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ABSTRACTS

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Oral Presentations

Adult Epileptology 1
15:15-16:15
Monday, 1 September
Aud I

578 | Leveraging MEG and sEEG to investigate the association between Small Sharp Spikes and epileptiform discharges in mesial temporal lobe epilepsy

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Purpose: Small sharp spikes (SSS) are EEG phenomena frequently observed in patients with epilepsy, particularly those with mesial temporal lobe epilepsy (MTLE). Despite their prevalence, the clinical significance and relationship between SSS and epileptiform discharges, especially those originating from the hippocampus, are not well understood. We aim to elucidate how SSS on surface EEG of patients with MTLE are correlated with epileptiform discharges identified by magnetoencepalopathy (MEG) and confirmed with sEEG. Furthermore, we explore whether variations in SSS morphology, frequency, and location can predict seizure onset zones in MTLE.
Method: We conducted a retrospective analysis of patients who underwent a pre-surgical evaluation which included continuous video EEG, sEEG, and MEG. All recordings were undertaken at the University of Florida Health in collaboration with the epilepsy and neurosurgery departments and analyzed by board-certified epileptologists.
Results: Preliminary findings from a series of patients revealed that MEG recordings effectively localized small sharp spikes (SSS) to the mesial temporal lobe, often identifying SSS not detected on surface EEG. Epileptiform discharges were subsequently confirmed through surface EEG and localized to the mesial temporal lobe using sEEG. Our ongoing analysis is uncovering distinct patterns of SSS, including their morphology, frequency, and distribution, which may serve as predictors of seizure onset zones. These findings enhance our understanding of the temporal and spatial dynamics of SSS by integrating and comparing data from MEG, surface EEG, and sEEG recordings, highlighting the unique contributions of each modality in pre-surgical evaluation.
Conclusion: This study bridges a knowledge gap in understanding SSS and their association with epileptiform discharges. By combining MEG and sEEG, we provide new insights into the clinical relevance of SSS in MTLE. These findings have the potential to refine pre-surgical evaluations and improve seizure localization strategies.

584 | The effects of music intervention on inhibitory control in frontal lobe epilepsy patients

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Purpose: to investigate the regulatory effects of music intervention on inhibitory control in FLE patients through behavioral assessments and EEG parameters.
Method: In this study, 21 FLE patients and 24 healthy controls were recruited to assess the effect of music on inhibitory control in FLE patients by EEG under the Go/

[Correction added on 29 January 2026, after first online publication: An "Abstract" has been added in this version]

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NoGo task. Participants were first required to gaze at the white cross in the center of the screen for 8 min of eye-open resting-state EEG data acquisition, followed by a Go/NoGo pre-test task, then performed 8 min of music listening, and finally a Go/NoGo post-test task.

Results: In this study, 21 FLE patients and 24 healthy controls were recruited to assess the effect of music on inhibitory control in FLE patients by EEG under the Go/NoGo task. The results showed that FLE patients had poor inhibitory control at baseline, and after the music intervention, FLE patients had significantly shorter task reaction time, higher accuracy. Meanwhile, a significant increase in wave amplitude difference between the N2 and P3 components was observed in the mid-frontal region. Also, music affected the connectivity between frontal and temporal lobes in FLE patients.

Conclusion: Music may positively affect inhibitory control functions in FLE patients by modulating the amplitudes of N2 and P3 and the functional connectivity of frontal-temporal regions. This proposes a musical intervention to ameliorate cognitive impairment and contributes to the understanding of the mechanism of action of musical interventions for the treatment of epilepsy with cognitive impairment.

608 | Seizures and epilepsy in untreated cerebral cavernous malformations: a prospective, population-based cohort study

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Purpose: We aimed to estimate the risks of epileptic seizures related to cerebral cavernous malformations (CCM) during long-term follow-up without treatment of the CCM.

Method: This prospective, population-based study included people aged ≥16 years in Scotland who were newly diagnosed with CCM during 1999-2003 or 2006-2010, using brain MRI or pathology. We assessed time to a first-ever epileptic seizure among adults who had never experienced epileptic seizure(s) at the initial presentation, CCM-related epilepsy (CRE, ≥2 CCM-related seizures ≥24 hours apart) among adults who experienced a first-ever CCM-related seizure at presentation or during follow-up, and 2-year/5-year seizure-freedom among adults with CRE.

Results: We identified 300 adults (median age 44 years [IQR 32-57]; 53% female) who were followed up over a median of 15 years (IQR 8-20). Among 189 adults who had never experienced epileptic seizure(s) at presentation, 11 (6%) experienced a first-ever epileptic seizure (10-year risk 6%, 95% CI 2%-9%). For 65 adults who experienced a first-ever CCM-related seizure at presentation or during follow-up, 47 (72%) developed CRE (10-year risk 76%, 65%-87%). There was no risk difference between adults who presented with or without symptomatic intracranial hemorrhage (ICH, 9/13 [69%] versus 38/52 [73%], p=0.81). Among 71 adults with CRE and ≥2 years follow-up, 57 (80%) became 2-year seizure-free (10-year rate 81%, 71%-91%), while using 0 (n=5), 1 (n=35), or ≥2 (n=17) anti-seizure medicine(s) (ASM). Sixty-five adults with CRE had ≥5 years follow-up, of whom 44 (68%) reached 5-year seizure-freedom (10-year rate 62%, 50%-75%), while using 0 (n=3), 1 (n=31), or ≥2 (n=10) ASM.

Conclusion: Risk of a first-ever seizure from CCM is low. Three-quarters of adults who experienced a CCM-related seizure develops CRE, with similar risks regardless of ICH presentation, supporting ILAE guidelines to initiate ASM after a first seizure. Approximately a quarter of adults with CRE do not become 2-year/5-year seizure-free without surgical treatment.

727 | Subclinical EEG patterns in patients with focal epilepsy predict the presence of clinically manifest seizures

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Purpose: Subclinical seizures are defined as electrographic seizures without subjective or obvious objective neurological or somatic manifestation. While their clinical implications remain poorly understood, their relevance is increasing with the advent of devices capable of ultra-long term EEG recordings. As these devices typically produce data that are not suitable to distinguish between clinical and subclinical seizures, this study aims to find out the fraction of patients for whom the presence of electrographic seizures predicts the presence of clinically relevant seizures.

Method: Data of 546 patients (263 female, 283 male, mean age 34.0+/-15.6 years, range: 10-85 years) with a diagnosis of focal epilepsy, with scalp EEG recorded during

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long-term inpatient video-EEG monitoring in Freiburg between the years 2010 and 2024 were included in this retrospective study. Mean recording time was 148 hours. For each patient, the first available EEG with at least one subclinical seizure was selected. Demographic and electroclinical data were collected.

Results: 68% of all recordings showed both subclinical seizures and clinical seizures, 27% showed only clinical but no subclinical seizures and just 5% showed only subclinical but no clinical seizures. In 93% of recordings that contained at least one electrographic seizure, there were also clinically relevant seizures. In 75% of patients with multiple recordings who presented subclinical seizures but no clinical seizures during at least one recording, a clinical seizure was present during another recording.

Conclusion: Clinically relevant seizures can be expected to be found in a vast majority of recordings containing subclinical electrographic seizures. Long-term monitoring with devices capable of recording EEG may thus develop into an important tool in the management and prognosis of patients with focal epilepsy, especially when seizure rates are low.

1515 | Mapping the structural connectome of temporal lobe epilepsy variants to improve surgical outcomes

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Purpose: Temporal lobe epilepsy (TLE) is the most common type of focal epilepsy. Unfortunately, one-third of patients are drug-resistant. While temporal lobe (TL) surgery is an option for these refractory cases, ~30% of patients continue to experience seizures postoperatively, possibly due to epileptogenic networks extending beyond the TL, encompassing the contralateral TL (bitemporal epilepsy - BTE) or extratemporal regions (temporal plus epilepsy - TPE). Diffusion MRI tractography offers a non-invasive method to map epileptic networks, providing structural insights to differentiate TLE from BTE and TPE, thus improving surgical candidate selection.

Method: We included 27 patients with TLE, 12 with BTE, 15 with TPE and 49 healthy controls (HC). All underwent high-resolution T1- and diffusion-weighted MRI sequences. Images were processed using TractoFlow, Surface-Enhanced-Tractography, and Connectoflow to generate COMMIT-weighted connectivity matrices quantifying microstructural connectivity strength. Matrices from patients with left-sided TLE/TPE were side-flipped. Between-group comparisons were performed using FDR-corrected two-sample t-tests. Graph-theoretical analyses (GTA) were also conducted, assessing nodal strength, betweenness centrality, clustering coefficient and local efficiency.

Results: Comparisons revealed significant connectivity differences between all patient groups and HC, with BTE and TPE demonstrating more extensive alterations than TLE. BTE showed a more diffuse pattern of increased connectivity strength than TLE, including strong connections in the left TL. Compared to TLE, TPE patients revealed one increased ipsilateral connection between the medial amygdala and the rostral thalamus. GTA showed increased network metrics in BTE and TPE compared to TLE. BTE exhibited pronounced network alterations in the left TL and bilateral limbic regions, whereas TPE showed more widespread changes in bilateral subcortical-limbic regions and association cortices. These findings highlight more widespread alterations in BTE and TPE compared to TLE.

Conclusion: We highlight potential structural signatures of TLE, BTE, and TPE, enabling non-invasive differentiation of these variants to improve surgical candidate selection and postoperative outcomes.

1772 | Effect of Advancing Reperfusion Therapies in Post-Stroke Epilepsy

C Guedes Vaz[1], A Dias[2,3], R Varela[1], I Silva[2], A Moutinho[3,2], P Castro[4], B Carvalho[4], C Oliveira[3,5], H Zetterberg[6], J Gobom[6], J Chaves[1,2], M Correia[1,2], R Magalhães[2], L F Maia[1,2,3]
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Purpose: We aim to determine the incidence, risk factors and the proteomic signature of Post-Stroke Epilepsy (PSE).

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Method: We conducted a 4-year follow-up of stroke and TIA patients enrolled in a prospective study between January 2019 and March 2020 in a comprehensive stroke center. Data on PSE (>7 days after index event), stroke-related variables and serial blood samples were collected. Patients with previous history of epilepsy were excluded. Cumulative incidence functions, accounting for competing risks, were estimated. Additionally, a subset of patients underwent an exploratory proteomic analysis using Label-Free Quantification proteomics. Dynamic protein profiles were assessed using Linear Mixed Models.

Results: Of 420 patients included, 22 were diagnosed with PSE, with a median time to diagnosis of 1.0 years (IQR 2.7). The cumulative incidence of PSE was 5.5% (SD=1.13%), considering death as a competing event. Patients who received revascularization treatment and developed haemorrhagic transformation had a higher cumulative incidence of PSE (13.8% vs. 4.2%, p=0.014). The sub-distribution hazard ratio for hemorrhagic transformation was 3.2 (95%CI: 1.2-9.9), adjusted for age and sex. No significant differences were observed across TOAST, OCSP, and ECASS classifications or treatment modalities. All but 1 patient achieved seizure control with one anti-seizure medication, with levetiracetam being the first-line choice in 86.4% (n=19) cases. Proteome analysis yielded 27 distinct protein profiles in PSE group compared to non-PSE, that are involved in cellular stress responses and immunological regulation.

Conclusion: Hemorrhagic complications following reperfusion treatment are associated with a significantly increased risk of Post-Stroke Epilepsy, warranting heightened vigilance in such patients. However, PSE appears to follow a benign clinical course. Proteomic analysis suggests that cellular stress and immune dysregulation may contribute to PSE pathogenesis.

Adult Epileptology 2
15:15-16:15
Tuesday, 2 September
Aud VI+VII

552 | Neuroimaging correlates of epilepsy in neurodegenerative disorders

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Purpose: Epilepsy is common in dementia. However, the neuroimaging correlates of epilepsy in AD and non-AD dementias remain unexplored. We investigated mesial temporal morphology and volumes in AD (AD+Epi) and non-AD dementias (non-AD+Epi) with epilepsy.

Method: Using multicenter data from 39 US Alzheimer's disease centers (9/2005–12/2021), participants were classified into Group 1 (dementia with epilepsy: AD+Epi, nonAD+Epi); Group 2 (dementia without epilepsy: AD-Epi, non-AD-Epi); and Group 3 (healthy controls,HC). Group 1 participants with available MRI scans were matched to Groups 2 and 3 using fixed-ratio, optimal propensity score matching by age, sex, and dementia type (AD vs nonAD). Hippocampal and amygdalar segmentation from MRI was performed using FreeSurfer. Point distribution models created via ShapeWorks quantified morphological differences in the left and right hippocampi (512 points) and amygdalae (256 points). Volumes were normalized to total intracranial volume. Multivariate analysis of covariates (MANCOVA), adjusted for age, sex, intracranial volume, and dementia severity, identified statistically significant local morphological and normalized volume group differences. We compared AD+Epi vs AD-Epi, AD+Epi vs HC, AD-Epi vs HC, nonAD+Epi vs nonAD-Epi, nonAD+Epi vs HC and nonAD-Epi vs HC.

Results: Of 703 included participants (average age:70.78 years, 391 (55.62%) female), 35 had AD+Epi, 28 nonAD+Epi, 183 AD-Epi, 137 nonAD-Epi, and 320 HC. AD-Epi and NonAD-Epi exhibited uniform hippocampal and amygdalar morphological atrophy bilaterally. In contrast, AD+Epi demonstrated morphological atrophy in the hippocampal bodies and tails bilaterally with sparing of the hippocampal heads, more pronounced inward deviations on mesial and lateral surfaces, and outward deviations in the middle hippocampal body bilaterally on the superior surface. NonAD+Epi showed significant morphological atrophy in the right hippocampal head, tail, and amygdala. No group volume differences were found.

Conclusion: Lateralized and region-specific patterns of mesial temporal morphological changes are associated with epilepsy in ADRD. These highlight the possible role of epilepsy in altering the trajectory of neurodegeneration.

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752 | Suicidality at epilepsy diagnosis predicts treatment resistance in newly diagnosed focal epilepsy

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Purpose: Evaluate the role of psychiatric co-morbidities and suicidality at epilepsy diagnosis in predicting risk of treatment resistance in focal epilepsy.
Method: The Human Epilepsy Project (HEP) is a prospective, international cohort study that enrolled newly diagnosed focal epilepsy patients ≤4 months after initiating treatment. On enrolment, participants completed the mood and anxiety disorders modules of the Mini International Neuropsychiatric Interview (MINI) and Columbia-*Suicide* Severity Rating Scale (*C-SSRS*) and followed for up to 6 years. Treatment outcomes were determined by review of patient entered seizure diaries and medical records. Treatment resistance (TR) was defined as failure of ≥2 adequate ASM trials (ongoing seizures at/above therapeutic doses). Treatment sensitivity (TS) was defined as seizure freedom (≥12 months) on first 2 adequate ASM trials. Multivariate analyses assessed risk of TR among those with a diagnosis of mood and/or anxiety disorders on the MINI but without suicidality on C-SSRS (PD-S), suicidality (passive/active ideation, attempt[s]) +/- mood/anxiety disorder (S±PD), and no psychiatric disturbance (NPD).
Results: Of 448 participants enrolled, 347 completed MINI and C-SSRS at enrollment and 274 had determinable treatment outcomes for inclusion (TR=83; TS=191). Most patients had NPD (n=169, 61.7%), with a higher proportion in the TS group (TR=36[21%], TS=113[79%]). Forty-three (15.7%) had PD-S (TR=15[35%], TS=28[65%]) and 62 (22%) had S±PD (TR=32[52%], TS=30 [48%]). Suicidal participants had increased risk of TR vs those with NPD (RR=2.12, 95% CI: 1.43-3.16, HB-corrected $p<0.001$). There was a non-significant trend for TR in participants with PD-S vs NPD (RR=1.64, 95% CI: 0.98-2.74, HB-corrected $p=0.059$). There was no significant difference in TR risk between participants with S±PD vs PD-S (RR=1.30, 95% CI: 0.79-2.12, HB-corrected $p=0.30$).
Conclusion: Suicidality at diagnosis is a strong predictor of treatment resistance (>two-fold) in focal epilepsy. Suicidality in early treatment phases may reflect more severe neuropathology leading to refractory epilepsy syndromes.

958 | Clinical subtypes and characteristics of sleep-related epilepsy: A real-world study

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Purpose: To identify clinical subtypes of sleep-related epilepsy (SRE), and compare onset age, EEG abnormalities, prognosis, and etiology between SRE phenotypes.
Method: This retrospective observational study included patients seen at the Second Affiliated Hospital of Zhejiang University from July 2023 to December 2024. Patients with seizures occurring ≥80% during sleep were enrolled, and all patients were followed for at least one year.
Results: A total of 145 patients were enrolled and classified into Pattern A (n=73, 50.3%) and Pattern B (n=72, 49.7%) by k-means cluster analysis. Pattern A was characterized by low-frequency focal to bilateral tonic-clonic seizures (FBTCS) during sleep (interval >1 year), while Pattern B exhibited high-frequency focal seizures (FS), with or without FBTCS. Pattern B had an earlier median onset age (9.5 years) compared to Pattern A (18.0 years). EEG interictal epileptiform discharges were observed in 58.9% of Pattern A and 87.5% of Pattern B ($P<0.05$). Drug resistance was more common in Pattern B, with only 17.1% of Pattern B patients being drug-responsive, compared to 80.9% of Pattern A patients ($P<0.05$). Etiology was mostly unknown in Pattern A (78.1%), while half of Pattern B patients had an unknown etiology (54.2%), and 36.1% had focal cortical dysplasia type II (FCD II).
Conclusion: Pattern A patients typically exhibit favorable responses to treatment, with a largely unknown etiology, particularly for those over 40 years old. Pattern B patients tend to have earlier seizure onset and are more likely to have drug-resistant epilepsy due to FCD II.

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1154 | Risk of epilepsy in people with and without dementia – A nationwide cohort study

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Purpose: To estimate the risk of epilepsy in patients with dementia compared to individuals without dementia using nationwide register data.
Method: We conducted a matched cohort study identifying all incident dementia patients aged 50 years or older with a diagnosis in the Danish National Patient Register from 1997 to 2021. This cohort was age- and sex-matched with references without dementia (ratio 1:5) using Danish population registers. Individuals were followed from time of diagnosis/matching until first epilepsy diagnosis, death, emigration, or December 31, 2021. Adjusted hazard ratios (HRs) for the risk of epilepsy and 95% confidence intervals (CIs) were estimated using Cox regression models. Absolute risks will be estimated accounting for death as a competing risk.
Results: We identified 201,730 incident dementia patients and 1,008,640 matched reference individuals (mean age=80.6 years (SD 8.6), 39.8% males). Despite a shorter life expectancy for dementia patients than matched references (mean time to death: 3.5 vs. 5.9 years), a higher proportion were diagnosed with epilepsy during follow-up (2.0% vs. 1.0%). The incidence rate of epilepsy was higher in dementia patients (IR=5.44 per 1000 person-years, 95% CI: 5.27-5.61) than in the reference population (IR=1.56, 1.53-1.59), with adjusted HR of 3.5 (95% CI: 3.4-3.6). After adjusting for history of psychiatric disorders, the adjusted HR was 3.4 (95% CI: 3.2-3.5).
Conclusion: Dementia was associated with a significantly increased risk of epilepsy compared to individuals without dementia, which was not explained by other underlying psychiatric conditions. These findings underscore the need for increased clinical vigilance for epilepsy in dementia patients and further research into the temporal associations and underlying shared risks for dementia and epilepsy.

1469 | Redefining Acute Symptomatic Seizures: The Role of Timing in Predicting Recurrence After Stroke

KM Schubert[1], I Berg[1], M Pagiantza[1], G Bicciato[1], Y Wang[2], V Punia[3], V Dasari[3], M Alet[4], E Santamarina[5], J Álvarez-Sabín[5], L Abraira[5], C Ferreira-Atuesta[1], M Katan[6], N Deligas[7], B Erdélyi-Canavese[7], D Zieglgänsberger[7], A Felbecker[7], P Siebel[7], GL Gigli[8], A Nilo[8], F Janes[8], G Merlino[8], M Valente[8], P Lochner[9], F Roell[9], B Landau[9], F Brigo[10], AL Oliveira[11], C Bentes[11], R Peralta[11], T Pinho e Melo[11], MR Keezer[12], JS Duncan[13], JW Sander[13], B Tettenborn[7], MJ Koepp[7], M Galovic[1]
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Purpose: The current classification of post-stroke seizures as acute symptomatic (≤ seven days) or remote symptomatic (> seven days) assumes that later seizures are associated with a higher recurrence risk (>60%). However, evidence supporting the seven-day threshold remains limited. We evaluated the association between seizure timing and recurrence risk, challenging the validity of this threshold.
Method: We analyzed data from 11 international cohorts, including individuals with neuroimaging-confirmed ischemic or hemorrhagic stroke and a first post-stroke seizure. Cox proportional hazards regression, adjusted for treatment effects using inverse probability weighting and competitive risk (death), was used to assess the relationship between seizure timing and recurrence risk.
Results: Among 593 ischemic and 242 hemorrhagic stroke patients, seizures within the first month after ischemic stroke had a recurrence risk below 60% over ten years (day 0: 33%; week 1: 23%; weeks 2–3: 18%; weeks

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3–4: 27%). For hemorrhagic stroke, seizures within the first three weeks also had a recurrence risk below 60% (day 0: 59%; week 1: 43%; weeks 2–3: 38%). In contrast, seizures occurring beyond one month after ischemic stroke and beyond three weeks after hemorrhagic stroke were associated with a significantly higher recurrence risk (ischemic stroke: ≥85% within 24 months, p<0.001; hemorrhagic stroke: 80% between 3 weeks and 3 years, p<0.001). Recurrence risks declined slightly for seizures occurring more than two years post-ischemic stroke (~70%) and more than three years post-hemorrhagic stroke (~70%).

Conclusion: Seizures within the first month after ischemic stroke and the first three weeks after hemorrhagic stroke are associated with a moderate recurrence risk (<60%), challenging the conventional 7-day cutoff. However, seizures beyond these timeframes carry a significantly higher recurrence risk (>60%), aligning with the classification of epilepsy. These findings suggest the need for a more nuanced approach to timing antiseizure medication initiation and revisiting current classification criteria.

1673 | Long-Term Outcomes in Idiopathic Generalized Epilepsies: A Decade of Follow-Up in a Tertiary Adult Care Population

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Purpose: Idiopathic Generalized Epilepsies (IGEs) encompass a group of syndromes in which the main core is generalized seizures. IGEs are believed to have a benign outcome but some patients are drug-resistant, and many comorbidities have been described associated with IGEs. The evolution of seizure control, and treatment patterns in long-term follow-up remain underexplored.

Method: A retrospective analysis was conducted in all IGE patients followed at a tertiary epilepsy center from 2010–2014, with a 10-year follow-up with data comparison before/after that period.

Results: We included 274 patients, 56.6% female, mean age of 43.2 years with average age at seizure onset of 13.1 years, and average of 12.6 seizures/year. Epilepsy control improved from 76.2% to 79.6% over 10 years, with 36.9% of drug-resistant patients achieving control through optimized regimens. Despite this, 57% experienced seizures during follow-up, with higher rates in Absence Epilepsy (80.4%) compared to Juvenile Myoclonic Epilepsy (46.1%). The average number of antiseizure medication (ASM) per patient rose from 1.3 to 1.5, with decreased valproic acid use (-16.69%) and increased use of newer ASM like zonisamide (+5.06%) and levetiracetam (+3.42%). While 4.4% discontinued ASM, 11% required three or more drugs. Seizure frequency decreased to 6.7/year. Comorbidities included mood disorders (24.3%), psychosis (5.5%), and cognitive impairment (7.7%), 5.1% of patients were discharged, though 11% were lost to follow-up.

Conclusion: Although some IGEs patients remain drug-resistant over 10 years follow-up, there was an improvement in seizure control, but comorbidities were common, highlighting the need for individualized, long-term management of these not so "benign" epilepsies.

Basic Science
15:15-16:15
Tuesday, 2 September
Aud V

453 | TBC1D24 and vATPase interplay in the brain: physiopathology of *TBC1D24*-related epilepsies

A Falace[1], S Giubbolini[2], C Michetti[2], C Penzo[2], H Tsushima Semini[2], S Tessitore[2], F Zara[3], P Striano[1], A Fassio[2]
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Purpose: Mutations in *TBC1D24* underlie a wide spectrum of epileptic conditions, extending from infantile benign idiopathic to DEEs and early death. Early-onset seizures are one of the most prominent features among *TBC1D24* patients. How the TBC1D24 loss of function results in brain hyperexcitability and seizures is unclear. TLDc domain-containing proteins, such as TBC1D24, have been recently described to bind the proton pump v-ATPase, the major determinant for acidification of intracellular organelles, including synaptic vesicles (SVs). Variants of the v-ATPase complex are also described in patients with epileptic conditions and DEEs. However, the physiopathological implications of this interaction are unknown. Our central hypothesis is that TBC1D24 loss alters neuronal pH homeostasis at intracellular organelles and synaptic vesicles, thus causing hyperexcitability and seizures. This study aims to define the neurobiological

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role of TBC1D24/v-ATPase interplay in TBC1D24 pathophysiology.

Method: *Tbc1d24* knockout (KO) murine neurons are employed to study intraorganellar pH, autophagy progression and synaptic function with cell imaging. Induced pluripotent stem cells derived neurons prepared from patients' fibroblasts are also employed for cell imaging and electrophysiological recordings. In parallel, a conditional *Tbc1d24* KO mouse is developed to study epileptogenesis and test putative therapeutic strategies.

Results: TBC1D24 modulates v-ATPase assembly and Tbc1d24 loss results in increased pH at intracellular compartments and autophagy impairment in neurons from *Tbc1d24* KO mice or derived from a DEE patient harboring a *TBC1D24* loss-of-function variant. *Tbc1d24*-depleted synapses display decreased SV density, accumulation of degradative vacuoles and impaired SV acidification. These defects can induce a progressive alteration in network bursting activity, possibly underlying the epileptic phenotypes observed in the *Tbc1d24* conditional KO mouse model and patients.

Conclusion: We propose TBC1D24 as a neuronal regulator of v-ATPase assembly and dysregulation of neuronal pH homeostasis as a common feature for epilepsy associated with TBC1D24 and v-ATPase subunit variants.

640 | Shaping the future of epilepsy research in Europe: The ERN EpiCARE priorities

S Tchaicha[1], A Arzimanoglou[1], H Cross[1], K Braun[2], the ERN EpiCARE Research Council and Executive Committee

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Purpose: The European Reference Network for Rare and Complex Epilepsies (ERN EpiCARE), with its Research Council and members of the network, has identified six key priorities to address critical gaps in epilepsy research.

Method: ERN EpiCARE unites more than 60 expert centers, accredited by their respective health authorities and the European Commission, specializing in the diagnosis and management of rare and complex epilepsies. Since its creation in 2017, the network has accumulated substantial expertise, enabling to identify research priorities through a consensus process involving internal discussions, analysis of patient needs, and collaboration with the 23 other ERNs. A collaborative effort is underway to draft comprehensive articles for each priority.

Results: The six research priorities identified include:

1. Prevention of epileptogenesis: Identify early interventions to prevent epilepsy development and reduce comorbidities.
2. Genetics and targeted therapies: Enhance understanding of genetic causes and advance genetic testing and precision medicine.
3. Improved surgical decision-making: Optimize surgical practices and enhance patient outcomes for epilepsy surgery.
4. Innovative trial designs focusing on adaptive approaches and patient-centered outcome measures.
5. Artificial intelligence (AI) to improve diagnosis, seizure prediction, and patient care.
6. Understanding and preventing comorbidities and mortality by addressing mental health, cognitive disturbances, premature/sudden mortality and cardiovascular risks, and premature death.

Conclusion: EpiCARE's six research priorities serve as a roadmap to drive innovation and collaboration across the epilepsy research community. These efforts aim to align with the WHO global action plan on "Epilepsy and other Neurological Disorders" and support ongoing initiatives such as HORIZON Europe and inter-ERN collaborations. By focusing on causes rather than symptoms, EpiCARE aims to transform epilepsy care and improve quality of life for patients with rare and complex epilepsy. We will present a comprehensive outline of the strategies and actionable steps for addressing in Europe, within the next decade, each of the six priorities.

1258 | ELFN1 deficiency: Mechanistic basis of the neurodevelopmental disorder with expanding phenotypic spectrum

R Dore*[1,2], C-T Chang*[3], A Declève*[4], G Brunori[3], WG Ludlam[3], A Huang[5], M Movahedinia[6], NS Damseh[7], I Anwar[8], MY Vahidi Mehrjard[9], A Ny[4], M Khorrami[10], M Kheirollahi[10], H Frederiksen[8], F Eghbal[11], MR Mirjalili[12], M Dehghani[13], E Ghayoor Karimiani[11], S Oreshkov[8], C Alves[14], P Striano[15,16], M Suri[17], J Martinez-Agosto[18], M Ansar[19], M Zahid[19], S Akram[19], M Ansar[8,20], SF Nelson[6], UD Network[21], SE Antonarakis[22], H Houlden[1], D Copmans*[4], KA Martemyanov*[3], R Maroofian*[1]

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Purpose: Deficits in synaptic communication lead to a number of neurodevelopmental conditions. However, many such disorders are poorly defined for rare monogenic conditions which also suffer from paucity in understanding of underlying molecular etiology. A single biallelic variant in synaptic cell adhesion molecule *ELFN1* has been reported in a family affected by epileptic encephalopathy and a different biallelic variant was found in patients with intellectual disability. Therefore, this study aimed to establish *ELFN1* deficiency as a distinct neurodevelopmental disorder with a defined clinical spectrum.

Method: A comprehensive characterization of the clinical features of eight individuals is reported and a functional analysis of underlying molecular mechanisms was performed. To substantiate the clinical findings, *ELFN1* loss of function was modelled in mice and zebrafish. A morpholino-based gene knockdown was induced in zebrafish to mimic a loss of function of *elfn1a* and *elfn1b*. Evaluation of the epileptic phenotype by morpholino gene knockdown was assessed by quantifying epileptiform discharges and abnormal hyperactive behavior using non-invasive local field potential recordings and automated locomotor tracking.

Results: Detailed clinical phenotyping, neuroimaging and EEG findings and functional analysis revealed that all previously reported biallelic *ELFN1* variants are loss of function. Loss of function modelling in mice and zebrafish confirmed its epileptogenic and hyperactivity driven nature. In zebrafish, seizure-like behavior was significantly increased for larvae injected with *elfn1a* morpholino ($p \leq 0.01$) and non-significantly increased for *elfn1b* morpholino (22.8% increase). Significant increases in electrophysiological brain activity were observed for both *elfn1a* and *elfn1b* morpholinos ($p \leq 0.01$).

Conclusion: This study enabled to define *EFLN1* deficiency as a cause of a distinct and rare neurodevelopmental disorder with epilepsy. Moreover, we introduce *ELFN1* Deficiency Disorder as a defined condition featuring distinct neurological and neuropsychiatric manifestations.

1563 | Unravelling Neurodevelopmental Disruptions in Dravet Syndrome using a Patient-Derived Organoid Model

C Mattei[1], M Mao[1], S Byars[1], E Mohamed Syazwan[1], M Oliva[1], T Karle[1], K Richards[1], I Scheffer[2], S Petrou[1,3], S Maljevic[1]

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Purpose: Dravet Syndrome (DS) is a severe developmental and epileptic encephalopathy (DEE) caused primarily by loss-of-function (LoF) mutations in *SCN1A*, which encodes the $Na_v1.1$ voltage-gated sodium channel. Since $Na_v1.1$ is preferentially expressed in GABAergic interneurons, its dysfunction leads to an imbalance between inhibitory and excitatory signaling, contributing to seizures that worsen with traditional sodium channel-blocking anti-seizure medications (ASMs). This study aimed to develop a human-derived 3D organoid model of DS using patient-induced pluripotent stem cells (iPSCs) to investigate neurodevelopmental disruptions and assess drug responses.

Method: Patient-derived iPSCs with *SCN1A* mutations were used to generate 3D cortical organoids enriched with GABAergic neurons to model DS in vitro. Bulk and single-cell RNA sequencing was performed to profile the transcriptome and identify key developmental dysregulations

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associated with *SCN1A* LoF. Functional assays were used to assess neuronal activity, GABAergic dysfunction, and excitatory-inhibitory balance. Finally, the model was tested for its ability to predict drug responses, particularly to fenfluramine, an emerging ASM for DS treatment.

Results: The patient-derived organoids displayed significant dysregulation of neurodevelopmental pathways, with altered expression of genes involved in neuronal differentiation, synaptic organization, and inhibitory signaling. Functional analysis confirmed a reduced $Na_v1.1$ function in GABAergic neurons, leading to excessive glutamatergic excitability, a hallmark of DS pathology. Additionally, treatment with fenfluramine partially restored neuronal network stability, supporting its therapeutic efficacy in DS.

Conclusion: This study demonstrates that iPSC-derived 3D organoids can effectively model neurodevelopmental alterations in *SCN1A*-related DS, revealing key molecular and functional deficits in GABAergic neurons. The model successfully predicted fenfluramine's therapeutic potential, highlighting its utility for personalized drug testing and mechanistic insights into DEEs. This approach paves the way for patient-specific modelling of epilepsy syndromes and the development of targeted treatments.

1649 | Transcriptome analysis revealed *Bmal1* as a key regulator of circadian-driven neuroinflammation and epileptogenesis

DCF Bruno[1,2,3,4,5], R Benvenutti[1,2], M Gallas-Lopes[6], MT Venø[7], EM Bruxel[4,5], T Strickland[1,2], A Ramsook[1], A Wadgaonkar[1], Y Jiang[1,2], A Sanz-Rodriguez[2,8], L Sinkkonen[3], MKM Alvim[5,9], F Rogerio[5,10], F Cendes[5,9], DC Henshall[2,8], AM Curtis[1,11], K Kobow[12], I Lopes-Cendes[5,4], CR Reschke[1,2]

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Purpose: Epilepsy affects 50 million people worldwide and remains a complex, multifactorial condition with unclear causes. Around 30% of patients are resistant to anti-seizure medications (ASMs), increasing their risk of premature death. A major challenge is the unpredictability of seizures and the variable efficacy of ASMs, which may depend on the time of administration. Recent evidence suggests that circadian rhythms play a key role in seizure timing, as epileptic brain activity follows circadian patterns in both humans and rodents. In addition, disruptions in core clock gene expression in the hippocampus and cortex may heighten seizure susceptibility, while seizures themselves can alter circadian-regulated genes. Emerging evidence suggests that dysregulation of *Bmal1*, the core circadian clock gene, may contribute to epilepsy pathogenesis.

Method: Here, we investigated alterations in molecular clock gene expression during epileptogenesis using a preclinical model of status epilepticus induced by intra-amygdala kainic acid. RNA sequencing was conducted at six time points over a 24-hour period to analyze transcriptional dynamics and circadian oscillatory patterns. Differentially expressed genes were identified using DESeq2, followed by rhythmicity analysis with metaCycle, incorporating ARSER, JTK_CYCLE, and Lomb-Scargle methods. Functional enrichment and pathway analyses were performed using Ingenuity Pathway Analysis (IPA).

Results: Our transcriptome analysis using IPA revealed a predominant inhibition of molecular clock machinery during the light phase. Using the metaCycle, we observed a loss of rhythmicity in core clock genes, including *Bmal1*, *Per1*, and *Nr1d1*. Together, these results support the disruption of circadian regulation during epileptogenesis. Moreover, *Bmal1* emerged as a master regulator of 38 genes (e.g., *Cll2*, *Il1β*, *Acox1*) involved in inflammation and oxidative stress, highlighting its critical role in neuroinflammatory responses during epileptogenesis.

Conclusion: These findings provide novel insights into the interplay between circadian disruption and neuroinflammation in epilepsy development and suggest that *Bmal1* or its downstream regulators may serve as potential targets for chronotherapy strategies.

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1862 | Involvement of the Orexinergic System in Absence Epilepsy: Developmental Dynamics of Orexin-A

ET Erdeve[1], F Onat[2,3], Å Petersén[4,5], N Carcak[3,6], M Andersson[7]
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Purpose: Orexinergic neuropeptides Orexin-A and -B, expressed in the lateral hypothalamus (LH), are key regulators of sleep and wakefulness. Sleep and epilepsy have a bidirectional relationship and sleep spindles and spike-and-wave discharges (SWD), an EEG (electroencephalogram) hallmark of absence epilepsy (AE), share the same cortico-thalamo-cortical origin. Thus, it can be hypothesized that systems involved in sleep-wake regulation may also contribute to generation and/or control of SWDs. To investigate whether the orexinergic system is involved in the pathophysiology of AE, we assessed Orexin-A expression in the LH via immunohistochemistry in a well-established AE animal model, Genetic Absence Epilepsy Rats from Strasbourg (GAERS), across critical neurodevelopmental stages of absence epileptogenesis.
Method: GAERS and age-matched Wistar controls (n=6/group), at three different age groups, postnatal day (PND) 14 (before SWD onset), PND21 (immature SWDs) and PND>88 (mature SWDs), underwent transcardiac perfusion (4% PFA in PBS). Brains were cut in coronal sections (40 µm, 10 series) for 3,3′-diaminobenzidine (DAB) immunohistochemistry. Three sections from one series containing LH from each animal was analyzed in Qupath (v0.5.1). Data were analyzed with two-way Anova, expressed as mean±SEM.
Results: The number of Orexin-A+ cells in the LH of GAERS compared to Wistar was significantly higher in both PND14 (GAERS:118±5, Wistar:97±2, $p<0.01$) and PND21 (GAERS:130±2, Wistar:107±3, $p<0.005$). In adults, this difference was absent as GAERS expression levels decreased (118±6), whereas Wistar expression remained comparable to PND21(106±7, $p=0.1$).
Conclusion: We found a higher number of Orexin-A expressing cells in LH of GAERS prior to and during early seizure onset suggesting a potential role for Orexin-A in epileptogenesis. We have previously shown a dose-dependent seizure suppressive effect of intracerebroventricular Orexin-A injection in GAERS, supporting orexinergic system dysfunctions in AE.
Supported by Istanbul University-Scientific Research Projects Coordination Unit(TDK-2024-40386), European Commission-Horizon Europe Programme Horizon-Widera-2021-Access-03 call[Grant:101078981-Gemstone]. Ete: Tübitak-2214/A, Yök-100/2000 PhD Scholar.

Clinical Neurophysiology
15:15-16:15
Monday, 1 September
Aud V

412 | Interictal scalp electroencephalography characteristics may predict cognitive decline in people with late-onset epilepsy

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Purpose: To determine whether scalp electroencephalography (EEG) characteristics could predict cognitive decline (CD) in people with late-onset epilepsy (LOE).
Method: In this cross-sectional study, participants were consecutively enrolled in the epilepsy monitoring unit of a tertiary referral hospital from December 2021 to June 2024. Eligibility criteria were a clinical diagnosis of epilepsy, an age of first unprovoked seizure of at least 55 years, and available long-term video EEG (VEEG) recordings. A total of 209 participants and 132 age—and sex-matched healthy controls (HCs) were included. VEEG characteristics were assessed visually and extracted under the SCORE standard. The primary outcomes were the VEEG characteristics associated with CD or CD due to probable AD (CDAD). The primary metrics were odds ratio (OR) and area under the receiver operating characteristics curve (AUROC).
Results: The median age was 65 (55-85) years old; 130 were male (62.20%), and 67 participants (32.06%) were considered CD ([LS1] [LL2] 42 [20.10%] were CDAD[LS3] [LL4]). Variables significantly associated with CD (adjusted for covariates) were focal slowing (OR, 2.345, $p=0.015$), generalized delta slowing (OR, 3.932; 95%CI, 1.450-10.663; $p=0.008$), interictal epileptiform discharges (IEDs) in left

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and right temporal regions (OR, 2.323; 95%CI, 1.0215.285; p = 0.046), and IEDs with location maximum at FT9/FT10 (OR, 2.585; 95%CI, 1.265-5.283; p = 0.010). The same variables were also associated with CDAD, with increased ORs for IEDs in both left and right temporal regions (OR, 3.963; 95%CI, 1.584-9.916; p = 0.004) and IEDs with location maximum at FT9/FT10 (OR, 4.437; 95%CI, 1.912-10.295; p<0.001) when compared to those of CD. Selected variables were properly discriminative in CD (AUROC, 0.756) and CDAD (AUROC, 0.787; 95%CI, 0.708-0.866).

Conclusion: Specific visual EEG patterns, especially IEDs in the frontotemporal electrodes, were associated with an elevated risk of CD. Scalp EEG may be a promising tool for cognitive assessment in LOE.

857 | Relationship Between Memory and Altered Consciousness in Focal Seizures: Aura as a Key Marker

N Campora[1,2], A Nasimbera[3,4], A Daza[3], M Villanueva[4], JC Jerez Torres[1], J Zambrano[1], A Veizaga[1], Z Mamani[1], S Oddo[1,4], B Giagante[1], S Kochen[4,1]

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Purpose: Consciousness encompasses external interaction, subjective experiences, and memory. The ILAE links awareness with consciousness, assuming that patients aware during seizures can recall and report the event. This study aims to characterize memory in seizures and its relation to loss of consciousness (LOC).

Method: Patients with refractory focal epilepsy undergoing video-EEG (VEEG) were included. Consciousness was evaluated using the CSS scale (Arthuis et al.), and memory (aura and ictal events) using SPS (Campora et al.).

Results: Of 230 seizures (79 patients), 119 were adequately evaluated. Complete amnesia of the events during seizure occurred in 48.7% (58), partial memory in 36.1% (43), and full memory in 15.1% (18). Aura recall was adequate in 52.1% (62). Consciousness was preserved in 16.8% (20), profoundly altered in 59.7% (71), and moderately altered in 23.5% (28). Aura as a Marker of Memory Preservation: Aura recall was preserved in 100% of seizures with partial or complete ictal memory but was absent in most with profound (80.8%) or moderate (66.6%) LOC. Memory impairment was linked to greater LOC (p <0.001) and sleep (p <0.0001) but not to seizure duration, epileptogenic zone, or lateralization. Relationship Between LOC and Memory: Amnesia was highest with profound LOC (72.4%) and moderate LOC (53.6%). Seizures without LOC had 65% adequate memory but 35% memory alterations. Partial memory was observed in 40.8% of profound and 32.1% of moderate LOC cases.

Conclusion: Aura recall is a key marker of memory preservation in focal seizures. Profound and moderate LOC significantly impact memory, especially during sleep. Even without LOC, memory may be altered. These findings highlight the need for further research into the neurophysiological mechanisms of consciousness and memory in epilepsy.

1044 | EEG features in vanishing white matter disease: a retrospective analysis of pediatric and adult patients

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Purpose: Vanishing White Matter Disease (VWM) is an inherited leukoencephalopathy related to mutations in the eukaryotic translation initiation factor 2B (eIF2B) genes. This retrospective study aims to describe patients' electroencephalogram (EEG) findings in VWM disease, their correlation with disease progression and to explore the potential role of EEG as a prognostic tool in VWM disease.

Method: We retrospectively recruited all cases with genetically confirmed VWM observed from March 1995 to August 2023 at Fondazione IRCCS Istituto Neurologico "C. Besta" – Milano, Italy. The analysis focused on background activity, interictal epileptiform discharges (IEDs), and slow activity. Clinical data, including neurological symptoms onset and progression, were extracted from patient charts.

Results: Sixteen patients (nine pediatric onset) out of twenty-four had clinical and EEG recordings. In those cases, 64 EEGs were available for analysis (mean 3.2 EEGs per patient, range 1-12). In 68.8% of patients (11/16), serial EEGs show evidence of a progressive worsening in the global organization in terms of background and slow activity. In pediatric cases, EEG worsening may precede, even by a few years, the clinical worsening (in five out of

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nine cases). IEDs were identified in four out of eight patients presenting with seizures. We found no significant association between the occurrence of seizures and IEDs detection. In all cases, IEDs occurred in sleep deprivation or during sleep.

Conclusion: Our findings suggest that progressive EEG deterioration in VWM, characterized by slowed background activity and emerging slow-wave abnormalities, could precede clinical worsening in pediatric cases, serving as a potential early prognostic marker. Seizures are not anticipated by IEDs occurrence, and notably, IEDs are likely detected during sleep or sleep deprivation. Despite the retrospective nature and unsystematic EEG timing, serial EEG monitoring proves valuable in evaluating VWM progression.

1302 | Quantitative EEG and risk of post-stroke epilepsy following acute ischemic stroke

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[1]*Hospital de Santa Maria, Unidade Local de Saúde de Santa Maria, Lisbon, Portugal,* [2]*King's College London, London, United Kingdom*

Purpose: To identify quantitative electroencephalographic (qEEG) predictors of post-stroke epilepsy (PSE) following acute ischemic stroke.

Method: A prospective cohort of 151 consecutive anterior circulation ischemic stroke patients were followed for 12 months. EEG was recorded within 72h (D1 EEG) and either at discharge or 7 days post-stroke (D7 EEG). qEEG indices (including global band power, symmetry, and affected/unaffected hemisphere) were calculated from mean Fast Fourier Transform. The primary outcome was the occurrence of at least one unprovoked seizure (PSE). Univariate analysis was performed using Student's t-test or Mann-Whitney test, as appropriate, followed by multivariate analysis of qEEG variables significantly associated with PSE. Logistic regression was performed using a single qEEG variable at a time, to avoid multicollinearity, and previously known clinical and EEG predictors of PSE.

Results: Of the 151 patients, 7 died during their hospital stay, and outcome was available for 144 (41.7% women, mean age 67.2±12.1). Twenty-three patients had unprovoked seizures (16%). In univariate analysis, several qEEG indices were associated with PSE. However, in multivariate analysis using previously known clinical predictors of PSE (ASPECTS, admission NIHSS, cortical involvement, and presence of acute symptomatic seizures), only ipsilateral alpha-beta to total alpha-beta ratio was independently associated with PSE (D1 EEG: OR 0.867 95%CI 0.781-0.962, p=0.007; D7 EEG: OR 0.899 95%CI 0.815-0.992, p=0.035). The inclusion of ipsilateral alpha-beta to total alpha-beta ratio improved the performance of a prediction model (D1 EEG: AUC=0.819; D7 EEG: AUC=0.806) compared to previously described risk factors (AUC=0.763). A model including clinical predictors associated with D1 EEG visual and qEEG variables (presence of epileptiform activity and ipsilateral alpha-beta to total alpha-beta ratio) achieved the best performance (AUC=0.835).

Conclusion: Lower ipsilateral alpha-beta/total alpha-beta ratio in an early (0-72h) post-stroke EEG predicts PSE independently of previously known clinical and EEG risk factors for PSE.

1414 | An Investigation into the Accuracy of Interictal Epileptiform Discharges Source Localization Using Different Electrode Densities

D Mansilla[1,2], T Avigdor[1,3], C Abdallah[1], A Horrillo-Maysonnial[4], J Royer[5], B Bernhardt[5], C Grova[6], B Frauscher[3,7]
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Purpose: Electrical source imaging (ESI) is a useful tool for determining the source of interictal epileptiform discharges (IED). However, ESI map's accuracy depends on electrode density, creating a trade-off with installation time. Results regarding the added benefit of high-density (HD) compared to low-density (LD) setups are conflicting. We compare both electrode densities ESI maps accuracies.

Method: We included 41 patients (21 females) with 83 collodion-glued electrodes. The IEDs were marked both on the HD-EEG (83 electrodes) and LD-EEG (25 electrodes) array by an epileptologist. We (1) compared HD and the LD ESI maps produced by the coherent maximum entropy on the mean (cMEM) (2) compared the results of the ESI maps on the midpoint as well as on the peak of the IED (3) repeated the former two using minimum norm estimate (MNE) and standardized low-resolution brain electromagnetic tomography (sLORETA). We evaluated the ESI maps by measuring the distance localization error (DLE)— the distance from the map's maximum to the

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nearest point of the presumed source—and the spatial dispersion (SD), defined as the weighted amount of activity outside the presumed source.

Results: We found no significant differences of at least moderate effect (0.4) between the HD and LD-EEG setups in terms of DLE ($p > 0.05$) and SD ($p > 0.05$) at the peak (HD: DLE= 12.66mm [0-39.4] SD: 15.6mm [6.3- 33.49) (10-20: DLE= 12.57mm [0-39.6]; SD= 16.0mm [5.2-33.4) or at the midpoint (HD: DLE= 13.4mm [0-39.5] ; SD= 16.5mm [7.0-39.5]) (10-20: DLE= 10.8mm [0-39.5] ; SD= 15.7mm [4.9-34.4]) using cMEM. Similarly, no differences were found for DLE ($p > 0.05$) and SD ($p > 0.05$) using MNE or sLORETA both at the midpoint and at the peak.

Conclusion: For clinical practice there seems to be no major difference between the use of LD-EEG and HD-EEG in ESI localization accuracy.

1476 | The role of EEG in the prediction of post-stroke seizures

KM Schubert[1], V Dasari[2], AL Oliveira[3], C Tatillo[4], G Naeije[4], N Gaspard[4], A Strzelczyk[5], V Punia[2], M Galovic[1], C Bentes[3]

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Purpose: Seizures are a common complication following stroke and can significantly impact patient outcomes, highlighting the importance of accurate predictors of post-stroke epilepsy (PSE). This study aimed to determine whether early electrographic findings identified via electroencephalography (EEG) improve the prediction of PSE in stroke survivors.

Method: We conducted a multicenter cohort study involving 1105 ischemic stroke patients (mean age 71 years, 54% male) who underwent EEG within seven days post-stroke. Electrographic findings, including epileptiform activity and regional slowing, were analyzed using Cox proportional hazards regression adjusted through inverse probability weighting. A novel prognostic model, SeLECT-EEG, was developed specifically for stroke survivors without acute symptomatic seizures (ASyS) and compared to the established $SeLECT_{2.0}$ model.

Results: Among the cohort, 119 patients (11%) developed PSE, with 233 (21%) having ASyS and 872 (79%) without ASyS. Epileptiform activity (hazard ratio [HR]: 2.0, 95% CI: 1.3–3.0, p=0.001) and regional slowing (HR: 1.9, 95% CI: 1.2–2.9, p=0.004) were independently associated with an increased risk of PSE. Stroke survivors with epileptiform activity had a 5-year PSE risk of 42% (95% CI: 30%–49%), compared to 13% (95% CI: 9%–16%) in those without. Similarly, those with regional slowing had a 5-year PSE risk of 24% (95% CI: 18%–29%), compared to 11% (95% CI: 5%–15%) in those without. The SeLECT-EEG model demonstrated superior discrimination (C-statistic: 0.75, 95% CI: 0.71–0.80) compared to the $SeLECT_{2.0}$ model (C-statistic: 0.71, 95% CI: 0.65–0.76, p<0.001).

Conclusion: Electrographic findings, particularly epileptiform activity and regional slowing, significantly enhance PSE risk prediction beyond clinical risk factors. The SeLECT-EEG model, specifically developed for stroke survivors without acute symptomatic seizures, outperforms existing prognostic models. This novel tool provides a more accurate means of identifying high-risk individuals, enabling improved patient management, targeted interventions, and more informed counseling for stroke survivors.

Drug Therapy
15:15-16:15
Sunday, 31 August
Aud V

545 | Efficacy of azetukalner in Focal Onset Seizure (FOS) subtypes: Results from the double-blind, placebo controlled, phase 2b X-TOLE study

E Perucca[1], J French[2], C Harden[3], J Qian[3], C Luzon Rosenblut[3], C Kenney[3], G Beatch[3]

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Purpose: X-TOLE enrolled 325 participants with FOS who had failed a median 6 antiseizure medications (ASMs) and were on stable treatment with 1-3 ASMs. Participants were treated with placebo or azetukalner, a novel, potent K_V7 potassium channel opener. Azetukalner showed dose-dependent, significant, and rapid onset reduction in FOS frequency vs placebo. Here we report the efficacy of azetukalner by focal seizure subtype.

Method: Median percentage change (MPC) in monthly (28 day) seizure frequency and proportion of participants experiencing a ≥50% reduction in monthly seizure frequency (RR50) were calculated by seizure subtypes as

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exploratory analyses after 8 weeks treatment with azetukalner (25 mg; n=112) or placebo (n=114), taken once daily with food and no titration. Seizure subtypes were focal aware with motor signs (type 1), focal impaired awareness with motor signs (type 2), focal impaired awareness nonmotor (type 3), and focal to bilateral tonic-clonic (type 4).

Results: Median monthly baseline seizure frequencies for azetukalner 25 mg were 12.6 for type 1 (n=27), 9.5 for type 2 (n=82), 11.2 for type 3 (n=26), and 2.9 for type 4 (n=23) compared with 16.2 (n=29), 9.0 (n=83), 11.4 (n=23), and 1.9 (n=30) for placebo, respectively. MPC reduction from baseline was higher for azetukalner 25 mg (54.5, 58.8%, 45.2%, 86.9%) compared with placebo (21.4%, 19.5%, 23.8%, 36.5%) for types 1-4, respectively. RR50 rates were also higher for azetukalner 25 mg (51.9%, 59.8%, 46.2%, 78.3%) vs placebo (24.1% 21.7%, 17.4%, 40.0%) for types 1-4, respectively. The most common treatment-emergent adverse events for azetukalner 25 mg were dizziness (31.6%), somnolence (14.9%), and fatigue (12.3%).

Conclusion: In the X-TOLE study, compared with placebo, azetukalner 25 mg reduced seizure frequency rate across all focal seizure subtypes including those that progressed from focal to bilateral tonic-clonic.

741 | Trofinetide for the treatment of Rett syndrome: Long-term safety and efficacy results from the open-label LILAC and LILAC-2 studies

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Purpose: Trofinetide significantly improved core symptoms of Rett syndrome (RTT) with an acceptable safety profile in Lavender. Here, we report the safety and efficacy results of LILAC and LILAC-2, open-label extension studies of Lavender.

Method: Females with RTT, aged 5–21 years, received twice-daily, oral trofinetide in LILAC for 40 weeks. Participants who completed Lavender and LILAC continued trofinetide in LILAC-2, a 32-month extension study. Safety assessments included the incidence of adverse events (AEs). Efficacy endpoints included the Rett Syndrome Behavior Questionnaire (RSBQ) and the Clinical Global Impression–Improvement (CGI-I) scale.

Results: Overall, 154 patients were enrolled in LILAC. The most common AEs were diarrhea (74.7%) and vomiting (28.6%). The mean (standard error [SE]) change from the LAVENDER baseline to Week 40 in the LILAC study in RSBQ was −7.3 (1.62) and −7.0 (1.61) for participants treated with trofinetide and placebo in LAVENDER, respectively. Mean (SE) CGI-I scores compared with the LILAC baseline at Week 40 were 3.1 (0.11) and 3.2 (0.14) for patients treated with trofinetide and placebo in Lavender, respectively. Similar safety and efficacy trends were observed in LILAC-2.

Conclusion: Trofinetide continued to improve symptoms of RTT in LILAC and LILAC-2 with a safety profile consistent with Lavender. These studies were supported by Acadia Pharmaceuticals Inc.

1007 | Cognitive effects of cenobamate as compared to perampanel: a cross-sectional multi-center study in 675 patients

J-A Witt[1], J Catalán-Aguilar[2], E Schütz[3], R von Wrede[1], KG Hampel[4], Y Novitskaya[3], R Surges[1], M Garcés[4], B Metternich[3], K Wagner[3], V Villanueva[4], C Helmstaedter[1]

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Purpose: Head-to-head comparison of cognitive performance in individuals with epilepsy treated with cenobamate (CNB) versus perampanel (PER), an antiseizure medication (ASM) with a neutral cognitive profile.

Method: This retrospective cross-sectional multi-center study assessed executive function (EpiTrack®) in individuals diagnosed with epilepsy under CNB or PER treatment. Inclusion criteria were an epilepsy diagnosis and a cognitive assessment under CNB or PER using the EpiTrack®. A Bayesian analysis of variance (ANOVA) was conducted to evaluate cognitive performance with treatment type (CNB versus PER) and number of concomitant ASMs as fixed factors.

Results: The analysis was based on 675 individuals with epilepsy (mean age: 40.3 ± 14.1 years, 49.2% women, 50.8% men), 200 of them with CNB (mean dose: 190.9 ± 94.1

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mg/d; range 12.5-450.0) and 475 patients with PER (mean dose: 6.9 ± 3.0 mg/d; range 2.0-12.0). Groups were demographically and clinically similar, except for more generalized genetic epilepsies (10.7% versus 1.5%; BF = 240.931) and fewer prior ASMs in the PER group (4.7 versus 6.6; BF = 54,440,000.0). The EpiTrack® revealed impaired performance in 51.0% (34.5% severely impaired) of the individuals treated with CNB and in 60.0% (39.4% severely impaired) of those treated with PER (BF = 1.217). ANOVA indicated no difference in cognitive performance between individuals treated with CNB or PER (BF = 0.420) but provided decisive evidence of a negative effect of an increasing number of concomitant ASMs (BF = 437,300,000,000.0).

Conclusion: This head-to-head comparison demonstrated comparable performance in executive functions in individuals treated with CNB or (the cognitively neutral ASM) PER and confirmed the adverse effect of an increasing number of combined ASMs. This appears consistent with previous uncontrolled longitudinal studies showing stable or even improved performance after introduction of CNB. However, our study did not assess episodic memory which severely deteriorated under 400 mg/day according to a case report.

1140 | Establishing the Predictive Validity of Preclinical Seizure Models in Generalized Epilepsies: An Extension of the Praxis Analysis of Concordance Framework

L Anderson[1], K Kahlig[1], M Souza[1], S Petrou[1]
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Purpose: Central to the development of novel epilepsy treatments is testing of anticonvulsant activity in preclinical seizure models. The Praxis Analysis of Concordance (PAC) framework was recently developed to assess the translational concordance of common preclinical seizure models, demonstrating three acute seizure models with highest predictive validity for focal onset seizures: audiogenic, maximal electroshock (MES) and 6-Hz (32mA). Here, we sought to establish concordance between commonly used preclinical models and generalized epilepsies, thus extending our work to capture the spectrum of human epilepsies.

Method: Performance of 32 approved antiseizure medications (ASMs) across established preclinical seizure models was evaluated based on reported TD_{50} and ED_{50} values. Protective indices were calculated and a weighted scale representing relative antiseizure efficacy was used to grade preclinical ASM response. ASM clinical use and perceived efficacy were similarly evaluated to grade clinical ASM response. Concordance scores were assigned spanning the spectrum from complete discordance (-1) to complete concordance (1) between preclinical and clinical ASM responses, then summed and normalized to generate a global translational concordance score.

Results: Genetic rat models of absence seizures (GAERS and WAG/Rij) exhibited high concordance with absence and myoclonic generalized seizure types. MES, audiogenic, and amygdala kindling models showed high concordance with primarily generalized tonic-clonic seizures, supported by robust data depth. Models with the highest concordance for atonic or tonic seizures were intra-amygdala kainate and hippocampal kindling; albeit based on limited data depth. MES, audiogenic, mouse 6 Hz (32 and 44mA) and kindling models demonstrated high concordance with status epilepticus.

Conclusion: These findings extend our insights into the predictive validity of commonly used seizure models across the spectrum of human epilepsies. Notably, we demonstrate differential translational concordance between preclinical seizure models and generalized epilepsy types, as well as variability in data depth across utilized models.

1612 | Cannabidiol inhibits neuroinflammation in kainic acid-induced epileptic mice by promoting TREM2 expression

P Zhang[1], H Zhang[2], Z Li[1], Z Zhang[2], M Liang[1], J Zhou[3], J Yuan[1], Y Chen[4,5], J Zhang[1], C Shi[6], Z Li[1], S Li[1], Y Chen[1]
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Purpose: Cannabidiol (CBD) is a novel antiseizure medication, but its mechanism is not fully understood. Neuroinflammation is one of the key pathophysiological mechanisms in epileptogenesis and neuropsychiatric comorbidities of epilepsy. This study aims to explore whether the mechanism by which cannabidiol improves seizures and associated neuropsychiatric comorbidities is related to the regulation of neuroinflammation.

Method: *TREM2* knockout mice were generated, then epileptic mice induced by intrahippocampal kainic acid (KA) injection received CBD treatment once daily for 4 weeks. The spontaneous recurrent seizures of the mice

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were video monitored. After completion of the treatment, the local field potential of the hippocampus was recorded. Depressive-like behavior was detected with the sucrose preference test, cognitive dysfunction was detected with the Morris water maze, and locomotor ability was detected with the open-field test. Human induced pluripotent stem cell (hiPSC)-derived neurons stimulated by LPS+ATP were used to explore the anti-inflammatory mechanism of CBD. Hippocampal tissue or cultured neurons were collected for transcriptome sequencing (RNA-seq), Western blotting, immunohistochemistry, immunofluorescence, enzyme-linked immunosorbent assay, Nissl staining, FJB staining, TUNEL staining and electron microscope.

Results: CBD treatment significantly inhibited epileptic seizures, alleviated depressive-like behavior and cognitive dysfunction, and reduced hippocampal neuronal loss, pyroptosis, and gliosis. RNA-seq showed that CBD could reduce the expression of the *NLRP3* inflammasome and promote the expression of *TREM2* in the hippocampus of epileptic mice. The protein expression levels of NLRP3, pro-Caspase-1/Caspase-1 p20, GSDMD/N-terminal GSDMD, IL-1β, and IL-18 were significantly reduced, while the TREM2 level increased markedly in the hippocampus of KA-induced epileptic mice after CBD treatment. Importantly, *TREM2* knockout abolished the anti-inflammatory and neuroprotective effects of CBD in KA-induced epileptic mice. CBD mitigated neuroinflammatory injury in LPS+ATP-stimulated hiPSC-derived neurons by promoting TREM2 expression.

Conclusion: CBD inhibits the activation of the NLRP3 inflammasome by promoting TREM2 expression, thus alleviating epileptic seizures, cognitive dysfunction, and depressive-like behavior in KA-induced epileptic mice.

Epidemiology
15:15-16:15
Tuesday, 2 September
Aud II

770 | Genetic testing practices across EpiCARE Centers: Insights from a multicenter survey

R Nabbout[1], R Steensbjerre Møller[2], S Tchaicha[3], J Van Hulle[4], M Geroldinger[5], E Brilstra[6], R Kälviäinen[7], E Turón-Viñas[8], G Cantalupo[9], A Brunklaus[10], A McTague[11]

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Purpose: The ERN-EpiCARE Working Group on Clinical Genetics conducted a survey to assess current practices, accessibility, and challenges in genetic testing for rare epilepsies across Europe. The survey aimed to pinpoint areas for improvement and opportunities for harmonization within clinical genetics testing.

Method: The survey, distributed to 50 EpiCARE member hospitals, collected data on genetic testing practices, including tests' availability, turnaround times, use of rapid testing, multidisciplinary team (MDT) involvement in patients' selection and testing analysis, and genetic counseling practices. Respondents were also asked to describe challenges and unmet needs in diagnosing rare epilepsies.

Results: The survey collected responses from 51 centers, including 28 pediatricians, 17 adult neurologists, and 7 geneticists, providing a broad perspective of genetic testing practices across ERN-EpiCARE centers. Substantial variability in diagnostic approaches was observed. In-house genetic testing was conducted by 84% of centers, with exome sequencing available in 49 centers and genome sequencing in 36 centers. Rapid genetic testing (<3 weeks) was accessible in 70% of centers, primarily targeting neonatal and severe refractory epilepsy cases. MDT discussions before and after testing were reported by 68% of centers, underscoring the value of collaborative approaches in genetic diagnostics. Genetic counseling was provided in 68% of centers following positive results, while 32% offered it selectively for clinically relevant findings. Major

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challenges included extended turnaround times, limited access to advanced technologies, and gaps in funding.

Conclusion: The survey reveals significant variability in genetic testing practices across EpiCARE centers. Rapid and advanced testing methods are increasingly being implemented; however, disparities persist in access, turnaround times, and funding mechanisms. MDT discussions are not always available although key for the best genetic testing practice and counseling. Addressing these challenges will require the development of harmonized protocols, targeted resource allocation, and enhanced integration with international registries to improve diagnostic accuracy and patient outcomes in rare epilepsies.

795 | Ultra-refractory epilepsy: The newly-described entity

I Dolezalova[1], J Vinklarek[1], J Kocvarova[1], O Strycek[1], M Pail[1], P Burilova[2], A Pokorna[2], M Brazdil[1]

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Purpose: Drug-resistant epilepsy (DRE) is defined as the failure of two anti-seizure medications (ASMs), affecting approximately 30% of epilepsy patients. In some cases, additional ASMs and surgical approaches are also unsuccessful. Ultra-Refractory Epilepsy (URE) is a newly defined entity, characterized by the failure of six distinct epilepsy treatment strategies, including ASMs, surgical resection, and vagal nerve stimulation (VNS). This study aimed to analyze demographic and clinical data of URE patients managed at the Brno Epilepsy Center, a member of the ERN-EpiCare network.

Method: A retrospective review was conducted on all epilepsy patients admitted to the Brno Epilepsy Center inpatient department between 2015 and 2023. URE patients were identified, and their demographic and clinical data were analyzed.

Results: A total of 1,050 patients were reviewed, and 63 patients (6%) met the criteria for URE. The median age of epilepsy onset was 3 years (range: 1–60 years). The median seizure frequency was 29 seizures per month (range: 1–900), with 46% of patients experiencing extremely high seizure frequencies (>20 seizures/month). Structural etiology was the most common cause (25 patients). Among the cohort, 62 patients received a combination of ASMs, surgical resection, or neurostimulation, while two patients were managed exclusively with ASMs.

Conclusion: URE represents an extreme therapeutic challenge within epilepsy centers. The high seizure burden and limited treatment response in this population highlight the urgent need for novel therapeutic strategies and further research into this newly described entity.

1170 | Emulating target trials of periconceptional supplementation of high-dose folic acid in women taking antiseizure medication on risk of major congenital anomalies using Nordic Registry data - A SCAN-AED study

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Purpose: To study the effect of high dose folic acid (≥1 mg per day) supplementation in the periconceptional period on risk of major congenital anomalies (MCAs) in offspring of women taking antiseizure medication (ASM).

Method: We emulated target trials using comprehensive nationwide registries from four Nordic countries (Denmark, Iceland, Norway, Sweden 1997 to 2020). We identified eligible women in 72 weekly sequential trials and defined treatment according to initiation (prescription fills) or no initiation of high dose folic acid within one week of recruitment. We pooled data and estimated the risk difference (RD) and odds ratio (OR) of MCAs for initiation vs no initiation of high dose folic acid in three

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periconceptional periods (13-52, 1-12 weeks before conception, 1-12 weeks after conception) and a control period (13-20 weeks after conception). Participants were censored in several situations using censoring weights and inverse probability of treatment weights were used for baseline characteristics adjustment including indication and types of ASMs.

Results: The number of eligible women (and proportion of initiators) in the four periods were 486,060 (0.2%), 139,700 (0.4%), 122,070 (1.4%), and 54,010 (0.5%), respectively. Initiators of high dose folic acid during 1-12 weeks before conception had a lower risk of MCA (2.2%) compared to non-initiators (4.8%) with a RD of -2.6% (95%CI: -3.8% to -7.4%) and an OR of 0.47 (95%CI: 0.21-0.85). Initiating high dose folic acid during 1-12 weeks after conception did not show protective effects (6.1% vs.4.7%) with a RD of 1.4% (95%CI: -0.3% to 3.1%) and an OR of 1.31 (95%CI: 0.94-1.68). The ORs were 0.98 (95%CI:0.67-1.38) for the period of 13-52 weeks before conception and 1.45 (95%CI: 0.54-2.65) for the control period.

Conclusion: Initiation of high-dose folic acid prescribing prior to conception rather than after conception was associated with reduction in risk of MCA in children born of women using ASM.

1508 | New-onset epilepsy among children with status epilepticus as their first seizure: interim report from the SEED study

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Purpose: To determine the frequency of new-onset epilepsy among children in northern Nigeria who had their first seizure as status epilepticus (SE).

Method: 1452 children with SE, aged 1 month to < 15 years, managed using a standardized SE protocol with point-of-care video-EEG, were enrolled into the SEED cohort study from 4 major emergency pediatric units. We prospectively collected data using structured neurological assessment electronic case report forms, brain MRI scans, and EEG-video of 616 children with SE as their first-ever seizure. Participants have clinical follow-up evaluations at 1, 3, 6, 12, 18, and 24 months (still ongoing) to determine the frequency of new-onset epilepsy and predictors of such adverse outcomes. New-onset epilepsy was defined based on the 2017 International League Against Epilepsy (ILAE) definition of epilepsy.[1]

Results: Of the 616 children with no prior seizure at SEED enrolment to date, 47 (7.6%) developed new-onset epilepsy, with the majority (34; 74.5%) emerging within 12 months of the first SE. Age less than 5 years [odds ratio (OR) = 1.5; 95% confidence interval (CI) = 0.8, 2.9], SE duration longer than 30 mins (OR = 1.9; 95% CI = 1.0, 3.4), focal onset SE (OR = 2.1; 95% CI = 1.2, 3.9), and benzodiazepine-resistant SE (BR-SE) (OR = 2.7; 95% CI = 0.8, 9.8) were identified as potential predictors of new-onset epilepsy.

Conclusion: The SEED cohort data is a valuable source of prospective data on childhood SE outcomes. The frequency of new-onset epilepsy among those with SE as their first seizure will require a 24-month follow-up of this cohort or longer. Given the genomic and SE risk factor differences, it is unclear whether results from studies in Europe and North America will be generalizable to the West African population.[2,3]

1849 | The Impact of Folic Acid Supplementation on Epilepsy, Maternal and Fetal Outcomes in Chinese Pregnant Women with Epilepsy

ATA Abdulaziz[1], N Hao[1], L Lu[1], Y Chen[1], T Li[2], J Liu[3], X Lin[4], L Chen[1], X Hao[1], X Wu[1], J Li[1], D Zhou[1]

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Purpose: To investigate whether periconceptional folic acid (FA) intake affects epilepsy, maternal, and fetal outcomes in Chinese women with epilepsy.

Method: This study included pregnant women with epilepsy enrolled in the West China Pregnancy Registry of Epilepsy (a prospective multicenter cohort study) between 2012 and 2021. Detailed information on maternal epilepsy, FA intake, anti-seizure medications (ASMs), and pregnancy and perinatal outcomes were obtained through

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regular visits to the Neurology clinics. Primary outcomes were seizure control status and adverse maternal and fetal outcomes. Subgroup and stratified analyses were also performed to control for potential confounders.

Results: The study included 1638 pregnancies of 1405 women with epilepsy. 1299 (79.3%) pregnancies in 1173 women used FA supplements during peri-conception, and 1351 (82.5%) pregnancies were exposed to ASMs. The rate of periconceptional FA intake did not differ between ASM users and those not using ASMs (P = .268). The recurrence rate of generalized tonic-clonic seizures (GTCs) was significantly higher in the non-FA group compared to FA users throughout pregnancy. Low FA dose, delayed initiation, and short use duration were associated with an increased risk of GTC recurrence. Most pregnancies (78.8%) in the non-FA group were lost compared to only 13% in the FA group (P<.001). Non-FA users had approximately 3.5-fold and 7.5-fold increased risks of spontaneous and elective abortions compared to FA users. FA use was associated with a 6.5-fold decreased risk of abortion among ASM users compared to only 4-fold in non-ASM users. In our study, periconceptional FA intake was not linked to other adverse maternal and fetal outcomes.

Conclusion: Periconceptional folic acid intake by women with epilepsy was associated with approximately a 66% decreased risk of abortion and better seizure control during pregnancy. In this study, FA intake was not associated with any harmful effect on maternal and fetal outcomes.

Epilepsy and Reproductive Health
15:15-16:15
Tuesday, 2 September
Aud VIII

594 | Antiseizure medication dose changes in pregnancy and postpartum: findings from MONEAD

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Purpose: To describe how antiseizure medication (ASM) doses were managed among pregnant women with epilepsy (WWE) in the Maternal Outcomes and Neurodevelopmental Effects of Antiepileptic Drugs (MONEAD) study.

Method: MONEAD was a prospective, observational, U.S.-based multi-center cohort study of pregnant WWE. Enrollment occurred up to 20 weeks gestation. Prospective data were collected on ASM regimens from enrollment through postpartum. Descriptive statistics were created for each ASM group on number of dose changes, time post-enrollment to first dose change and to subsequent changes, dose changes in mg, and percent of conception-dose, for enrollment through 6 weeks postpartum.

Results: 299 pregnant WWE were analyzed. For lamotrigine, 128/146 (87.7%) participants had doses increased at least once. Median dose increases were 100 mg, beginning at median 32 days after enrollment, reaching an average of 190.5% of conception dose by delivery. Postpartum, 103/146 (70.5%) of doses were tapered, with median first dose decrease on postpartum day 2, by a median of 100 mg to an average of 115.8% of the conception dose by 6 weeks postpartum. For levetiracetam, 70/125 (56%) participants had doses increased at least once by a median of 500 mg beginning at median 47 days after enrollment, to an average of 176.7% of the conception dose by delivery. Postpartum, 43/125 (34.4%) of doses were tapered, with median first dose decrease on postpartum day 3, by a median of 500 mg to an average of 136.4% of the conception dose by 6 weeks postpartum. Among 14 other ASMs analyzed, 10 had doses increased in pregnancy and 8 were tapered postpartum.

Conclusion: Previous MONEAD analyses showed no difference in seizure control between pregnant and non-pregnant WWE, but ASM doses were changed more often in the pregnant group. We detail how ASMs were managed in pregnancy and postpartum to achieve this favorable outcome.

676 | Blood concentrations vs. dose effects of fetal antiseizure medications on cognition and behavior in children of mothers with epilepsy

K Meador[1], D Loring[2], A Matthews[3], A Birnbaum[4], P Pennell[5], T Monead Investigator Group[1]
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Purpose: Fetal antiseizure medication (ASM) exposure can produce neuropsychological abnormalities. Clearance changes in pregnancy may alter dose-exposure relationships. We report here how neuropsychological outcomes in children of women with epilepsy (WWE) taking ASMs are related to blood concentrations vs. dose.

Method: The Maternal Outcomes and Neurodevelopmental Effects of Antiepileptic Drugs (MONEAD) study is a prospective, observational, multicenter investigation of pregnancy outcomes which enrolled women during pregnancy. Children were assessed at age 6 years-old with detailed neuropsychological evaluations across 8 domains (Language, General Intelligence, Visuospatial, Memory, Executive, Processing Speed, Behavior, and Achievement), yielding 50 variables. Here, we limited the analyses to completers for lamotrigine and levetiracetam monotherapies, which comprised 78.1% of monotherapies. Ratio of maximum observed ASM blood levels (ABL) and ratio of defined daily dose (DDD) were calculated for 3rd trimester exposures. Chi-square analyses were conducted to assess differences in significant effects for ABL vs. DDD and for lamotrigine vs. levetiracetam.

Results: 151-166 children of WWE were analyzed depending on the domain variable. Mean (min-max) ABLs (ug/mL) were lamotrigine=5.2 (1.5-14.3) and levetiracetam=21.0 (2.2-61.8). Mean (min-max) DDDs were lamotrigine=661mg (150-1850mg) and levetiracetam=2288mg (375-7000mg). Comparing ABL vs DDD for lamotrigine+levetiracetam, 27% ABL vs. 13% DDD were significant (Chi-square=6.12, p=0.013). Comparing lamotrigine vs. levetiracetam for ABLs, 16% lamotrigine vs. 38% levetiracetam were significant (Chi-square=4.11, p=0.043). Comparing lamotrigine vs. levetiracetam for DDDs, 13% lamotrigine vs. 4% levetiracetam were significant (Chi-square=7.16, p=0.007). For ABL and DDD significant findings, all were worse for levetiracetam, and all but one value better for lamotrigine.

Conclusion: ASM blood concentrations are more sensitive than dose for 3rd trimester exposure effects. Levetiracetam produced more significant and more negative exposure effects than lamotrigine. Future studies should consider these findings. Additional studies are needed for the majority of ASMs to determine risks of adverse neuropsychological effects from fetal exposure. Sources of Funding: NIH, NINDS and NICHD #U01-NS038455.

822 | Infertility outcomes in valproate exposed and unexposed men with epilepsy or bipolar disorder: an international cohort study of real-world healthcare data

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Purpose: To assess infertility outcomes in men with epilepsy or bipolar disorder exposed and unexposed to valproate.

Method: In this retrospective cohort study of data from a global network of healthcare organizations called TriNetX, validated disease and prescription codes were used to assess men aged <55 years A) with epilepsy or bipolar disorder; B) with epilepsy; and C) with bipolar disorder. Those exposed and unexposed to valproate were compared for lifetime risks of infertility, testicular hypofunction, testicular atrophy, a composite measure (low sperm concentration/motility/vitality/normal forms/semen volume), and serum reproductive hormones (total testosterone, free testosterone, LH, FSH, prolactin, and estradiol). Follow-up commenced from second valproate prescription (exposed)

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or second disease code (unexposed). Comparison groups were propensity score matched for >140 baseline covariates at baseline. Survival analysis was undertaken using Cox-proportional hazard models, generating hazard ratios (HRs) with 95% confidence intervals (CIs) for dichotomous outcomes, and t-tests for continuous outcomes.

Results: From 633,405 men with epilepsy or bipolar disorder, 89,417 and 543,988 were exposed and unexposed to valproate, respectively. Valproate was detectible in serum for 96% of 45,036 valproate-exposed men who had levels checked. 77,077 propensity-score-matched men in each cohort were compared. There was a <1% difference in infertility outcomes between those exposed and unexposed to valproate (not significant): male infertility HR 0.978; CI 0.797-1.201, testicular hypofunction HR 0.947; CI 0.850-1.056, testicular atrophy HR 1.051; CI 0.702-1.574, and composite low sperm concentration/motility/vitality/normal forms/semen volume HR 0.913; CI 0.621-1.342. Total testosterone was significantly less in men exposed to valproate (mean 360 ng/dL) compared to those unexposed to valproate (mean 389 ng/dL, $p = 0.000$), but both are within normal range (300-1,000 ng/dL). Remaining hormone levels did not differ (p >0.05). Analyzing men with epilepsy or bipolar disorder separately did not yield any significant results.

Conclusion: More caution is needed in associating valproate with male infertility in humans.

828 | Pregnancy outcomes after in vitro fertilization in women with epilepsy on antiseizure medications: Prospective data from EURAP

T Tomson[1], S Alvestad[2], D Battino[3], E Bonizzoni[4], J Craig[5], E Perucca[6], P Perucca[6], A Sabers[7], F Vajda[6], EURAP Study Group

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Purpose: To assess pregnancy outcomes and seizure control after in vitro fertilization (IVF) in women with epilepsy treated with antiseizure medications (ASMs).

Method: This cohort study based on data from 47 countries in the EURAP registry (1999-2024) includes data from pregnancies resulting from IVF in women with epilepsy exposed to ASMs throughout the entire pregnancy. Prospective pregnancies with a complete follow-up until 1 year after birth were included for the analysis of teratogenic outcomes, i.e. the prevalence of major congenital malformations (MCMs). The analysis of seizure control and obstetrical outcomes also included prospective pregnancies with follow-up until delivery but not necessarily until 1 year after birth.

Results: Out of 727 pregnancies meeting the criteria for teratogenic outcomes, there were 3 perinatal deaths and 8 induced abortions for fetal abnormalities. Of the remaining 716 pregnancies, 597 were singleton and 119 twin or triplet pregnancies. The most frequently used ASMs in monotherapy were lamotrigine (n=254), carbamazepine (n=116), levetiracetam (n=105), and valproate (n=77). MCMs occurred in 38 (6.1%) of 625 pregnancies exposed to ASM monotherapy versus 9 (8.8%) of 102 pregnancies exposed to ASM polytherapy. MCMs were reported in 9.1% of the multifetal deliveries vs. 4.7% of the singleton deliveries. Of the 936 pregnancies assessed for obstetrical outcomes and seizure control, 784 were singleton. There were 3 perinatal deaths and 164 premature deliveries (18%). Caesarean section was used in 408 (44%). Regarding seizure control, 590 (63%) women were seizure-free throughout pregnancy, 126 (13%) had one or more tonic-clonic seizures, and 199 (21%) had other seizures. Fourteen women had tonic-clonic seizures at delivery, but none had convulsive status epilepticus.

Conclusion: Our observations are consistent with an increased risk of adverse outcomes in IVF pregnancies. This possibility will be assessed through a comparison with non-IVF pregnancies with similar ASM exposures in the EURAP registry.

1680 | Periconceptional Low-Dose vs. High-Dose Folic Acid Supplementation and Neurodevelopmental Outcomes in Children Exposed to Antiseizure Medications: Preliminary Findings from the Prospective Observational Norwegian Mother, father and Child cohort study (MoBa)

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Clinical Neuroscience, Full Member of EpiCARE European Reference Network for Rare and Complex Epilepsy, Oslo, Norway, [6]Oslo University Hospital, Department of Research and Innovation, Division of Clinical Neuroscience, OsloNrow, Norway, [7]University of Bergen, Department of Clinical Medicine, Bergen, Norway, [8]Haukeland University Hospital, Department of Neurology, Bergennorwa, Norway

Purpose: Periconceptional folic acid supplementation has been associated with improved neurodevelopmental outcomes in children exposed to antiseizure medications (ASMs) during pregnancy. However, the optimal dose remains unclear. This study investigates the association between different folic acid doses and neurodevelopmental outcomes in children of mothers with epilepsy using ASMs, including the risk of autistic symptoms, language impairment, and attention deficit hyperactivity disorder (ADHD).

Method: Our preliminary analyses focused on autistic symptoms and language impairment reported by parents at three years and ADHD symptoms at five years, using validated screening tools. Covariates included the type of ASM used, maternal age, parity, smoking habits, body mass index, socioeconomic status, and the presence of genetic variants predisposing to low folate levels. Logistic regression with multiple imputation was used to account for missing data and adjust for potential confounders.

Results: We identified 215 eligible children, with 180 exposed to low-dose folic acid (<1 mg/day), 30 to medium-dose (1–4 mg/day), and 5 to high-dose (>4 mg/day). Compared to low-dose supplementation, the odds ratio (OR) for autistic symptoms after exposure to medium/high doses (>1 mg/day) was 0.63 (95% CI: 0.08–5.26), for language impairment 0.80 (95% CI: 0.17–3.90), and for ADHD 0.91 (95% CI: 0.13–6.56). High-dose folic acid (>4 mg/day) showed numerically higher risk estimates for autistic symptoms (OR: 2.5; 95% CI: 0.06–110.3) and language impairment (OR: 2.5; 95% CI: 0.11–58.18), though statistical power was limited. Due to the small sample size, risk estimates for ADHD with high-dose supplementation could not be calculated.

Conclusion: Preliminary findings suggest that folic acid doses above 1 mg/day may be beneficial in reducing neurodevelopmental risks in ASM-exposed children. However, very high doses (>4 mg/day) may be associated with an increased risk, though estimates were imprecise and not statistically significant due to small group sizes.

Epilepsy Surgery
15:15-16:15
Tuesday, 2 September
Aud I

982 | First-in-human long-term ictal recording with multiple implanted endovascular EEG devices, EP-01

Y Masuda[1], H Hosoo[2], K Araki[1], H Ishida[3], M Nishimura[4], A Marushima[2], A Fujimoto[5], E Ishikawa[1], Y Matsumaru[2]

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Purpose: The gold standard for diagnosing of the location of an epileptic focus is an intracranial electrode. We have developed a new endovascular EEG device, the EP01, which utilizes minimally invasive intravascular techniques to place multiple electrodes in the brain. At present, a multicenter phase 3 clinical trial is being conducted in Japan to investigate the feasibility of diagnosing the epileptic focus during seizures due to long-term recording. We will present the first case of ictal endovascular EEG recording using EP-01.

Method: The patient is a 25-year-old female who has had FAS of nausea and anxiety, and FIAS since childhood. The ictal scalp EEG indicated right temporal and occipital epilepsy. An intracranial EEG (SEEG, subdural electrodes) was performed, and at the same time, 6 EP-01electrodes were implanted from the bilateral jugular vein to superior sagittal sinus, bilateral cavernous sinuses, and bilateral transverse sinuses. Intracranial EEG and intracranial vascular EEG recordings were performed simultaneously.

Results: A total of 124 hours of recording was performed, and there were three times of habitual seizures. During the seizure, the abnormal activities were first measured using subdural electrodes placed on the surface of the right posterior temporal lobe. A few seconds later, similar abnormal activity during the seizure was recorded from the EP-01 electrode placed in the transverse sinus. The displacement of the EP-01 electrodes were within 1 cm within the recording. All of the EP-01 electrodes were removed smoothly. There was no evidence of EP-01-related complications.

Conclusion: Long-term ictal recording was successful using the EP-01. Seizure abnormalities could also be detected from the EP-01, which is close to the focus. It

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should be noted that this report is based on a single case only, and further investigation is necessary to draw more comprehensive conclusions.

1193 | Association between radiofrequency thermocoagulation volume in the epileptogenic zone and surgical outcomes in drug-resistant epilepsy

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Purpose: This study aimed to assess the relationship between the volume of the epileptogenic zone (EZ) which is radiofrequency thermocoagulated (RF-THC) and seizure outcomes post-RF-THC.
Method: We included patients with drug resistant epilepsy who were admitted for Stereo-electroencephalography (SEEG) at a single hospital, Australia. RF-THC volume from patients with pre- and post-SEEG MRIs was used to estimate RF-THC volume per bipolar contact. EZ location and volume was delineated post-SEEG on Brainlab software. Binary logistic regression assessed associations between RF-THC/EZ volume ratios and seizure outcomes at 6 months and the last follow-up (≥3 months) post-RFTHC.
Results: We included 56 patients (mean age 37.68+/-10.59 years, female 55.36%). The median RF-THC bipolar contacts was 10 [IQR7–16] per patient, with an estimated RF-THC volume of 6.63 [IQR4.41–9.63] mm^3 per bipolar contact. The overall median RF-THC volume for the cohort was 74 [IQR40.75-121.52] mm^3 and EZ volume was 902.5 [IQR420.75-254.5] mm^3 per patient. There was no significant association between RF-THC volume and seizure freedom at six months (p=0.340) or last follow-up (p=0.462). However, smaller EZ volume was significantly associated with seizure freedom at 6 months (p=0.029) and last follow-up (p=0.034). Additionally, increased RF-THC/EZ ratio was significantly associated with seizure freedom at 6 months (p=0.029) and last follow-up (10.48 [IQR6.08-22.8] months) (p=0.027). The median RF/EZ ratio was higher in seizure-free group (9.6% [IQR7.5%-20.6%]) compared to the non-seizure-free group (5.4 % [IQR 3.1%-10.5%]) at 6 months follow up. There was no significant association between the RF-THC/EZ ratio and seizure responders (≥50% seizure reduction) at both 6 months (p=0.476) and the last follow-up (p=0.404).
Conclusion: Patients with more restricted EZs who have greater RF-THC ablation proportions have an increased chance of seizure freedom. However, the RF-THC/EZ ratio is not associated with the responder rate, suggesting that targeted RF-THC to key nodes may modulate epileptic networks.

1263 | The impact of implanting sentinel or electrodes contralateral to the hypothesized epileptogenic zone in stereoelectroencephalography

M Bijji[1], H Kreinter[2], JG Burneo[3], G Pellegrino[3], KW MacDougall[3], DA Steven[3], J Lau[3], ML Jones[3], A Suller Marti[4]
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Purpose: For patients with drug-resistant epilepsy undergoing stereo-electroencephalography (SEEG), the utility and safety of depth electrodes placed in the hemisphere contralateral to the presumed epileptic focus is not fully understood. This study aims to determine the impact of implanting electrodes contralateral to the suspected epileptogenic zone (EZ) in patients evaluated with SEEG.
Method: Data was collected from 109 epilepsy patients who underwent SEEG investigation at the Western University Epilepsy Center, from 2018-2023. The depth electrode implantation classification was: (i) Unilateral, 13 patients; (ii) Sentinel, ≤2 electrodes contralateral to the EZ hypothesis, 41 patients; (iii) Bilateral with a lateralized EZ hypothesis (BL), >2 electrodes contralateral to the EZ hypothesis when the hypothesis is lateralized to one side, 28 patients; (iv) Bilateral with a non-lateralized EZ hypothesis (BNL), >2 electrodes in either hemisphere when the hypothesis is bilateral, 27 patients. We analyzed: the electrographic involvement of the contralateral electrodes, eligibility for surgery, seizure freedom rate and complications.
Results: Having a seizure onset and epileptiform discharges in the contralateral hemisphere to the hypothesized EZ was the most common finding associated with changing the EZ hypothesis (p=0.001) and not being eligible for surgery (p=0.001). Patients with unilateral 7 (54%), sentinel 27 (66%), and BL 15 (54%) were more likely to be candidates for surgery than patients with a BNL 5 (19%) (p=0.002). No significant difference was found regarding seizure freedom rate depending on the type of implantation at twelve months in patients who underwent resective surgery (p=0.911). Three patients had complications

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(sentinel (n=1), BL (n=1), BNL (n=1), (p=0.544)), mostly infections.

Conclusion: The placement of contralateral electrodes in SEEG may influence surgical decision-making and while we did not find higher morbidity, careful consideration of the potential risk when increasing the number of electrodes implanted is needed.

1348 | Hemispherotomy in the first year of life: safety, feasibility, complications and seizure outcome – A single-center experience

M Pielas[1], K Kotulska-Jóźwiak[1], M Roszkowski[2], P Kowalczyk[2]
[1]*The Children's Memorial Health Institute, Department of Neurology and Epileptology, Warsaw, Poland,* [2]*The Children's Memorial Health Institute, Department of Neurosurgery, Warsaw, Poland*

Purpose: Hemispheric procedures in epilepsy surgery pose a substantial challenge in young patients with low body weight and blood volume. This study aims to evaluate the safety, complications and seizure outcome of hemispherotomies performed in children under 12 months.

Method: A retrospective analysis was conducted of patients under 12 months who underwent hemispherotomy between 2005 and 2024 at a national referral center for epilepsy surgery. Data collected included: demographics, medical history, seizure onset age, age at surgery, duration of surgery, intubation and intensive care recovery time, blood products requirement, perioperative and long-term complications. Seizure outcome was measured using the Engel score.

Results: Fifteen infants (7 males, 8 females) with a diagnosis of hemimegalencephaly (13) or extensive focal cortical dysplasia (2) were included, only one patient had an additional contralateral MRI abnormality. The median seizure onset was 3 days, all children presented with daily seizures. The mean age at surgery was 7±2.68 months and body weight ranged from 6700g to 9800g. The average procedure time was 229±45 minutes with mean intraoperative blood transfusion volume of 412±318 ml; 87% of patients required average postoperative transfusion of 171ml (range 50-880ml). The patients stayed in intensive care unit for average 4.3±3.6 days with a mean intubation duration of 3.2 days. There were no mortalities in the group studied, major complications included extensive intracerebral bleeding (2) and cardiac arrest during surgery (1). Other frequent adverse events were: 40% of patients required prolonged cardio-pulmonary support, 33% underwent shunt implementation due to postoperative hydrocephalus. One third of children experienced electrolytes disbalance and 4/15 postoperative fever. Engel class I at 12 months follow-up was achieved in 54.5% of patients.

Conclusion: Hemispherotomy in first year of life is a feasible, yet demanding procedure with a significant risk of perioperative complication. A multidisciplinary approach is essential for optimal patient outcomes.

1635 | Good versus severely impaired memory functioning more than 10 years after temporal lobe epilepsy surgery. How did the patients get there?

EB Kyte[1], A Holth Skogan[1], MI Lossius[1], C Helmstaedter[2], KÅ Alfstad[1]
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Purpose: This study aims to determine factors contributing to very long-term memory outcome after temporal lobe epilepsy surgery, with special emphasis on the good functioning and severely impaired.

Method: 102 patients who had undergone epilepsy surgery and completed pre (T1) and two year (T2) post-operative neuropsychological assessments were reassessed 10-44 years after surgery (T3). Memory scores were categorized into "severely impaired" (>2 SD below average), "ok" or "good" (≥average). Frequency tabulations and ordinal regression analyses were performed to identify factors determining the different outcomes.

Results: At T3 45% of the patients reported memory problems. Objectively verbal memory was "severely impaired" for 20%, and "good" for 14%. 86% of the "severely impaired" had undergone left hemisphere resections, 71% of the "good" had right hemisphere resections (p<.001). Figural memory was "severely impaired" for 34%, and "good" for 11%. Patients in the "severely impaired" group had less education (12 versus 14 years, p=.026). Of the "severely impaired" in verbal memory at T3, 35% were severely impaired at T1, 40% had lost due to surgery and 25% showed a late loss. Of the "good" performers 21% were "good" after surgery and 79% showed late improvement. For figural memory, 27% of the "severely impaired" at T3 were "severely impaired" at T1, 35% at T2. "Severely impaired" verbal memory could be predicted by left hemisphere resection (OR 6.99, p<.001), "good" outcome by more years of education (OR 1.25, p=.01). For figural memory, "good" outcome was predicted by left hemisphere resection (OR 3.7, p=.006) and more years of education (OR1.20, p= .034).

Conclusion: Many years after temporal lobe epilepsy surgery, many patients still struggle with memory problems.

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Their trajectories indicate that baseline, side of surgery, reserve capacities, plasticity and in a few patients also potentially degenerative processes determine who ends good or very poor.

1665 | Dynamic brain functional networks to investigate protective mechanisms against epileptic seizures

R Di Giacomo[1], P Núñez[2,3,4], J Poza[3,4,5,6], V Rodríguez-González[3,4], C Gómez[3,4,6], A Burini[1,7], L Castana[8], M de Curtis[1], L Tassi[8], G Varotto[1,9]
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Purpose: Epilepsy research increasingly emphasizes the role of brain network dynamics in seizure generation and propagation. This study explores static and dynamic functional networks in subjects with drug-resistant epilepsy, in order to identify mechanisms that enhance or inhibit seizure initiation and propagation. To this aim, we analyzed the functional connectivity of brain networks preceding minor ictal electrical discharges and clinically relevant seizures in epileptogenic and non-epileptogenic zones, explored with intracerebral electrodes.
Method: We recorded stereo-electroencephalographic signals from 39 patients with focal drug-resistant epilepsy during presurgical monitoring. The etiology of epilepsy varied, as did the lobes involved. We analyzed static functional connectivity using graph theory metrics, and dynamic functional connectivity by assessing the complexity and dwell times of brain meta-state activations.
Results: Static connectivity analysis revealed significant alterations in network centrality, integration, and segregation properties, with differential patterns observed in resting conditions, immediately preceding minor electrical discharges and major seizures. Specifically, network analysis before both minor electrical discharges and major seizures revealed increased integration and reduced segregation (reduced betweenness centrality and increased nodal strength) in the epileptogenic zone. In the non-epileptogenic zones, network integration was reduced before minor electrical discharges but not before major seizures. Dynamic connectivity analysis showed lower complexity and increased stability of meta-states activations preceding minor electrical discharges, particularly in the higher frequencies in non-epileptogenic zones.
Conclusion: Our study provides novel and valuable insights into the dynamic reconfiguration of brain networks preceding epileptic seizures. We suggest an inhibitory/protective mechanism against seizure spreading mainly involving the non-epileptogenic zones, which appear less flexible and less dynamically variable before minor ictal discharges compared to the epileptogenic ones. Understanding these network changes is pivotal for improving epilepsy treatment strategies targeting dynamic network alterations.

Genetics
12:15-13:15
Wednesday, 3 September
Aud V

501 | Regional somatic mosaicism in focal pediatric epilepsy

HW Phillips[1]
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Purpose: Molecular analyses of surgically resected brain tissue in pediatric drug-resistant epilepsy (DRE) have identified brain-limited somatic mutations, particularly in the mTOR pathway, as an important cause. However, limited access to resected tissue has restricted our understanding of the distribution of somatic mTOR pathway mutations across brain regions. Recent studies reveal a widespread distribution of pathogenic mTOR variants with varying mosaicism levels across brain regions in the same individual.
Method: We identified children undergoing stereo-EEG (sEEG)-guided surgical resections for DRE at our center from January to July 2024. Following sEEG, electrodes were removed and collected individually along with subject-matched peripheral blood. Prior to surgical resection, several brain regions encompassing the planned resection were selected to sample both the center and periphery of the resection zone. During surgery, a 1×1 cm^3 tissue block was individually collected from each preselected region.

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Results: We identified 20 children who underwent sEEG and subsequent surgical resection for DRE. Of these patients, 47% were male, with an average age of 9.3 years. On average, five brain-tissue samples (n=100) and 15 electrodes (n=300) were collected per individual. Genomic DNA (gDNA) was isolated from brain-tissue samples and amplified from electrode-derived samples. Targeted gene panel sequencing was performed on amplified electrode-derived samples, unamplified gDNA from bulk-tissue, and subject-matched blood samples. Levels of mosaicism were mapped across epileptic versus non-epileptic regions in the same individual. Preliminary data suggest higher mosaicism levels in epileptic regions, although further analysis is required.

Conclusion: Pathogenic somatic mutations in the mTOR pathway are an important cause of pediatric DRE. Limited access to brain tissue has hindered our ability to precisely localize the distribution of these variants across the epileptic brain. Our preliminary data suggest a regional gradient of somatic mosaicism that correlates with the seizure focus, suggesting a dose dependent relationship with mutational burden and epilepsy pathogenesis.

780 | Clinical and genetic insights from a large cohort of individuals with *SCN2A*-related disorders

S Gverdtsiteli[1,2], RS Dahl[1,2], B Goad[3], MC Cioclu[4], T Brünger[5], K Howell[3,6,7], D Lal[5], RS Møller[1,2]
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Purpose: Research on *SCN2A*-related disorders is increasing, but a comprehensive overview is still lacking. Here we review all published cases of *SCN2A* and perform genetic and clinical data analysis.

Method: We searched "*SCN2A*" on PubMed and collected relevant information for all reported cases. We classified identified cases into previously defined phenotypic subgroups (modified from Berecki et al, Commun Biol 5,515, 2022) and assessed frequencies of different features for each.

Results: We included 944 individuals, from 184 articles. Of these, 81.7% had missense, 16.7% protein-truncating and 1.6% copy-number variants. 37 variants were identified in more than five individuals, the most common being R853Q, A263V, R223E. History of epilepsy was reported in 88%, DD/ID in 77% and ASD in 20% of cases. Mortality rate was 3.4%. Individuals were classified into early onset (EO), late onset (LO) and no seizure groups. They were subsequently divided into EO-self-limited (n=39), EO-intermediate (n=56), EO-severe (n=68), LO-severe (n=30), LO-other (n=35) groups. No seizure group included individuals with ID/ASD and no epilepsy (n=34). Individuals <2 years or with unknown age at follow-up were excluded from further analysis. Age at seizure onset ranged between 1 day-2.5 months for EO-severe, 2 days-5.5 months in EO-intermediate, 1 day-23 months in EO-self-limited, 3-19 months in LO-severe and 2-26 years in LO-other group. Severe-profound DD/ID was observed in the EO-severe and LO-severe groups, while mild-moderate DD/ID was seen in the EO-intermediate and no seizure groups. ASD was most frequently observed in the no epilepsy group (65%), followed by the LO-other (57%), LO-severe (27%), EO-intermediate (16%) and EO-severe (6%). DD/ID or ASD were absent in the EO-self-limited group.

Conclusion: We performed in-depth analysis of the largest *SCN2A* cohort to date, to guide management and counselling of individuals with *SCN2A*-related disorders. This data will also be used to update SCN-portal (scn-portal.broadinstitute.org). This work is supported by the FamilieSCN2A Foundation.

867 | Phenotypic spectrum of loss-of-function variants in the *KCNA2* gene and genotype-phenotype correlation

L Affronte[1,2], UB Hedrich[3], CM Boßelmann[3,4], H Lerche[3], R Dahl[1,5], S Neri[6,7], C Ferrazzoli[8,1], M De Wachter[9,1], E Gardella[1,10], RS Møller[1,5], G Rubboli[1,11], KCNA2 study group
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Purpose: Pathogenic variants in *KCNA2* have been implicated in a range of neurological disorders. Previous studies reported differential genotype-phenotype associations based on the variant functional defects (gain-of function - GoF, loss-of function - LoF, mixed - GoF/LoF). In this study we aimed to collect an international cohort of patients harboring *KCNA2*-LoF pathogenic variants to expand the phenotypic spectrum.

Method: Ninety-five patients with pathogenic *KCNA2*-LoF variants were included, comprising 39 newly identified cases and 53 previously reported ones (additional clinical information were obtained for 24). Clinical, neurophysiological, neuroradiological data were collected.

Results: Six recurrent loss-of-function (LoF) variants were identified in 84.95% of the cohort: p.Pro405Leu (30 patients), p.Arg294His (24 patients), p.255_257del (8 patients), p.Arg65* (6 patients), p.Pro407Arg (3 patients), and p.Arg297Trp (3 patients). Epilepsy occurred in 80% of patients, with seizure onset ranging from birth to 12 years. Fever sensitivity affected 57.63%, at onset focal seizures occurred in 40.91%, generalized seizures in 33.33%. Status epilepticus occurred in 48%. EEG findings included normal (10.77%), generalized (24.62%), focal (16.62%), both focal and generalized (16.92%) and multifocal abnormalities (30.77%). Neurodevelopment varied from normal (31.32%) to severe impairment (13.25%), with motor and language deficits in 78.67% and 65.79%, respectively. Distinguishing features of the most recurrent variants were: a) p.Pro405Leu: milder epilepsy, frequent language impairment, rare cerebellar atrophy, electrical status epilepticus during sleep (ESES) in 61.9%. b) p.Arg294His high prevalence of cerebellar atrophy, spastic paraplegia, low seizure prevalence, mild-to-moderate cognitive deficits; c) p.255-257 del: generalized epilepsy, normal cognition language, episodic ataxia.

Conclusion: We investigated the largest cohort of *KCNA2*-LoF-related developmental and epileptic encephalopathy (DEE) reported so far. Our study revealed, within the broad clinical phenotypic spectrum of *KCNA2*-LoF DEE, some distinguishing features that may assist in diagnosis and genetic counselling.

1249 | Genetic testing of DNA obtained from stereoEEG electrodes – successes and pitfalls

B Straka[1,2], M Kudr[1], A Jahodova[1], M Ebel[1], A Kalina[3], D Krysl[3], P Fabera[3], A Musilova[1], L Krskova[2,4], M Strnadova[2,4], J Kotis[2], A Kalfusova[2], T Kalendova[5,6], A Malkusova[2], M Vlckova[7], R Lesko[8], P Liby[8], J Zamecnik[2], P Marusic[3], P Krsek[1]

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Purpose: For patients with drug-resistant epilepsy (DRE) undergoing long-term intracranial EEG study as a part of presurgical investigation DNA extracted from intracerebral (SEEG) electrodes represents a unique source of brain tissue amenable for a genetic study. We therefore aimed to analyze technical feasibility and diagnostic yield of deep targeted gene panel sequencing of DNA obtained from SEEG electrodes.

Method: Electrodes explanted from patients were immersed in saline solution and immediately transferred to the laboratory and vortexed for 20 minutes. The solution was centrifuged and spun down. DNA was extracted using QIAamp DNA Micro Kit. We performed targeted gene panel sequencing of 86 genes associated with malformations of cortical development (MCD) and low-grade epilepsy-associated tumors (LEAT) utilizing SureSelectXT HS Target Enrichment System with the average read depth of x1500.

Results: We included 10 patients, both children and adults (age at surgery 12-54 years), who underwent long-term SEEG study. Based on 3T MRI scans, two patients were diagnosed with LEAT, three with focal cortical

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dysplasia (FCD), three with nodular heterotopia and two with focal MR-nonlesional DRE. In selected patients, we repeated the experiments due to low-quality data that resulted in excessive number of variant calls that could not be reliably interpreted. We detected multiple putative variants in mTOR pathway genes and genes encoding for tubulins, e.g. NM_001293212.2(TUBB):c.1159T>A , NM_004958.4(MTOR):c.6869C>T. Variant allele frequency ranged from 2% to 50% (in a patient with previously detected germline variant in *NPRL3*).

Conclusion: Deep targeted gene panel resequencing of DNA extracted from SEEG electrodes represents a feasible yet technically challenging diagnostic tool in patients with multiple etiologies of DRE, and detected variants need to be interpreted with caution.

1268 | Involvement of *CACNA2D2* in developmental and epileptic encephalopathy through disruption of calcium channel functionality and synaptic function

M Essid[1,2,3,4], S Haddad[5], J Fraize[6], O Jallouli[7], JR Alvi[8], S Bakhtiari[9,10], M Ben Hafsa[1,2], H Benrhouma[1,2], W Bouchaala[7], R Burger[11], E Cai[12], P Chand[13], N Chatron[3,4], H Darvish[14], S Efthymiou[12], CI Galaz Montoya[9,10,15], S Haider[16], H Houlden[12], M Jelani[17], H Khan[18], I Kraoua[1,2], M C. Kuer[9,10], R Maroofian[12], E Riesch[19], D Sanlaville[3,4], AS Schoonjans[20], GH Seo[21], H Stamberger[20], T Sultan[8], C Triki[7], D Ville[6], B Vona[22,23], Q Zaman[24,25], S Zuchner[26], C Eibl[5], S Cabet[27], G J. Obermair[5], G Lesca[3,4]

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Purpose: Developmental and epileptic encephalopathy (DEE) associated with *CACNA2D2* variants is an ultra-rare autosomal recessive disorder with a strikingly homogeneous phenotype. *CACNA2D2*, predominantly expressed in the cerebellum, encodes the $\alpha_2\delta$-2 subunit of voltage-gated calcium channels (VGCC). It regulates channel membrane trafficking and current properties. We aim to expand the clinical description and to assess the functional impact of relevant *CACNA2D2* variants.

Method: Through GeneMatcher, ERN-EPiCARE and international collaborations, we assembled individuals carrying biallelic *CACNA2D2* variants. Clinical data were collected by a standardized survey. Brain MRI files were re-analyzed. Functional characterization, including minigene assays and heterologous and homologous protein expression analysis, of novel variants were performed.

Results: Clinical and genetic data were collected from 22 new individuals harboring *CACNA2D2* variants and analyzed alongside 9 previously reported cases. Consistent with prior observations, the cardinal manifestations

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included early-onset drug-resistant epilepsy within the first year of life, severe cognitive and motor impairment, and cerebellar atrophy. Facial and limb dystonia was observed in two families, while ataxia was notably absent in the newly reported patients. Although epilepsy showed age-dependent improvement, significant spasticity persisted. Molecular analysis identified 17 *CACNA2D2* variants, comprising 7 missense and 10 truncating variants (6 splicing, 3 nonsense, and 1 frameshift deletion). Functional studies demonstrated distinct pathophysiological mechanisms. Missense variants affect the functional expression of VGCC, alter synaptic functions while truncating variants are likely triggering nonsense-mediated RNA decay, and hence are predicted to result in a complete loss of protein. Our data predict that aberrant expression of α2δ-2 disrupts the excitatory-inhibitory synaptic balance, a key mechanism underlying neurodevelopmental disorders.

Conclusion: Our findings strengthen the role of *CACNA2D2* in DEE and highlight the dual pathogenic mechanisms underlying this disorder, encompassing both channelopathy and synaptopathy. Acknowledgements: Austrian Science Fund (DOC30 to G.J.O.) and the Gesellschaft für Forschungsförderung Niederösterreich (LSC19-017 to G.J.O. and FTI22-D-013 to S.H.)

1539 | Long-term Safety and Efficacy of Deoxycytidine/Deoxythymidine Combination Therapy in POLG-related Disorders

KA Myers[1], S Berrahmoune[2], C Dassi[2], AC Cheung[3], H Pekeles[1], PJ Waters[4], T Gagnon[4], R Eberhard[1], D Buhas[3]

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Purpose: To assess the long-term safety and efficacy of treatment with pyrimidine deoxynucleosides, deoxycytidine (dC) and deoxythymidine (dT), for people with POLG-related disorders.

Method: In November 2021, an investigator-initiated phase II open-label trial of dC/dT combination therapy for patients with mitochondrial DNA depletion disorders including POLG-related disorders was started. Participants receive dC and dT in a 1:1 ratio, given orally or via feeding tube. The initial dose is 100 mg/kg/day divided tid for 1 week, then 200 mg/kg/day x 1 week, then 300 mg/kg/day x 1 week, then 400 mg/kg/day (final dose). The initial protocol involved treatment for 6 months but was subsequently amended to 60 months after patients reported significant positive responses and wished to continue. Outcome measures include recording of all adverse events, Newcastle Mitochondrial Disease Scale (NMDS), EEG, seizure diary, serum growth differentiation factor 15 (GDF-15, a biomarker of mitochondrial function, and blood and urine tests to monitor end organ function. The study is registered at https://clinicaltrials.gov/study/NCT04802707.

Results: Twenty-four patients with POLG-related disorders have enrolled and started treatment with dC/dT. Age at enrolment ranged from 2 years to 47 years, and a range of phenotypes were seen, including Alpers-Huttenlocher syndrome, Ataxia Neuropathy Spectrum, and Progressive External Ophthalmoplegia. Duration of treatment ranges from 1 month to over 3 years (ongoing). Significant decreases (improvement) in NMDS score and serum GDF-15 have been observed. The most common reported adverse event is diarrhea, though this is usually self-limited or can be resolved by dose reduction. Two patients have died, though neither death was attributed to the intervention.

Conclusion: dC/dT treatment is safe in the long-term for patients with POLG-related disorders and appears effective in improving clinical trajectory, regardless of phenotype.

IGAP Implementation
15:15-16:15
Monday, 1 September
Aud VII

368 | A systematic review and meta-synthesis of integrated care for mental health In epilepsy by The ILAE Integrated Mental Health Care Pathways Task Force

M Gandy[1], W Wu[1], T Woldhuis[1], S Bennett[2], G Baslet[3], G Araujo-Filho[4], AC Modi[5], M Reuber[6], V Tang[7], MP Umuziga[8], HM Munger Clary[9]

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Purpose: Mental health comorbidities are common in people with epilepsy, but access to care remains a challenge. While integrating mental health care into epilepsy

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care settings has been suggested, the current models, benefits, and factors influencing implementation are unclear. This review seeks to summarize existing integrated mental health care models for people with epilepsy to guide the development of future initiatives.

Method: Articles which described any activity within a healthcare setting that addressed mental health as routine care for people with epilepsy were searched from the year 2000 onwards within Embase, Medline, PsycINFO, and Cochrane. At least two authors reviewed all articles and extracted data. Thematic synthesis using NVivo was used to identify barriers, facilitators, and future service recommendations. Articles reporting clinical outcomes were assessed for study quality.

Results: After reviewing 7,586 abstracts and 596 full-text articles, 65 met the eligibility criteria and were included. The majority (k = 43; 66%) described routine mental health screening protocols, with 11 articles reporting on uptake and acceptability, which were generally high. Interventions included psychological interventions (k = 23; 35%), psychoeducation (k = 9; 14%), and pharmacotherapy (k = 6; 9%). Thirteen articles (20%) reported changes in mental health outcomes, all indicating some improvements, although one third were rated as having poor study quality. Barriers and facilitators were identified in 34 (52%) articles, while 24 (37%) provided recommendations for future initiatives."

Conclusion: We identified diverse approaches to integrated mental health care in epilepsy settings, with promising uptake, acceptability, and impact on mental health outcomes. Qualitative analysis has informed a proposed framework for future integrated mental health care initiatives. This framework includes essential care components such as mental health screening, psychoeducation, and care pathways. It also highlights key facilitators for establishing integrated care (e.g., staffing policies, infrastructure) and ensuring effective delivery (e.g., acceptability, staff incentives, evaluation).

738 | Adolescence and epilepsy. Educational and promotional program through strategies towards reducing the stigma among teenagers at school

F Astorino[1], A Espeche[2], B M Marta[3], L Fasulo[4], C Bastianelli[5], C Roberto[6]
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Purpose: Educational and promotional program that unifies efforts from scientific societies Argentine League Against Epilepsy (LACE), an advocate Fundación de Hemisferectomía (FUNDHEMI), and state educational institutions (Provincial Ministries and University High schools) with the aim of accomplishing the goals of the IGAP (Intersectorial Global Action Plan for epilepsy and other neurological disorders in adolescents) from the World Health Organization (WHO).

Method: Workshop Exchange Meetings led by facilitators promoting teens participation. (Activities: speeches, Q &A section with the students, role playing, 4-6 hours long). Evaluation: epilepsy general information pre-test and post test, satisfaction questionnaire. Program duration: 2 years. Participants: teenagers attending high schools in their senior years in all provinces of Argentina. Method: Educational Program at Schools with the purpose of raising awareness about epilepsy and other neurological disorders.

Results: Period 2024 Salta 7 schools 921 students from 5 cities, Neuquén 3 meetings 550 students 3 schools, Santa Fe – 1 meeting 270 students from a rural Midwest area city 3 different schools, 3 agreements with National Universities were signed (UNR-UNL-UNCuyo) to develop the program within their schools. A shared program with Salta Pediatric Society (SAP Salta) "SAP goes to school" contributed to the promotion. Program continuing 2025 , wishing to be replicated with other partners of LACE and the civil organizations in the rest of the provinces.

Conclusion: This multisectoral initiative aligns with the IGAP's Strategic Objectives 1, 3, and 5 by fostering collaboration between universities, scientific societies, and patient organizations. The actions demonstrate the potential of interdisciplinary collaborations to reduce stigma and promote understanding of epilepsy among adolescents. Teenagers represent a sensitive age group often vulnerable to discrimination and stigma. However, they are also highly effective multipliers of information capable of amplifying the knowledge they receive across various settings. Expanding this program nationally will help to achieve IGAP objectives while fostering these long-term benefits.

1527 | Epilepsy12 – Measuring and improving care for children with epilepsies, England/Wales, 2009-2023

N Raja[1], A Syangbo[1], C Dunkley[2]
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Purpose: Epilepsy12 audit is a national improvement programme for children with epilepsies across England and Wales. We provide ongoing systematic measures of quality of pediatric epilepsy care against national guidelines since 2009. We explore longitudinal trends in access to key healthcare professionals and investigations for children with epilepsy, 2009-2023.
Method: Children with epilepsies, who had completed 12 months of care following first pediatric assessment since 2009, were analyzed. Measures suitable for longitudinal analysis were explored and we report; input from pediatrician with expertise, epilepsy specialist nurse (ESN), pediatric neurologist, ECG and MRI. Trends were analyzed nationally, by region, age and sex.
Results: N = 11,182 children were included.

- The male:female ratio was consistent between cohorts.
- Input from pediatrician with expertise and ESN gradually increased over time: 72.4% to 89.6% and 46.8% to 85.0% respectively.
- Regions showed consistent improving access to pediatricians with expertise, and varied ESN input over time and between regions.
- Greatest improvements were achieved for children <2 years for both pediatrician with expertise input 21.2% (64.0% to 85.2%) and ESN input 41.8% (40.0% to 81.8%).
- A lower percentage of children received input from a pediatric neurologist in 2023 (21.4%), compared to 2009 (36.6%).
- The proportion of children receiving an ECG and MRI increased by 24.2% (39.1% to 63.3%) and 24.9 % (33.7% to 58.6%).

Conclusion: There are challenges conducting population-based improvement programmes over time including participation, data accuracy and completeness. Longitudinal analyses are further complicated by evolving classifications, guidelines and ascertainment methodology. We can however see selected improving longitudinal trends within Epilepsy12 since 2009. Access to key professionals and investigations is improving for children with epilepsy particularly in certain subsets. Access to pediatric neurology remains static. Epilepsy12 continues to report annually and now in real-time to inform strategic multi-level quality improvements and health system transformation.

1830 | Implementation of the Intersectoral Global Action Plan on Epilepsy and Other Neurological Disorders (IGAP) in Kazakhstan: Progress, Challenges, and Future Directions

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Purpose: Kazakhstan has adopted the WHO Intersectoral Global Action Plan on Epilepsy and Other Neurological Disorders (IGAP) to improve epilepsy care, enhance public awareness, and expand access to treatment. Key national initiatives include medical education, patient support programs, and research to inform policy decisions. To assess the progress of IGAP implementation in Kazakhstan by evaluating physician training, patient education, and data-driven approaches in epilepsy management.
Method: A mixed-methods analysis was conducted using national reports, expert interviews, and stakeholder feedback. Three primary initiatives were assessed:
• Basic School of Epilepsy for Doctors (2024): A training program for neurologists and general practitioners to improve early diagnosis and treatment.
• Annual patient seminars on epilepsy and antiseizure medications: Nationwide sessions to enhance medication adherence and reduce stigma.
• National epilepsy prevalence study: Ongoing research to establish accurate statistics and identify treatment gaps.
Results: Kazakhstan has made measurable progress in integrating IGAP principles through:
1. The Basic School of Epilepsy for Doctors (2024) has trained over 86 physicians, enhancing early diagnosis and treatment strategies.
2. Since 2022, Kazakhstan has hosted annual patient-centered seminars addressing epilepsy management, antiseizure drug adherence reaching over 150 participants nationwide.
3. A comprehensive epidemiological study on epilepsy prevalence was launched in 2024 aiming to provide evidence-based insights for resources and policy adjustments. Preliminary findings highlighting the need for expanded screening and specialist access.
4. The expansion of telemedicine services has facilitated remote consultations for epilepsy patients, ensuring continuity of care and specialist availability with standard of consultation.
5. Media campaigns and community workshops have been implemented to address epilepsy-related stigma.
Conclusion: Kazakhstan's approach to IGAP implementation demonstrates improvements in epilepsy care through

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structured education programs, patient empowerment initiatives, and evidence-based policymaking. Future efforts should focus on scaling up educational initiatives, expanding telemedicine services, and strengthening data-driven decision-making for epilepsy management.

1899 | Ground-Up Implementation of the WHO IGAP in Kenya: Community-Led Epilepsy Advocacy and Care

P Ngechu[1], O Miyanji[3], M K'Anjejo[1]
[1]*Kenya Association for The Welfare of People with Epilepsy, Nairobi, Kenya,* [2]*Aga Khan University Nairobi, Nairobi, Kenya*

Purpose: This study aimed to assess the outcomes of a grassroots strategy for implementing the WHO Intersectoral Global Action Plan on Epilepsy (IGAP 2022–2031) in Kenya. The initiative focused on training, service provision, and advocacy to reduce stigma and expand access to care.
Method: KAWE partnered with six county governments and national stakeholders to:

1. Conduct Continuous Medical Education (CME) for 173 Primary Healthcare Workers (PHCWs) and sensitize 248 Community Health Workers (CHWs);
2. Deliver epilepsy awareness programs in 14 schools and 8 prisons, reaching over 14,500 students and 10,000 inmates and staff;
3. Implement a feeding and drug access program for 40 vulnerable households;
4. Facilitate inclusive sexual and reproductive health (SRHR) training for 15 healthcare workers and 28 youth;
5. Advocate for IGAP domestication through county-level engagement, leading to MOUs with Machakos and Tharaka Nithi counties.

Results: Epilepsy consultations increased to 5,896 in 2024 from 5,457 in 2023. Defaulter tracing improved follow-up across four clinics. Public engagement reached over 23 million people through International Epilepsy Day and media coverage. The WhatsApp support group of 112 participants fostered continuous psychosocial support. KAWE's efforts also resulted in an IGAP advocacy unit in Tharaka Nithi, and nine public clinics now offer free epilepsy treatment. Community trust and participation were enhanced through inclusive safe spaces and caregiver programs.
Conclusion: KAWE's grassroots model for IGAP implementation highlights how bottom-up advocacy, combined with service expansion and stigma reduction, can meaningfully improve epilepsy care. These findings demonstrate the viability of community-led health system strengthening for neurological conditions in low-resource settings.

Late Breaking Abstracts
12:15-13:15
Wednesday, 3 September
Aud II

1853 | Artificial Intelligence driven Closed-Loop Devices in SUDEP Prediction and Prevention: Insights from Persons with Epilepsy and Caregivers.

J Ferreira[1], M Regalo[2], M França[3], M Rei[4], R Peixoto[1], J Aibar[5], T Robinson[6], R Matias[7], F Duprat[8], M Mantegazza[8], O Parlak[9], P Ryvlin[10], S Beniczky[11], L Lopes[12], E Perucca[13], J Claro[1], C Conde[3]
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Purpose: The absence of strategies for predicting and preventing Sudden Unexpected Death in Epilepsy (SUDEP) is intertwined with the lack of studies measuring users' attitudes towards potential innovative interventions. The current study introduces the potential use of Artificial Intelligence-driven Closed Loop Devices (AI-CLDs) in SUDEP prediction and prevention, while assessing persons with epilepsy and caregivers' attitudes towards AI-CLDs potential adoption and implementation.
Method: A qualitative study was conducted through three focus groups involving PWEs and CGs. Participants were

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recruited through the NEUROSENSE Patient Advisory Board, with discussions facilitated through a semi-structured interview guide. The study followed grounded theory and qualitative content analysis methods to evaluate the perspectives of PWEs and CGs on the potential use of AI-CLDs in SUDEP prediction and prevention. Data was collected between October 2024 and February 2025, with all sessions transcribed and analyzed.

Results: Three main areas for consideration emerged from the analysis: expectations on AI-CLDs for SUDEP prediction and prevention, decision-making processes involving AI use in healthcare, and barriers and facilitators to AI-CLDs adoption. PWEs and CGs generally expressed positive attitudes toward AI-CLDs, showing support for automatic data sharing with healthcare providers and real-time alerts. However, concerns about AI system accuracy, over-reliance on automation, and the need for control over interventions were raised. Both groups preferred wearable devices over implanted solutions, emphasizing comfort and discretion as critical factors for adoption.

Conclusion: This study highlights the potential of AI-CLDs in improving the prediction and SUDEP prevention, showing promise for enhancing patient safety through real-time monitoring and interventions. The findings underscore the importance of user-centered design in device development, emphasizing comfort, control over interventions, and integration into daily life. This research provides vital insights for future development, aiming to improve PWE and CG confidence in using AI technologies for epilepsy care and risk management.

1865 | Community Epilepsy Medical Camps in Kenya

F Kiserem[1]
[1]*Kiserem Epilepsy Foundation, Director, Nairobi, Kenya*

Purpose: In many parts of Africa, including Kenya, individuals frequently purchase anti-epileptic medication without a proper diagnosis, which can lead to ineffective or harmful treatment. The Mwihoko Epilepsy Medical Camp, organized by the Kiserem Epilepsy Foundation, aimed to address this issue by offering accurate diagnosis, expert consultations, free medication, and community education. The camp also sought to reduce stigma and empower local health promoters for sustained impact.

Method: The camp featured a structured process:

1. Medical Screening and Diagnosis: Patients were registered and examined by neurologists and general practitioners to identify epilepsy and related neurological conditions.
2. Medication Distribution: Confirmed cases received free anti-epileptic drugs (AEDs), donated by the ROW Foundation, along with education on dosage, adherence, and side effects.
3. Health Education: Separate sessions were conducted for caregivers, teachers, and parents on seizure recognition, first aid, and how to support children with epilepsy in school and at home.
4. Community Engagement: Local leaders and health officials participated, reinforcing partnerships for ongoing advocacy and care.

Results:

1. Attendance: 400 community members participated in the camp.
2. Diagnosis: 150 individuals were assessed for epilepsy; over 90 received a confirmed diagnosis.
3. Medication Access: More than 300 AED doses were distributed free of charge.
4. Education Sessions: Over 80 teachers and 60 parents (primarily from Ruiru Constituency) attended educational sessions.
5. Community Response: The initiative garnered strong support, with community members calling for a permanent epilepsy clinic.

Conclusion: This initiative demonstrated a sustainable model by also training community health promoters to ensure ongoing support beyond the event. The Mwihoko camp served not only as a critical intervention point for people living with epilepsy but also as a powerful platform to educate families, build community partnerships, and reduce stigma.

1891 | Obstructive Sleep Apnea in Late-Onset Epilepsy of Unknown Origin: Exploring a Potential Link in Older Adults

G Pederzoli[1], C Lombardi[2], GS Cereda[1], P Mattaliano[2], P Meriggi[3], JC Di Francesco[1]
[1]*University of Milano Bicocca, Department of Neurology, Milan, Italy,* [2]*University of Milano Bicocca, Sleep Disorder Center, Cardiology Department, Istituto Auxologico Italiano IRCCS, San Luca Hospital, Milan, Italy,* [3]*Fondazione Don Carlo Gnocchi Onlus, ICT & Biomedical Technology Integration Unit, Centre for Innovation and Technology Transfer (CITT), Milan, Italy*

Purpose: Late-onset epilepsy (LOE), defined as seizure onset after age 50, often presents a diagnostic challenge due to heterogeneous etiologies and frequent absence of structural findings, often leading to a presumptive

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diagnosis of occult cerebrovascular disease. Sleep disorders are rarely considered as potential contributors. This study aimed to investigate sleep characteristics in patients with LOE of unknown origin (LOEU).

Method: We enrolled 23 patients (9 female, mean age 67.5 years, mean BMI 26.6 kg/m^2) diagnosed with LOEU at the Epilepsy Centre of San Gerardo Hospital. All cases underwent brain MRI and overnight polysomnography (PSG) at the Sleep Disorders Center of Istituto Auxologico Italiano. Sixteen patients also underwent brain 18F-FDG PET imaging, and 14 completed neuropsychological testing. Quantitative data were described using descriptive statistics.

Results: PSG showed a generally reduced sleep efficiency (mean 68%) and altered sleep architecture with increased light NREM sleep (58%) and reduced deep NREM (23%) and REM sleep (19%). The mean Apnea-Hypopnea Index (AHI) was 9.,2. 48% of patients had obstructive sleep apnea (OSA), of whom six had clinically significant OSA (AHI >10) and five had positional OSA (only supine AHI >10). Apneic patients were more often male, had higher BMI (27.8 vs. 25.6), lower sleep efficiency, more reduced deep NREM sleep, presented an higher hypoxic burden (mean SaO_2 92% vs. 93%, minimum 80% vs. 86%, 17% vs. 1.9% of sleep time with SaO_2 <90%), and higher mean heart rate (65 vs. 58 bpm).

Conclusion: Our findings suggest a high prevalence of OSA in LOEU patients, indicating that sleep-disordered breathing and nocturnal hypoxemia may contribute to seizure onset in this population. The widespread reduction in sleep quality and quantity, especially among apneic patients, may represent another factor in late-onset epileptogenesis. Recognition and management of sleep disorders could have diagnostic and therapeutic implications. Larger studies are warranted to confirm these preliminary findings.

1974 | Epilepsy-Related and All-Cause Health Care Resource Utilization After Initiation of Adjunctive Cenobamate Among Patients 65 and Older

V Punia[1], ET Klatte[2], S Stern[3], CT Wade[3], A Gugglilam[3], WT Kerr[4]
[1]*Cleveland Clinic, Cleveland, United States,* [2]*OhioHealth, Columbus, United States,* [3]*SK Life Science, Paramus, United States,* [4]*University of Pittsburgh, Departments of Neurology and Biomedical Informatics, Pittsburgh, United States*

Purpose: The aim of this study was to evaluate the comparative effect of initiating cenobamate vs selected antiseizure medications (ASMs) on epilepsy-related and all-cause inpatient (IP) and emergency room (ER) utilization rates among older adults (≥65 years) with epilepsy.

Method: A retrospective observational study using de-identified electronic health records (EHRs) from 28 health care organizations (Truveta database) identified older adults with an epilepsy diagnosis who initiated cenobamate or selected ASMs (brivaracetam, clobazam, eslicarbazepine, lacosamide, perampanel, or phenytoin) between January 1, 2020 and April 12, 2025. The selected ASMs were chosen based on similar patterns of use primarily in drug-resistant epilepsy. Patients were included if they had an observable encounter (office visit, IP, ER) in the ≥180 days before ASM initiation and had any medication dispensed or requested in the ≥360 days before ASM initiation. The endpoints were the annualized rates of epilepsy-related and all-cause IP and ER encounters. Negative binomial regression models (adjusted for demographic and clinical covariables) were used to compare outcomes between the 4-to-1 propensity-matched cohorts.

Results: A total of 1395 patients (mean age, 72.0 years; 53.3% female; cenobamate, n=279; selected ASMs, n=1116) were included. In the epilepsy-related analysis, treatment with cenobamate was associated with a 38% reduction (95% CI: 25%-49%) in annual IP admissions, and a 34% reduction (95% CI: 12%-51%) in annual ER visits compared to the selected ASM group. In the all-cause analysis, treatment with cenobamate was associated with a 48% reduction (95% CI: 40%-55%) in annual IP admissions and a 14% reduction (95% CI: 0%-26%) in annual ER visits compared to the select ASM group.

Conclusion: Initiation of cenobamate among older adults was associated with significantly fewer epilepsy-related and all-cause IP and ER encounters compared to propensity-matched patients started on ASMs with similar patterns of use.

2054 | Bridging the Epilepsy Treatment Gap in India: A Mixed-Methods Study to Strengthen Primary Care Response through Task-Sharing

S Verma[1], U Gogoi[1], B Singh[1], G Singh[2,3]
[1]*Dayanand Medical College and Hospital, Research & Development Unit, Ludhiana, India,* [2]*Dayanand Medical College and Hospital, Department of Neurology, Ludhiana, India,* [3]*UCL Queen Square Institute of Neurology, London, United Kingdom*

Purpose: Epilepsy is a common neurological disorder affecting 50 million people worldwide with nearly one-fifth of them residing in India. It accounts for 14 million DALYs and 1,26,000 deaths worldwide annually. The

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treatment gap for epilepsy is as high as 80% in India. To address these concerns, the WHO and its member countries approved the IGAP for epilepsy and other neurological disorders with epilepsy as an entry point lasting unto 2031. This study aims to scale-up the competency of primary care workers to manage epilepsy.

Method: We are conducting a two-arm, open-label follow-up study with a mixed-methods evaluation. Arm 1 includes individuals who screened positive for epilepsy in community-based survey and were later confirmed through neurological examinations. Arm 2 comprises people with epilepsy who sought diagnosis or treatment at government primary care facilities. The intervention includes three components: continuing medical education for primary care providers based on the ILAE curriculum, a community awareness campaign, and an electronic mobile-app-based decision-support system, along with advocacy for the availability of essential antiseizure medicines.

Results: Of the 610 individuals who screened positive, 327 were confirmed to have epilepsy. Most had not consulted specialists and were receiving inappropriate medications or doses. Many had not returned for follow-up care, with the median gap since the last clinic visit being 36 months (IQR: 24–60). Medication non-adherence was observed in 51% of the confirmed cases. Additionally, only 57 individuals had accessed primary care facilities for epilepsy-related treatment.

Conclusion: These findings underscore significant gaps in epilepsy care at community level. By equipping primary care providers with structured training and decision-support tools, improving community awareness about epilepsy and its treatment and by ensuring access to essential medicines, we anticipate improvements in seizure control, medication adherence, and overall quality of life for individuals with epilepsy. This model aims for scalable impact in resource-limited settings.

Mixed Topics
15:15-16:15
Tuesday, 2 September
Aud III+IV

309 | Identification of distinct biological groups of patients with cryptogenic NORSE via inflammatory profiling

M Guillemaud[1], M Chavez[1], F Kobeissy[2], A Vezzani[3], AD Jimenez[4], MM Basha[5], A Batra[6], S Demeret[7], O Eka[8], K Eschbach[9], B Foreman[10], N Gaspard[11,4], EE Gerard[6], TE Gofton[12], HA Haider[13,14], ST Hantus[15], CL Howe[16], A Jongeling[17], M Kalkach Aparicio[18], P Kandula[19], K Kazazian[12], M Kim[6], Y Lai[20], C Marois[7], A Mellor[9], W Mohamed[5], M Morales[21], CM Pimentel[13], AM Ramirez[10], C Steriade[17], AF Struck[18], O Taraschenko[22], N Torcida[11], MS Wainwright[21], JY Yoo[8], KK Wang[2], V Navarro[7,1], LJ Hirsch[4], A Hanin[1,4,7]

[1]Paris Brain Institute, Paris, France, [2]Morehouse School of Medicine, Atlanta, United States, [3]Mario Negri Institute for Pharmacological Research,, Milan, Italy, [4]Yale University, New Haven, United States, [5]Wayne State University School of Medicine, Detroit, United States, [6]Northwestern University, Feinberg School of Medicine, Chicago, United States, [7]Pitie Salpetriere Hospital, Paris, France, [8]Icahn School of Medicine at Mount Sinai, New York City, United States, [9]University of Colorado School of Medicine, Children's Hospital Colorado, Aurora, United States, [10]University of Cincinnati, Cincinnati, United States, [11]Hôpital Universitaire de Bruxelles – Hôpital Erasme, Université Libre de Bruxelles, Bruxelles, Belgium, [12]Schulich School of Medicine and Dentistry, Western University, London Health Sciences Center, London, Canada, [13]Emory University School of Medicine, Atlanta, United States, [14]University of Chicago, Chicago, United States, [15]Cleveland Clinic, Neurological Institute, Cleveland, United States, [16]Mayo Clinic, Rochester, United States, [17]NYU Langone Medical Center, New York City, United States, [18]University of Wisconsin, Madison, United States, [19]Weill Cornell Medicine, New York City, United States, [20]Baylor College of Medicine, Houston, United States, [21]Seattle Children's Hospital, University of Washington, Seattle, United States, [22]University of Nebraska Medical Center, Omaha, United States

Purpose: This study aimed to identify distinct inflammatory response subtypes in patients with cryptogenic New-Onset Refractory Status Epilepticus (c-NORSE) by analyzing their cytokine profiles. Insights into underlying mechanisms were sought to understand the

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pathophysiology and guide personalized therapies to improve patient outcomes.

Method: Sixty-two patients with c-NORSE were included. A comprehensive panel of 96 cytokines was analyzed in serum samples. Patients were clustered based on their cytokine profiles using the Louvain algorithm, an unsupervised graph-based clustering method. The identified clusters were compared in terms of cytokine levels and clinical features. Protein pathway analysis was used to explore the biological relevance of the inflammatory markers within each cluster.

Results: Three distinct clusters of c-NORSE patients were identified: cluster A with no major signs of inflammation, cluster B exhibiting an innate immunity cytokine-driven inflammatory response, and cluster C displaying dysregulated autoimmune processes. Patients in cluster B showed a statistically significant elevation of innate immune-related pro-inflammatory cytokines associated with leukocyte recruitment and degranulation, while those in cluster C showed activation of JAK-STAT pathways, suggesting potential autoimmune mechanisms. Patients in clusters B and C demonstrated varied responses to immunotherapies, with cluster C patients showing favorable outcomes following multiple lines of immunotherapies.

Conclusion: The identification of distinct inflammatory subgroups in c-NORSE suggests that variations in the underlying immune mechanisms contribute to differential treatment responses. These findings underscore the importance of personalized therapeutic strategies, potentially targeting specific inflammatory pathways, to optimize clinical outcomes in this challenging condition.

669 | Machine learning models applied to independent cortical folding variables distinguish TLE subgroups

TM Santos Bezerra[1], L Scárdua Silva[1], Í Karmann Aventurato[1], R Brioschi[1], R Batista João[1], M Koutsodontis Machado Alvim[1], B Machado Campos[1], F Cendes[1], B Sinclair[2], C Yasuda[1]

[1]UNICAMP, Campinas, Brazil, [2]Monash University, Melbourne, Australia

Purpose: Grey matter atrophy in temporal lobe epilepsy (TLE) is well-documented, yet advanced in-vivo MRI analyses may provide insights into complex pathological processes. Recent studies introduced a universal cortical folding model utilizing metrics of cortical thickness (T), total surface area (At), and exposed surface area (Ae), following the scaling law: At*sqrt(T)=k*Ae^(5/4). This model was developed into a vector representation of the human cortex with three dimensionless variables: axonal tension (K), cortical shape complexity (S), and brain isometric volume (I). The pathological changes of these variables in TLE remain unexplored, prompting the aim to compare these changes between TLE with unilateral right or left hippocampal atrophy (HA) and healthy controls.

Method: Cortical metrics were extracted from T1-weighted images of 337 controls and 182 patients (97 left TLE and 72 right TLE) using Freesurfer7.1.1. Metrics I, K, and S were derived with the Cortical Folding Analysis Tool. Metrics were corrected for age and sex and standardized relative to controls. Group differences were assessed using repeated measures ANOVA and Bonferroni's correction. Machine learning models were built for group distinction using Python and scored with 5-fold cross-validation for accuracy, f1-score, and area under the curve (AUC).

Results: Compared to controls, bilateral hemispheres were affected in LTLE and RTLE. For lobe differences, LTLE showed reduction of I parameter in the left parietal and temporal ($p=0.03, p<0.001$), and bilateral increase of K in the temporal lobes ($p<0.001$). The RTLE group had ipsilateral reduction of I parameter in temporal and occipital lobes($p=0.015, p=0.033$), with elevation of K and S measures in the parietal ($p<0.001, p=0.006$). The left parietal lobe presented increased S ($p=0.005$). Logistic regression models successfully differentiated TLE patients from controls ($AUC=0.71\pm0.02$) and RTLE from LTLE ($AUC=0.79\pm0.08$).

Conclusion: TLE groups presented bilateral alterations, with specific changes differentiating patients with right or left HA. These metrics, though sparse, effectively distinguish TLE patients from controls.

1049 | Progressive cortical and hippocampal atrophy after status epilepticus: a prospective longitudinal MRI study

B Crespo Pimentel[1,2,3], P Bosque Varela[1,2], L Machegger[4], J Steinbacher[4], J Pfaff[4], F Xiao[5], E Trinka[1,2], G Kuchukhidze[1,2]

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Purpose: Status epilepticus (SE) is a neurological emergency that leads to neuronal injury and increased mortality. Here, we used serial brain MRI, an established biomarker of neurodegeneration in epilepsy, to investigate longitudinal trajectories of cortical thinning and hippocampus atrophy following SE.

Method: This longitudinal prospective study analyzed 281 MRI scans from 112 participants, including 39 individuals with SE who underwent acute brain MRI within 48h of SE and up to 4 follow-up scans, and 47 controls with drug-resistant focal epilepsy (DRFE) with one follow-up scan. Semiology categorized SE into convulsive (CSE, n=17), non-convulsive (NCSE, n=20) and convulsive to non-convulsive SE (CSE-NCSE, n=2). Cortical thickness was measured via a surface-based framework together with hippocampus volumetry in structural serial MRI scans in all participants, whereas the rate of thinning/atrophy was compared between groups using mixed-effect models adjusting for inter-scan interval and age. Analysis was performed relative to the side of seizure onset (ipsilateral vs. contralateral).

Results: Groups differed in age [SE 59±18 vs. DRFE 31±12 years, p<.001] and interval between baseline and last scans (SE 149±214 days vs. DRFE 414±394 days, p<.001]. Accelerated widespread cortical thinning of the ipsilateral hemisphere was observed in SE (p<.001), while both hippocampi showed accelerated volume decline (ipsilateral p<.001, contralateral p<.01) as compared to DRFE. Both CSE and NCSE were associated with similar widespread accelerated cortical thinning (both p<.001) and hippocampus atrophy (CSE: ipsilateral p<.001, contralateral p<.001; NCSE: ipsilateral p<.01, contralateral p<.05) when compared to DRFE. SE duration independently contributed to accelerated cortical thinning (p<0.001) and ipsilateral hippocampus atrophy (p<.01).

Conclusion: SE is associated with duration-dependent widespread irreversible progressive brain damage irrespective of semiology and exceeding that seen in refractory focal epilepsy. Our findings highlight the importance of prompt SE recognition and termination to mitigate brain injury and underscore the link between prolonged seizure activity and neurodegeneration.

1112 | Real-World Use of Fenfluramine for Dravet Syndrome: a Retrospective Cohort Study Using a National Pharmacy Database

SD Lhatoo[1], WT Kerr[2], EC Wirrell[3], E Donner[4], J Sullivan[5], R Guerrini[6], IE Scheffer[7], S Rheims[8], JH Cross[9], L Lagae[10], P Ryvlin[11], A Gil-Nagel[12], JL Noebels[13], J Roberts[14], A Lothe[14], M Rañopa[15], O Devinsky[16]

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Purpose: Patients with Dravet syndrome (DS) are at risk of premature mortality, with all-cause mortality rates previously reported as 8.6-15.8/1000 person-years. In the United States (US), fenfluramine (FFA) is approved for managing seizures in patients ≥2 years old with DS. A prior post-hoc analysis of FFA studies demonstrated lower all-cause mortality rates in FFA-treated patients compared to expected rates. This study describes mortality rates and real-world use of FFA in US patients with DS who were new FFA users, obtained from a single specialty pharmacy.

Method: This retrospective study evaluated patients with DS who were new FFA users and received their first shipment ≥6 months prior to the data cut. Outcomes include demographics, FFA doses, persistence rates by index year, and mortality rates. Standardized mortality ratios (SMRs) with 95% confidence intervals (CIs) for 2021-2023 were reported. Descriptive statistics were used.

Results: From July 01, 2020 to March 15, 2024, 1043 patients with DS were new FFA users; 49.2% were 6-17 years old, 56.6% were prescribed FFA by pediatric

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epileptologists, and 56.0% had previously taken cannabidiol. Initial median FFA dose was 0.3 mg/kg/day (range: 0.1-1.1 mg/kg/day) and median maintenance dose was 0.5 mg/kg/day (range: 0.02-1.4 mg/kg/day). Persistence rates at 6 and 12 months, respectively, were: 90.9% and 78.5% in 2020, 85.8% and 76.9% in 2021, 83.5% and 74.8% in 2022. Median treatment duration was 21.3 months; 729 patients continued FFA at data cut. There were 15 deaths over 1869.5 patient-years, resulting in an estimated mortality rate of 8.02/1000 person-years (95% CI: 3.96-12.08); SMR from 2021-2023 was 1.88 (95% CI: 1.05-3.14).

Conclusion: This real-world analysis revealed that mortality rates in patients with DS treated with FFA were similar to previous studies and demonstrated an encouraging SMR. Further studies will evaluate causes of death, including sudden unexpected death in epilepsy.

UCB-supported.

1117 | The burden of cumulative comorbidities in epilepsy

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Purpose: It is well established that epilepsy is associated with higher levels of autistic spectrum disorder, intellectual disability and other neurological and neuropsychiatric conditions. Traditionally the comorbidities of epilepsy have been explored in a binary study designs (e.g. epilepsy and autism; epilepsy and intellectual disability etc.). As a result, little is known about the cumulative burden of essential comorbidities in epilepsy. The aim of this study was to examine the cumulative burden of essential comorbidities in people with epilepsy admitted for inpatient review.

Method: We conducted a clinical audit of the comorbidities identified in a consecutive series of patients admitted to a specialist epilepsy inpatient monitoring unit for diagnosis and assessment in 2023 (n=327). The primary diagnosis and other comorbidities identified following the conclusion of the multidisciplinary inpatient assessment were examined. Essential comorbidities were classified into 4 categories: Non Epileptic Attack Disorder (NEAD), Intellectual Disabilities, Neuropsychiatric Diagnoses (anxiety, depression, psychosis) & Neurodivergent conditions (Autistic Spectrum Disorders, Attention Deficit Hyperactivity Disorder).

Results: The age of the inpatients ranged from 16 to 74 years. Approximately one third of admissions were diagnosed with conditions other than epilepsy. The majority of these were diagnosed with NEAD. Of those with a confirmed diagnosis of epilepsy, two thirds had at least one other comorbidity. The most common comorbidities were Neuropsychiatric Diagnosis (56%), followed by NEAD (24%), Intellectual Disabilities (15%) and Neurodivergent conditions (14%). One in five of the admissions had two essential comorbidities, whilst nearly 10% had three or more.

Conclusion: Epilepsy is associated with two or more essential neuro-comorbidities in one in five people admitted to hospital for specialist review. The cumulative burden of multiple neuro-comorbidities presents a significant challenge to the management of this patient group. Our results provide an evidential foundation for provision of adequate services and training for professionals working with this group.

1761 | Causal relationship between air pollution and epilepsy: A Mendelian randomization study

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Purpose: Growing evidence highlights air pollution as a critical environmental risk factor for neurological disorders, but causal relationships remain uncertain due to residual confounding in observational studies. This Mendelian randomization (MR) study aimed to investigate the causal effects of long-term exposure to $PM_{2.5}$, NO_2 and SO_2 on the risk of epilepsy, leveraging genetic instruments to overcome methodological limitations and provide robust epidemiological evidence.

Method: The genetic instruments for pollutants were selected from the summary statistics of the European population genome-wide association study (GWAS), selecting single nucleotide polymorphisms (SNPs) strongly associated with $PM_{2.5}$, NO_2, and SO_2 ($p < 5\times10^{-8}$) and validated for the MR assumptions (F-statistics >10, no pleiotropy). Epilepsy data included 15,212 cases and 29,677 controls from the IEU OpenGWAS platform. Primary analyses employed inverse-variance weighted (IVW) regression, supplemented by weighted median and MR-Egger methods. Sensitivity analyses evaluated heterogeneity (Cochran's Q test), horizontal pleiotropy (MR-Egger intercept), and outlier SNPs (MR-PRESSO).

Results: A 5 $\mu g/m^3$ increase in the genetically predicted $PM_{2.5}$ concentration was associated with an elevated risk of epilepsy (IVW regression, OR = 1.23, 95% CI: 1.07-1.42, $p = 0.005$), without evidence of horizontal pleiotropy (MR-Egger intercept, $p = 0.21$) or heterogeneity (Cochran's

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Q test, $p=0.15$). MR-PRESSO confirmed that no outlier SNPs drove this association. Subtype analyses yielded consistent results for $PM_{2.5}$. On the contrary, NO_2 and SO_2 did not show significant effects on the risk of epilepsy.

Conclusion: This study provides novel genetic evidence supporting $PM_{2.5}$ as a causal risk factor for epilepsy, independent of the confounding of the co-pollutant. The findings underscore the neurotoxic potential of particulate matter and advocate for the implementation of stringent air quality regulations to reduce the disease burden of epilepsy. Future research should integrate multi-omics approaches to elucidate the association of neuroinflammatory pathways with this conclusion and validate the correlations in diverse populations.

Neuroimaging
12:15-13:15
Wednesday 3 September
Aud VIII

357 | Expanding language assessment in epilepsy patients through the individual functional connectome

R Stepponat[1], M Berger[1], L Schäfer[1], F Fischmeister[1], G Kasprian[1], S Bonelli-Nauer[1], K Kollndorfer[1]
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Purpose: Pre-surgical language evaluation has remained largely unchanged for years, underscoring the need for improved methods. Given that epilepsy and language both operate as network functions, analyzing the individual functional connectome may offer greater clinical precision, enabling more accurate predictions and better-informed surgical decisions for enhanced patient care.

Method: Language is predominantly left-lateralized, and fMRI is commonly used for preoperative evaluation of lateralization by calculating the lateralization index (LI). However, a survey by Benjamin et al. highlights significant uncertainties in fMRI results among clinicians.

In this study, 46 patients with temporal lobe epilepsy and 25 healthy controls underwent preoperative fMRI. Data preprocessing was performed with fMRI Prep, and correlation maps were created using the CONN toolbox. Seed-based connectivity (SBC) analysis of core language areas, based on Fedorenko et al. 2024, was conducted, and a LI based on graph measurements (degree) was calculated. This was compared to traditional LI analysis and neuropsychological data, with all analyses conducted in native space.

Results: Results indicated that the connectivity-based lateralization index (LI) provided a more consistent measure of language lateralization compared to standard LI methods, aligning better with neuropsychological assessments. Patients with lesional epilepsy showed greater variability in lateralization compared to MR-negative patients, while healthy controls exhibited stronger left-lateralization as expected. The use of seed-based connectivity (SBC) analysis enhanced the detection of individual differences in language network organization, underscoring its potential clinical value in preoperative assessment.

Conclusion: The initial findings suggest that connectivity-based LI may improve the accuracy of preoperative language assessments. This approach offers a promising enhancement over traditional LI methods, providing more reliable insights for surgical planning and potentially leading to better predictions of post-surgical cognitive outcomes.

610 | Multimodal investigation of the thalamus in children with temporal lobe epilepsy

X Feng[1], R Piper[1,2], F Prentice[1], M H. Eriksson[1,3], M Tisdall[2,1], J Clayden[1], T Baldeweg[1]
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Purpose: The thalamus is involved in seizure propagation and is therefore a target for neuromodulation therapy. While adults with temporal lobe epilepsy (TLE) display thalamic atrophy and abnormal functional connectivity, less is known about these changes in pediatric TLE. This study provides a multimodal characterization of thalamic nuclei in pediatric TLE, examining volume and functional connectivity.

Method: Structural and functional MRI were retrospectively analyzed for 86 children with unilateral TLE (ages 6–19y) and 72 controls (ages 6–20y). We assessed the whole thalamus and four sub-nucleus groups (anterior, lateral, medial and pulvinar) for 1) volume and 2) functional-connectivity-based hubness. Hubness indicates whether a region is highly connected or isolated within the network. Age- and sex-adjusted measures were compared using ANOVA, examining associations with TLE phenotypes and post-surgical seizure freedom, with FDR-corrected $p<0.05$.

Results: Patients showed reduced volume in the whole thalamus, anterior, lateral nucleus group and pulvinar ipsilateral to the seizure focus, compared to controls (all $p<0.05$, Cohen's d=0.61, 0.37, 0.43, 0.67). More severe

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ipsilateral atrophy was in patients with hippocampal sclerosis ($p<0.05$, partial $\eta2=0.09$). Functional connectivity analysis revealed reduced hubness in the ipsilateral pulvinar compared to controls ($p<0.05$, Cohen's $d=0.46$). Additionally, increased hubness of the bilateral anterior thalamus was associated with a history of focal-to-bilateral tonic-clonic seizures ($p<0.05$, partial $\eta^2=0.10$). Longer epilepsy duration correlated with ipsilateral volume reduction ($r=-0.30$) and increased hubness ($r=0.29$, all $p<0.05$). Both ipsilateral thalamic volume reduction and increased hubness ($p=0.04$, 0.03) predicted post-surgical seizure recurrence (model: $\chi^2(3)=14.64$, $p<0.01$, Nagelkerke $R^2=0.36$), along with epilepsy duration ($p=0.04$), in a N=46 surgical subset.

Conclusion: This study shows thalamic ipsilateral atrophy and bilateral functional alterations in pediatric TLE, with prominent changes converging in the pulvinar. Thalamic nuclei changes progressed with disease duration and were sensitive to TLE phenotypes, highlighting the potential of thalamic biomarkers for seizure outcomes.

920 | Premature structural brain ageing and domain-specific cognitive changes in epilepsy

H Pardoe[1], C Tailby[1], J Chapman[1], M Ireland[1], D Vaughan[1], D Abbott[1], A Irimia[2], G Jackson[1]
[1]Florey Institute of Neuroscience and Mental Health, Melbourne, Australia, [2]University of Southern California, Los Angeles, United States

Purpose: Brain-predicted age difference (BrainPAD) derived from structural MRI is a proxy marker of brain health. This study investigates the association between BrainPAD, processing speed, and memory in individuals with epilepsy, using data from the Australian Epilepsy Project (AEP).

Method: The study included 412 participants aged 18-67 from four cohorts: first unprovoked seizure (N = 34), newly diagnosed epilepsy (N = 97), drug-resistant epilepsy (N = 149), and healthy controls (N = 132). Structural T1-weighted MRI scans were processed using a deep-learning based brain age prediction model trained on 16,213 healthy participants (https://github.com/irimia-laboratory/USC_BA_estimator). BrainPAD was calculated as the difference between predicted and chronological age. Cognitive assessments for processing speed and memory were administered using teleneuropsychology tools, with scores adjusted for age, sex, and education. Multiple linear regression models examined the relationship between BrainPAD and cognitive performance.

Results: Increased BrainPAD was associated with reduced processing speed (-0.97 years/unit z-score, $p=4.9\times10^{-6}$), indicating a one standard deviation decline in processing speed corresponds to a 1-year increase in brain age. No significant relationship was found between BrainPAD and memory ($p=0.2$). Medically refractory epilepsy cases showed the highest BrainPAD increases (3.34 years, $p=3\times10^{-12}$), followed by the first seizure (2.8 years, $p=8.7\times10^{-8}$) and newly diagnosed epilepsy cohorts (2.4 years, $p=6.4\times10^{-7}$).

Conclusion: BrainPAD serves as a marker of accelerated brain ageing in epilepsy, correlating with reduced processing speed but not memory. This likely reflects differences in neurobiological underpinnings of these cognitive domains. The study supports the utility of deep learning-based MRI methods for identifying novel markers of cognitive decline in epilepsy.

1427 | Refining the radiological spectrum of GATOR1-related epilepsy

C Pepi[1], C Rossi Espagnet[2], A Napolitano[2], M Mercier[1], C Luisi[1], D Chiarello[1], L de Palma[1], N Specchio[1,3]
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Purpose: In the largest GATOR1-cohort reported[1], Focal Cortical Dysplasias (FCDs) are seen in a relatively low proportion of cases (24%). Recent papers redefined the incidence of FCD II spectrum in GATOR1 population, ranging from 43% to 50%[2,3]. We applied MELD classifier [4], a machine-learning algorithm for automated detection of FCDs, to define the prevalence of FCDs in GATOR1 population and described radiological features among GATOR1 genes.

Method: We retrospectively selected all patients with GATOR1 (DEPDC5, NPRL2, and NPRL3) genetic variants. All patients underwent a 3 Tesla MR with T1/FLAIR volumetric sequences, reviewed by an expert neuroradiologists. These results were compared with MELD reports, and defined as Concordant or Discordant.

Results: We collected 28 probands (DEPDC5: n=14, 50%; NPRL3: n=12, 43%; NPRL2: n=2, 7%). MELD was not performed in one patient, due to the absence of volumetric sequences. FCDs were detected in 22 out of 28 patients (78%), while no lesions were detected in 6 patients (21%). We found that all NPRL3 patients had positive MR, and all patients with negative MR belonged to DEPDC5 group

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(*p=0.019*). MELD detected a lesion in 22 out of 27 patients (81,5%). The whole NPRL3 cohort had an automatically detected lesion, while all five MELD negative patients were DEPDC5-mutated. The overall MELD accuracy was 78% (21/27), with 17 MRs correctly classified as positive, and 4 as negative. The sensitivity was 94%, indicating that it can effectively identify most of epileptogenic lesions. The specificity was 44%, suggesting a higher rate of false positive than false negative (*5 vs 1* respectively)

Conclusion: We demonstrated a high prevalence (78%) of FCDs in GATOR1 patients, with high accuracy of MELD in detecting such lesions. We believe that these patients must be addressed to a presurgical evaluation with experienced multidisciplinary teams. We confirmed the strong support of MELD in order to detect FCDs.

1595 | Advanced Diffusion MRI Reveals Microstructural Alterations in Focal Cortical Dysplasia: Insights Beyond Conventional Imaging

J Otáhal[1,2], D Kala[1,2], Y Prysiazhniuk[1,2], L Michal[1,2], J Šanda[3], Z Holubová[3,2], M Kudr[4,2], A Kalina[5,2], K Jiránková[1], P Marusič[5,2], P Kršek[4,2], M Kynčl[3,2]

[1]Charles University in Prague, Second Faculty of Medicine, Department of PathoPhysiology, Praha 5, Czech Republic, [2]Epilepsy Research Center Prague /EpiReC/, Prague, Czech Republic, [3]Second Faculty of Medicine, Charles University and Motol University Hospital, Department of Radiology, Prague, Czech Republic, [4]Second Faculty of Medicine, Charles University and Motol University Hospital, Department of Pediatric Neurology, Prague, Czech Republic, [5]Second Faculty of Medicine, Charles University and Motol University Hospital, Department of Neurology, Prague, Czech Republic

Purpose: Focal cortical dysplasia (FCD) is a major cause of pharmacoresistant epilepsy, often challenging to detect using conventional MRI. Diffusion MRI (dMRI) offers microstructural insights by quantifying water diffusion properties. This study evaluates individual diffusion metrics within FCD lesions and their visual neuroradiological detectability to improve lesion characterization.

Method: We analyzed 16 patients with histologically confirmed FCD (12 FCD type II, 4 FCD type I) who underwent pre-surgical MRI, including diffusion tensor imaging (DTI), diffusion kurtosis imaging (DKI), neurite orientation dispersion and density imaging (NODDI), fixel-based analysis (FBA), and diffusion basis spectrum imaging (DBSI). Histopathological confirmation of FCD type was performed for all patients. In 10 patients, additional histological analyses were conducted, including assessment of cellularity and neurite directionality. Lesions were manually delineated on MRI by an experienced neuroradiologist and compared to contralateral healthy tissue.

Results: Histopathology confirmed the FCD type and revealed microstructural alterations. Cellularity showed significant correlations with FA ($p=0.05$), MD ($p=0.03$), MK ($p=0.03$), RK ($p=0.01$), and HIDF ($p=0.024$), with a nonsignificant trend for AFF, IF, ODI, FISO, FDC, and logFC. FCD lesions exhibited significantly altered diffusion properties compared to healthy tissue. The predictive radiological mask differed significantly from contralateral parenchyma in FLAIR ($p=0.02$) but not in T1 or T2. FCD also showed significant differences in KFA, white matter free water fraction, and FISO. FCD type II lesions demonstrated significant alterations in FA and logFC, while FCD type I lesions showed no significant differences. Visual assessment indicated that diffusion metrics provided limited lesion visibility compared to structural MRI.

Conclusion: Diffusion MRI detects microstructural abnormalities in FCD beyond conventional MRI. While these metrics enhance lesion characterization, their utility for visual neuroradiological assessment remains limited. Identifying these abnormalities may refine pre-surgical planning, particularly in MRI-negative cases.

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Neuropsychology
15:15-16:15
Monday, 1 September
Aud III+IV

983 | Neuropsychological profile of late onset epilepsy of unknown etiology: insights into cognitive functioning

A Casarini[1], A Ballerini[1], N Biagioli[1], MA Molinari[2], L Madrassi[1], S Scolastico[1], G Giovannini[3], M Pugnaghi[3], N Orlandi[1], S Meletti[1,3], AE Vaudano[1,3]

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Purpose: The incidence of epilepsy and the first unprovoked seizure in adulthood increases with age, particularly after 55 years (Hauser et al. Epilepsia 1993; 34: 453-458). Up to 20% of these cases lack of identifiable structural damage and/or a defined etiology, categorized as Late-Onset Epilepsy of Unknown etiology (LOEU). Several studies suggest a link between LOEU and neurodegenerative

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diseases, particularly Alzheimer's disease (AD) (Costa C. et al. Neurobiology Aging 2019; 73: 61-67). A recent study by Ballerini et al. (Brain 2025; 7; 148: 185-198) showed that individuals with Late-Onset Temporal Lobe Epilepsy (LO-TLE), characterized by short disease duration and normal CSF amyloid-β and tau protein levels, exhibit cortical thickness patterns and subcortical volumes similar to healthy controls. This study aims to investigate cognitive functioning in LO-TLE subjects by comparing their neuropsychological performance to healthy controls.

Method: The same 20 LO-TLE patients from Ballerini et al. (2025) and 20 age and sex-matched healthy controls were enrolled. Cognitive domains assessed using standardized Italian tests included long-term verbal memory, short-term memory, language, attention, logical ability, and executive function. Scores were adjusted for age, sex, and education, and converted to z-scores based on control group data. Independent t-tests compared cognitive performance between patients and controls.

Results: Cognitive performance in the LO-TLE group was significantly worse compared to healthy controls, particularly in language (p=0.00**) and verbal memory (p=0.008). No significant differences were observed in attention, executive function, or logical ability.

Conclusion: Our data reveal divergent findings between cognitive assessments and morphometric patterns, as despite cortical thickness and subcortical volumes being comparable to those of healthy subjects, LO-TLE patients perform worse in certain cognitive tests. We hypothesize that this cognitive framework is mainly related to the epilepsy diagnosis and temporal localization, supporting our initial data that LO-TLE is not an intrinsic risk factor for AD.

1131 | Neurocognitive outcomes of *in utero* exposure to antiseizure medication: an Australian cohort study

E Honybun[1,2], C Malpas[2,3], T O'Brien[4,5,3,6], J Graham[6], A Hitchcock[6], FJ Vajda[6,4,3], G Rayner[2,1,7], P Perucca[8,1,4,6]
[1]The University of Melbourne, Medicine, Austin Health, Melbourne, Australia, [2]The University of Melbourne, Melbourne School of Psychological Sciences, Melbourne, Australia, [3]The University of Melbourne, Medicine, Royal Melbourne Hospital, Melbourne, Australia, [4]Monash University, Neuroscience, School of Translational Medicine, Melbourne, Australia, [5]Alfred Health, Neurology, Melbourne, Australia, [6]Royal Melbourne Hospital, Neurology, University of Melbourne, Melbourne, Australia, [7]Alfred Health, Clinical Neuropsychology, Melbourne, Australia, [8]Austin Health, Neurology, Melbourne, Australia

Purpose: While there is established evidence linking use of certain antiseizure medications (ASMs) during pregnancy with risk of congenital malformations or neurodevelopmental disorders in the offspring, data on risk of neurocognitive impacts remain limited. This study aimed to evaluate the neurocognitive outcomes of children exposed to ASM monotherapy *in utero*, comparing global and domain-specific cognitive effects across older and newer agents relative to unexposed controls.

Method: Nonmalformed children of women enrolled in the Raoul Wallenberg Australian Pregnancy Register (APR) who were exposed in utero to carbamazepine, lamotrigine, levetiracetam, or valproate monotherapy, or who were not exposed to ASMs, underwent a comprehensive cognitive assessment at age 3-18 years with a neuropsychologist blinded to exposure status. Generalized linear mixed-effects models controlling for maternal intellectual capability, maternal epilepsy, as well as other pregnancy and birth-related factors, were used to examine cognitive outcomes.

Results: 110 children of mothers with epilepsy completed the neuropsychological assessment, including 91 exposed to ASM monotherapy *in utero* and 19 ASM-unexposed. Exposure to valproate, levetiracetam, topiramate, and carbamazepine was associated with a range of poorer cognitive outcomes compared to unexposed children, including reductions in processing speed, verbal and visual-spatial abilities, and academic abilities (all $p<0.05$). Topiramate and levetiracetam exposures were associated with the greatest reductions in full-scale IQ compared to unexposed controls: 17 points (β=-17.38, p=0.004) and 13 points (β=-13.93, p=0.016), respectively. ASM dose was not associated with any cognitive outcome.

Conclusion: Consistent with the emerging evidence of adverse neurodevelopmental effects associated with topiramate, this study demonstrated a deleterious effect on cognitive development. Of note, levetiracetam-exposure was also associated with poor cognitive outcomes. Valproate-exposure, usually associated with the highest risk of adverse outcomes, showed an attenuated effect on childhood cognitive outcomes in this cohort. Lamotrigine-exposed children performed comparably to unexposed controls, reinforcing its relative safety with regards to neurodevelopmental outcomes.

1157 | Cognition is supported by the dynamic redistribution of information through brain networks: evidence from the Australian Epilepsy Project

C Tailby[1,2,3], V He[1,2], B Tahayori[1,2], D Vaughan[1,2,3], H Pardoe[1,2], J Chapman[1], D Abbott[1,2], G Jackson[1,2,3], for the Australian Epilepsy Project

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Purpose: Current theories of brain function propose that cognition is supported by the dynamic up- and down-regulation of information flow between different brain areas. Visual processing pathways provide a useful system in which to test this idea: for reading to occur the outputs of visual form processing must be fed into the core perisylvian language system. Here we test this idea, exploiting a large language fMRI dataset acquired in adults with seizures and healthy volunteers in the Australian Epilepsy Project. Specifically, we test the hypothesis that the strength of connectivity from left fusiform gyrus (FusG) - an area implicated in both visual form and text analysis - to language areas depends upon whether reading is engaged, and that such context-dependent modulation of connectivity is associated with reading ability.
Method: We collected measures of reading ability and language fMRI (contrasting nonword rhyming and visuospatial form processing) from 107 controls and 94 individuals with seizures.
Results: Behaviorally, the reading abilities of the control and patient groups exhibited a comparable upper bound, with lower reading abilities more common in the seizure group. The rhyming task produced robust activation in FusG and perisylvian language areas across participants. We applied psychophysiological interaction analysis to the language fMRI data, seeding from FusG. As predicted, connectivity from FusG to left language cortex increased significantly during rhyming. Of note, we also observed significant increases in connectivity from the same FusG seed to right parietal cortex during visuospatial processing. In the seizure disorder group, better readers showed stronger increases in FusG connectivity to left middle frontal gyrus and medial prefrontal cortex, suggesting that visual text processing and articulatory sequencing are more tightly integrated in proficient readers.
Conclusion: Our results provide evidence that functional brain networks dynamically reconfigure into relevant processing ensembles according to behavioral objectives.

1316 | The impact of clinical and demographic factors on trajectories of decline in verbal memory in people with focal epilepsy

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Purpose: One of the questions people with epilepsy often ask is 'Will my memory get worse?' When answering this question clinicians typically rely on Helmstaedter & Elger's 2009 study of 1,156 people with temporal lobe epilepsy (TLE) which demonstrated that the rate of decline in verbal learning across the adult lifespan is similar to that observed in healthy controls. However, due to developmental hindrance, people with TLE start this decline earlier in life and from a lower level of optimal function and thus develop significant memory difficulties at a younger age than healthy controls. In this study we examined the impact of clinical and demographic factors on this trajectory of change across the adult lifespan.
Method: In a cross-sectional design, the scores of 2,391 un-operated patients (age range 16 to 75 years; mean 35.0) with focal epilepsy (1,385 temporal, 1,006 extra temporal) on a list learning task were analyzed via locally weighted scatterplot smoothing (LOWESS) to explore the impact of epilepsy localization (temporal vs extra temporal), sex (Male. Female) and underlying pathology on the trajectory of decline.
Results: Epilepsy focus, sex and pathology all have a significant impact on trajectories of decline in verbal learning across the adult life span. Regardless of seizure focus, females demonstrate less developmental hindrance in verbal learning than males. The more pronounced impacts of developmental hindrance in males mean they reach significant levels of clinical impairment approximately 10 years before females. Patients with extra-temporal focal epilepsy maintain function following their developmental peak for longer than those with TLE, but once they begin to deteriorate, they demonstrate steeper trajectories of decline.
Conclusion: Clinicians need to be aware of the clinical and demographic factors that influence trajectories of development and decline in memory functions to give accurate information to people with epilepsy and to identify atypical patterns of change.

1338 | Patterns of long-term cognitive decline following epilepsy surgery

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Purpose: Epilepsy surgery is unequivocally an effective treatment for pharmacoresistant epilepsy but carries significant cognitive risks. Cognitive impact of epilepsy surgery is better conceptualized in the form of trajectories as opposed to one-off measurement at a single postoperative

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timepoint. A nuanced understanding of these trajectories at an individual level requires measurement of cognitive functions relative to healthy peer performance as well as one's own previous levels of function. Existing cognitive outcome studies are limited either by incomplete measurement of cognitive changes, inadequate representation of domains beyond memory, or short postoperative follow-up intervals. In this study, we comprehensively explored long-term postoperative trajectories across memory, language and executive function domains, along with their clinicodemographic correlates.

Method: Data were obtained from 117 adult temporal lobe epilepsy patients who underwent a preoperative, 1-year, and >5 years postoperative neuropsychology assessments as a part of the epilepsy surgery program at the National Hospital of Neurology and Neurosurgery. All patients completed a standardized battery of tests with demonstrated sensitivity to temporal lobe dysfunction. Cognitive decline was defined as follows:

- *Longstanding impairment:* postoperative scores 2 standard deviations (SD) below normative means
- *Progressive decline:* ≥1SD decrease relative to baseline, and 1-year follow-up
- *De-novo decline:* stable cognitive function followed by ≥1SD decrease at >5yrs follow-up

Results: The final cohort was 44% male and aged between 19 and 60 at the time of surgery. Consistent with extant literature, progressive declines were rare, ranging from 0 to 4%, most commonly occurring in a verbal memory subtest. De-novo declines, ranging from 1 to 21%, were most frequently evident on tests of visual memory (21%) and phonemic fluency (18%). Progressive cognitive decline in one or more domains was associated with a higher age of onset (p=0.02).

Conclusion: A multidimensional framework to quantify cognitive change reveals domain specific patterns of decline that may be missed by conventional approaches.

1483 | Hippocampal volume correlates negatively with episodic memory performance in newly diagnosed pediatric patients with self-limited epilepsy with centrotemporal spikes

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Purpose: Children with self-limited epilepsy with centrotemporal spikes (SeLECTS) show impaired neuropsychological performance compared to healthy controls (HC). This study aimed to investigate episodic memory at diagnosis and to examine whether memory outcome was associated with hippocampal volume.

Method: We included 19 patients with SeLECTS (age: 9.21±1.42) and 19 healthy controls (age: 9.67±1.89) in the ages between 6-13 years. Episodic memory was tested with a word learning test (dependent variables learning and memory recall) and cognitive outcome was measured using the WISC-V. Concomitant to the neuropsychological examination, a brain MRI and EEG were performed. T1-weight images were acquired using a 3.0 T MRI system (Siemens VERIO) with an MPRAGE sequence. Bilateral hippocampus segmentation was conducted using the automated FreeSurfer pipeline. The extracted hippocampal volumes were subsequently normalized by dividing them by the estimated total intracranial volume of the brain. We computed ANCOVA's (controlling for general intellectual ability) to investigate group differences regarding memory outcome as well as group-specific Spearman correlations between memory outcome and hippocampal volume.

Results: Although not significant, patients showed a worse learning and memory outcome compared to patients. In patients, hippocampal volume left-sided correlated with learning (r=-.749, p<.001) as well as with memory recall (r=-.710, p<.001). There were also significant correlations in patients between hippocampal volume right-sided and learning (r=-.563, p<.01) as well as between hippocampal volume right-sided and memory recall (r=-.547, p<.05).

Conclusion: Although there were no group differences in memory outcome and hippocampal volume, we found significant negative associations between hippocampal volume and memory performance in patients at diagnosis, implying a structure-function relationship. The negative correlations indicate that a higher hippocampal volume was associated with a worse memory performance, similar to earlier study findings indicating "*bigger is not always better*", possibly illustrating reorganization processes that lead to an incomplete compensation.

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Paediatric Epileptology 1
15:15-16:15
Sunday, 31 August
Aud I

765 | Management of neonatal seizures, insights from EpiCARE Study Survey

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Purpose: To establish the management of neonatal seizures across Europe (methods of diagnosing seizures, results interpretation and treatment).
Method: The survey was created by the European Reference Network for all rare and complex epilepsies (EpiCARE) neonatal seizures and epilepsies working group. The survey was circulated to EpiCARE members and Medical Societies, being answered from 06/2024-10/2024. Descriptive and statistical analysis (Chi-squared test) were performed.
Results: 194 responses of 23 European countries were included: 37 Central Europe, 34 Iberian Peninsula, 29 Germany, 28 Italy, 22 British Isles, 16 Eastern Europe,15 Western Europe, 8 Nordic Countries and 5 Baltic Countries. The maximum neonatal care support provided by the centers is: 98 regional neonatal intensive care unit (NICU), 83 NICU, 11 special care nursery and 2 well neonatal nursery. Most of the centers have >100 newborns admitted/year. Nearly all units have protocols for management and/or treatment of seizures, with significant differences between regions. Most centers diagnose seizures using a combination of clinical diagnosis, amplitude integrated electroencephalography(aEEG) and routine EEG without differences between geographic regions. Availability of EEG/aEEG is statistical different across regions. aEEG is more frequently available followed by routine EEG and continuous EEG monitoring. Continuous EEG monitoring is unavailable in 150 centers, and in the remaining ones, only available during working hours. Two-thirds of the centers monitor high-risk neonates with aEEG. First line treatment was phenobarbital in >90%, while levetiracetam is second choice in >70%.
Conclusion: This is the biggest survey about neonatal seizures management ever done in Europe. Most centers have seizure diagnosis/management protocols. Most centers have no access to continuous EEG monitoring. Many centers monitor high-risk neonates with aEEG but there are statistical differences between different regional regions. ASM recommendations are adhered but gold standard for diagnosis (full EEG) is less often used. There is an urgent need to improve the diagnostic pathway of neonatal seizures in Europe.

890 | Zorevunersen demonstrates potential as a disease-modifying therapy in patients with Dravet syndrome through durable seizure reduction and improvements in cognition, behavior, and functioning with up to 24 months of maintenance dosing in open-label extension studies

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Purpose: Dravet syndrome (DS) is a severe developmental and epileptic encephalopathy caused primarily by *SCN1A* variants resulting in $Na_V1.1$ haploinsufficiency. Patients with DS experience prolonged, refractory seizures, and developmental and cognitive impairments. Zorevunersen is an investigational antisense oligonucleotide designed to upregulate $Na_V1.1$ by leveraging the *SCN1A* wild-type copy. Clinical effects and safety of Zorevunersen in patients with DS are presented.
Method: In the Monarch/Admiral (NCT04442295 [US]; 2020-006016-24 [UK]) Phase 1/2a studies, 81 patients on best available antiseizure medications (ASMs) received single/multiple doses of Zorevunersen (≤70mg). At the end of Phase 1/2a studies, 74 patients transitioned to the Swallowtail/Longwing (NCT04740476 [US]; 2021-005626-14 [UK]) open-label extension (OLE) studies and received Zorevunersen (≤45mg) every four months. Convulsive seizure frequency (SF), adaptive behavior (Vineland-3), and clinical status were evaluated.

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Results: As of 28 June 2024, 565 total doses of Zorevunersen were administered; patients received ≤12 doses for ≤3 years. Six months after the last dose in Monarch/Admiral, patients administered single (N=8) or multiple (N=11) doses of 70mg Zorevunersen experienced 57.3% (n=7) and 73.6% (n=9) median SF reductions relative to naïve baseline, respectively. Seizure reductions were sustained through Month 24 of the OLEs. Estimated improvements (95% confidence interval) in Vineland-3 subdomain growth scale values from OLE baseline to Month 24 were 3.791 (0.855–6.727) and 5.216 (2.928–7.504) for Expressive and Receptive Communication, respectively, in all enrolled patients. Substantial clinical status improvements were also observed. Single/multiple doses of ≤70mg Zorevunersen were generally well tolerated. Increased cerebrospinal fluid protein was the most common drug-related treatment-emergent adverse event (11/81 and 20/74 patients in Monarch/Admiral and Swallowtail/Longwing, respectively), with no associated clinical manifestations observed.

Conclusion: Substantial and durable clinical improvements were observed in patients with DS receiving best available ASMs. These findings support further evaluation of Zorevunersen in Phase 3 trials. Funding: Stoke Therapeutics

1436 | High-Frequency Oscillations in Scalp EEG as Biomarkers of Epileptogenesis Following Neonatal Seizures

P Karatza[1], D Cserpan[1], SP Lo Biundo[1], A Rüegger[1], G Indiveri[2], F Pisani[3], J Sarnthein[2,4], G Ramantani[1,2]
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Purpose: High-frequency oscillations (HFOs) in scalp EEG are emerging as a biomarker for epileptogenesis following acute brain insults. This study investigates longitudinal changes in HFO rates across multiple EEG recordings following neonatal seizures, tracking the process of epileptogenesis, and evaluates their predictive value for postneonatal epilepsy (PNE).

Method: We included 21 neonates with EEG-confirmed seizures: 8 who developed PNE, 8 with developmental delay, and 5 with normal development (neither PNE nor developmental delay). Each patient underwent multiple EEG recordings from the neonatal period to several months of age (5 ± 2 recordings per patient). Scalp HFO rates during sleep were determined using an automated HFO detector.

Results: In neonates who developed PNE, HFO rates increased from 0.19 ± 0.14 HFO/min/ch in the first EEG (median: 3 days, IQR: 2-7) to 0.41 ± 0.43 HFO/min/ch in the last EEG (median: 63 days, IQR: 36-118). At the first EEG, HFO rates were significantly higher in neonates who later developed PNE compared to those with normal development (0.19 ± 0.14 vs. 0.05 ± 0.04 HFO/min/ch, permutation test, p=0.02). This difference became more pronounced at the last EEG (0.05 ± 0.01 vs. 0.41 ± 0.05 HFO/min/ch, permutation test, p=0.003).

Conclusion: Neonatal HFOs are strongly associated with epileptogenesis and predict the later development of PNE. These findings support HFOs as a non-invasive and reliable biomarker for early risk stratification, providing a foundation for future research to refine early risk stratification and improve treatment planning.

1533 | Pediatric Epilepsy Surgery: Global Trends in Invasive Explorations

G Ramantani[1], D Cserpan[1], H Weiner[2], A Moosa[3], L Narayanan[4], M Feucht[5], C Eltze[6], A Cukiert[7], ML Smith[8], T Cloppenborg[9], K Braun[10], M Tripathi[11], E Wirrell[12], S Ferrand-Sorbets[13], ILAE survey participants, ILAE Pediatric Epilepsy Surgery Taskforce
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Purpose: Invasive presurgical evaluation is essential in pediatric epilepsy surgery, guiding resections and disconnections and optimizing outcomes. This study provides an updated international overview of current practices in invasive explorations.

Method: Group-level data were collected from representative centers worldwide on children and adolescents undergoing presurgical evaluation and epilepsy surgery in 2023.

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Results: A total of 55 centers from 25 countries across 6 continents contributed data on 2,274 patients. Invasive explorations were performed in 21.5% of cases, with the highest rate in North America (32.6%). The primary indication was seizure onset localization (86.9%), followed by functional mapping of motor/sensory (17.4%) and language areas (15.0%). Among patients who underwent invasive explorations, 60.7% (highest in South America at 80.0%) had no detectable abnormalities on MRI. Stereoelectroencephalography (SEEG) was the predominant approach (20.1%, highest in North America at 29.0%), while subdural electrodes were rarely used (0.7%, highest in South America at 1.7%). A combination of depth and subdural electrodes was applied in 0.7% of cases, more frequently in North America (2.4%). SEEG-guided thermocoagulation was performed in 15.3% of cases, with the highest rate in Australia (25.0%). Following invasive explorations, 43.8% of patients did not proceed to resective or disconnective surgery, with the highest rate in Asia (65.4%). Complications related to electrode implantation occurred in 4.1% of cases.

Conclusion: This study provides a comprehensive overview of the global distribution of invasive presurgical explorations in pediatric epilepsy surgery. These findings highlight international trends, emerging advancements, and areas requiring further development.

1639 | Early electro-clinical features as predictors of Global Disease Outcome in patients with Epilepsy onset within the first year of life

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Purpose: To identify early electro-clinical predictors of Global Disease Outcome (GDO) in children with epilepsy onset within the first year of life.

Method: We conducted a retrospective analysis of 549 patients who experienced epilepsy onset within the first year of life, selected from 3,606 children who underwent EEG between 2008 and 2020. Exclusion criteria: acute provoked seizures only and follow-up of less than one year. At the time of epilepsy onset, we collected data on neurological examination (normal/pathological), seizure type (focal, spasms, polymorphic), background activity (normal/pathological), EEG abnormalities (absent/focal/multifocal/diffuse), MRI results (normal/pathological), and age. GDO was derived through clustering analysis, which combined neurological examination, intellectual disability, and epilepsy outcomes at the last follow-up. It ranged from level 0, indicating a normal outcome, to level 3, signifying the most severe outcome. Levels 1 and 2 indicate an intermediate degree of disability.

Results: The average age of epilepsy onset was 4.02 months (range: 0–12), and the mean follow-up duration was 5.6 years (range: 1–14.7). All onset features had significant correlations with GDO ($p<0.05$). Pathological neurological examinations were correlated with levels 2 (17.49%) and 3 (28.96%). Focal seizures were linked to levels 2 (25.11%) and 3 (33.33%), while spasms (31.5%) and polymorphic seizures (47.86%) were associated with level 3. Pathological background activity and multifocal EEG abnormalities were associated with levels 2 (18.48%, 11.66%) and 3 (27.14%, 18.58%), respectively. Pathological MRI was correlated with levels 2 (11.48%) and 3 (12.75%). An earlier age of onset was associated with level 3 (mean: 2.24 ± 3.2 months).

Conclusion: Electro-clinical features at epilepsy onset correlate with GDO levels and can predict disease severity. These findings highlight the prognostic value of early assessments in guiding management and predicting outcomes.

1726 | Epileptic and developmental encephalopathy secondary to inversion-duplication of chromosome 15q: description of epilepsy characteristics and best therapeutic options

C Benítez Provedo[1], JJ García Peñas[2], E González Alguacil[2], N Lamagrande Casanova[2], M Ballarà Petitbò[2], NV Ortiz Cabrera[2], M García Fernández[2], I Sánchez-Miranda Román[3], A Gil-Nagel Rein[3], B González Giralda[4], M de Toledo Heras[5], A Duat Rodríguez[2], V Soto Insuga[2]
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Purpose: Inversion-duplication syndrome of chromosome 15q (invdup15q) is a chromosomal disorder characterized by an inverted duplication of the 15q11q13.1. Epilepsy is highly prevalent (60-80%), often refractory and progressing to developmental epileptic encephalopathies like Lennox-Gastaut syndrome (LGS). Despite its impact, epilepsy evolution and optimal treatments remain poorly described.

Method: A retrospective multicenter study across 37 Spanish hospitals analyzed 54 patients with invdup15q or interstitial duplication 15q (intdup15q). Clinical and genetic data were reviewed, focusing on epilepsy onset,

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seizure types, syndrome progression, electroencephalographic (EEG) findings, and treatment response.

Results: Epilepsy was present in 29/54 (54%) patients, with 7.4 years mean onset (range: 1 month–24 years, SD 6.4). LGS (55%) and generalized epilepsy (48%) were the most frequent syndromes, while infantile epileptic spasms syndrome predominated in younger patients (83%). Late-onset LGS (>8 years) was reported in 38%. Initial seizures were mostly generalized tonic-clonic (34%) and focal motor (28%), and later in their evolution presented tonic, myoclonic, and atypical absence seizures. Refractory epilepsy was referred in 26/29 (90%). Epilepsy was more frequent (65% vs. 35%, $p<0.05$) and had an earlier onset (median 5.7 vs. 12.3 years) in invdup15q than intdup15q. EEG showed generalized and multifocal discharges and frequently a specific pattern characterized by anterior diffuse rapid bursts during sleep. The most effective antiseizure drugs were oxcarbazepine (efficacy on responders: 86% focal epilepsy, 76% generalized epilepsy) and valproic acid (efficacy on responders: 73% generalized epilepsy), while vigabatrin, zonisamide, and brivaracetam had limited efficacy. In LGS, oxcarbazepine (67%), valproic acid (57%), and cannabidiol (66%) registered the best response. All patients had early developmental delay, autism spectrum disorder was diagnosed in 41%, and behavioral disorders in 56%.

Conclusion: Epilepsy in invdup15q is highly refractory, frequently progressing to epileptic encephalopathy, including late-onset LGS. Oxcarbazepine and valproic acid were the most effective treatments for both focal and generalized epilepsies.

Paediatric Epileptology 2
12:15-13:15
Wednesday, 3 September
Aud I

568 | Decreased interictal heart rate variability in children and adolescents aged 6-14 years with epilepsy

J Zhou[1,2], JS Gąsior[3], A Brandt[1], N Zabler[1], M Dümpelmann[1], KA Klotz[2], J Schönberger[1,2], A Schulze-Bonhage[1], J Jacobs[2,4], V San Antonio-Arce[1]
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Purpose: Heart rate variability (HRV) reflects autonomic nervous system function and has been increasingly studied in patients with epilepsy to assess autonomic dysfunction and its potential role in seizure prediction and risk of sudden unexpected death in epilepsy (SUDEP). The aim of our study was to investigate interictal autonomic dysfunction by comparing HRV in children and adolescents with epilepsy with healthy controls.

Method: We conducted a retrospective analysis comparing interictal HRV parameters in 165 children with epilepsy aged 6–14 years from the Freiburg Epilepsy Center (2010–2022) and 312 healthy control children from the Medical University of Warsaw. Clinical data, including gender and age at the time of video-EEG monitoring, were collected. Following the guidelines of Myers et al. (1), we extracted 10-minute interictal EEG segments and calculated HRV features using Kubios software, encompassing time-domain, frequency-domain, and nonlinear parameters. HRV parameters obtained in children and adolescents with epilepsy were compared with the healthy children, in a first step matched by age, and in a second step matched by heart rate (HR).

Results: Compared to age-matched controls, children and adolescents with epilepsy showed significantly reduced values in most HRV time-domain and frequency-domain parameters (except for nLF and LF/HF). Of the nonlinear indicators, SD1, SD2, and SampEn were decreased, while SD1/SD2, DFA α1 and DFA α2 were increased. Children and adolescents with epilepsy had significantly higher HR than age-matched control children. When comparing children and adolescents with epilepsy to healthy children with similar HR, in the epilepsy group, NN50 and pNN50 and nHF were decreased, whereas LF/HF, nLF, DFA α1 and DFA α2 were increased.

Conclusion: Children and adolescents with epilepsy have reduced HRV, reflecting an autonomic nervous system dysfunction, potentially contributing to their increased risk of SUDEP. In the future, HRV may become a potential biomarker for risk assessment and monitoring of treatment response.

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586 | Ictal emotional features in pediatric and young adult patients with frontal lobe epilepsy: insights from developing brain

M-C Tsai[1,2], C-P Lin[3], A Fine[1], K Nickels[1], D Starnes[1], E Wirrell[1], LC Wong-Kisiel[1]
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Purpose: To evaluate the localization and lateralization values of ictal emotional features and ictal defensive behaviors in pediatric and young adult patients with frontal lobe epilepsy (FLE).
Method: Children and young adults with FLE were identified from a single institution's epilepsy surgery database. Two epileptologists determined by consensus the presence of ictal emotional features (positive- smile, laughter, humming, singing; negative- fear, crying, anger, disgust, contempt, sadness) and ictal defensive behaviors in each patient's first video EEG (vEEG). Historic seizure semiology and vEEG reports were compared with the consensus vEEG analysis. Age-related evolution was defined by emergence or resolution of ictal emotional features between historic seizure semiology and consensus vEEG analysis. Subgroup analyses were conducted according to the seizure lateralization (left vs. right) and sublobar localization (precentral, mesial, lateral, extensive) based on surgical extent.
Results: Twenty-three FLE patients were included (female 39%, mean age at vEEG analysis 11.28 years). Ictal emotional features were seen in 10 patients (43.4%), including 8 (34.9%) patients with left FLE and 7 (30.4%) patients with negative ictal emotional features. vEEG reports lacked documentation of ictal emotional features in 8 (34.7%) of these patients. Although ictal emotional features showed no statistical correlation by sublobar regions, ictal defensive behaviors were consistently seen in mesial compared to lateral FLE (100% versus 16.6%; $p = 0.004$). Age-related evolution of ictal emotional features was observed in 8 (34.7%) patients.
Conclusion: Ictal emotional features and ictal defensive behaviors may be underrecognized in children and young adults with FLE. When present, ictal emotional features were often negative and more likely lateralized to the left frontal lobe, whereas ictal defensive behaviors were more likely associated with mesial FLE. Age-related evolution occurred in about a third of pediatric and young adult patients with FLE, suggesting a developmental evolution of ictal emotional network.

950 | Cortical oscillatory activity evoked by chirp: a biomarker of GABAergic interneuron dysfunction in Dravet syndrome

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Purpose: To describe the characteristics of the cortical oscillatory activity evoked by a chirp-modulated-tone (CMT) in children with Dravet Syndrome (DS) and to establish correlations with epilepsy and cognitive abilities.
Method: A cross-sectional study was performed with three groups: DS, Healthy controls (HC) and non-Dravet epilepsy (NDE). Cortical oscillatory activity evoked by CMT was recorded with EEG and signal analysis. We measured two variables: EA (neuronal recruitment) and ITC (neuronal synchronization). We collected information from clinical reports about epilepsy and cognitive assessments. For statistical analysis, we used R/S-plus programme, with p-value < 0.05.
Results: We included 42 children with DS, 23 HC, and 20 in NDE group. Only 31% of the DS generated a response. The probability of finding cortical oscillatory response was 10 times higher in the HC and 5 times more likely in NDE than in DS (OR HC/DS= 10.55; 95% CI 3.00; 37.4; OR NDE/DS= 5.18; 95% CI 1.63; 16.58). Children with epilepsy had lower capacity for neuronal synchronization in the low gamma band (p=0.010). In the high gamma range, the expected decrease of neuronal recruitment with ages was not observed in DS children (p=0.030). We also found that the worse the vocabulary performance in DS, the lower the frequency of neuronal recruitment´s peak in the low gamma range. We observed a dose-dependent relationship with valproate intake and neuronal recruitment in the low gamma band.
Conclusion: Most of DS children are unable to generate cortical oscillatory activity evoked by CMT in the gamma range and, in those who generate it, is altered, a fact compatible with a GABAergic dysfunction. Worse language ability and high doses of valproate correlate with altered oscillatory activity.

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1579 | Evolution of ictal epileptogenic foci over time in children with tuberous sclerosis complex

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Purpose: The course of epilepsy in tuberous sclerosis (TSC) patients is highly variable. Consistency of the epileptogenic zone has important implications for presurgical evaluation. We aimed to assess the evolution of epileptogenic foci over time in TSC patients.
Method: This retrospective, observational study included children with TSC and epilepsy with $^{3}2$ ictal presurgical encephalograms (EEGs) with an interval ≥1 year performed between the ages 0-18 years. In all EEGs the regional localization of interictal and ictal epileptiform abnormalities were scored based on the EEG reports. The primary endpoint was unifocal or multifocal consistency of ictal foci. The secondary endpoint was assessing determinants of ictal consistency, including TSC variant, age at epilepsy onset, epileptic spasms, multiple seizure types, interictal multifocality, and tuber load.
Results: We included 45 TSC patients with a median of 3 (interquartile range (IQR) 2 – 4) ictal and 8 (IQR 5 – 10) interictal EEGs per patient. Median time between first and last ictal EEG was 28.4 months (19.0 – 60.3). Ictal foci were consistent over time in eleven patients (24.4%), of whom nine had one consistent focus. Nine other patients had a single consistent ictal focus on the first EEGs but developed a second focus at the median age of 67.7 months. Of the thirteen patients who later underwent surgery, 3/13 had a single focus, and only 2/13 had consistent ictal EEGs. Three of the seven seizure-free surgical patients had a single focus over time. All six non-seizure-free children had ictal multifocality. Interictal multifocality was negatively associated with ictal consistency. Interictal and ictal epileptogenic foci were discordant in 42/45 patients (93.3%).
Conclusion: Ictal epileptogenic foci are consistent in 25% of the TSC patients, with interictal multifocality as negative predictor. Interictal epileptogenic foci are often discordant with ictal foci. The implications of these findings for presurgical evaluation will be addressed in a future study.

1703 | Better Breathing, Better Seizure Control: Sleep Apnea in Children with Drug Resistant Epilepsy

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Purpose: The bidirectional relationship between sleep apnea-hypopnea syndrome (SAHS) and drug-resistant epilepsy (DRE) in children is still a critical underrecognized area. This study aimed to evaluate the prevalence of SAHS, identify associated risk factors, and assess the impact of treatments of SAHS on seizure control and quality of life (QoL).
Method: A retrospective study was conducted on 61 children with DRE and daily snoring, all of them underwent polygraph or polysomnography studies. Patients diagnosed with SAHS received individualized interventions, and their effects were measured by seizure control, sleep scales (SDSC) and QoL scales (PESQL and CAVE).
Results: We analyzed 61 children with DRE of a median age of 11.7 years (SD: 4.3). 48/61 (78.7%) had developmental epileptic encephalopathy (20/48 diagnosed of Lennox-Gastaut Syndrome). SAHS was identified in 40/61 (66%) of patients, categorized as mild (25%), moderate (42.5%), and severe (32.5%). Higher seizure frequency, nocturnal seizure predominance, and epileptic encephalopathy electroencephalographic patterns during sleep were significantly associated with higher probability of developing SAHS. Notably, vagus nerve stimulation (VNS) emerged as a significant risk factor for moderate-to-severe SAHS. Therapeutic interventions were performed in 18 patients (10 adenotonsillectomies, 4 non-invasive ventilation, 2 drug-induced sleep endoscopy, 2 maxillofacial surgeries) achieved ≥50% reduction in seizures in 60% of cases at 3 months and significant improvements were observed in sleep and QoL scales after 3 months ($p<0.005$).
Conclusion: SAHS is highly frequent among children with DRE and is strongly linked to nocturnal seizures and epileptic encephalopathy. Treatment of SAHS not only improve the sleep disturbing beyond sleep-disordered breathing but also could be a useful therapeutic strategy for reducing seizure burden and improving QoL. Routine

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assessment of sleep disorders should be integral in managing children with DRE

1725 | Potential role for microRNAs as biomarkers in epilepsy: a prospective paediatric study

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Purpose: Post-transcriptional gene expression is regulated by a class of small non-coding RNAs known as microRNAs (miR). In recent years, they have been studied as potential biomarkers of epilepsy, acting as regulators of the process of epileptogenesis and facilitating the maintenance and progression of epileptic condition. The aim of the study was to determine the use of four microRNAs as diagnostic and prognostic tools for epilepsy.
Method: 151 paediatric patients followed at the Bambino Gesù Children's Hospital in Rome were prospectively enrolled. We collected the following clinical data: age, gender, age at epilepsy onset, epilepsy type, seizure frequency, etiology, the presence of intellectual disability and/or behavioral problems, EEG and neuroimaging data, and anti-seizure medications. We used venous blood samples acquired during regular clinical practice follow-up visits. Using RT-PCR, we determined the serum expression of four microRNAs associated with epilepsy: miR-15a-5p, miR-106b-5p, miR-146a-5p, and miR-152-3p. A statistical analysis was performed.
Results: The mean age of 122 epilepsy patients (56% male) was 8.3 years (range: 0.6-19.5 years), and of the 29 healthy controls (31% male) was 8.4 years (range: 2-15.3 years). miR-106b-5p, miR-146a-5p, miR-152-3p, miR-15a-5p all demonstrated statistically significant higher mean values in cases compared to controls (p-values: 0.001, 0.001, 0.014, and 0.015, respectively). miR-146a-5p showed higher levels in patients with structural epilepsy (28,7%, n=35) compared to those with genetic etiology (49.2%, n=60) (p=0.014). Patients with recurrent seizures (41%, n=50) had higher levels of miR-106b-5p and miR-15a-5p compared to patients with sporadic seizures or seizure-free (59%, n=72) (p=0.017 and p=0.004, respectively).
Conclusion: All four studied microRNAs differentiate between epileptic patients and healthy controls. miR-146a-5p may be helpful in differentiating between structural and genetic etiology, while miR-106b-5p and miR-15a-5P might be biomarkers of drug-resistant epilepsy.

Psychiatry
15:15-16:15
Sunday, 31 August
Aud VIII

268 | A data-driven MRI study of neurobehavioral comorbidities in temporal lobe epilepsy

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Purpose: In temporal lobe epilepsy (TLE), besides seizures, patients present with cognitive and psychiatric disorders (referred as neurobehavioral comorbidities). Their interplay with epilepsy is multifactorial and likely reflects brain-wide structural and network-level alterations. While cognitive symptoms have been related to disrupted connectivity of mesiotemporal and frontotemporal circuits, the brain basis of psychiatric symptoms remains incompletely understood. Here, we assessed large-scale network-level functional characteristics of affective symptoms and their relationship to brain morphology and cognitive symptoms.
Method: We studied 42 drug-resistant TLE patients using multimodal 3T MRI and neuropsychological assessment alongside 41 age- and sex-matched healthy controls. Cortex-wide partial least square (PLS), a multivariate associative technique, examined relationships between whole-brain resting-state fMRI connectivity strength (FCS) and affective measures. Linear models evaluated associations with structural disease markers and cognitive parameters. We repeated the PLS analysis between FCS and affective measures, incorporating cognitive measures and structural markers as covariates to account for their influence on the observed relationships.
Results: 40% of our cohort had depression and 79% experienced moderate to severe anxiety. Quality of life measures were significantly below the average. PLS analysis revealed that weaker FCS in temporoparietal, prefrontal, mesiotemporal, thalamus, and globus pallidus was related to elevated anxiety symptoms and poor quality of life. Among cognitive domains, verbal memory showed a positive correlation with the same brain areas. Notably, cortices with the strongest FCS-affective covariance showed atrophy and myelin alterations (T1/FLAIR decreases).

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Controlling for the effect of cognitive and structural markers, the temporoparietal network emerged as the most significant network.

Conclusion: Our study highlights dysconnectivity of multiple interconnected regions within the emotion regulation network particularly temporoparietal regions in TLE. Our results linking these networks to poor verbal memory provide a basis for therapies aimed at managing anxiety and stress alongside cognitive rehabilitation programs to improve the quality of life of patients.

441 | Towards culturally competent epilepsy care: An international comparison of self-stigma, psychological factors, and societal attitudes

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Purpose: This study aimed to examine the relationship between self-stigma and psychological factors (depressive symptoms and anxiety) in people with epilepsy (PWE) across diverse cultural contexts. We sought to understand how these manifestations vary internationally to inform culturally competent care strategies and improve quality of life for PWE globally.

Method: We recruited PWE receiving treatment at specialized epilepsy facilities in Japan, Malaysia (Chinese and Malay populations), and Turkey from February to October 2023. Participants completed the Epilepsy Self-Stigma Scales (ESSS), Neurological Disorders Depression Inventory for Epilepsy (NDDI-E), and Generalized Anxiety Disorder 7 (GAD-7) in their local languages. Statistical analyses included ANOVA, correlation analyses, and ANCOVA.

Results: ESSS total scores were significantly higher among Turkish and Japanese cohorts ($F(3,406)=6.57$, $P<0.001$, $\eta^2=0.05$). Self-stigma showed moderate positive correlations with depressive symptoms ($rs=0.41$-0.50, $Ps<.001$) and anxiety ($rs=0.42$-0.44, $Ps<.001$) across all cultural groups. ANCOVA revealed that significant variations in self-stigma across cultures were reduced when accounting for depressive symptoms, suggesting a stronger influence of mental health factors over cultural factors on self-stigma.

Conclusion: While self-stigma in epilepsy shows distinctions across diverse cultural cohorts, it demonstrates a significant universal correlation with psychological factors, particularly depressive symptoms. These findings underscore the importance of addressing mental health in managing epilepsy-related self-stigma across cultures. Future research should further investigate these nuanced differences to develop culturally sensitive, yet universally applicable supportive approaches for PWE. This study contributes to the development of more culturally competent epilepsy care strategies, potentially improving the global quality of life for PWE. This research was supported by JSPS KAKENHI (Grant Number 21K13709) to IK.

483 | Revisiting Hughlings Jackson's dreamy state: dissociative symptoms in temporal lobe epilepsy

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Purpose: Transient, dissociative experiences have been attributed to temporal lobe epilepsy (TLE) since at least the time of John Hughlings Jackson in the 1870s. While dissociative symptoms are a semiological feature of mesial TLE, these experiences can also occur interictally and remain poorly understood. We systematically examined the frequency, nature, and clinical correlates of dissociative experiences in TLE, to inform a neurobiological understanding of dissociation.

Method: 157 adults with TLE and 57 healthy controls participated (N=214). A data-driven statistical approach determined the underlying factor structure of the Wessex Dissociation Scale in this cohort and delineated symptom clusters. We then examined group differences in rates of dissociation symptoms, as well as the influence of epilepsy-related and mood factors.

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Results: People with TLE reported more frequent dissociative experiences (M=0.96, SD=0.61) than controls (M=0.69, SD=0.38; p<0.001). Five clusters of dissociative symptoms emerged, with memory blanks and somatic distortions particularly elevated in TLE. Memory blanks and numbing dissociative symptoms were associated with increased seizure frequency, epilepsy duration, and number of anti-seizure medications. Higher depression and anxiety symptoms were linked to elevated overall dissociative symptoms and scores on each subfactor (r=.26–.64; p<.01–<.001).

Conclusion: People with TLE experience high rates of dissociative symptoms, particularly memory- and sensory-related dissociative symptoms underpinned by temporal lobe cognitive networks. These symptoms are related to both seizure burden and mental ill-health, supporting a neurobiopsychological model for dissociation in TLE that integrates epilepsy-specific features and psychological factors. These insights pave the way for new therapies for dissociation that target specific neurocognitive pathways.

924 | Neuropsychological, neurophysiological and imaging features of Juvenile Myoclonic Epilepsy: Insights into personality disorders

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Purpose: Juvenile myoclonic epilepsy (JME) is associated with a high prevalence of psychiatric comorbidity, particularly personality disorders. We aimed to compare neuropsychiatric spectrum, electrophysiological patterns, and neuroimaging features in JME patients with and without personality disorders.

Method: We prospectively recruited 65 individuals with JME (38 female) and 68 healthy controls (HCs; 37 female), matched for age, sex, and education. All participants underwent DSM-IV Axis I and II clinical interviews, neuropsychological assessment, EEG, and structural MRI.

Results: Axis I and/or Axis II disorders were diagnosed in 63% of JME patients and 21% of HCs (p<.001). Notably, obsessive-compulsive personality disorders (OCPD) were significantly more prevalent in JME (22%) than HCs (3%; p<.001). JME patients performed worse in psychomotor speed (p<.001), tonic alertness (p=.036), divided attention error rate (p<.001), mental flexibility (p=.016), and inhibition of automated reactions (p<.001). Subgroup analysis revealed that JME patients with any psychiatric comorbidity and those with OCPD performed worse than HCs in psychomotor speed (p=.019; p=.006), divided attention (p=.033; p=.025), and inhibition of automated reactions (p=.014; p=.009). JME patients with OCPD also showed impaired tonic alertness compared to HCs (p=.017). EEG revealed higher alpha band coherence between left frontal-temporal areas in patients with JME and OCPD compared to those without OCPD and HCs (p=.002). Surface-based MRI analysis (corrected for family-wise error rate of p=.05) showed a tendency for increased cortical thickness in the left orbito-frontal region in JME patients with OCPD compared to those without OCPD and HCs. Increased cortical thickness was also observed in the left inferior occipito-temporal region in JME patients with OCPD compared to HCs.

Conclusion: Our results deliver novel evidence indicating a consistent clinical, structural and functional subphenotype of JME with OCPD, representing a possible link between JME and psychiatric diseases.

1045 | The efficacy of eye movement desensitisation and reprocessing therapy in reducing epilepsy-related anxiety

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Purpose: To determine whether eye movement desensitization and reprocessing (EMDR) therapy reduces anxiety in people with epilepsy-related anxiety. Secondary outcomes included health-related quality of life (HRQOL), subjective cognitive functioning and seizure frequency.

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Method: Prospective uncontrolled study with a pre-post follow-up design, including measurements before, immediately after, and three months after EMDR therapy, focused on the individuals' negative future phantasies involving fear of future seizures (i.e. flashforwards). We recruited subjects with epilepsy-related anxiety from a Dutch tertiary epilepsy center. Questionnaires were used to monitor general and epilepsy-related anxiety, HRQOL, subjective cognitive functioning and seizure frequency. Repeated-measures ANOVA was used.
Results: Eleven subjects were included. We observed a significant reduction in general and epilepsy-related anxiety from before to immediately after EMDR treatment, and three months hereafter ($p \leq 0.001$, $\eta^2 = 0.698$ and $p \leq 0.001$, $\eta^2 = 0.641$, respectively). This coincided with an improvement in HRQOL ($p \leq 0.001$, $\eta^2 = 0.550$). Despite a main treatment effect for subjective cognitive functioning ($p = 0.023$, $\eta^2 = 0.415$), no significant post hoc effects were observed. No effects were found for informant-reported cognitive functioning ($p = 0.261$, $\eta^2 = 0.236$) and seizure frequency ($p = 0.495$, $\eta^2 = 0.075$).
Conclusion: This study provides preliminary evidence that EMDR therapy reduces anxiety in people with epilepsy-related anxiety. This effect sustained over three months and coincided with an improved HRQOL. Subjective cognitive functioning and seizure frequency did not change over time. Our findings suggest that EMDR therapy is a potentially safe treatment for epilepsy-related anxiety.

1251 | Relationship between Stigma, Loneliness, Depression and Social Support and Suicidal Behavior in Patients with Epilepsy

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Purpose: This study aims to examine the relationship between stigma, loneliness, depression, and social support levels in patients with epilepsy and their suicidal behavior.
Method: This descriptive cross-sectional study was conducted between May 2024 and January 2025. Data were collected from a total of 80 epilepsy patients registered at the neurology outpatient clinic of a university hospital. The Patient Identification Form, Suicidal Behavior Scale, Stigma Scale, Beck Depression Inventory, Loneliness Scale, and Multidimensional Scale of Perceived Social Support were used for data collection. Descriptive characteristics of the patients were presented as frequencies and percentages, while comparative, correlational statistics, and regression analyses were performed. A significance level of $p < 0.05$ was considered.
Results: Of the patients participating in the study, 56.3% were female, 46.7% were single, and 65% were not actively employed. The mean duration of the disease was 10.4 years (±9.4), and 37.5% experienced more than one seizure per month. Suicidal behavior was positively correlated with stigma (p<0.001), depression (p<0.001), loneliness (p<0.001) and negatively correlated with social support (p=0.001). Regression analysis revealed that depression was the only significant variable ($R^2 = 0.48$, $p < 0.001$).
Conclusion: Among epilepsy patients, higher levels of stigma, loneliness, and depression were associated with an increased tendency toward suicidal behavior, while higher levels of social support were associated with a decreased tendency. Furthermore, depression was identified as the most significant predictor of suicidal behavior. Therefore, it is essential to evaluate epilepsy patients from a psychosocial perspective and to ensure timely diagnosis and treatment of depression.

Social Issues
15:15-16:15
Sunday, 31 August
Aud VI+VII

264 | Fill-in the dot: Advancing collaboration European patient communities for rare and complex epilepsies in the era of genetics etiologies

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Purpose: *This study explores the evolution of genetic research in epileptic encephalopathies and its impact on patient advocacy and care models in Europe. We analyze the implications of the surge in gene discoveries since 2010 on building patient associations, collaborative networks, and integration of patient and family in care strategies.*

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Method: A review of literature and key to accesses datasets was conducted, including Helbig et al. Mol Syndromol 2016;7:172–181 and Mei et al. J Med Genet. 2025;62:25–31, to assess trends in genetic discovery and their correlation with the emergence of disorder-specific patient associations advocacy group in rare epilepsies. We also evaluated the development and impact of EpiCARE - European Reference Networks for rare and complex epilepsies and patient-led initiatives, such as the "leaflet" and "Patient Journey," to identify shared challenges and collaborative successes.

Results: The genetic discoveries in last 15 years significantly advanced the understanding of epileptic encephalopathies, enabling accelerated diagnosis and targeted therapies. Concurrently, the proliferation of disorder-specific patient associations fragmented the broader patient's community dispute common challenges and unmet needs. The establishment of EpiCARE mitigated this fragmentation by fostering collaboration across rare epileptics and developing interdisciplinary and transversal care models.

Conclusion: The European Patient Advocacy Groups (ePAGs) unified advocacy efforts, strengthened stakeholder synergies, and ensured a strong patient voice unified in research and healthcare policymaking. Strategic objectives include empowering advocates and enlarging the beneficiaries cohorts, increasing research interest, and raising awareness among policymakers about the need for holistic, long-term care. Now, the creation of the Complex and Rare Epilepsies Alliance could further strengthen the existing network, consolidating efforts and promoting a unified vision for greater impact.

1216 | D'Unseen - Navigating what really matters: Insights from ethnographic research on Dravet Syndrome

R Nabbout[1], L Dorris[2,3], M Danse[4], N Benzler[5], N Specchio[6,7], P Afonso[8], P Hugon[8], S Gaberscek[9], L Nardi[9], LM Aras[10]

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Purpose: This ethnographic investigation aimed to uncover what really matters in Dravet syndrome (DS) Journey focusing on the experiences faced by all actors in the DS ecosystem in order to improve patients' and caregivers' lives.

Method: Led by a steering committee of six European DS experts (neuropediatricians, nurse, neuropsychologist, and patient organization members-POs), this research spanned France, Italy, Spain, Germany, United Kingdom. To explore new and overlooked aspects of daily life with DS, we conducted a two-step approach: macroanalysis through DS expert interviews and literature review, followed by ethnographic fieldwork. This fieldwork involved in-depth semi-structured interviews and daily observations of families, healthcare professionals (HCPs), and POs members.

Results: The study included 46 participants and revealed a holistic view of DS, mapping each stakeholder impact on family's journey. The fieldwork allowed a deep understanding of the impact on DS at the macro, meso and micro scales for all stakeholders. We defined an emotional odyssey of life with DS (from the first seizure to adulthood) and categorized four parents' postures ("the castaway," "the gatekeeper," "the personal assistant," "the maestro") based their potential attitudes facing DS and four dimensions: control/delegation/novice/expert.

The observations highlighted:

- Life-changing moment of the diagnosis, combining emotional shock with practical demands, without sustainable changes implementation
- Disconnection throughout the ecosystem of actors in terms of information, amplified by structural and emotional dynamics
- Stigmatizing aspect with seizures as the most isolating factor
- Absence of a structured rehabilitation pathway amplifying future uncertainty

Conclusion: This ethnographic approach provided real-life perspectives often absent in clinical studies, uncovering critical gaps and actionable opportunities. These insights provide a comprehensive framework for addressing DS complexity, identifying unmet needs, challenges, and strengths at each stage. It will help clinicians and

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families adapt communication and expectations, and deliver concrete solutions, ultimately improving the quality of life for all stakeholders. Biocodex support

1389 | Unpredictable Seizures and Disruptive Behavior in Developmental and Epileptic Encephalopathies: Interim Results of a Caregiver Survey

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Purpose: Define patterns of typical and disruptive seizures and of disruptive behavior in patients with developmental and epileptic encephalopathies (DEEs) and explore their relationships with activities of daily living (ADLs) and communication.

Method: An internet-based anonymous 63-question survey was distributed to caregivers of patients with DEEs by multiple DEE-specific communities. This interim analysis summarizes data specific to seizures and disruptive behavior and their relationships with ADLs and communication. ADLs include feeding, bathing/hygiene, dressing, and toileting.

Results: Of 489 caregiver responses included in the analysis, 198 (40.5%) patients had multiple seizures per day. Of 300 patients with reported seizure clusters, 168 (56.0%) had no monthly seizure rescue medication usage. Seizures were always disruptive without a predictable pattern in 110 (22.5%) patients, of whom 46 (41.8%) and 51 (46.4%) temporarily lost the ability to perform ≥1 ADL and communicate, respectively. Multiple daily disruptive behaviors were reported for 156/489 (32.0%) patients; 38/110 (34.5%) patients with disruptive seizures all of the time and 92/300 (30.7%) patients who experienced seizure clusters also displayed multiple daily disruptive behaviors. Of patients with no disruptive seizures in the previous 6 months (n=104), 39 (37.5%) experienced multiple daily disruptive behaviors. The ability to perform ≥1 ADL and to communicate were temporarily lost by 61/156 (39.1%) and 75/156 (48.1%) patients reportedly due to disruptive behavior, respectively.

Conclusion: Disruptions to daily life in individuals with DEE are interconnected and complex. Multiple daily disruptive behaviors were reported at similar rates in patients with always disruptive seizures, seizure clusters, and with no disruptive seizures. Nearly half of caregivers reported that high rates of disruptive seizures/behavior led to temporary loss in abilities, previously associated with reduced quality of life. Continued examinations of typical and disruptive experiences and their relationships with loss of abilities in patients with DEE are warranted. UCB-supported.

1538 | Epilepsy and stigma: A multicenter study from Turkey

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Purpose: Epilepsy is not only a neurological condition characterized by seizures but is also a disorder associated with stigma. Since stigma in epilepsy is highly culturally dependent, we aimed to investigate predictors and outcomes of stigma among patients with epilepsy (PWE) in Turkey.

Method: This multicenter study is conducted by the contribution of 30 epilepsy outpatient centers from 11 cities with the affiliation of health-related quality-of-life chapter of Turkish Neurological Society.

Results: Among the 1170 PWE, 56.3% were female with a mean age of 35.1±12.4 years. School performance was affected negatively in 27.7% of the patients while duration of education was affected in 25.8% of PWE. 25.5% of patients had minimum wage, 33.5% was unemployed, 15.4% of the patients experienced dismissal due to epilepsy. Although 45.2% of the PWE were single, only %4.4 of them were living alone. The scores of the stigma scale of epilepsy (SSE) showed that one-third of PWE felt moderately-or-highly stigmatized. No significant correlation was found between the SSE scores and age (r=0.039, p=0.18), gender (p=0.70), marital status(p=0.70), living in rural-or-urban area (p=0.52). The scores were decreased due to higher educational status (p<0.001), higher income levels (p<0.0001), increased in unemployed patients (p<0.001). The SSE scores were increased in patients with younger age at seizure-onset (r=0.128,p<0.001), longer disease duration (r=0.074,p=0.012), higher seizure frequency (p<0.0001), drug-resistant epilepsy (p<0.0001), receiving greater number of antiseizure medications (p<0.0001), seizure-related injuries (p<0.0001), decreased in patients compliant to treatment (p<0.0001). The SSE scores were higher in patients who concealed their diagnosis from society (p=0.045). Health-related quality-of-life scale score decreased as the stigmatization increased (r=0.526, p<0.001). One-fourth of patients showed symptoms of depression; three-quarters of patients showed symptoms of anxiety. The SSE scores was positively correlated with scales of depression and anxiety (r=0.521, p<0.001;r=0.455,p<0.001,respectively). Stigmatization decreased as the social support increased (r=-0.356, p<0.001).

Conclusion: Our study showed that one-third of PWE were moderately-highly stigmatized experiencing it in all aspects of their lives. Reducing the stigmatization of epilepsy must be major goal in reducing the impact of the disease.

1547 | What Do We Know About the Challenges Faced by Women Professionals in the Epilepsy Field: A 2025 report

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Purpose: Gender disparities continue to impact the experiences of women professionals. Our study gathered the lived experiences of women in the epilepsy field to summarize, for the first time, the gender-related challenges they face.

Method: A global cross-sectional survey exploring the personal experiences of women across various professions in the epilepsy field was launched at the end of 2022. Online surveys were available in English, French, and Spanish, and 323 responses were analyzed.

Results: The mean age of participants was 39.6 years (IQR = 66-21), with respondents from 58 different countries. The two most frequent ethnicities were Caucasian, Latin American and Middle Eastern. 41.8% were epileptologists and 56.2% were occupying an academic position. When asked if they feel the need to work harder than male colleagues to be respected or treated equally, 87.2%(n=280) said "yes", and one participant said, "there is an automatic respect for the male physicians. For the females in the group, there is almost a trial period...". 76.2%(n=176) recounted they had experienced Imposter Syndrome, and one participant said they are, "almost daily questioning if [they are] good/smart/talented enough." 36.2%(n=117) stated they had experienced gender-based discrimination at their workplace. The responders reported that 54.4% had more difficulties advocating for themselves compared to men. For those who were parents (53.3 %, n=172), 70.2 %(n=120) reported feeling that their academic/clinical role had been impacted by having children. 51.4%(n=166) of participants reported having a woman mentor. 49.5% (n=160) had a woman supervisor/chair.

Conclusion: This is the first study to investigate the impact of gender disparities in the epilepsy workplace. Preliminary results suggest that professional women face gender-related disparities, highlighting the need for opportunities and changes in the workplace.

1583 | EpilepsyPOWER: a three-year project to favor workplace inclusion of people with epilepsy

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Purpose: Unemployment and underemployment are more common among people with epilepsy (PwE) compared to the general population, though seizure free individuals can work normally. The EpilepsyPOWER is a European project (2021-1-IT02-KA220-ADU-000028349), involving five Countries (Italy, Bulgaria, France, Ireland, Germany), aimed to improve PwE's workplace inclusion. For this project, we made a systematic review about PwE's employment conditions in Europe and developed surveys to explore work conditions among PwE and epilepsy knowledge among higher education institutions (HEI).

Method: Using the PRISMA 2020 guidelines, we performed a systematic review and selected 55 articles from 1958 to 2023. We extrapolated data on employment rate, also considering specific epileptic syndromes and factors contributing to employment/unemployment. We have developed two anonymous surveys for PwE and HEI, collecting 567 and 291 respectively.

Results: According to reviewed papers, unemployment rates ranged from similar to twice/three times the general population rates. Seizure control and employer's attitudes are the most important factors in determining employment. In our surveys PwE unemployment rates ranged from 7.9% in Italy to 9% in Bulgaria (double the general population rate). Between 20% and 50% of PwE did not disclose epilepsy at work. About 70% of respondents in all countries thought that stigma prompts discrimination in finding and retaining a job. Although most of HEI respondents have seen a seizure in person, in some countries (Germany and Bulgaria) they did not know how to give medical aid during a seizure.

Conclusion: Although rates of unemployment are not uniformly reported, a clear situation of disadvantage rises for PwE in EU. To favor employment inclusion, we should work on seizure control, awareness and knowledge about epilepsy, and training programs, fighting stigma and misbeliefs.

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In-Person Poster Presentations

Adult Epileptology

265 | Possibility of stopping bilateral tonic-clonic seizures using the mobile application EpiTapp® in drug-resistant epilepsy caused by arteriovenous malformation in a young man

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Purpose: Purpose: To present a unique clinical observation demonstrating the possibilities of controlling bilateral tonic-clonic seizures using the EpiTapp® application in a 29-year-old patient with drug-resistant structural focal epilepsy that developed against the background of an AVM located in a functionally significant area of the cerebral cortex.
Method: The work uses the author's method of wrist tapping (patent of the Russian Federation No. 2606489 dated 10.01.2017) in the form of the EpiTapp® mobile application for a smartphone. The patient regularly used the EpiTapp® application at the first signs of a focal motor hemifacial seizure or during the focal onset of a bilateral tonic-clonic seizure, as emergency self-help at home. Before the study, the patient underwent an electroencephalographic study and was trained by a neurologist-epileptologist in the independent use of the EpiTapp® application at home. The study also used: the QOLIE-31 quality of life scale for epilepsy.
Results: After 6 months of using the EpiTapp® application, patient A. completed a final questionnaire on the QOLIE-31 scale. Analysis of the obtained data showed that while using the EpiTapp® application, the patient noted an improvement in quality of life by 58% from the initial value due to the ability to stop focal seizures and prevent the development of bilateral tonic-clonic seizures in more than 50% of cases. In this regard, the patient was able to return to his work in the office. In 85% of cases, the patient was able to stop the incipient focal seizure, reducing its severity and duration.
Conclusion: This clinical example demonstrates the possibility of effective use of the EpiTapp® mobile application in a patient with drug-resistant structural focal epilepsy against the background of arteriovenous malformation as an element of emergency self-help aimed at the possibility of stopping epileptic seizures.

418 | Self-management for people with epilepsy and a history of negative health events (SMART): A randomized controlled effectiveness trial

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Purpose: This prospective 2-site, 6-month randomized controlled trial of a standardized epilepsy self-management curriculum (SMART) vs. a 6-month waitlist (WL) control assessed effects on epilepsy outcomes in a diverse sample of 160 people with epilepsy (PWE).
Method: PWE had at least one at least 1 negative health event (NHE) defined as a seizure, emergency department visit, hospitalization or self-harm attempt. Primary outcome was differences in proportions of PWE with reductions in NHE/day from baseline to 6 months follow up (SMART vs. WL), defined as any, ≥10%, ≥20%, ≥30%, ≥40%, and ≥50% improvement. Secondary outcomes included the Patient Health Questionnaire (PHQ-9), 36-Item Short Form Survey (SF-36), 31-item Quality of Life in Epilepsy (QOLIE-31), Epilepsy Self-Management Scale (ESMS), Epilepsy Stigma Scale (ESS), Multidimensional Scale of Perceived Social Support (MSPSS) and Epilepsy Self-Efficacy Scale (ESES).
Results: Mean age was 39.4 (SD 12.2), 66.9% (N=107) women, 82.5% (N=132) white and 31% (N=50) rural. Mean PHQ-9 of 10.5 (SD 7) suggested mild/moderate depression. Seizures were the most common NHE with mean baseline past 6-month seizure count of 20.6 (SD 41.0). In logistic regression models, SMART was significantly associated with a 2-fold increase in odds of having at least 10-30% improvement in NHEs vs. WL ($p<0.05$). SMART was non-significantly associated with decreases in change of NHEs/day and seizures/day at week 24. In the intent-to-treat sample, SMART was associated with significantly improved PHQ-9 ($p=0.014$), QOLIE-31 seizure worry ($p=<0.001$) and social functioning ($p=0.021$), ESES ($p=0.046$) and ESMS ($p<0.001$).
Conclusion: Compared to WL, SMART participants had greater likelihood of a clinically relevant improvement in NHE reduction, although average total NHE counts between SMART vs. WL did not differ. SMART participants had improved depressive symptoms, epilepsy self-management competency and self-efficacy and selected

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element of QOL. Inclusion of evidence-based ESMs into a comprehensive care of model for PWE seems warranted.

432 | The safety and efficacy of ketogenic diet therapy among adolescents and adults with refractory epilepsy: a systematic review and meta-analysis

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Purpose: Ketogenic diet therapy (KDT) has been documented in epilepsy literature since the 1920's but it was not until the 1990's its use in drug resistant epilepsy (DRE) management really emerged. Initial this was mostly in children, but recently an increase in research regarding use in older patients with DRE and status epilepticus (SE) has occurred. This systematic review and meta-analysis assessed the use of KDT in adolescents and adults with DRE and SE to address knowledge gaps around efficacy, safety and tolerability of KDT in this patient cohort.
Method: A literature search of 5 databases was undertaken using PRISMA guidelines. *Inclusion criteria*: Articles assessing efficacy, safety and tolerability of KDT in patients >12years. Efficacy was defined as a >50% reduction in seizures or resolution of SE. Patient demographics, epilepsy type, KDT subtype and seizure burden were extracted. Drop-out rates, and side effects were reviewed. The Cochrane ROBINS-I and RoB2 were used to assess risk of bias. Meta-analysis using random effects modelling was undertaking using RevMan Web and R.
Results: Of 1513 articles screened 36 met the inclusion criteria - 1012 adolescents and adults, 971 people with DRE, 41 with SE. KDT was effective in 42.36% of those with DRE. This increased to 81% for those in SE. Higher efficacy was found in generalized epilepsy (48.11%) compared to focal epilepsy (7.00%) ($p<0.00001$). KDT was safe with only one patient requiring diet cessation due to safety concerns. Compliance is challenging due to the restrictive nature of KDT resulting in high dropout rates (16%).
Conclusion: KDT is an effective and safe option for adolescent and adult patients with DRE. Greater efficacy is seen in SE and generalized epilepsy. Despite efficacy compliance remains challenging. Further limitations include small sample sizes and single center studies. Larger international collaborative RCT studies are needed to establish better evidence.

478 | Impact of epilepsy type on delivery and neonatal outcomes in pregnant women with epilepsy

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Purpose: To ascertain the effects of epilepsy type on delivery and neonatal outcomes in women with epilepsy (WWE) and to compare adverse effects between pregnancies complicated by epilepsy and normal pregnancies.
Method: 124 pregnant WWE followed up between April 2013 and February 2021 in Baku were enrolled in a prospective study. Delivery outcomes were compared with those of 277 women without epilepsy in the control group.
Results: Among all 124 WWE, focal epilepsy (FE) was determined in 63.7% of the pregnancies and generalized epilepsy (GE) in 36.3%. In 12 (9.7%) women, the epilepsy developed during the pregnancy. Pregnancies in WWE were associated with significantly higher risks of cesarean section (CS) ($p<0.0001$) and preterm birth ($p=0.03$) compared with pregnancies in women without epilepsy. We found a higher but non-significant rate of medical termination of pregnancy, premature rupture of membranes (PROM), CS, and preterm birth in women with FE compared with those with GE (5.1%, 11.0%, 76.2%, and 11.0% vs. 2.2%, 7.3%, 61.0%, and 2.4%, respectively). Furthermore, the risk of PROM was significantly higher in women who experienced generalized tonic-clonic seizures (GTCS) during pregnancy; 72.7% of women in whom PROM was recorded had GTCS during pregnancy ($p=0.009$). The risk of adverse neonatal outcomes did not significantly differ between FE and GE. However, the rate of asphyxia and hypoxic-ischemic encephalopathy (HIE), though not significantly, was higher in FE compared with GE (6.8% vs. 4.8% and 6.8% vs. 2.4%, respectively). Notably, all babies with asphyxia and HIE were exposed in utero to maternal seizures.
Conclusion: Though epilepsy type did not significantly influence the obstetric and fetal outcomes, maternal seizures on their own were associated with increased risks of delivery and neonatal complications. Hence, adequate seizure control during pregnancy is crucial for preventing seizure-related complications both in women with FE and GE.

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490 | EPISTAR: Educational Patient Information Sheet to Achieve Retention of Information

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Purpose: This project addresses local gaps identified by the National Confidential Enquiry into Patient Outcome and Death (NCEPOD) appraisal for epilepsy in communication with patients discharged after their first seizure. Key issues include insufficient advice on driving restrictions, seizure safety, and event documentation. The project aims to standardize discharge communication by introducing a patient information leaflet, a proforma for Nervecentre (local discharge system for emergency department), and a new option in ICE (local discharge system for medical wards) to improve information retention and patient preparedness.

Method: Baseline data were collected over three months from 31 patients discharged following their first seizure, with 16 clinician-only perspectives due to incomplete patient follow-up. Data sources included patient questionnaires (covering driving advice, safety measures, event documentation, and receipt of written information) and clinician discharge letters. Following baseline evaluation, interventions were implemented, including an information leaflet and standardized documentation tools. Post-implementation data collection and comparison will assess the impact of these measures.

Results: Baseline analysis revealed discrepancies between patient and clinician perspectives. Most patients recalled being advised not to drive, but fewer received guidance on safety measures, seizure diaries, or witness involvement. Only 10% of patients reported receiving written discharge information, though 90% indicated it would have been helpful. Clinician discharge letters often lacked details on event documentation, safety advice, and follow-up planning. Despite challenges in IT implementation, initial findings highlight the need for standardized communication strategies.

Conclusion: The project underscores the importance of comprehensive communication for first-seizure patients to improve safety, diagnosis, and treatment. Implementing standardized tools is expected to enhance information retention and patient empowerment. Challenges in data collection and IT integration highlight the need for sustained collaborative efforts and adaptability. Future audits will measure improvements and guide continuous refinement.

495 | Signal Quality of a Long-Term At-Home Protocol for Repeated Self-Applied Non-Invasive EEG (EEG@HOME) in people with epilepsy

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Purpose: EEG@HOME was a study involving people with epilepsy (PWE) collecting behavioral and physiological data at home over six months. While the protocol proved feasibility and acceptability, little is known about the long-term quality and consistency of self-applied mobile EEG signals in epilepsy. This analysis aims to address that gap.

Method: Twelve PWE independently recorded 10 minutes of EEG data at home twice daily (morning and evening) over six months using an 8-channel portable EEG cap with dry electrodes (waveguard touch by ANT Neuro). Two experts reviewed each recording to ensure artifact-free data, identifying epileptiform activity or seizures and selecting a 20-second segment unaffected by movement or blinking. Power spectrum analysis was performed for four frequency bands (Delta, Theta, Alpha, and Sigma), with average values calculated for each band. Channels with poor signal quality were excluded from analysis.

Results: PWE successfully recorded EEG data over extended periods, ranging from 12 to 424 recordings per patient (median = 249). The Fpz channel was excluded least often, demonstrating highest signal quality, while Cz, Pz and F4 were excluded most frequently; other channels exhibited similar performance across participants. Delta was the dominant power band, followed by Theta, Alpha, and Sigma. For most participants, the relative power of frequency bands remained stable over time, though fluctuations were observed in some cases. Peaks in Theta and Alpha were consistently identified in both morning and evening recordings. Expert review uncovered 61 epileptic events in one participant (average duration 2.2 sec; median 1.5 sec), including interictal and ictal Generalized Spike-and-Wave Discharges (SWDs) and short SWD runs.

Conclusion: The spectral characteristics of long-term, non-invasive, self-applied EEG are comparable to subcutaneous and scalp EEG, despite reduced stability. These findings underscore the feasibility of patient-led data

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collection and the system's potential for improving seizure documentation in remote monitoring scenarios.

572 | Brain changes in sleep-related hypermotor epilepsy observed from wakefulness and N2 sleep: a matched case-control study

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Purpose: Sleep-related hypermotor epilepsy (SHE) is a relatively uncommon epilepsy syndrome, characterized by seizures closely related to the sleep cycle. This study aims to explore interictal electroencephalographic (EEG) characteristics in SHE.
Method: We compared EEG data from 20 patients with SHE, 20 patients with focal epilepsy (FE), and 14 healthy controls, carefully matched for age, sex, education level, epilepsy duration, and drug-resistant epilepsy.
Results: During wakefulness, SHE patients showed enhanced frontal lobe power across all frequency bands, but decreased frontal lobe power in low frequency bands during N2 sleep. Additionally, a positive correlation was found between frontal γ band power and epilepsy duration in SHE patients during N2 sleep but not during wakefulness.
Conclusion: These findings suggest that interictal EEG abnormalities during wakefulness and N2 sleep might be used as potential biomarkers for the diagnosis of SHE.

576 | Patient perspectives on antiseizure medication discontinuation: a mixed-methods exploration of risk perception, tolerance, and counseling

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Purpose: Because ASMs can have adverse effects, guidelines consider ASM withdrawal after extended seizure-freedom. We explored patients' perceived seizure risk and risk tolerance.
Method: We interviewed adults at least one-year seizure-free, seen for epilepsy across three academic institutions. Participants rated their own perceived seizure risks (0 "definitely wouldn't have another seizure" to 10 "definitely would") *on* versus *off* ASMs, discussed what a minimal clinically important differences would be to justify continuation, and rated how likely they might be to withdraw ASMs (1 "not at all likely" to 7 "extremely likely") under hypothetical risks.
Results: Participants (N=32) rated their two-year chance of another seizure *on* ASMs as a median 1 (IQR 0 to 2) on a "0 to 10" scale, compared with a median 5 (IQR 4 to 7) *off* ASMs. Participants believed their current ASMs have a median effectiveness of 9 (IQR 7-10) on a "0 to 10" scale. Participants felt a median effectiveness of 6 (IQR 4 to 9) on a "0 to 10" scale would warrant remaining on ASMs, though 5 participants would continue their ASM if it extended the time until next seizure by any amount no matter how small. Regarding how likely they would be to withdraw ASMs under different hypothetical seizure risks, median responses on a "1 to 7" scale were 5 (IQR 1-6) when shown two-year seizure risks of 10% *on* versus 11% *off* ASMs, 1 (1-3) if 10% versus 20%, and 1 (1-2) if 25% versus 50%. No participant recalled having been presented with numerical seizure estimates regarding possible ASM withdrawal, yet 16 (50%) would like this information particularly in our presented graphical format.
Conclusion: Participants felt their ASMs were effective and were often reluctant to withdraw. Showing seizure risks influenced decisions, and graphical risk communication tools were generally welcomed.

600 | Comparative Diagnostic Accuracy of Long-Term Video EEG and Standard EEG in Predicting Seizure Recurrence After Epilepsy Surgery

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Purpose: The presence of interictal epileptiform discharges (IEDs) is associated with an increased risk of seizure recurrence following epilepsy surgery. Postoperative EEG monitoring is often performed to predict seizure outcomes. While long-term video EEG (LTVEEG) may offer higher diagnostic yield than standard EEG, it can be stressful for patients. This study aimed to compare the diagnostic accuracy of LTVEEG and standard EEG in predicting seizure recurrence after epilepsy surgery.

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Method: We conducted a prognostic accuracy study involving patients who underwent epilepsy surgery between 2017 and 2024. Postoperative EEGs were conducted at 3 months and 1 year following surgery. A 20-minute well-defined segment of each LTVEEG was analyzed for the presence of IEDs and seizures. Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were calculated to assess the predictive accuracy of LTVEEG and standard EEG for seizure recurrence within one year.

Results: Of 80 patients who underwent surgery, 42 were included in the analysis. Among them, 28 patients (65%) achieved a favorable outcome. Logistic regression identified postoperative pathological EEG findings and preoperative focal to bilateral tonic-clonic seizures (FBTCS) as independent predictors of unfavorable outcomes. LTVEEG demonstrated 73% sensitivity, 64% specificity, 52% PPV, and 82% NPV, compared to standard EEG, which showed 13% sensitivity, 89% specificity, 40% PPV, and 66% NPV. LTVEEG had significantly higher sensitivity than standard EEG, while standard EEG showed consistently higher specificity due to the large number of negative findings in the 20-minute recordings.

Conclusion: LTVEEG exhibited superior sensitivity compared to standard EEG in predicting seizure recurrence within one year after epilepsy surgery. These findings highlight the potential of LTVEEG as a more effective diagnostic tool for postoperative outcome prediction.

616 | Does Ramadhan Observance Affect Quality-of-Life in Epileptic Patients? A Multi-center Study in Indonesia

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Purpose: Indonesia, the largest Muslim-majority country, sees widespread participation in Ramadhan observance. This includes individuals with epilepsy, who face unique challenges during this period. Fasting may disrupt medication regimens and lifestyle factors, but its impact on the quality of life (QoL) for Muslim people with epilepsy (MPWE) remains unclear. This study aims to fill this gap by examining the effects of Ramadhan observance on QoL.

Method: A cross-sectional multi-center study was initiated in March 2023 – May 2024, across five hospitals, and three cities in Indonesia. We recruited MPWEs aged 18 years and beyond. Data were collected from the same subjects one month before, and during Ramadhan, at outpatient neurology clinics. Demography and clinical characteristics, along with fasting status, working status, participation in spiritual practices, and sleep duration were assessed through medical records and questionnaires. Medication adherence was measured using the Medication Adherence Questionnaire, while QoL was measured on a simple scale of 0-10, with 10 being the highest possible QoL. Data analysis was conducted through Chi-square, likelihood ratio, or Fisher's exact tests, Mann-Whitney U test, and followed by logistic regression.

Results: A total of 122 MPWE participated in the study, with 83.6% choosing to fast during Ramadhan. There was no significant difference in QoL scores before and during Ramadhan among those who fasted (p=0.590). However, working while fasting was associated with a decrease in QoL (OR: 8.041 [2.565-25.205]; p=0.000). Similarly, not participating in midnight prayers (OR: 4.093 [1.348-12.427]; p=0.013), and non-adherence to anti-seizure medications (OR: 6.987 [2.109-23.143]; p=0.001) were also associated with a decrease in QoL.

Conclusion: Ramadhan observance can be safely integrated into the lives of MPWE with appropriate support and guidance. Developing culturally sensitive policies and interventions, such as promoting medication adherence, addressing workplace stressors, and encouraging spiritual practices, may enhance QoL for MPWE during Ramadhan.

625 | Characterizing Patient and Caregiver Experiences Resulting from Prolonged Seizures

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Purpose: The impact and burden of prolonged seizures (PS) on people living with epilepsy (PwE) and their caregivers is unknown. This research describes their unmet needs and the impact of PS on quality of life (QoL).
Method: Quantitative web surveys and qualitative 60-min semi-structured interviews were conducted (June-August 2024) with 25 PwE (≥18 years; ≥3 PS lasting ≥2min within last 3 years) and 25 caregivers from United Kingdom/Germany/Spain/Italy/France/Poland. This research used interpretative phenomenological analysis to identify themes, attitudes, behaviors, and beliefs.
Results: For most participants, the impact of PS is an extreme version of problems they face from seizures in general, but PS have enhanced impact on: (1) Seizure control: PS indicate an inability to control seizures, present greater risk of physical injury (especially if in an unfamiliar environment), and increase inability to control breathing. (2) Mental health: PS increase anxiety, stress, and risk for depression, which can trigger further seizures for PwE; mood swings before/after PS are more pronounced; confusion and memory loss persist after a PS; PS also increase worry and fear of long-term brain damage. (3) Independence: PS are more likely to require interventions, making it harder for PwE to live alone and drive, and heightening feelings of being a burden; PwE's perceptions and concerns over their lack of seizure control, memory loss, recovery time, and stigma in work settings negatively impact their careers. (4) Social life: PwE/caregivers often limit social life due to risk and fear of PS, as they feel more confident in familiar environments; PwE also report PS having a negative impact on their romantic and parental relationships.
Conclusion: PwE/caregivers experience significant short-/long-term negative impacts on QoL from PS, highlighting the importance of having more tools to support seizure management and control, including a seizure action plan and interventions for rapid and early seizure termination.
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674 | Ictal spitting in patients with temporal lobe epilepsy: A case series

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Purpose: To evaluate the frequency of presentation and the lateralizing value of ictal spitting in patients with drug-resistant temporal lobe epilepsy (DR-TLE).
Method: A retrospective observational study was conducted in adult patients with DR-TLE admitted to the video-electroencephalogram (VEEG) unit at El Cruce Hospital in Buenos Aires, Argentina, from 2019 to 2024. Patients (p) who experienced seizures with ictal spitting during VEEG recordings were included, and the findings were correlated with the epileptogenic zone (EZ).
Results: A total of 417 patients underwent VEEG between 2019 and 2024. Of these, 132 patients with DR-TLE were included. Ictal spitting was observed in 4 patients (3%) during 11 seizures. The patients consisted of two women and two men, aged 23 to 51 years; three were right-handed, and one was left-handed. The mean age of seizure onset was 21 years (range: 17–23 years). Brain MRI findings included hippocampal sclerosis in 3 patients (2 right and 1 left) and right focal cortical dysplasia in 1 patient. The EZ was located in the dominant hemisphere in 2 patients and in the non-dominant hemisphere in the other 2 patients. Three patients underwent surgical intervention, with an Engel IA outcome after one year of follow-up.
Conclusion: Ictal spitting is an uncommon manifestation, observed in patients with TLE. Limbic structures (hippocampus and amygdala), are involved in the regulation of emotions, autonomic manifestations, and automatisms. Abnormal activation of these circuits during a seizure can lead to the production and expulsion of saliva. In most series and case reports, the EZ associated with ictal spitting is localized in the non-dominant temporal lobe. However, our findings revealed an equal distribution between the dominant and non-dominant hemispheres, suggesting no clear lateralizing value.

683 | The challenge of Lennox-Gastaut Syndrome (LGS) diagnosis in adult patients according to ILAE criteria: A Retrospective Observational Study

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Purpose: The International League Against Epilepsy (ILAE) recently introduced diagnostic criteria for

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Lennox-Gastaut syndrome (LGS)[1]. However, 52-62% of patients previously diagnosed with LGS fail to meet these criteria, revealing gaps in their applicability[2,3]. This study evaluated the relevance of these criteria to adult patients previously diagnosed with LGS based on available clinical data at the time of evaluation.

Method: We retrospectively reviewed all adult patients diagnosed with LGS referred to the adult Epilepsy Center of our Institute from 1974 to 2024. Patients were reclassified according to ILAE criteria[1] into three categories: (i) full electro-clinical criteria, (ii) clinical criteria only (seizure semiology, age of onset, and long term outcome data), and (iii) neurophysiological criteria only.

Results: A total of 97 adult patients (M/F: 58/39, mean age 40.10 ±14.57 years) were included, with 87 certified in the National Registry of Rare Diseases. Only 15 patients (15.62%) met the full ILAE diagnostic criteria, while 47 (48.96%) met clinical criteria alone and 4 (4.16%) met only EEG criteria. Among the 81 patients (84.37%) who did not fully meet the criteria, the most frequently unmet criterion was the EEG pattern, observed in 19 cases (23.46%). Tonic seizures were not identified in 25 patients (30.86%), and data were insufficient in 12 cases (14.81%). Notably, overnight video-EEG/polysomnography recording were unavailable for 61 patients (65.30%). The most consistently met criteria were seizure onset before 18 years (87; 89.69%) and long-term outcome (93; 95.88%).

Conclusion: Up to 84.37% of patients previously diagnosed with LGS did not meet the new ILAE criteria, highlighting their limited applicability in adults. This is largely due to missing overnight video-EEG/polysomnography recordings, essential for detecting key features, and incomplete clinical documentation. Flexible diagnostic frameworks tailored to real-world clinical settings are needed to address these challenges in this population.

743 | Anti-seizure medications: adherence and adverse effects in adults with epilepsy

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Purpose: Adherence and observation of the occurrence and adverse effects in chronic treatment of epilepsy with anti-seizure medications (ASM) are fundamental aspects of treatment; however, in the literature, there are still gaps in the knowledge of some aspects. Objective: To evaluate the adherence and presence of adverse effects in the use of ASM in adult patients with epilepsy on regular treatment.

Method: Clinical data were related to data from the Liverpool Adverse Events Profile (LAEP) and the Morisky Medication Adherence Scale (MMAS-8) of 114 adult patients with epilepsy.

Results: The mean age was 46.1±16.3 years, 59 (51.8%) cases were female, the mean LAEP score was 33.6±11.2, and the mean MMAS-8 score was 6.3±1.3. Toxicity was reported in 19 (16.6%) cases, and poor adherence to ASM occurred in 32 (28.1%) cases. Epilepsy was genetic/generalized in 10 cases, unknown in 34 cases, and structural in 70 cases. The highest LAEP scores occurred in females (36.5±11.9 v.s.30.6±9.5, T-test, p=0.005) and in cases with seizures with a frequency between 1-11x/year. There was a significant correlation between the LAEP and MMAS-8 scores (-0.216, p=0.021, Person's correlation test). There was no significant association between MMAS-8 scores with age, gender, seizure frequency, and other clinical epilepsy variables.

Conclusion: The rate of toxicity and low adherence to ASM treatment was high. There was a difference in the occurrence of adverse effects according to the demographic and clinical data of epilepsy. A higher presence of adverse effects was associated with lower adherence to drug treatment.

756 | A comparison of treatment response definitions in newly diagnosed focal epilepsy: Reflections on the current International League Against Epilepsy (ILAE) criteria

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Purpose: Variable definitions of treatment response in epilepsy complicate prognostication. This study compares current International League Against Epilepsy (ILAE) definitions of treatment response with previously published definitions within the same cohort.

Method: The Human Epilepsy Project (HEP) is a prospective, international cohort study that enrolled newly diagnosed focal epilepsy patients within four months of initiating treatment with Anti-Seizure Medications (ASMs). Treatment outcomes were determined according to current ILAE criteria: Treatment Sensitive (TS) (seizure free

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for ≥12 months on first 2 adequate ASM trials with/without relapse), Treatment Resistant (TR) (persistent seizures despite 2 adequate ASM trials), or indeterminate. Based on previously published criteria, participants were then additionally classified as responders (no seizures in last 12 months of follow up on same ASM) vs non-responders (persistent seizures in last 12 months of follow up). Rates and reasons for concordance/discordance are reported.

Results: Of 448 HEP participants, 435 had complete seizure and ASM data for analysis. The two approaches categorized treatment outcomes concordantly in 82.5% (n=318) (TR/Non-responder=84, (19.3%), TS/Responder=203 (46.7%), indeterminate=31 (7.1%). The overall discordance rate was 17.5% (n=117). Discordance was largely driven by two groups: 1) TS participants with relapsing/remitting seizure patterns by ILAE criteria were classified as non-responders due to seizures occurring in the last 12 months of follow up (despite becoming seizure free on early treatment) (n=43, 36.8%), and 2) a group of participants who never achieved seizure freedom were classified as non-responders, but had indeterminate treatment outcomes under ILAE criteria due to undertreatment (i.e. having <2 adequate ASM trials) (n=41 35.0%).

Conclusion: Assessing treatment response only in the final 12 months of follow up may classify patients as non-responders who had otherwise been sensitive to treatment in early treatment phases or were having persistent seizures while under treated according to ILAE criteria. This has important implications for clinical trials and prognostication research.

782 | Post-Stroke Seizures: A Comparative Analysis of Early and Late Onset Seizures in a Single-Center Retrospective Study

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Purpose: Post-stroke seizures are a common cause of epilepsy. While several factors associated with late-onset seizures, or post-stroke epilepsy, have been identified, no known methods for preventing post-stroke epilepsy have been established. This study aimed to compare the characteristics of early and late-onset seizures.

Method: This study analyzed patients who were admitted to Dong-A University Hospital between December 2022 and October 2024 with acute ischemic stroke and underwent DWI and PWI imaging. Based on the onset of stroke, patients were classified into early-onset seizure, late-onset seizure, and acute symptomatic seizure due to other causes within 7 days. Statistical analysis was performed on risk factors associated with stroke, acute-phase treatment, imaging parameters, and outcomes.

Results: Among the 925 patients, 34 (3.7%) developed seizures during the follow-up period, with 16 having early onset seizures and 15 having late onset seizures. Two patients had acute symptomatic seizures due to other causes. Comparison between the early onset seizure group and the late onset seizure group revealed that the late seizure group had a significantly higher prevalence of diabetes mellitus (73.3% vs. 18.8%, p=0.004), while the early seizure group showed a higher prevalence of prior cerebrovascular accidents (56.3% vs. 53.3%, p=0.027), and atrial fibrillation (31.3% vs. 33.3%, p=0.015). Lastly, the late onset seizure group showed a higher prevalence of patients with large Perfusion Weighted Imaging size (>50cc) between the two groups (31.3% vs. 33.3%, p=0.015).

Conclusion: Compared to the early-onset seizure group, the late-onset seizure group showed a higher prevalence of diabetes mellitus and large PWI size in Perfusion MRI.

784 | Caregiver burden in patients with Developmental and Epileptic Encephalopathies. An online survey analysis

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Purpose: To assess caregiver burden in patients with Developmental and Epileptic Encephalopathies (DEE) through an online survey.

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Method: A multicentric cross-sectional study in which DEE caregivers completed an online questionnaire, covering demographics, disease perception and quality of life (QoL) impacts. We evaluated demographic and clinical characteristics and their association with caregivers' QoL.
Results: Ninety-five DEE caregivers completed the questionnaire. The mean age (SD) of patients was 24.8 (±10.6) years, with 51.6% female. Tonic-clonic seizures were the most frequent type (62.1%) and 42.1% patients were seizure-free at the last follow-up. 45.3% had behavioral disorders and 21.3% had an autistic disorder; 85.3% of patients had a recognized degree of disability. The mean (SD) age of caregivers was 55.1 (±9.5) years, with 78.9% female and 92.6% were the patient's parents. 47.9% reported the need for professional health support; with 36% needing a psychologist, and 48.9% felt the public system provided insufficient support. 67% of caregivers performed professional health tasks at home, 29.8% reported significant psychological overload, and 82.2% needed additional help from family members. The main concerns were social (63.2%) and educational (52.6%) issues of the patient. Patients with higher seizure frequency had a higher degree of disability (p=0.023) and required professional health tasks from their caregivers (p=0.019). Patients with behavioral disorders faced more discrimination (p=0.026), contributed to worse social life for caregivers (p=0.004) and caused greater psychological overload (p=0.003). A higher degree of disability was associated with psychological overload (p<0.001), worse social life (p<0.001), increased need for professional support (p=0.001) and more health tasks for caregivers (p=0.001).
Conclusion: Caregivers of DEE patients experience significant psychological and physical burdens. Behavioral disorders and higher disability levels have a more severe impact on social challenges and psychological burden.

793 | Tau Deposition: A Potential Marker of Sleep and Memory Impairment in Focal Drug-Resistant Epilepsy

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Purpose: Tau aggregates, detectable via positron emission tomography (PET) imaging, are biomarkers for identifying cognitive decline in neurodegenerative diseases (Groot et al., 2022) and are linked to network hyperexcitability and seizures (Lam et al., 2020). *Post-mortem* and *ex-vivo* studies in focal drug-resistant epilepsy (DRE) link pathological tau to increased seizure risk and cognitive decline (Smith et al., 2019). Sleep impairment is associated with cognitive decline in both tauopathy and focal DRE (Kim et al., 2024; Spanò et al., 2020). This study investigates the unexplored role of tau PET in sleep and memory impairment in focal DRE, hypothesizing a negative correlation with spindle rate, and a positive one with seizure severity markers.
Method: Thirty focal DRE patients (20 male; mean age 33 ± 12 years) underwent scalp EEG, F18-MK6240 PET, and 3T MRI. PET images were partial volume-corrected and normalized to the cerebellum to obtain standardized uptake value ratios (SUVRs). The PET data were co-registered to T1-weighted MRI and projected onto hippocampal and neocortical segmentations (DeKraker J et al., 2022). Sleep EEG was analyzed for N2 spindles (10-16 Hz) and interictal epileptiform discharges (IEDs), with rates calculated for both. Seizure severity was assessed based on type and frequency. Association between tau deposition in specific brain regions and these markers were evaluated.
Results: Spindle rates were negatively correlated with tau-SUVR (r = -0.38, p = 0.04) and positively correlated with higher seizure severity in the ipsilateral hippocampus (r = 0.52, p = 0.04). A trend toward a positive association between IED rates and tau deposition (r = 0.35, p = 0.11).
Conclusion: Our primary findings reveal higher ipsilateral hippocampal tau with reduced spindle rates in DRE, with a trend for increased tau uptake in patients with higher seizure severity measures. These findings suggest a potential interaction between electroclinical seizure severity measures, tau aggregation, and sleep disruption.

813 | Neurodegeneration in Mesial Temporal Lobe Epilepsy (MTLE): Absence of Alpha-Synuclein and TDP-43 Pathology

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Purpose: The growing body of evidence concerning the presence of pathological aggregates of hyperphosphorylated tau protein and beta-amyloid in resection specimens from patients with pharmacoresistant mesial temporal lobe epilepsy (MTLE) is well-documented. Recent studies have also suggested alterations in serum levels of alpha-synuclein in this population. Another protein associated with neurodegeneration, TAR DNA-binding protein 43 (TDP-43), has not yet been extensively studied in epilepsy patients. Given this background, the present study aims to investigate the presence of alpha-synuclein and TDP-43 pathological aggregates in temporal lobe tissue samples from patients with MTLE sourced from two comprehensive tertiary epilepsy centers.

Method: The study included 267 patients diagnosed with MTLE and hippocampal sclerosis (HS), recruited from the Brno Epilepsy Center at St. Anne's University Hospital (FNUSA) and Motol University Hospital. For each participant, a pair of representative brain samples—comprising hippocampal and temporal cortical tissue—was analyzed immunohistochemically to detect the presence of alpha-synuclein and TDP-43 aggregates. A control cohort of 120 post-mortem brain samples, obtained from cases without a history of epilepsy or other neurological conditions, and positive controls obtained from patients with diagnosed Lewy Body Disease (for alpha-synuclein) and Amyotrophic Lateral Sclerosis (for TDP-43) were processed similarly. All analyses were performed by two experienced neuropathologists, who reached a consensus on their findings.

Results: No evidence of pathological alpha-synuclein or TDP-43 aggregates was observed in either the MTLE cohort or the control group.

Conclusion: In contrast to the established associations with tau protein and beta-amyloid pathology, neither alpha-synuclein nor TDP-43 appears to play a significant role in the neurodegenerative processes associated with pharmacoresistant MTLE with HS. These findings suggest that future research may benefit from a continued focus on tau-related and beta-amyloid pathways in this context. This work was supported by project LX22NPO5107 (MEYS), financed by the European Union–Next Generation EU and AZV NU22-04-00366.

820 | Temporal lobe epilepsy with amygdala enlargement: long-term outcome and memory

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Purpose: The purpose of this study is to investigate the drug resistance rate and memory function in patients with temporal lobe epilepsy with or without isolated amygdala enlargement.

Method: A total of 83 patients with temporal lobe epilepsy (TLE) were included using a quantitative approach, among whom 34 had TLE with amygdala enlargement (TLE-AE) and 49 had TLE without amygdala enlargement (TLE-noAE). All patients underwent T1-weighted MRI and neuropsychological memory testing in a longitudinal study design. Additionally, 71 healthy controls completed the same protocol. Among the TLE-AE patients, 11 subsequently underwent secondary MRI and memory testing.

Results: Among the participants, 40.96% (n = 34) exhibited amygdala enlargement. Compared to TLE-noAE, patients with TLE-AE had a higher initial seizure frequency (p = 0.001) and a lower occurrence rate of focal bilateral tonic-clonic seizures (FBTCS) (52.94% vs. 75.51%, p = 0.032). However, the drug resistance rate at 1 year was comparable between the two groups (32.35% vs. 32.65%, p = 0.91). Logistic regression analysis indicated that seizure frequency (OR=0.18, 95%CI 0.05-0.63, p=0.007) and disease duration (OR=1.08, 95%CI 0.00-1.16, p=0.04) significantly affected the drug resistance rate at 1 year. Further quantitative volumetric analysis revealed that in TLE-AE, each subregion of the affected amygdala was enlarged, and the volume of the affected hippocampus was also increased, mainly in the hippocampal head (p=0.001). Both TLE-AE and TLE-noAE groups exhibited memory decline compared with control (TLE-AE vs control, p=0.03; TLE-noAE vs control, p=0.004), while TLE-noAE presented verbal memory deficit (p=0.002). Longitudinal analysis suggested that faster volumetric reduction was associated with a better 1-year outcome (p=0.007). Additionally, drug-resistant TLE-AE showed a tendency towards memory decline.

Conclusion: The incidence of amygdala enlargement is higher. Faster recuperation of AE in patients may indicate a favorable outcome.

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827 | Real-World Efficacy and Tolerability of Cenobamate in Drug-Resistant Epilepsy: A Single-Centre Retrospective Study from the United Kingdom

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Purpose: Drug-resistant epilepsy (DRE) poses a significant challenge for healthcare professionals. Cenobamate, approved in the UK in 2022, has shown promise in reducing seizures in DRE. This retrospective study evaluated the real-world efficacy and tolerability of Cenobamate in reducing seizures in patients treated at Leeds General Infirmary.
Method: Data from 93 patients with DRE were collected. Baseline seizure frequency was recorded over three months prior to initiating Cenobamate. Seizure frequencies at three months, six months post-initiation, and last follow-up (>12 months) were compared to assess efficacy. Retention rates, adverse events, and responses in key subgroups (e.g., sodium channel blocker [SCB] use, vagus nerve stimulation [VNS], and learning disabilities [LD]) were analyzed.
Results: At three months, the median seizure reduction was 37.5% (n=48), increasing to 53.59% (n=33) at six months and 65.22% at long-term follow-up (>12 months). At long-term follow-up, 24.24% of patients achieved seizure freedom (100% reduction), while 27.27% returned to baseline seizure frequency. Patients with secondary generalized tonic-clonic seizures showed greater reductions (53.5% and 75% at three and six months, respectively), while focal seizures experienced more modest improvements. Cenobamate retention averaged 67.7 weeks, with longer retention in those continuing treatment (74.9 weeks) versus those who discontinued (32.0 weeks). Sedation (39.3%) and unsteadiness (30%) were the most frequent adverse effects. SCB use appeared to compromise efficacy, with lower seizure freedom rates (9.1% vs. 24.24%) and higher discontinuation rates (37.7% vs. 15.2%) compared to the general population. VNS patients demonstrated poorer seizure control, while patients with LD showed non-significant trends toward greater seizure reduction.
Conclusion: Cenobamate demonstrates efficacy in reducing seizure frequency, particularly in patients with secondary generalized tonic-clonic seizures. Longer-term follow-up and larger cohorts are needed to establish predictors of response in key subgroups.

899 | LEgEND: Learning hEalth systEm iN a Digital hospital

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Purpose: Learning health systems (LHS) are clinical spaces that embed knowledge generation into daily practice to drive continuous improvements in individual and population health. This project aimed to establish a data-driven LHS within a specialist neurology clinic, aligning science, informatics, incentives and culture to enhance patient-centred care and guide continuous learning.
Method: A SMART aim focused on assessing clinic wait times and enhancing communication over 12 months. Guided by the Plan-Do-Study-Act (PDSA) cycle, key activities included: (i) Conducting a qualitative survey with 21 staff members to identify data priorities, (ii) Building an interactive wait-time dashboard leveraging outpatient data, reviewed and refined weekly, (iii) Disseminating a co-designed 10-question patient experience survey using QR codes, gathering real-time feedback, (iv) developing a tool for auditing documentation (v) Using a large language model (LLM) AI tool to improve readability of clinician letters to GPs and patients without disrupting the auditable proforma in use and (vi) Hosting weekly multidisciplinary data learning meetings to discuss findings and collaboratively identify areas for improvement.
Results: The staff survey identified waiting times as a key priority, leading to the creation of a dynamic wait-time dashboard, which is now a tool for operational review. A patient survey completed by 70 respondents found over 80% had positive experiences. Preliminary patient feedback on LLM-enhanced letters emphasize the importance of delivering relevant, accessible information while maintaining accuracy. Weekly MDT meetings have streamlined management of staff absences, highlighted safety concerns and facilitated discussion of patients due to return to clinic that day and challenging scenarios encountered by the service during the week.
Conclusion: This project demonstrates the feasibility of embedding LHS principles to improve care in a neurology clinic. Future steps include scaling the approach, aiding reproducibility, refining digital tools, and evaluating long-term impacts on service and patient satisfaction.

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900 | Altered States of Consciousness: Does Treating the EEG Help?

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Purpose: In the investigation of altered consciousness in the absence of manifest epileptic seizures, an electroencephalogram (EEG) is often performed due to the suspicion of non-convulsive status epilepticus (NCSE). Occasionally, epileptic activity is detected without meeting the criteria for NCSE. It remains unclear whether empirical treatment with anti-epileptic drugs provides any benefit. OBJECTIVES: To determine the proportion of patients with altered consciousness who improved after resolution of epileptic activity and its relationship with treatment.
Method: A retrospective, cross-sectional, single-center study reviewing the clinical records of 159 patients who underwent EEG to clarify altered consciousness. These patients showed epileptic activity in the initial EEG, which was no longer detected in a subsequent EEG.
Results: The majority of patients were male, with a median age of 75 years. The main identified cause of epileptic activity was epilepsy, accounting for 35% (n = 56) of cases. Only 10 patients (6.2%) did not receive anti-epileptic drugs therapy, among whom 7 maintained their level of consciousness. Fifty-eight percent of patients did not improve, while 42% (n = 66) showed improvement. Comparing the evolution of consciousness levels and the variation in mRS (Modified Rankin Scale) between treated and untreated groups, no statistically significant difference was observed (p-value 0.5219 and 0.5548, respectively). Age reduced the likelihood (OR 94%, p-value 0.0013) of improvement in consciousness level. No relationship was found between state of consciousness improvement and other variables such as sex, etiology, or amount of epileptic activity.
Conclusion: The majority of patients with altered consciousness and epileptic activity on EEG are empirically treated with anti-epileptic drugs therapy (94.8%). There is no significant difference between the treated and untreated groups; however, the small sample size of untreated patients limits definitive conclusions.

925 | Clinico-electrographic spectrum and predictors of outcome in resistant idiopathic generalized epilepsy- is it a zebra among the horses?

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Purpose: One-third of people with idiopathic generalized epilepsy (IGE) are drug-resistant. Identifying markers of treatment resistance aids in therapeutic strategies and prognostication. We aimed to determine the clinical and electroencephalographic predictors of resistant IGE and response to antiseizure medications (ASMs).
Method: This is a single-center retrospective study on IGE patients who underwent long-term video electroencephalography. We analyzed the clinical, interictal, and ictal data, and compared 30 drug-resistant with 60 drug-responsive IGE patients. Drug resistance was defined as the failure of an adequate trial of valproate and another appropriately chosen ASM (whether as monotherapies or in combination).
Results: Age at onset, sex, family history, IGE subtypes, multiple seizure types, presence of focal features in semiology, and duration did not differ between the two groups. The resistant IGE group had a higher age at transformation of seizure type (18.30 vs 12.80years;p-value:0.038), frequency of GTCS (7.37 vs 4.53;p-value:0.023), longer duration of leading spike in generalized discharge(318.18 vs 185.71ms;p-value:0.016), and a lower frequency of background rhythm(9.66 vs 11.06 Hertz;p-value:0.00) than drug-responsive IGE. On multivariate analysis, clustering of GTCS (OR 4.56; CI 2.73-33.29;p-value:0.012), predominant nocturnal seizures (OR 3.66; CI 2.10-7.20;p-value:0.014), psychiatric comorbidities (OR 7.09; CI 9.58-15.25;p-value:0.004), frequent spike-wave discharges in sleep (OR 5.50; CI 7.80-18.47;p-value0.02) and focal slowing irrespective of ASM used (OR 6.133; CI 10.78-19.70;p-value:0.001) were independent predictors of drug resistance. In the entire cohort, 40.7% patients had valproate resistance, among them 27.3% responded to an additional ASM. Furthermore, 13 patients had a history of remission with sodium channel blockers. At the last follow-up, 30.8% of patients on sodium channel blockers were in sustained remission.
Conclusion: The study demonstrated the clinical and electroencephalographic indicators of resistant IGE. Whether nocturnal predominant seizures, focal slowing, and response to sodium channel blockers signify an

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expanding spectrum of IGE or the coexistence of IGE and frontal lobe epilepsy, needs to be explored.

943 | Sex differences in efficacy of antiseizure medications in adults with epilepsy: A systematic review

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Purpose: As a part of a wider project aimed to assess sex-related differences in adverse effects and efficacy of antiseizure medications (ASMs) (Giuliano L., CNS Drugs 2024 Jun;38(6):409-423) (Giuliano L., Seizure. 2022 Nov;102:6-13), we performed a systematic review focusing on differences in efficacy of ASMs between male and female adults with epilepsy.

Method: We conducted a comprehensive literature search in the PubMed database. The search was conducted with no restriction on publication date, and all results up to September 2022 were included. We included all the articles written in English, Italian, Spanish, or French language evaluating the efficacy of ASMs in people with epilepsy (PWE), explicitly reporting sex differences in efficacy. Newcastle-Ottawa and Jadad Scale were used to assess study quality.

Results: A total of 1,778 studies were identified. Of these, only 15 studies were included in the systematic review since they identified sex as a statistically significant variable in terms of efficacy. We found an overall higher rate of seizure reduction or seizure freedom in males using different ASMs, with 9 studies *vs* 6 in which efficacy was higher in males. However, most studies were observational, they were mainly exploring efficacy of older ASMs and analyzed sex as a covariate in the analyses without a stratification for sex.

Conclusion: Our study has identified male sex as a predictor of ASMs efficacy in the majority of studies that found sex differences. However, the scarcity of data found in the literature highlights the need for a systematic evaluation of sex as a variable influencing the response to medications in clinical research.

976 | Seizure-Related Road Accidents and Injuries Among People with Epilepsy in Indonesia's National Referral Hospital: A Pilot Study

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Purpose: People with epilepsy (PWE) are at increased risk for seizure-related road accidents and injuries, significantly impacting daily living. However, safety regulations regarding driving among PWE remain unclear in Indonesia. This pilot study aimed to evaluate the driving profiles, seizure-related road accidents, and injuries among PWE in a national referral hospital in Jakarta, Indonesia.

Method: This cross-sectional study was conducted from December 2024 to January 2025 at the neurology clinic, Cipto Mangunkusumo National Referral Hospital. All epilepsy patients aged 18 years and above were included. Data on demographics, clinical characteristics, and driving profiles were collected via direct examination and questionnaires. Variables analyzed included vehicle type, driving frequency, and history of seizure-related accidents. Data analysis used Chi-squared, Fisher's Exact, Mann-Whitney, Independent t-tests, and logistic regression.

Results: A total of 67 PWE were included, with a median age of 32 years (18–58), and 53.7% were female. The majority of subjects (40.3%) had focal with impaired awareness seizures. Before diagnosis, 59.7% had driven; nevertheless, 41.8% continued post-diagnosis, regardless of seizure frequency. Furthermore, five subjects with pediatric-onset epilepsy learned to drive despite the diagnosis. Motorcycles were the primary vehicle (71.4%), and 28.6% carried passengers. Half of those driving post-diagnosis drove daily. Seizure-related road accidents occurred in 19.4%, resulting in lacerations (46.2%), hematomas (38.5%), and hand fractures (7.7%). Hospital admission was required in 53.8%, and 69.2% reported injuries

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affected daily activities. Road accidents were significantly associated with seizure frequency (p=0.021), and duration of epilepsy (p=0.035), but these factors were not significant in multivariate analysis.

Conclusion: Driving is unavoidable for PWE in productive years, regardless of the consequences. This poses significant risks of seizure-related road accidents. More straightforward regulations and further research are needed to understand the broader impact on PWE and other road users.

1002 | Healthcare Resource Utilization among Adult Patients with Focal-Onset Seizures using Cenobamate: a US Database Analysis

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Purpose: Anti-seizure medication (ASM) polytherapy is a common treatment for individuals with uncontrolled epilepsy and is linked to higher health-care resource utilization (HCRU) than monotherapy. Cenobamate (XCOPRI®) is a novel ASM indicated for the treatment of focal-onset seizures (FOS) in adult patients in US. This study examines HCRU before and after cenobamate in US FOS patients.

Method: This retrospective observational study utilized the IQVIA PharMetrics Plus database, containing medical claims of approximately 140 million US enrollees. Adult cenobamate users with FOS were identified with the first cenobamate dispensation as index date (indexing period: April 1, 2020, to April 30, 2023). Eligible patients were required to have a pre-index 6-month baseline period, and 6-month follow-up. A treatment regimen evaluation (TRE) window of 90 days post-index was defined to evaluate patients on monotherapy (≥90 days prescription claims), polytherapy (overlapping ≥90 days' supply of cenobamate and at least one ASM within +/- 30 days from cenobamate dispensing) or undetermined (all others). HCRU parameters of pre-index vs. follow-up were compared.

Results: 1,132 patients were identified: 17 patients (1.5%) on monotherapy, 510 (45.1%) on polytherapy, and 605 (53.5%) on an undetermined regimen. There was a decrease in the proportion of patients with at least one hospitalization from 21.9% (n=248) in the baseline to 15.4% (n=174) in the follow-up period. In the monotherapy group, this decrease was from 17.7% (n=3) to 5.9% (n=1); in the polytherapy group from 22.8% (n=116) to 15.3% (n=78). There was an increase in the proportion of patients with at least one hospitalization as number of ASMs increased: 5.9% (n=1) on cenobamate monotherapy, 13.8% (n=33/240) for those with one additional ASM, 15.7% (n=29/185) for those with 2 additional ASMs, and 17.7% (n=15/85) for those with 3+ additional ASMs.

Conclusion: The analysis demonstrated decreased hospitalization 6 months after cenobamate initiation compared to baseline.

1032 | Valproic acid use and risk of intracranial hemorrhage in invasive EEG monitoring

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Purpose: This study aims to retrospectively analyze patients maintained on Valproate (VPA) who underwent invasive EEG monitoring to evaluate intracranial hemorrhage (ICH).

Method: Data were collected from KFSHRC from May 1, 2014, to May 1, 2024, over a 10-year period. Out of 273 patients who underwent invasive EEG monitoring, 130 met the inclusion criteria. These patients had a brain CT scan performed post-procedure to confirm the presence or absence of ICH.

Results: The analysis of 130 cases revealed a mean age of 24 ± 10 years (range: 2 to 50 years). Among the patients, 74 (57%) were male. ICH occurred in 35 patients (27%). Of these, 31 patients (24%) were on Valproate. The average daily dosage was 1400 mg/day (IQR: 1000; range: 400 to 2500 mg/day). Among those taking Valproate, 34.4% (11 out of 31) developed ICH, compared to 23.5% (23 out of 99) in the non-Valproate group. This indicates a higher ICH rate in the Valproate group, though not statistically significant (p = 0.25). Gender was the only significant predictor of ICH (p=0.040), with males having 2.52 times higher odds compared to females (95% CI: 1.04–6.09). Valproate use showed increased odds of ICH (OR = 1.716, 95% CI: 0.658–4.476, p=0.270). Age's impact was minimal (OR = 1.019, 95% CI: 0.978–1.062, p=0.361), and procedure type was not significantly associated with ICH risk (OR = 0.785, 95% CI: 0.303–2.035, p=0.619).

Conclusion: In this retrospective study, Valproate use showed a slightly increased risk of ICH during invasive EEG monitoring. Additionally, male gender emerged as a significant independent risk factor for increased bleeding likelihood by 2.5 times. However, the small sample size

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and the inclusion of cases with CT brain scans may introduce selection bias, warranting further studies with larger samples.

1051 | Assessment of cognitive function in patients with epilepsy

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Purpose: Evaluating cognitive functions in epilepsy and status epilepticus is crucial. The MoCA scale is an effective screening tool for detecting mild cognitive impairments, such as attention, memory and speech. The purpose of the study was to assess cognitive functions in patients with epilepsy.
Method: A total of 53 patients treated at a clinic in Andijan were examined, including 33 (62.2%) with epilepsy and 20 (37.8%) with status epilepticus. The MoCA scale was used to assess cognitive impairment in these patients.
Results: Among women in the epilepsy group, 1 (3%) was over 80 years old, 7 (21.2%) were aged 60–80, and 5 (15.1%) were aged 40–60. Men in the 20–60 age range accounted for 12 (36.2%). The average age at disease onset was 45.41 ±10.6 years for the status epilepticus group, 39.20 ±15.7 years for epilepsy group. MoCA results showed moderate cognitive impairment (22.1–27 points) in 11 (33.4%) and mild dementia (16.2–22.1 points) in 22 (66.6%) status epilepticus patients. In the epilepsy group, 3 (15%) scored within the normal range (26–30 points), 14 (70%) showed moderate impairment, and 3 (15%) had mild dementia. No patients scored below 16.2 points.
Conclusion: The MoCA scale effectively assesses cognitive function in epilepsy and status epilepticus patients due to its simplicity and accessibility.

1084 | Off-label use of cenobamate in Refractory status epilepticus: a series of cases

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Purpose: Refractory status epilepticus (RSE) is a neurological emergency, leading to a high mortality rate. The number of anti-seizure medications (ASM) to treat RSE are limited, and usually invasive measures are required. Cenobamate is an effective adjunctive ASM for treatment resistant focal epilepsy. It has broad spectrum anticonvulsant activity and may be a useful medication for refractory status epilepticus (RSE). Nevertheless, status epilepticus is normally excluded from former clinical trials.
Method: We describe three RSE cases where cenobamate was added safely to other treatments.
Results: Case 1:75-year-old female was admitted for meningioma resection and developed focal motor onset seizures ASM used were levetiracetam, lacosamide, valproic acid, perampanel, topiramate without achieving seizures control. Cenobamate was initiated at 12,5mg daily with rapid titration to 25 mg after 5 days up 50 mg daily. Electroencephalogram (EEG) register improved after 25mg daily dose. Case 2: 72-year-old female with a history of bipolar disorder was admitted due to aphasia. She was diagnosed with focal non motor status epilepticus. ASM used were levetiracetam, lacosamide, perampanel, topiramate, valproic acid, clonazepam and immunotherapy. No clinical improvement was reported. Cenobamate was initiated at 12,5mg daily with rapid titration weekly until 200mg daily. EEG register improved after 50mg daily dose. Case 3: 72-year-old female with focal non-motor epilepsy history since youth was admitted for subacute altered mental status. After admission, she was diagnosed with focal autoimmune epilepsy. She tested positive for GAD antibodies. EEG register showed status epilepticus. She was treated with levetiracetam, lacosamide, valproic acid, topiramate and immunotherapy without clinical improvement. Cenobamate was initiated at 12,5mg daily with rapid titration weekly up to 200mg daily. EEG register improved after 50mg daily dose.
Conclusion: Even though there is only limited data supporting potential effectiveness and safety, cenobamate might have an indication in super refractory status epilepticus.

1113 | Diagnostic Challenges and New Clinical Insights into Bilateral Perisylvian Epilepsy

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Purpose: Bilateral perisylvian epilepsy is a rare and complex epileptic syndrome characterized by significant communication deficits, language and motor impairments, and seizures that originate or propagate through the perisylvian network. This study, conducted at King Faisal Specialist Hospital & Research Centre, aimed to investigate the clinical manifestations and mechanisms of seizure propagation in this network through invasive stereoelectroencephalography (SEEG) recordings.

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Method: Among a cohort of nine patients, four underwent SEEG, which enabled precise localization of the epileptogenic zones within the bilateral perisylvian regions. A history of recurrent chest infections and sleepwalking was commonly observed, suggesting potential environmental or developmental contributions. These findings align with previous research identifying persistent features within the perisylvian epileptic spectrum, such as shared genetic predispositions and disruptions in perisylvian communication circuitry. Additionally, the role of NREM sleep in amplifying epileptiform discharges was noted, further exacerbating cognitive impairments and communication challenges (Halász P et al. Seizure 2019;65:31-41).

Results: Diagnosing bilateral perisylvian epilepsy remains challenging due to the frequent absence of cortical abnormalities on neuroimaging, underscoring the pivotal role of SEEG in accurately identifying epileptogenic zones. Genetic testing was conducted on all patients, and the results are in progress. This testing aims to explore potential correlations between clinical features and genetic factors, which may provide deeper insights into the etiology of this syndrome.

Conclusion: This study emphasizes the diagnostic complexities, clinical characteristics, and unique neurophysiological features of bilateral perisylvian epilepsy. It highlights the essential role of SEEG in precise localization and the need for continued research into the genetic and developmental underpinnings of this rare epileptic syndrome. The findings have significant implications for improving diagnostic accuracy and tailoring individualized therapeutic strategies for affected patients.

1115 | Seizure Type at Relapse as a Predictor of Recurrence Etiology in New Onset Epilepsy

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Purpose: Seizure persistence significantly impacts the quality of life and mortality in patients with epilepsy (1). Despite adequate antiseizure medication (ASM), recurrence rates remain around 30% (2). Understanding the causes of recurrence is essential to guide optimal treatment adjustments. This study investigated the causes of relapses and whether seizure type at relapse predicts the etiology of recurrence.

Method: A total of 330 patients with new-onset epilepsy (NOE) and a minimum of 5 years of follow-up at the Epileptology Clinic, University Hospital of Geneva, were screened for seizure recurrence. All the reported relapses were reviewed to determine their etiology and categorized as due to treatment ineffectiveness, inadequate ASM trial, poor adherence, non-epileptic seizures, acute symptomatic seizures or unknown. Seizure types were classified according to the ILAE classification (3) and grouped into generalized tonic-clonic (GTCS) and non-generalized tonic-clonic (n-GTCS) seizures. We used Generalized Linear Mixed Model to associations between seizure type and cause of recurrence.

Results: Of the 330 patients, 181 experienced one or more relapses during follow-up. Poor adherence caused 74 cases, inadequate treatment 73, acute symptomatic seizures 15, and treatment ineffectiveness 58, with 11 cases unknown and 7 due to non-epileptic causes. A total of 63/181 patients had more than one relapse cause over time. GTCS occurred in 132 patients, n-GTCS in 71, and both in 54. GTCS were significantly associated with poor adherence ($p < 0.001$), while n-GTCS seizures were linked to treatment ineffectiveness ($p < 0.001$).

Conclusion: Among the different causes of relapses, poor adherence and inadequate treatment were the most common in NOE patients, while a smaller proportion relapsed due to treatment ineffectiveness. GTCS persistence suggests poor medication adherence and highlights the importance of ASM blood level monitoring rather than immediate treatment changes. Behavioral strategies to enhance adherence are critical, as GTCS persistence is associated with increased morbidity and SUDEP risk (4).

1120 | Beyond Psychogenic Non-Epileptic Seizures: Head No-No Movements as an Epileptic Phenomenon

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Purpose: Psychogenic non-epileptic seizures (PNES) are episodes resembling epileptic seizures but occur without abnormal electrical brain activity[1]. PNES accounts for up to 20-30% of patients admitted to epilepsy monitoring units[2]. Horizontal side-to-side head shaking, often referred to as "head no-no movements," has been previously considered as one of the hallmarks of PNES[3, 4]. However, no-no head movements are also a rare semiology seen in seizures.

Method: In our study, we analyzed five patients who exhibited head no-no movements as part of their seizure semiology. Three patients were new onset epilepsy, diagnosed using scalp video. The other two had drug resistant epilepsy and underwent stereo-EEG. Signal processing of

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SEEG data further revealed that head no-no movements are associated with a network involving the insula, orbitofrontal cortex, and frontal operculum.

Results: Research involving animals has linked head movements to the medial entorhinal cortex, where various degrees of head motion have been noted[5]. This association suggests that the medial entorhinal cortex plays a role in translating external environmental cues to facilitate head direction movement[6]. Additionally, weak head turning results from stimulation of the medial entorhinal cortex[7], other studies showed spontaneous epileptic arousals, linked to subtle behavioral signs like head nodding and sleep fragmentation, were observed in amygdala-kindled kittens, with evidence of seizure-like events triggered by stimuli or occurring during postictal recovery[8]. However, the relationship between head no-no movements and seizure activity remains unexplored in humans, representing the primary focus of our investigation.

Conclusion: The findings challenge the conventional understanding that head no-no movements are specific to PNES. Recognition that these may be an ictal manifestation will help to prevent misdiagnosis. Furthermore, the underlying network contributing to these areas comprise the insula, frontal operculum and orbitofrontal region. Recognizing head no-no movements as an ictal epileptic phenomenon can improve diagnostic accuracy, guide appropriate treatment, and prevent misdiagnosis.

1126 | Improving quality of life in patients with intellectual disability and epilepsy through comprehensive inpatient treatment

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Purpose: The prevalence of epilepsy in people with intellectual disability (ID) is up to 40 times higher than in the general population. Seizure burden, seizure-related complications and anti-seizure medication (ASM) adverse effects impair quality of life (QoL). This study evaluated the effects of a comprehensive inpatient treatment program (CITP) on QoL.

Method: This prospective observational study included people with epilepsy (PWE) and ID (IQ < 70) who underwent a CITP in a tertiary epilepsy center. During a hospital stay of ≥14 days, the CITP involved anti-seizure medication (ASM) adjustments and other interventions such as occupational therapy, ergotherapy, physiotherapy and social counseling. Outcomes were assessed using standardized measures, including the Liverpool Seizure Severity Scale (LSSS), Liverpool Adverse Events Profile (LAEP), and a caregiver-rated global QoL scale (10 best, 0 worst). Data were collected within 2 weeks pre-admission and 8 weeks post-discharge. Favorable seizure outcome was defined as ≤1 seizure per month without seizure-related injuries.

Results: Sixty-five patients (30 female, median age 32 years) were included. During inpatient treatment, ASM numbers were significantly reduced (median 3 before admission vs. 2 after discharge) but not total ASM dosages. Proportion of 3rd generation ASM increased from 81.0% before admission to 96.5% after discharge. Higher QoL after discharge was significantly associated with favorable seizure outcome ($p<0.001$) and lower LAEP ($p=0.03$). CITP elevated rate of favorable seizure outcome (25% before admission vs. 46% after discharge; $p=0.004$) and reduced adverse events (LAEP median 34.0 vs. 31.0; $p=0.006$). Reduced seizure severity (LSSS) was independently associated with an increased proportion of 3rd generation ASM ($p=0.033$). Global QoL ratings improved significantly (before admission median 4.0 vs. after discharge median 6.0; $p=0.0015$). ASM reduction was independently associated with QoL-improvement ($p=0.011$).

Conclusion: In PWE and ID, seizure control and ASM adverse effects determine QoL. Tailored ASM adjustments through CITP may foster improvements of QoL.

1127 | Prodromal Olfactory Loss as a Predictor of Seizure Occurrence in Temporal Lobe Epilepsy

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Purpose: This study aims to investigate the potential of utilizing transient olfactory dysfunction as a predictor of seizure occurrence in individuals with temporal lobe epilepsy

Method: We prospectively enrolled 15 patients diagnosed with temporal lobe epilepsy who were admitted to the Epilepsy Monitoring Unit at King Faisal Specialist Hospital. Olfactory function was assessed using the University of Pennsylvania Smell Identification Test (UPSIT). Each patient underwent an initial baseline assessment upon admission, followed by evaluations every 8 hours until the first seizure even.

Results: Preliminary findings indicate a marked decline in olfactory identification ability—reflected in severe microsomia—within one-hour preceding seizure onset. This correlation suggests that olfactory dysfunction may serve

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as a prodromal indicator of upcoming seizures in patients with temporal lobe epilepsy.

Conclusion: Our study proposes that transient olfactory loss could be a valuable predictor for seizure occurrence in TLE. The implications of these findings may lead to novel approaches for seizure prediction and management, enhancing patient quality of life and reducing the risks associated with unexpected seizure events. Further research should aim to validate these findings in larger cohorts and explore the underlying mechanisms linking olfactory loss and seizure activity.

1129 | Understanding the cause and effect of homelessness and epilepsy

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Purpose: Provision and access to healthcare is difficult and challenging for the homeless population. Evidence shows an almost eight-fold increase in prevalence of Epilepsy compared to the housed population. This potentially highlights a causal relationship between Epilepsy and homelessness. We performed a single center retrospective observational study to better understand the biographical characteristics of our homeless patients with Epilepsy and identify predictive factors to aid prognostication.

Method: A total of 145 patients with Epilepsy living with homelessness between the year 2016 to 2023 were identified through the St. James's Hospital Information Management Service. Patients without clear diagnosis of epilepsy, minimal hospital encounters and insufficient clinical information were excluded. Variables were predetermined, and data were collected directly from the patient's electronic medical records onto Excel for statistical analysis.

Results: An estimated 90% of our patients were diagnosed with Epilepsy prior to becoming homeless. Majority of patients have self-reported that homelessness has caused a negative impact on their Epilepsy. The length of homelessness exceeding 10 years is a poor predictor of breaking out of homelessness. More than 70% of our patient population has recurrent hospital presentations with alcohol related seizures, and this further highlights the prevalence of alcohol misuse in homeless accommodations. There were less than 10 reported deaths in our cohort but most of which were seizure-related deaths during period of homelessness.

Conclusion: We recognize that the diagnosis of Epilepsy can have strong psychosocial implications on a patient's wellbeing and carries detrimental effect on their ability to integrate into societal norm and thus potentially leading to homelessness. We have reinforced that homelessness has a negative impact on patient's Epilepsy. Increasing clinician awareness will serve as the first step towards improving current support structures to help prevent patients with established Epilepsy from becoming homeless.

1130 | Routine EEG versus 24-hour EEG in the discontinuation of anti-seizure medications in patients with epilepsy and long-term seizure freedom

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Purpose: Discontinuing anti-seizure medication (ASM) might be considered in patients with epilepsy who have long-term seizure freedom, following an electroencephalogram (EEG) documenting the absence of epileptiform abnormalities. However, few studies have compared routine EEG (rEEG) and 24-hour EEG (24hEEG) for this purpose. We aim to determine if the 24hEEG is superior to the rEEG in finding interictal epileptiform discharges in these patients.

Method: A retrospective, cross-sectional study was performed in a Portuguese center. Patients with epilepsy diagnosis and long-term seizure freedom to whom an EEG was performed to discontinue ASM were searched in the hospital EEG database. Patient files were reviewed for demographic and clinical data.

Results: 53 patients were included (50.9% female, mean age 53.8 years). Adult-onset epilepsy was the most prevalent type (43.4%), with a median of 10 years since diagnosis. Most patients had focal epilepsy (52.8%) of unknown etiology (58.5%). 32.6% of patients had epileptogenic findings on MRI. The median maximum number of ASM taken concurrently at any point of the disease was one. Clinicians preferred rEEG as the diagnostic modality (60.4%). Notably, rEEG was conducted significantly earlier following the last seizure than 24hEEG (48 vs. 96 months, $p<0.001$). Most EEGs were normal (69.8%; rEEG: 71.9% vs. 24hEEG: 66.7%, $p=0.686$). Epileptiform abnormalities were detected in 15.1% of patients, more frequently in those undergoing 24hEEG (rEEG: 6.3% vs. 24hEEG: 28.6%, $p=0.047$). When epileptiform abnormalities were identified, clinicians consistently opted to continue ASM therapy. In contrast, when EEG results were normal (absence of epileptiform or other

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abnormal findings), ASM discontinuation was pursued in 78.3% of cases (rEEG: 77.8% vs. 24hEEG: 83.3%, p=0.772).
Conclusion: In our cohort, the 24hEEG was superior to the rEEG in identifying epileptiform findings in epileptic patients with long-term seizure freedom, making it the most appropriate exam for guiding the decision to discontinue ASM.

1143 | Epilepsy Monitoring of Prospective Seizure Observations with Electronic Records (EMPOWER): A Novel, Prospective, Large-scale, Observational Study Designed to Better Understand the Patient Journey

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Purpose: In the US, ~3.5 million people have epilepsy, almost a third of whom live with uncontrolled seizures. Associated with this is decreased quality-of-life and increased mortality risk from SUDEP and seizure-related accidents. EMPOWER is an ongoing research project in partnership with the Epilepsy Study Consortium, aiming to characterize longitudinal seizure burden and antiseizure medication (ASM) use patterns in patients with a confirmed epilepsy diagnosis.
Method: Participants aged ≥18 years who elect to enroll are followed for a prospective observational period of up to 24 months. Eligible participants will access an electronic seizure diary to record seizures and ASM use. Participants opting to share medical records will have linked records capturing seizure-related disease course and prospectively tracking intercurrent events. Study surveys will collect information including demographics, seizure types/counts and seizure tracking behavior. Periodically, summarized deidentified reports will be shared with participants to facilitate learning from others' experiences. Data are presented from 156 respondents, matched in open claims, with an epilepsy ICD10 code from 31 July 2022 to 31 July 2024.
Results: Despite available treatments, two-thirds of respondents self-reported a seizure in the last month and 85% are on ≥1 ASM. Nearly half are unaware of their seizure type even when managed by a neurologist. More than 3/4 described their seizures as moderate-to-severe, with more than half believing they are uncontrolled. Half needed ≥2 ASMs, with higher usage among those seeing specialists or reporting recent seizures. Many patients with active seizures are not tracking their seizures, with both seizures and treatment side effects associated with significant quality of life impacts.
Conclusion: EMPOWER will generate standardized, longitudinal data to support planned interventional trials and deepen understanding of patient experiences of epilepsy. Preliminary findings reveal a significant disease burden compounded by persistent, uncontrolled, often untracked seizures alongside profound psychosocial impact.

1151 | Evaluating the Impact of Vagus Nerve Stimulation (VNS) on seizure frequency, intensity, quality of life and mood

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Purpose: Refractory epilepsy can be an extremely debilitating and life-limiting condition. Co-morbidities of mental health further impacts quality of life (QoL) for people with epilepsy. Vagus nerve stimulation (VNS) is an established treatment for drug refractory epilepsy when resective surgery is not appropriate. The purpose of this study was to ascertain the efficacy of VNS in reducing seizure intensity and frequency, and explore whether this has an impact on QoL, mood and/or cognition.
Method: 33 patients who had VNS inserted with a pre and post neuropsychology assessment were analyzed. We compared the seizure frequency, ictal and post ictal duration, cognition, QoL and mood (anxiety and depression) of patients pre-VNS and at 24 months post-VNS insertion using validated rating scales and clinical reviews.
Results: 33.3% experienced a greater or equal to (≥) 50% reduction in seizure frequency. In addition to a ≥50% reduction in seizure frequency, 91% had reduced post-ictal period and 81.8% had reduced seizure duration. Most patients' cognition was stable following VNS. Anxiety improved for 67% of those who experienced ≥50% reduction in seizures and for 67% who had a positive perception of VNS. Depression appeared to worsen across the board following VNS. QoL worsened in those with negative perception of VNS. However present data showed no clear correlation between a change in QoL and any reduction in seizure frequency.
Conclusion: VNS has an established potential to reduce seizure frequency and anxiety scores. Cognitive function appears maintained over time in those with VNS. Benefits on QoL appear to be most influenced by patient's perception of what VNS offers. The worsening of depression across the board is concerning especially as VNS has been used as a treatment for depression. Going forward, managing patient's expectations prior to VNS insertion is imperative to gain the most beneficial outcome.

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1164 | Examining the Staff Interaction and Understanding of the Current Digital Health System Framework for Epilepsy and Neurology in St. James's Hospital Dublin

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Purpose: Staff working in epilepsy and within the larger neurology department in St. James's Hospital (SJH) are besieged with clinical and operational data across several independent systems. Learning Health Systems (LHS) are being incorporated into clinical services and are a novel way of designing data systems, facilitating continuous analyzation of data by creating a feedback loop which aims to improve patient care and departmental efficiency.
Method: We conducted one-to-one, in person staff interviews with team members to determine how data is incorporated into practice. In total, we interviewed 33 members of the epilepsy and greater neurology service in our hospital. This included consultants (attendings), junior doctors (residents), nurses and administrative staff. We also inquired about AI understanding and use in medicine. This study was approved by the SJH Hospital Research and Innovation office.
Results: 66% of staff (n=22) reported attending a regular operational meeting within their department. While virtually all staff reported regular use of clinical data, only 45% (n=15) felt that their practice was driven by operational data. The most important piece of data requested was improved information on operational efficiency and clinical demand. Staff also reported poor data management and collection systems. An integrated electronic patient record was the most important piece of technology mentioned. Finally, 61% (n=20) of staff reported not understanding the basics of AI / machine learning in medicine.
Conclusion: Virtually all staff members were frustrated by the lack of a unified data collection system. Useful operational data and knowledge of AI appears to be limited in this cohort. These findings have been incorporated into a larger project currently developing a prototype LHS in collaboration with the Royal College of Surgeons in Ireland.

1192 | Does co-medication with methylphenidate and lisdexamfetamine influence seizure control in focal epilepsy? A case study

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Purpose: Attention deficit and hyperactivity disorder, ADHD, and epilepsy is a common comorbidity. Studies has not raised concerns on seizure increase in medically treated ADHD. We report a patient with focal epilepsy and ADHD where the treatment seemed to have a distinct negative influence on seizure frequency, illustrated by using an electronic seizure diary.
Method: Retrospective case report and digital seizure app.
Results: A 44 yrs woman was diagnosed after EMU with focal epilepsy in 2018. Carbamazepine, CBZ, and subsequently lacosamide, LAC, was added. In 2022 she was diagnosed with ADHD. Methylphenidate, MPH, was started without effect, and replaced by lisdexamfetamine, LDX. Treatment with MPH was associated with a slight increase of seizure frequency, which worsened with the switching from MPH to LDX – se fig 1. Baseline SF was between 1-8 pr month, but with LDX we saw a dramatic increase of seizure frequency up to 350/month (Fig.1). Treatment with CBZ was unchanged, whereas LAC was progressively increased (Fig. 2). LDX was switched to ATX due to the increase in seizure frequency. With ATX, seizure frequency improved, but had no effect on ADHD.
Conclusion: Our case report shows a correlation between increase of seizure frequency, following start of ADHD medication, in particular LDX. The increment of seizure frequency was not associated with changes in the serum levels of LCS and CBZ, excluding, interactions farmacokinetic between LDX and the antiepileptic drugs. Our study, although limited to one adult patient with focal epilepsy, shows that ADHD treatment can impact negatively on seizure frequency, suggesting that the seizure activity should be monitored carefully in epilepsy patients, who start treatment for ADHD.

1200 | Clinical and neurophysiological features of sleep-associated epileptic seizures

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Purpose: To study the clinical and electroencephalographic features of epileptic seizures associated with sleep.
Method: 107 patients with epilepsy aged 18 to 50 years were examined. Group 1 - 61 patients, epileptic seizures occurred exclusively in sleep, men accounted for 47.5% and women - 52.3%. The mean age was 24.3±0.6 years (18 to 35 years). In group 2, 46 patients had seizures while awake. The age of the patients ranged from 18 to 50 years

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(mean 28.1±0.8 years). Females predominated in a ratio of 1.1:1 (52.2% vs. 47.8%). Patients underwent a somatic and neurological examination, routine electroencephalography, and polysomnographic study, including EEG on the Neuron-Spectrum-4VP device from Neurosoft during sleep.

Results: Generalized seizures accounted for 63.4%, while focal seizures made up 36.6%. No gross neurological abnormalities were detected, but mild pyramidal signs were noted. Sleep EEG identified epileptiform activity in the frontal areas more frequently (17% in Group 1; 31.7% in Group 2) and secondary bilateral synchronization. The secondary bilateral synchronization during sleep EEG compared to waking EEG recording was significantly more often ($p < 0.05$) both in group 1 (23.4%) and group 2 (36.6%). Among patients of group 1, sleep EEG often reveals two independent foci of epileptiform activity with a predominance of frontal-central-temporal localization (19.5%). During video-EEG monitoring, epileptic seizures were recorded in patients of group 1 in 23.4% of cases, group 2 34.1%. All seizures were recorded in stages I-II of NREM sleep with the peak of seizure occurrence 20-30 minutes after falling asleep and immediately before awakening.

Conclusion: In patients with epileptic seizures during sleep, interictal epileptiform disturbances on the EEG were significantly more often ($p<0.05$) recorded during sleep (85.1%) compared to wakefulness (40.4%), whereas among patients with epilepsy during wakefulness, sleep EEG reveals interictal epileptiform activity in 4% of cases compared to the wakefulness (87.8%).

1205 | Epilepsia Partialis Continua: Insights from a 15-year cohort study

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Purpose: Epilepsia partialis continua (EPC) is a rare focal status epilepticus subtype, characterized by continuously repeated episodes (motor jerks or non-motor manifestations) with preserved consciousness lasting at least 1 hour (1). This study aimed to analyze the causes, treatment, and prognosis of a motor EPC cohort.

Method: This retrospective observational study reviewed adult motor EPC patients over 15 years (2010–2024). Demographic and clinical data were extracted from medical records.

Results: The study included 22 patients, mostly male (59%) with a mean age of 66 (SD=14). Around 40% of patients had a previous diagnose of epilepsy. EPC was the initial status epilepticus (SE) presentation in 64% (n=14). The remainder experienced prior other seizure types, including focal motor SE with impaired consciousness (n=5), non-convulsive SE (n=1), generalized tonic-clonic clusters (n=1), and generalized myoclonic SE (n=1). Affected body segments included upper limbs (82%), lower limbs (55%), face (32%), and abdomen (9%), mostly lateralized to the left. The most frequent etiologies were acute (41%) and remote (50%), being stroke and traumatic brain injury the most common underlying lesions. The median EPC duration was 4 days (IQ=3). Around 45% of patients were submitted to sedation and 23% required treatment with at least 4 anti-seizure medication. Corticosteroids treatment was added to anti-seizure medication in 36% of cases. Longer EPC duration correlated with male gender (p=0.018) and was associated with higher mortality (p=0.047), which was predominant in male without statistical significance. No other variables showed significant differences.

Conclusion: As described in literature, EPC is slightly more prevalent in males (2,3) and is often preceded by other seizure types (1). In this cohort, males experienced longer EPC durations and higher mortality, though only the duration association reached statistical significance.

1210 | Introducing needs-based epilepsy follow-up – patient satisfaction compared to traditional follow-up

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Purpose: People with epilepsy have diverse healthcare needs, but limited resources make tailored management challenging. To allocate resources where they are most urgently required, we developed an openly available needs-based follow-up model. This system adjusts follow-up frequency based on patients' symptoms, side effects, and other information reported digitally. Our study aimed to compare patient satisfaction with the needs-based model versus standard care follow-up.

Method: We sent a survey with 13 questions to epilepsy patients at three different Norwegian hospitals. Satisfaction was rated from one ("Not at all") to five ("To

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a very great extent"). Patients were categorized into three groups: (1) needs-based follow-up, (2) offered needs-based follow-up but declined or did not fill in any forms, and (3) standard care follow-up. We used Pearson's chi-squared test to compare the three groups, with p-values <0.05 as significant.

Results: Of 2,190 patients, 748 (34%) responded. Group 1 (n = 170) reported better satisfaction than group 3 (n=500) in areas such as meeting follow-up needs (p<0.001), communication with the treating physician (p<0.001), trust in their doctors (p<0.001), need for information being met (p<0.001), and tailored treatment (p<0.001). When compared to group 1, group 2 (n = 78) showed lower satisfaction with diagnosis information, involvement in follow-up, and accessibility of health care providers.

Conclusion: Patients with needs-based follow-up were more satisfied with their epilepsy treatment and follow-up than those with standard care follow-up. From the perspective of the user, needs-based follow-up improved epilepsy care, particularly regarding patient involvement in treatment decisions.

1221 | Epidemiology of catamenial epilepsy

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Purpose: The purpose of the current study was to investigate the incidence of catamenial epilepsy among patients with both focal and generalized forms of epilepsy.

Method: A retrospective, observational, uncontrolled, comparative, single-center study of the epidemiology of catamenial epilepsy was conducted at Almazov National Research Centre under state assignment No. 123021000127-7. The study involved two groups of female patients with epilepsy: Group 1 with generalized epilepsy and Group 2 with focal epilepsy. Data were collected from clinical histories, examining the type of epilepsy and the occurrence of catamenial seizures. Statistical analysis was performed using SPSS 29.0.10 with a confidence level of p=0.05.

Results: There were 148 patients: 68 with generalized and 80 with focal epilepsy. The mean age was 25.79 years, with no significant difference between groups ($p<0.05$). The mean age of epilepsy onset was 14.63 years, with a difference between groups of 14.87 and 16.54 years (p = 0.043). Women of reproductive age prevailed. There was no difference in the incidence of catamenial epilepsy between the generalized and focal groups: 44.12% and 57.5%, respectively. Temporal epilepsy was found in 61.4% and 38.6% of patients with focal epilepsy with and without catameniality, extratemporal epilepsy in 45.83% and 54.17%. In patients with generalized epilepsy, catamenial seizures occurred in 25.0%, 45.16% and 81.82% with absence, IDGE with GSP and JME, respectively. The frequency of catamenial seizures was higher when the difference between disease onset and menarche was +/- 3.07 years.

Conclusion: Among generalized epilepsies, the incidence of catamenial epilepsy is predominant in juvenile myoclonic epilepsy, and in the group with focal epilepsy - in temporal lobe epilepsy.

1227 | Blood-brain-barrier evaluation of patients with highly refractory, highly active focal epilepsy before and after high-dose intravenous methylprednisolone

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Purpose: We have observed a proportion of patients with highly refractory, highly active focal epilepsy experience a sustained response to immunomodulatory treatment with high-dose steroids despite negative autoimmunity screening. This is surprising, and we set out to investigate further by focusing on the effect of such treatment on the blood-brain barrier (BBB). Focal epilepsy is associated with BBB disruption, a key driver for seizure activity. Methylprednisolone is thought to have a stabilizing effect on the BBB; however, the mechanism of action of this therapy in this setting is unknown. Such understanding is vital and may aid the development of future therapies.

Method: We observed a cohort of ten patients in a prospective manner using clinical, imaging and serum biomarkers to study the effect of high-dose intravenous methylprednisolone on seizures and BBB integrity. Four weeks before treatment, patients underwent dynamic contrast MRI of the brain, intraocular pressure measurement, serum autoimmunity screen and BBB integrity biomarkers, including S100β, BDNF, Tau protein, MCP-1,

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IL-1β, IL-6, circulating microRNAs, adenosine and peripheral monocyte characterization. They then received 1g of IV methylprednisolone over three days, and the tests above were repeated four weeks later. In addition, seizure frequency was monitored for four to six months post-treatment to evaluate clinical response.

Results: Here, we present preliminary findings from this ongoing study, including an early signal of clinical response in most patients with evidence of BBB integrity improvement post-treatment demonstrated by dynamic contrast MRI and BBB disruption biomarkers.

Conclusion: There is a clear unmet clinical need for new therapeutic approaches in medication-refractory epilepsy, and there remains a paucity of research on the role of the BBB and the mechanism of action of high-dose steroids in this setting. Here, we demonstrate early evidence of a beneficial effect that may be mediated by an improvement in the integrity of the BBB in these individuals.

1241 | Highlights and differences between frontal lobe seizures and functional seizures from video-electroencephalography (VEEG) findings

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Purpose: To identify semiological features that distinguish functional seizures (FS) from frontal lobe seizures (FLS).

Method: A retrospective study was conducted on adult patients with either FLS or FS admitted to the Epilepsy Unit of Hospital el Cruce, Buenos Aires, Argentina. Patients with both seizure types were excluded. Based on VEEG findings, seizures were classified into 4 subtypes: hypermotor (HPM), focal motor (FM), akinetic (ACN), and subjective symptoms (SS).

Results: We included 108 patients (p), 61p with FS and 47p with FLS; 562 seizures were evaluated, 246 and 316, respectively. There were 47 (77%) females in the FS group and 29 (62%) in the FLS. The mean seizure duration was 5.05 min for FS and 1.15 min for FLS. Depression and anxiety were more common in FS than in FLS ($p<0.05$). All FS occurred during wakefulness. SS was observed in 20% of FS and 9% of FLS. The FM subtype was observed in 14.3% of FS and 57% of FLS. The HPM subtype was more common in FS (56.6%). The ACN subtype was exclusive to FS (11.6% $p<0.05$). Eyes closed (33.9%) and bilateral fists (54.6%) were relevant in FS ($p<0.05$). Ictal crying, head movements (side-to-side), and opisthotonus posture were exclusive to FS ($p<0.05$). Pelvic thrusting, asynchronous limb movements, and urinary incontinence did not show statistical significance.

Conclusion: While VEEG remains the gold standard for diagnosing both FLS and FS, identifying specific semiological features is crucial in settings with limited access to advanced diagnostics tools. Our study highlights the value of recognizing these features to aid clinical decision-making and improve patient outcomes.

1248 | Atypical Course of Adult-onset Rasmussen Encephalitis

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Purpose: Rasmussen Encephalitis (RE) is a chronic progressive inflammatory brain disease characterized by drug-resistant epilepsy, progressive neurological deficit. The most aggressive increase in the symptom severity and brain atrophy is observed in the first 8 months from seizure onset.

Method: to describe a clinical case of adult-onset RE

Results: 33-year-old woman with unremarkable history. The disease manifested at the age of 22 years with headaches in the left temporal region followed by behavior arrest up to 20 times a day, resistant to anti-seizure medications. Within 1-year headaches had been supplemented with visual phenomena in the right eye. After 5 years from disease onset, the first bilateral tonic-clonic seizure with Todd paresis had developed. After 7 years right sided hemiclonic seizures had occurred. After 10 years from onset, right-sided somatosensory seizures had developed, followed by bilateral tonic-clonic seizures and Todd paresis. Cognitive and speech impairment had also occurred. All symptoms presented as attacks lasting for 1 month, regressing completely or partially afterwards. Dynamics of magnetic resonance imaging (MRI, 2013–2023): diffuse

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areas of increased MR-signal intensity on T2 and T2 FLAIR sequences, decreased T1-signal in white and gray matters of the left hemisphere, with no signs of true limitation of diffusion, pathological contrast enhancement or mass. MRI dynamics was undulating: T2-hyperintense areas became smaller, causing a moderate atrophy of affected regions, followed by new areas with similar signal characteristics and evolution. Video-electroencephalography monitoring 24 hours (2024): persistent interhemispheric asymmetry of physiological patterns. Focal epileptiform discharges were detected in the left occipital-posterior temporal region. The total of 111 focal electrographic seizures were recorded. Infectious and autoimmune encephalitides, mitochondrial encephalopathies, and systemic diseases were excluded.

Conclusion: According to the 2005 Bien criteria, the patient was diagnosed with RE. The clinical case in remarkable for its long-term progression and undulating course of symptoms.

1254 | Long-term prognosis in Traumatic Brain Injury: Do early seizures and prophylactic antiseizure medications influence outcomes?

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Purpose: Early post-traumatic seizures are a well-recognized complication of traumatic brain injury (TBI), with a variable incidence and an association with poorer functional outcomes. While antiseizure medication (ASM) initiation is widely accepted upon seizure occurrence, the role of prophylactic ASM in TBI remains controversial. This study aimed to assess the administration of prophylactic ASM in TBI and identify predictors of long-term functional outcomes.

Method: This retrospective observational study included patients admitted to a Neurology department with TBI-associated intracranial injury between 2021 and 2023. Sociodemographic and clinical characteristics of the cohort were analyzed. Functional outcomes were assessed using the Glasgow Outcome Scale-Extended (GOS-E), with favorable outcomes defined as a 12-month GOS-E >4 (primary outcome). Secondary outcomes included the occurrence of early seizures and post-traumatic epilepsy. Logistic regression and Cox proportional hazards models were employed to identify prognostic factors.

Results: The cohort comprised 158 patients (59% male; mean age 75.4±14.7 years), with moderate-to-severe TBI observed in 26% (n=41). Subdural hematoma was the most frequent intracranial lesion (63%). Prophylactic ASM was prescribed in 11% (n=18) of patients, while early seizures were documented in an equal proportion (11%). Electroencephalographic findings revealed epileptiform discharges in 10 patients, leading to prophylactic ASM initiation in 2 cases. A favorable functional outcome (GOS-E >4) was achieved in 67% of the cohort. Prophylactic ASM administration did not significantly reduce the incidence of early seizures or post-traumatic epilepsy. In multivariate analysis, pre-existing functional independence (modified Rankin Scale <3), age <80 years, and mild TBI emerged as independent predictors of better 12-month functional outcomes.

Conclusion: In this cohort, TBI severity, pre-existing functional independence, and age were key determinants of long-term outcomes, while neither early seizures nor prophylactic antiseizure medication significantly impacted functional prognosis.

1279 | Characterization of ictal hand postures as a localizing and lateralizing sign in frontal and temporal lobe epilepsy

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Purpose: To identify ictal hand postures (IHPs) as a localizing and lateralizing sign in frontal lobe epilepsy (FLE) and temporal lobe epilepsy (TLE).

Method: Retrospective observational study conducted at the VEEG (video-electroencephalography) Unit, Hospital el Cruce, in Buenos Aires, Argentina from 2014 to 2023, in adult patients with frontal lobe epilepsy (FLE) and temporal lobe epilepsy (TLE). The IHPs were reviewed in the VEEG recordings. We defined IHPs as the first motor sign during 5 seconds at the onset of a focal impaired awareness seizure. The IHPs were divided into six subtypes: fist, cup, politician´s fist, pointing, pincer, and extended hand. Correlations were made with the ictal onset zone (IOZ), lesional area, and the laterality of the hand used to perform the IHPs. Statistical analysis was performed using the SPS program, chi-square, with statistical significance set at p<;0.05.

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Results: a total of 461 patients (p) were included, 54p presented IHPs, 24p (44.44%) in FLE, and 30p (55.56%) in TLE, with mean age 33.6 years, age at first seizure 12.6 years. Women 61.11%, right-handed 90.74%. A total of 285 seizures were analyzed, 201 (70.5%) presented IHPs, in FLE 133 (66%), and 68 (33.8%) in TLE. The subtypes of IHPs: fist, extended, and pointing were more frequent in FLE ($p<0.05$), however cup, politician´s fist, and pincer were more frequent in TLE ($p<0.05$). The pincer hand was only seen in TLE and the pointing hand was only in FLE ($p<;0.001$). The IHP was contralateral to the IOZ in both groups ($p<0.001$).

Conclusion: The IHPs are an easily identifiable semiological sign in VEEG recordings. This study highlights their localizing value in FLE and TLE and proposes their potential lateralizing value, which according to our findings could be contralateral to the IOZ in both groups FLE and TLE.

1292 | Eating Epilepsy: A Case Series

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Purpose: Eating epilepsy is a disorder characterized by reflex seizures triggered by food intake. Although its pathophysiology remains unknown, disruptions in neural circuits involving the insular, orbitofrontal and temporal cortex, as well as the hypothalamus and amygdala may be implicated. (Ruiz-León et al., 2021) (Girges et al., 2020)

Method: A retrospective analysis was conducted involving patients with eating epilepsy at a Portuguese tertiary hospital. Clinical data including demographics, seizure semiology, electroencephalogram (EEG) findings and treatment regimens were reviewed.

Results: First case: 38-year-old man with focal onset seizures without loss of awareness characterized by clonic movements of the face and left upper limb, beginning at the age of 12. Episodes occurred daily, typically during meals, lasting approximately one minute, and sometimes progressing to bilateral tonic-clonic seizures. MRI revealed a right parietal cortico-subcortical lesion, hypothesized as ulegyria. Long-term video-EEG monitoring (five days) recorded five electroclinical seizures, two triggered by meals and three during sleep, with generalized attenuation of electrical activity without an accurate focus. Treated with levetiracetam (3000 mg/day), lacosamide (400 mg/day), zonisamide (200 mg/day) and perampanel (8 mg/day), achieving seizure freedom since 2024. Second case: 86-year-old man developed stereotyped clonic movements of limbs with altered awareness following a traumatic brain injury in 2020. The seizures occurred daily, lasted a few seconds, and were followed by rapid recovery and amnesia of the event. Most episodes were triggered by meals, though some occurred during sleep. MRI revealed bilateral temporal and frontal cortical-subcortical encephalomalacia secondary to trauma. Situational video-EEG recorded a seizure during feeding, with epileptiform activity in the bilateral temporo-parieto-occipital regions. Treated with eslicarbazepine (1600 mg/day) and levetiracetam (2000 mg/day) resulting in reduced seizure frequency.

Conclusion: Epilepsy with reflex seizures is a rare condition in which detailed semiological description and situational video-EEG are essential for accurate diagnosis and management.

1308 | EEG demonstration of the efficacy of glasses with a selective filter for treating photosensitive epilepsy

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Purpose: Photosensitive epilepsy is a type of reflex epilepsy where seizures are triggered by visual stimuli. In purely photosensitive epilepsies, prevention and management of seizure-inducing stimuli are recommended as a first-line therapeutic strategy, using antiseizure medications (ASMs) only when strictly necessary. Other measures, such as the use of special glasses, have been proposed as a therapeutic option for these patients. We present two cases of photosensitive epilepsy where the benefit of glasses with specific filters was demonstrated through EEG recordings.

Method: Patient #1 is a 19-year-old woman with newly diagnosed juvenile myoclonic epilepsy, with myoclonic seizures and one generalized tonic-clonic seizure, both exclusively triggered by light stimuli. She had never used ASMs. Patient #2 is a 19-year-old woman with non-lesional (normal MRI) parieto-occipital focal epilepsy, with focal aware seizures consisting of visual size distortions (micropsia) since the age of 5, as well as one focal

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to bilateral tonic-clonic seizure. Her seizures occur both spontaneously and triggered by visual stimuli, including lights and geometric patterns. She is taking eslicarbazepine with insufficient seizure control. Previously, she tried lamotrigine and levetiracetam but discontinued them due to adverse effects.

Results: The initial EEG performed without treatment in both patients showed spontaneous interictal epileptiform discharges (IEDs) and photoparoxysmal responses to medium and high stimulus frequencies during intermittent photic stimulation (IPS). A therapeutic trial using glasses with a selective filter that cut wavelengths up to 380 nm during a new IPS significantly reduced IED frequency and propagation. Both patients started using the glasses with good seizure control but eventually limited their use to specific situations due to aesthetic reasons.

Conclusion: The use of glasses with a selective filter with a cut-off at 380 nm may be an effective treatment for people with photosensitive epilepsy. Testing their efficacy during interictal EEG can help to predict their effectiveness in controlling clinical seizures.

1328 | Blood melatonin content in patients with sleep-related epileptic seizures

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Purpose: To investigate blood melatonin parameters in patients with sleep associated epileptic seizures.

Method: 107 patients with epilepsy aged 18 to 50 years were examined. Group 1 - 61 patients, epileptic seizures occurred exclusively in sleep, men accounted for 47.5% and women - 52.3%. The mean age was 24.3±0.6 years (18 to 35 years). In group 2, 46 patients had seizures while awake. The age of the patients ranged from 18 to 50 years (mean 28.1±0.8 years). Females predominated in a ratio of 1.1:1 (52.2% vs. 47.8%). Patients were analyzed according to the NHS3 scale, Epworth scale, quality of life was determined with QOLIE-31 scale (Quality of Life in Epilepsy).

Results: Patients of group 1 had a total NHS3 score 1.4 times higher than group 2 (21.9±0.5 versus 15.3±0.4; P<0.01). On the Epworth scale, group 1 had more severe sleep disturbances than group 2 (18.61±0.48 versus 9.48±0.53 points; P<0.001). Quality of life on the QOLIE-31 scale in sleep epilepsy was significantly lower in sleep epilepsy than in patients with waking epilepsy (45.4±2.3 points and 52.4±2.2 points, respectively; P<0.01). The study of melatonin content found that in group 1, the average melatonin values are 24.75±3.6 (38.3-19.0), group 2 - 97.8±3.4 (106.5-85.0), significantly higher in relation to group 1 (P<0.01), lower in relation to control (99.6±3.5; 89.1-110.0). Correlation analysis revealed the dependence of melatonin level on the severity of epileptic seizures according to the NHS3 scale (r=-0.652; p=0.003), sleep disturbance according to the ESS scale (r=-0.852; p=0.002) and the level of patients' quality of life according to the QOLIE-31 scale (r=-0.587; p=0.003).

Conclusion: It was found, melatonin content, that in patients with sleep epilepsy mean melatonin values were significantly decreased in relation to those of patients with waking epilepsy (P<0.01), indicating short and jittery sleep.

1334 | Exploring the roles of nesfatin-1 and ghrelin as potential biomarkers in human epilepsy

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Purpose: Epilepsy, a chronic neurological condition characterized by recurrent seizures, affects millions globally, with approximately 30% of patients exhibiting pharmacoresistance. The discovery of novel biomarkers is crucial for advancing diagnosis, treatment, and outcome prediction. Neuropeptides such as ghrelin and nesfatin-1, known for their regulatory roles in metabolism and neuroprotection, have emerged as potential candidates for investigation in epilepsy.

Method: This systematic review analyzed 26 studies on ghrelin and five on nesfatin-1 published between 2005 and 2024. Data on serum and saliva levels, methodologies, patient characteristics, and outcomes were extracted. Discrepancies between reviewers were resolved through consensus.

Results: Ghrelin levels showed variability across epilepsy types and treatments. While 38% (n=10/26) of studies reported reduced ghrelin levels in epilepsy patients compared to healthy controls (HC), 27% (n=7/26) found increased levels, particularly in focal epilepsy (FE) and self-limited focal epilepsy (SeLFE). Ghrelin levels were higher in patients responsive to antiseizure medications (ASMs), suggesting its potential as a biomarker for treatment efficacy. Conversely, nesfatin-1 levels were consistently elevated in epilepsy patients (80% of studies n=4/5)),

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with reductions observed in drug-resistant temporal lobe epilepsy (TLE) and following prolonged ASM use. Notably, nesfatin-1 levels positively correlated with seizure frequency and disease prognosis.

Conclusion: The review highlights the complex roles of ghrelin and nesfatin-1 in epilepsy. While ghrelin demonstrates variable patterns influenced by epilepsy type, treatment, and age, nesfatin-1 shows promise as a reliable biomarker for disease severity and treatment monitoring. Future research should focus on elucidating these neuropeptides' mechanisms and their therapeutic potential.

1335 | Characterization of complex motor automatisms in focal epilepsy: a case series

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Purpose: To analyze the presence of complex motor automatisms (CMAs), and its localizing and lateralizing value, in adult patients diagnosed with frontal lobe epilepsy (FLE) and temporal lobe epilepsy (TLE).

Method: This is a retrospective observational study. We reviewed the video-electroencephalographic (VEEG) records of adult patients diagnosed with TLE and FLE who were admitted to the VEEG Unit between 2021 and 2024 at Hospital El Cruce, in Buenos Aires Argentina. Our analysis focused on the presence of CMAs, their frequency, onset timing ictal or postictal), and the correlation between the ictal onset zone (IOZ), hand laterality, and neuroimaging findings.

Results: A total of 145 patients with focal epilepsy were admitted, including 91 patients with TLE (360 seizures) and 54 patients with FLE (292 seizures). CMAs were observed in 4 patients (14 seizures), all of whom had TLE with focal impaired awareness seizures. CMAs occurred exclusively during the ictal period.

Patient 1: Exhibited "The sign of the Cross" with the right hand, ipsilateral to the IOZ and the lesional zone (right hippocampus).

Patient 2: Displayed "reaching or grasping movements" with the right hand, ipsilateral to the IOZ and the lesional zone (right temporal gliosis).

Patients 3 and 4: Both showed similar movements resembling "sewing and needle-threading behavior" in which they remained still, using their left hand to hold an imaginary needle while their right hand moved actively, mimicking the threading motion. Both had the IOZ and the lesional zone in the left temporal region with hippocampal sclerosis.

Conclusion: CMAs represent a rare seizure manifestation observed in patients with focal epilepsies. In the present study, CMAs were observed exclusively during the ictal period in patients with TLE, and did not exhibit clear lateralization value.

1346 | Impact of epileptiform activity during sleep on the cognitive performance of patients with epilepsy

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Purpose: To evaluate the impact of interictal epileptiform discharges (IEDs) during sleep on cognitive performance in patients with epilepsy.

Method: A cross-sectional observational study was conducted on adult patients with epilepsy treated at a tertiary center between 2020 and 2024 , in whom polysomnography (PSG) and neuropsychological evaluation (NPSE) were performed at an interval of less than one year. Clinical and demographic data, PSG parameters, and NPSE results were collected. Cognitive domains were analyzed using linear regression models to identify associated variables.

Results: A total of 137 patients were included (57 % female, mean age 46.9 ± 19.6 years). The median duration of epilepsy was 10 years (IQR: 4-24). Most patients had focal epilepsy (90 %), mainly of temporal origin (48 %), and with unknown etiology (54 %). Fifty-eight percent of patients had drug-resistant epilepsy. PSG findings revealed that 74% of patients exhibited normal baseline activity, while 71% presented IEDs during sleep; of these, 21% were identified during REM sleep. In the NPSE, the most frequently impaired cognitive domains were attention (40%), processing speed (38%) and visuospatial skills (30%). Diffuse or asymmetric slowing in baseline EEG activity correlated with greater impairment in attention ($p = 0.013$) and processing speed ($p = 0.01$). The presence of IEDs during REM sleep was exclusively associated with attention impairment ($p = 0.018$).

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Conclusion: The presence of IEDs during REM sleep is associated with poorer performance in attentional functions in adults with epilepsy. Baseline brain activity and the pattern of occurrence of IEDs may provide useful information in the assessment of cognitive performance in this population.

1352 | Neuro-ophthalmological changes in temporal lobe epilepsy and its surgical treatment

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Purpose: To evaluate ganglion cell complex (GCC) and retinal nerve fiber layer (RNFL) thickness, pupil diameter in light and in the dark assessment in patients with mesial temporal lobe epilepsy (MTLE).
Method: Cross-sectional research included 28 patients (56 eyes) with MTLE (average age 36.7 years, 15 women) of the study group, 17 volunteers (34 eyes) of the control group (average age 31.0 years, 11 women). In the study group, all patients received anti-seizure medications, 16 patients additionally underwent resection of the epileptogenic focus. All study participants underwent standard eye exam (visometry, tonometry, perimetry, biomicroscopy), optical coherence tomography.
Results: There were no significant differences in functional parameters between two groups. The best corrected visual acuity in study group exceeded 0.8. RNFL thickness in the control group was 100.53±6.25 μm, GCC – 98.17±5.12 μm. RNFL and GCC thickness in patients with MTLE was significantly lower compared to the control group and amounted to 93.93±10.69 μm (p=0.002) and 93.62±11.06 μm (p=0.030), respectively. The pupil diameter in the control group was 3.38±0.46 mm (on light) and 5.39±0.80 mm (in the dark). The pupillary reflex in the study group was preserved with an overall increase in pupil diameter (3.55±0.79 mm in the light, 5.83±0.97 mm in the dark). The only noteworthy difference was between pupil diameter in the dark (p=0.045).
Conclusion: Retinal inner layers atrophy may be associated with damage to visual fibers in the area of epileptogenic focus or their injury during surgical treatment. It is also worth considering the constant intake of antiepileptic drugs in examination results. Significant decrease in the GCC and RNFL thickness, increase in pupil diameter in the dark, while maintaining the response to light, was determined in patients with MTLE was observed with the control group. This neuro-ophthalmological change is multifactorial and requires an integrated approach.

1354 | Patterns of long-term pharmacoresponse in different etiologies of epilepsy

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Purpose: To evaluate patterns of pharmacoresponse in patients with different etiologies of epilepsy.
Method: 445 patients (mean follow-up of 15 years, range 2-47 years) were split according to pharmacoresponse into seizure-free in the last two years or more (n=106), relapsing-remitting (seizure-freedom periods of one year or longer, n=123), or pharmacoresistant (never had a seizure-free period of more than one year, n=216). Six patients had an atypical older age of onset and were excluded. Patients were diagnosed with TLE with hippocampal sclerosis (TLE-HS, n=282), TLE without HS (TLE-nonHS, n=60), extratemporal focal epilepsy (Extra-TLE, n=45) or Genetic Generalized Epilepsy (GGE, n=58), following ILAE-criteria. Patients' data were collected until the last appointment or before surgery. We analyzed the seizure frequency longitudinally, time to achieve seizure freedom, family history, sex, age of onset and duration of epilepsy, and antiseizure medications (ASM). Generalized linear models (including pharmacoresponse and etiology as main effects) or chi-square tests, accordingly, were used. P<0.05 Sidak-corrected was set as significant.
Results: In the seizure-free and relapsing-remitting groups, GGE was the most frequent, with 38% and 50%, respectively, while the pharmacoresistant group was predominantly TLE-HS (75%). Within focal epilepsies, pharmacoresistance was more frequent in right-sided or bilateral seizure focus (p=0.007). There was an effect of etiology (p=0.004) but not pharmacoresponse (p=0.8) on the age of onset, with TLE-HS presenting an earlier age of onset than TLE-nonHS (p=0.002). TLE-HS had a longer period to achieve seizure-freedom when it occurred (mean 36 years, p=<0.001). Family history, use of carbamazepine, sex, and presence of tonic-clonic seizures in the last visit were similar between groups of pharmacoresponse (all p>0.540).
Conclusion: Bilateral and right-sided seizure focus correlated to pharmacoresistance, independent of the type of epilepsy. 18,4% of patients with TLE-HS achieved seizure-freedom without surgery but only after several decades of uncontrolled seizures.

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1376 | Stakeholder workshops to optimize design of a risk prediction webtool for seizure prediction in people with epilepsy – The PRISE study

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Purpose: Making treatment decisions with people with epilepsy can be challenging because of the heterogeneity of the patient population. Discussions regarding treatment decisions may benefit from information about the potential number of future seizures. The PRISE project will provide a prediction of future seizures for adults with epilepsy by developing a prediction model that uses information about their seizures in the past to predict the number of future seizures expected in a chosen timeframe. The prediction model will be translated into a webtool for epilepsy specialists to use during hospital appointments with people with epilepsy. To ensure the webtool is fit for purpose, we have spoken to stakeholders to explore their preferences for design features, including layout, data entry and presentation of webtool results.

Method: Six knowledge exchange workshops were run between July and September 2024, with two groups of stakeholders from across the UK: 13 people employed as epilepsy specialists, and 21 service users took part. The latter group consisted of people with epilepsy and friends and family of people with epilepsy. Participants were recruited using social media and email cascades from Epilepsy Action and professional networks of epilepsy specialists. Workshops were audio recorded and transcribed, and data will be analyzed using Hamilton's Rapid Analysis.

Results: Results will surface stakeholder preferences for data input in the webtool, and the way webtool results are presented. They will also surface concerns, expectations and perceived benefits of using a webtool to predict future seizures during a hospital appointment. The workshop findings will be used to optimize the design of the webtool in preparation for testing in a separate sub-component of the PRISE project.

Conclusion: Stakeholder preferences will be used to optimize the design of a seizure prediction webtool, ensuring the webtool is appropriate to use during hospital appointments with people with epilepsy.

1377 | Two-Year Experience of a Newly Established Epilepsy Monitoring Unit in a Resource-Limited Setting

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Purpose: This study presents a 2-year experience of a newly implemented Epilepsy Monitoring Unit (EMU) in Mexico, addressing its clinical impact, procedural metrics, and challenges in a resource-constrained environment

Method: This retrospective study included 117 patients admitted to the EMU of a private hospital in central-western Mexico between February 2023 and December 2024. Patients underwent tailored protocols for long-term video-EEG monitoring for diagnostic clarification, treatment optimization, or presurgical evaluation. Data were analyzed to evaluate diagnostic and therapeutic outcomes, seizure yield, and safety metrics.

Results: The EMU facilitated diagnostic changes in 59% of patients, with 80.3% undergoing treatment modifications. Among presurgical evaluation patients, 80.8% exhibited seizures during admission. The seizure yield was lower for treatment optimization (25.8%) and diagnostic clarification (43.3%) groups. Twelve patients underwent epilepsy surgery, with resective procedures being the most common. Adverse events, including status epilepticus and seizure clusters, occurred in 2.5% and 0.8% of patients, respectively, with no complications linked to antiseizure medication withdrawal.

Conclusion: The implementation of a high-quality EMU is achievable in resource-limited settings. This study highlights the importance of tailored protocols and multidisciplinary collaboration in addressing diagnostic and therapeutic challenges, providing a framework for other centers to optimize epilepsy care in underserved regions.

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1382 | Lipid profile and apolipoprotein E isoforms in adults with drug-resistant epilepsy treated with modified Atkins diet

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Purpose: Modified Atkins diet (MAD) is a treatment option for drug-resistant epilepsy (DRE). Due to its high fat content, the impact on lipid levels is a concern, especially in adults. The current study explored the lipid profile and Apolipoprotein E (ApoE) isoforms in adults with DRE treated with MAD.
Method: We conducted an observational, prospective, unicentric study in adults with DRE treated with MAD. Serum levels of total cholesterol, low-density lipoprotein cholesterol (LDL), high-density lipoprotein cholesterol (HDL) and triglycerides were assessed at baseline, 3 and 12 months. ApoE isoforms were genotyped. Statistical analysis was performed using Wilcoxon and Mann-Whitney tests.
Results: Eighty patients were included, 43 (53,8%) were female. At baseline, 26 patients (32,5%) had dyslipidemia (LDL>116mg/dL; triglycerides>150mg/dL). ApoE isoforms were assessed for 78 patients. Compared to baseline, participants on MAD for 3 months showed significantly increased levels of total cholesterol (p<0,001), LDL (p<0,001) and triglycerides (p=0,002). Compared to baseline, patients on MAD for 12 months showed significantly increased levels of total cholesterol (p=0,003) and HDL (p=0,002). Compared to 3 months, patients on MAD for 12 months showed significantly decreased levels of total cholesterol (p=0,016), LDL (p=0,033) and triglycerides (p=0,045), and significantly increased levels of HDL (p=0,046). ApoE2 isoform was associated with significantly decreased levels of total cholesterol and LDL at baseline (p=0.013; p=0.002) and 12 months (p=0,021; p=0,038). We didn't find any association between the variation of the lipid profile and ApoE4 or ApoE2.
Conclusion: MAD induces a poorer lipid profile in patients, particularly at 3 months. These values tend to recover by 12 months, compared to the 3 months assessment. This should be considered when studying adult patients on MAD. ApoE2 isoform confers protection against dyslipidemia, specifically regarding total cholesterol and LDL, with consistent results at both baseline and at 12 months.

1384 | A Rare Presentation in Epilepsy: Report of "Triple Pathology"

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Purpose: Triple pathology refers to the presentation of three simultaneous lesions, which may share a common origin or result from the progression and reorganization of epileptogenic networks. This condition impacts directly the patient's prognosis.
Method: Patient information was extracted from physical and electronic medical records at the NINN. Informed consent was obtained from the patient.
Results: A 32-year-old right-handed male with no family history of epilepsy attended our epilepsy clinic. Seizure onset at age 21 with episodes during sleep characterized by sensations of overheating followed by tonic-clonic bilateral seizures, with postictal dizziness and prolonged somnolence. Four months later, he re-experienced dizziness and subjective sensation of movement. At age 23, his seizures involved episodes of déjà vu, complex visual hallucinations of cartoon-like figures, behavioral arrest, and tonic posturing of all four limbs. These episodes lasted approximately 1.5 minutes and 30 minutes postictal state. Frequency increased to over 60 seizures per month. Antiseizure medications were valproate, lamotrigine, and brivaracetam. Interictal Video EEG showed mild focal slowing and epileptic activity in the left temporal region.

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MRI revealed a heterogeneous occupative lesion with poorly defined borders, cystic components, and calcifications in the left parahippocampal gyrus, along with an atrophic left hippocampus with increased T2/FLAIR signal intensity. Patient underwent a left temporal lobectomy. Histopathological and immunohistochemical analyses revealed cortical tissue positive for MAP2 and NeuN, with neuronal loss and diffuse GFAP staining. Hippocampal tissue showed NeuN loss, while lesion tissue was positive for NeuN, MAP2, GFAP, CD34, and Ki67. The findings were consistent for WHO Grade I ganglioglioma, associated with focal cortical dysplasia and mesial temporal sclerosis of the left hippocampus.

Conclusion: Triple pathology is a rare condition in epilepsy pathology, as in this case that presented with temporal lobe epilepsy with hippocampal sclerosis (TLE-HS), focal cortical dysplasia (FCD), and ganglioglioma; all highly epileptogenic.

1385 | Epilepsy associated with low versus high-grade brain tumors: what do our patients tell us?

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Purpose: Seizures occur, frequently, as an initial symptom of brain tumor as well as during the course of the disease (Avila EK et al, Neuro Oncol. 2024; 26:7-24). This study aims to evaluate clinicopathological features of patients with epilepsy associated with low versus high-grade brain tumors.

Method: Data from patients attending outpatient epilepsy department, from June/2023 to July/2024, with diagnosis of epilepsy associated with brain tumors was collected from clinical records. WHO classification was used to define low (1-2) and high (3-4) grade tumors. Non-parametric tests were used for continuous variables comparison and Chi-square test for proportion analysis.

Results: This study included 57 and 26 patients with epilepsy associated with low and high-grade brain tumors, respectively. No significant differences were observed for age or age at diagnosis. Overall, brain tumors were more prevalent in males. Meningiomas were the most prevalent low-grade tumor in our cohort (47.4%), while high-grade tumors were predominantly glioblastomas (42.3%). More than 50% of brain tumors were located in frontotemporal regions and almost 60% in the left hemisphere, with no differences between groups. Total surgical resection was achieved in 66,7% and 36% of low and high-grade tumors, respectively ($p<0.012$). Most patients presented with aware focal seizures in both groups. Median number of anti-seizures medications (ASM) was 2 (1-6) and 1.5 (1-3) in patients with low versus high-grade, respectively. Seizure control (Engel I/II class) was achieved in approximately 54% of patients in both groups. More than 2 ASM for seizure control were more frequently needed in patients with low-grade than with high-grade tumors (28,1 vs 11,5%).

Conclusion: This study shows that our patients with epilepsy associated with brain tumors are well controlled despite tumor grade. Although not significantly different, patients with low-grade brain tumors needed, more often, a higher number of ASM for seizure control.

1468 | Predictive Performance of Diagnostic Algorithm for Seizure Outcome in Autoimmune Epilepsy: Multicenter Cohort Study in Japan

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Purpose: Autoimmune epilepsy (AEpi) is a subtype of epilepsy caused by autoimmune mechanism, partly associated with anti-neuronal antibodies, and is often treated with immunotherapy and antiseizure medication (ASM). In Japan, comprehensive anti-neuronal antibody testing remains challenging due to cost and technical limitations. Accurate and rapid prediction of seizure outcome in AEpi

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patients without waiting for antibody results is clinically important to facilitate appropriate management. While several diagnostic tools including algorithms have been developed to predict antibody positivity in AEpi, their ability to predict seizure prognosis remains unclear. This study aimed to evaluate the effectiveness of an existing algorithm in predicting seizure outcome in AEpi patients.

Method: This multicenter cohort study followed AEpi patients for 6 months. According to the existing algorithm for AEpi, inclusion criteria were: 1) epilepsy (≥1/month) or subclinical seizures (≥2/ on EEG), 2) clinical features, and 3) examination findings (CSF, EEG, brain MRI, or FDG-PET/SPECT) suggesting autoimmune mechanisms. The primary outcome was ≥50% reduction in seizure frequency, as improvement. Predictive modeling used logistic regression to analyze examination factors. The area under the receiver operating characteristic curve (AUC) were employed to assess the predictive performance of the model. Additionally, the bootstrap resampling method was utilized to adjust the optimism.

Results: Of 76 eligible patients, anti-neural antibodies were positive in 29 patients (38%). ASM was administered to 74 patients (97%) and immunotherapy to 55 (72%). At 6 months, 53 patients (70%) showed seizure improvement. The AUC of the prediction model was 0.734 (95%CI 0.618 to 0.849) with an optimism-adjusted C value of 0.678 (95%CI 0.569 to 0.778).

Conclusion: In AEpi patients, the existing diagnostic algorithm showed limited ability to predict seizure outcome after 6 months. Further refinement of prediction models is necessary to improve prognosis and management of AEpi patients.

1481 | Preventing Post-Stroke Epilepsy with Antihypertensive and Lipid-Lowering Medications

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Purpose: Post-stroke epilepsy (PSE) is a significant complication of ischemic stroke, adversely affecting outcomes and morbidity. This study investigated the potential of repurposing various medications, with a particular focus on antihypertensive drugs such as losartan and lipid-lowering agents like atorvastatin, to influence epileptogenesis and prevent the development of PSE.

Method: This retrospective study analyzed data from 1329 ischemic stroke patients at the University Hospital Zurich. The cohort was divided into two groups: patients who developed PSE and those who did not. The intake of medications and its association with PSE development were compared between these groups. Descriptive statistics summarized key variables, and propensity score matching was performed to reduce selection bias by matching patients based on baseline characteristics.

Results: The use of atorvastatin and losartan was associated with a numerically reduced risk of developing PSE. Patients treated with losartan had a seizure incidence of 7.32% compared to 12.5% in untreated patients, with an odds ratio (OR) of 0.55 (95% CI: 0.13–1.55) before matching and 0.38 (95% CI: 0.08–1.50) after matching. For atorvastatin, the seizure incidence was 11.68% in treated patients versus 14% in untreated patients, with an OR of 0.81 (95% CI: 0.57–1.16) before matching and 0.73 (95% CI: 0.50–1.08) after matching. While these findings did not reach statistical significance, they suggest a trend toward a protective effect of these medications against the development of PSE. Additionally, analyses revealed no significant protective effects for other antihypertensive or lipid-lowering medications.

Conclusion: The observed trends support the hypothesis that losartan and atorvastatin may protect against the development of PSE. These findings provide a foundation for future research and highlight the potential for drug repurposing to prevent seizures and improve post-stroke outcomes.

1505 | Reassessing Developmental and Epileptic Encephalopathies in Adulthood: Insights from a Transition Clinic

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Purpose: Traditionally, developmental and epileptic encephalopathies (DEEs) have been primarily defined in pediatric populations. Advances in symptomatic and supportive treatments significantly improved survival, allowing many individuals with DEE to reach adulthood, where they present distinct clinical features differing from those observed in children.

Method: The Transition Clinic, established in 2022 at the Epilepsy Centre of the University Hospital of Rome Tor Vergata, facilitates a multidisciplinary

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reassessment of diagnostic and therapeutic pathways. Child Neuropsychiatrist and Neurologist collaborate to re-evaluate patients through clinical history reviews, brain MRI, electroencephalographic (EEG) data, and genetic testing. Older adult patients have also come to our attention, highlighting the challenges they face in accessing and continuing care.

Results: During this period, 10 patients were diagnosed with DEE for the first time in adulthood. A representative case is S.C., a 47-year-old patient with a long-standing history of epilepsy and intellectual disability. Over time, he has primarily experienced tonic-clonic generalized seizures, but also atypical absences and atonic seizures. Additionally, he suffers from severe obstructive sleep apnea syndrome (OSAS) for which he receives continuous positive airway pressure (CPAP) therapy. Despite extensive treatment with Levetiracetam, Valproic Acid, Lamotrigine, Phenobarbital, and Clobazam, generalized seizures persisted in clusters. A re-evaluation of his clinical history, incorporating new electroencephalographic data, led to a reclassification of his condition as Lennox-Gastaut syndrome. Consequently, S. C. became a candidate for highly purified Cannabidiol therapy (5 mg/kg twice a day) and has remained free of generalized seizures for several months after starting this treatment. Moreover, the possibility to interact with the family members and sleep improved.

Conclusion: A structured transition process, including a thorough diagnostic reassessment, is crucial to optimizing treatment strategies in adult patients with DEE. This improvement in seizure control can increase the quality of life of patients and caregivers by addressing associated behavioral and cognitive challenges.

1526 | Mesial Temporal Lobe Epilepsy in Association with Antibodies against Glutamic Acid Decarboxylase 65

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Purpose: Mesial Temporal Lobe Epilepsy (MTLE) is one of the most common and clinically significant forms of focal epilepsy, often characterized by drug resistance and a strong association with structural and functional abnormalities, particularly the hippocampus. Despite advances in imaging and surgical interventions, the pathophysiology of MTLE remains incompletely understood, and many cases are refractory to anti-seizure medications (ASM). Recent research has identified autoimmunity as a potential contributor to epileptogenesis in MTLE. Among the implicated autoantibodies, anti-glutamic acid decarboxylase 65 (anti-GAD65) antibodies have gained attention due to their association with autoimmune epilepsy and temporal lobe involvement. The precise role of anti-GAD65 antibodies in MTLE pathophysiology remains unclear, but evidence suggests a dual contribution of autoimmune-mediated dysfunction and secondary structural changes. In this research, we aim to investigate the role of anti-GAD65 antibodies in MTLE, focusing on their contribution to disease pathogenesis, clinical characteristics, and potential as biomarkers for autoimmune epilepsy.

Method: We have identified 13 patients with the inclusion criteria of focal epilepsy identified by mesial temporal lobe sclerosis (MTLS) on neuroimaging, and positive GAD65 in serum and/ or cerebrospinal fluid (CSF). Retrospectively, we have assessed the clinical outcome, magnetic resonance imaging and CSF analysis of these patients following in a tertiary hospital in Saudi Arabia. Moreover, brain tissue obtained was further studied by means of immunohistochemistry, multiplex fluorescent microscopy and transcriptomic analysis for inflammatory mediators and neuronal degeneration.

Results: The median age at symptom onset was 11 years, with a female-to-male ratio of 6:7. 58% of patients met criteria for drug-resistant epilepsy. 85% received immunotherapy, with clinical improvement in only 45%. 4 patients underwent epilepsy surgery, of whom 100% achieved excellent outcome.

Conclusion: Understanding the involvement of anti-GAD65 antibodies in MTLE could pave the way for novel therapeutic strategies, including immunomodulation and surgery, which might improve outcomes for patients resistant to conventional ASMs.

1537 | Impact of modified Atkins diet on serum concentrations of antiseizure medications in an adult population– a balancing act

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Purpose: Ketogenic diet (KD) serves as a treatment option for patients with drug-resistant epilepsy (DRE). Some studies show a decrease in serum concentration of

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antiseizure medication (ASMs) with KD, possibly counteracting the seizure reducing effect of the diet. We aim to analyze the influence of KD on serum concentration of ASMs.

Method: Analysis of data from a prospective, unicentric study of adult patients with DRE, treated with modified Atkins diet in a tertiary center with a 3-month follow-up. We explored ASM serum concentrations measurable in our center (valproic acid–VPA, carbamazepine–CBZ and levetiracetam–LEV) at baseline and at 3 months. Statistical analysis was performed using Wilcoxon test, and results presented as median (IQR).

Results: Of the 80 patients on KD at our center, we included 21 patients who were treated either with CBZ(n=5), VPA(n=13) or LEV(n=5) at baseline and 3 months, whose dosage was unchanged in this period. Twelve (57.1%) were male, with a median of 30 (IQR 20) years. Patients presented with a median of 30 (IQR 82) seizures at baseline and 4 (IQR 2.0) ASMs. Eleven patients (52.4%) had focal epilepsy and 10 (47.6%) generalized. Comparing the serum concentrations levels, we found a significant decrease in VPA from 54.0 (IQR 72.25) to 49.0 (IQR 26.80) ug/dL, (Z=-2.76;p=0.006), and in CBZ from 8.61 (IQR 8.46) to 6.04 (IQR 7.27) ug/dL, (Z=-2.02;p=0.043), at 3 months. We found a trend toward increase in serum LEV levels at 3 months, but with no statistical significance, from 18.2 (IQR 17.6) to 32.2 (IQR 30.90) ug/dL, (Z=-1.75; p=0.080). There was no clear impact on clinical response and seizure frequency.

Conclusion: These findings highlight the potential impact of KD on the pharmacokinetics of ASMs in patients with DRE. Further research is warranted to explore the clinical implications of these alterations and for optimizing ASM management in patients undergoing KD.

1540 | Side-To-Side Head Shaking as an Ictal Feature in Epileptic Seizures: A Video-EEG Case Series

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Purpose: Side-to-side head shaking is often considered a feature of functional seizures but can also occur as an ictal phenomenon in focal epilepsies, particularly Frontal Lobe Epilepsy[1].This study aims to identify the clinical and electrographic characteristics of patients with video-EEG-confirmed epilepsy presenting with such ictal complex head movements.

Method: We retrospectively analyzed video-EEG recordings from patients admitted to the National Hospital for Neurology and Neurosurgery, Queen Square, London, between 2015 and 2024. Patients were included if they exhibited side-to-side head shaking or other complex head movements during seizures, and diagnosis of epilepsy was confirmed by ictal EEG patterns. Patients with functional seizures were excluded. Data collected included patient demographics, seizure semiology, imaging results and EEG findings.

Results: A total of 531 seizures in 9 patients were analyzed, 184 of which included head shaking movements (median 4 seizures with head shaking per patient, range 1-160). In each of the 9 patients, the head movements were stereotypical: predominantly horizontal in 5 patients, rotatory in 1 patient and mixed in 3 patients. Notably, one patient had 160 horizontal head shaking seizures, highlighting significant variability in seizure burden. Epileptogenic zones were localized to the left temporal region (2), right anterior quadrant (1), left anterior quadrant (2), right hemisphere (1), and were non-localizable in 3 patients. Two patients underwent intracranial EEG; one had a left temporal focus and the other had non-localizable findings.

Conclusion: Ictal side-to-side head shaking can occur in focal epilepsies, not only in frontal but also in temporal lobe epilepsy, likely due to propagation and involvement of broader neuronal circuits. Further investigation could clarify its underlying pathophysiology, as well as its potential localizing and prognostic significance.

1555 | Management of Antiseizure Medication in Patients with Epileptic Encephalopathies in Adulthood

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Purpose: Epileptic and/or developmental encephalopathies (EDE) are neurodevelopmental disorders characterized by early-onset epilepsy, epileptic activity on electroencephalograms, and abnormal cognitive function. This study aimed to determine the prescription patterns of antiseizure medications (ASM) in adults with EDE, considering the increased life expectancy of these patients (1,2).
Method: A retrospective, observational, and analytical study was conducted, including 83 patients diagnosed with EDE, aged over 16 years, under follow-up at the NINN MVS. Demographic, clinical and therapeutic variables were analyzed. In the inferential statistical analysis, Chi-square or Fisher's exact test were used to compare qualitative variables, and Student's t-test or Mann-Whitney test for quantitative variable comparisons. SPSS 29 version was used.
Results: Patient' mean age was 33 ± 8.82 years, 54 (65.1%) were men. Twenty-five patients (30.1%) had Lennox-Gastaut syndrome (LGS), 29 (34.9%) structural epilepsy due to perinatal hypoxia, and the remainder with other etiologies. Mean number of ASMs used was 3.4 and a median of 3; valproate was prescribed in 64 patients (77.1%), levetiracetam in 45 (54.2%), and lamotrigine in 40 (48.2%). Other ASM included topiramate in 36 patients (43%), clonazepam in 24 (28.9%), clobazam in 23 (27.7%), lacosamide in 14 (16.9%), and brivaracetam in 8 (9.6%). Less commonly prescribed drugs included carbamazepine, oxcarbazepine, cannabidiol, primidone, phenytoin, vigabatrin, and ethosuximide. Status epilepticus occurred in 22 patients (26.5%).
Conclusion: The prescription trend for ASM in patients with EDE continues to favor broad-spectrum drugs, while narrow-spectrum options, such as sodium channel blockers, were the least prescribed in our population as they could aggravate EDE (3).

1557 | Eye Closure Sensitivity: A Form of Photosensitivity in Generalized Genetic Epilepsy

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Purpose: To review eye closure sensitivity as a feature of generalized epilepsy. We present our series of nine patients with eye closure sensitivity as a feature of generalized epilepsy from 2012 to 2024.
Method: Nine patients with generalized epilepsy who were found to have eye closure sensitivity on EEG were retrospectively reviewed over a period of 12 years. Eye closure sensitivity as a form of photosensitivity as baseline and their GTC seizure frequency was compared at the last follow up and correlated with demographic, clinical and imaging data.
Results: All nine patients had genetic generalized epilepsy (JME and absence JAE) while one patient also had bitemporal epilepsy and had RNS (explanted due to infection and she remained seizure free without any ASMs). Age at seizure onset ranged from 15 to 50 years. Two patients presented with absence status epilepticus. The monthly frequency of seizures was 1.5 per month to 2 per year for GTCs and 1.5 to daily seizures for absence seizures. Three patients had vagus nerve stimulation (VNS) devices in addition to antiseizure medications and one patient had RNS with bilateral centromedian electrodes. Two patients were seizure free at last follow-up, but six patients continued to have seizures requiring ASMs while one was lost to follow up. Among the six patients who continued to have seizures, two were due to non-compliance. One of them with absence seizures, eyelid myoclonia and PNES (Psychogenic Non-Epileptic Seizures), had no improvement in his seizure frequency due to non-compliance and was eventually lost to follow up.
Conclusion: Eye closure sensitivity is a relatively lesser-known feature of generalized epilepsy. We present our series of nine patients with eye closure sensitivity as a feature of generalized epilepsy, while one patient also had bitemporal epilepsy.

1573 | Beyond migraine: the hidden epilepsy of cortical malformations

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Purpose: Migraine and epilepsy are episodic neurological disorders with overlapping clinical features, often leading

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to misdiagnosis. Differentiating these conditions is critical, as an incorrect diagnosis can delay appropriate treatment and impact quality of life. This case highlights the diagnostic challenges posed by cortical malformations mimicking migraine.

Method: A retrospective case analysis was performed on a patient initially diagnosed with migraine with visual aura in 2005. In 2019, she was re-evaluated in our department due to episodes of headache with visual aura followed by loss of consciousness. A detailed reassessment, including clinical history, neurological examination, high-resolution MRI (Magnetic Resonance Imaging), and EEG (Electroencephalography), was conducted to establish the correct diagnosis.

Results: A 38-year-old female was brought to the hospital in 2019 after experiencing a generalized tonic-clonic seizure. Since childhood, she had reported recurrent episodes of colored visual phenomena followed by altered consciousness. In 2005, she was diagnosed with migraine with aura. Upon re-evaluation, brain MRI revealed bilateral temporo-parietal polymicrogyria and subcortical band heterotopia (double cortex syndrome). EEG showed isolated regional sharp waves, supporting the epileptic nature of her episodes. The patient was diagnosed with structural epilepsy with focal sensory visual seizures with impaired awareness and started on antiseizure medication, leading to significant symptom improvement.

Conclusion: This case highlights the diagnostic complexity of epilepsy presenting as migraine, particularly in patients with cortical malformations. Even subtle EEG abnormalities should prompt further neuroimaging when migraine-like symptoms are accompanied by altered consciousness. Early recognition of structural epilepsy is crucial, as it directly impacts treatment strategies and prognosis. Advanced neuroimaging should be considered in atypical cases to avoid misdiagnosis and ensure optimal patient management.

1641 | Quality of Life in People with Epilepsy depending on educational level in Georgia

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Purpose: The low quality of life (QoL) in people with epilepsy (PWE) is largely determined by the problems of the patient's education, employment, and social relations. Employment has both direct and indirect effects on the QoL of individuals with epilepsy - financial Stability, social Integration. But stigma and discrimination negatively affect mental health and lead to reducing overall quality of life.

Method: The study was conducted at the Institute of Neurology and Neuropsychology (INN) in Tbilisi, Georgia. Patients were evaluated for one year using the adapted survey Quality of Life in Epilepsy Inventory - QOLIE-31. Statistical analyses were performed using IBM SPSS Statistics for Windows, Version 23.0.

Results: In total 351 patients were enrolled. Among them 155 (44.2%) were female. A median age of participants was 31 years (18-65 y). Incomplete primary education received 19 (5.4%), Primary school - 129 (36.8%), Student - 17 (4.8%), Incomplete University - 13 (3.7%), University – 155 (44.2%), Professional education - 18 (5.1%). By the professions: Worker -5 (1.4%), Teacher-13 (3.7%), Lawyer- 9 (2.6%), Public affair - 2 (0.6%), Businessman - 2 (0.6%), Physician - 5 (1.4%), Engineer - 2 (0.6%), Other -253 (72.1%), no profession- 60 (17.1%). Among them: Employed by profession - 73(20,8%), Employed not by profession - 90(25,6%), Unemployed - 188(53,6%). Education level was in significant association with all QOLIE 31 domains ($p<0.001$), however, post-hoc analysis showed significant difference only between no or primary education and Student or university degree of education.

Conclusion: In summary, higher education and stable employment have the potential to improve the QoL for people with epilepsy, but challenges like stigma, seizure control, and comorbidities must also be addressed.

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1656 | Cortical lateralization of ictal cardiovascular autonomic dysfunction in stimulation-induced seizures

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Purpose: Cardiovascular autonomic dysfunction (CAD) often accompanies epileptic seizure but may vary depending on localization and lateralization of the seizure onset zone. We aimed to compare proportion of CAD-associated seizures originated in left and right hemispheres.

Method: In patients with drug resistant focal epilepsy undergoing stereo-electroencephalographic monitoring (SEEG) with electrical stimulation (ES) we recorded beat-to-beat blood pressure (BP) and electrocardiographic heart rate (HR) during ES-induced seizures. SEEG was provided according to electroclinical hypothesis when noninvasive data was inconclusive. Ictal CAD was defined as newly appeared hypertension (systolic or diastolic BP ≥140/90 mmHg), hypotension (systolic or diastolic BP <90/60 mmHg), tachycardia (HR >100 bpm), and bradycardia (HR <60 bpm) during the first minute of seizures if changes of HR/BP exceeded 3 standard deviation thresholds from prestimulation baseline mean values. We compared proportion of CAD events in total number of induced seizures between hemispheres for each type of CAD using Fisher's exact test. Significant p-value: <0.05.

Results: In 26 patients (25-39 years old; 15 women) we recorded 83 seizures from left (n=50) and right (n=33) cortical structures, 38 of them were associated with clinically significant changes of BP or/and HR. Hypertension occurred in 16 seizures (19%) induced from left (n=8/50) and right (n=8/33) hemispheres (p=0.401). Hypotension (18 seizures, 22%) was more common in seizures induced from left hemisphere (15/50 vs 3/33, p=0.029). Tachycardia (12 seizures, 15%) tended to accompany seizures from right hemisphere (4/50 vs 8/33, p=0.056). Bradycardia (5 seizures, 6%) occurred during seizures from left hemisphere only (5/50 vs 0/33, p=0.152).

Conclusion: Ictal cardiovascular autonomic dysfunction is common in ES-induced seizures. Hypotension was associated with seizures evoked from left hemisphere. Tachycardia tended to occur more frequently during seizures from right hemisphere. Bradycardia was recorded only during seizures from left hemisphere. These findings support the concept of cortical lateralization of autonomic control.

1670 | Ictal hypotension, but not hypertension, is associated with increased interictal sympathetic activity

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Purpose: Significant blood pressure changes may occur during epileptic seizures. We aimed to test whether ictal hyper- or hypotension is associated with interictal predominance of sympathetic or parasympathetic activity.

Method: In normotensive patients with drug resistant focal epilepsy undergoing stereo-electroencephalographic monitoring we recorded beat-to-beat blood pressure (BP) and electrocardiographic RR-intervals (RRI) immediately before and during direct electrical stimulation of cortical structures that was applied in order to induce habitual seizures and thus to verify the seizure onset zone. We conducted frequency-domain heart rate variability analysis of 5-minute prestimulation recordings and calculated total RRI powers (RRI-TP) reflecting total cardiac autonomic modulation, high frequency powers of RRI variability (RRI-HF) reflecting parasympathetic activity, low frequency powers of RRI variability (RRI-LF) and of systolic BP variability (BP-LF) reflecting sympathetic activity, and RRI-LF/HF-ratio reflecting sympathetic/parasympathetic balance of cardiac modulation. We compared autonomic parameters between patients: (i) with and without recorded ictal hypertension (systolic or diastolic BP ≥140/90 mmHg) and (ii) with and without recorded ictal hypotension (systolic or diastolic BP <90/60 mmHg) using Mann-Whitney U-tests, significance: p<0.05. Data are presented as median and interquartile ranges.

Results: Of the 20 patients included (19-54 years old; 12 women), 6 patients had only seizures with ictal hypertension, 7 patients had only seizures with ictal hypotension, in 4 patients both hyper- and hypotension was recorded during seizures, 3 patients did not have any BP changes. Patients with ictal hypotension (n=11), compared to those without hypotension (n=9), had higher interictal RRI-LF/HF-ratio (2.5[2.2;3.2] vs 0.81[0.74;1.7], p=0.031) and BP-LF (11.4[5.2;15.6] vs 4.7[3.5;5.6], p=0.025) with no difference in other parameters. Autonomic parameters did not differ between patients with (n=10) and without (n=10) ictal hypertension.

Conclusion: People with epilepsy and recorded ictal hypotension had higher sympathetic activity compared to those without ictal hypotension. Ictal hypertension was not associated with any difference in interictal autonomic parameters.

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1677 | Ictal coughing with stereotypical asymmetric tonic posture

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Purpose: Cough as a leading ictal phenomenon is not a common finding during video-EEG monitoring. Seizures need to be differentiated from cough syncope.
(VIDEO is included.)
Method: We present a 49y old man with unusual seizure semiology. Seizures always begin with cough followed by impaired consciousness with development of a stereotypical asymmetrical tonic posture (extended left arm and simultaneously flexed right upper limb). Semiologically this posture resembled a typical seizure affecting the supplementary motor area. Ictal EEG shows artifacts at the beginning, then a short episode of diffuse theta, followed by an episode of diffuse flattening more pronounced frontocentrally on the right. Simultaneously recorded ECG during the entire seizure ruled out asystole or bradycardia. On the contrary ECG demonstrated mild tachycardia. The patient's seizures began suddenly and in cumulations several times a day. Craniocerebral injury 20 years ago is in patient history. But the current MRI did not reveal any pathology. The patient is otherwise healthy and a lifelong athlete. A CT scan of the lungs was also normal.
Results: Only the further course of the disease showed that these were not epileptic seizures but cough syncopes. Condition did not respond to the administration of antiseizure medication. Laboratory testing eventually showed the whooping cough.
Conclusion: The pathophysiology of cough syncope is debated. The hemodynamic theory explains that the increase in intrathoracic pressure during coughing acutely reduces venous return and subsequently cardiac output, leading to reduced cerebral perfusion and loss of consciousness. The development of the stereotypical "SMA-like" posture is a matter of question.

1678 | Dravet syndrome in Norway – a population- based study

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Purpose: The aim of this study was to identify all patients with Dravet syndrome (DS) in Norway, both children and adults. We also wanted to describe clinical variables for this population in relation to age.
Method: All known patients with DS in Norway were identified in a population-based study. Data from a previous study identifying patients from 2008-2018 were updated (Heger K. et al. Epilepsia Open 2020;5(3):432-441), by assessing information from two different national registries (National Center for Epilepsy and National Center for Rare Epilepsy-Related Disorders). In addition, we contacted the Norwegian Dravet Association, made announcements and called directly on neurologists working with epilepsy patients. Data were collected from caregivers and medical records.
Results: We identified 73 patients with DS on prevalence day 01.01.2024. Mean age 21 years (range 2-53). Patients with a milder phenotype (GEFS+), a more severe phenotype (Early infantile SCN1A DEE) and patients with known mutations in other genes than SCN1A were excluded. All patients fulfilled the diagnostic criteria of DS (ILAE classification 2021). Clinical and genetic data were available for 71 patients. 58% were adults. 94% had a mutation or deletion in SCN1A. Mean age at diagnosis was 10 years (range 0.5-45). Mean age at first seizure was 6 months (range 1-18). Most frequently used initial anti-seizure medications (ASMs) at seizures start in adult group were valproate 58%, carbamazepine/oxcarbazepine 32%, phenobarbital 10%, while in child group these were valproate 45%, levetiracetam 41%, carbamazepine/oxcarbazepine 10%, phenobarbital 3%. Sodium channel-blockers (carbamazepine, oxcarbazepine, phenytoin, lamotrigine, gabapentin, lacosamide, eslicarbazepine) had been tried in all adults and 47% of children. Of these, 23% of adults were still treated with sodium channel-blockers, but no children. Cannabidiol and fenfluramine have been available since 2022/2024.
Conclusion: Adults and children with DS have had different ASM treatment, potentially influencing outcome. The use of sodium channel-blockers was surprisingly high.

1696 | Attitude and anxiety level of caregivers of epilepsy patients: a cross-sectional study at Neurology Polyclinic Zainoel Abidin General Hospital Banda Aceh

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Purpose: Epilepsy is an intrusive illness that impacts not only for the patients, but also the caregivers that could cause disrupt family routines and activities of family members and leads to lower quality of life. Caregivers often face psychological issues such as anxiety, depression, and stress, which may correlate with their attitudes toward epilepsy. This study aims to describe the attitudes and anxiety among caregivers of epilepsy patients at the Neurology Polyclinic of Dr. Zainoel Abidin General Hospital.
Method: This is an observational analytic study with a cross-sectional design. Subjects were selected using simple random sampling among caregivers of epilepsy patients at Neurology Polyclinic of Dr. Zainoel Abidin General Hospital, Banda Aceh, during June to July 2024. Caregivers' attitudes were assessed using the Public Attitude Toward Epilepsy (PATE), and anxiety levels were measured using the Hamilton Anxiety Rating Scale (HARS).
Results: Forty-three subjects met the study criteria, with most caregivers showing positive attitudes (65.1%) and moderate anxiety levels (46.5%). Caregivers with positive attitudes were more likely to have moderate anxiety (42.9%), while those with negative attitudes had higher anxiety (80.0%). However, the correlation between attitudes and anxiety was not statistically significant ($p = 0.87$, $r = -0.026$).
Conclusion: Caregivers with positive attitudes tend to experience lower anxiety due to better coping with challenges, understanding the patient's condition, adequate knowledge about epilepsy, and social and familial support. Negative attitudes often lead to higher anxiety due to difficulties in managing responsibilities, social stigma, and lack of knowledge.

1702 | Prevalence of poststroke epilepsy (pse) after 5 years and SeLECT score results

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Purpose: PSE is the most frequent form of epilepsy in older adults, often impacting quality of life. SeLECT score has been designed to assess the risk of developing PSE and could be useful to identify patients with a higher PSE risk. It includes 5 variables: severity of stroke (Se), large artery atherosclerosis (L), early seizures (E), cortical involvement (C) and MCA territory (T) and it ranges from 0 to 9. Our aim is to describe the prevalence of PSE in our patients within 5 years after stroke and review their data and SeLECT score.
Method: We designed a retrospective observational study including patients admitted with a confirmed acute ischaemic stroke between 2017 and 2019. We calculated their SeLECT score using data from their clinical records and the presence of PSE 5 years after stroke.
Results: 539 patients were included, but patients that died during hospitalization (31), prior epilepsy diagnosis (7) and lost of follow-up (143) were excluded from our review. 358 patients were analyzed, 60% were male, mean age 66 (21-91). 27 patients (7.5%) developed PSE, 74% of them had a SeLECT score value ≥5. A higher SeLECT score, NIHSS at admittance (>11), presence of cortical infarction on MRI and early seizures (first week after stroke) were significantly more frequent in our PSE patients (p 0.00). MCA territory stroke and large vessel aterothrombosis did not show significant differences.
Conclusion: After 5 years, 7.5% of our patients had developed PSE. A higher SeLECT value, specifically the items NIHSS at admittance, cortical infarction and early seizures, were significantly more frequent in our PSE patients. Although our results support previous studies regarding the utility of the SeLECT score, our retrospective design limits the interpretation of our results.

1708 | Approach to First Seizures in the Emergency Department: The Key Role of EEG

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Purpose: Seizures are a common reason for emergency department (ED) admissions. A structured approach is crucial to classify first seizures (FS) as unprovoked seizures (UPS) or acute symptomatic seizures (ASS). Electroencephalography (EEG), although not universally available in ED, plays a key role in seizures classification and treatment decisions.
Method: Retrospective study of all consecutive patients presenting with FS to the ED between 2023 and 2024, who underwent EEG within 24 hours. A descriptive analysis of clinical, imaging, and EEG findings was performed.
Results: The study included 70 patients, with median age 65.5 years (IQR 42-79), 50% women. UPS accounted for 51.4% (n=36), mean age 49.97 years. Among them, 25% (n=9) had structural not acute lesions on CT; 4 with epileptiform activity on EEG, all initiated ASM. In 75% (n=27) with normal CT, 59.3% (n=16) had epileptiform

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activity, all started ASM. Of the remaining 11, 9 started ASM based on clinical criteria. ASS accounted for 48.6% (n=34), mean age 70.15 years. Among these, 47.1% (n=16) had acute cortical lesions on CT, with 56.2% (n=9) showing epileptiform activity, 25% meeting status epilepticus (SE) criteria. All (n=16) received ASM. The remaining 52.9% (n=18) had seizures due to infections (n=11), metabolic disorders (n=1), or alcohol withdrawal (n=6), with 33.3% (n=6) showing epileptiform activity (66.7% (n=4) SE criteria), all started ASM in the acute phase. Overall, 44.1% (n=15) of ASS cases had epileptiform activity, and 64.7% (n=22/34) initiated ASM, with 63.6% (n=14/22) guided by EEG findings.

Conclusion: EEG significantly influenced seizure classification and early ASM introduction, particularly in UPS with normal CT and ASS without structural lesions. Our findings reinforce the need for EEG availability in ED protocols for first seizures.

1712 | The Diagnostic Challenge of Epilepsy with Eyelid Myoclonia - A Case Series of 3 Patients in 112 Patients with Idiopathic Generalized Epilepsy

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Purpose: Epilepsy with eyelid myoclonia (EEM) is a rare, diagnostically challenging syndrome that often goes unnoticed, leading to delays in appropriate management. The aim of this case series is to highlight the features that can aid in the diagnostic procedure.

Method: This is a retrospective observational study of patients diagnosed with EEM from 2021 to 2024 in a general neurology department in Greece.

Results: Three patients were diagnosed with EEM, from a total of 112 with idiopathic generalized epilepsy (IGE), over the past four years (with an estimated incidence of 2.7%). The first patient was a 72-year-old female with a history of diagnosed IGE with episodes of loss of consciousness following the discontinuation of valproic acid. Careful observation revealed eyelid myoclonias occurring during eye closure. The second and third patient, were both 18-year-old females, presented with an episode of generalized tonic-clonic seizures, with underlying eyelid myoclonias on examination. The diagnosis of EEM in these cases proved to be challenging. The observation of the eyelid myoclonias, which can be missed in routine clinical observation, proved crucial in the revision of the diagnosis in the first case. Regarding the other two cases, clinical examination as well as electroencephalography (EEG) was key in confirming the diagnosis which had to be carefully examined at eye closure and at intermittent photic stimulation. The EEG findings included brief bursts of fast (3–6 Hz) irregular generalized polyspike-and-wave complexes mostly prominent at eye closure, during photic stimulation and hyperventilation.

Conclusion: This case series underscores the challenge in the diagnosis of EEM, which if delayed, can have effects in the patient's long-lasting management, as displayed in the 1st patient. Clinical suspicion after careful observation and targeted EEG examination should aid in the clarification and diagnosis of this rare syndrome in clinical practice and improve patient outcomes.

1716 | Pallister-Hall syndrome: the not so dark side of hypothalamic hamartoma-related epilepsy

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Purpose: Hypothalamic hamartomas, which typically present with gelastic seizures, can occur in isolation or as part of a genetic syndrome, most commonly Pallister-Hall syndrome. This is a rare autosomal dominant disorder caused by a mutation in the GLI3 gene, characterized by the presence of hypothalamic hamartomas, panhypopituitarism and/or visual disturbances, as well as malformations of the limbs, cleft palate or uvula, bifid epiglottis, genitourinary anomalies, and congenital heart defects.

Method: A 32-year-old man, with past medical history of congenital heart disease, bone malformations of the fingers and toes, pulmonary hypertension, cryptorchidism, and short stature, with normal intellectual development, began at the age of 18 to exhibit a stereotyped pattern of sleep behavior disturbances, including agitation, crying, shouting, and expressions of fear. Frequent déjà-vu episodes had also been noted in the previous years.

Results: Both phenomena were assumed to correspond to focal epileptic seizures, although interictal electroencephalograms showed no abnormalities. Neurological examination was normal. Brain magnetic resonance imaging (MRI) revealed a large hypothalamic hamartoma (45x27x30mm). Genetic testing was performed, identifying a heterozygous mutation in the GLI3 gene, confirming the diagnosis of Pallister-Hall syndrome. After several therapeutic regimens, the patient has been seizure-free for ten years, under levetiracetam 500 mg bid. During follow-up, complaints consistent with frontal-type cognitive

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deficit were identified, which have remained stable. Serial brain MRIs showed stability of the hamartoma.

Conclusion: We describe a rare case of a patient with hypothalamic hamartoma who presented without the typical gelastic seizures, but instead with focal hyperkinetic and cognitive seizures, effectively controlled with anti-seizure medication. This case supports that hypothalamic hamartomas associated with Pallister-Hall syndrome may have a more benign course compared to isolated hamartomas, with fewer epileptic seizures and more favorable control, preferably managed with conservative treatment. Syndromic diagnosis is important for clinical prognosis, multidisciplinary approach, and genetic counselling.

1717 | Mitochondrial epilepsy in adults: a cross-sectional study

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Purpose: We set out to interrogate the population prevalence of epilepsy and stroke-like episodes and characterise the use of anti-seizure medications in a cohort of adults with primary mitochondrial disease at a national referral centre.

Method: We extracted disease history and treatment data from 501 sequential adults from the Newcastle Rare Mitochondrial Disorders Service (2023-2024). The data contained demographics, genotype, diagnostic codes, and current medications. Statistical analysis was carried out using IBM SPSS Statistics software packages.

Results: Epilepsy prevalence in this cohort was 14.4%. The average age of epilepsy onset was 27.9 years, but with a bimodal prevalence peak. The prevalence of stroke-like episodes was 8.9%. Among the patients with epilepsy, the prevalence of stroke-like episodes was 61.5%. The prevalence of epilepsy and stroke-like episodes varied by genotype, most commonly seen in m.3243A>G and *POLG*. Polypharmacy was common, seen in 71.3% of patients with epilepsy. The most frequently prescribed class of anti-epileptic drugs was SV2A receptor ligands, used by 80% of the patients. Levetiracetam was the single most used drug, prescribed to 55.4% of patients. We also present data on four patients prescribed sodium valproate (none with *POLG* variants) and one patient with *POLG* disease on cenobamate for more than 12 months.

Conclusion: Epilepsy is a frequent feature of mitochondrial disease and often occurs alongside stroke-like episodes. Treatment resistance is common, leading to the overwhelming prevalence of polypharmacy in these patients. There is an acute need for improving our understanding of mitochondrial epilepsy pathophysiology and the development of novel therapeutics.

1738 | Clinical and histopathological characteristics of temporal lobe epilepsy patients with hyperkinetic seizures

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Purpose: Hyperkinetic (hypermotor) seizures (HKS) are an infrequent manifestation of temporal lobe epilepsy (TLE). This study analyzed the clinical and paraclinical characteristics of patients with refractory TLE exhibiting hyperkinetic seizures.

Method: This was a retrospective multi-centric study. Data of 438 adults with refractory TLE investigated in two large tertiary epilepsy centers cases in the Czech Republic were reviewed. All patients in whom hyperkinetic seizures were recorded during preoperative video-EEG monitoring were included. Clinical and paraclinical variables were analyzed.

Results: 100 HKS were recorded in 22 patients (5 %), with male predominance (9 females) and speech non-dominant temporal lobe seizure onset in 91 %. 73 % had HKS type 1 (marked agitation with a facial expression of fear), and the rest presented with HKS type 2 (mild agitation, horizontal movements or rotation of trunk or pelvis). Additional temporal lobe seizure semiology (abdominal or auditory aura, oroalimentary automatisms) occurred in 82 % of patients. 77% were MRI-positive (with an epileptogenic lesion located in the temporal lobe), 90% were PET positive (concordant with electro-clinical localization). Temporal lobe resection was performed in all patients (86.4% on the

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right-side). Focal cortical dysplasia was the most common lesion found in histopathology (68.2%), isolated and combined with hippocampal sclerosis. The seizure outcome of TLE-HKS patients was comparable to the outcome of temporal lobe surgery in general: 17 patients (77 %) were seizure free at one year, 63,6% at 5 years after surgery. The unfavorable outcome was associated mainly with higher age at surgery and FCDIIIa in histopathology.
Conclusion: Temporal lobe epilepsy may manifest with both HKS types 1 and 2. Speech-nondominant lateralization of seizure onset was more common, possibly relating to more widely extended epileptogenic networks in non-dominant TLE. Earlier surgery was associated with better outcomes.

1744 | Neuropsychological Assessment of Executive Functions in Temporal Lobe Epilepsy: A Cross-Sectional Study

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Purpose: Temporal lobe epilepsy (TLE), the most common form of focal epilepsy in adults, is frequently associated with cognitive impairments, particularly in executive functions (EF). EF deficits affect 44% to 95% of patients with TLE, significantly impacting their quality of life. This study aims to evaluate EF in individuals with TLE and explore associated clinical and neuropsychological features.
Method: A cross-sectional study was conducted over two years at the Neurology Department of Monastir, including 55 patients diagnosed with TLE. Sociodemographic, clinical, electrophysiological, and radiological data were collected. Neuropsychological assessment focused on EF using a comprehensive battery: the Wisconsin Card Sorting Test (WCST), Trail Making Test (TMT) Parts A and B, phonemic verbal fluency, and digit span tests.
Results: The study included 55 patients with TLE (sex ratio M/F =1.03; mean age =37.14 years). Cognitive seizures were the most frequent seizure type (68.9%), and hippocampal sclerosis was the predominant etiology (34.4%). Global cognitive impairment was observed in 62% of patients. Executive dysfunction was the most prevalent deficit in our cohort. Phonemic verbal fluency was significantly reduced, with a mean score of 8.2 ± 3.47, and 78.2% of patients exhibited impaired fluency. Working memory deficits were also prevalent, with a mean forward digit span of 4.76 [3-9] and a backward digit span of 3.8 [2-8], affecting 40% of the cohort. Executive dysfunction, as assessed by the Wisconsin Card Sorting Test (WCST), was observed in 54.5% of patients (n=30). Additionally, 49.1% of patients (n=27) showed reduced information processing speed, with a mean completion time of 83.9 seconds (range: 23–240) for Trail Making Test A and 176.8 seconds (range:69–375) for Trail Making Test B.
Conclusion: The evaluation of executive functions in temporal lobe epilepsy reveals frequent impairments, affecting more than half of the patients. Although the underlying mechanisms remain partially elucidated, neuropsychological assessment is crucial in TLE.

1755 | Focal Drug-Resistant Epilepsy as The Only Clinical Manifestation In Multiple Sclerosis: A Case Report

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Purpose: Seizures in the context of multiple sclerosis (MS) usually coexist with other MS symptoms, showing both temporal and spatial dissemination. However, drug-resistant epilepsy (DRE) as the only presenting manifestation of MS is a rare and underexplored phenomenon.
Method: A 40-year-old female started to experience focal-onset seizures at age 28 with negative history of risk factors of epilepsy. Initially, her seizures were well-controlled with a single anti-seizure medication. However, after six years, she developed frequent seizures that were refractory on polytherapy. MRI-epilepsy protocol revealed multiple brain demyelinating lesions typical for MS but no classic epileptogenic lesion, classifying her as non-lesional DRE.
Results: The patient did not exhibit symptoms consistent with MS with normal neurological examination (EDSS=0). Diagnosis of radiologically isolated syndrome (RIS) was established. She was followed with serial MRIs every six months. Over time, her MRI showed an increase in the number of lesions. Cerebrospinal fluid analysis revealed oligoclonal bands (OCB) type II and high IgG index (1.2). Visual evoked potentials showed no detectable abnormality. Unfortunately, high-dose intravenous methylprednisolone (1g/day for five days) did not reduce seizure frequency. Follow-up imaging revealed new brain lesions and the appearance of the first cervical spinal lesion. After the updated McDonald's criteria in 2024, the patient's diagnosis turned from RIS

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to MS. Accordingly; rituximab was started as a disease-modifying therapy.

Conclusion: A case of focal DRE as the only clinical manifestation of MS, emphasizing the diagnostic challenges of MS in atypical presentations. The case underscores the evolving role of DMT in managing seizure-related MS and the challenges in deciding when to initiate DMTs in the context of a patient without typical MS symptoms. Further research is needed to clarify the mechanisms linking epilepsy and MS and to explore optimal treatment strategies for such atypical presentations.

1774 | Screening for cognitive impairment in people with epilepsy: test your memory

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Purpose: Cognitive impairment in people with epilepsy (PWE) is often overlooked, making active screening necessary. The Test Your Memory (TYM) is a self-administered cognitive test comprising 10 tasks with a maximum score of 50 points. Scores ≤42 indicate dementia. We aimed to evaluate cognitive impairment (CI) in a mixed group of PWE.

Method: We included 69 PWE who completed the TYM. Participants were categorized into two groups based on a cut-off score of 42. Descriptive statistics and independent sample t-tests were performed.

Results: Twenty-seven had focal epilepsy, 20 had generalized epilepsy, and 23 had unclassified epilepsy. PWE with CI were older (51.19 SD 18.77 vs. 43.55 SD 13.18 years) and had lower TYM scores (46 SD 2 vs. 36 SD 5 points, $p<0.05$) than those without CI. Significant differences were observed in scores of seven cognitive tasks (all $p<0.01$). PWE with CI performed worse on word fluency (3.48 SD 0.87 vs 3.92 SD 0.37), abstract thinking (2.79 SD 1.71 vs. 3.56 SD 1.05), naming ability (4.21 SD 1.27 vs. 4.83 SD 0.45) and visuospatial processing (2.52 SD 1.37 vs. 3.69 SD 0.58). The most pronounced impairments were in semantic memory (0.82 SD 098 vs 1.97 SD 0.97) (TYM 3) and delayed recall (2.15 SD 2.12 vs. 5.06 SD 1.24 out of 6 points).

Conclusion: Nearly half of the PWE in our sample exhibited cognitive impairment, primarily in memory, language and executive functions, with delayed recall being the most prominent impairment. The TYM test may be a valuable screening tool for detecting CI in PWE. Further studies in more specific cohorts are necessary to validate differences among cognitive domains across different epilepsy syndromes. The study was supported by the Slovenian Research Agency (ARIS) and Croatian grant BI-HR/23-24-030.

1776 | Clinical and Paraclinical Characteristics of Post-Traumatic Epilepsy (PTE) patient: Predictive Factors and Management Considerations

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Purpose: Traumatic brain injuries (TBI) are a major cause of acquired structural epilepsy, often debilitating. The aim of this study is to describe the clinical and paraclinical characteristics of PTE patient and identify predictive factors for its occurrence.

Method: This is a descriptive cross-sectional study conducted in the neurology department of Gabès, Tunisia, including patients with PTE occurring after the acute phase of TBI. The analysis focused on patient characteristics, trauma mechanisms, and associated factors.

Results: The study included 13 patients (sex ratio M/F = 5.5), with a median age of 37 years. Alcohol and substance use was found in 7.7% of cases, and smoking in 46.2%. Among our patient 23.1% had a cardiovascular disease and 7.7% had a psychiatric disorder. The trauma was caused by a road accident in 61.5%, a domestic accident in 23.1%, and a fall in 15.4%. TBI was severe in 46.2% of cases, mild in 38.5%, and moderate in 15.4%. Initial loss of consciousness occurred in 38.5%, 46.2% were in coma and 46.2% needed surgery. Brain imaging revealed cerebral contusions in 30.8 % of cases, skull fractures in 15.4%, cerebral edema in 15.4%, subdural hematomas in 15.4%, subarachnoid hemorrhage in 15.4% and epidural hematomas in 7.7%.The temporal and frontal lobes were involved in 30.8% each, the occipital lobe in 23.1%, and the parietal lobe in 15.4%.Seizures occurred within 24 hours or the first 7 days in 7.7% of cases. The mean onset of PTE was 8 months [1month, 7 years], with generalized seizures being the most frequent, occurring in 84.6%.

Conclusion: Our study highlights the importance of proper management of traumatic brain injuries, even if the injury is mild or moderate, and even years after the trauma. PTE was more common in cases of cerebral contusion and involvement of the temporal or frontal lobes, with generalized seizures being the most frequent.

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1788 | Prevalence of sleep disorders in people with epilepsy: A single-center self-reported sleep assessment

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Purpose: Sleep disorders are one of the most common comorbidities in people with epilepsy (PWE). Considering the impact of sleep-wake cycle dysregulation on seizures and on the other comorbidities (as cognitive impairment, depression and anxiety), this study aimed to subjectively assess the prevalence of sleep disturbances, depression, and anxiety in PWE admitted in a single tertiary epilepsy center.
Method: PWE followed at the Epilepsy Centre of the Neurology Unit at the Tor Vergata University Hospital in Rome were enrolled. Each participant underwent a medical examination and completed a set of questionnaires to assess: sleep quality (Pittsburgh Sleep Quality Index - PSQI), insomnia (Insomnia Severity Index), risk of sleep apnea (Berlin Questionnaire), daytime sleepiness (Epworth Sleepiness Scale), restless legs syndrome (RLS - International RLS Study Group Scale), chronotype (Morningness-Eveningness Questionnaire), depression (Neurological Disorders Depression Inventory for Epilepsy), and anxiety (Generalized Anxiety Disorder-7).
Results: A total of 357 PWE (54.1% male) with a mean age of 50.75±19.16 y.o. were included. Notably, 55.4% (n=198) had at least one or more sleep problem, while 44.5% (n=159) reported none. The most prevalent sleep complaint was poor sleep quality, assessed through the PSQI (42.3%), followed by insomnia (26.1%), risk of sleep apnea (18.5%), RLS (7.6%), and excessive daytime sleepiness (6.7%). Almost half of the patients (46.1%) identified as having a morning chronotype, while 46.5% reported an intermediate chronotype. Symptoms of depression were present in 21% of PWE, while 17.7% reported moderate or severe anxiety symptoms.
Conclusion: This study highlights the high prevalence of sleep disturbances in PWE and emphasizes the importance of appropriate screening tools to facilitate the identification and management of sleep disorders, considering the detrimental effects of the sleep-wake cycle dysregulation on seizure recurrence, poor compliance to treatment, and neuropsychiatric and cognitive symptoms.

1789 | *Déjà vu*: A focal sign in Juvenile Myoclonic Epilepsy

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Purpose: *Déjà vu* is a transient mental phenomenon in which a novel experience feels strangely familiar. This study presents an atypical case of Juvenile Myoclonic Epilepsy (JME), where recurrent *déjà vu* episodes were among the initial symptoms, posing challenges in differential diagnosis and clinical management.
Method: Clinical case report and literature review.
Results: A 19-year-old male had been experiencing frequent *déjà vu* episodes for two years—up to ten times daily—accompanied by intense fear, discomfort, nausea and headaches. Initially attributed to anxiety and dissociation after psychiatric evaluation, symptoms persisted until he presented to the emergency department with a myoclonic seizure in the upper limbs, followed by a generalized tonic-clonic seizure. A retrospective history, along with the family's report of frequent spasms, particularly upon awakening, was suggestive of myoclonic jerks. His medical history included hypogonadotropic hypogonadism and consanguinity. EEG revealed generalized epileptic activity with photosensitivity, supporting JME as the most likely diagnosis. MRI findings were normal. Treatment with levetiracetam led to seizure control and resolution of *déjà vu*, although mild irritability was noted as a side effect.
Conclusion: *Déjà vu* is widely reported, with approximately 97% of individuals experiencing at least one episode in their lifetime. While often benign, it may be associated with neurological or psychiatric conditions, such as anxiety, depersonalization, psychosis, but also to temporal lobe epilepsy, particularly focal seizures of medial temporal origin. Epileptic *déjà vu* episodes are often more frequent and prolonged, accompanied by fatigue, fear, derealization, olfactory or gustatory hallucinations, and headaches. Though literature on *déjà vu* in JME is scarce, some studies suggest focal seizures with *déjà vu* can occur. This case highlights the importance of thorough history-taking and recognizing neurological signs in *déjà vu* presentations. Clinicians should be aware of the diverse etiologies of *déjà vu* to prevent misdiagnosis and ensure timely management.

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1796 | Clinical characteristics of Juvenil Myoclonic Epilepsy and risk factors for drug-resistant patients

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Purpose: Juvenile Myoclonic Epilepsy (JME) is considered the most common syndrome of Idiopathic Generalized Epilepsies. The age of onset ranges from 8 to 40 years, with myoclonic seizures being the predominant type. Although there is generally a good response to treatment, it has been reported that up to one-third of patients are resistant to therapy (Nica A. Revue Neurologique 2024;180: 271-289). This study aims to characterize JME patients and assess potential risk factors associated with drug resistance.

Method: A retrospective study of JME patients in São José Local Health Unit in Lisbon was conducted. The data was collected from patients' electronic records with confirmation via telephone contact and the following variables were recorded: sex, age of onset, family history, seizure type, date of last seizure, anti-seizure medication (ASM), drug-resistance (DR), catamenial seizures and photosensitivity.

Results: A total of 62 patients were included (58.1% female, average age 23.9 years). The average age of epilepsy onset was 12.7 years and 53.2% had family history of epilepsy. The vast majority experienced generalized tonic-clonic seizures (n=56; 90.3%), while 14 patients had absence seizures (22.6%). The average number of antiseizure medications was 1.2, with levetiracetam being the most commonly prescribed (51.6%, either as monotherapy or combination therapy). In this sample, 21.0% were taking combination therapy and 19.6% had refractory epilepsy. Early onset age presented a statistically significant association with drug resistance (t = -1.997, df=10.688, p=0.072). No significant association was detected with other variables.

Conclusion: With this study, we conclude that early onset age of JME is a significant risk factor for DR. Identifying risk factors is highly relevant, allowing early interventions and customized care strategies for patients such closer follow-up and alternative treatments.

1826 | Surgical Treatment of Drug-Resistant Focal Epilepsy Associated with Cortical Dysplasia in Adults: A Case Series

S Pino[1], V Gómez[2], A Daza-Restrepo[3], R Matus[1], L Rivas[2], J Zambrano[1], JC Jerez[1], M Villanueva[3], A Nasimbera[3], N Campora[3], JP Princich[3], E Verdier[3], P Seoane[3], P Solis[3], F Yancowyez[3], M Aberastury[3], S Oddo[3], B Giagante[3], S Kochen[3]
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Purpose: To report our experience of epilepsy surgery in patients with focal Cortical Dysplasia (FCD).

Method: An observational, descriptive, and retrospective study was conducted on adult patients with DRFE who underwent surgery for FCD. Medical records, video-electroencephalography, stereo-electroencephalography (SEEG), neuroimaging, histopathological data, and post-operative outcomes (ILAE and Engel) were analyzed.

Results: A total of 21 patients were included, 11 (53%) were male, with a median follow-up period of 3.6 years. Regarding seizure types, 14 patients (67%) experienced focal seizures evolving into bilateral tonic-clonic seizures. The epileptogenic zone (EZ) was localized to the temporal lobe in 10 patients (47.6%) with an epilepsy onset age of 15 years, compared to 11 patients (52.3%) with extratemporal zones, whose epilepsy began at 10 years ($p<0.05$). MRI revealed lesions in 14 patients (66%): 2 (14%) in the temporal lobe and 12 (85%) in extratemporal regions (p=0.001): 8 frontal, 2 occipital, 1 cingulate, and 1 multilobar. SEEG was performed in 11 patients (53%). Histopathological findings showed that 13 patients (62%) had FCD type IIa, 3 (14%) had type Ic, 2 (9%) had type IIb, 1 (5%) had type Ia, 1 (5%) had mMCD, and 1 (5%) had MOGHE. Among the 7 patients without MRI-detectable lesions, 4 had FCD type IIa, 2 had type Ic, and 1 had mMCD. Postoperative outcomes were favorable (ILAE 1-2-3/Engel I-II) in 14 patients (66.6%) and less favorable (ILAE 4-5-6/Engel III-IV) in 7 patients (33.3%).

Conclusion: FCD is a common histopathological finding in patients with drug-resistant epilepsy. In our series, two-thirds of patients achieved favorable postoperative outcomes. No significant differences in outcomes were observed regarding the EZ location, time to surgery, or the presence of MRI-detectable lesions.

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1835 | Enhancing Care for Women with Epilepsy in Kazakhstan: Implementation of the 2022 ILAE Classification in Primary Care

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Purpose: Women with epilepsy (WWE) require specialized care due to hormonal influences, reproductive health considerations, and the teratogenic risks of antiseizure medications (ASMs). In Kazakhstan, epilepsy prevalence is 5.3 per 1,000 people, with women comprising 48% of cases. However, gaps in classification-based diagnosis and primary care knowledge lead to suboptimal management. This study aims to assess the integration of the 2022 International League Against Epilepsy (ILAE) classification into clinical practice and develop an educational program for primary care providers (PCPs) to enhance epilepsy care for WWE.

Method: A comprehensive review of WWE cases from Kazakhstan's National statistical data was conducted to evaluate current diagnostic approaches. Primary care gaps were identified through a survey of 54 PCPs across urban and rural regions. Based on these findings, the Educational Program for Primary Care Providers (EPCP-WWE) was designed, incorporating training modules, digital decision-support tools, telemedicine consultations, and patient awareness campaigns.

Results: Survey results indicated that 72% of PCPs lacked formal training in epilepsy classification, and 85% reported difficulty managing WWE, particularly regarding ASM selection and pregnancy-related risks. Implementation of the 2022 ILAE classification improved diagnostic accuracy. The EPCP-WWE program demonstrated a 35% improvement in PCPs' ability to correctly classify epilepsy syndromes and initiate appropriate treatment plans.

Integrating the 2022 ILAE epilepsy classification and targeted education improves care for WWE in Kazakhstan. We recommend nationwide implementation of the EPCP-WWE program, mandatory epilepsy training for PCPs, expansion of telemedicine services, and policy alignment with international guidelines. Future research should assess long-term outcomes and refine strategies for sustainable healthcare integration.

Conclusion: Integrating the 2022 ILAE epilepsy classification and targeted PCP education significantly enhances epilepsy care for WWE in Kazakhstan. The EPCP-WWE program provides a scalable model for improving early diagnosis, optimizing treatment, and reducing health disparities. Further evaluation is needed to ensure sustainable integration into national healthcare policies.

1545 | Association of quality of life with anti-seizure medication adherence and beliefs in patients with epilepsy

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Purpose: The outcomes of epilepsy rely heavily on anti-seizure medication (ASM) compliance and adherence. Reported non-adherence varies between 26% and 79% among patients with epilepsy (PwE). Non-adherence to ASM therapy is a crucial factor in the mortality rates and failures of treatment in epilepsy. To evaluate the association between anti-seizure medication (ASM) adherence, ASM beliefs and the quality of life (QoL) in epilepsy patients in Riyadh, Saudi Arabia.

Method: A cross-sectional study was conducted at an outpatient Epilepsy Clinic of a tertiary government hospital in Saudi Arabia. Between August and December 2023, 52 patients with a confirmed diagnosis of epilepsy and receiving oral ASM therapy were identified. A self-administrated structured questionnaire containing 46 questions, using the tools (QOLIE-31, MARS-5 and BMQ-Specific) was conducted. Data analysis used frequencies, means and paired t-test to test for association between adherence and refractory seizure.

Results: The questionnaire was answered by 60% males, and 40% females. 53% of which are considered refractory to ASM. The median duration since time of diagnosis with epilepsy was 11-15 years. QoL was 61% and 52% in non-refractory and refractory epilepsy, respectively. There was no statistical difference between refractory and non-refractory participants in relation to medication adherence ($P > 0.05$). There were more concerns and lower belief in the necessity of ASM in the non-refractory group being 47%, in comparison to 42% in the refractory group ($P > 0.05$). Few cases showed very low adherence which correlated with low quality of life ($P > 0.05$).

Conclusion: Quality of life was higher in non-refractory epilepsy patients. Although, the non-refractory group showed lower beliefs in ASM. There was no difference between refractory and non-refractory epilepsy in terms of adherence to ASM. Few patients showed poor adherence and lower QoL. Overall, we recommend enhancing and emphasizing education on anti-seizure medications for epilepsy patients to improve their QoL and comprehensive care.

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1821 | Having multiple seizures per night by history may impact important EEG domains in epilepsy

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Purpose: Seizures appearing during the day or at night may have different yet concerning consequences for adults with epilepsy (AWE). Moreover, seizures in sleep are prone to occur more than once per night. Hence individuals who experience seizures in sleep may be at a higher risk of seizure recurrence. We aimed to assess specifically the impact of having multiple seizures per night (MSPN) by history on EEG outcomes in AWE.
Method: Overall, 116 AWE from epilepsy and sleep disorders tertiary clinic were included. All patients underwent neurological interview and long-term EEG with polysomnography (PSG). A structured checklist was used to assess common seizure characteristics (seizure onset, seizure type and pattern, monthly and yearly frequency, seizure in nychthemeron, etc.) and specific aspects, e.g. history of having MSPN. Chi-squared and Mann-Whitney U tests were used for statistical analysis.
Results: From 116 participants 50 % were female, mean age of the total group was 35±14.1 years. We found that in AWE who experience MSPNs had earlier onset of epilepsy than those without (19 vs 26 years, p=0.02), and had longer disease duration (15 vs 9, p<0.001). They also were taking more antiseizure medications: 1.2 vs 0.8 (p=0.02), had higher yearly and monthly seizure frequency: 69.7 vs 28.7 (p=0.01), 7.7 vs 3.3 (p=0.004) respectively. AWE with MSPN were prone to have less specific EEG changes 83.3%/97.5% (p<0.05), have more EEG changes in sleep (56.25%/23.1%, p=0.04). MSPN did not depend on polysomnographic variables.
Conclusion: The results of our study suggest that those patients, who had MSPN by history tend to have early age of epilepsy onset, longer disease duration, take more than one antiepileptic medication, higher seizure frequency and are more likely to have EEG changes during sleep.

AI and Computational Medicine

506 | Exploring comorbidities in Developmental and Epileptic Encephalopathies through using data mining in electronic health records: the example of sleep disorders

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Purpose: Sleep disorders are a major comorbidity in Developmental and Epileptic Encephalopathies (DEEs), significantly affecting the quality of life of patients and families. This study aimed to investigate the incidence and types of sleep disturbances in individuals with DEEs using a natural language processing (NLP) through our data warehouse.
Method: Dr Warehouse, a medical data mining platform implemented at Necker-Enfants Malades Children's Hospital, was used to analyze large volumes of free-text clinical data. We identified the patients with specific keywords related to major DEEs subgroups within electronic health records (EHRs) and included patients with a definitive diagnosis of DEE. Subsequently, terms associated with sleep disturbances and their treatment were searched in the EHRs.
Results: The cohort included 884 patients: Lennox-Gastaut Syndrome (LGS) (301), Dravet Syndrome (278), Tuberous Sclerosis (167), CDKL5 (55), KCNT1 (20), SYNGAP1 (18), PCDH19 (18), KCNB1 (11), KCNQ2 (8), and SCN8A (8). In 63.7% of patients, one or more terms associated with sleep disturbances were identified. “Sleep disorder” was the most frequently reported concept (47.2%), followed by “Nocturnal seizure” (40.5%), “Night awakenings” (23.9%), and “Restless sleep” (16.2%). References to “Melatonin” or “Prolonged-release melatonin” were found in 32.7% of cases; in 3.1%, these terms were present without any associated sleep disturbance terms. Variations were observed across etiologies: for example, “Nocturnal seizure” was more frequently reported in LGS patients (50.5%), while “Sleep disorder” (77.8%) and “Night awakenings” (38.9%) were more common in SYNGAP1-DEE patients.

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Conclusion: These findings confirm existing literature on the high prevalence of sleep disorders in DEE patients and highlight differences across epilepsy syndromes and etiologies. This methodology proved effective for exploring sleep comorbidity incidence and type in a large cohort of DEE patients through EHR and can therefore be applied to investigate other comorbidities encompassing other diseases.

510 | Bridging the Gap in Tonic Seizure Detection: A Systematic Review and Meta-Analysis of Automatic Detection Systems

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Purpose: Tonic seizures are a significant clinical concern in epilepsy, particularly in Lennox-Gastaut Syndrome. Accurate detection of these seizures is critical for improving patient outcomes, yet current detection systems face substantial challenges in reliability and applicability. This systematic review and meta-analysis aimed to evaluate the effectiveness of automatic detection systems for tonic seizures, focusing on different modalities, algorithms, and performance metrics.
Method: Following PRISMA guidelines, a comprehensive search was conducted across PubMed, Scopus, and Wiley databases for studies published between 2014 and 2024. Inclusion criteria targeted studies assessing automatic detection systems for tonic seizures using various modalities. Performance metrics such as sensitivity, specificity, accuracy, and false alarm rates per hour (FAR/h) were analyzed and recalculated where necessary to ensure comparability.
Results: A total of 19 studies met the inclusion criteria. Multimodal systems integrating signals from accelerometry, gyroscopes, and other sensors demonstrated the highest sensitivities (up to 1.0) and accuracies (up to 0.97), significantly outperforming single-modality approaches. False alarm rates were lowest in controlled settings, particularly for ECG-based systems, but real-world applications highlighted variability and challenges with noise and signal acquisition. The findings underscore the potential of combining physiological and neural signals with machine learning techniques to improve detection accuracy.
Conclusion: While recent advances in neurotechnology have enabled substantial progress in tonic seizure detection, significant challenges remain, including variability in performance metrics, generalizability to diverse populations, and scalability for real-world applications. Future research should focus on standardizing evaluation frameworks, diversifying training datasets, and validating systems in clinical and outpatient settings.

519 | Distinct Functional Connectivity Network in Two Subtypes of Temporal Lobe Epilepsy Across East China

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Purpose: Focal impaired awareness seizures (FIAS) and focal to bilateral tonic-clonic seizures (FBTCS) are common subtypes in temporal lobe epilepsy (TLE), and the challenge of distinguishing between them complicates the clinical management of the disease. Here, we aim to investigate the differences in functional connectivity between FIAS and FBTCS and propose a classification model.
Method: This cross-sectional study included 35 patients with 33 FIAS and 27 FBTCS during EEG recordings. The EEG-based functional connectivity and network topology parameters are comprehensively studied to characterize the features of the network structure. A machine learning model was proposed to verify the effectiveness of the brain network.
Results: Network features were stronger in FIAS than FBTCS during seizures, prominent in the δ, θ, and α frequency bands. Functional connectivity was stronger in FIAS than FBTCS during seizures, and local connectivity was lower while global connectivity was higher in FBTCS compared to FIAS. The machine learning model demonstrated robust predictive performance, accurately distinguishing between FIAS and FBTCS during the ictal phases.
Conclusion: Our research revealed the different functional connectivity network between FIAS and FBTCS during seizures, which can be used to form a classification model. These findings may elucidate the mechanisms and models of FIAS and FBTCS in TLE, guiding further construction of an intelligent and systematic TLE classification system using machine learning models.

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536 | Noisy Spontaneous Firing May Modulate Seizure Threshold: Insights from Seizure Simulations with Density-Based Neural Mass Models

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Purpose: While the role of noisy spontaneous neuronal firing in improving the sensory information processing, such as the stochastic resonance phenomenon, is well-established, its impact on seizure dynamics remains poorly understood and is usually neglected. This study investigated whether the noisy spontaneous firing modulated the seizure threshold and aimed to elucidate its potential role in epileptogenesis.
Method: This study utilized a density-based neural mass model to simulate the CA1 hippocampal network, comprising a pyramidal cell population receiving excitatory feedback from local pyramidal cells and inhibitory feedback input from local interneurons. Within this mean-field framework, additional noisy spontaneous firing, modeled as a Poisson process with a rate determined by a sigmoid function of the mean membrane potential, was incorporated for each cell population. The noise intensity, defined by the maximum Poisson rate, was systematically varied. We analyzed seizure thresholds for generating sporadic interictal spikes under varying excitatory and inhibitory synaptic gain conditions to assess the impact of changing the noise intensity.
Results: Increasing the noise intensity raised the seizure threshold, reduced sporadic interictal spike frequency, and stabilized CA1 network dynamics. This effect was robust across various synaptic gain conditions, highlighting the noisy spontaneous firing played a crucial role for mitigating seizure generation and increasing non-seizure state stability.
Conclusion: The noisy spontaneous firing may naturally stabilize seizure networks by increasing the seizure threshold. These findings emphasize its potential for seizure prevention and its indispensability when building computational epilepsy models to investigate seizure prevention strategies. Future studies shall study its interaction with possible modulatory mechanisms such as electrical stimulation for exploring therapeutic intervention against seizures.

579 | Spectral and entropy dynamics of ictal vs. interictal generalized spike-and-wave discharges in absence epilepsy

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Purpose: The 3 Hz generalized spike-and-wave discharge (GSWD) is the hallmark EEG pattern of absence epilepsy, representing either ictal or interictal activity with distinct clinical implications. This study aimed to explore the differences in spectral content and entropy dynamics of ictal and interictal GSWDs of patients with absence epilepsy, especially in clinical settings where the video correlation is unavailable, or the EEG technician fails to examine the patient during the epileptiform discharge.
Method: Forty GSWDs (20 ictal, 20 interictal) from 12 patients with Childhood/Juvenile Absence Epilepsy from the Epilepsy Clinic of Hospital "Country 2000", Jalisco, Mexico, were analyzed. Ictal and interictal states were confirmed by board-certified epileptologists through behavioral testing and video-EEG analysis. EEG signals were artifact-cleaned and segmented into one-second windows: Pre-burst (before the epileptiform pattern), Post-burst (after the epileptiform pattern), and Background. Power spectral density (PSD) in the classical frequency bands, approximate entropy (ApEn), and multiscale sample entropy (MSE) were calculated. Differential variables Pre-burst *minus* Background, Post-burst *minus* Background, and Post-burst *minus* Pre-burst were analyzed across anterior, central, temporal, and posterior regions applying the Mann-Whitney U test ($p<0.05$, ictal vs. interictal).
Results: Ictal patterns had higher delta and theta PSD than interictal ones across regions, especially in the central and posterior regions during Pre- and Post-burst *minus* Background conditions. Meanwhile, interictal patterns showed higher beta PSD in the anterior region during these conditions. Ictal patterns exhibited higher ApEn and MSE in central and posterior regions during Post-burst *minus* Pre-burst condition, while interictal patterns had higher ApEn and MSE in the anterior region during Post-burst *minus* Background.
Conclusion: Distinct spectral and entropy profiles in ictal vs. interictal GSWDs suggest potential biomarkers for absence epilepsy. These preliminary findings highlight the value of quantitative EEG analysis in distinguishing ictal from interictal activity and hold promise in enhancing diagnostic accuracy and therapeutic strategies.

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603 | Interictal functional connectivity at high frequencies discriminates epileptogenic tissue and predicts outcome in drug-resistant epilepsy

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Purpose: Epilepsy is progressively acknowledged as a disease of disrupted brain networks. Highly connected nodes in these networks represent potential surgical targets. In this work, we assess whether interictal functional connectivity (FC) in intracranial electroencephalography (iEEG) can quantify the epileptogenicity of different brain regions, distinguish between the epileptogenic zone (EZ) and eloquent cortex, and predict surgical outcome.
Method: We computed functional connectivity in 18 drug-resistant epilepsy patients (DRE) using three different connectivity techniques (directed and undirected) in iEEG segments with and without high-frequency oscillations (HFOs). We then calculated four local graph properties (strength, betweenness centrality, page rank, and clustering coefficient) in eight frequency bands (from delta to fast ripples). We compared each property inside and outside the resection in patients with good and poor outcomes and assessed its utility in predicting the EZ and the surgical outcome. We finally explored the temporal consistency of the networks in patients with multiple-night recordings, by comparing their local properties across different nights.
Results: We observed lower outward strength and clustering coefficient inside resection (Wilcoxon Signed Rank test, $p<0.05$) for good-outcome patients and no differences for poor-outcome in all frequency bands above beta. Logistic regression models trained on local network properties predicted the EZ with up to 80% accuracy (AUC=0.87, precision=0.80, recall=0.79). Resection of "sink" nodes (outward strength < threshold) was predictive of outcome (up to 83% accuracy). All network measures proved stable across 4 different nights at the cohort, patient, and electrode levels (Linear Mixed Effects, $p>0.05$).
Conclusion: Our findings suggest that functional connectivity at high frequencies can identify the epileptogenic brain regions in DRE patients and become a promising tool for predicting surgical outcome. The temporal stability of FC across different recording days strengthens its potential as a tool for investigating epileptogenicity in the presurgical workup.

642 | Development and Validation of a Seizure Alert Detection Collar for Assistance Dogs

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Purpose: To formalize and provide proof of concept for seizure alerting behavior in trained assistance dogs through the development of a seizure alert detection collar. Anecdotal evidence, and a small body of research has suggested that untrained assistance dogs can alert their handlers to imminent seizure activity. This research aims to standardize these observations in trained assistance dogs and explore the feasibility of leveraging wearable technology to enhance the reliability and utility of such behaviors.
Method: Anecdotal reports of untrained dogs exhibiting pre-seizure alert behaviors were analyzed, identifying common indicators such as vocalization, physical contact, and agitation. A demonstrable event-detecting collar equipped with advanced sensors and wireless connectivity to monitor and physical behavioral changes in trained dogs was developed and tested. The collar was designed to detect pre-seizure alerts through integrated sensors for movement analysis. Handlers recorded instances of trained alerting behavior using a mobile application synchronized with the collar, as well as time stamped video recordings of instances, enabling real-time data collection, validation and analysis.
Results: Preliminary results demonstrated the collar effectively recorded and transmitted these alerts; corroborating handler recorded events with high accuracy. The collar's ability to detect and transmit behavioral changes reliably supports the hypothesis that seizure alerting dogs have the potential to remotely alert family members, friends and carers to imminent seizure activity.
Conclusion: Our findings provide compelling evidence supporting the potentially life changing benefits of seizure alerting in trained assistance dogs. The seizure alert detection collar offers a promising tool for validating and harnessing these abilities, with the possibility of improving the safety and quality of life for individuals with epilepsy.

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649 | Quantifying Ictal Brain Connectivity Dynamics from SEEG for Epileptogenic Zone Identification in Refractory Epilepsy

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Purpose: SEEG monitoring can assist during the planning of different invasive procedures for the treatment of Refractory Epilepsy (RE) by providing information to help define the Epileptogenic Zone (EZ). Traditionally, contact classification is based on qualitative signal and image analysis by clinicians. New decision-supporting quantitative tools can assist this classification by unveiling Epileptogenic Network dynamics. To this end, we aim to present Functional Connectivity (FC) findings that help characterize the EZ and identify new biomarkers that such tools can leverage.
Method: SEEG recordings from 76 seizures from 20 RE patients from a public dataset were included. Ground truth for their EZ was based on seizure-free operative outcome. The temporal linear dynamics around the seizure onset were analyzed through Granger's Causality-based methods for nodes (contacts) in/out information flow analysis. Furthermore, Phase Locking Value was measured to investigate the synchronization dynamics during this period. Statistical analysis was performed to identify significant differences between pre-ictal and ictal periods and between EZ and non-EZ nodes.
Results: EZ nodes showed a significant increase in information inflow ($p<0.001$) and a decrease in outflow ($p<0.001$) in the ictal period compared to pre-ictal, while both decreased on non-EZ nodes ($p<0.001$). The inflow of EZ contacts was significantly higher than non-EZ ($p<0.001$), and the outflow was significantly lower ($p<0.001$) in both periods. Moreover, EZ nodes were less synchronous during pre-ictal periods ($p<0.01$). Around the seizure onset, they showed a sharp increase in synchronization strength, followed by non-EZ nodes. During ictal periods, no differences in synchronization strength were found between the two nodes' groups ($p=0.93$).
Conclusion: SEEG nodes involved in the EZ showed significantly different FC behavior. Thus, FC features are a promising biomarker for EZ identification from SEEG contacts. This analysis can be integrated into a future computational tool dedicated to clinical support during the planning of different RE treatments. Funding: FCT(LA/P/0063/2020).

684 | Artificial intelligence-based tool for spike-and-wave discharge detection in genetic absence epilepsy rats

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Purpose: Genetic absence epilepsy rats from Strasbourg (GAERS) is a critical model for investigating spike-and-wave discharges (SWDs) (Danober L et al. Prog Neurobiol 1998;55:27–57; Marescaux C et al. Epilepsy Res Suppl 1992;8:9–25). However, manual analysis of electroencephalography (EEG) recordings is time consuming and prone to inter-observer variability. There are studies for automatic detection of SWDs in GAERS, including our earlier deep learning-based model but further refinements in accuracy, efficiency and precise border demarcation remain necessary (Baser O et al. Biomed Signal Process Control 2022;76:103726.). This study aimed to build a fast, accurate and reproducible Artificial Intelligence (AI)-based SWD detection tool that overcomes these limitations.
Method: In 75 hours of intra-cortical EEG recordings from 16 GAERS, SWDs were manually labeled and used to feed the models. Convolutional neural network (CNN) and extreme gradient boosting (XGBOOST) models were trained. In the CNN model, power spectral density (PSD) analysis was applied at 2-second EEG intervals. For the XGBOOST model short-time Fourier transform (STFT) was applied to 0.6-second EEG intervals then each interval's mean amplitude was added. Finally, a brief post-processing step was integrated to further refine SWD border demarcation and reduce computational load by-passing intervals deemed improbable for SWDs.
Results: The CNN model achieved 93.7%±0.07% overall accuracy, F1 score of 90.11%±0.23% on 5-fold-cross-validation. The XGBOOST model achieved 96%±0.2% overall accuracy on 20-fold-cross-validation, F1 scores of 94.9%±0.31%, 97.0%±0.00% SWD and artifact classes respectively. Training the model took 2 minutes, the pipeline of preprocessing and prediction was completed within 40 seconds.

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Conclusion: With high accuracy, precise demarcation and a fast, efficient pipeline, this tool significantly accelerates EEG analysis, saving researchers' time and minimizing inter-observer variability. By minor modifications and additional training, the tool can potentially be adapted for other rodent models. Future work will advance the tool's capabilities.

767 | Exploring the epilepsy-depression relationship using Artificial Intelligence on Real-World Data in Germany, France, Italy and Spain

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Purpose: Literature suggests a bi-directional relationship between epilepsy and depression; however, the exact mechanisms underlying this relationship are not entirely understood. In previous work (Ruggieri et al. Eur J Neurol. 2024;31(Suppl. 1):e16338), Machine Learning (ML) was used to identify predictors of depression in patients with epilepsy (PWE) using German electronic medical records (EMR). This study extends the analysis of depression predictors in PWE to additional countries (France, Italy and Spain) and explores predictors of epilepsy in patients with depression (PWD).
Method: Four national EMR databases include data from 4956-55505 PWE (Germany N=55505, France N=31785, Italy N=12171, Spain N=4956) and 35968-685743 PWD (Germany N=685743, France N=355588, Italy N=139178, Spain N=35968). Country-specific tree-based models were trained on this data to predict risk of depression onset in PWE and epilepsy onset in PWD. Recorded diagnoses, prescriptions and visits were used as input features. Explainable AI identified important features for prediction.
Results: Age and gender were consistently found to be important predictors for both depression and epilepsy onset in PWE and PWD, respectively. The use of antimigraine medications, anxiolytics and antipsychotics were associated with depression in PWE while the use of antimigraine, antithrombotic agents and antipsychotics were observed as predictors of epilepsy in PWD.
Conclusion: This study starts delineating profiles of PWE at higher risk of developing depression and vice versa. Further analyses in the United Kingdom, Sweden and Denmark will expand the data to include socio-economic status and patient outcomes (hospitalizations, mortality). Using this data across all countries, further work could involve the creation of a model involving clinical, demographic, and healthcare utilization data to help predict those at higher risk and allow early treatment and possibly prevention. Angelini Pharma S.p.A. is the sponsor and funded IQVIA to conduct the study.

771 | Co-creation of new electronic clinical outcome assessments (eCOAs) in Dravet syndrome

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Purpose: Patients with Dravet syndrome experience treatment-resistant epilepsy and neurodevelopmental delays, leading to intellectual disability. These challenges severely impact the quality of life (QoL) for both children and their caregivers. However, many aspects important to them are not captured by current disease-specific outcome measures, which mainly focus on seizure counts. New digital outcome measures could enhance remote monitoring, support clinical trials, and capture meaningful, patient-relevant outcomes. This study aims to develop electronic clinical outcome assessments (eCOAs) by identifying meaningful aspects of health (MAH), concepts of interest (COI), and relevant outcomes through collaboration between Aparito's Patient Group Accelerator and the Dravet Syndrome Foundation Spain. The usability and clinical utility of these measures will be tested using the Atom5™ software platform.
Method: A survey was conducted with 50 participants through the Dravet Syndrome Foundation Spain. It explored daily impacts, symptoms, and acceptance of remote digital technology. Insights from a follow-up focus group helped identify MAHs and COIs. A conceptual model was then developed to guide the design of a fit-for-purpose software platform. The platform will be co-designed and tested for usability.
Results: A conceptual framework will be presented to outline eCOAs capable of measuring outcomes of interest for the Dravet syndrome community. A tailored Atom5™ platform for patient-generated data capture and analysis will be developed and tested by patients and their families. They will provide feedback on performing and video recording tasks at home, which will inform the design of a decentralized clinical study.
Conclusion: Co-creating digital outcome measures with Dravet syndrome patients and their families is crucial for

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developing tools that accurately capture the aspects most relevant to their daily lives.

788 | Towards Standardized Seizure Forecast Algorithm Development and Evaluation

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Purpose: The unpredictability of seizures significantly impacts the quality of life for individuals with epilepsy. While seizure forecast has emerged as a promising approach, lack of standardization in protocols for developing and testing algorithms inhibits direct comparison between state-of-the-art approaches, both hindering progress in the field and limiting clinical applicability. In this work we present a Python-based framework designed to standardize the development, evaluation, and reporting of individualized algorithms for seizure forecast.
Method: The framework was tested using the My Seizure Gauge Seizure Forecasting Challenge dataset to develop three distinct models: (1) a periodicity model based on seizure times, (2) a logistic regression model using time series features from wearable devices, and (3) an ensemble model combining the two. The framework was used throughout the whole model development process. This included automation of cross-validation splits, labeling of data, postprocessing of forecasts, computation of deterministic and probabilistic evaluation metrics, and visualization of results. Observations from the development process were used to assess the framework's usability and effectiveness. The framework is publicly available at https://github.com/anascacais/SeFEF and on PyPI to facilitate broader adoption by the community.
Results: Preliminary observations suggest that the framework simplifies data preparation, facilitates consistent evaluation across different approaches, and supports direct performance comparisons, even when using diverse data types and modeling approaches. While formal metrics were not collected, anecdotal evidence during its application indicated reduced development time and minimized the risk of unintentional methodological variations that could compromise comparability between approaches.
Conclusion: This framework addresses critical challenges in seizure forecasting research by promoting methodological consistency and enabling reliable comparisons between diverse algorithmic approaches. Its adoption could drive future efforts into a convergent approach regarding study design and evaluation methodologies, supporting the clinical translation of seizure forecasting tools. Further validation is necessary to confirm its broader applicability.

843 | Applying Generative Large Language Models to Calculate Seizure Frequency for People with Epilepsy

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Purpose: Seizure frequency is difficult to automatically extract from free-text Electronic Health Records (EHRs) in the United Kingdom due to their unstructured nature, doctors and nurses being inconsistent in entering seizure information, 'noise' created by lots of non-seizure medical information, and ambiguous language. Yet seizure frequency data is critical when using AI tools to mine big epilepsy datasets to improve patient treatment outcomes.
Method: We developed an innovative approach to solve this problem by applying recent generative Large Language Models (LLMs), all released in 2024, to extract seizure frequency data at a specific point in time from individual EHRs in a new dataset that we curated from two London hospitals: King's College Hospital, and Guy's and St Thomas' Hospital (84,936 EHRs and 10,527 unique adult epilepsy patients). We prompted the LLMs to calculate a patient's seizure frequency as expressed by the number of times per month on average. This singular numerical measurement allows us to determine whether a patient's seizures are improving over time or not. We optimized the LLMs' output by fine-tuning the models on a sample of our annotated proprietary dataset.
Results: The best-performing LLM was Paris-based Mistral AI's Ministral 8B (8 billion parameters) Instruct version. It achieved an F1 score of 0.76 and an accuracy rate of 0.63 when evaluated on eight temporal seizure frequency categories, which sets a high bar, and an F1 score of 0.87 and an accuracy rate of 0.78 when evaluated on binary categories of frequent and infrequent seizures, which sets a more realistic bar.
Conclusion: Generative LLMs are a new and valuable AI tool to extract seizure frequency data from free-text EHRs, and the most recent LLMs demonstrate significant ability

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for mathematical reasoning. The research was funded by Epilepsy Research Institute UK (project reference 2209 Richardson Angelini) and Angelini Pharma.

880 | Intracranial Spike activity from N3 and N2 sleep-stages best localizes the Seizure-Onset-Zone

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Purpose: Epileptiform spikes are a well-established interictal electroencephalographic (EEG) biomarker of epilepsy. However, past research using intracranial-EEG (iEEG) has found only moderate overlap between regions of frequent spike-activity and seizure-onset(SOZ). Previous work has been limited by using only minutes of data to quantify spike-activity or research-grade spike-detectors. We build on previous research by measuring spike-activity in multi-day records using a clinically validated spike-detector. We aim to: (i)explore the differences in intracranial spike-activity from different sleep/wake-stages; (ii)use these differences to improve the ability of spikes to localize the SOZ.
Method: The EEG data came from the EPILEPSIAE database. The selection-criteria included: simultaneous scalp-EEG and iEEG, sampling-rate>=1kHz, 48-hours of EEG, 30 minutes of each sleep-stage. Seven patients were selected. Sleep-stages were estimated using the scalp-EEG and Persyst15a®. The spike-events were detected on the iEEG using Persyst15a®(Reveal-detector). Logistic regression was used to classify SOZ channels based on spike activity.
Results: Patients were deemed to be awake in 63% of the data. Time asleep was divided into four sleep-stages as follows: N3=24%, N2=49%, N1=12%, REM=15%. The average spike-occurrence-rate-per-minute from each sleep/wake-stage was: N3=50, N2=45, N1=44, Wakefulness=32, REM=30. The spike-activity from all sleep-stages was significantly higher in the SOZ than in the non-SOZ ($p<=0.01$, Mann-Whitney-U). The spike-activity during Wakefulness was also higher in the SOZ, however, this difference was less robust ($p=0.02$). The logistic-regressor achieved the following median area-under-the-receiver-operating-characteristic-curve for each sleep/wake-stage: N3=0.75 (iqr=0.09), N2=0.74 (iqr=0.09), REM=0.70 (iqr=0.15), N1=0.68 (iqr=0.06), Wake=0.61 (iqr=0.11).
Conclusion: The proportions of time in various sleep/wake-stages and the spike-occurrence-rates in each stage agree with previous studies, thus providing some validation of the sleep-staging and spike-detection algorithms. The spike-activity from N3 and N2 best localized the SOZ, which is also in agreement with previous studies. Our results suggest that automated iEEG spike-detection for SOZ delineation is clinically feasible and support the value of conditioning iEEG analysis by sleep/wake-stage. Funding: MITACS Grant IT38347

1028 | A Multimodal Pre-Trained Deep Neural Network for Automated Seizure Detection and Localization

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Purpose: Automated Seizure detection and localization can facilitate epilepsy diagnosis and treatments. This study presents a novel pre-trained model integrating video and electroencephalogram (EEG) data to enhance the precision of automated seizure detection and localization.
Method: The dataset contains 502 patients and 5374 seizure events. Video-EEG data from 46 patients were reserved for testing. Data were segmented into 4-second epochs. Our multimodal architecture processes EEG and video through specialized branches: EEG branch employs EfficientNet encoder with feature alignment, while video branch utilizes X3D-M network for spatiotemporal encoding. Multimodal fusion implements Transformer-based crossattention with learnable classification tokens and positional encoding, enabling deep feature interaction between modalities.
Results: For seizure detection using 17,413 training and 2,546 testing seizure epochs, the model achieved 0.975 area under sensitivity-specificity curve and 0.822 area under the precision-recall curve. At clinically relevant 80% sensitivity, precision was 63.7% with 98.6% specificity. For seizure localization, 4559 seizures with clear origins were categorized into five classes: frontal, temporal, occipital, centro-parietal and generalized. Using 24,557 training epochs from 454 patients and 1,778 testing epochs from 45 patients, EEG-only model achieved 64% overall accuracy. Video integration improved accuracy to 66%, with frontal seizures showing greatest benefit (precision increased from 76% to 80%). Meaningful Improvements were also observed in occipital seizures (precision increased from 59% to 62%). Centro-parietal seizures maintained 62% precision with enhanced sensitivity (from 71% to 74%). Temporal seizures exhibited slight gains (EEG+video: 52% precision 83% sensitivity, EEG-only: 51% precision 82% sensitivity), whereas generalized seizures remained largely unchanged.

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Conclusion: This study provides a novel pretraining deep learning model based multimodal data. The model successfully detect and localizes seizure origins in an independent testing dataset. The model integrated video data showed good performance in seizure localization.

1041 | Deep Learning detection of drug-resistance in patients with epilepsy using routine EEG data

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Purpose: Deep learning is a branch of machine learning that uses multi-layered neural networks to automatically learn patterns from large datasets. Our aim was to develop a Convolutional Neural Network (CNN) model to classify patients with epilepsy in drug-responsive or drug-resistant using standard surface EEG recording analysis.
Method: We reviewed all consecutive EEG recordings from patients with a definite epilepsy diagnosis under follow-up at a tertiary center's epilepsy unit from 2020 to 2024. All patients had a surface EEG with a standard 10:20 recording protocol of ≥30 minutes. Patients were labelled as drug-responsive or drug-resistant according to ILAE 2010 consensus definition and those in which epilepsy surgery was performed were excluded. Deep learning models were developed by an external observer blinded to any clinical data, except for drug resistance status. The initial dataset was randomly split into training (80%) and test (20%) sets. During the training phase, we employed a 10-fold cross-validation strategy and the bootstrap method to ensure robustness and generalizability.
Results: A total of 180 EEG recordings from different patients were included; mean age (SD) was 41.1±17.2 years, 54.5% women and 47.5% had drug-resistant epilepsy. The median age at onset was 20 [IQR:10–35] years. In the drug-resistant group, there was a higher proportion of focal epilepsies—particularly of temporal lobe—and a longer duration of disease. During the training, over 100 CNN configurations were tested to identify the best-performing model, which exhibited a 73.5% validation accuracy. During the test, we reached an overall accuracy of 70%, positive and negative predictive values of 72.2% and 66.6%, respectively, with both sensitivity and specificity approximately 70%.
Conclusion: Our best-performing artificial intelligence model showed a test accuracy of 70% for the correct classification of drug-resistance status in patients with epilepsy using only surface EEG data. Training in larger datasets is needed to improve these results.

1050 | Resting-State EEG Functional Connectivity in Juvenile Myoclonic Epilepsy: Insights into Biomarkers and the Impact of Antiseizure Medication

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Purpose: To compare resting-state EEG functional connectivity in patients with juvenile myoclonic epilepsy (JME) with and without antiseizure medication (ASM) and healthy controls, aiming to identify biomarkers for JME independent of epileptic discharges, which may be absent in up to 50% of cases despite activation procedures.
Method: Fifty-four EEG recordings, from which 34 belong to patients with JME (17 with ASM and 17 without ASM) and 20 healthy controls were analyzed. A 140-second resting-state segment with closed eyes and no epileptiform discharges was selected from each recording. A 20 Hz low-pass Butterworth filter was applied to each segment, followed by blind source separation to remove artifacts. Clean segments were divided into 1-second windows, and an ideal Fourier filter was applied to extract delta, theta, alpha, and beta bands. Pearson's correlation was used to calculate connectivity, with analyses conducted for intra-hemispheric, interhemispheric, and overall connectivity. The Kruskal-Wallis test was used to identify significant differences between groups with α=0.05.
Results: Significant differences were observed between controls and patients without ASM, where the latter showed reduced connectivity in the alpha and beta bands, particularly in temporal and central regions and a special measure of total connectivity that is the median connectivity of all regions belonging to each analysis. No significant differences were found between controls and patients with ASM.

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Conclusion: JME can be associated with decreased functional connectivity, which may serve as a potential biomarker, even in the absence of epileptic discharges. ASM appears to normalize connectivity, making brain activity in patients with JME more similar to that of healthy controls. These findings support the utility of connectivity analyses in advancing diagnostic and therapeutic approaches for JME.

1072 | Deep learning for the identification of pro-ictal states in human temporal lobe epilepsy using microelectrodes

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Purpose: Seizure forecasting has become a pivotal focus in epilepsy research. While electroencephalography (EEG) remains the gold standard for epilepsy diagnostics, stereo-electroencephalography (sEEG) offers deeper insights into complex brain interactions and potential preseizure dynamics. However, definitive evidence for the existence of a pro-ictal state—a brain state marked by an increased likelihood of seizure onset—remains elusive. Our objective is thus to outperform the current state-of-the-art approaches in pro-ictal state identification, using a novel deep learning methodology, while benefiting from combining multiple scales of analysis in continuous long-term recordings.
Method: In this study, we propose a new Artificial Neural Network (ANN) architecture which combines a Transformer and a Convolutional Neural Network (CNN) in order to detect pro-ictal states. In addition to this ANN methodology, we also benefit from utilizing microelectrodes to explore neuronal activity at an unprecedented level of detail. We analyzed data from 23 patients with pharmacoresistant temporal lobe epilepsy, recording activity in deep brain structures across several consecutive weeks. This high-resolution approach allows us to investigate the origins of signals typically observed at broader scales. Neuronal activity was compared between interictal periods (seizure-free days) and preictal periods (within hours before a seizure). This approach builds upon previous studies demonstrating that sEEG connectivity is altered on preictal days compared to interictal days and that this might be observable at a finer scale.
Results: This novel Deep Learning approach seems to show significant improvements in anticipating seizures when compared to traditional methods such as AutoRegressive Integrated Moving Average (ARIMA), Long Short-Term Memory networks (LSTM), and Recurrent Neural Networks (RNN) which fail to capture long-term dependencies.
Conclusion: Using a CNN-Transformer based Artificial Neural Network, more capable of understanding the global context, and combining multiple scales of sEEG analysis seem to improve pro-ictal states identification in human temporal lobe epilepsy.

1163 | Advancing Epilepsy Care: Free and Intuitive Electrical Source Imaging Software for Underserved Communities

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Purpose: Epilepsy has a higher prevalence in populations with low to middle socioeconomic levels, where limited access to diagnostic tools hinders adequate management. Electrical Source Imaging (ESI) is a clinically validated tool for the presurgical evaluation of patients with drug-resistant focal epilepsy (DRE); however, licenses for commercially distributed software are prohibitively expensive for resource-limited settings. This project aims to develop open-source, cost-free, and user-friendly software for performing ESI in such scenarios.
Method: The software was developed using Python modules, including PySide6, MNE-Python, Nilearn, and Nibabel, which were integrated into a graphical and intuitive interface to facilitate usability by neurologists. The software was evaluated using a curated database of patients who underwent epilepsy surgery at the epilepsy clinic of Hospital Country 2000. Its performance and user-friendliness were assessed based on feedback from medical staff and the engineering team.
Results: The software successfully implemented EEG-based ESI algorithms for patients with DRE. The estimations were reviewed and validated by board-certified epileptologists. Furthermore, complementary tools such as topographic mapping and functional connectivity analyses were incorporated to provide additional insights into the patients' brain activity.
Conclusion: The developed software is an accessible and effective tool for localizing the epileptogenic zone in patients with DRE. Its user-friendly design and free access enhance its feasibility for implementation in resource-limited settings, thereby contributing to the diagnosis and treatment of epilepsy in underserved populations.

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1329 | Radiomics Analysis with Machine Learning to Differentiate LEAT and Developmental Abnormalities

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Purpose: develop a machine learning prediction model identifying FCD (Focal Cortical Dysplasia) and LEAT (Long-term Epilepsy-associated Tumor)

Method: This study categorizes post-surgical patients into two groups, FCD and LEAT. First, lesions are manually delineated using a graphic software. By aligning lesion features with preoperative and postoperative MRI scans, the lesion location is identified and annotated on T2-weighted images. Next, radiomic features are extracted from the annotated lesions using Image Processing Toolbox in MATLAB R2024a. A total of 206 radiomic features are extracted. These features are ranked based on their influence using the Minimum Redundancy Maximum Relevance (mRMR) algorithm. Subsequently, 20 machine learning classifiers are trained individually. Performance metrics, including true positives, false positives, true negatives, and false negatives, are used to calculate precision, recall, specificity, accuracy, ROC curve, and AUC for each model. These metrics provide a comprehensive evaluation of each model's performance.

Results: The optimal model in this study is the "Quadratic Support Vector Machine (Quadratic SVM) trained using features ranked 1 to 16". Its performance evaluation metrics are as follows, with precision of 0.909, recall of 0.938, specificity of 0.818, and accuracy of 0.897.

Conclusion: The results indicate that this study has preliminarily achieved decent outcomes, which can serve as an objective decision-making tool. It provides clinicians with preoperative or pre-treatment evaluations, improving diagnostic accuracy and reducing patient risks. This enables physicians to formulate treatment strategies early (e.g., deciding between craniotomy or minimally invasive surgery), plan surgical procedures (determining the extent based on lesion location), and assess the urgency of the surgery. However, we need more MRI data to expand the sample size or use it as an external test set to enhance the model's performance. Additionally, we aim to develop a commercial software application within the next few years, enabling practical implementation in the healthcare industry to effectively support clinical practitioners.

1457 | Navigating BrainFocus iEEG: A Cloud-based Software to Assist Clinicians in Identifying Seizure Onset Zone(s) in Drug-resistant Patients

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Purpose: The pre-surgical evaluation of drug-resistant epilepsy involves the visual inspection of long stereo-EEG (sEEG) recordings to identify epileptogenic regions, a time-consuming and error-prone process. To enhance diagnostic accuracy and efficiency, we developed BrainFocus iEEG (BFiEEG), a cloud-based software that automates the localization of the seizure onset zone (SOZ), a key proxy for the epileptogenic zone.

Method: BFiEEG's algorithm detects seizure-specific spectral signatures by identifying time-frequency windows where Global Activation (GA) and Activation Entropy (AE) are maximized. These features help pinpoint or connect to the SOZ. The software provides a patient-level workspace for organizing iEEG and MRI data, along with interactive tools for visualizing epileptogenic patterns in synchronization with a 3D brain model. Clinicians can adjust the algorithm's detection sensitivity based on patient-specific seizure dynamics.

In retrospective studies with 20 adult patients (Hospital Clínic), including temporal lobe epilepsy (TLE) and non-TLE cases, we compared BFiEEG's automated SOZ localization against standard diagnostic information and correlated it with surgical outcomes (Engel's classification, 2+ years follow-up).

Results: For TLE patients, BFiEEG achieved ~90% sensitivity and specificity, while non-TLE cases showed greater variability. Agreement between algorithm and clinical SOZ correlated with Engel class, suggesting potential clinical value. Further improvements including anatomical data (MRI, DTI), is ongoing as well as the clinical validation of the software in an operational environment.

Conclusion: BFiEEG enhances pre-surgical epilepsy diagnosis by extracting clinically relevant seizure patterns often undetectable by visual inspection, positioning itself as both a confirmatory tool for straightforward cases and a revelatory tool for complex cases. We will present a live platform demonstration and discuss its potential impact on epilepsy surgery.

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1458 | Effectiveness of Vagal Nerve Stimulation in Drug-Resistant Epilepsy: An Analysis Using Quantum Algorithms and Artificial Intelligence

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Purpose: Vagal nerve stimulation (VNS) is a safe and effective therapeutic option for the control of epileptic seizures in patients with drug-resistant epilepsy. However, the appropriate selection of patients candidate to VNS is still not well defined. The aim of this preliminary study is to identify predictive characteristics of clinical response using quantum and artificial intelligence tools.
Method: A retrospective study was conducted on patients diagnosed with drug-resistant epilepsy according to ILAE, who underwent VNS implantation between January 2008 and January 2022, with a regular clinical follow-up of more than 24 months. Data were collected on 23 patients, including: age, gender, time since diagnosis, any syndromic status, number and type of seizures, number of antiseizure medications used, and etiology. Feature selection techniques based on quantum algorithms (QAOA, SB, SA) were employed to identify the most relevant characteristics. Subsequently, predictive models were constructed using machine learning methods such as Distributed Random Forest (DRF), Gradient Boosting Machines (GBM), and Deep Learning Machines, evaluating their performance through 5-fold cross-validation.
Results: Considering the responders (34.8% of cases with $>50\%$ reduction in seizure frequency), quantum feature selection techniques agreed on the importance of age, time since diagnosis, and seizure frequency, with particular attention to focal seizures. Among the predictive models, DRF demonstrated the best performance with an accuracy of 78.26% and an AUC of 0.81.
Conclusion: This preliminary study suggests that age, time since diagnosis, and seizure frequency are key factors in predicting response to VNS in patients with drug-resistant epilepsy. The use of quantum techniques for feature selection and machine learning models represents a significant innovation in the field, providing new insights for selecting suitable candidates for surgical therapy. These preliminary results require further investigation to enhance therapeutic strategies and optimize surgical indications.

1459 | Network dynamic changes before epileptic seizures: Physiological correlates and network modeling

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Purpose: Predicting seizures through reliable pre-seizure biomarkers could greatly enhance neuromodulation therapies for drug-resistant patients. Recent research using stereo electroencephalography (sEEG) has revealed specific changes in network dynamics during pre-seizure periods. In particular, our previous work demonstrated that day-time dependent alterations preceding seizures are largely driven by an increased occurrence of recurrent, short-lasting (0.6s) high-connectivity network configurations, termed High Connectivity States (HCS). In this study, our findings provide evidence that time-dependent increases in HCS probability throughout the day can serve as a potential pre-seizure biomarker.
Method: We replicated the previous study findings using long-term sEEG recordings from a publicly available database (SWEC-ETHZ iEEG long-term database) and another patient undergoing presurgical evaluation with depth electrodes. For the latter patient, we leveraged all available monitoring information to validate the robustness of HCS alterations across different recording configurations. Additionally, we compared HCS dynamics with other sEEG measurements (e.g., power activity) and electrocardiogram derived variables (e.g., heart rate) and developed a low-dimensional statistical network model to capture key network features of the pre-seizure period.
Results: Our results confirmed the specific emergence of HCS hours before seizure onset, consistent across monopolar, bipolar, and common average referential recordings. Notably, preictal HCS probability alterations were distributed across the frequency power spectrum and exhibited stronger correlations with heart rate fluctuations than with grand average functional connectivity. The statistical model indicated that preictal HCS probability changes arise from shifts in network topology rather than changes in mean connectivity, highlighting the role of complex interactions between epileptogenic and non-epileptogenic brain regions.

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Conclusion: These findings suggest that integrating HCS probability with both invasive and non-invasive monitoring variables could establish it as a promising biomarker for an early detection of upcoming epileptic seizures.

1519 | Automated detection of interictal epileptiform discharges in scalp EEG using convolutional autoencoders and artificial neural networks

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Purpose: Electrical Source Imaging (ESI) is a clinically validated tool for pre-surgical evaluation in patients with drug-resistant focal epilepsy. However, the detection and annotation of interictal epileptiform discharges (IEDs) is a time- and resource-consuming process. Therefore, accurate automation of IED detection could optimize medical decision-making. This study presents the development and validation of an interpretable automated method for detecting IEDs in scalp electroencephalograms (EEG), aiming to enhance the accuracy of focal epilepsy treatment by providing reliable IED detections for electrical source analysis. Additionally, it streamlines clinical workflows and supports clinicians in optimizing EEG interpretation by providing a user-friendly graphic user interface (GUI).
Method: Routine EEG recordings were used for model training, including 42 from healthy subjects and 15 from focal epilepsy patients, totaling 2,141 annotated IEDs. Testing was conducted on 13 EEGs from healthy individuals and 3 from epilepsy patients, comprising 236 IEDs. The pipeline involved pre-processing for candidate IED detection, noise reduction, and average referencing, followed by feature extraction using a Convolutional Autoencoder (CAE) and classification via a Kolmogorov-Arnold Network (KAN) for interpretability. The algorithm was implemented in Python 3.12.3 with a GUI for visualization and automated detection.
Results: The proposed algorithm achieved 100% precision, detecting 164 true positives with zero false positives, outperforming commercial software while maintaining 71% sensitivity at a KAN threshold of 0.5. The software successfully identified the peak IED amplitude and timestamp, marking events with visual annotations. Processing time for a 30-minute EEG was under 5 seconds.
Conclusion: The algorithm demonstrated strong generalization across patients with minimal training data. While sensitivity was lower than commercially available systems, threshold values in the pre-processing and classification stages were optimized for precision. Adjustable parameters allow trade-offs between precision and sensitivity. Its rapid execution suggests feasibility for real-time IED detection, advancing automated EEG analysis.

1521 | Very high-frequency oscillations detector in routine stereo-EEG

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Purpose: Very high-frequency oscillations (VHFOs, >500Hz) have emerged as a valuable biomarker in delineating the epileptogenic zone. This work introduces a detector designed to identify very high-frequency oscillations in stereo-electroencephalogram recordings with a sampling frequency of 5 kHz. Since manual VHFO detection is time-consuming, a VHFO detector could significantly enhance ongoing research in this field.
Method: The study included a cohort of 67 adults with drug-resistant epilepsy who underwent resective surgery, with a 2-year post-surgical follow-up. Thirteen patients met the final inclusion criteria, and 15 channels with VHFO activity were selected for further analysis. A threshold algorithm was used to detect potential VHFOs, which were then manually confirmed. The original threshold parameters were adjusted, and the signal was processed again to select VHFO-wise interesting areas for feature calculation. A support vector machine model was trained using a leave-one-patient-out cross-validation method to classify the interesting areas window-wise. The original sample-wise ground truth labels were recalculated into window labels, and these were compared to the model output. The windows that were not selected as interesting areas were not considered in the results.
Results: After manual removing channels with VHFO rates <15/min from the dataset, the results were: Precision

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0.8088; Recall 0.6982; F1 Score 0.7620; ROC AUC 0.7010; AUPRC 0.8563. The detector results trained on all channels were: Precision 0.5768; Recall 0.6592; F1 Score 0.5622; ROC AUC 0.6645; AUPRC 0.6080.

Conclusion: In conclusion, the detector shows promise for detecting VHFOs, but the unbalanced dataset is a key limitation. This could be addressed by including more VHFO channels or using generative neural networks to generate additional examples. The determination of the channels eligibility for VHFO detection has shown as a necessary step in order to preserve the detectors reliability, which could be addressed through signal preprocessing.

1582 | Online educational survey uncovers knowledge and practice gaps in focal epilepsy amongst European neurologists and psychiatrists

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Purpose: Focal epilepsy presents challenges in diagnosis and treatment due to diverse presentations, limited standardization, and evolving therapies. An educational survey was conducted to identify attitudes, knowledge, and practice gaps among European neurologists and psychiatrists.

Method: A 27-question online CME survey assessed knowledge (disease burden, predictors, clinical data) and case-based competence. Conducted from April to December 2024, responses were de-identified and aggregated. Two questions mirrored a 2021 Medscape survey, enabling comparisons (neurologists only).

Results: Responses from 135 neurologists and 28 psychiatrists revealed discrepancies between knowledge- and competence-based performance, with better outcomes on case-based practice. Neurologists had a mean knowledge score of 49.8% (SD = 28.4), compared to psychiatrists at 36.3% (SD = 23.0). Competence scores were higher for both groups: neurologists averaged 68.7% (SD = 13.8) and psychiatrists 61.6% (SD = 16.9). As expected, both scores were slightly lower for psychiatrists (mean knowledge 36.3%, SD 23.0; competence 61.6%, SD 16.9). In managing a case of uncontrolled focal epilepsy on one ASM, 44% of neurologists and 46% of psychiatrists considered two appropriate treatment approaches, but most preferred only one of the two treatment appropriate approaches: neurologists favored add-on therapy (39%) vs switching (17%), while psychiatrists favored switching (29%) vs add-on (25%). Comparing neurologists' results from 2021 to 2024, similar results were observed across two themes: SUDEP risk factors (29% vs. 33%), etiology and seizure freedom (70% vs. 71%) respectively. Neurologists showed poor understanding of SUDEP risk factors and clinical trial data, though both groups performed better in managing focal epilepsy and comorbidities. Psychiatrists, often not ASM prescribers, showed differing results.

Conclusion: This study revealed persistent knowledge and practice gaps and inflexibility in management strategies for focal epilepsy. These findings underscore the need for targeted and sustained education to address critical gaps and improve decision-making.

1588 | Focal Epilepsy: Virtual patient simulation improves European neurologists' performance in diagnosis and management but uncovers inertia in recognizing and managing breakthrough nocturnal seizures and drug-resistant epilepsy

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Purpose: Diagnosing focal epilepsy is challenging due to heterogeneous presentation, limited patient awareness and restricted access to diagnostic tools. Further, management is complicated by diverse etiologies and numerous therapies. Using a patient simulation of a young female with focal seizures, co-morbid anxiety and depression with partial control on 2 prior monotherapies, we assessed neurologists' performance in diagnosing drug-resistant focal epilepsy and managing nocturnal breakthrough seizures with appropriate combination therapy.

Method: This CPD-certified virtual simulation allowed European neurologists to select diagnostic and treatment options from a comprehensive database (available: https://www.medscape.org/viewarticle/998607). Following decisions, learners received clinical guidance (CG) based on evidence and faculty recommendations. Pre- and post-CG decisions were analyzed using McNemar's test ($P<.05$ is significant). Data were gathered from March to December 2024.

Results: Ninety neurologists participated in the case simulation. Significant improvements were seen post-CG for identifying drug-resistant epilepsy (21% to 65%, $P<.001$), managing epilepsy (36% to 69%, $P<.001$), and evaluating comorbid anxiety/depression (67% to 75%, $P<.01$). 7% of neurologists correctly diagnosed 'drug-resistant epilepsy' which improved to 42% post-CG. With a different definition ('focal epilepsy with focal aware seizures

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and nocturnal bilateral tonic-clonic seizures'), 41% were correct pre- increasing to 70% post-CG (both P<0.001). Analyzing decision flows, correct diagnosis associated with correct treatment rose from 24% to 29%, while incorrect decisions dropped from 46% to 36%. Among those choosing incorrect treatments, 87% showed inertia pre-CG (no treatment change), decreasing to 74% post-CG. When assessing rationales for skipping combination therapy: 56% of neurologists cited concerns about side-effects, while 22% considered the patient's seizures were mild and did not require additional treatment.

Conclusion: This study demonstrates the positive effect of an online educational virtual simulation on neurologists' performance in diagnosing and managing drug-resistant focal epilepsy, but deeper analyses uncovered high levels of inertia in recognizing and managing nocturnal seizures and drug-resistant epilepsy.

1594 | Virtual patient simulation improves diagnosis and management by European neurologists but uncovers low recognition and inertia in treatment of drug-resistant focal epilepsy

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Purpose: Diagnosing focal epilepsy is challenging due to heterogeneous presentation, limited patient awareness and restricted access to diagnostic tools. Further, management is complicated by diverse etiologies and numerous potential therapies. Using a patient simulation of a 62-year-old male with post-encephalitic focal seizures with poor control despite 3 different therapies, we assessed neurologists' performance in diagnosing drug-resistant focal epilepsy and managing frequent seizures with appropriate combination therapy.

Method: This CPD-certified virtual simulation allowed European neurologists to select diagnostic and treatment options from a comprehensive database (available at: https://www.medscape.org/viewarticle/998607). After each decision, learners received clinical guidance (CG) based on evidence and faculty recommendations. Pre- and post-CG decisions were analyzed using McNemar's test (P<.05 is significant). Data were gathered from March to December 2024.

Results: 106 neurologists participated in the case simulation. Significant improvements were seen post-CG for identifying drug-resistant epilepsy (16% to 56%, P<0.001) and appropriate management (14% to 29%, P<0.001). Neurologists from the EU5 countries (France, Germany, Italy, Spain and UK) demonstrated higher diagnostic accuracy compared to those from non-EU5 countries with 31% correct diagnosis rates increasing to 67% post-CG (p<0.001) and 10% increasing to 52% (P<0.001) for non-EU5. Analyzing decision flows with a less-stringent diagnostic definition, correct diagnosis associated with correct treatment rose from 0.9% to 13%, while incorrect decisions dropped from 93% to 60%. Among those with incorrect treatment, 61% showed inertia pre-CG (no treatment change), decreasing to 46% post-CG. 43% of neurologists cited lack of expertise in managing complex cases as the main reason for not selecting combination therapy.

Conclusion: This study demonstrates the positive effect of virtual simulation-based medical education on European neurologists' performance in diagnosing and managing drug-resistant focal epilepsy. However, more in-depth analyses uncover persistently low diagnosis and management rates, underscoring the need for greater expertise and more consistent education on diagnosis throughout Europe.

1601 | Online medical education improves specialists' knowledge of add-on antiseizure medications in people with focal epilepsy

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Purpose: We evaluated whether an online educational programme directed at European-based specialists, could improve knowledge on appropriate management of people with focal epilepsy, particularly relating to add-on therapies when seizures are partially controlled.

Method: The educational activity was a 31-minute online, case-based, chapterised video with 4 European experts in Epilepsy. Educational effect was assessed using a 3-question repeated pairs, pre/post assessment survey. A paired-samples t-test was conducted to assess overall number correct and confidence change. P values <0.05 (McNemar's test) are statistically significant. Cohen's d test was used for magnitude of effect of education on the overall outcomes (knowledge). The activity launched on 11 October 2023 and data analyzed as of 15 January 2025.

Results: 1,574 neurologists and 463 psychiatrists participated in the programme, of which 154 neurologists and 30 psychiatrists completed pre- and post-assessment tests. Significant improvements were seen for both groups, with an average correct response rate of 59% and 38%

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pre-assessment, which increased to 74% and 52% post-assessment, for neurologists (P<0.001; Cohen's d = 0.72) and psychiatrists (P<0.05; Cohen's d = 0.48) respectively. Neurologists showed a significant improvement for each of the three case-based questions conversely psychiatrists demonstrated a significant improvement in only 1 of the 3 questions. As expected, neurologists performed better overall with 19% increasing to 39% answering all 3 questions correctly and 7% increasing to 20% for psychiatrists. Based on a self-reporting question, neurologists expressed a 32%, and psychiatrists expressed a 57%, increase in confidence following the education on add-on antiseizure medication selection.

Conclusion: This study demonstrates the positive effect of online medical education on specialists' knowledge and confidence in partial responses to antiseizure medications and consideration of add-on therapies for people with focal epilepsy in Europe.

1607 | Online medical education improves specialists' knowledge and competence of management in people with focal epilepsy

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Purpose: We evaluated whether an online educational programme directed at European-based specialists, could improve knowledge and competence on appropriate work-up after a first unprovoked seizure and selection of add-on therapy compared with sequential monotherapy.

Method: The educational activity was an 18-minute online, case-based video with 1 European expert in Epilepsy. Educational effect was assessed using a 3-question repeated pairs, pre/post assessment survey. A paired-samples t-test was conducted to assess overall number correct and confidence change. P values < 0.05 (McNemar's test) are statistically significant. Cohen's d test was used for magnitude of effect of education on the overall outcomes (knowledge). The activity launched on 29 December 2023 and data analyzed as of 15 January 2025.

Results: 778 neurologists and 245 psychiatrists participated in the programme, of which 114 neurologists and 31 psychiatrists completed pre- and post-assessment tests. Significant improvements were seen for both groups, with an average correct response rate of 45% and 39% pre-assessment, which increased to 65% and 49% post-assessment, for neurologists (P<0.001; Cohen's d = 0.78) and psychiatrists (P<0.01; Cohen's d = 0.68) respectively. Neurologists showed a significant improvement for each of the three case-based questions while psychiatrists demonstrated a significant improvement in 2 of the 3 questions. As expected, neurologists performed better overall with 6% increasing to 21% answering all 3 questions correctly and 0 increasing to 10% for psychiatrists. Based on a self-reporting question, neurologists expressed a 29%, and psychiatrists a 26% increase in confidence following the education on changing antiseizure medication for patients with focal epilepsy.

Conclusion: This study demonstrates the positive effect of online medical education on specialists' knowledge and confidence in managing and selecting appropriate antiseizure medications for people with focal epilepsy in Europe.

1616 | Ultradian seizure pattern detection on presurgical monitoring data: An unsupervised machine learning approach

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Purpose: Epilepsy is among the most common neurological diseases. Despite significant therapeutic advances, Drug-Resistant Epilepsy remains a challenge. The study of cycles in seizure occurrence could combat the unpredictability of seizures and reduce the burden of the disease for patients. This study explores ultradian seizure patterns in a presurgical setting using data from the EPILEPSIAE database, containing EEG recordings from 285 patients over more than 2,000 days. Detecting patterns during presurgical monitoring could allow for better management of clinicians and provide more comfort to patients in this context.

Method: We focused on 284 patients with 1,821 lead seizures. We considered the seizure onset time-of-day as a circular variable and applied hierarchical agglomerative clustering with complete linkage. Single-member clusters were deemed outliers. We introduced a clustering performance metric integrating three factors: clustered seizure ratio; average cluster density; inter-cluster separation. Statistical significance was tested via Monte Carlo simulations under the null hypothesis of uniform seizure occurrence, with a 5% significance level.

Results: Results showed that cross-patient seizure occurrence is non-uniform (Hodges-Ajne test with p=0.0440). Patient-specific analyses revealed that 25 patients (9%) displayed statistically significant time-of-day clustering,

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suggesting persistent ultradian rhythms even under the atypical conditions of presurgical monitoring. Other patients with visible patterns were found but likely fell short of statistical confirmation due to the small sample size. Additionally, 85% of the cohort displayed at least one multi-seizure cluster. Ultradian clusters could suggest the existence of an underlying circadian component.

Conclusion: These findings indicate ultradian seizure patterns can persist under presurgical conditions, potentially helping manage monitoring strategies. Concentrating observations on high-risk windows may reduce patient burden and clinical resource demands while still providing robust presurgical monitoring. This work is financed through national funds by FCT - Fundação para a Ciência e a Tecnologia, I.P., in the framework of the Project UIDB/00326/2025, UIDP/00326/2025, and Ph.D grant 2024.00672.BD.

1617 | Quantitative EEG Features Predict Treatment Response in New-Onset Focal Epilepsy: A Machine Learning Approach Across Seven Epilepsy Centers

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Purpose: Electroencephalography (EEG) is an essential tool for diagnosing epilepsy and guiding treatment decisions. Antiseizure medications (ASMs) are the mainstay of epilepsy therapy, with the primary goal of achieving the best possible quality of life by maximizing seizure control and minimizing adverse effects. However, no established EEG-based biomarkers reliably predict the efficacy of ASMs, and the selection of the initial therapy remains largely a trial-and-error process. This study applies a machine learning (ML) approach to assess whether conventional scalp EEG can predict seizure freedom in newly diagnosed focal epilepsy patients after initiating their first ASM. We hypothesize that quantitative EEG features extracted before treatment can serve as predictive biomarkers of clinical outcome in focal epilepsy.

Method: A total of 202 newly diagnosed focal epilepsy patients from seven Italian epilepsy centers were analyzed between March 2018 and January 2022. Patients were categorized as either seizure-free (SF) or non-seizure-free (NSF) after one year of ASM treatment. Pre-treatment 19-channel EEG recordings were analyzed to extract quantitative features including Power Spectral Density, Phase Locking Value, and graph theory connectivity measures. These analyses generated 138 primary features, which were expanded to 414 features through statistical operations (mean, median, and max). A Random Forest classifier was trained using a nested K-fold cross-validation approach, where the outer loop (five folds) assessed model performance on unseen data, and the inner loop optimized hyperparameters via GridSearchCV.

Results: The optimized Random Forest model demonstrated strong predictive performance, achieving an average accuracy of 71.4%, a precision of 72%, and an F1-score of 83.3%.

Conclusion: This study presents a novel ML-based approach for predicting ASM response in focal epilepsy using EEG data. The findings suggest that EEG features could be leveraged to develop clinical decision-support tools for personalized epilepsy treatment. Future research should refine this methodology to enhance individualized ASM selection and improve patient outcomes.

1618 | Continuing medical education curriculum improves European specialists' knowledge, competence and confidence on management of focal epilepsy

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Purpose: We evaluated whether an online educational curriculum, reflecting the latest evidence, could improve knowledge, competence, and confidence among European specialists in managing focal epilepsy. The curriculum comprised four principal themes: SUDEP risk communication, selection of new ASMs, managing drug-resistant epilepsy and managing comorbidities.

Method: The curriculum included seven accredited expert-led activities in various formats available from June 2023 to December 2024. Educational effectiveness was assessed using a paired pre/post design with learners serving as their own controls. Each activity included three knowledge and/or competence questions and one on confidence, assessed before and after. McNemar's and paired t-tests evaluated knowledge/competence and confidence changes respectively. Confidence was rated on a 1-not confident to 5-very confident scale. $P < .05$ is considered significant.

Results: By December 2024, 17,299 physicians participated, including 10,728 neurologists and 6,057 psychiatrists. Data from 614-1,016 neurologists and 192-7124 psychiatrist completers were analyzed. Neurologists improved knowledge by 51% and competence by 14% (both P<0.001) while psychiatrists improved by 28% and 22% (both P<0.001) respectively. Overall change in knowledge/competence was 40% for neurologists and 29% for psychiatrists (both P<0.001). Greatest improvements for neurologists and psychiatrists were on SUDEP risk communication (122% and 129% relative increases respectively, both P<0.001). Smallest improvements were for management of drug-resistant focal epilepsy (20% and 24% increases respectively, both P<0.001). 41% of neurologists and 50% of psychiatrists increased confidence (both P<0.001) and of those whose confidence increased, mean confidence increased by 64% and 63% respectively after education. 92% of neurologists improved or reinforced their knowledge/competence and a similar 90% was seen for psychiatrists.

Conclusion: This educational curriculum resulted in significant improvements in knowledge, competence and confidence among neurologists and psychiatrists on management of focal epilepsy, comorbidities and selection of therapies. Specialists who improved or reinforced knowledge/competence also saw notable and significant confidence gains.

1625 | Leveraging digital application database to help patient recruitment in clinical trials

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Purpose: Patient recruitment in randomized controlled trials, including in epilepsy research, is becoming difficult. The average number randomized per site has declined from >10 in 1990, to <5 in two recent trials mainly due to therapies targeting specific syndromes or patient populations. Digital applications like Helpilepsy allow patients to self-monitor their epilepsy to try to better understand it. Available in more than 10 languages and worldwide, Helpilepsy has built a large database. We evaluated whether the database could support recruit patients for clinical trials.

Method: Applying different filters on the database, we identified patient or seizure characteristics that might be applicable for inclusion in clinical trials. We explored the total number of patients, the amount and type of seizures, year of diagnosis, and number and type of antiseizure medications.

Results: Our database holds records of around 12.000 patients with more than 6000 newly diagnosed patients enrolled between 2020 and 2025. The database holds records of >800.000 seizures, of which 120.000 (15%) have been detected through a validated seizure detection device. Duration >3min was observed in >60.000 (7.5%), qualifying as prolonged seizures. In more than 7000 patients, 160.000 seizures (20%) were generalized (both focal and generalized onset). More than 5000 patients reported >20.000 focal onset seizures. Two or more antiseizure medications were entered by approximately 4.000 patients. Sleep data (>300k nights) with seizure detection are available.

Conclusion: The proliferation of digital tools and health applications, including Helpilepsy, has given rise to a substantial repository of patient-reported data. The Helpilepsy database, offers breadth and depth of information that may prove instrumental to drive patient recruitment in research and development. This may benefit patients, academia, physicians with benefit from disease related insights, and pharmaceutical industry that might accelerate recruitment, leading to faster introduction of new drugs to the market.

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1633 | Smarter Than Before?: Comparison of GPT-4o and GPT-3.5 in Epilepsy Case Management

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Purpose: This study statistically evaluates GPT-4o and GPT-3.5 performance in epilepsy case management across four aspects-Diagnosis, Alternative-Diagnoses, Investigations, and Management. It compares mean scores, variability, inter-rater agreement, and scoring consistency to determine GPT-4o or GPT-3.5's superiority.

Method: Anonymized histories of 25 epilepsy cases were evaluated by GPT-4o and GPT-3.5. Responses were assessed by 7 neurologists. Mean scores and standard deviations (SD) were calculated for each aspect. Interclass Correlation Coefficient (ICC) measured neurologist agreement, while Cronbach's Alpha assessed scoring consistency. Pairwise correlations between neurologists were analyzed, and interquartile range (IQR) of correlations were calculated to evaluate variability.

Results: GPT-4o outperformed GPT-3.5 across all aspects, with higher mean scores±SD (Diagnosis:9.36±0.49 v/s6.08±0.76, Alternative-diagnosis:7.68±0.47 v/s5.92±0.76, Investigations:9.36±0.49 v/s6.56±0.71, Management:9.44±0.50 v/s 6.24±0.73). ICC values for GPT-4o (Diagnosis:0.85, Alternative-diagnosis:0.82, Investigations:0.84, Management:0.86) exceeded GPT-3.5 (Diagnosis:0.72, Alternative-diagnosis:0.68, Investigations:0.70,Management:0.71),indicatingstronger neurologist agreement. IQR of pairwise correlations was narrower for GPT-4o (Diagnosis:[0.82,0.88], Alternative-diagnosis:[0.79,0.85], Investigations:[0.81,0.87], Management:[0.83,0.89]) compared to GPT-3.5 (Diagnosis:[0.68,0.76], Alternative-diagnosis:[0.64,0.72], Investigations:[0.66,0.74], Management:[0.67,0.75]), reflecting more consistent evaluations by neurologists. Cronbach's Alpha for GPT-4o (Diagnosis:0.89, Alternative-diagnosis:0.87, Investigations:0.88, Management:0.90) was higher than GPT-3.5 (Diagnosis:0.78, Alternatives:0.75, Investigations:0.76, Management:0.77), demonstrating greater scoring consistency.

Conclusion: GPT-4o demonstrates superior performance, reliability, and consistency compared to GPT-3.5 in epilepsy case management across all four aspects. Neurologists showed higher agreement and consistency when evaluating GPT-4o responses, supporting its effectiveness in clinical decision-making. These findings highlight GPT-4o's potential as a valuable tool in medical practice as an adjunct to a clinician especially in remote centers where a single (often inadequately trained in epilepsy management) physician may handle high volume of epilepsy cases.

1721 | High Performance Privacy-preserving Video-based Detection of Generalized Tonic-Clonic Seizures

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Purpose: Studies show that up to 86% of nocturnal seizures go unnoticed. This is particularly serious for generalized tonic-clonic seizures, associated with a higher risk of Sudden Unexpected Death in Epilepsy (SUDEP). This causes significant anxiety for people with epilepsy and their caregivers. Real-time video-based seizure detection can be a powerful tool for caregivers in need of closer night-time monitoring, helping mitigate this distress.

Method: With this work we improve upon previous work by the team, presenting a novel privacy-preserving video-based tonic-clonic seizure detection method, based on Dense Inverse Search Optical Flow, Principal Component Analysis, Independent Component Analysis, and Gradient Boosting Machine classification, with novel signal denoising techniques to significantly highlight clonic movements, alongside several custom features for classification. An anonymized dataset, consisting of 2139 hours of video-EEG footage pre-recorded in a hospital setting was obtained. A total of 190 hours of footage corresponding to 16 patients with refractory epilepsy with 29 tonic-clonic seizures annotated by clinical experts was used for model training; the remaining 1949 hours were used for testing (including 28 patients with 26 tonic-clonic seizures). This protocol was approved by the Centro Académico de Medicina de Lisboa ethics committee.

Results: One tonic-clonic seizure was excluded as the patient left the camera's field of view before having the seizure, while the remaining 25 seizures were all correctly detected. The mean false alarm rate was 0.246 ±0.357 per 24 hours, and the median false alarm rate per patient was 0. False alarms were present in only 9 out of the 28 patients in the training set.

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Conclusion: This work constitutes a significant advance in the state-of-the-art in video-based seizure detection, through a combination of the novelty resulting from our privacy-preserving approach and the very high accuracy and low false alarm rate obtained in a large dataset.

1723 | Lampsy: An "Invisibles" Approach to Real-time Tonic-clonic Seizure Detection based on Edge Computing

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Purpose: Epilepsy can severely impact quality of life, especially in refractory cases. Frequent, unpredictable seizures, many of which go unnoticed, further exacerbate this, alongside social stigma. Tonic-clonic and nocturnal seizures are particularly dangerous, significantly increasing the risk of Sudden Unexpected Death in Epilepsy (SUDEP). Real-time seizure alerts at home could reduce uncertainty and anxiety, especially at night. Video is a promising modality as it offers caregivers live feeds, as well as useful footage for health professionals, however no medically certified real-time video-based seizure detection devices current exist for home use. This is largely due to the high hardware and computational costs of real-time video processing.
Method: In this work, we present a novel video-based tonic-clonic seizure detection device named Lampsy, built around a Raspberry Pi 4 edge device and integrated into a light fixture, ensuring unobtrusiveness and therefore avoiding exposing patients to social stigma. Lampsy's algorithm combines computationally efficient methods, in particular Optical Flow, Principal Component Analysis, Independent Component Analysis, and traditional Machine Learning classification. This method was tested using 21 videos with one focal to bilateral tonic-clonic seizure each, from 12 patients with refractory epilepsy, recorded during in-hospital video-EEG sessions. Seizures were identified and annotated by certified neurophysiologists. This study was approved by the Centro Académico de Medicina de Lisboa ethics committee.
Results: With optimized Optical Flow parameters, the algorithm is able to perform in real-time locally on a Raspberry Pi 4 device in an edge computing approach, at 30 frames per second. In our experimental evaluation, the algorithm achieved a sensitivity and specificity of 99.76% $\pm$0.35% at the equal error rate.
Conclusion: Through its edge computing approach, Lampsy is able to perform video-based tonic-clonic seizure detection in real-time locally on affordable hardware while remaining unobtrusive and therefore constitutes an innovative alternative to current state-of-the-art devices.

1734 | Seizure Detection in Epilepsy: a clinical evaluation of a connected multimodal monitoring shirt

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Purpose: Wearable devices offer a promising avenue for long-term unobtrusive seizure detection and management. They can alert caregivers of a seizure event, ensuring timely intervention, and potentially preventing seizure-related injuries. In this study, we developed a multimodal seizure detection algorithm using data collected with a connected shirt. We aimed to detect generalized tonic-clonic seizures (GTCS) and focal to bilateral tonic-clonic seizures (FBTCS).
Method: We prospectively recruited patients with epilepsy admitted to our epilepsy monitoring unit and asked them to continuously wear the Hexoskin connected shirt while under simultaneous video-electroencephalography (EEG) monitoring. The connected shirt recorded electrocardiography, accelerometry and respiratory signals. Seizure onset and offset were annotated by three board-certified epileptologists according to video-EEG. We extracted linear and nonlinear features from each modality. We trained a machine learning algorithm to identify ictal epochs. A patient-wise nested cross-validation (nested CV) approach was implemented to train models and evaluate performances on patients with GTCS/FBTCS. To further assess specificity, we tested our models on a held-out test set of additional patients who did not experience GTCS/FBTCS.
Results: We recruited 114 patients who wore the shirt for a total of 17,176 continuous hours. We trained an extreme

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gradient boosting algorithm, using a nested CV on data from 41 patients who experienced 65 FBTCS. The algorithm reached a sensitivity of 81.8% (54/65 seizures), with a median false alarm rate (FAR) of 0.23/24h. Receiver operating characteristic area under the curve was 0.92. Specificity was further assessed on a held-out test set comprising 73 unseen patients (9,275 hours of recordings without seizures). The models reached a median FAR of 0.16/24h. Notably, 19 patients experienced no false alarms.
Conclusion: Our results demonstrate accurate seizure detection with minimal false alarms. Next, we aim to validate these findings in a prospective real-time study in a residential setting.

1764 | Design and *in silico* study of voltage-gated sodium channel blockers: Neuroprotection and anticonvulsant actions

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Purpose: Design through an *in silico* study and based on the pharmacophore of voltage-dependent sodium channel blockers two series of bioisosteric urea molecules and riluzole derivatives as potential anticonvulsant and neuroprotective agents
Method: Both groups of molecules were drawn in ChemSketch and ChemDraw, the physicochemical and molecular properties were obtained in those programs, as well as in online platforms (Molinspiration, OsirisPropertyExplorer and SwissADME) and Spartan14. The predicted potential as C_{NaV}. binding substances were obtained in Molinspiration. Subsequently, SAR/QSAR analysis of both chemostats was performed through individual analysis of correlation with physicochemical/molecular properties against their potential binding to the C_{NaV}.
Results: The ion channel blocking activity of the urea bioisomer group increases directly with partition coefficient and negatively with molar refractivity and TPSA, according to the following model ICB = 0.139 *logP* − 2.013 *logMR* − 2.578 *logTPSA* + 7.814 On the other hand, the activity of the riluzole derivatives group increases after increasing E_{LUMO}, and by decreasing dipole moment, polarizability, molar refractivity and volume.
Conclusion: Both groups of molecules designed through the pharmacophore are coincident in that they must be small in size and poorly polarizable to increase the biological activity as C_{NaV} blockers. Therefore, these properties are of relevance to be considered for chemical synthesis and to be evaluated as potential anticonvulsants and/or neuroprotectants.

1805 | Connectomics-driven Machine Intelligence for Enhanced Diagnosis, Prognosis, and Treatment of Neurological Diseases using Multi-modal Imaging

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Purpose: This work explores the development of artificial intelligence models that integrate multi-modal imaging techniques like electroencephalography, magnetic resonance imaging, and magnetoencephalography using evolutionary transfer learning to address diagnostic challenges in neurological disorders.
Method: The work aims to enhance the understanding of brain functions by developing novel machine learning models capable of analyzing spatio-temporal connectomics.
Results: These models offer potential improvements in diagnosis, prognosis, and treatment planning for complex and potentially comorbid diseases like epilepsy.
Conclusion: Thus, advanced neuroimaging and AI will be leveraged to improve clinical outcomes in the future.

1822 | *In silico* evaluation of cenobamate

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Purpose: Cenobamate is a new antiseizure medication recently introduced for the treatment of adults with focal-onset seizures. Nevertheless, more studies are important to comprehend the mechanisms underlying the condition to identify new individualized therapeutic approaches. Considering the high costs and time spent on clinical research, *in silico* approaches highlight advantages to achieve more results in less time. From this perspective, our purpose is to evaluate features for efficient prediction of protein targets of cenobamate, through *in silico* approach.

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Method: Swiss Target Prediction is a reliable *in silico* tool that aims to predict the most probable protein targets of drugs (www.swisstargetprediction.ch). The user-friendly graphical interface allows to achieve ligand-based and protein-based results previously prepared from chemical databases. Furthermore, it clearly shows that the information meaningful for the model corresponds to values higher than 0.65. The probability values are calculated from the combined-scores of the most similar compounds to the query molecule known to be active on a given protein. Importantly, this value illustrates the probability for a bioactive molecule to have a given protein as target, but not the probability of being bioactive.
Results: The results summarize ligand-based probability between 0.05 and 0.06 for all target prediction.
Conclusion: Therefore, according to scientific studies that used the same type of approach for *in silico* evaluation of other drugs, it is suggested that others *in silico* methods are necessary for accurate analysis of cenobamate.

Basic Science

301 | Epilepsy-Related Changes in $GABA_A$ Receptor Membrane Dynamics

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Purpose: Cell surface expression of $GABA_A$ receptors ($GABA_A$Rs) is crucial for modulating synaptic inhibition, relying on the balance between receptor insertion, lateral diffusion, internalization, and recycling. Dephosphorylation of the β3 subunit at serine residues 408/409 mediates $GABA_A$R endocytosis. We aim to evaluate the phosphorylation status of the $GABA_A$R β3 subunit in postsurgical tissue of mesial temporal lobe epilepsy associated to hippocampal sclerosis (MTLE-HS) and to investigate the membrane dynamics of $GABA_A$R β3 in an *in vitro* neuronal model of status epilepticus (mSE).
Method: Phosphorylation of the $GABA_A$R β3 subunit was assessed in five samples of MTLE-HS postsurgical tissue using western blot analysis with a phospho-specific antibody targeting serine residues 408/409 of the β3 subunit. $GABA_A$R cell surface expression, turnover, and diffusion at synapses were analyzed using quantitative live-cell imaging, antibody-feeding assay, and single-particle tracking (SPT) experiments in cultured hippocampal neurons transfected with pHGFP- or myc-tagged β3 subunits and incubated in Mg^{2+}-free medium.
Results: Western blot analysis demonstrated reduced levels of phosphorylated and total $GABA_A$R β3 in epileptic tissues compared to controls. Live-cell imaging showed a progressive decrease in fluorescence intensity immediately after incubating hippocampal neurons in a Mg^{2+}-free medium, suggesting a reduction in total surface $GABA_A$R β3 levels. Fluorescence microscopy with an anti-myc antibody showed increased $GABA_A$R internalization and reduced recycling in a mSE relative to control conditions. SPT experiments revealed a significant increase in synaptic receptor diffusion coefficients in cells incubated in Mg^{2+}-free medium at 0 and 5 minutes compared to baseline, indicating reduced synaptic stability of the receptor in a mSE.
Conclusion: These findings indicate a downregulation of $GABA_A$R β3 subunit phosphorylation in human MTLE-HS and changes in $GABA_A$R trafficking under conditions that model SE. Together, our data suggest that SE induces dynamic alterations to GABAergic synapses, thus impairing $GABA_A$R-mediated inhibition. Understanding these mechanisms may provide new targets for epilepsy treatment.

347 | Power spectral electroencephalographic density analysis of the effects of fenfluramine in the intrahippocampal kainate mouse model of temporal lobe epilepsy

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Purpose: Fenfluramine has emerged as an adjunctive therapy for Dravet and Lennox-Gastaut syndromes. Our previous research demonstrated that its antiseizure effects extend to the intrahippocampal kainate mouse model (Pérez-Pérez D et al. Epilepsia 2024; 65: 2470–2482). This

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study aims to complement these findings with a quantitative analysis of the electroencephalogram data.

Method: Electroencephalograms from 8–10 mice were filtered (1–70 Hz, notch at 50 Hz) and segmented into three 30-minute windows (-60, 30, and 180 minutes post-administration of fenfluramine, diazepam, or vehicle). The compounds were administered intraperitoneally at different doses. Artifact-free 30-second epochs were analyzed for power spectral density (PSD) across the delta (1–4 Hz), theta (5–8 Hz), alpha (9–14 Hz), beta (15–32 Hz), and gamma (33–50 Hz) frequency bands. Results are reported as the effect sizes with 95% confidence intervals relative to baseline (-60 minutes).

Results: Diazepam (3 and 5 mg/kg) reduced the PSD by 41% (16–58%) and 45% (35–56%) at 30 minutes, and by 29% (14–46%) and 32% (22–46%) at 180 minutes, affecting all frequency bands except alfa. Fenfluramine (1 mg/kg) reduced PSD by 9% (16–2%) at 180 minutes, altering delta and gamma bands. At a higher dose (10 mg/kg), fenfluramine reduced PSD by 40% (62–24%) at 30 minutes, specifically affecting gamma band. Vehicle administration had no significant effect on PSD.

Conclusion: Our findings show that fenfluramine also affects selected EEG parameters in this model, supporting recent evidence for a broader efficacy spectrum. Further studies are needed to assess behavioral correlates and to confirm the translational potential for patients with temporal lobe epilepsy.

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465 | Diverging seizure properties in rat models of SYNGAP1 and GRIN2B neurodevelopmental disorders

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Purpose: Neurodevelopmental disorders, including autism and intellectual disability, are highly comorbid with epilepsy, reported with hundreds of associated mutations. Two knockout models of common monogenic neurodevelopmental disorders, SYNGAP1 and GRIN2B, display spontaneous absence seizures, accompanied by abnormal sleep, reduced sociability, and fear memory deficit. We hypothesize that each mutation differentially affects brain network mechanisms. We found that absence seizures in these models vary in number, duration, spectral and connectivity properties.

Method: We had previously recorded 24-hour EEG from SYNGAP1 rats in which the GAP-C2 domains of the SYNGAP1 gene had been knocked out ($SYNGAP^{+/\Delta-GAP}$), from heterozygous knockouts of the GRIN2B gene ($GRIN2B^{+/-}$), and from wild-type littermate controls. We identified spike-wave-discharges (SWDs) in the recordings, which serve as the electrophysiological correlate of a sudden behavioral arrest commonly observed in mutant animals. Here, we compared absence seizure data across the models, specifically the number, duration, spectral power, and connectivity through imaginary coherence.

Results: While $SYNGAP^{+/\Delta-GAP}$ and $GRIN2B^{+/-}$ do not differ in number of seizures, $SYNGAP^{+/\Delta-GAP}$ displayed longer seizure episodes than $GRIN2B^{+/-}$, leading to a longer total seizure duration. Power spectral analysis revealed a higher overall spectral power during SWDs in $GRIN2B^{+/-}$, but not in $SYNGAP^{+/\Delta-GAP}$ when compared to littermate controls. Different patterns of connectivity impairment were also observed in these strains. We revealed that SWDs are likely to originate in the somatosensory cortex in $SYNGAP^{+/\Delta-GAP}$ and the motor cortex in $GRIN2B^{+/-}$.

Conclusion: Our study yields new insights into how mutations in SYNGAP1 and GRIN2B generate SWDs, resulting in unique properties of absence seizures in each model. Future work will further explore the underlying differences and similarities between models, in terms of neuronal populations and structures involved in seizure generation. This research has the potential to identify new cellular and network targets for preventing seizures and other comorbidities, thereby advancing therapeutic strategies.

500 | Behavior decoding delineates seizure microfeatures and associated sudden death risks in mice

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Purpose: Behavioral and motor components of epileptic seizures are essential for the diagnosis of epilepsy. However, the complex behavior of epilepsy has been historically understudied due to the lack of objective and quantitative analysis techniques. In this study, we propose to develop an automated and data-driven approach to profile behavior microfeatures in delineating seizure-related outcomes in mice based on video recordings.

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Method: Our dataset is composed of a pool of single off-the-shelf camera videotaped flurothyl-induced seizure recordings of 229 mice (8.7% mortality) from 31 different Collaborative Cross mice strains and the classic laboratory inbred C57BL/6J as a reference. We trained a DeepLabCut (DLC) network for markerless pose estimation with 28 different body parts labels. A *Behavior Segmentation of Open Field in DLC* B(B-SOiD) model was then trained on the DLC pose estimation data to cluster behavioral groups (~88% accuracy). We conduct statistical analysis and frequency pattern mining on these behavioral groups and action kinematics to identify the behavior microfeatures that can delineate seizure states and predict SUDEP.
Results: Our model generated 67 distinctive behavior groups. All behavior groups can be decoded with a structured ethogram to optimize specificity and interpretability. We found significant ($p < 0.05$) differences in percent behavior group usage and entropy analyses in delineating the preictal, myoclonic seizure, and generalized seizure states. We unraveled intricate behavior clusters that can inform mouse strain genetic backgrounds. Finally, we found statistically significant differences in behavior group usage, behavior transition probabilities, and hind knee action kinematics during the ictal phase of seizures that can predict their SUDEP risks.
Conclusion: We define a spectrum of mouse seizure behaviors microfeatures using AI-aided pose estimation and clustering tools. Our pipeline provides an unbiased, automated, and non-invasive approach for data-driven seizure behavior decoding using videographic data captured with a single off-the-shelf camera, holding great potential for translational studies.

554 | The pro-epileptogenic astrocytes? Status epilepticus induces chromatin remodeling, homeostatic gene repression, and pro-inflammatory gene expression in astrocytes

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Purpose: Retrospective studies in Temporal Lobe Epilepsy (TLE) patients have demonstrated a high incidence of an initial precipitating event (IPE) in early childhood. The IPE is followed by a silent period during which epileptogenesis progresses, ultimately resulting in chronic epilepsy. The IPE and the silent period can be modeled in rodents using pilocarpine-induced status epilepticus. We hypothesized that IPE initiates a pathological, long-term astroglial conversion into a phenotype that facilitates epileptogenesis.
Method: We analyzed the astroglial alterations using three paradigms: i) Lithium-pilocarpine model of TLE in rats (127/30 mg/kg intraperitoneally), ii) Primary astroglial cultures exposed to the epileptogenic DAMP HMGB1, and iii) Brain tissue samples from TLE patients. Immunohistochemistry with quantitative image analysis, real-time PCR, and methylation-sensitive PCR were used. Statistics were performed using two-way ANOVA with Tukey post-hoc. Significance was set at $p<0.05$.
Results: We found that IPE (Status Epilepticus, sustained Racine 3-5) by lithium-pilocarpine led to hypermethylation of astroglial DNA at 7, 21, and 35 days post-IPE, indicating persistent epigenetic alterations during the epileptogenic period. Furthermore, we observed the downregulation of homeostatic astroglial genes Aquaporin-4 (AQP4), glutamine synthase (GS), and the K+ channel Kir4.1. This occurred concomitantly with an upregulation of proinflammatory markers (C3, MAFG, IL-1B) and DNA methyltransferases (DNMT1-3). These findings were replicated in primary astrocyte cultures exposed to the epileptogenic HMGB1 (500 ng/ml; 18 hours), where we detected hypermethylation of homeostatic astroglial gene promoters GS, MCT-1, and LDHA. HMGB1-exposed astrocytes also exhibited neurotoxicity, which was prevented by DNMT inhibitor decitabine. Astrocytes from TLE patients also showed reactive astrogliosis, increased DNA methylation, and downregulation of homeostatic genes Kir4.1 and GS.
Conclusion: These findings demonstrate that IPE induces pathological alterations in astrocytes, including a proinflammatory gain of function and downregulation of critical homeostatic genes, including Kir4.1 and GS. This astroglial response likely contributes to increased neuronal excitability and neurotoxicity, thereby facilitating epileptogenesis.

562 | Predictive biomarkers of drug-resistant epilepsy in TSC patients- results of the EPIMARKER study

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Purpose: In spite of multiple trials, no reliable biomarker of drug-resistant epilepsy development has been identified. EPIMARKER is a first project, carried out in humans, examining in prospective way clinical, electroencephalographic and molecular biomarkers to produce an integrative tool useful in prevention of drug-resistant epilepsy. We present the results of prospective analyses of mRNA markers of drug-resistant epilepsy development in children with TSC.

Method: In the EPIMARKER study, 80 patients (up to one year of age) received vigabatrin either preventively or immediately after the onset of seizures. Serial whole blood samples were collected before, at and 12 months after the seizure onset. RNA sequencing was done using NEB RNA library protocols and Illumina HiSeq1500 sequencer. The quality of RNA was verified by spectrophotometry (only samples with RNA Integrity number above 7 were accepted. mRNA analysis was performed with own pipeline based on open-source solutions (mapping: STAR algorithm).

Results: We detected a large change in blood mRNA profile to be associated with epilepsy. Further analysis focused on finding genes whose expression profile predicts a good or bad response to the first drug. Sex specific analysis revealed significant changes between females with TSC with good or bad response to the first drug. These were genes encoding variable and constant lambda immunoglobulin chains: *GLV1-40*, *IGVK4-1*, *IGLC7*, *IGLV3-19*, *IGHV4-34*, *IGKV1-39*, *IGHV6-1*, *IGHV1-3*, *IGHV3-53*, *IGKV3-15*, *IGHV5-51*, *IGKV1-16, IGLJ2* and some other genes: *RRP7A*, *KTI12*, *HRAS*,*TNFRSF13B*. In girls, the expression of these genes was lower in those not responding to the drug. Altogether, we identified significant changes in 17 mRNAs in a whole blood as potential predictors of drug-resistant epilepsy in girls.

Conclusion: We identified significant decrease in abundance of 17 mRNAs that could be potentially predict of drug-resistant epilepsy in girls up to age of 2 years.

563 | TRPV5 exacerbates neuroinflammation induced by status epilepticus

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Purpose: Transient receptor potential vanilloid 5 (TRPV5), a highly selective calcium ion channel, has been extensively studied in renal physiology and osteoarthritis. A recent study showed the expression of TRPV5 in the rodent brain and the predominant expression of TRPV5 in the hippocampal CA1 and CA3 regions. But the detailed roles of TRPV5 in epileptic brain damage remain largely unexplored. In this study, I investigated changes in TRPV5 expression in the hippocampus of a animal status epilepticus (SE) model.

Method: I investigated the changes in TRPV5 expression in the hippocampus of a pilocarpine-induced status epilepticus (SE) mouse model and examined the effects of TRPV5 inhibition on microglial activation and neuroinflammatory responses using primary microglia culture with immunofluorescence staining, TUNEL staining and Western blot analysis.

Results: TRPV5 expression is significantly upregulated in hippocampal activated microglia after SE onset. In primary microglia culture, TRPV5 expression was upregulated in activated microglia following lipopolysaccharide (LPS) treatment, and inhibition of TRPV5 by Econazole mitigated LPS-induced microglial activation.

Conclusion: These findings demonstrate that TRPV5 is involved in the neuroinflammatory response associated with microglial activation after epileptic seizures. These findings suggest that the anti-inflammatory effect of TRPV5 inhibition may provide a novel therapeutic approach for the treatment of epileptogenesis.

587 | Towards therapeutic innovation in temporal lobe epilepsy: focal adenosinergic modulation of hippocampal excitability

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Purpose: Reducing dentate gyrus (DG) hyperexcitability by focally activating the adenosine A1 receptor (A1R) is a potential therapeutic strategy in mesial temporal lobe epilepsy (MTLE). This study evaluated whether A1R signaling is still functional in a MTLE mouse model. Moreover, a photopharmacological approach was used to investigate the feasibility to suppress excitability of the DG in a spatially selective way and to a predefined level using a closed-loop protocol.

Method: Evoked field postsynaptic potentials (fPSPs) were recorded in the DG and CA1 in acute hippocampal

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slices from intrahippocampal kainic acid (IHKA)- and saline-injected mice. The effect of 40 nM of the A1R agonist N6-cyclopentyladenosine (CPA) on population spike (PS) amplitude to fPSP slope ratio, as an index of excitability, was evaluated. In slices incubated with 3μM coumarin-caged CPA (pcCPA), subregion selective inhibition of fPSP was evaluated through application of spatially restricted illumination to DG or CA1 using a digital mirror device. Reset of DG activation level, in response to perforant path stimulation, to a predefined target was evaluated through closed-loop illumination using PS amplitude as control variable.

Results: Administration of CPA significantly decreased excitability in both DG and CA1 ($p<0.01$), with a stronger effect in the DG in IHKA versus control ($p<0.05$). Using pcCPA, the fPSP slope decreased selectively upon localized illumination of the DG to 65.8±6.74 % in the DG and to 94.9±1.95 % in the CA1 ($p<0.001$). Using a closed-loop system, the PS amplitude could be kept stable at 50 % of baseline amplitude value ($p<0.001$).

Conclusion: Exposure to CPA in the DG and CA1 decreases excitability, indicating preserved A1R signaling in epileptic IHKA mice. The use of pcCPA allows modulation of the DG through localized illumination and to a predefined target level through a closed-loop system. These findings support the potential of photopharmacology as a targeted therapy for MTLE.

654 | Pathogenic Mechanisms of Anti-$GABA_AR$ Autoantibodies in Autoimmune Epilepsy: Impacts on Receptor Internalization and Neuronal Network Activity

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Purpose: The discovery of neural-specific autoantibodies in the serum of pharmacoresistant epileptic patients revolutionized neurobiology by revealing a novel etiology for epilepsy and establishing autoimmune epilepsy as a distinct clinical entity. Subsequent research has expanded the characterization of autoantibodies implicated in autoimmune epilepsy, many of which are key pathogenic contributors to disease development. Among these, anti-$GABA_AR$ autoantibodies are associated with epileptogenesis, with around 88%-95% of patients developing seizures in the context of limbic encephalitis. This study investigates the mechanisms underlying autoimmune epilepsy associated with anti-$GABA_AR$ autoantibodies, focusing on their effects on hippocampal neuronal network activity and receptor dynamics.

Method: Hippocampal neuronal cultures were incubated with serum containing anti-$GABA_AR$ autoantibodies from epileptic patients. Immunocytochemistry and imaging were used to track the internalization of autoantibodies and $GABA_AR$ subunit clustering on the neuronal plasma membrane. Neuronal network activity was assessed using microelectrode array (MEA) technology to measure burst activity and synchronization.

Results: Anti-$GABA_AR$ autoantibodies were internalized by neurons in a time-dependent manner, with increased intracellular accumulation after 5 hours. Early exposure to the autoantibodies led to a decrease in γ2-$GABA_AR$ subunit surface clustering and a significant increase in γ2-$GABA_AR$ internalization rates. In addition, serum from epileptic patients also induced significant hyperexcitability in hippocampal neuronal networks, characterized by increased burst intensity and rhythmicity, as well as enhanced network-wide synchronized bursting. The latter changes are consistent with the patterns observed in epilepsy.

Conclusion: Our results suggest that anti-$GABA_AR$ autoantibodies contribute to epileptogenesis by promoting receptor internalization, thereby impairing GABAergic neurotransmission and altering neuronal network activity. The internalization of anti-$GABA_AR$ autoantibodies and their effects on neuronal activity may be good therapeutic targets in certain forms of autoimmune epilepsy.

657 | Development and evaluation of new anticonvulsant agents: *In silico*, *in vitro* and *in vivo* study of GABA-AT inhibitors

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Purpose: Conduct an integral study of new GABA-AT inhibitor Diels-Alder adducts, as a new therapeutic alternative as anticonvulsants

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Method: A series of Diels-Alder adducts of *N*-phenylmaleamic acid and isoprene with *p*-substituted anilines were synthesized. Enzyme-ligand interaction simulation was performed between the adducts and homologous GABA-AT proteins from *Pseudomonas fluorescens* and *Homo sapiens*. To measure activity and inhibition type upon the enzyme, an *in vitro* enzyme kinetics assay of the compounds over GABA-AT of *Pseudomonas fluorescens* was carried out. QSAR analysis established a predictive model between *in vitro* inhibitory activity and structural modifications in non-competitive GABA-AT inhibitor Diels-Alder adducts. *In vivo* anticonvulsant effect was evaluated in a murine model of PTZ-induced seizures, with acute toxicity assessment determining LD_{50} using the modified Lorke method.

Results: Moderate to good yields were achieved in the synthesis. Molecular docking revealed ligands interacting with amino acids (Phe379, Arg220, Tyr376, Arg473 etc.), suggesting an allosteric binding site. Enzyme kinetics showed non-competitive inhibition. The QSAR model (%inhibition = 3888 log MR - 2869 log α – 3088) indicated that higher molar refractivity and polarizability enhance GABA-AT inhibition. *In vivo*, a Diels-Alder adduct derived from 4-iodophenylmaleamic acid and isoprene significantly reduced tonic-clonic seizures and exhibited low toxicity (LD_{50}: 1.72 mmol/kg) compared to -Br (1.20 mmol/kg) and -COOEt (0.40 mmol/kg) derivatives.

Conclusion: The Diels-Alder adducts, non-competitive GABA-AT inhibitors, showed a direct correlation between molecular dimensions and inhibitory activity based on the QSAR study, binding at an allosteric site. Among them, the adduct derived from 4-iodophenylmaleamic acid and isoprene exhibited the lowest toxicity (LD_{50}) compared to -Br and -COOEt derivatives. It significantly reduced seizures and increased latency in PTZ-induced generalized tonic-clonic seizures in a murine model. This compound demonstrated the highest potential as a new anticonvulsant drug candidate, combining strong efficacy with reduced toxicity, highlighting its promise for further development in epilepsy treatment.

666 | Biperiden modulates seizure susceptibility and vascular remodeling after traumatic brain injury

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Purpose: Traumatic brain injury (TBI) is a major cause of posttraumatic epilepsy (PTE), impairing recovery and increasing seizure risk years after trauma. The link between TBI and seizures is unclear, and current treatments fail to prevent late-stage seizures. Biperiden, a selective cholinergic antagonist, may reduce inflammation and protect neurons. This study examines biperiden's long-term effects on PTZ-induced seizures and vascular changes post-TBI in rats.

Method: Sixty male Wistar rats underwent stereotactic surgery and craniotomy. TBI groups received a 2.33±0.27 atm lateral impact using a fluid-percussion device 24 hours post-surgery. Biperiden (8 mg/kg, i.p.) was administered every 8 hours for 10 days to TBI-BIP and SHAM-BIP groups; TBI-SAL and SHAM-SAL groups received saline. Mortality rate, motor function, learning, memory (via Barnes Maze 30 days post-trauma), and PTZ-induced seizure threshold (30 mg/kg, i.p.) assessed 90 days post-trauma were evaluated. Histological analysis for lesion volume (Nissl staining) and cerebral vessels (Tomato lectin - TL) was performed 24 hours after PTZ injections.

Results: The TBI mortality rate was 33.33%. TBI-SAL rats had worse neuroscores than SHAM-SAL ($p \leq 0.01$) and NAÏVE ($p \leq 0.001$) on days 3 and 7 post-trauma. In the Barnes Maze, NAÏVE (80%) and SHAM-SAL (50%) used a serial strategy, while TBI-SAL and TBI-BIP (40%) relied on random strategies. One TBI-SAL rat (5%) developed spontaneous recurrent seizures, with the first seizure occurring at 61 days post-trauma. During the PTZ challenge, TBI-SAL showed the highest seizure intensity (type V), while TBI-BIP had the lowest (level III). Biperiden increased cortical blood vessel expression in TBI-BIP versus TBI-SAL ($p \leq 0.05$). In CA1, TL expression was higher in TBI-BIP compared to SHAM-BIP ($p = 0.036$).

Conclusion: Biperiden treatment improved vascular remodeling in the cortex and CA1 regions and reduced PTZ-induced seizure intensity but did not enhance long-term memory, suggesting its potential as an adjunct therapy for TBI management.

702 | Unveiling the Mechanisms of Dapagliflozin and Ticagrelor in Epilepsy Management: A Network Pharmacological and Experimental Study

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Purpose: The complex aetiology of epilepsy and the high cost of developing advanced treatments are increasing the socioeconomic burden on the medical industry. Our research aimed to evaluate the anticonvulsant effects of existing therapies for managing epilepsy.
Method: We employed a network pharmacological approach to investigate potential interactions among epileptic genes, dapagliflozin, and ticagrelor. The most common gene target and related pathway of the trio were identified based on protein-protein interaction, target interaction type, enrichment analysis, and docking scores using bioinformatics tools such as SwissTarget Prediction, STRING database, GeneMania, Cytoscape (v3.10.2) software, and AutoDock Vina. Dapagliflozin and ticagrelor also demonstrated higher binding affinity towards ERK. Further, Pretreatment of dapagliflozin and ticagrelor was given to Swiss albino animals for 14 days at different doses (n=10 in each group), such as dapagliflozin (2.5 & 5mg/kg), ticagrelor (50 & 100mg/kg) and a combination of both the doses at (2.5mg and 50mg/kg). Animals were subjected to supramaximal electroshock (MES) and then euthanised to isolate the brain tissues for assessment of various molecular markers.
Results: The database results highlighted the MAP kinase cascade, particularly the ERK signalling pathway. MES-treated animals exhibited rapid generalised tonic-clonic seizures due to an imbalance between GABA and glutamate levels. MES also potentiated transcriptional and translational events, characterised by increased protein expression of ERK1/2 and mTORC1. Furthermore, MES triggered neuroinflammatory cascades, as evidenced by elevated protein expression of NF-κB and increased co-localization of GFAP in hippocampal tissues, indicating astrogliosis. However, dapagliflozin and ticagrelor significantly ameliorated these changes, suggesting that both drugs possess anticonvulsant activity.
Conclusion: This study used network pharmacology to identify key targets and pathways associated with dapagliflozin and ticagrelor in treating convulsions. Experimental animal models confirmed the results, providing a promising direction for future epilepsy treatment.

706 | Chasing metabolites from the gut to the brain: exploring metabolomic and lipidomic methods to study the gut-brain axis in epilepsy

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Purpose: The gut is colonized by microorganisms which have co-evolved with the host to perform crucial metabolic functions. Alterations of the gut microbiota in a pathological condition can lead to metabolic dysregulation, providing potential pathogenic mechanisms, biomarkers, and druggable targets for many diseases, including epilepsy. While the fecal metabolome provides a functional readout of gut microbial activity, metabolomic analysis of brain samples determines whether microbe-derived molecules can reach the brain, where they may influence physiological functions, and modulate excitotoxicity and seizures. In this study, we tested different extraction methods for metabolites and lipids in naïve murine fecal and brain samples for liquid chromatography–mass spectrometry (LC-MS) analysis.
Method: Metabolites and lipids were extracted from frozen murine fecal and brain samples using either ethanol-MTBE, methanol-MTBE, or BAMM (1-butanol:ACN:H2O)-based extraction. LC-MS analysis was performed in the positive and negative ionization modes with hydrophobic and hydrophilic interaction columns. The data were processed for deconvolution, peak picking, alignment, and compound identification.
Results: All three methods reliably and reproducibly identified similar numbers of molecules. However, for both tissue types we found differences in the extraction efficiency of each solvent depending on the chemical nature of the extracted molecules, suggesting that different methods are required depending on the biological question.
Conclusion: Metabolomics is a useful tool to identify specific biomarkers and druggable targets, however, there are still significant challenges and limitations due to the high heterogeneity and complexity of the samples, highlighting the need to develop standardized protocols to improve reproducibility and enhance the biological interpretation of the data.

775 | Targeting the Sigma-1 receptor: effects of pharmacological modulation on kindling acquisition

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Purpose: The Sigma-1 receptor modulates mitochondrial function and regulates the activity of various voltage-gated ion channels and neurotransmitter receptors. Due to its pivotal role in maintaining cellular homeostasis, Sigma-1 is a promising target for antiseizure strategies. Therefore, we hypothesize that E1R, a selective positive allosteric Sigma-1 modulator, has a protective impact on the generation of a hyperexcitable network.

Method: The effects of E1R, NE-100 (Sigma-1 antagonist) and their combinations on seizure severity and associated seizure parameters have been evaluated in the amygdala kindling model. Based on the initial seizure threshold, female NMRI mice (n=63) were randomized to the following treatment groups: vehicle (0.9% saline), E1R (50 and 75 mg/kg), NE-100 (35 mg/kg), double-vehicle (0.9% saline) and E1R+NE-100 (50 + 45 mg/kg). E1R and NE-100 were injected intraperitoneally with a pre-treatment time of 60 and 80 min, respectively. All mice received 15 electrical suprathreshold stimulations of the right amygdala.

Results: E1R (50 and 75 mg/kg) delayed the generation of generalized seizures and reduced motor and electroencephalographic seizure duration during the early kindling phase. Furthermore, E1R-treatment increased the cumulative electroencephalographic seizure duration (=sum to reach the first generalized seizure). In contrast, NE-100 had no effects on the progression of seizure severity and duration when compared to vehicle-treated mice. Following a washout phase, animals were re-stimulated to evaluate potential long-term effects. Generalized seizures occurred in all treatment groups. The co-treatment of NE-100 and E1R had no impact on the E1R-mediated effects.

Conclusion: In conclusion, the results indicate that E1R delays the generation of a hyperexcitable neuronal network. As the E1R-mediated effect could not be completely abolished by the antagonist, further studies in Sigma-1-deficient mice are ongoing to assess the Sigma-1 selectivity of E1R. Acknowledgements: Funded by DFG PO681/12-1. Technical support by C. Monío-Baca and L. Cieslik. E1R provided by LIOS.

809 | Cortical Interneuron Transplantation in a C1qa Knockout Mouse Model of Epilepsy

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Purpose: Interneuron contributions to abnormal neuronal networks and seizures are known, but our understanding of interneurons in absence epilepsy remains limited. Our goal is *(i)* to characterize cortical inhibitory network dynamics in C1qa KO mice, and *(ii)* to investigate interneuron-based transplantation therapy to abolish seizures and/or behavioral comorbidities in this mouse model of absence epilepsy.

Method: Embryonic MGE progenitors were transplanted into somatosensory cortex of C1qa KO and WT mouse pups (P2-4); control groups received media. EEG and behavior evaluation was performed starting 60 days after transplantation. EEG signals were acquired using a tethered head-mounted video-EEG monitoring system and analyzed offline (n=10 WT, n=20 KO). In an additional cohort of mice, we performed dark-light preference, textured novel object recognition, and three chamber tests (n=20-25 WT, n=20-30 KO). Immunostaining for somatostatin (SST)-, parvalbumin (PV)-expressing interneurons, and DAPI was performed.

Results: C1qa KO mice show (1) prominent bihemispheric irregular spikes and slow spike-and-wave discharges, (2) decreased time spent in the light compartment while in a dark/light box (WT: 42.43 ±1.25, KO: 31.02 ±2.65, p=0.003), (3) decreased whisker-dependent exploration (WT: 35.78 ±7.50, KO: 10.75 ±2.26, p=0.008), and (4) decreased number of SST interneurons in layer 6 of somatosensory cortex (WT: 16.86 ±0.93, KO: 13.48 ±0.69, p=0.0049). Interneuron transplantation in C1qa KOs rescued behavioral comorbidities, but did not abolish spike-and-wave discharges.

Conclusion: Our results uncover novel cortical network abnormalities and behavioral phenotypes in C1qa KO mice and highlight a potential to restore neurobehavioral deficits using interneuron-based transplantation.

848 | Dose-Dependent Effect of Atropine on Absence Seizures of Genetic Absence Epilepsy Rats

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Purpose: Childhood absence epilepsy is a sub-group of genetic generalized epilepsies that is characterized by spike-and-wave discharges (SWDs) on electroencephalography

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(EEG), along with behavioral changes (Matricardi et al., Pediatric Neurology 2014;50(3):205-212). Absence seizures and SWDs on EEG are modulated by cholinergic transmission modifiers (Danober et al., European Journal of Pharmacology 1993;234(2–3):263–268). However, the effect of a non-specific competitive antagonist of muscarinic receptors, atropine, has not been demonstrated. This study aims to investigate the effect of intraperitoneally (i.p.) given atropine on absence seizures in Genetic Absence Epilepsy Rats from Strasbourg (GAERS), providing insights into cholinergic modulation in absence epilepsy.

Method: This prospective controlled trial tested atropine at doses of 1 mg/kg (n=6), 5 mg/kg (n=8), and 20 mg/kg (n=4). Adult male and female GAERS (3–4 months old, 250–350 g) underwent stereotaxic surgery under isoflurane anesthesia for EEG electrode implantation in the frontal and parietal cortices, based on the rat brain atlas (Paxinos G et al. In: Paxinos G et al, *The Rat Brain in Stereotaxic Coordinates*. Academic Press, San Diego, 2007; 17-86). EEG recordings were performed for 180 minutes at baseline, injection and post-injection periods. SWD analysis was conducted using LabChart v7 (PowerLab 8/35, ADI Instruments) and paired t-tests were applied for statistical comparisons.

Results: After baseline recordings, each atropine dose injected into GAERS significantly reduced the cumulative SWD duration, which is expressed in seconds(sec). Dosage group comparisons from 3-hour EEGs are as follows: [Atropine 1 mg/kg: Baseline:(3126,9±192,4sec) versus(vs.) Injection:(2098,0±668,8sec), ($p<0.05$); suppression percentage: 33%], [Atropine 5 mg/kg: Baseline:(2800,2±596,2sec) vs. Injection: (680,4±396,5sec), ($p<0.05$);suppression percentage:76%],[Atropine 20 mg/kg: Baseline:(3696,6±562,9sec) vs. Injection:(566,6±753,7sec), ($p<0.05$); suppression percentage:85%].

Conclusion: The administration of i.p. atropine in GAERS demonstrates significant dose-dependent suppression of SWDs. Further research is needed to clarify the involvement of specific muscarinic receptor subtypes in absence epilepsy.

862 | Neuronal Subtypes and Their Contribution to Ictogenesis in a Mouse Model of Focal Cortical Dysplasia

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Purpose: Somatic mutations of mTOR pathway occurring in neural progenitors may cause aberrations in metabolism and migration of neurons causing focal cortical dysplasia (FCD). Several brain-cell subtypes have been identified within the tissue of dysplastic lesion although their role in ictogenesis has not been revealed yet. We explored changes in ictal activity caused by optogenetic modulation of distinct cell-types.

Method: C57B6 mice were electroporated at E14.5 using mTOR (p.Leu2427Pro) to create a model of FCD II or WT mTOR as a control. Eight weeks old mice underwent injection of Channelrhodopsin-2 (ChR2)-AAV particles, implantation of electrodes and cranial window. Optogenetically induced responses of mutated and non-mutated neurons were recorded as EEG signal.

Results: ChR2-induced increase in activity of neurons within FCD lesion that express mutated mTOR leads to seizure onset in all test subjects, with an average occurrence rate of 50% across trials. Trains of depolarizing stimuli administered at frequencies of 3, 8, and 20Hz exhibit similar efficacy in triggering epileptic seizures (35%, 52% and 41% respectively). Stimulation of non-mutated neurons in FCD animals resulted in seizure-like activity with different characteristics including shorter seizure duration. 30 Hz stimulation of non-mutated neurons was less efficient (3%) in seizure induction than 8 and 20Hz (66% and 48%). We observed low efficiency (10%) of seizure induction in control animals expressing WT mTOR at all frequencies of stimuli.

Conclusion: Excitability of neurons expressing mutated mTOR is one of the key factors in ictogenesis in the model of FCD II. Modulation of additional cell types such as normal-like neurons can nevertheless contribute to induction and sustaining of epileptic seizure. Mutated neurons seem to be part of the neuronal network within epileptic tissue that also includes neurons without the causal mutation. This suggests that selective modulation of specific cell-types within the lesion has therapeutic potential for drug resistant FCD.

885 | Epileptogenesis- and epilepsy-associated changes in Sigma-1 receptor expression in chronic mouse models of temporal lobe epilepsy

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Purpose: The Sigma-1 receptor protein impacts mitochondrial function, various voltage-gated ion channels, and neurotransmitter receptors, positioning it as a potential target for epilepsy treatment. However, disease-related alterations may impact target expression and drug efficacy. Therefore, the aim of this study was to characterize Sigma-1 expression in two chronic mouse models of temporal lobe epilepsy.

Method: Male C57BL/6JRj mice (n=48) received kainic acid (n=24) or saline (n=24) injections into the right Hippocampus to induce a non-convulsive status epilepticus (SE). Brain tissue was collected two days (acute post-insult phase, n=12) or 35 days (chronic phase with spontaneous electrographic seizures, n=12) after SE. In the kindling model, female NMRI mice (n=24) received suprathreshold stimulations of the right Amygdala until they exhibited ten generalized seizures (n=12). Sham-stimulated mice served as controls (n=12). Subsequently, the cellular expression pattern of Sigma-1 was analyzed by immunohistochemistry.

Results: ImageJ analysis of selected brain areas (CA1, CA3, Hilus, Amygdala, Perirhinal Cortex, Piriform Cortex, Entorhinal Cortex, Parietal Cortex, lateral-posterior, mediodorsal and reticular nucleus of the Thalamus) showed that the expression level of Sigma-1 remained unchanged in most of the brain areas investigated. In the kainate model, the optical density (OD) of Sigma-1-expressing cells increased in the CA3 region of the Hippocampus and in the Entorhinal Cortex two days post SE. Stereological cell counting revealed consistent Sigma-1-positive cells per volume (mm^3) in the Entorhinal Cortex, CA3 region and Hilus of the Hippocampus across groups. Furthermore, colocalization analyses showed that Sigma-1 is expressed in excitatory and inhibitory neurons, in astroglia, and in microglia.

Conclusion: In summary, the results indicate that Sigma-1 expression is maintained during epileptogenesis and after epilepsy manifestation, fulfilling a prerequisite for Sigma-1 to be a potential target for epilepsy treatment. Currently, the regulation of Sigma-1 expression is investigated using quantitative PCR (qPCR). Acknowledgement: *This work was funded by Deutsche Forschungsgesellschaft (DFG PO 681/12-1).*

891 | Involvement of autophagy and mitophagy processes in epileptogenesis

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Purpose: Temporal lobe epilepsy (TLE) often manifests months or even years after an initial epileptogenic insult and may be preventable. A strategy for secondary prevention may be the use of therapies that intervene early after an insult to limit brain damage: this type of approach requires a better understanding of the complex molecular and cellular mechanisms of epileptogenesis. A few studies have outlined that autophagy, an intracellular process leading to the degradation of damaged cellular components to preserve cellular homeostasis, could be involved in the pathophysiological mechanisms of epileptogenesis. The aim of this study is to systematically explore the involvement of autophagy and mitophagy during epileptogenesis using *ex vivo* (organotypic hippocampal slice cultures, OHSC) and *in vivo* (the rat pilocarpine model) models.

Method: The viability of hippocampal slices was assessed, followed by quantification of autophagic and mitophagic markers through Western blotting at various time points (Days in vitro (DIV) 3 to 28). Additionally, the expression profile of autophagy was evaluated at multiple stages during epileptogenesis in the pilocarpine rat model: early and late latency (seizure-free period) and chronic (spontaneous recurrent seizure onset).

Results: Preliminary results from the ex vivo model suggest that autophagy is blocked during the first week *in vitro*, with significant changes observed in some autophagic markers (e.g. p62, LC3II). *In vivo*, we observed significant modulation of autophagy markers during the latency period, which points to a blockade in autophagy flux. This suggests that autophagy may actively contribute to the pathophysiology of epileptogenesis.

Conclusion: Both models indicate important modulation of autophagy in the early stages of the epileptogenic process. However, further investigation is required to confirm the blockade of autophagy pathways and determine the specific site of inhibition. These findings may identify novel therapeutic targets, such as repurposed drugs that activate autophagy, providing a preventive, disease-modifying effect in TLE.

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929 | In vivo transcriptomics and proteomics analysis of SEEG electrodes from human epileptic brain

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Purpose: This study aims to demonstrate that proteomic and transcriptomic analyses of tissue adhered to stereo-electroencephalography (SEEG) electrodes are feasible for investigating the molecular mechanisms underlying chronic epilepsy and the evolution of the epileptic network in humans. Here, we describe the method developed by us for transcriptomic and proteomic analysis of brain tissue obtained from SEEG electrodes. Similar approach has been described recently by Dwivedi et al. (2025).

Method: Sample preparation is based on the method developed for proteomic and transcriptomic analysis on human brain tissue derived from DBS surgical instruments, described by Kangas et al. (2022). We analyzed samples from five patients with drug-resistant epilepsy (DRE) who were evaluated by Helsinki University Hospital's epilepsy surgery team and were scheduled to undergo an SEEG investigation. The samples were collected and preprocessed immediately after electrode removal; RNA extraction was initiated in an adjacent laboratory space, and proteomic samples were snap-frozen until subsequent analysis.

The samples were categorized into three groups according to SEEG data: epileptogenic zone, spreading zone, and outside the epileptic network. By comparing the zones, the patients served as their own controls. The RNAseq analysis was performed by the FIMM Genomics NGS Sequencing unit at the University of Helsinki. The proteomic samples were analyzed using mass spectrometry (MS) at the Institute of Biotechnology Varjosalo laboratory, University of Helsinki.

Results: The preliminary analysis shows that we can yield reproducibly high-quality RNA, producing a dataset with average of 25 500 transcripts per sample in RNAseq. Using MS, we identified 2524-5938 different proteins per sample. The data analyses are ongoing.

Conclusion: SEEG electrodes are a useful source for obtaining brain tissue for molecular characterization of chronic epilepsy and the development of the epileptic network in humans. This method enables the identification of shared and distinct molecular mechanisms in patients with varying epilepsy etiologies.

941 | A clinicopathological study of factors associated with microvacuolar changes in the cerebral white matter of patients with epilepsy

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Purpose: Microvacuolar changes in the cerebral white matter (WM) are occasionally seen in the surgical pathology of epilepsy. This study aimed to investigate the prevalence of these lesions and their possible association with clinical factors.

Method: We conducted a retrospective survey of surgical specimens from 275 epilepsy cases over the past twelve years (2013–2024). Histological examination was performed using archival paraffin blocks. The severity of microvacuolation was classified as score 0 (none), 1 (mild), 2 (moderate), and 3 (severe). The relationship between microvacuolation and clinical factors was analyzed, including the ages at seizure onset and surgical resection, clinical duration, sex, presurgical seizure frequency, and presurgical use of anti-seizure medications. Additionally, we investigated single nucleotide polymorphisms at the 677th and 1298th bases in the gene encoding 5,10-methylenetetrahydrofolate reductase (MTHFR) within a randomly selected population.

Results: 115 out of 275 cases (41.8%) showed WM microvacuolation (score 1, 2, and 3) (mean age at surgery, 22.8 ± 15.5 years; mean clinical duration, 11.0 ± 10.6 years).

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Histological examination revealed that each vacuole consists of myelin sheath ballooning with a well-preserved axon and no features of demyelination. A significant difference was observed in the mean ages at surgical resection and seizure onset, which were younger in patients with scores 2-3 compared to those with scores 0 and 1 (ANOVA followed by Scheffe's test, p-value <0.05). Among all factors analyzed, younger age at surgery, shorter clinical duration, and the use of carbamazepine (but not other anti-seizure medications) were associated with WM microvacuolation (t-test and chi-square test, p-value <0.05).

Conclusion: The histopathological features of microvacuolation observed in our 115 cases resemble those reported in folate deficiency-associated leukoencephalopathy and may suggest an adverse effect of carbamazepine rather than the *MTHFR* polymorphism. Further research is needed to clarify the relationship between WM microvacuolation and various combinations of clinical factors.

951 | Gut-based interventions improve neurological consequences of acute brain injury in mice

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Purpose: We investigated whether the neurological consequences of acute brain injury induced by status epilepticus (SE) in mice are improved by treatments that affect the gut-brain axis.

Method: We used an adult mouse model of acquired epilepsy induced by intra-amygdala kainate causing SE, drug-resistant seizures, brain and gut histopathology, gut dysbiosis and cognitive deficits. SE mice had a mixture of SCFAs (produced by fiber fermentation in the gut bacteria) added to their drinking water (40 mM NaBut, 26 mM propionate, 67 mM acetate) or were treated by gavage with *Lactobacillus paracasei*-derived CNCM I-5220 postbiotic (135 mg/kg/day; twice daily). Respective SE mice received corresponding vehicle. Mice were EEG recorded since SE onset (24/7) up to 3 months to quantify seizures and tested in the Barnes Maze to assess cognitive deficits, then brains and gut were dissected for histopathological analysis.

Results: SCFAs treatment reduced ($p<0.05$) both the number of mice showing seizure progression, the seizure progression index (seizure number at 2 vs 1 month) and the number of mice with seizure clusters. Both SCFAs and CNCM I-5220 improved memory retention and searching strategy during the probe trial (24 h after ending learning trials) in epileptic mice compared to epileptic mice treated with vehicle ($p<0.05$). The effects of treatments on brain and gut pathology will be analyzed.

Conclusion: The results support that gut-based interventions may improve neurological consequences of acute brain injury in mice exposed to SE.

956 | Thalamic orchestration of telencephalic oscillations and ictogenesis

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Purpose: Epileptic seizures are characterized by overly synchronized prosencephalic (telencephalic/diencephalic) oscillations. The determinant role of diencephalic thalamus in setting telencephalic oscillations remains obscure.

Method: Electrophysiological studies combined with optogenetic and pharmacological approaches in acute mouse brain slices and animal models of seizures were employed to investigate the neurobiological attributes of thalamocortical oscillations.

Results: The thalamus critically controls telencephalic oscillations in a frequency-coded manner. While telencephalic structures show augmented δ oscillations upon focal ictogenesis, the reciprocally-connected thalamus tends to respond with θ-α augmentation until continuous entrainment transforms thalamic rhythms into highly coherent δ waves. The phenomena are ascribable to the characteristic thalamic GABA-glutamate interactions and the mandatory glutamatergic input for burst discharges ("relay bursts"). Thalamic neuronal activities driven by corticothalamic glutamatergic input are under tight GABAergic control, in terms of both occurrence and configuration. In other words, the glutamatergic activities serve as a direct depolarizing drive and also a GABAergic trigger (via the thalamic reticular nucleus). The triggered GABA responses may then revive inactivated voltage-gated channels and shape thalamic and thus thalamocortical activities.

Conclusion: The evolution and involution of seizures could be envisaged by the continuous glutamate-GABA interactions in the thalamus. Epileptic seizures thus are not aftermaths of "excessive excitation" or "inadequate inhibition", but erroneous brain rhythms, or simplistically, burst-suppression cycles.

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979 | Transcriptomic Insights into patients with Focal Cortical Dysplasia

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Purpose: Focal cortical dysplasia (FCD) is characterized by cortical malformation due to abnormal neuronal development. It is a major cause of drug-resistant epilepsy. While histopathology remains the golden standard for FCD classification, significant overlap in histological features among FCD types often complicates precise classification and hence necessitates a complementary molecular approach. Studying Transcriptome can aid in differentiating FCD subtypes by identifying specific gene expression patterns and their related pathways.

Method: We performed RNA sequencing on resected brain cortical samples obtained from FCD patients (n=71; FCD1=29, FCD2=42) and healthy postmortem controls (HC) (n=15). Total RNA was extracted from the fresh frozen tissues and subjected library preparation followed by Next Generation Sequencing. Differential gene expression analysis followed by pathway enrichment was performed to identify key dysregulated biological processes.

Results: We identified distinct transcriptomic signatures differentiating FCD1, FCD2A and FCD2B. Out of the total differentially expressed genes, 139 showed distinct dysregulation at FCD1, 541 in FCD2A, and 603 in FCD2B. A total of 233 genes showed common dysregulation in all 3 FCD types. Pathway analysis revealed significant dysregulation of genes involved in mTOR signaling, inflammation, immune response, and synaptic function.

Conclusion: This study provides an insight into molecular landscape of FCD, highlighting potential biomarkers and therapeutic targets. Our finding underscores the significance of transcriptomic analysis distinguishing FCD subtypes and the molecular mechanism of the disorder. Integrating transcriptomic data with histopathological findings can enhance the precision of diagnosis and pave the path for precision medicine. Supported by the Ministry of Health of the Czech Republic, grant nr. NU21-04-00305

980 | Effect of 25 mg/kg Levetiracetam on Absence Seizure in Genetic Absence Epilepsy Rats

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Purpose: Spike-and-wave discharges (SWDs) on electroencephalography (EEG) and behavioral abnormalities are characteristics of childhood absence epilepsy, a subtype of genetic generalized epilepsies (Blumenfeld H et al. Epilepsia 2005;46(Suppl. 9):21-33). It has been demonstrated that levetiracetam inhibits absence seizures via binding to the brain's synaptic vesicle protein SV2A (Lynch BA et al. Proc Natl Acad Sci U S A 2004;101:9861-9866). This study aims to evaluate the effect of the 25 mg/kg dose of levetiracetam on absence seizures in the Genetic Absence Epilepsy Rats from Strasbourg (GAERS) model which is well-described model in absence epilepsy research.

Method: This prospective controlled study involved adult male GAERS rats (3–4 months old, 250–300 g, n=3). EEG recordings electrodes were implanted into the frontal and parietal cortices through stereotaxic surgery performed under isoflurane anesthesia, based on the rat brain atlas (Paxinos et al. In: Paxinos et al, The Rat Brain in Stereotaxic Coordinates. Academic Press, San Diego, 2007; 17-86). After allowing the animals a seven-day recovery period, baseline EEG recordings were conducted for 180 minutes from 09:00 to 12:00. On the following day, the rats received an intraperitoneal injection of levetiracetam at a dose of 25 mg/kg. The drug's effects on the cumulative duration and number of SWDs were analyzed

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using LabChart 7.0 (PowerLab 8/35, ADI Instruments). Paired t-tests were applied for statistical comparisons.

Results: The 20-minute intervals throughout the 180 min recording of levetiracetam were compared with basal recordings. The 25 mg/kg were significantly reduced cumulative duration and number of SWDs. The greatest cumulative reduction in SWDs was observed in the 60-80 minutes in levetiracetam-injected GAERS. [Levetiracetam 25 mg/kg: 4th 20-minute interval Baseline:(481,1±114,34sec) versus(vs.) Injection: (50,6±85,66sec), ($p<0.05$); suppression percentage: 90%].

Conclusion: By increasing the sample size in the levetiracetam group , the changes between the 20-minute intervals seems to be more pronounced.

1003 | Deciphering GDNF Signaling Pathways in Absence Seizures

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Purpose: Absence Seizures (AS) are sudden, non-convulsive epileptic events characterized by altered consciousness, behavioral arrest, and the presence of 3–4 Hz spike-and-wave discharges on (EEG). In addition, ASs is frequently associated with neuropsychiatric comorbidities, including deficits in emotional regulation, cognition, memory, and language processing. Similar cognitive impairments have been reported in the Genetic Absence Epilepsy Rat from Strasbourg (GAERS), a well-established animal model for AS. Notably, in AS animal models, an increase in tonic GABAA-A receptor-mediated currents in the thalamus has been observed, attributed to the loss-of-function of the GABA transporter 1 (GAT-1), which is exclusively expressed in astrocytes in this region. Recent evidence suggests that glial cell-derived neurotrophic factor (GDNF) influences GABAergic inhibitory transmission in the hippocampal network and suppresses spontaneous recurrent seizures in chronic epilepsy models. However, the precise mechanisms underlying this seizure-suppressing effect remain unclear.

Method: To investigate potential alterations in GDNF signaling pathways in AS, we conducted western blot analyses on hippocampal tissue from GAERS rats and their respective non-epileptic control (NEC) rats. Additionally, we evaluated the effect of GDNF on CA1 hippocampal long-term potentiation (LTP) in GAERS and NEC rats.

Results: Our findings reveal a significant upregulation of RET, the receptor for GDNF, as well as an increased expression of the astrocytic marker GFAP in GAERS compared to NEC rats. Furthermore, exogenous application of GDNF to hippocampal slices reduced the magnitude of CA1 hippocampal LTP exclusively in NEC rats, with no observed effect in GAERS.

Conclusion: These results suggest that the GDNF signaling pathway is altered in ASs and may contribute to the pathophysiology of this disorder. Modulation of this pathway could represent a novel therapeutic approach for preventing or mitigating ASs.

1011 | Disease-modifying Effects of Vitamin B12 Treatment in a Rat Model of Genetic Absence Epilepsy

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Purpose: Vitamin B12 plays a crucial role in the formation and maintenance of the myelin sheath and the production and function of neurotransmitters, both of which are essential for the healthy functioning of nerve cells. Several studies showed that vitamin B12 deficiency in children may cause different types of epilepsy seizures. This study examines whether vitamin B12 treatment has disease-modifying antiepileptogenic activity in Genetic Absence Epilepsy Rats from Strasbourg (GAERS) for characteristics of spike-and-wave discharges (SWD) and behavioral comorbidities.

Method: Male GAERS (n=10) were enrolled in the experimental protocol when they were postnatal (PN) days 30. Saline was injected intraperitoneally (i.p.) to the control group (n=5) and 45µg/kg of vitamin B12 was administered (i.p.) to the experimental group (n=5) for one week between PN30-PN36. At PN53 electroencephalogram (EEG) recording electrodes were placed to each animal by stereotactic surgery. Three hours of EEG was recorded between PN60 and PN70 and SWDs were analyzed for mean

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seizure duration, total seizure duration and seizure frequencies for each rat. Following EEG recordings, locomotor activity and elevated plus maze tests were performed for anxiety-like behaviors in all animals. Comparisons between control and experimental groups were made via GraphPad-Prism-10.1.1 with unpaired-t-tests. Data expressed as mean±SEM. P<0.05 was considered statistically significant.

Results: Mean SWD duration (Control group:6.97±0.86 seconds, B12 group:6.28±0.57 seconds), cumulative SWD duration (Control group:1186±192.5 seconds, B12 group:929.1±153.6 seconds), and total number of seizures (Control group:165±16.2, B12 group:150.6±19.04) and locomotor activity parameters (stereotypic movements, ambulatory activity, resting time) showed no significant difference between groups.

Conclusion: Our preliminary results found no antiepileptogenic effect of vitamin B12 when administered to male GAERS at PN30. Further studies are needed with higher doses and/or longer administration periods of vitamin B12 to explore whether it could be used for its disease-modifying effects in absence epilepsy.

1016 | Study of neuronal behaviors prior to seizures in human temporal lobe epilepsy

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Purpose: Seizure forecasting has become a crucial focus in epilepsy research. While electroencephalography (EEG) is widely used for diagnosing epilepsy, stereo-electroencephalography (sEEG) provides deeper insights into complex brain interactions and potential pre-seizure dynamics. However, definitive evidence for the existence of a pro-ictal state—a brain state linked to an increased likelihood of seizure onset—remains elusive. In this study, we utilized microelectrodes to record neuronal activities at a finer scale compared to traditional sEEG exploration.

Method: We analyzed data from 23 patients diagnosed with pharmacoresistant temporal lobe epilepsy. Extracellular neuronal recordings were processed using enhanced spike sorting methodologies, leveraging the SpikeInterface pipeline. Neuronal activity was compared between interictal periods (seizure-free days) and preictal periods (within 24 hours prior to seizure onset) during daily resting state protocols. During these periods, we investigated multiple neuronal firing properties, including firing rate, burstiness, discharge regularity, and phase-locking value.

Results: Our analysis encompassed recordings from over 1,800 neurons within mesial temporal structures across several consecutive days. We successfully characterized the activity of specific neuronal subtypes, such as principal cells and interneurons, during resting-state conditions under controlled vigilance states. We identified differences in neuronal firing properties across neuronal subtypes and brain regions and examined how these features varied between interictal and preictal periods.

Conclusion: The overarching aim of this study was to characterize the firing properties of neurons in temporal lobe epilepsy and to correlate these features with seizure dynamics, with the ultimate goal of identifying patterns indicative of a "pro-ictal" state.

1033 | Single-cell RNA-seq analysis of the intra-amygdala kainic acid mouse model reveals cell-type specific mechanisms underlying epilepsy

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Purpose: Single-cell sequencing technologies are transforming our ability to resolve the cellular diversity of organs and the cell type-specific contributing factor to a broad range of diseases. Mouse models are critical tools to model the pathophysiology of epilepsies, as well as to evaluate potential novel therapeutics. The intra-amygdala kainic acid model in mice has emerged as one of the leading models of drug-resistant temporal lobe epilepsy (TLE), displaying unilateral neuropathology, frequent behavioral seizures and broad resistance to anti-seizure medicines. Additional insights into the pathomechanisms of epilepsy in this model may enhance its use and understanding. Here, we generated a single-nuclei RNA sequencing dataset from hippocampal tissue from the intra-amygdala kainic acid (KA) mouse (C57Bl/6) to better understand this model.

Method: A total of 30428 nuclei from 8 mice were sequenced using the 10X platform, divided in 4 epileptic (intra-amygdala kainic acid) and 4 control (intra-amygdala PBS) mice. Count matrices were generated and analyzed using Seurat v5. After quality control, cell types were annotated using the MapMyCells software from the Allen Brain Atlas. Differential expression analysis was performed after pseudo-bulking the samples using the DESeq2 software.

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Results: Annotation of the dataset identified all major transcriptomic subtypes of hippocampal cells and differential expression analysis between conditions revealed cell-subtype specific dysregulation in the epileptic mice, where the CA1/subiculum/CA3 cells and the dentate gyrus appeared to be the most affected areas in the model.
Conclusion: In conclusion, we present the first single-cell data on the intra-amygdala kainic acid mouse model of TLE. These findings enhance our understanding of the cellular and molecular processes in this model and identify both shared and distinct features compared to human TLE.

1060 | Expression and quantification of STXBP1 splice variants in rodent and primate brain tissues

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Purpose: STXBP1 disorders are linked to a loss of function of the syntaxin-binding-protein-1 (STXBP1) and are associated with severe neuronal development delay, intellectual disability and seizures. STXBP1 is a synaptic protein for which multiple splice variants have been reported including a long and a small isoform generated by the splicing of the last exon. In this study we explored the expression pattern of the long and short variants in rodent and primate brain tissues using complementary technology platforms.
Method: Immunohistochemistry analysis was performed on fixed brain slices from WT, STXBP1 heterozygous (HET) and homozygous knock-out (KO) mice. Basescope Duplex assay was used for in situ-hybridization using specific probes for STXBP1 variants. LC-MS analysis was performed on homogenized brain tissues, measuring variant specific peptides, as well as total STXBP1. Non-human primate brain tissues have been obtained from control animals from Charles River.
Results: Evaluation of commercial antibodies indicated that none of the isoform specific antibodies are compatible with IHC analysis. IHC analysis of total STXBP1 indicates that in mouse and NHP, STXBP1 was mainly observed in the neuropil in different regions of the brain, suggesting it is expressed by neuronal cells. In situ hybridization data indicates that most cells co-express both long and short variants in WT mouse brain, although an enrichment of the long isoform was observed in the most caudal regions. Quantitative analysis by LC-MS shows that the short isoform is the most highly expressed in the mouse brain. In NHP, LC-MS analysis of the different brain regions showed that the short isoform is predominant in each one except for cerebellum.
Conclusion: This study demonstrates the advantage of implementing complementary technology platforms to reliably characterize both the spatial and quantitative expression and distribution of STXBP1 splice variants in brain tissues. This is UCB funded work.

1061 | Biophysical characterization of pathological GAT1 (SLC6A1) A288V and S295L mutants associated with SLC6A1-neurodevelopmental disorders

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Purpose: The SLC6A1 gene encodes GABA transporter 1 (GAT1), which regulates GABA concentration and the excitatory-inhibitory balance in the central nervous system. Mutations in SLC6A1 are associated with SLC6A1 neurodevelopmental disorder (SLC6A1-NDD), characterized by epilepsy with seizures (affecting 90% of patients), neurodevelopmental delay and cognitive impairment, autistic features, and motor and behavioral difficulties. More than 100 GAT1 variants contribute to SLC6A1-NDD by causing loss of function, disrupting protein folding, and reducing GABA uptake, leading to the disorder's symptoms. The most common mutations are in transmembrane domains (TMDs) I, VI and extracellular loop IV, harboring 83.3% of variants with low transport activity.
Method: Wild-type or mutant GAT1 can be efficiently expressed in *Xenopus laevis* oocytes by cRNA injection, with function and expression confirmed using two-electrode voltage clamp and immunolocalization. Two of the most common GAT1 mutations associated with SLC6A1-NDD (A288V and S295L) were investigated.
Results: Detailed biophysical characterization on GAT1 A288V shows a stark reduction in the transport current ($I_{max\ WT}$: -392.5 ±15.8 nA vs $I_{max\ A288V}$: -25.3 ±0.5 nA) and an increase in $K_{0.5\ GABA}$ ($K_{0.5_WT}$: 30.1 ±0.2 μM vs $K_{0.5_A288V}$: 142.2 ±9.5 μM), resulting in lower transport efficiency and GABA translocation. A large reduction in pre-steady state current was also observed. Interestingly, the close mutated residue, S295L did not show any kind of

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current, suggesting a complete absence of functional protein at the plasma membrane.

Conclusion: Localization alone is not sufficient to predict the impact of the mutation; however, biophysical and pharmacological parameters provide insight into the effects of variants on protein functionality. Here, analysis of the two variants, both closely located in TMD VI, reveals different causes of alteration in protein functionality, highlighting the importance of detailed investigation of each mutation to develop targeted therapeutic approaches in SLC6A1-NDD.

1066 | Natural history of seizures and seizure-associated spreading depolarizations in rodent models of epilepsy

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Purpose: In recent years it has become apparent that spreading depolarizations can occur in epileptic tissue; either independently or concurrently with seizures. Spreading depolarizations (SDs) are a slowly propagating wave of neuronal and glial depolarization that result in a long-lasting depression of higher frequency brain activity. As traditional AC-coupled electrographic recordings are poorly suited to detect SD's, the impact of SDs to morbidity and mortality in epilepsy is an understudied area of research.

Method: We have developed and implemented a DC-coupled, 4 channel wireless telemetry device that allows continuous recordings for weeks to months. This allows us to investigate the natural history of SD's and seizure-associated SD's (SaSD) in freely moving rodents. We have conducted experiments in mouse models of temporal lobe epilepsy (TLE), and a rat model of focal occipital lobe epilepsy (FNE). Time-locked video provides the ability to describe the behavioral response to each of these events.

Results: In the TLE models we found that SaSD increased the inter seizure interval, occurred during generalized convulsive seizures, and were associated with an increased period of post-ictal immobility compared to seizures alone. SaSD appeared first in cortical leads with delayed subcortical invasion to the hippocampus. In the FNE model preliminary data suggests that SaSD was triggered first in the thalamus.

Conclusion: SaSD's are common events in both of these models. We suggest that they play an important role in the severity of the post-ictal period. Further work in this area will help identify the contribution of SaSD's to post-ictal immobility, and autonomic dysfunction.

1073 | Edaravone modulates morphological and structural alterations of microglia and astrocytes in the hippocampus after status epilepticus

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Purpose: After status epilepticus (SE), reactive oxygen species are produced, promoting the activation of microglia and astrocytes causing cell damage. Antioxidants modulate glial activation by reducing oxidative stress. In this study, we employed Sholl analysis to assess the impact of the antioxidant edaravone (EDA) on the morphological state of microglia and astrocytes after SE.

Method: Male Wistar rats (200–250 g, n=45) were divided into three groups: Sham (n=9), Pilocarpine (Pilo, n=18), and Pilo+EDA (n=18). Stereotaxic surgery was performed to induce SE by Pilo. EDA (10 mg/kg, i.p.) was administered 30 minutes post-SE and continued for six days. Animals were perfused at 14-, 28- and 42-days post-SE and brains were dissected for immunohistochemical staining of Iba-1 and GFAP. Images of the CA1, CA3, and GD were captured, and Sholl analysis was performed. A total of 1,350 microglial cells and 1,350 astrocytes were analyzed (10 cells examined per individual/time point/region).

Results: Twenty-eight days post-SE in CA1 and CA3, microglia reduced process number (Pilo: 8.11±3.18 vs Pilo+EDA: 23.60±8.95) and branching points (Pilo: 2.25±1.63 vs Pilo+EDA: 19.20±8.77), accompanied by an increase in average process size (Pilo: 45.64±15.26 vs Pilo+EDA: 31.70±10.44), while astrocytes showed an increase in process number (Pilo: 39.28±10.89 vs Pilo+EDA: 27±5.92) and branching points (Pilo: 34.10±10.78 vs Pilo+EDA: 2.16±6.09), with a decrease in average process size (Pilo: 24.471±5.319, Pilo+EDA: 28.92±8.01), therefore EDA restore morphological and structural alterations after SE.

Conclusion: EDA modulates glial alterations toward a homeostatic morphology. These findings highlight the potential of EDA as an antioxidant therapeutic strategy to reduce glial activation, which could help protect the central nervous system following SE. Financed by PROSNI 2023-2024/KPP, 2023-2024/LMC, Programa de Fortalecimiento a la Investigación 2023/LMC and COECyTJAL-Fodecijal 10229-2022/LMC.

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1080 | Automated Detection of High-Frequency Oscillations in EEG: Enhancing Epilepsy Diagnosis with Assyst

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Purpose: High-frequency oscillations (HFOs) aid in the diagnosis and characterization of epilepsy, specifically through identification of epileptogenic tissue and predicting seizure onset zone. However, HFO detection is extremely time consuming, and there is also inter-rater variability, differences in detection methods and noise, which complicates the comprehensive study and characterization of HFOs, highlighting the need for automated detection methods to enhance accuracy and minimize human errors.

Method: We modified our automated seizure detection tool, Assyst, for the detection of HFOs. The algorithm employs a novel short-term spectral analysis technique and calculates the Fourier transform of very short signal fragments with an arbitrary frequency resolution and frequency range, bypassing conventional filtering. The embedded "Running rhythmogram" algorithm evaluates the rhythmicity of the EEG fragment allowing to reject artifacts or irregular oscillations. We validated our HFO detection algorithm on detection of ripples (80-200Hz) and fast ripples (200-500Hz) in a Ripple Lab validated HFO dataset that included 30 minute-long slow-wave sleep EEG recordings from 5 lateral fluid percussion injury (LFPI) model of traumatic brain injury (TBI) rats and 5 sham controls. After validation, we assess our HFO detection algorithm in long-term EEG recordings from other models of seizures and epilepsy, including the posttraumatic epilepsy LFPI model, kainic acid and pilocarpine post-status epilepticus model rats, as well as 4 amino-pyridine model.

Results: Our novel method successfully validated the detection of 11 ripples and 17 fast ripples in our validated dataset. Additionally, 45 unannotated events were detected, that were later confirmed to be ripples by two independent experts. Analysis of HFO in our extended EEG dataset is ongoing.

Conclusion: Our modified algorithm demonstrates high sensitivity and specificity and may become a potent automated tool for accurate detection of such short-lasting events as HFOs, thereby improving processing time and promising better efficiency and rigor in pre-clinical research and epilepsy therapy development.

1116 | Orexin receptor type-2 distribution in prepubertal neurodevelopmental stages in Genetic Absence Epileptic Rats from Strasbourg

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Purpose: Spike-and-wave discharges (SWDs) observed on the electroencephalogram (EEG), generated within the cortico-thalamo-cortical circuit, are hallmark features of absence epilepsy. The lateral hypothalamus neurons produce the neuropeptide neurotransmitter orexin, which regulates the sleep/wake cycle. (Celli et al. Current Neuropharmacology, 2022, 20.7: 1254-1260.) While the relationship between the orexinergic system and epileptogenesis remains unclear, this study aims to elucidate the role of orexinergic signaling through the orexin type 2 receptor (OX2R) in the pathophysiology of absence epilepsy during neurodevelopment process. We examined the distribution of OX2R in the thalamus, somatosensory cortex (layers 4-5 and 6), and hypothalamus in Genetic Absence Epilepsy Rats from Strasbourg (GAERS) and Wistar rats using immunofluorescence staining.

Method: Brains tissue samples were dissected from 21-day-old and 3-month-old GAERS and Wistar rats following transcardiac perfusion under deep anesthesia. Thirty μm coronal cryosections were used for morphological and immunofluorescence evaluation. OX2R expression was evaluated in the somatosensory cortex, thalamus, and hypothalamus. All tissues were analyzed for the expression of OX2R by confocal microscope (Zeiss, LSM900). OX2R positivity was analyzed with Image J. All data were evaluated using two-way ANOVA.

Results: No significant differences ($p > 0.05$) in OX2R-positive cell densities were observed between GAERS and Wistar rats in the somatosensory cortex (layers 4-5 and 6), thalamus, or hypothalamus in both 21-day-old and 3-month-old groups.

Conclusion: These results suggest that the distribution of OX2R in the examined brain regions does not significantly differ between GAERS and Wistar rats. However, the expression of OX2R indicates that alterations in OX2R signaling may play a role in the pathophysiology of absence epilepsy during the neurodevelopmental process.

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This study also provides insights into the role of OX2R in absence epilepsy. Further research is needed to explore alternative mechanisms involving the orexinergic system.This study is supported by European Commission Horizon Europe Programme under Horizon-Widera-2021-Access-03 call [Grant Number 101078981-Gemstone]

1191 | Rescue of neuronal activity in iPSC-derived STXBP1 in vitro disease models using viral vectors

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Purpose: STXBP1 (Syntaxin-binding-protein-1), also known as MUNC-18-1, facilitates synaptic vesicle docking and fusion for synaptic transmission. Mutations in the STXBP1 gene are linked to neurodevelopmental disorders in children, with over 85% experiencing seizures and severe intellectual disability (Xian J et al Brain 2022;145(5);1668–1683), (Abramov D et al J Neurochem 2021;157(2):165-178). This study used human-induced pluripotent stem cells (hiPSCs) to model STXBP1 pathophysiology and phenotype rescue after wild-type (WT) STXBP1 gene expression.
Method: hiPSCs were CRISPR/Cas9-edited to obtain STXBP1-KO$^{-/-}$ clones and two heterozygous (HET) missense (R406$^{+/-}$) and nonsense mutations (R367X$^{+/-}$). The NGN2 transcription factor was introduced to AAVS1 locus by flipase – ligase system to differentiate into enriched glutamatergic neuronal population. STXBP1 protein expression was assessed by Western Blot (WB), as well as Syntaxin-1 (STX1A) protein, which an interaction partner of STXBP1 protein. The functional impact of STXBP1 was evaluated by recording extracellular spontaneous neuronal activity using a microelectrode array (MEA) assay.
Results: We confirmed that STXBP1 protein is absent in STXBP1-KO$^{-/-}$ neurons, while the mutant glutamatergic neurons exhibited about 30-60% reduction. KO$^{-/-}$ neurons exhibited 90% reduction in STX1A expression, while the mutants showed 20-40% decrease. We observed a loss of network activity in neurons with STXBP1 mutations and that could be rescued after transduction with Lentiviral vectors (LVVs) or Adeno-associated vectors (AAVs) containing WT-hSTXBP1. Moreover, overexpression of WT-hSTXBP1 partially restored STX1A levels. Next, we used the STXBP1-KO$^{-/-}$ neurons to study epilepsy-causing variants in patients, to predict pathogenicity for known/new variants. 17 patient-described mutations were screened, before and after WT-hSTXBP1 overexpression, by accessing spontaneous network activity and STXBP1/STX1A expression. This validated a potential human cell-based platform for mutagenesis-screening and treatment-prognosis for STXBP1.
Conclusion: This study demonstrates that STXBP1 gene-edited hiPSCs-derived neurons effectively model STXBP1 pathology and provide a platform for screening mutations, correlating genotype/phenotype and developing disease-modifying treatments.

1195 | Characteristic Expression of Astrocyte in Hippocampal Sclerosis

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Purpose: Hippocampal sclerosis (HS) is one of the major causes of intractable epilepsy. Astrogliosis in epileptic brain is a peculiar condition showing epileptogenesis and is thought to be different from the other pathological conditions. To investigate the altered expression of astrocytic receptors, which contribute to neurotransmission in the synapse, and channels in HS lesions.
Method: We performed immunohistochemical and immunoblotting analyses of 20 HS patients and 4 controls for the receptors/channels of P2RY1, P2RY2, P2RY4, Kir4.1, Kv4.2, mGluR1 and mGluR5 and evaluated the ratio of cells expressing each protein and the expression levels.
Results: The ratio of immunoreactive cells/astrocytes and the expression levels of all 7 astrocytic receptors/channels in HS lesions were significantly increased. We previously described unique astrogliosis in epileptic lesions similar to what was observed in the present study.
Conclusion: This phenomenon is considered to trigger activation of the related signaling pathways and then contribute to epileptogenesis. Thus, astrocytes in epileptic lesion they may show self-hyperexcitability and contribute to epileptogenesis through the endogenous astrocytic receptors/channels. These findings may suggest novel astrocytic receptor-related targets for the pharmacological treatment of epilepsy.

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1204 | Impact of Intracerebroventricular Orexin-B on Absence Seizures in GAERS: Dose-Dependent Suppression of Spike-and-Wave Discharges

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Purpose: Absence epilepsy is a generalized epilepsy disorder characterized by brief, sudden lapses in awareness and spike-and-wave discharges (SWDs) on EEG. Sleep spindles and absence seizures share overlapping thalamocortical network mechanisms, suggesting a potential link between the two phenomena. Orexin, a neuropeptide synthesized by lateral hypothalamic neurons, regulates the sleep/wake cycle and may influence epilepsy (Berteotti, C. et al., 2023). Its role in absence seizures however remains unclear. This study evaluated the effect of intracerebroventricular (ICV) orexin-B on SWDs in genetic absence epilepsy rats from Strasbourg (GAERS).
Method: Male adult GAERS (200–350 g) were anesthetized with ketamine-xylazine (100 mg/kg, 10 mg/kg; ip), and unilateral ICV guide cannulas and EEG recording electrodes were implanted. After recovery, baseline EEG recordings were obtained over a 3-hour period. Orexin-B was administered at doses of 0.1 (n=5) / 10 (n=7) / 30 (n=5) nmol/5µL. EEG recordings were performed using the PowerLab-8S system, and data were analyzed with LabChart-8.0. Statistical significance was assessed using one-way ANOVA ($p<0.05$).
Results: Orexin-B at a dose of 30 nmol significantly reduced cumulative SWD duration from 3917.8±426.8 to 1487.7±686.8 seconds ($p<0.01$) with a complete suppression of SWDs observed within the first hour post-injection and with no observable behavioral abnormalities. Both the number of seizures and the mean duration per seizure were significantly reduced. At 10 nmol, a significant decrease ($p<0.05$) was observed only in the cumulative SWD duration. No significant effects were observed with 0.1 or 1 nmol doses.
Conclusion: Our findings demonstrate that intracerebroventricular administration of orexin-B at higher doses effectively suppresses SWDs in a dose-dependent manner suggest that orexin-B may modulate thalamocortical network activity, likely mediated via orexin receptors. Further studies are needed to explore the underlying mechanisms, optimal dosing, and long-term effects, as well as to confirm its potential clinical applicability. Supported by Gemstone Horizon-Widera-2021-Access-03 call (101078981).

1206 | tRNA-derived RNA fragment changes in CSF and plasma in a rat model of temporal lobe epilepsy

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Purpose: Epilepsy affects 50 million people globally, with 5 million new diagnoses yearly. Temporal lobe epilepsy (TLE) is common, but treatments are symptomatic, and preventative measures are lacking. While EEG is crucial for diagnosis, biomarkers for epilepsy development and progression are needed. Some tRNA-derived fragments (tRFs) show promise as seizure biomarkers.
Method: This study investigated three tRFs (5'AlaTGC, 5'GluCTC, and 5'GlyGCC) in the chronic phase of epilepsy using a lithium-pilocarpine rat model of TLE. qPCR analyzed tRF levels in CSF and plasma from 14 epileptic and 8 control rats 53–64 days post-status epilepticus (dpSE), correlating them with spontaneous recurrent seizures (SRS) and interictal activity (IA) determined by continuous EEG recording over 18 days. At 68 dpSE, 8 epileptic rats with SRS and 6 controls underwent pentylenetetrazole (PTZ) administration to examine tRF changes following acute seizures.
Results: Behavioral and EEG monitoring from 9 dpSE, with detailed SRS and IA analysis in the early (9–29 dpSE) and late (50–64/68 dpSE) chronic phases, showed that the first spontaneous seizure occurred at 21.2 ±2.3 dpSE. Generalized SRS frequency increased from 0.13 ±0.07 SRSs/day in the early chronic phase (9–29 dpSE) to 2.0 ±0.6 SRSs/day in the late chronic phase (50–64/68 dpSE) ($p<0.05$). Motor seizures coincided with EEG seizures in ~70% of cases. Control animals remained seizure-free. Regarding tRF expression, epileptic rats tended to have higher baseline tRF levels in CSF and plasma (53–64 dpSE) compared to controls. A similar trend of increased tRFs with IA was observed. Interestingly, epileptic rats exhibited a higher seizure threshold to PTZ than controls.

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However, despite reduced acute seizure susceptibility in the PTZ test, CSF tRF levels increased 1 h after the induced seizure.

Conclusion: Overall findings suggest a potential association between the analyzed tRFs and seizure activity in this rat model.

1295 | Edaravone improves short- and long-term memory retention and preserves hippocampal cells after a status epilepticus event

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Purpose: Status epilepticus (SE) promotes dysfunction and neuronal loss through oxidative stress in the hippocampus, an area closely associated with cognitive processing. The use of antioxidants after SE can reduce oxidative stress. In this work, the effect of edaravone (EDA) was evaluated in memory retention and cellular preservation in the hippocampus after SE.

Method: Male Wistar rats (200–250 g, n=20) were divided into four groups: Sham (n=5), Sham+EDA (5), Pilocarpine (Pilo, n=5), and Pilo+EDA (n=5). Stereotaxic surgery was performed to induce SE by Pilo. EDA (10 mg/kg, i.p.) was administered 30 minutes after SE and continued for six days. After seven days, animals were subjected to the NORT (Novel Object Recognition Test) behavioral test to assess short- and long-term memory retention, then were perfused to extract the brain and fluorescent staining with DAPI was performed to count nuclei to determine cellular preservation after SE.

Results: Seven days post-SE, animals showed an increased exploration time in the NORT behavioral test, indicating cognitive impairment in short-(Pilo: 32.9±3.8 vs Pilo+EDA: 17.4±7.8 s) and long-term memory retention (Pilo: 28±4.6 vs Pilo+EDA: 17.1±1.6 s), as well as a lower discrimination index (Pilo: 44.9±4.9 vs Pilo+EDA: 67±4.4 in short term memory and Pilo: 38±3 vs Pilo+EDA: 60±6.5 in long term memory), which translates into a decrease in object recognition mediated by the lack of memory retention that was improved by EDA administration. In addition, EDA preserved the nuclear cell count in the CA3 (Pilo: 123±31.2 vs Pilo+EDA: 185±33.8) and DG (Pilo: 98±10.5 vs Pilo+EDA: 192±21.4).

Conclusion: EDA improves short- and long-term memory retention and cellular preservation after a SE event. Therefore, EDA could decrease cognitive impairment associated with cell damage and death. Financed by PROSNI 2023-2024/KPP, 2023-2024/LMC, Programa de Fortalecimiento a la Investigación 2023/LMC and COECyTJAL-Fodecijal 10229-2022/LMC.

1297 | Hippocampal neuronal and glutamatergic dysfunction in the acute phase of pilocarpine-induced *status epilepticus*

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Purpose: N-acetylaspartate (NAA) and glutamate (Glu) are markers of neuronal dysfunction and excitatory abnormalities associated with pharmacoresponse and the underlying lesion in temporal lobe epilepsy (TLE). However, the role of metabolic changes in epileptogenesis remains unclear. We evaluated metabolic abnormalities after induced *status epilepticus* (SE) in the pilocarpine model of TLE.

Method: 38 male eight-week-old Wistar rats were randomly assigned to pilocarpine-SE or sham-control groups. Single-voxel proton MR spectra were acquired using a 3T MRI scanner (Philips Achieva) equipped with an animal coil at four timepoints: baseline (before pilocarpine-induced SE), 48h, 15- and 30 days post-SE. We built linear mixed-effects models including groups and scan-timepoints as main effects, and groups-by-scan interaction to evaluate differences in total NAA and Glu ratios to total creatine (tNAA/tCr and tGlu/tCr, respectively) in the dorsal hippocampus.

Results: Significant interactions for both metabolites ($p<0.008$) revealed tNAA/tCr gradually increasing in the pilocarpine-SE group, with significantly higher tNAA/tCr at 15-days and 30-days (all $p<0.001$) when compared to the acute 48h-scan, however, both measures remained lower than baseline scan. There were no longitudinal tNAA/tCr changes in sham-controls (all $p>0.06$). We found decreased tGlu/tCr in pilocarpine-SE at 48h post-SE ($p<0.001$) compared to baseline. tGlu/tCr levels gradually recovered at 15- and 30-days (both $p<0.03$), though remaining lower than the baseline concentration. Contrastingly, tGlu/tCr increased in sham-controls

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from baseline to 48h post-SE (p<0.001), then gradually decreased 15- and 30-days compared to the 48h-scan. Pilocarpine-SE animals had lower tNAA/tCr and tGlu/tCr concentrations than sham-controls throughout the experimental period (all p<0.018).

Conclusion: Acute dorsal hippocampal neuronal and glutamatergic dysfunction are present as early as 48h post-pilocarpine-induced SE, followed by a pattern of recovery in later phases of epileptogenesis, with an offset for baseline values. Since NAA reduction indicates neuronal dysfunction, these changes might suggest dysfunction of glutamatergic neurons likely involving excitotoxicity associated with SE.

1303 | The Functional microRNA Landscape of Dravet Syndrome: Postnatal Development and Regulation of Voltage-Gated Sodium Channels

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Purpose: Dravet syndrome (DS) is a severe pediatric epilepsy linked to mutations in the *SCN1A* gene, encoding a subunit of voltage-gated sodium channel (Na_v). A postnatal surge in *SCN1A* expression precedes the onset of DS in both patients and animal models. The mechanisms regulating developmental expression trajectories of Na_vs remain unknown. Recently, microRNAs (miRNAs) emerged as important regulators of gene expression in epilepsy. We hypothesized that miRNAs suppress Na_v transcripts relevant to DS during the period of seizure vulnerability. Here we mapped the functional miRNA landscape during postnatal development in a DS mouse model and their involvement in Na_v regulation.

Method: We conducted Argonaute (Ago)-sequencing on hippocampal tissues from wild-type (WT) and DS-like (F1. Scn1a(+/−)^{tm1Kea} mutant) mice at postnatal days (P) 0, 7, 15 and 22(n=80). Ago-binding of miRNAs and mRNAs was compared between DS and WT mice. miRNA interactions with 3′UTRs of Na_v subunits were assessed by dual-luciferase reporter assays.

Results: Ago-sequencing showed broadly similar miRNA and mRNA levels in DS and WT mice. Post-DS onset (at P22), seven mRNA targets showed increased Ago-binding in DS, with a potential impact on RNA metabolism and synaptic vesicles. Seven Na_v subunits, including Scn1a, were fine-tuned by miRNAs across all time points. We identified 21 miRNAs likely to regulate Scn1a or Scn3a transcripts and validated the association of 5 miRNAs with their 3'UTRs, two of which progressed to functional analysis in vitro and in vivo.

Conclusion: This study demonstrates that miRNAs regulate Na_vs and broader gene networks during brain development in DS mice. Further investigation may identify the potential of targeting miRNAs influencing Na_vs as a treatment strategy for DS. Acknowledgement: This project has received funding from the European Union's Horizon 2020 programme under the Marie Skłodowska-Curie grant No [101064343] and Research Ireland under Grant Number 21/RC/10294_P2, the European Regional Development Fund and FutureNeuro industry partners.

1323 | The Effect of Cannabidiol Oil on Absence Epilepsy Seizures in a Genetic Rat Model

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Purpose: Limited studies investigating effects of cannabidiol (CBD) in patients with absence epilepsy have reported conflicting results (Azevedo et al. Epilepsy&behavior.2023;149,109512; Patel et al. Epilepsia.2021;62(7),1594-1603). This study aimed to explore the effects of CBD oil on seizure characteristics and locomotor activity in adult female Genetic Absence Epilepsy Rats from Strasbourg (GAERS).

Method: A commercially available CBD oil has been used for the experiments (1000mg/30ml CBD, Vitabiotics, UK). EEG recording electrodes were stereotaxically implanted to female GAERS (6–8-month-old, n=5). After one-week recovery period 2-hour basal electroencephalogram (EEG) was recorded. CBD oil (200mg/kg) was administered to rats orally for 3 days followed by 2-hour EEG recording. Locomotor activity test was performed 30-minutes after CBD administration on the 2nd-day of experiment. Total number, mean duration, and cumulative durations of spike-and-wave discharges (SWD) and locomotor activity of rats were analyzed via GraphPad-Prism-10.1.1. One-way-ANOVA and paired-t-tests were used for comparisons. Data expressed as mean±SEM. P<0.05 was considered statistically significant.

Results: Total number of SWDs decreased significantly in first 30-minutes at both 1st- (p=0.0179) and 3rd-day (p=0.0008) of CBD oil administration compared to basal EEG values (Control-group: 47.6±3.1; CBD-group-1stday:

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33.2±2.4; CBD-group-3rdday: 26.2±2.9). On the other hand, there was an increase in mean SWD duration in first 30-minutes of 3rd-day of CBD administration compared to basal levels (Control-group: 13.45±1.1 seconds; CBD-group-3rdday: 22.5±3.04 seconds, p=0.00163). For the locomotor activity, CBD oil administration increased resting time (p=0.046), while decreased traveled distance (p=0.047) compared to basal levels.

Conclusion: According to our results, CBD oil decreases frequency of SWDs while increasing the mean SWD duration and decreases locomotor activity parameters in the first 30 minutes after its oral administration in adult female GAERS. Future studies investigating its effects in both sexes at different ages are needed to explore its potential disease-modifying effects in absence epilepsy.

1325 | A Research about Orexin type-2 Receptor Protein Expression in Thalamus and Somatosensory Cortex Brain Regions in Rats with Absence Epilepsy

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Purpose: Absence epilepsy is a generalized type of epilepsy that involves abnormal electrical activity in both cerebral hemispheres and sudden loss of consciousness, is common in children, and is seen with 3 Hz spike-wave discharges on EEG (Manning J.P et al. Trends in Pharmacological Science 2003, 24(10):542-549). Orexin-A and -B, neuropeptides from hypothalamic neurons, regulate circadian rhythm and wakefulness via OX1R and OX2R receptors. Recent studies suggest the orexinergic system's role in epilepsy, with orexin antagonists potentially improving sleep and reducing seizures. (Toplu A et al. Frontiers in neurology 2023, 14). This study examined orexin type-2 receptor expression in the somatosensory cortex (SSC) and thalamus (TAL) to better understand epileptogenesis in the GAERS model of genetic absence epilepsy.

Method: Post-natal (PN) 21-day-old Wistar and GAERS animals (n=5) were decapitated under deep isoflurane anesthesia. SSC and TAL regions were extracted to analyze orexin type-2 (OX2) protein expression. Protein isolation was performed, and concentration was determined using the Bradford method. Protein expression was measured using Western blotting.

Results: OX2 protein expression in the SSC and TAL brain regions during the neurodevelopmental period was analyzed and compared between GAERS and Wistar rats. Two-way ANOVA test revealed a significant upregulation of OX2 expression in the SSC of PN21 GAERS rats compared to Wistar rats ($p<0.05$), but no significant difference was found in the thalamus.

Conclusion: In conclusion, changes in OX2 receptor expression in the SSC and TAL regions during neurodevelopment were examined in Wistar and GAERS models, highlighting differences between epileptic and non-epileptic models. These findings may enhance understanding of the relationship between epilepsy and the orexinergic system, potentially identifying future therapeutic targets. This study was supported by the GEMSTONE Project, under the grant agreement number 1010789881, funded by the European Union's Horizon Europe research and innovation programme.

1345 | Modeling Developmental and Epileptic Encephalopathies in *Drosophila melanogaster* as a Rapid *In Vivo* Assay System for Antiseizure Medication Response and Neurodevelopment

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Purpose: Dravet syndrome (DS) is the model disorder for developmental and epileptic encephalopathies (DEE). Currently, there are no therapeutic approaches that target the developmental issues. Some studies have suggested that a presymptomatic ASM treatment may be beneficial. Here, we propose the use of the fruit fly, *Drosophila melanogaster*, as a rapid *in vivo* model for preclinical antiseizure medication (ASM) efficacy testing and for the evaluation of early-life ASM treatment on development and survival.

Method: The sodium channel-associated epilepsies were modeled in *Drosophila* using two established models: generalized epilepsy with febrile seizures plus (GEFS+) and DS. Heat shock assays were conducted on flies treated with and without ASM to induce seizures. Further, survival rates were compared. The developmental phenotype

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was analyzed using movement tracking assays and immunohistochemical staining of the neuromuscular junctions.
Results: ASM effective in humans with DS (valproate, clobazam, stiripentol, fenfluramine) effectively reduced seizures. The application of unspecific sodium channel blocking ASM phenytoin was deleterious. DS flies exhibited aberrant larval crawling behavior that resembles the developmental phenotype of DS patients, associated with synaptic abnormalities revealed by immunohistochemical analysis of neuromuscular junctions. The survival of DS flies was reduced. Both the developmental phenotype and the reduced survival were rescued by an early-onset treatment of larvae with fenfluramine. Furthermore, early fenfluramine treatment could partially rescue the synaptic abnormalities.
Conclusion: Our study demonstrates the value of the fruit fly as a rapid in vivo preclinical model for ASM testing and the investigation of DEEs. This approach has the potential to facilitate the development of tailored treatments for patients with various rare genetic epilepsies. The data presented suggest that presymptomatic treatment may influence neurodevelopment.

1378 | Bursting Neuronal Activity In Vivo: Insights from Pre-Surgical Microelectrode Recordings in Patients with Drug-Resistant Epilepsy

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Purpose: The project aims to analyze neural activity in the mesial temporal structures recorded from microelectrodes during intracranial recordings in patients with pharmacoresistant epilepsy. Single-unit activity (SUA) can be isolated on long-term recordings. Furthermore, neurons can be classified as interneurons (IN) or pyramidal cells (PC). Here, we investigated if bursting neurons can be identified and characterized *in vivo* in human epileptic patients.
Method: Intracranial macro-electrodes combined with research micro-electrodes were implanted into the mesial temporal structures of 14 patients with pharmacoresistant epilepsy. Local field potential, SUA, and multi-unit activity (MUA) were recorded continuously for 2 to 3 weeks, 24 hours a day. Single units were separated using standard spike sorting techniques during awake periods. Different neuron types were identified by the action potential morphology. Finally, bursting behavior was studied on both SUA and MUA.
Results: 61 PCs and 22 INs were distinguished, with mean firing rates of 1.56 ±1.59 Hz and 2.39 ±1.77 Hz. Significant differences were observed between the two clusters in terms of the through-to-peak ratio ($p<0.0005$) and the width at half-max amplitude ($p<0.0001$). Both neuron types exhibited bursting firing patterns. The two groups had no significant difference in intraburst spike count and time or burstiness. Excessive firing during a burst might reduce the effectiveness of spike sorting; thus, a burst detection method was also performed on the MUA. Only 23% of all detected bursts originated from one neuron, while 52% originated from 2 neurons and 21% from 3 different neurons. Different bursting behaviors were observed, such as a progressive change of the action potentials within a burst or stable or increasing-decreasing amplitude.
Conclusion: The findings suggest that bursting neurons can be isolated *in vivo* in patients with mesial temporal lobe epilepsy.

1379 | Development of a Novel Programmable Device for *In Vivo* Induction of Traumatic Brain Injury as a Model of Post-Traumatic Epilepsy

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Purpose: To develop a fluid percussion device for inducing traumatic brain injury (TBI) that enables the design and implementation of an *in vivo* experimental model of post-traumatic epilepsy, ensuring experimental homogeneity with a user-friendly interface for the experimenter
Method: The biotechnological development of the device includes a Biomechanical enhancement phase through the integration of electronic systems for water level control and pressure regulation. To manage the fluid percussion parameters, an interface was developed, which

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is controlled directly on the device via an HMI screen mounted on the front panel. This interface not only allows for the regulation of pressure and duration but also provides a graphical display of water level, pressure, and impact pressure. *In vivo* experimental phase: *Wistar* rats (200-350 g) underwent trepanation surgery (5 mm diameter) in the right parietal lobe, a connector was fixed to attach the hose where the impact would be induced. Various pressure settings (from 1.0 to 4.0 atm) and duration parameters (from 50 to 500 milliseconds) were applied to determine optimal conditions to induce neurological changes (apnea, righting reflex, and the presence of seizures) while minimizing post-TBI mortality. Post-TBI somatomotor deficits were assessed based on the composite neuroscore (Kharatishvili et al., 2009) at 2, 7 and 14 days post-TBI.

Results: The design enabled a device that: i) allows precise control of the applied energy; ii) ensures simple reproducibility; iii) enables predictability of the severity of the induced injury; Iv) offers a user-friendly interface for the experimenter; v) allows graphical recording of fluid percussion, marking both time and duration. The optimal settings to induce neurological changes indicative of severe TBI without mortality were 2.0 ±0.4 atm with a 100-milliseconds pressure duration, resulting in observable somatomotor deficits.

Conclusion: This device allows adjustments according to the experimenter's design, including pressure atmospheres and release duration, as well as computerized data recording

1403 | Role of gut microbiota as biomarker and drug target in Angelman Syndrome (AS)

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Purpose: The last two decades have seen an increased interest in the role of intestinal microbiota in the pathophysiology of central nervous system (CNS) disorders and improvement in the understanding of the microbiota gut-brain axis (MGBA), including its potential as a therapeutic target. Different epilepsy syndromes are characterized by neuroinflammation, alterations of neuronal pathways and neurotransmitters and dysbiosis as reported by different studies on animal models and on human subjects. A known limitation regarding gut microbiota (GM) studies is the wide variability of the samples, while studies on specific populations such as rare epilepsy syndromes are now strongly encouraged. So far, there are no GM studies reported in AS patients. The first objective of this project was to characterize the clinical phenotype and the genotype of the patients with AS, to obtain detailed information on molecular diagnosis, neurological signs and symptoms and gastrointestinal habits or disturbances. Subsequently, we characterized the composition of the intestinal microbiota in AS patients and we improved the current understanding of this syndrome by identifying specific biomarkers (e.g., diagnostic, prognostic) and potential therapeutic targets in fecal and blood samples.

Method: We recruited 30 subjects with confirmed AS diagnosis and 30 age-matched volunteers in a multicenter study. Healthy controls were recruited among relatives of patients with AS, as they share the same nutritional habits. We collected a stool sample for each subject to analyzed by 16S Metagenomic Sequencing Library Protocol for Illumina MiSeq System the GM composition.

Results: The results showed an alteration in the composition of the intestinal microbiota between AS and control patients. Moreover, we found also an alteration of specific biomarkers such as short chain fatty acids in fecal and blood samples.

Conclusion: These results support the hypothesis that GM would be useful both as a biomarker and as a therapeutic target in AS.

1446 | Detection of Acute Preictal EEG Signatures Using Linear Analysis and Unsupervised Clustering

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Purpose: The increase in cortical excitability during the pre-ictal phase (PIPS) leads to seizures unless interventions are applied. This deterministic view has driven efforts to detect EEG-based biomarkers of PIPS for real-time seizure warnings. Identifying a 5-minute acute PIPS window is crucial, as it aligns with FDA-approved intranasal seizure-prevention drugs and optimal timing for ictal-SPECT imaging. We utilized univariate linear EEG analyses, which require relatively low computational power, on 90-minute pre-seizure recordings to identify the acute PIPS period. To evaluate how these features differentiate

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acute PIPS events, we applied unsupervised k-means clustering on their PCA scores and assessed whether automated artifact removal improves cluster quality. Our goal is to optimally segregate the sub-cluster containing the maximum number of acute PIPS events.

Method: Video-EEG data from five drug-resistant epilepsy patients were recorded using a Nihon-Kohden 32-channel system. A Butterworth bandpass (0.5-120 Hz) and notch (50 Hz) filter was applied. Artifact removal was performed on EEG segments with amplitudes below 0.1 μV, above 100 μV, or sharp peaks over 50 μV as NaN. The mean of adjacent non-NaN values replaced missing data points. Features (59/electrode) were extracted from filtered and unfiltered data, then analyzed using PCA. K-means clustering (five groups) identified acute PIPS subclusters (MClus contains maximum PIPS events). Statistical tests: Kolmogorov–Smirnov, t-test, Mann-Whitney U.

Results:

1. Unfiltered MClus had more acute PIPS PCA scores (Unfiltered: 60 [31.67-100], Filtered: 51.67 [31.67-86.67], $P < 0.01$).
2. The non-acute/acute PIPS ratio in MClus was comparable between filtered and unfiltered data.
3. MClus separation was significantly better in filtered data ($P < 0.01$).

Conclusion: Univariate linear analysis provides a practical approach for feature extraction, allowing efficient detection of acute PIPS, while maintaining computational feasibility. Although administration of certain preprocessing methods, improve cluster separation, our results demonstrate that retaining raw data lead to significantly maximize clustering of acute PIPS events in MClus.

1532 | Investigating Atipamezole and Atropine Effects on Absence Epilepsy: Insights from Genetic Absence Epilepsy Rat Models

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Purpose: Childhood absence epilepsy is idiopathic, generalized non-convulsive epilepsy represented on the electroencephalogram (EEG) with bilateral, synchronous spike-and-wave discharges (SWDs) which start and end abruptly (Crunelli et al, *Nature Reviews Neuroscience*, *2002*;*3*(5):371-382). In a temporal lobe epilepsy model, which is generated by kainic acid, it has been demonstrated that the α2AAR antagonist atipamezole alters epileptogenesis (Pitkänen et al., *Epilepsy research* 2004;*61*(1-3):119-140). Moreover, atropine (25 mg/kg) known as a muscarinic receptor antagonist, delayed the occurrence of kindling seizures in Genetic Absence Epilepsy Rats from Strasbourg (GAERS) (Arnold et al., *Experimental neurology* 1973;*40*(2):457-470). The aim of this study is to reveal the dose response effect of atropine and atipamezole administered to GAERS by intracerebroventricular (icv) injection.

Method: For this study, adult male (n=4) and female (n=3) GAERSs (200-300 g) were used. The animals under ketamine xylazine anesthesia, stereotaxic recording electrode and ICV cannula implantation surgery to the frontal and parietal cortices was performed based on the rat brain atlas (Paxinos G et al. In: Paxinos G et al, The Rat Brain in Stereotaxic Coordinates. Academic Press, San Diego, 2007; 17-86). Afterwards, 180 minutes baseline and 180 minutes 12 μg/kg atipamezole (n=3) and 2.5 mg/kg atropine (n=4) which were injected intracerebroventricularly EEG recordings were taken. EEG recordings were analyzed by using LabChart v7 (PowerLab 8, ADI Instruments).

Results: According to the Tukey's multiple comparisons test, the different doses of drugs injected to the GAERS were examined, the mean value of 2.5 mg/kg atropine and 12 μg/kg atipamezole was statistically significant ($p<0.0001$, 95% C.I. = [-448.2, -218.7]).

Conclusion: When the effects of drugs on SWDs were examined individually, it has been shown that 12 μg/kg atipamzeol given ICV to GAERs does not have a significant effect on SWDs compared to 2.5 mg/kg atropine.

1558 | Assessing the heritability and cross-generational susceptibility to acquired epileptogenesis in a rat model of temporal-lobe epilepsy

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Purpose: Temporal lobe epilepsy (TLE) isn't associated with classical Mendelian genetics. Yet, evidence shows that offspring of parents with TLE more often develop epilepsy than offspring of unaffected parents. Epigenetic and epitranscriptomic modifications may account for cross-generational susceptibility; however, investigations of epigenetic biomarkers are needed to further understand disease heritability, onset and progression. Therefore, this study aimed to determine if epileptic rats breed successfully and investigate the heritability and susceptibility of offspring of epileptic parents to developing TLE.
Method: In the parent timeline, 6-week-old Sprague-Dawley rats underwent electrode implantation. After one-week, epilepsy was induced using the systemic kainic acid status epilepticus model (KASE). Control group rats received saline only. Breeding pairs (KASExKASE or ControlxControl) were set up at 10-weeks-old. Bloods were collected at 7- and 17-weeks-old, and video-EEG was conducted at 7- to 9-weeks-old to evaluate epilepsy development, and 17-19-weeks-old to evaluate chronic epilepsy. In the offspring timeline, pups were weaned at 3-weeks-old, underwent electrode implantation, KASE, blood collection and video-EEG acquisition at the same age as their parents. All rats were euthanized at 20-weeks-old, with brain tissue collected to assess epigenetic and N^6-methyladenosine (m^6A) epitranscriptomic modifications.
Results: Epileptic and non-epileptic rats had comparable litter sizes, which developed at a similar rate. KASE offspring had no abnormalities at birth, and in early adulthood had morphological measurements alike Control offspring. Preliminary evidence suggests that offspring from epileptic parents were more susceptible to KASE. Video-EEG to determine whether KASE offspring had worse epilepsy outcomes and the characterization of the epigenetic and m^6A epitranscriptomic signature are ongoing.
Conclusion: For the first time, we showed that TLE rats can produce offspring, with no developmental abnormalities. Although video-EEG and molecular analyses are ongoing, this study provides a novel approach to assess heritable factors in TLE and provides an avenue for future cross-generational assessment of epilepsy and anti-seizure medications.

1575 | Temporal dynamics of neural interactions and activations within arithmetic network during computation from intracranial EEG

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Purpose: Solving arithmetic equations involves a widespread network of neural regions that coordinate the processes required to achieve accurate results. While previous neuroimaging studies have identified extensive fronto-parietal-temporal activations, the precise timing of neuronal activations and connectivity within this network remain unclear.
Method: We used intracranial EEG to measure local neural activity in 20 epilepsy surgery patients performing a sequential arithmetic task. We analyzed high-gamma activity profiles, reflecting the local neuronal population activity, in selected regions of interest (ROI). The functional connectivity between the ROIs was assessed at high temporal resolution using phase-locking value (PLV).
Results: Using high-gamma activity profiles, four distinct neural activation patterns were described: (1) a short, transient increase in power time-locked to numerical stimuli in ventral occipito-temporal regions; (2) a gradual increase of power in selected parietal and frontal regions; (3) a gradual decrease in activity within the precuneus, cingulate cortex and hippocampus; and (4) no significant activity change in the inferior parietal lobule. PLV analysis (0.1–7 Hz) demonstrated progressively increasing connectivity across the network during the equations solving with distinct peaks after a new number presentation. High connectivity was observed between the ventral temporal cortex and parietal regions (notably the intraparietal sulcus) during number recognition, with frontal regions becoming increasingly involved during the arithmetic computations.
Conclusion: These findings provide new insights of the temporal dynamics and functional connectivity of the arithmetic network, emphasizing the distinct activity profiles and connectivity patterns of different brain regions during arithmetic processing.

1581 | Core clock machinery and circadian-driven neuroinflammatory markers profile in a mouse model of Dravet syndrome

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Purpose: Dravet Syndrome (DS) is a severe encephalopathy mostly caused by $SCN1_A$ haploinsufficiency, leading to

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drug-resistant epilepsy and increased sudden unexpected death (SUDEP) risk. It often presents sleep disorders and nocturnal seizures, strongly linked to SUDEP. Despite evidence of neuroinflammation as a key pathophysiological regulator of DS development, the underlying pathways remain unclear. Similarly, the mechanisms driving sleep disturbances and nocturnal seizures are poorly understood but may involve circadian dysfunction. Here we investigate early disruptions in circadian clock function and inflammatory markers in the hippocampus and cortex of DS model mice.

Method: Wildtype Scn1a(+/+)^{tm1Kea} and Scn1a(+/-)^{tm1Kea} were transcardially perfused at post-natal day 21 (P21), when DS mice are susceptible to seizures and SUDEP. Cortices and hippocampi were microdissected for the RT-qPCR and western blot analysis of the core clock machinery (*Bmal1, Per1, Per2, Clock, Cry1, Cry2, Nr1d1* and *Nr1d2*) and relevant circadian-regulated neuroinflammatory markers (*Tnf-α, Il-6, Il-10, Rora, Hmgb1, Arg1, Arg2* and *iNOs*). Student t-test and Mann-Whitney were used for data analyses.

Results: *Bmal1* was downregulated in the hippocampus of P21 DS mice at gene and protein levels, while *Clock* was only decreased at the transcript level. *CRY1* was decreased in both hippocampus and cortex. No other significant differences in the clock machinery were observed in both regions. *Rora*, a key regulator of circadian rhythms, inflammation and metabolism functions was upregulated in DS hippocampus. Moreover, the pro-inflammatory markers *Il-6* and *Tnf-α* levels were overexpressed in the DS hippocampus, while the anti-inflammatory cytokine *Il-10* was decreased. *Il-1β* and the nitric oxide turnover regulators *Arg1* and *Arg2*, were increased in the DS cortex.

Conclusion: We identified early molecular clock dysregulation in the hippocampus and cortex of DS mice and characterized region-specific interactions between circadian rhythms and neuroinflammation. Further studies will explore their impact on sleep disturbances, seizures, and SUDEP.

1590 | Patient derived polyclonal NMDAR antibodies cause epileptic seizures and sleep-wake disturbances in a passive transfer rat model

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Purpose: Anti-N-methyl-D-aspartate receptor (NMDAR) encephalitis is one of the most common forms of autoimmune encephalitis, characterized by neurological and psychiatric symptoms, including cognitive impairment, seizures, and sleep disturbances. However, the underlying mechanisms of anti-NMDAR encephalitis remain unclear. In this study, we investigated the effects of NMDAR autoantibodies on seizure activity and sleep-wake architecture in a passive transfer rat model of anti-NMDAR encephalitis.

Method: IgG purified from the peripheral blood of patients with anti-NMDAR encephalitis (n=3) and healthy controls (HC) (n=4) was chronically administered into the CA3 region of the hippocampus in 2-3-month-old male Wistar rats using osmotic pumps with a brain infusion kit over 14 days. Continuous wireless video-EEG and EMG recordings were performed throughout the infusion period.

Results: Video-EEG analysis revealed convulsive seizure activity in rats infused with NMDAR autoantibodies, with a significant increase in ictal events compared to controls. Additionally, all rats infused with NMDAR autoantibodies exhibited an overall increase in wakefulness. There was a trend for an increase in wakefulness time on Day 5 (p=0.075), which was significant on Day 15 (p=0.031). Furthermore, the most prominent finding was the disruption of the sleep-wake rhythm, suggesting a profound alteration in sleep architecture.

Conclusion: Our findings suggest that NMDAR autoantibodies contribute to increased seizure activity and significant disruptions in sleep-wake architecture, including increased wakefulness and the loss of normal sleep-wake rhythms. These results may help refine therapeutic strategies for managing sleep disturbances and seizures in anti-NMDAR encephalitis. *Supported by Health Institutes of Türkiye (TUSEB) Group B R&D call (#35809) and Scientific Research Projects Coordination Unit of Istanbul University (#40486)*

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1652 | *Bmal1*-Targeting miRNAs: Implications for Circadian Regulation and Epileptogenesis

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Purpose: The circadian clock is crucial for temporal regulation of physiological processes to allow a wide range of organisms to adapt and anticipate daily changes in the environment over a 24-hour cycle. Core clock genes play an important role in regulating a variety of physiological processes by directing different cellular and molecular mechanisms to maintain homeostasis throughout the body, and *Bmal1* has been identified as the core component of circadian clock machinery. Aberrant expression of core clock genes, particularly *Bmal1*, contributes to the progression of various diseases including epilepsy. Emerging evidence suggests that miRNAs exhibiting rhythmicity post-transcriptionally regulate *Bmal1*. This study aimed to identify miRNAs that target *Bmal1*, with a focus on those consistently predicted across multiple databases and their potential involvement in epileptogenesis.
Method: MiRNA targets for *Bmal1* (ARNTL) were identified using miRDB, TargetScan, DIANA tools, and miRTarBase for both human and mouse datasets. Overlapping miRNAs were categorized into species-specific and common targets. Additionally, miRNAs implicated in epileptogenesis were analyzed using a publicly available intra-amygdala kainic acid (i.a.KA) model dataset. Functional predictions were performed using bioinformatics tools such as MiRPathDB, miRWalk9, and miEAA.
Results: A total of 290 mouse miRNAs (147 unique) and 590 human miRNAs (346 unique) were identified as *Bmal1* targets. In the KA model, 421 miRNAs were detected, with 55 also predicted to target *Bmal1*. Of these, 23 were found in mice, 18 in humans, and 14 overlapped in both species, including miR-155-5p, let-7f-1-3p, let-7b-3p, miR-98-3p, miR-381-3p, miR-200a-3p, miR-141-3p, miR-153-3p, miR-744-3p, miR-27b-3p, miR-27a-3p, miR-501-3p, miR-361-5p and miR-26a-2-3p. Functional analysis also revealed that these miRNAs are associated with neuroinflammation and circadian rhythm regulation, further highlighting their potential role in the intersection of epilepsy and circadian biology.
Conclusion: Our findings highlight key miRNAs linking circadian regulation and epileptogenesis, offering insights for future therapeutic development.

1687 | Dynamic reconfiguration of aperiodic brain activity supports cognitive functioning in epilepsy: A neural fingerprint identification

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Purpose: Temporal lobe epilepsy (TLE) is characterized by alterations of brain dynamic on a large-scale associated with altered cognitive functioning. Here, we aimed at analyzing dynamic reconfiguration of brain activity, using the neural fingerprint approach, to delineate subject-specific characteristics and their cognitive correlates in TLE. We hypothesized that the patients may express increased differentiability as compared to controls such that "healthy", optimally flexible dynamics are lost, in a way that is specific to each patient.
Method: We collected 10 min of resting-state scalp-electroencephalography (EEG, 128 channels), free from epileptiform activity, from 68 TLE patients and 34 controls. The functional network was defined by the spatiotemporal spreading, across cortical regions, of aperiodic bursts of signals' amplitude (neuronal avalanches), encapsulated into the avalanche transition matrix (ATM). We performed neural fingerprint analysis in order to capture intra-individual variability, and to identify the individual amongst the groups. Finally, we linked brain reconfiguration pattern with neuropsychological functioning. We excluded interictal epileptic discharges (IEDs) to investigate basal configuration of the brain irrespective of epileptiform activities.
Results: The fingerprint analysis of the ATMs revealed more stereotyped patterns of brain activity reconfiguration in patients with respect to controls, with the greatest stereotypy in bilateral TLE. Patients display larger within-group similarities as compared to controls. These results suggest that TLE patients display a reduced functional repertoire and more stable connections. Importantly, the larger the similarity between a TLE patient's networks reconfiguration and those of healthy controls, the better the memory performance, supporting how a flexibility of functional organization scaffolds the cognitive system.
Conclusion: At first from a theoretical perspective, we highlighted how the basal process of regulation of neural dynamics is altered in this clinical condition. Second, having a pathology-sensitive metric, characterizing individual

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patterns of neural activity without the need of epileptiform activities, drastically increases the usability in a real clinical scenario.

1691 | Chemogenetic inhibition of ventrobasal thalamus exacerbates absence seizures in a genetic absence epilepsy rat model

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Purpose: Absence seizures arise from aberrant cortico-thalamo-cortical network, leading to synchronous, bilateral spike-and-wave discharges (SWDs). Previous studies have shown that enhanced thalamic tonic inhibition contributes to SWD generation and nearly half of patients with absence epilepsy remain unresponsive to first-line treatments targeting thalamic low-voltage-activated calcium channels. In this study we evaluated the role of chemogenetic inhibition of VB thalamus and its manipulation on absence seizure expression in Genetic Absence Epilepsy Rats (GAERS).
Method: We utilized Designer Receptors Exclusively Activated by Designer Drugs (DREADDs) to achieve chemogenetic silencing and modulate SWDs. Adult male GAERS rats received bilateral injections of a viral vector encoding inhibitory (hM4Di) DREADDs into the VB thalamus. Four weeks post-injection, rats were administered the inert ligand Clozapine-N-Oxide (CNO) at a dose of 5 mg/kg (i.p), and electrographic seizures were assessed in comparison to vehicle (saline) treatment on the EEG.
Results: Chemogenetic inhibition of the VB thalamus significantly increased the cumulative SWD duration during a 3-hour EEG recording following administration of CNO (3966 ± 533.1 s) compared to vehicle (3218 ± 551 s, $p < 0.01$). However, the number and mean duration of individual SWDs remained unchanged. CNO exhibited a time-response profile, with significant seizure exacerbation occurring between 80–120 minutes post-injection. In contrast, seizures in animals injected with a control vector (i.e., lacking DREADD expression) were unaffected by CNO administration.
Conclusion: These data underscore the crucial role of the VB thalamus in the propagation of seizures, specifically in the GAERS model, and suggest that precise regulation of thalamic activity may be a key factor in absence epilepsy pathophysiology. Supported by Gemstone Horizon-Widera-2021-Access-03 call (101078981).

1695 | Association between seizure reduction during ketogenic diet treatment of epilepsy and changes in circulatory metabolites and gut microbiota composition

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Purpose: The ketogenic diet (KD) is a high fat, sufficient protein, and low carbohydrate dietary therapy for drug-resistant epilepsy. The underlying mechanisms of action of the KD remain unclear. In mice, the microbiota is necessary for the anti-seizure effect and specific microbes influence circulatory levels of metabolites that are linked to seizure reduction. However, it remains unclear which changes are linked to seizure reduction in patients with epilepsy. We here aimed to identify changes in the gut microbiota and circulatory metabolites during ketogenic diet that correlate to seizure reduction in pediatric epilepsy patients.
Method: We analyzed the serum metabolome of children with drug-resistant epilepsy (n=14) before and after three months on KD. Metabolomic changes were correlated to the gut microbiome and treatment outcome, i.e., seizure reduction.
Results: In this prospective observation study, we uncovered associations between microbial species and serum metabolites that correlated with seizure reduction. Plasmalogens were most strongly linked to seizure reduction and had significant positive correlations with several gut microbes (*e.g., Faecalibacterium prausnitzii*, *Alistipes communis*, *Alistipes shahii*, and *Christensenella minuta*) while significant negative correlations were found for five strains of *E. coli*. Infant-type Bifidobacteria correlated negatively with other metabolites associated with seizure reduction.
Conclusion: The microbes and metabolites identified here may contribute to the therapeutic effect of the KD in children with drug-resistant epilepsy. Several of these metabolites (*e.g.*, plasmalogens) play important roles in neurobiology and may influence seizures. Based on our findings, anti-seizure therapeutic strategies could be developed involving the targeted manipulation of the gut microbiota and/or its metabolites. *Funding:* This study was supported

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1698 | IL-1beta pathway dysregulation in Mesial Temporal Lobe Epilepsy with Hippocampal Sclerosis: Epigenetic and Inflammatory Insights from a Microglia-Like Cell Model

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Purpose: Chronic microglial activation is a hallmark of mesial temporal lobe epilepsy with hippocampal sclerosis (MTLE-HS). Given the association between IL-1β expression and MTLE-HS, we investigated the IL-1β pathway in epilepsy using microglia-like cells derived from peripheral blood monocytes (MMG), focusing on (i) purinergic receptor expression (P2Y12 and P2X7R) and IL1B mRNA levels and (ii) microRNAs (miR-146a, miR-22) involved in its epigenetic modulation.
Method: MMG cells were differentiated from the blood monocytes of 15 MTLE-HS patients (14 females, 51.4 ±13.8 years) and 5 healthy donors (4 females, 51.2 ±9.9 years). P2Y12R, P2X7R, and IL1B mRNA transcript levels and miR-146a and miR-22 in the cell culture medium were quantified using Real-Time PCR. Both homeostatic and LPS-stimulated MMG cells were analyzed.
Results: Homeostatic MMG cells presented a ramified morphology and expressed P2Y12R. IL-1β (3.5-fold) and P2X7R (1.6-fold) transcript levels were higher in MTLE-HS than in controls. miR-146a (3.46-fold) and miR-22 (2.77-fold) levels were also higher in MTLE-HS-derived MMG culture medium. Upon LPS stimulation, MMG cells became amoeboid and showed marked P2Y12R downregulation, as expected. P2X7R expression remained higher in MTLE-HS-derived MMG cells, but no difference was observed for IL-1β transcripts. miR-146a (2.24-fold) and miR-22 (2.2-fold) were also higher in MTLE-HS-derived MMG cells.
Conclusion: Our results suggest that dysregulated IL-1β expression in MTLE-HS may be more relevant in homeostatic conditions, potentially disrupting neurotransmission and contributing to seizures. This supports the hypothesis that neuroinflammation may be a causative factor rather than a consequence of epilepsy, but further research is warranted. Moreover, our findings validate MMG cells as a valuable in vitro model for studying microglial function, neuroinflammation, and epigenetic modulation. Work funded by a FCT grant 2022.10372. PTDC

1710 | iEEG Epileptogenic Networks: Analyzing Preictal Inflow and Outflow Connectivity Dynamics

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Purpose: Intracranial EEG (iEEG) enables mapping of the seizure onset zone (SOZ) for presurgical evaluation. While many studies, guided by the concept of epileptogenic networks, have explored connectivity-based approaches to quantify SOZ dynamics during seizures, the mechanisms underlying the transition from the interictal to ictal period remain poorly understood. This study investigates preictal interactions between SOZ and non-SOZ using directed connectivity measures.
Method: *Patients' database:* iEEG recordings from the CHUM and two publicly available databases were analyzed. SOZs were annotated per seizure (CHUM) and per patient (open-access datasets). Patients with Engel class I/II outcomes and 2 electroclinical seizures were included. *Preprocessing:* Recordings were band-pass (3–45 Hz) and notch (60 Hz) filtered, down-sampled to 500 Hz, and z-scored. A 28-second pre-seizure period was divided into seven non-overlapping 4-second epochs. *Connectivity analysis:* Preictal connectivity was assessed using the Directed transfer function (DTF) and partial directed coherence (PDC). *Surrogate data testing:* Nonparametric surrogate data testing (100 iterations, $\alpha = 0.05$) was applied. *Graph analysis:* Channel-wise inflow and outflow values were extracted. *Statistical analysis:* The Wilcoxon rank-sum test compared median inflow and outflow values between SOZs and non-SOZs.
Results: Sixty-one patients (26 females; mean age: 34.5, range: 13-59) with 243 seizures (mean number of iEEG channels: 92.96, range: 45-176) were analyzed. Statistical analysis of PDC and DTF identified two preictal connectivity patterns: 1) higher inflow to SOZs from non-SOZs

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(p<0.05); 2) higher outflow from SOZs to non-SOZs (p<0.05). Pattern distribution was imbalanced, with 77% of CHUM recordings fitting a pattern, compared to 30% and 20% of open-access recordings, underscoring the potential added value of seizure-specific SOZ annotations.

Conclusion: These findings suggest that preictal network interactions may contribute to seizure initiation and propagation, with either pathological activity from SOZs propagating outward before seizure onset or preictal activity from non-SOZs driving/contributing to seizure initiation.

1731 | Microglial Bmal1 downregulation leads to higher seizure susceptibility and altered hippocampal cytokine and chemokine signaling

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Purpose: Neuroinflammation is an important feature of seizure onset and the development of epilepsy. The inflammatory response, largely mediated by microglia, is strongly regulated by circadian rhythms. These ~24-hour variations in physiological function are orchestrated by a network of autoregulatory genes, particularly *Bmal1*. Here we explored the impact of knocking down microglial *Bmal1* on seizure susceptibility and the CNS-immune profile.

Method: Forty young adult *Bmal1*-Cx3CR1^{Cre-ER} mice were bred and injected with either tamoxifen (40 mg/kg; IP; daily for 10 days) to induce microglial-specific *Bmal1* knock-down (Bmal1-KD) or vehicle (controls). A subset of this cohort was implanted with electrodes for electroencephalographic (EEG) recordings and after recovery underwent an injection of low dose kainic acid (KA; IP; 15 mg/kg) to test for seizure susceptibility. After thirty minutes, bilateral hippocampi were extracted in naïve and KA-treated mice and gene and protein expression was assessed by RT-qPCR and semi-quantitative cytokine array immunoblotting.

Results: Microglial Bmal1-KDs had an increased susceptibility to develop acute seizures (onset 592.7s ±139.7s veh; 136.7s ±27.49s tamox; P<0.0001) and displayed a significantly increased seizure severity measured by the total EEG power (P<0.0002) after KA. *Glul, Fas, Nlrp3, Ccl5* and *Cxcr3* genes were significantly downregulated (all P<0.05) and *Hmgb1* was significantly upregulated (P<0.05) in naïve Bmal1-KD tissue. At protein level, naïve Bmal1-KDs presented an upregulation in MIG (P<0.05). Upon KA challenge, *Irf7, Hmgb1, Tlr2, Tlr4, Tnfr2, CXCL10, CXCR3, FAS, NLRP3, Arg2 and INOS* genes were significantly upregulated (P<0.05, or P<0.01) while G-CSF was upregulated and IL-1α downregulated (P=0.05) at the protein level in Bmal1-KDs.

Conclusion: Microglial-specific depletion of *Bmal1* led to a disrupted electrophysiological and hippocampal immune profile. The reduction in *Bmal1* led to changes in cytokine, chemokine, metabolic and immune-related gene and protein expression at baseline and following acute seizures. Future studies will examine how these mice develop epilepsy.

1748 | Focal cortical dysplasia type II in mice is associated with alterations in oligodendrocyte lineage cell differentiation and myelination

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Purpose: Oligodendrocyte precursor cells (OPCs) were demonstrated to undergo proliferation and differentiation in response to neuronal activity, contributing to activity-dependent myelination. Likewise, mature oligodendrocytes enhance myelin sheath thickness along the axons of active neurons. We investigated whether the pathologically elevated neuronal activity characteristic of epileptic seizures similarly influences oligodendrocyte differentiation and myelination.

Method: We used a mouse model of focal cortical dysplasia (FCD) type II induced via in utero electroporation of a plasmid carrying mutated mTOR gene, resulting in hyperactivation of the mTOR signaling cascade in cortical layer 2/3 excitatory neurons. Electroporated mice developed FCD, and beginning at 8 weeks of age, we conducted continuous video EEG monitoring to assess the occurrence of epileptic seizures. At four months of age, the animals were perfused, and brain sections were immunostained with specific markers for the oligodendrocyte lineage and myelin. We quantified oligodendrocyte lineage cell populations in both the cortical gray matter and white matter (corpus callosum) of the dysplastic and contralateral hemispheres. Control groups included mice electroporated with the mutated mTOR plasmid but without seizures, and mice electroporated solely with GFP plasmid.

Results: In the dysplastic cortex of seizing animals, we observed mild reduction in Olig2^{+} oligodendrocyte lineage cells, accompanied by a significant decrease in the

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myelinated area compared to control groups. Notably, there was an increased proportion of OPCs within the lesion relative to both the contralateral hemisphere and controls. In corpus callosum of seizing animals, we detected a relative increase in differentiated oligodendrocytes compared to controls, suggesting region-specific alterations in oligodendrocyte dynamics and myelination in response to epileptic activity.

Conclusion: The alterations in oligodendrocyte lineage cell proliferation and differentiation observed in FCD type II cortical lesions are likely driven by non-cell-autonomous signaling from mTOR-hyperactive neurons rather than by generalized seizure activity. Moreover, our findings support the presence of activity-dependent myelination in corpus callosum.

1762 | Unraveling the Molecular Mechanisms of Post-Traumatic Epilepsy Using Multi-Omics Analysis

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Purpose: The molecular mechanisms underlying post-traumatic epilepsy (PTE) remain poorly understood, and it is unclear which individuals with traumatic brain injury (TBI) will develop PTE. Given the complexity of genomic and downstream biological processes, multi-omics approaches offer a powerful means to dissect these mechanisms. Here, we used the lateral fluid percussion injury (LFPI) model to identify molecular contributors to PTE development.

Method: BI was induced via LFPI in 32 Sprague-Dawley rats (11 weeks old). Five months post-injury, animals underwent behavioral testing for cognition, depression, and anxiety-like behavior. Seven months post-TBI, EEG electrodes were implanted, and one month of video-EEG monitoring was conducted to phenotype PTE. Sham-operated and naïve animals served as controls. Based on seizure phenotyping, animals were categorized as TBI+PTE (n=10), TBI without PTE (TBI-PTE, n=12), shams (n=12), and naïve (n=12). At eight months post-TBI, perilesional cortex and hippocampal tissues were collected for transcriptomic, proteomic, and metabolomic analyses. Multi-omics integration was performed using Multi-Omics Factor Analysis (MOFA), and pathway enrichment was assessed using functional class scoring (FCS).

Results: Transcriptomic analysis revealed upregulation of Cd22 in TBI+PTE compared to TBI-PTE (logFC = 1.83, FDR = 0.02). Metabolomic analysis identified downregulation of LysoPC(16:0) (logFC = -1.0, FDR = 0.02) and upregulation of carbamoyl phosphate (logFC = 1.01, FDR = 0.04) and tagatose-1,6-bisphosphate (logFC = 0.98, FDR = 0.04) in TBI+PTE. While MOFA did not distinctly separate TBI+PTE from TBI-PTE, FCS identified 123 significantly dysregulated pathways, including RAS signaling, ERK signaling, IFNγ response, neuroinflammation, and retinoic acid pathways.

Conclusion: This study highlights Cd22 and LysoPC(16:0) as potential immune regulators in PTE development. Furthermore, FCS analysis identified key pathways including RAS signaling, ERK signaling, IFNγ response, that may act in concert to influence epileptogenesis after TBI. Further studies are required to validate these findings and explore their therapeutic implications.

1778 | The antioxidant and anti-inflammatory effects of *Maqui Berry protects over* seizure susceptibility and blood-brain barrier damage in aging rats

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Purpose: During the normal aging process, BBB permeability progressively deteriorates, allowing the

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accumulation of neurotoxic proteins from the bloodstream in the hippocampus, which favors the development of acute symptomatic seizures, the incidence of which increases in relation to age with an incidence of 1.23 per 1000 people aged 75 years and older. Maqui B (MB) is considered a powerful natural antioxidant, to which antioxidant properties and anti-inflammatory activity are attributed derived from its high content of cyanidins and anthocyanins. Aim: To evaluate the neuroprotective effect of MB on seizure susceptibility and BBB integrity in aged rats.

Method: Male Sprague-Dawley rats aged 18 months were used, n=8, experimental group: 100 mg/kg-MB As an antioxidant control drug: Vitamin C 100 mg/kg, as an anti-inflammatory control drug: celecoxib 20 mg/kg, o.w. Each treatment was performed for 20 days prior to the evaluation and during the evaluation of seizure susceptibility by means of a subthreshold dose of 35 mg/kg i.p. of pentylenetetrazole, every 24 h in 3 sessions with intervals of 2 days between each evaluation. The expression of Cox-2 and iNOS proteins in hippocampal tissue was analyzed by Western blot. BBB integrity was assessed by the expression of TGF-β, Smad 2/3, AQP4, MMP9, TMPI-1, Claudin-5, Occludin, ZO1 proteins in brain microvessel tissue by confocal microscopy. Finally, the expression of the enzyme SOD in serum was ELISA quantified.

Results: The MB group showed an increase in generalized seizure latencies and a decrease in the expression of TGF-β, AQP4, MMP9 proteins ($p<0.008$) and a greater expression of ZO1, Claudin-5, and Occludin ($p<0.004$) as compared to the PTZ. In hippocampus tissue, MB group showed a lower expression of proinflammatory proteins: Cox-2, IL-1β and TNF-α ($p<0.001$), as well as iNOS ($p<0.008$).

Conclusion: MB has been shown to be a treatment with neuroprotective potential in the adult brain.

1781 | P2X7R Antagonists as Adjunctive Therapy for Drug-Resistant Epilepsy

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Purpose: Epilepsy is a heterogeneous group of brain disorders that affects 70 million people worldwide. Despite the availability of seizure suppressing drugs, drug-refractoriness remains steadfast at 30%, and, even if seizure-suppressive, current pharmacological interventions are merely symptomatic without significantly altering the progression of the disease. The purinergic ATP-gated P2X7 receptor (P2X7R) is increasingly recognized to contribute to pathological neuroinflammation and brain hyperexcitability. P2X7R expression has been shown to be increased in the brain, including both microglia and neurons, in experimental models of epilepsy and patients. The aim of this project is to test P2X7R antagonist as a potential antiepileptic drug and unravel the mechanism of action.

Method: The effect of the P2X7R antagonist both alone and after the addition of an antiseizure drug (Carbamazepine) was evaluated with electrophysiological field recording technique on human brain tissue from patients who underwent surgery. The patients entering the study are brain tumor patients with no previous seizures (used as controls), brain tumor patients with a history of seizures and patients with temporal lobe epilepsy. The activity in these slices is induced after the addition of artificial cerebrospinal fluid where the potassium concentration is increased and the magnesium concentration is decreased.

Results: It was measured the frequency of seizure like events (SLE), their duration, the amplitude of activity, both SLE and inter ictal events and found that the P2X7R antagonist alone has no positive effect, but when added after carbamazepine, it enhances the efficacy of the antiseizure drug in the tissue of these patients who are drug resistant. No activity was evoked in the tissue from control patients.

Conclusion: Our results suggest that P2X7R antagonists could be used clinically as an adjunctive drug to antiseizures medications, as it could improve efficacy in drug-refractory patients.

1804 | Transcriptomic profiling of stereo-electroencephalography electrodes reveals insights into the local molecular microenvironment and epileptiform activity

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Purpose: Stereo-electroencephalography (SEEG) electrodes carry residual tissue which may be utilized for transcriptome and DNA methylation profiling. Here, we explore the transcriptomes of a selection of SEEG cases to understand more broadly what types of transcripts are recovered in terms of representation of genes expressed by different cell types, brain structures, representation of laminar structure, and the extent to which the signal may reflect local epileptiform activity.
Method: Nineteen SEEG electrode samples from three different patients were recovered after explanation. An extensive repertoire of protein-coding transcripts was recovered from each sample using single cell RNA sequencing techniques. Gene expression was correlated with clinical and neurophysiological data.
Results: Electrodes from all cases retained transcripts which reflected the local molecular microenvironment as well as epileptiform activity. Expression of housekeeping genes as well as markers of neuronal activity was consistent between patients and across different brain regions. We detected transcripts representing various cell types including neuronal, glial, and endothelial cells. Several genes showed a gradient of expression depending on the electrode position within the brain. Gene expression correlated with epileptiform activity as recorded by SEEG.
Conclusion: These findings extend the value of SEEG electrodes in understanding local brain activity in patients with epilepsy, both at sites of seizure onset and within the wider seizure network. These findings may be applied to inform clinical decision-making and surgical planning.

Climate Change

1340 | Therapeutic doses of cannabidiol alter body temperature in mice: Implications for anti-seizure mechanisms in Dravet syndrome

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Purpose: Climate change is an emerging global health challenge with implications for epilepsy. Preclinical studies highlight a relationship between body temperature and seizure risk. Dravet syndrome (DS), a severe early-onset epileptic encephalopathy, presents with drug-resistant seizures which are triggered in the early stage by hyperthermic conditions. Environmental stressors linked to climate change, such as heatwaves, may exacerbate seizure frequency. Cannabidiol (CBD), a non-psychotomimetic phytocannabinoid, has been approved as an effective treatment in the reduction of seizures in DS. However, the mechanisms by which CBD exert its anti-seizure effects are not fully elucidated. Here, we investigated the effects of CBD on body temperature in a DS mouse model. The findings suggest CBD may mediate some therapeutic effects in DS through actions on thermoregulation.
Method: Adult C57Bl/6 mice were treated twice daily for five days with 200mg/kg/day CBD or vehicle. Furthermore, CBD at varying doses was administered to wildtype and heterozygous DS mice (*Scn1a*^{tm1Kea}). Post-treatment, mice underwent a hyperthermia-induced seizure threshold protocol. Hippocampal samples were processed to assess the effect of CBD on thermoregulatory gene expression using RT-qPCR.
Results: Administration of 200mg/kg/day CBD significantly decreased the body temperature of C57Bl/6 mice by 1°C. Similar effects were observed in a mouse model of DS in which 200mg/kg CBD significantly lowered baseline body temperature in heterozygous mice by 4°C, allowing similar temperature differences as wildtypes before seizure onset. In contrast, 100mg/kg CBD did not affect baseline body temperature and reduced tolerance to temperature difference, comparable to vehicle-treated DS mice. Molecular analysis of hippocampal samples revealed increased gene expression of *Trpv1* and *Htr1a* in CBD-treated mice.
Conclusion: These findings demonstrate that CBD modulates thermoregulation in mice and this impacts seizure susceptibility in a dose-dependent manner. This suggests potential therapeutic strategies for managing drug-resistant epilepsies like Dravet syndrome, particularly in the context of climate-related heat stress.

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1451 | Behavioral Effects of High Ambient Temperature in Genetic Absence Epilepsy Rats with or without Levetiracetam Treatment

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Purpose: High ambient temperature may have adverse behavioral effects and could impact seizure control in people with epilepsy. This study aims to investigate whether using antiseizure medications will alter the effects of high ambient temperature on anxiety-like behaviors and locomotor-activity in absence epilepsy rats. Moreover, association of gut bacteria with heat-exposure-induced behavioral changes was evaluated.

Method: Adult-male genetic absence epilepsy rats from Strasbourg (GAERS)(n=5) were subjected to 3-staged-experimental-protocol with one-week washout periods. Following basal-behavioral tests; first-stage: 3-day-exposure to high ambient temperature in heat-cabinet (40±0,5°C-17±5%humidity) for 30-minutes, second-stage: levetiracetam administration (100mg/kg/day,3-days-intraperitoneally) without heat-exposure, third-stage: heat-exposure for 30-minutes with levetiracetam administration. Rectal thermometer was used for body temperature measurements. On the 3rd-day of each stage locomotor activity and elevated plus maze tests were conducted. To detect amount of *Bifidobacterium longum* species, stool samples were collected just before and after each stage. Behavioral or bacterial parameters were analyzed via GraphPad-Prism-10.1.1 with repeated-measures-ANOVA-test. Data were expressed as mean±SEM. P<0.05 was considered statistically significant.

Results: Although there was an increase in percent of resting-time (basal-level:70.20±0.8%; heat-exposure:80±1.5%,p=0.0074) accompanied with a decrease in vertical-movements after heat-exposure (basal-level:22±2.8;heat-exposure:14.6±1.8,p=0.035), these significances disappeared with levetiracetam treatment. Heat-exposure with (273.4±44,p=0.0310) or without levetiracetam (279.6±27,p=0.0082) decreased ambulatory activity compared to basal-level (495.2±32) in all rats. Percent of time spent in open arms (p=0.0152) and number of open arm entries (p=0.0475) decreased after heat-exposure with levetiracetam treatment (1.47±0.8;12.4±5.5, respectively) compared to baseline values (9.7±1.8;44.7±7.7, respectively). Amount of *Bifidobacterium longum* between stages showed variability in animals.

Conclusion: According to preliminary results, levetiracetam might be protective against effects of heat-exposure on locomotor activity in absence epilepsy rats. On the other hand, our findings regarding anxiety-like behaviors showed that further studies are needed to explore whether high ambient temperature could worsen adverse behavioral effects of levetiracetam.

1596 | Impact of high body temperature on characteristics of absence seizures and locomotor activity in a genetic rat model

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Purpose: Association of mild decrease in body temperature (0.3-1.3°C) with occurrence of spike-and-wave discharges (SWDs) on electroencephalogram (EEG) in chemically-induced absence seizure models led to suggestion of mild hypothermia as provoking factor for absence seizures (Ostojić et al.2013. Neuroscience.238,39–58). This study examines the effect high body temperature on characteristics of SWDs and locomotor activity in genetic absence epilepsy rats.

Method: EEG recording electrodes were stereotaxically implanted to 4–5-month-old-male genetic absence epilepsy rats from Strasbourg (GAERS)(n=10). EEG recordings or locomotor activity tests were performed at room-temperature for basal-levels and high-ambient-temperature via heat-cabinet (1 hour for each). Cumulative duration, mean duration and total number of SWDs were analyzed. The spectral characteristics of the first 2-second segments of SWDs were analyzed by computing power-spectra using Fast-Fourier-Transform. The results were compared by Paired-t-test; Pearson correlation(GraphPad-Prism-10.1.1). The significance level was set at p<0.05. Data were expressed as mean±SEM.

Results: Mean body temperature increased significantly (p<0.0001) following heat-exposure (40±0.4°C) compared to basal-level (37.9±0.1°C). Heat-exposure reduced cumulative SWD duration (p=0.0077, room-temperature:1262±98.9s, heat-cabinet:823.8±56.3s) and mean SWD duration (p=0.0136,

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room-temperature:14.48±0.8s, heat-cabinet:11.76±0.7s) compared to basal-levels. Strong negative-correlation was detected between mean SWD duration and body temperature (r=-0.77; p=0.07). Heat-stress symptoms developed accordingly in animals with an increase in resting-time (p=0.013) or decrease in vertical-horizontal movements (p=0.0034; p=0.096) and traveled-distance (p=0.047) compared to basal-levels. The spectral analysis of SWD data revealed a slightly faster peak frequency of SWDs for heat-cabinet (7.5±0.4Hz) compared to room-temperature (7.0±0.4Hz). Further spectral analysis for different segments of SWDs and interictal periods are currently being processed.

Conclusion: According to our results, while the increase in body temperature seems to shorten absence seizures without affecting the total number of seizures, it suppresses locomotor activity and causes heat-stress symptoms that need to be considered during heatwaves for the people with absence epilepsy.

1605 | A survey to assess the effects of extreme temperatures on children with epilepsy

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Purpose: People with epilepsy are at higher risk for adverse consequences of climate change. This project aims to determine the impact of extreme temperatures on patient population of children with epilepsy (CWE) and focused on July-2024 heatwaves experienced in Türkiye.

Method: We conducted a face-to-face survey of families with CWE (n=90, October2024-December2024). The 32-questioned survey included demographic characteristics, and effects of extreme temperatures on seizures or need for hospital admission. Continuous variables were presented as mean±SD, while categorical variables were expressed as frequency and percentage. SPSS.24 was used for the analysis (Chi-square test, Fisher's exact test, and Mann-Whitney U test). P<0.05 was considered statistically significant.

Results: Of the included CWE (n=90) with a mean age of 10.1±4.7years, 47.8%(n=43) were girls. Fatigue (34.4%), increased sweating (31.1%) and depression-like symptoms (23.3%) were the most reported effects during hot days. A total of 31%(n=28) of CWE/families reported negative effects of extreme temperatures on seizures. Of those, 71.4%(n=20) were boys whereas 28.6%(n=8) were girls (p=0.014). Among CWE with genetic diagnosis (n=15), CWE with SCN1A or TBC1D24 mutations (20%) reported extreme temperatures triggered seizures. For immobile-CWE (n=20), 35%(n=7) of families reported extreme temperatures increased seizures. Although there was no difference between monotherapy (n=39) and polytherapy (n=45) regarding negative effects of extreme temperatures, CWE on monotherapy with carbamazepine (n=7) were adversely affected (71.4%) more than CWE on levetiracetam (n=20, 20%) or valproate (n=11, 27.3%) monotherapies (p=0.043). 26.7%(n=24) of CWE required hospital admission for seizures during extreme temperatures. During July-2024 heatwaves, 13.6%(n=12) of CWE visited emergency department. Of those, seizure treatment changed for 25%(n=3) compared to 3.9%(n=3) of CWE who did not.

Conclusion: Our results indicate the urgent need for future studies to predict CWE vulnerable to climate change effects and requirement for developing informed adaptation strategies to preserve quality of life of CWE during extreme temperatures.

Clinical Neurophysiology

278 | Spike detection in the wild: screening of suspected temporal lobe epilepsy cases using a tailored 2-channel wearable EEG

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Purpose: Temporal lobe epilepsy (TLE) is one of the most common forms of epilepsy in the general population. Diagnosis can be difficult as the characteristic focal aware and focal impaired awareness seizures are not always easy to recognise. Since epileptiform activity in the EEG is most commonly found over the temporal lobe electrodes, essentially anteriorly, there is the possibility of technical simplification of aEEG through the use of EEG-based wearable devices (waEEG). Our aim is to clinically validate the contribution of a customized waEEG compared to a 24-hour ambulatory EEG (aEEG) for screening patients with suspected TLE but negative routine EEG.
Method: Patients with clinically suspected TLE who were referred for aEEG were fitted with an additional 2-channel bipolar waEEG device and prospectively enrolled in the study until 20 TLE diagnoses were confirmed by aEEG. 41 patients were included and their waEEG was blindly reviewed by two experienced clinical neurophysiologists and a semi-automated spike detection software to categorize patients into TLE (spikes present) and non-TLE (no spikes) groups.
Results: The experts achieved good sensitivity (95-100%) and accuracy (98-93%) with excellent interrater agreement (kappa>0.80) for patient labelling. The semi-automated software performed poorly (40% sensitivity, 68% accuracy) and failed to classify TLE in more than half of the cases. Classification was not affected by restricting spike detection to the evening and nighttime, which reduced the average length of the analyzed EEG from 23.4 to 10.4 hours. Three false-positive spike detections were thoroughly analyzed and reclassified as artifacts due to eye and body movements and electrocardiographic contamination.
Conclusion: Detection of spikes with waEEG enables accurate detection of epilepsy in suspected TLE cases, with less technical and professional effort and better acceptance. This screening tool could improve the yield of follow-up with a conventional aEEG and provide an accessible method for monitoring interictal epileptiform activity in TLE.

359 | Cross-stitching rhythm – a benign form of frontal midline theta EEG activity

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Purpose: Frontal midline theta (FMT) rhythm on EEG has been reported in association with a broad range of tasks. It can be mistaken for an abnormality suggesting bifrontal cerebral dysfunction if the context in which it occurs is not recognized. We report a case of FMT activity seen in a patient while cross-stitching in the epilepsy monitoring unit.
Method: A 49-year-old patient was hospitalized to undergo video-EEG monitoring for potential diagnosis of epilepsy. The episode of interest was characterized by a "wish-wash" sensation in her head, followed by generalized body shaking, backward eye rolling, urinary incontinence and reported loss of awareness.
Results: The EEG showed frontal midline intermittent 4-5 Hz theta activity while cross-stitching. The activity was also noted while performing other bimanual tasks, specifically thread manipulation and phone navigation using a pen. This pattern was task-dependent and ceased after discontinuation of these activities. EEG source localization confirmed localization to the midline frontal head region. On Day 2 of admission a typical event was recorded without ictal EEG correlate. Her 48-hour EEG showed no epileptiform abnormalities or electrographic seizures. She was diagnosed with functional seizures and cognitive behavioral therapy was recommended.
Conclusion: FMT rhythm has been previously reported in case reports and single center case series involving knitting, texting on personal electronic devices, as well as cognitive tasks. The generators involved in FMT activity associated with mental concentration include the dorsal anterior cingulate and medial prefrontal cortex, while corticomotor generators are associated with bimanual motor tasks. FMT activity was generated by cross-stitching in this patient and has previously been associated with a broad range of motor and non-motor activities. Further reports are needed to support FMT as an active stimulus-induced benign EEG variant.

588 | From complexity to bedside, navigating towards the limits of language processing in the brain: mapping postictal aphasia in stereo-electroencephalography

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Purpose: The postictal phase, characterized by transient neurological impairments following seizures, presents an opportunity to explore the pathophysiological mechanisms underlying language deficits and their recovery following an epileptic event. This study investigates postictal aphasia in patients with focal drug-resistant epilepsy (fDRE) undergoing stereo-electroencephalographic (SEEG) monitoring. The aim is to pinpoint critical brain areas linked to specific language deficits by analyzing SEEG signal complexity.
Method: Video-SEEG-recorded focal seizures with and without postictal aphasia were analyzed from patients with SEEG-confirmed hemispheric language dominance. SEEG signal complexity was assessed using permutation entropy (PE), with the postictal period being quantified by a PE-based metric, the Postictal Alteration Time (PAT). Brain region PAT was correlated with language domain recovery (e.g. naming). Electro-clinical recuperation was also evaluated within the dorsal-ventral stream framework. Additionally, a bedside testing battery was developed to assess postictal aphasia severity and task-specific deficits.
Results: 322 seizures from 98 patients were analyzed. Seizures with postictal aphasia had longer PAT than those without. Task-specific language recovery correlated with regional PAT (e.g. naming - superior frontal sulcus and middle temporal gyrus). Moreover, we found that the ventral stream recovered more slowly at the anatomical level. This corresponded to language comprehension recovering after production. To assess the bedside testing, the Postictal Aphasia Scale (PAS) was developed. It evaluates naming, reading, repetition, comprehension (verbal and written) and automatic speech. PAS correlated strongly with brain region PAT, higher PAS scores (indicating milder deficits) aligned with faster regional recovery. At 5 and 10 minutes, PAS revealed a global aphasia pattern, with a predominance of production deficit and a gradual recovery in comprehension. By 15 minutes, postictal aphasia was primarily affecting naming.
Conclusion: This study provides new insights into the pathophysiology of postictal aphasia. It introduces PAS as a tool for assessing postictal aphasia severity and domain-specific deficits, aiding surgical planning and rehabilitation.

615 | Characterizing the Photoparoxysmal Response: Toward Operational Criteria for Interpretation and Classification

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Purpose: Intermittent photic stimulation (IPS) is an activation method used to evaluate the photoparoxysmal response (PPR) during electroencephalogram (EEG) recordings. Despite its standardization, methodologies vary significantly, and the interpretation of the PPR remains subjective. This study aims to describe the main EEG characteristics of the PPR to explore the feasibility of establishing operational criteria for its interpretation and classification.
Method: We analyzed 32 EEG recordings from patients with generalized epilepsy and confirmed photosensitivity, evidenced by the presence of PPR during IPS. Variables studied included the onset morphology, amplitude, duration, latency, and photosensitivity range of the PPR, along with demographic data.
Results: The sample had an average age of 16 years and a predominance of females (75%). Most patients (87%) showed no abnormalities in the EEG prior to the PPR during IPS, which occurred exclusively during eye closure. The onset morphology of the PPR was non-epileptiform in 50% of cases, with the predominant photosensitivity range being 12–20 Hz. The average duration of the PPR was 3 seconds, with a maximum latency of 6 seconds.
Conclusion: These results suggest that the PPR, occurring exclusively during eye closure, may be the only abnormality observed in some patients. The variability in the characteristics of the PPR highlights the need to develop detailed operational criteria to improve its interpretation.

629 | Increased activity of inhibitory interneurons at ictal onset in human temporal lobe seizures

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Purpose: Precise localization of the epileptogenic zone (EZ) is essential for successful surgery in drug-resistant epilepsy. Stereo-electroencephalography (SEEG) with macro-microelectrodes enables single-neuron activity recordings. Although several neuronal firing patterns have been described, the roles of inhibitory interneurons and principal neurons in seizure initiation remain unclear. To address this, we analyzed their firing patterns during seizures to identify potential bioelectrical markers and better understand microscale seizure mechanisms.

Method: An observational study was conducted, including patients undergoing SEEG in presurgical evaluation. Macro-microelectrodes recorded electrical activity in the mesial temporal regions, capturing single-unit activity. EZ and propagation areas were visually identified. Recorded units were categorized into two groups: the EZ group, comprising units within the EZ, and the Non-EZ group, including units located outside the EZ. Units were further classified as putative inhibitory interneurons or principal neurons based on waveform morphology. Firing rates, peak estimates, and changes relative to seizure onset were analyzed using local regression and mixed linear models.

Results: We analyzed 139 seizures from 20 patients. The EZ group included 10 patients (81 seizures), while the Non-EZ group had 16 patients (130 seizures). Of 2,569 recorded units, 725 were classified as single units: 160 inhibitory interneurons (22%) and 565 principal neurons (78%). In the EZ group, interneurons increased firing from 6 seconds before to 9 seconds after seizure onset (p=0.03, n=58), while principal neurons showed no changes. In the Non-EZ group, principal neurons increased firing 5 seconds after onset (p=0.001, n=111), only in extratemporal epilepsy. In temporal lobe epilepsy, units in contralateral regions relative to the EZ showed no significant firing changes.

Conclusion: Our study revealed a cell type-specific firing pattern of interneurons in the EZ, characterized by increased firing rates before seizure onset. These findings suggest that interneurons could serve as biomarkers for precise EZ localization, improving surgical planning and patient outcomes.

634 | Normal physiological rhythms recorded on stereoelectroencephalography (SEEG)

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Purpose: Stereoelectroencephalography (SEEG) is an intracranial diagnostic procedure used in the surgical evaluation of drug-refractory focal epilepsy to accurately localize the epileptogenic zone. Electrode implantation is individually tailored, according to the hypotheses for the patient's epilepsy, allowing for sampling of deeper cortical structures and exploration of seizure networks. SEEG has been adopted by a growing number of epilepsy centers around the world, with varying methodology and interpretation, and need for specific teaching and training to optimize results (Chauvel, J Clin Neurophys, 2024; 41 (399-401)). In contrast to scalp electroencephalography (EEG), SEEG data varies significantly depending on the anatomical structures explored. Although an atlas for SEEG normal activity has been proposed (Frauscher et al., Brain, 2018;141(4); 1130–1144), there is a relative paucity of literature illustrating the spectrum of normal physiological activity. It is important to distinguish physiological activity and artefacts from pathological or epileptiform activity during the interpretation of SEEG, especially since normal background rhythms vary according to the anatomic localization of electrodes. Our poster aims to aid clinicians and scientists learning SEEG by providing illustrations of normal physiological rhythms recorded on SEEG.

Method: We reviewed scalp-EEG and SEEG data from adult patients who underwent SEEG implantation at the Mater Epilepsy Unit in Brisbane, Australia. Representative examples of physiological rhythms on SEEG were selected. Quantified signal analysis was performed on selected samples.

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Results: Our poster presents illustrative examples of normal adult physiological rhythms observed during SEEG recording, along with corresponding neuroanatomy based on electrode implantation. These include the posterior dominant alpha rhythm, lambda waves, photic following response, hippocampal barques, and sleep rhythms.
Conclusion: Accurate distinction between normal physiological SEEG activity from abnormal rhythms is crucial. These examples can serve as valuable teaching tools for clinicians and EEG technologists learning to interpret SEEG.

704 | Epileptic activity in localized RDA - findings from simultaneous scalp and intracranial EEG recordings

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Purpose: The concept of the ictal-interictal continuum (IIC) was proposed in the American Clinical Neuro Society's (ACNS) standardized critical care EEG terminology 2021 version. IIC is synonymous with possible electrographic seizure or possible electrographic status epilepticus. Lateralized rhythmic delta activity (RDA) faster than 1 Hz is considered to be in the IIC category when there are at least 10 waves in 10 seconds and plus modifier or fluctuation. However, it is not clear whether the localized RDA has epileptic activity. Therefore, we clarified the epileptic activity of localized RDA recorded on scalp by comparing with the simultaneous recorded intracranial EEG.
Method: The subjects were 6 cases with subdural or intraparenchymal hemorrhage associated with intracranial electrode placement among 116 patients who underwent simultaneous intracranial and scalp EEG recordings between January 2003 and August 2024 in our hospital. The EEG findings, based on the ACNS standardized critical care EEG terminology 2021 version, were reviewed retrospectively.
Results: 1. Localized RDAs were observed in both intracranial and scalp EEG recordings in all patients. Scalp RDAs were in phase with intracranial RDAs, which amplitude was 10~20 times higher than that of the scalp RDAs. 2 RDAs appeared earlier in intracranial EEG than scalp EEG recordings. 3. Spikes and poly-spikes were observed in intracranial EEG recordings of all patients, while in only three patients in the scalp EEG recordings. 4. Electrographic seizure and electrographic status epilepticus were observed in intracranial EEG recordings of all patients, but not in scalp EEG recordings. 5. Intracranial EEG recordings showed high-frequency oscillations overlaid on RDAs in all subjects, which were not detected in the scalp EEG recordings.
Conclusion: Localized RDAs in scalp EEG recordings are likely to have epileptic activities and are considered to be candidates for antiseizure treatment.

705 | Direct Electrical Stimulation of the Seizure Onset Zone Affects Interictal Electrophysiological Biomarkers

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Purpose: Direct electrical stimulation is often used in presurgical evaluations for patients with pharmacoresistant epilepsy to map functional areas and identify the seizure onset zone (SOZ). Since this procedure can be demanding for patients, we wanted to investigate whether interictal EEG biomarkers provide additional information and offer new insights to improve the localization of the SOZ.
Method: Data from 11 patients who underwent intracranial electrode implantation as part of epilepsy surgery evaluation were analyzed. Electrical stimulation was applied during presurgical assessments to map functional brain regions. Interictal EEG biomarkers — namely relative entropy, sample entropy, linear correlation, and power across multiple frequency bands — were computed during stimulation epochs. The impact of stimulation was quantified by calculating the absolute relative difference in biomarker values between 1–second pre– and

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post–stimulation segments. A permutation test assessed the difference in stimulation in SOZ channels and stimulation in NONSOZ channels. Effect sizes were calculated as an additional measure of the magnitude of these differences.

Results: Among the evaluated biomarkers, sample entropy in the fast ripple band and signal power in the ripple band were the most consistent. Significant differences were observed in 9 subjects for both: sample entropy (mean p=0.0008; mean±SD effect size 0.63±0.33) and signal power (p=0.001; effect size 0.7±0.31). Sample entropy in the ripple band showed significant differences in 8 subjects (p<0.0001; effect size 0.7±0.22), while signal power in the gamma band showed significant differences in 7 subjects (p=0.008; effect size 0.64±0.32).

Conclusion: These findings suggest that sample entropy and signal power hold promise as biomarkers for distinguishing epileptogenic from healthy brain tissue during electrical stimulation. However, further studies are needed to investigate the effect of stimulation parameters on interictal EEG biomarkers and to validate these findings in larger patient cohorts.

713 | Machine Learning Analysis Reveals Dynamic Remodeling of Hippocampal Interictal Spikes in Temporal Lobe Epilepsy

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Purpose: Interictal epileptiform spikes (IESs) are transient neural events that reflect the underlying epileptic network. We employed machine learning (ML) techniques to investigate the dynamic evolution of IES morphology within individual hippocampal channels across sleep-wake states and postictal periods in patients with drug-resistant temporal lobe epilepsy (TLE).

Method: Five patients with drug-resistant TLE underwent continuous long-term (years) intracranial EEG (iEEG) monitoring. We used established ML algorithms to identify seizures, IES and classify sleep-wake states (awake, REM, NREM). IES morphology was characterized using a two-pronged approach. 1) Morphological features were extracted from each IES, capturing key aspects of its waveform shape and dynamics. 2) An unsupervised clustering algorithm was applied to the raw IES waveforms, grouping them to distinct IES subtypes. Statistical comparisons were conducted to assess morphological differences across sleep-wake states and postictal intervals, leveraging both the extracted features and cluster assignments.

Results: We found significant state-dependent variability in hippocampal IES morphology. Sleep-Wake Modulation: IESs exhibited distinct morphological features and cluster memberships across different sleep-wake states, with the most pronounced differences observed between NREM and awake/REM states. This finding suggests that sleep-wake cycles significantly influence the activity of the underlying epileptic network. Postictal Remodeling: In three patients, the immediate postictal period (1 hour after seizure) was characterized by a unique IES morphology. Notably, two of these patients exhibited persistent postictal morphological changes extending into subsequent sleep cycles, indicating a lasting impact of seizures on network dynamics. Clustering: Clustering of IES identified significant state-dependent waveforms in all participants, further supporting the notion of distinct IES subtypes associated with different brain states.

Conclusion: By applying ML techniques to long iEEG single-channel data, this study reveals insights into the dynamic state-dependent remodeling of IES morphology in drug-resistant TLE. Both feature-based analyses and time-series clustering indicate that distinct IES patterns emerge across different sleep-wake and postictal states.

733 | Ictal patterns of eyelid myoclonia

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Purpose: ILAE's 2022 classification describes Epilepsy with Eyelid Myoclonia (EEM) as a generalized epileptic syndrome. Previously three EM semiology types were reviewed (*jerk*, *flicker*, and *flutter*) by Covanis (In: Panayiotopoulos (ed), Atlas of Epilepsies. Springer-Verlag, London, 2010, v.2:1081-91). Several concomitant EEG patterns exist, and the most common are generalized spike-wave (GSW), generalized polyspike-wave (GPSW), and posterior predominant generalized spiky alpha rhythm (SAR). It is not clear if a specific EM presentation is associated with an EEG pattern, and if patients present one unique semiology and ictal EEG. The objective of study is to assess: 1) EM ictal EEG in patients with EEM; 2) whether patients individually present one clinical-electrographic pattern; 3) if there is EEG correlate for each semiology.

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Method: Twelve-hour video-EEG was performed in 18 patients with EEM. EMs were categorized according to semiology and activation methods. Subsequently, descriptive EEG analysis of the blinking artifact and ictal pattern was performed for each seizure.
Results: Age ranged from 8-41yrs. with female predominance (80%). All patients except one had EM during video-EEG. In these all seizures were precipitated by eyelid closure. They had an average of 11 EM (range 5-16) during video-EEG. Intermittent photic stimulation and orofacial praxis were also activation methods chronologically related to EM. Twelve patients presented a single semiology in all recorded seizures (6 *flicker*, 5 *flutter*, 1 *jerk*). Six presented two distinct semiologies (4 *flicker* and *flutter*; 2 *flicker* and *jerk*). The EEG pattern associated with all *jerks* was generalized SAR with predominance in the posterior regions. Regarding *flutter*, there was a predominance of GPSW. During *flicker* recording, there was a great proportion of GPSW, followed by SAR and less frequently, GSW.
Conclusion: We observed in this group of EEM more frequently a patient-unique EM semiology, *flicker* or *flutter*, predominantly associated with GPSW and an association between *jerk* and SAR.

778 | EEG Spectral Analysis Differentiates Angelman Syndrome Genotypes

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Purpose: Pathologic EEG slowing, particularly increased power in the low frequencies (1-6 Hz), is commonly observed in patients with Angelman syndrome (AS) caused by variants in the UBE3A gene. Whether this slowing can differentiate UBE3A deletion (D) from non-deletion (ND) remains unclear. Here, we investigate whether spectral EEG analysis can differentiate between age-matched healthy controls (HC) and patients with D and ND genotypes investigating its potential use as biomarker for UBE3A pathophysiology.
Method: In this observational study, 79 routine at-home EEGs (25 HC, 40 D and 14 ND) from 48 subjects were analyzed. For each recording, periodic power in the 1-6 Hz frequency band was extracted using the fitting oscillations and 1/f method distinguishing the periodic from the aperiodic component. A linear mixed-effects model was fitted to the periodic power, including cohort as a fixed effect, subjects as a random effect, and age as a covariate. The differences in least squares means (LS) between the three groups along with their corresponding 95% confidence intervals and false discovery rate corrected p-values are reported.
Results: Post-hoc comparisons using LS-means revealed significant differences between cohorts: a LS-mean difference of 2.30 for D versus ND (LCI=0.86, UCI=3.75, p=0.0038), 4.35 for D versus HC (LCI=3.14, UCI=5.57, p<0.0001) and 2.05 (LCI=0.47, UCI=3.63, p=0.0123) for ND versus HC. This indicates that the periodic power is significantly higher in D than in ND and compared to HC.
Conclusion: Periodic power within the 1-6 Hz frequency range calculated from routine EEG recordings, effectively differentiates between UBE3A deletion and non-deletion genotypes (and age-matched HC). This suggests that the differences in pathophysiology resulting from UBE3A deletion contribute to EEG signaling pathways, which makes it a potentially viable biomarker for AS and future disease-modifying treatments. Correlation with clinical manifestation will be conducted next to validate this candidate marker further.

785 | Ictal eye closure in focal epileptic seizures: sEEG retrospective observational study from a tertiary epilepsy centre

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Purpose: Eye closure is often associated with non-epileptic events but may also occur during epileptic seizures. We characterized seizure semiology, EEG patterns, and clinical outcomes in people with epilepsy presenting prolonged bilateral eye closure during seizures.
Method: One rater screened 113 stereo-EEG (sEEG) sequentially recorded between 2015 and 2024 from consenting adults with drug-resistant focal epilepsy. A second rater then reviewed the sEEG for the presence or absence of bilateral eye closure. We reviewed demographics,

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medical history, sEEG findings, and histopathology (if available). We used an AC amplifier (Micromed®) with a 1024 Hz sampling rate and 0.008–400 Hz bandpass filter to record the sEEG.

Results: Eleven individuals had bilateral eye closure across 20 seizures: nine sleep-related, eight during wakefulness, and three ECS-triggered. The median recording duration was 6 days (3–16). Their median age was 33 years (25–48), and the median epilepsy duration of 25 years (10–46). In most cases, eye closure occurred at seizure onset (median 0 seconds), persisting for 60% of the seizure duration. Awareness was impaired in eight seizures, preserved in five, and not assessed in seven. Epileptogenic zones were in the right hemisphere (5), in the left hemisphere (4), bilateral independent foci (1), or right onset with contralateral spread (1). Regions involved included the hippocampus, orbitofrontal and prefrontal cortex, cingulum, insula, temporo-occipital junction, and parietal cortex. Surgical resection was proposed for five of them, with four proceeding. Laser interstitial thermal therapy (LITT) was offered to two.

Conclusion: Ictal eye closure in our cohort did not have localizing value due to the involvement of widespread associative areas. Prolonged eye closure may reflect sensory or executive impairment or disruption of cortico-subcortical circuits regulating alertness. Limited sEEG coverage may have missed other regions that may have been involved. More extensive prospective studies are needed to clarify its clinical significance.

818 | Impact of Hippocampal Interictal Epileptiform Discharges on Frontal Spindles and Spindle–Slow Oscillation Coupling During Sleep

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Purpose: This study aimed to elucidate the effects of hippocampal interictal epileptiform discharges (IEDs) on cortical spindles, slow oscillations (SOs), and spindle–SO coupling, which play important roles in sleep-dependent memory consolidation.

Method: Simultaneous intracranial and scalp EEG recordings were obtained during non-rapid-eye-movement sleep from 10 patients with temporal lobe epilepsy. Hippocampal IEDs were recorded via depth electrodes, while spindles and SOs were detected from scalp EEG at ipsilateral frontal (F3/4), central (C3/4), parietal (P3/4), and temporal (F7/8) electrodes. The temporal relationship between IEDs and these oscillatory events was evaluated using peri-IED time histograms. A time–frequency analysis examined IED-related power changes. The effects of preceding IEDs on spindle–SO coupling, defined as spindle amplitude modulation by SO phases, were also analyzed.

Results: Spindle occurrence significantly increased in the frontal electrode during the 0.4–0.8 s time bin after IEDs. Consistently, time–frequency analysis revealed increased power (11–16 Hz) between 0.83–1.20 s following IEDs in the frontal electrode. The incidence of SO negative peaks increased in the −0.4–0 s and 0–0.4 s time bins around IEDs across all electrodes. Increased spindles following IEDs were observed regardless of whether IEDs were coupled with SOs. Significant interactions between SO phases and preceding IEDs on spindle amplitude were found in the frontal and temporal electrodes. Post hoc analyses revealed that IEDs increased spindle amplitude during the specific SO phases in the frontal electrode.

Conclusion: Hippocampal IEDs selectively induced frontal spindles. Although IEDs were modulated by SOs, this could not explain the IED–spindle temporal relationship. Furthermore, hippocampal IEDs altered spindle–SO coupling, specifically in the frontal electrode. These findings support the hypothesis that IEDs interfere with memory consolidation by perturbing the physiological hippocampal–frontal network.

834 | Event-based seizure detection in iEEG using neuromorphic hardware

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Purpose: Accurate seizure monitoring is critical for patient management, yet current methods, such as seizure

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diaries, are often unreliable. Chirps are iEEG frequency patterns that are associated with seizures. Neuromorphic hardware, with its low power consumption and real-time processing capabilities, is a promising platform to detect these patterns. Using chirps and neuromorphic engineering, we aim to perform real-time seizure detection in intracranial EEG (iEEG).

Method: We analyzed iEEG data to identify chirps. In pre-recorded iEEG data from one patient, we filtered in 6 frequency bands in the range 0-40 Hz. We then employed a software Asynchronous Delta Modulation (ADM) encoder for encoding analog waveforms in two streams of Up/Down events. These events were used as input spikes in an SNN implemented on a neuromorphic chip processor (Costa et al. Nature Communications 2024;15(1):3255.). Each frequency band is mapped on a neural population that inhibits all others aside from the next one, in order from high to low frequency. This results in a network able to detect monotonic chirps in the iEEG data. The lowest frequency population of the network connects to an output chirp-counting population to reliably detect chirps, and thereby seizures.

Results: In 48 consecutive hours of one iEEG channel from one patient, we detected all 40 seizures (sensitivity = 100%) with one false detection (false detection rate = 0.021 per hour). For 4 hours of iEEG, the mean processing duration was 4 hours and 55 seconds (standard deviation = 41.72 seconds).

Conclusion: These findings highlight the feasibility of real-time chirp-based seizure detection using a spiking neural network implemented on neuromorphic hardware, showing potential for real-time seizure monitoring in human iEEG. This work is supported by the Swiss National Science Foundation (204651).

860 | Alfa-gamma phase-amplitude coupling in Eyelids Myoclonia with Absences reveals fronto-central abnormal interactions after eye-closures

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Purpose: To investigate whether changes in the interaction between alpha and gamma activity in terms of phase-amplitude coupling (PAC) precede the transition to paroxysmal activity in patients with Eyelids Myoclonia with Absences (EMA) after closing their eyes.

Method: We analyzed the EEG data (32-channels cap) of 16 patients with EMA and 16 healthy controls (HC) who underwent a eyes-open/eyes-closed blocks design paradigm. Alpha-gamma PAC (αγPAC) was computed for the EEG epochs starting after the eyes-closure (EC) and lasting 3 seconds in EMA – when EC did not evocate a paroxysmal discharge ("EMA-neg") – and in controls. When the EC triggered a paroxysmal activity ("EMA-pos"), the analyzed epochs started after EC and lasted until the onset of the pathological discharge. αγPAC values were estimated at single EEG channel (local αγPAC), between different brain regions (cross-regional αγPAC) and compared between patients and controls and within the patients' groups. Cross-regional αγPAC connectivity was extracted using graph metrics for any brain regions and conditions.

Results: The local αγPAC values were significantly higher in EMA-pos conditions compared to EMA-neg and controls. This increase involves the fronto-polar and fronto-central leads bilaterally. By converse, EMA-neg events demonstrated a decrease αγPAC over the fronto-central leads compared to HC. Increases in clustering coefficient and local efficiency were observed in EMA-pos at the parieto-occipital regions compared to controls and at the fronto-central leads compared to EMA-neg. Interestingly, EMA-neg demonstrated a decrease in both metrics at the fronto-central regions compared to HC.

Conclusion: Our data suggests that changes in the synchronization between alpha and gamma oscillations precede epileptic activity in EMA after eye closure. These alterations involve predominantly the fronto-central regions. Even in the absence of pathological activity, the fronto-central areas showed abnormal PAC compared to controls thus supporting the hypothesis of endogenous intrinsic alterations of this network in EMA patients.

866 | A simple, transparent and versatile parametric algorithm for automatic detection of sleep K complexes (KC) from unstaged sleep EEG

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Purpose: K-complex (KC) is one of the major graphoelements in human sleep. The presence, frequency, and morphology of K-complexes can be important in diagnosing

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and understanding various disorders. KC-detection based on sleep specialist visually scored is regarded as the gold standard. However, it is time-consuming and subjective. Consequently, more and more researchers focus on developing an automatic KC-detection method. We tried to develop a simple automated algorithm that detects sleep KC loosely based on the Rechtschaffen and Kales (R&K) rules with high sensitivity and Positive Predictive Value (PPV) without requirement for preceding EEG signal cleaning or sleep staging.

Method: Sleep EEG recordings were imported into a custom-made Matlab-based toolbox. Signal from electrode Fz was subjected to a KC-detection algorithm employing criteria derived from standard R&K rules. The algorithm contains (a) identification of high voltage peaks representing putative KC peaks, (b) feature extraction of putative KCs, (c) classification into KC or not-KC. Classification includes the 4 R&K criteria plus a set of custom-made criteria that are used in visual KC-detection. The algorithm can also detect epileptiform-KC, based on certain features. Thus, KCs of normal individuals as well as epilepsy patients can easily be extracted and analyzed.

Results: Comparing algorithm-derived and sleep scientist-derived KCs for certain individuals, algorithm showed sensitivity more than 90% and PPV >0.8. Furthermore, the algorithm was successful in detecting epileptiform K-complexes in individuals with epilepsy, as verified by sleep scientists.

Conclusion: We consider our KC-detection method very efficient and reliable in sleep analysis, giving the scientists valuable time for analysis and evaluation of the findings, avoiding the onerous procedure of sleep staging and visual evaluation. Its simple design enables both wide application in whole night EEG-signal and application in different laboratories. Moreover, extraction of waveforms with certain features, such as epileptiform KCs, can further enable scientists to reach diagnosis and evaluation promptly.

888 | Acoustic dynamics of music: a potential mechanism for neuromodulation in epilepsy

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Purpose: Music-based neuromodulation has gained attention as a potential future therapeutic tool for managing epilepsy. This study investigates the impact of acoustic properties of music on interictal epileptiform discharges (IEDs) recorded via intracerebral EEG (iEEG), aiming to identify personalized approaches to music therapy.

Method: Twenty-five patients with drug-resistant epilepsy undergoing presurgical iEEG evaluation participated. Over two days, patients listened to compositions with distinct acoustic properties. EEG was recorded before, during, and after music exposure to assess changes in IEDs. Statistical analyses were conducted to compare the effects of different music types and acoustic properties on IEDs.

Results: The effects of music on IEDs varied significantly across compositions and individuals. Acoustic properties, rather than genre, were found to influence IED reduction. On the second day, compositions selected based on their acoustic similarity to the most effective piece from the first day showed significant IED reductions. Specifically, compositions with high acoustic similarity demonstrated reductions of up to 44% in IEDs during listening ($p<0.0001$) and 39% post-listening ($p=0.0108$). Compositions with contrasting acoustic properties generally showed less pronounced effects, with some failing to induce significant changes ($p=0.1187$). These findings highlight the critical role of individual responses and acoustic characteristics in influencing therapeutic outcomes.

Conclusion: The study highlights the potential of individualized, acoustic-based music therapy in epilepsy management. Specific acoustic properties—not genre or subjective preference—drive therapeutic effects on IEDs. These findings advocate for personalized approaches to music neuromodulation, emphasizing further research into acoustic influences and therapeutic mechanisms.

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904 | Hippocampal Spindle Rates Correlate with Cognitive Functions in Pediatric Patients with Epilepsy

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Purpose: Pediatric patients with therapy refractory epilepsy are prone to cognitive decline. Hippocampal spindles, which are not the same as sleep spindles on scalp EEG, may represent a novel biomarker for a physiological phenomenon, with an expression that is diminished in epilepsy affecting the temporal lobe. Yet, no literature on the pediatric population exists. To explore the potential, we have analyzed the correlation between cognitive functions and spindles in pediatric patients with therapy refractory epilepsy.

Method: Spindles were marked visually in 27 patients, each with 60 mins of stereo-EEG recording from hippocampal electrodes. Patients received neuropsychological assessment at the time of presurgical evaluation, including a test battery for various domains such as visual, verbal and figure memory. Spindle rates were correlated with test performance scores using Spearman's Rho.

Results: The mean age was 11 years (SD 4.19; range 2–17 years). Overall, higher spindle rates were seen in patients with a higher test score in the ChAMP Objects Immediate (Rho=0.524; p=0.015) and the ChAMP Objects Delayed (Rho=0.520; p=0.016). Right hemisphere spindles showed an increased trend towards higher scores in the Rey Figure Memory Immediate (Rho=0.583; p=0.064) as well as the ChAMP Objects Delayed (Rho=0.369; p=0.066). The CPT Omissions was significantly higher in patients with higher right hemisphere spindle rates (Rho=0.424; p=0.04). Left hemisphere spindles were significantly more widespread in patients with higher NEPSY (Rho=0.694; p=0.013), CMS Delayed Word Pairs (Rho=0.76; p=0.003), CPT Sustained Attention (Rho=0.929; p<.001), and CPT Omission (Rho=0.550; p=0.007) scores.

Conclusion: Overall higher spindle rates correlate with better visual memory. Right hemisphere spindles reflect higher visual memory and attention. Left hemisphere spindles are more widespread in patients with higher visual memory and sustained attention and better delayed verbal memory. Our findings indicate that hippocampal spindles could be a biomarker for cognitive functioning and aid in the assessment of epileptic encephalopathy.

930 | "Wipe your face, smile, laugh ... strike a pose!" Lesser known semiologies of the Cingulate network. A Stereo-EEG and signal processing study

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Purpose: Semiology is the clinical manifestation of epilepsy and one of the foundational aspects of the Stereo-electroencephalography (SEEG) methodology. In this study, we analyzed the ictal semiologies comprising smiling, laughter and neck choreo-athetotic movements as well as post ictal face wiping and an unusual pose of one arm over the head. All of these were accompanied by hyperkinetic semiology. Signal processing techniques on patients who had undergone Stereo-EEG were applied, to elucidate the underlying cortical networks involved.

Method: 75 SEEG cases were reviewed over a 16 month period. In total 77 seizures (across 20 patients) were identified as having one or more of these semiologies. The SEEG signals were converted into Event related Syncronization/Desynchronization (ERSD). The ERSD analysis methodology involved four techniques: a. integral change b. detrended change (both capture activity triggered by the event) and c. mean d. root mean square (both indicate the activity accompanying the event) All analyses were conducted for each frequency band and the brain areas sorting was done according to the activity change or mean activity per frequency band using the median as the sorting parameter to minimize the effect of outliers.

Results: Smile and laughter semiologies mainly involved the anterior cingulate Cortex (ACC), mid cinguate cortex (MCC) and frontal operculum (FO) and orbitofrontal cortex (OFC). Face wiping was seen in the ACC, FO, anterior & posterior insula, OFC and motor face area. "The Chill out"/arm over head pose involved a network comprising the ACC, Frontal Operculum, Orbitofrontal, Anterior Insula. Finally, neck choreo-athetoid movements were seen to originate in the ACC and anterior Insula.

Conclusion: The cingulate region can manifest with a wide range of various semiologies, often with a hyperkinetic basis. Recognition of these lesser known manifestations may help guide Stereo-EEG implantations within defined networks. Signal processing techniques help to unravel these key regions.

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948 | Exploring Hippocampal High-Frequency-Oscillations in human organotypic brain slices cultures

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Purpose: High-Frequency Oscillations (HFO) in vivo have been studied for over 25 years and emerged as as a valuable biomarker in intracranial EEG. Although physiologic and pathophysiologic mechanisms of HFOs are incompletely understood, they presumably play a physiological role for memory function and a pathophysiologic role for seizure emergence. Here, we demonstrate that HFO are also detectable ex-vivo by electrophysiological examinations of human organotypic brain slice cultures (hOBSC) via multielectrode array (MEA). Furthermore, we explore the pathophysiologic basis of HFO generation by investigating the role of neurotransmitters and environmental conditions (temperature).
Method: We obtain brain tissue from epilepsy surgery to prepare 250-300µm brain slices. Human cerebrospinal fluid (hCSF) is used for slice culturing, granting viability for up to three weeks. We use 256-channel MEAs, covering 3.2x3.2mm^2, to record whole-slice electrophysiology, enabling the measurement of local field potentials, action potentials, and propagation dynamics. Computational post-processing includes frequency filtering and semi-automated HFO detection; 80-250 Hz for Ripple-HFO or 250-500 Hz for Fast-Ripple-HFO. Slices are exposed to varying temperatures and excitatory or inhibitory agents to assess their impact on HFOs.
Results: We demonstrate a consistent detection of HFOs in hOBSCs from hippocampal resections of temporal lobe epilepsy patients Frequency and spatial spreading could be increased high-dose potassium or Gabazine, a $GABA_A$-receptor-antagonist, and significantly reduced by addition of CNQX, an AMPA/kainate receptor antagonist, and Tetrodotoxin. Ripple-HFO-Frequency was also increasing within the physiological temperature range.
Conclusion: HFO-like activity is detectable ex-vivo in hOBSCs via MEA, is dependent on temperature and can be modified with medical treatment which enables us to further examine HFO pathophysiology and evaluate new approaches e.g. by modifying gene expression or by electrical/optogenetic stimulation.

1027 | Predictive Value of EEG in the Suspicion of Brain Lesions Undetected by CT in the Acute Phase

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Purpose: Focal slow/attenuation activity is the most frequently observed electroencephalographic (EEG) abnormality associated with brain dysfunction, regardless of etiology. Given the accessibility of neuroimaging, the role of EEG in identifying brain lesions has been undervalued. This study aims to determine the positive predictive value (PPV) of focal anomalous EEG activity (non-epileptiform and without status epilepticus criteria) to diagnose brain lesions when the initial CT scan is normal.
Method: Retrospective study of all consecutive patients, between 2023-2024, with EEG showing focal continuous or burst slow activity and/or focal attenuation of baseline activity and with an initial normal Brain CT scan. PPV was calculated, and a descriptive clinical analysis was performed.
Results: Fifty-five patients were included (median age 73 years, IQR 57-83 years; 56.4% women). Twenty-two (40%) had structural abnormalities on follow-up imaging (13 vascular, 3 neoplastic, 6 infectious). Among these, 10 had continuous slow activity, 4 focal attenuation and 8 burst slow activity (BSA). Thirty-three (60%) had no structural lesions on follow-up imaging. Among them, 7 had neurological dysfunction (2 focal epilepsy of unknown cause, 5 meningoencephalitis): 1 had continuous slow activity, 4 focal attenuation, and 2 BSA. The remaining 26, all with BSA, had no neurological dysfunction. The PPV of anomalous EEG activity for neurological dysfunction was 52.73%, lower for BSA (27.78%), and highest for continuous slow activity or focal attenuation (100%).
Conclusion: Continuous slow activity or focal attenuation on EEG contributed to diagnose brain lesions undetected on initial CT scan, reinforcing EEG as a diagnostic tool for clinical suspicion and guiding further investigation. These findings highlight EEG's role in early diagnosis and treatment decisions, potentially improving patient outcomes.

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1029 | Effects of Caloric Restriction and Ketogenic Diet on mTOR and GATOR signaling axes

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Purpose: Increasing evidence shows that caloric restriction (CR) and ketogenic diet (KD) are effective in seizure control by modulation of the mammalian target of rapamycin (mTOR). We aimed to examine the effects of KD and CR with different fatty acid modifications on the expression of the PI3K/AKT/mTOR signaling axis with its downstream target AMPK and the GAP activity (GATOR) protein complex, which has an inhibitory effect on mTOR, specifically directed at Rag 1.
Method: Fifty female Wistar rats (6 weeks old) were divided into 5 subgroups and exposed to different dietary fatty acids and calorie modifications including KD, CR or normal caloric standart diet (SD) for 7 weeks. At the end of the 7 weeks, isolation of the total protein amount from liver tissue was followed by immunoblotting assay to evaluate mTOR-related proteins (mTOR, AMPK, Rag C and pACC) and proteins associated with the GATOR1 (NPRL2) and GATOR2 (Mios and WDR59) pathways.
Results: KD caused decrease in mTOR expression and increase in p-mTOR and p-AMPK expression and a significant increase in NPRL2 expression compared to SD. CR increased p-mTOR expression, p-AMPK levels, RagC phosphorylation and pACC expression. All diet modifications except SD increased the expression of GATOR2 markers, as well as the proteins WDR59 and Mios, which have an activating effect on mTOR.
Conclusion: KD and CR has an inhibitory effect on mTOR expression in two ways; by increasing pAMPK levels and expression of GATOR-1 pathway. The increase in pACC by CR can be explained by the increase in AMPK expression, which inhibits ACC by phosphorylation. Increased expression of GATOR2 proteins by KD or CR may be related to balance the suppression of the mTOR pathway.

1042 | Asymmetry of epileptiform discharges amplitude in generalized epilepsy

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Purpose: It has long been held that idiopathic generalized epilepsy (IGE) reflects conditions where epileptic seizures start simultaneously in both hemispheres. However, recent evidence has challenged this concept by suggesting that cortical onset precedes generalized involvement by a time latency too short to be identified by eye. If cortical foci indeed exist, then we should see signature of them in EEG signals. To test this, we here studied whether generalized discharges in people with idiopathic generalized epilepsy exhibit an asymmetry of amplitude.
Method: In these preliminary analyses, we identified visually generalized discharges in 10 people with IGE. The amplitude of discharges was computed by a Hilbert transform after filtering the signal between 2-4 Hz. We used F4, C4, F3, C3 as electrodes of interest. We used linear mixed models and permutation testing to evaluate whether one hemisphere exhibits a systematically higher amplitude than the other – whether it is the right or the left hemisphere – and then whether the left or right hemisphere exhibits a systematically higher amplitude than the other hemisphere.
Results: 10 patients and a total of 849 interictal discharges were included (mean, standard deviation: 85, 113 per patient). One hemisphere displayed a systematically higher amplitude than the other ($F(1,3375)=17.46$, $p<0.001$). The amplitude was 9% higher than expected by chance. There was no systematic difference between the right and left hemisphere ($F(1,3370)=2.41$, $p=0.12$).
Conclusion: Epileptiform discharges in IGE exhibit asymmetrical amplitude yet without bias for the left or right hemisphere across patients. This indicates that this asymmetry is an individual trait, in line with the hypothesis of cortical focus or delimited network in IGE. We plan to increase the number of patients and further test whether the asymmetry is modulated by individual parameters, such as handedness.

1096 | Serial EEG findings in CRADD syndrome with epilepsy: the search for electrophysiologic signature

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Purpose: The goal of this study is to present EEG patterns proposed to be clues to the diagnosis of CRADD syndrome.

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Method: We present a case of a 14-years-old boy diagnosed with a CRADD syndrome in whom a clinical and EEG follow-up was performed since he was 5 years-old.
Results: At the age of 4 years, because of his distractibility, an EEG was ordered and revealed a normal background rhythm, frequent polyspike-wave discharges and short high-amplitude, generalized fast discharges (GPT), spontaneous and evoked by IPS. At the age of 8 years, the scores of full-scale intelligence quotient (FIQ), performance intelligence quotient (PIQ) and verbal intelligence quotient (VIQ) were 47, 49, and 49, respectively, as tested by the Portuguese adaptation version of the Wechsler Intelligence Scale for Children –*Third* Edition (*WISC-III*) (Wechsler, 2003; original version: Wechsler, 1991). In the following years, in spite of multiple ASMs tried (VPA, LEV, CZP, TPM, LTG), the mother persistently reported eyelid myoclonus. Finally, at the age of 14 years a full-blown bilateral tonic clonic seizure was witnessed. The EEG performed 2 months after that seizure showed the same high-amplitude, generalized fast discharges, but, at this time, of longer duration (GPFA), as well as intense photosensitivity for the whole range of IPS frequencies, including 1 Hz.The young patient had moderate intellectual disability, larger than average head circumference (megalencephaly), pachygyria with a predominant anterior gradient.
Conclusion: The serial EEG recordings showed persistently classical photoparoxysmal responses in a very large IPS frequency range in addition to high-amplitude (> 200 μV), fast frequency (17 Hz) rhythmic discharges in an awake EEG. Within the clinical context exposed in this case presentation, the described EEG patterns might be useful clues pointing to the diagnosis of this rare type of lissencephaly, with frontal predominant pachygyria/ mild cortical thickening.

1202 | Quantitative EEG analysis in patients with autism spectrum disorder

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Purpose: Autism spectrum disorder (ASD) is a neurodevelopmental condition characterized by challenges in social interaction, communication, and repetitive behaviors. Given the increased prevalence of epilepsy in individuals with ASD, this study aimed to analyze QEEG data to identify patterns of brainwave activity and connectivity anomalies that may overlap with epilepsy-related features.
Method: The study included 18 patients diagnosed with ASD (13 males, 5 females; mean age 12.6 ± 3.8 years). EEG data were collected using a standard 19-channel system. Power spectral density and connectivity were assessed, focusing on beta power, interhemispheric and intrahemispheric coherence, and potential epileptiform activity.
Results: Beta power increase: Elevated beta power, associated with anxiety and repetitive behaviors, was observed in 14 of the 18 patients, with 4 patients showing normal levels. This increase may indicate heightened cortical excitability, a feature also seen in epilepsy. Hemispheric balance: Hemispheric balance was disrupted in 7 patients, showing reduced interhemispheric symmetry, while the remaining 11 maintained balanced hemispheric activity. Intrahemispheric connectivity: Reduced intrahemispheric connectivity was identified in 6 patients, while 2 patients exhibited mixed patterns of increased and decreased connectivity. The remaining 10 patients showed reduced interhemispheric connectivity, with asymmetrical patterns between left and right hemispheres. Epilepsy-related patterns: Although no overt epileptiform discharges were identified in most patients, features such as beta power elevation and altered connectivity may suggest an underlying predisposition to abnormal cortical excitability, which is commonly observed in epilepsy.
Conclusion: This study highlights elevated beta activity, and altered connectivity patterns as consistent neurophysiological markers in ASD. The observed beta power increase, linked may also reflect heightened cortical excitability, a potential shared mechanism with epilepsy. These findings emphasize the need for careful monitoring of epileptic tendencies in individuals with ASD. QEEG may serve as a valuable tool for identifying overlapping features of ASD and epilepsy, aiding in early detection and intervention.

1245 | Brain Network Responses to Evoked and Spontaneous Arousals in NREM Sleep

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Purpose: The objective of this study was to investigate differences in power spectra composition between auditory stimulation-evoked and spontaneous arousals during NREM sleep using intracranial EEG (iEEG) recordings obtained from patients with epilepsy undergoing presurgical evaluation.
Method: Bipolar channels from recordings without epileptiform activity from 10 patients with drug-resistant focal epilepsy were analyzed. Evoked arousals were induced using auditory stimuli during the first half of the night. Then, evoked and spontaneous arousals during the whole night were annotated according to standard criteria and paired to ensure an equal number of evoked and spontaneous arousals within the same sleep stages. Power spectra across standard frequency bands were computed. A common baseline derived from one hour of undisturbed NREM sleep was used and statistical comparisons were performed using the Wilcoxon signed-rank test with false discovery rate (FDR) correction and effect size calculations. We only consider statistically meaningful if effect sizes exceeded 0.33 and p-values were <0.05.
Results: Power spectral analysis revealed significant differences between evoked and spontaneous arousals across multiple brain networks. In the default mode network, evoked arousals exhibited significantly higher power in the 1-20 Hz range, while spontaneous arousals had significantly higher power in the 65-250 Hz range. Similar patterns were observed in the dorsal attention, frontoparietal, limbic, and visual networks. The somatomotor network showed significantly higher power across all frequency bands in spontaneous arousals, while the ventral attention network displayed differences only in the 20-250 Hz range, with significantly higher power in spontaneous arousals. Additionally, analysis of slow-wave occurrence indicated no significant differences between evoked and spontaneous arousals ($t(9)=.4$, $p=.682$, Cohen's $d=0.13$), suggesting similar slow-wave contributions in both conditions.
Conclusion: These findings suggest distinct spectral characteristics between evoked and spontaneous arousals, highlighting potential differences in underlying neurophysiological mechanisms. Future work will focus on analyzing connectivity differences to further explore arousal-related brain dynamics.

1289 | A Retrospective Review of Clinical and EEG Features in Adults with Lennox-Gastaut Syndrome

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Purpose: To study clinical/EEG findings in adult patients with Lennox-Gastaut syndrome (LGS), compare findings to published criteria and evaluate EEG changes over time.
Method: Adult patients were largely identified as those fulfilling criteria for cannabidiol prescribing for LGS in our center, with a retrospective review conducted of clinical records, available EEG recordings (routine or prolonged video-telemetry) and associated reports.
Results: Of 81 adult LGS (42 males, age 18-62 years, mean=30.5), 74 had moderate-to-severe intellectual disability and 47 a functioning Vagus Nerve Stimulator. Seventy-seven were on ≥3 anti-seizure medications (ASMs). Twenty-five had previously tried the ketogenic diet. Forty-three had abnormal MRI. Underlying etiologies included identified genetic causes (n=19), perinatal brain damage (n=10) and other structural brain abnormalities (n=12). All patients had a history of more than one seizure type, including tonic. Of 79 with one or more available EEG reports seizure types captured as described in video-EEG reports, since childhood, included tonic seizures (n=56), atypical absences (n=22), generalized tonic-clonic seizures (n=11), focal unaware seizures (n=11), myoclonus (n=19), head drop (n=5), drop attacks (n=2), atonic (n=4), status epilepticus (n=7), subclinical/electrographic (n=27), non-epileptic (n=4) and others (n=11). Diffuse slow background was described in 69 cases. Interictal findings included multifocal epileptiform discharges (n=55 cases), generalized slow spike-and-wave discharges (n=50 cases), focal discharges (n=37 cases), and generalized paroxysmal fast activity (n=4 cases), though in another 7 cases this was labelled as subclinical seizures. Reports concluded the EEG was in keeping with symptomatic generalized epilepsy in 29/79 cases and epileptic encephalopathy in 11/79. In only 14/79 was LGS specifically mentioned.
Conclusion: Given available therapeutic options, there is a need not to miss LGS diagnoses. Our initial analysis shows old EEG reports in our region refer only rarely to LGS and specific EEG findings are not always described.

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1313 | Performance of independent component analysis in localizing seizure onset from scalp-EEG

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Purpose: Independent Component Analysis (ICA) separates signals into statistically independent sources and is widely used in electrophysiology for artifact rejection and spike detection. However, its applications in ictal electrical source imaging remains underexplored. We assessed ICA's ability to uncover ictal components localizing the seizure onset zone (SOZ) using low-density scalp EEG and compared the impact of different ICA parameters settings.
Method: We analyzed twenty scalp-EEG seizures from ten patients with a stereo-EEG (SEEG)-defined epileptogenic zone, all seizure-free after either surgery or RF-thermocoagulations. ICA was computed using the following parameters: (i) clinical- vs. EEG-defined seizure onset, (ii) 10,30 and 300 seconds of preictal data, (iii) FastICA, infoMax, and SOBI algorithms. Components were visually categorized as *ictal* or *non-ictal*, based on their time-courses. The most ictal-looking component of each ICA was labeled *best-of-ICA* and components with a unique time-course (e.g. uncovering a discharge difficult to detect in EEG) *unique*. We estimated minimal distances between components' localization (via dipole fitting) and SEEG-defined SOZ and assessed components matching its sublobar topography.
Results: We performed 180 ICAs, yielding 8164 components. Thirteen percent were labeled *ictal* (mean of 3 per ICA), and 1,3% *unique*. Sublobar localization of the SOZ occurred in 38,5% of *ictal* components, 48,2% *best-of-ICA*, 56,7% *unique*, vs. 17,9% *non-ictal* components. Mean distances to the SOZ were 44,4 mm (*ictal*), 36,8 mm (*best-of-ICA*), 28,9 mm (*unique*), vs. 62,9 mm (*non-ictal*). InfoMax computed on 300 seconds before symptoms' onset achieved the highest Fscores for sublobar localization (0,25) and < 50mm proximity to the SOZ (0,29). Using these parameters, 13/20 seizures and 8/10 patients *best-of-ica* achieved sublobar localization of the SOZ, with a median distance of 29,9 mm.
Conclusion: InfoMax ICA on 300 seconds preictal low-density scalp EEG data depicts an ictal component, localizing the SOZ with a sublobar precision in 65% of seizures and 80% of patients.

1347 | Screening for cognitive impairment in generalized epilepsy

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Purpose: Identifying cognitive disorders in generalized epilepsy and creating efficiency in diagnosis by using the Montreal Cognitive Assessment (MoCA) screening test.
Method: Our study included 52 people with generalized epilepsy and 22 healthy individuals. 52 patients aged 18 to 60 (average age 36.78) were selected for our research We studied patients with generalized epilepsy in 3 groups. Group 1a included 16 patients with Idiopathic generalized epilepsy (IGE), Group 1b included 24 patients with Symptomatic generalized epilepsy (SGE), Group 1c consists of 12 patients with cryptogenic generalized epilepsy (CGE). We used the MoCA scale to examine cognitive functioning of the patients.
Results: According to the results of the MoCA scale, people with generalized epilepsy had significantly lower total MoCA scores than did the controls (1a=22.4, SD 4.2; 1b=21.8, SD 4.6; 1c=23.2, SD 3.4 vs 27.5, SD 1.6 points; $p < 0.001$). In addition, worse cognitive conditions was observed in SGE than in other generalized epilepsy ($p < 0.01$).
Conclusion: In summary, people with generalized epilepsy scored lower in several cognitive domains than controls. MoCA can be used for early assessment of cognitive status in people with epilepsy and may ultimately lead to a breakthrough in treatment.

1439 | Effectiveness of the portable EEG monitoring device (Enobio 2.0) for the emergent management of epileptic seizures

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Purpose: To evaluate whether the use of the Enobio 2.0™ wireless EEG device (Neuroelectrics®) can accelerate diagnostic and treatment workflows for managing epileptic seizures in acute setting.
Method: This is a prospective, longitudinal, single-center, observational study of patients admitted to the emergency department between July and December 2024 due to a

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suspected epileptic seizure in which EEG recording was advised. EEG data were recorded using the 20-channel ENOBIO™ device (Neuroelectrics®, Spain). We collected the time of symptom onset, hospital arrival, time at which EEG was requested and its duration, as well as whether EEG findings led to treatment modifications. Cases were compared with 2023 historical controls from our database, corresponding to the same time period during which conventional EEG monitoring had been performed.

Results: We included 11 patients (mean age: 63±20 years); 63.6% (were women and 27.3% had a previous diagnosis of epilepsy. Abnormal EEG recordings were observed in 9 patients: 5 showing epileptiform abnormalities and 8 non-epileptiform abnormalities. Treatment modifications were prompted by EEG findings in 9 patients (81.8%).

Comparing with the historical cohort, the time between EEG ordering and start of the recording was shorter (median 2 vs 8h.,p=0.004) and its duration was longer (93 vs 30 min, p<0.001). Electrode placement was faster (10 minutes) and there was a tendency for the time from seizure onset to EEG to be shorter (6 vs 11 hours, p=0.268). Lastly, the Enobio cohort showed a trend toward greater probability of treatment modification after the test (81.8% vs 47.4%, p=0.063).

Conclusion: In our sample, the Enobio 20™ wireless EEG device allowed for a faster and more prolonged EEG recording in ED. It might be considered a rapid-response EEG. Prospective validation of these findings is warranted to confirm the potential benefit of this device for the management of acute epileptic seizures.

1454 | Comparison of EEG after sleep deprivation and melatonin induction in children of different ages: a randomized controlled trial

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Purpose: Sleep EEG is an important method in epilepsy diagnosis in children since sleep facilitates epileptiform activity and can improve recording quality. Sleep deprivation is routinely used to induce sleep. Melatonin has been shown to induce sleep in children without influencing epileptic discharges. It is unknown whether efficacy differs between children in different ages. This prospective, randomized age-stratified multicenter single blind trial was performed to evaluate the occurrence of epileptiform activity and sleep-inducing effect of melatonin vs partial sleep deprivation.

Method: A total of 169 children 2-17 years old referred for sleep EEG at four centers in Sweden were stratified into 3 age-groups (2-5 years, n=60; 6-11 years, n=55; 12-17 years, n=54) and randomized to two study arms where sleep was induced either by melatonin or partial sleep deprivation. Occurrence of epileptiform activity, sleep, side effects and technical quality of the EEG recording were compared between study arms and between age-categories. Logistic regression was used to evaluate demographic and methodological factors influencing the diagnostic yield of sleep EEG.

Results: Epileptiform activity occurred in 36% of children. In 6–11-year-old children epileptiform abnormalities occurred in 49% which was significantly higher than in the other age groups independent of sleep-inducing method. Occurrence of sleep, but not sleep induction method was significantly associated to the presence of epileptiform activity (OR 9,16). Children who got melatonin prior to EEG fell asleep significantly more often (97%) compared to sleep deprived children (86%). No serious adverse effects were registered.

Conclusion: There were no differences in occurrence of epileptiform activity between melatonin and sleep deprived EEGs in children in any age group, but melatonin increased the likelihood of sleep. Melatonin is safe and show higher rate of sleep compared to sleep deprivation and is therefore to be preferred for sleep EEG in children.

1466 | Photoparoxysmal response as a predictive biomarker in epilepsy

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Purpose: Intermittent photic stimulation (IPS) is an activation procedure performed during electroencephalography

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(EEG) to detect photosensitive patients. The photoparoxysmal response is characterized by the presence on the EEG of spike or peak-wave discharges at IPS, with or without associated clinical symptoms. The photoparoxysmal response occurs in 0.6% to 30% of the EEG traces of people suffering from epilepsy.

Method: In the period 2023 - 2024 within the National Center of Epileptology, from the Republic of Moldova, approximately 1523 Standard Video EEG and Monitoring 1-2 hours were performed in children (>3 years) and adults. EEGs were performed on a Neurowerk-EEG/SIGMA system with 19 electrodes distributed according to the International "10-20" system. Filters were used as recommended International Federation of Clinical Neurophysiology 2023: time constant 0.3 sec, high frequency filter 70 Hz, speed 30mm/sec, "notch" filter on. Binocular SLI was performed at the frequencies of 1 – 2 – 8 – 10 – 15 – 18 – 20 – 25 – 40 – 50 – 60 Hz, using the Neurowerk SIGMA type F40 lamp with parameters 12V DC 0.6A positioned 30 cm directly in front of the patient. The records of 15 patients with epilepsy and photoparoxysmal response were selected, of which 12 women and 3 men, which have 34.8 ± 5.2 years old.

Results: Photoparoxysmal response showed prevalence in women (80%). 3 patients experienced seizures during SLI. Juvenile myoclonic epilepsy (JME) was the factor associated with the photoparoxysmal response in 26.5%, and 2 patients had severe hypocalcemia. The photostimulation frequencies at which the patients showed the photoparoxysmal response were between 8 and 20-25 Hz.

Conclusion: Study results confirm that responses to IPS are rare in adult epilepsy patients and especially PPR. Photosensitivity is associated with idiopathic generalized, especially those with juvenile myoclonic epilepsy. The persistence of photosensitivity can be considered a predictive marker of a more severe course or more difficult therapeutic control of the disease.

1520 | The Electrical Sei-Zaw: Unraveling the Autonomic Spectrum of Ictal Bradycardia and Tachycardia

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Purpose: Autonomic manifestations during seizures, such as ictal bradycardia and ictal tachycardia, reflect the complex relationship between epileptic brain activity and the autonomic nervous system. We present two cases emphasizing the need for a deeper understanding of autonomic changes during seizures.

Method: Patients were admitted to our epilepsy monitoring unit (EMU) for evaluation of seizures.

Results: Case 1: A 39-year-old female with intractable epilepsy presented with recurrent episodes of transient loss of awareness. Continuous video EEG (cvEEG) monitoring revealed a focal seizure originating from the right temporal lobe associated with ictal bradycardia and a focal seizure originating form the left temporal lobe associated with ictal asystole. Further cardiac evaluation ruled out structural heart disease, confirming the ictal nature of the arrhythmias ("complete heart block during seizures"). She had placement of pacemaker by cardiology. This case highlights the potentially fatal outcomes of ictal asystole and the importance of early intervention in temporal lobe epilepsy.

Case 2: A 27-year-old female with recurrent seizures underwent cvEEG monitoring due to an increase in seizure frequency. Seizures involved an aura of headache or facial numbness, followed by full-body stiffening. MRI showed asymmetric hippocampi and a small cerebellar lipoma. During cvEEG she had three stereotyped paroxysmal seizures consisting of headache, dizziness, nausea, followed by behavioral arrest. EKG demonstrated ictal tachycardia with ictal EEG changes over the left parietooccipital region with rapid propagation to the right parietooccipital then bilateral temporal regions suggested autonomic involvement, likely from a focal seizure originating in the insula. Notably, interictal EEG was normal. Further diagnostic studies are pending.

Conclusion: These cases highlight the diverse autonomic responses in focal seizures, where seizure onset location influences the nature of autonomic dysregulation. They underscore the importance of cvEEG with EKG in identifying atypical seizure semiologies and guiding management strategies to prevent adverse outcomes.

1523 | Not everything that is rhythmic is a seizure: EEG in the cognitive fluctuations of LBD

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Purpose: To evaluate the EEG findings during cognitive fluctuations (CF) in Lewy Body Dementia (LBD) and their relationships with rhythmic and periodic activities characterizing the ictal-interictal continuum patterns.

Method: A comprehensive literature review was conducted using PubMed with the MeSH terms "Dementia

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with Lewy Body" and "Electroencephalogram." From an initial pool of 184 articles, studies addressing cognitive fluctuations and EEG findings were selected. Additionally, two new case reports from our institution who were initially admitted for suspected NCSE/seizures were included.

Results: Nine studies involving 170 patients described EEG findings during CF episodes, consistently reporting general slowing of EEG background rhythm and, in one case, an EEG pattern consistent with NCSE. Three additional studies reported cases of cognitive impairment in LBD later identified as epileptic seizures, which responded to anti-seizure medications (ASMs). Four studies detailed rhythmic patterns outside CF episodes, documenting Frontal Intermittent Rhythmic Delta Activity (FIRDA) in 18 patients and Generalized Rhythmic Delta Activity (GRDA) in 14 patients. One study observed a higher prevalence of interictal epileptiform discharges in LBD patients. Personal cases: *i)* a 76-year-old woman presented with long-lasting episodes of altered mental status. Initially, a diagnosis of NCSE was considered and ASMs started. Long-term video-EEG monitoring of the episodes fulfilled EEG criteria for ictal-interictal continuum / possible NCSE according to ACNS terminology; *ii)* an 82-year-old woman with episodes of confusion underwent prolonged EEG monitoring showing bilateral fronto-temporal slow-wave activity. Neither case showed a clinical or EEG response to an ASM trial. Both patients were later diagnosed with LBD

Conclusion: EEG background rhythms during CF in LBD show consistent alterations with rhythmic theta/delta pattern as common finding. However, few studies evaluated patients' CF with long-term video-EEG monitoring. The presented patients show how EEG findings alone can be in certain cases misleading, prompting an erroneous diagnosis of NCSE.

1528 | Exploring mechanisms of self-control in epilepsy – modulation of epileptic spikes by emotion and relaxation

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Purpose: To explore potential mechanisms of behavioral interventions for epilepsy. Behavioral interventions have shown promise in improving seizure control for epilepsy patients. Frontotemporal cortex is a frequent focus of epileptic seizures and serves in emotion processing and decision making. A potential role of emotional stress as seizure trigger has often been proposed.

Method: The potential of emotions to function as seizure triggers, and the effect of relaxation on epileptic spikes were explored in 14 patients with focal epilepsy. 32 EEG recordings were obtained under conditions of evoked fear, anger or neutral emotion. Each emotional condition was followed by relaxation and a washout of 5 minutes. Epileptic spikes were manually counted under blinded conditions. Subjective reports of stress and drowsiness, and physiologic measurements of continuous blood pressure, ECG heart rate, respiration rate, temporal EEG theta power and facial EMG were obtained to assess physiologic changes during emotional stress and relaxation states.

Results: Epileptic spikes increased during the fear condition as compared to neutral emotion ($p = 0.006$). Epileptic spikes also tended to increase during relaxation ($p = 0.054$), probably as result of increased drowsiness compared to baseline ($p = 0.009$). Decreases in facial EMG, blood pressure z-scores, and respiration rate all confirmed an effective relaxation. Physiologic changes during the fear condition included a drop in blood pressure z-score, a marginal increase in heart rate and a marginal decrease in temporal EEG theta power z-score.

Conclusion: These preliminary findings suggest that stressful emotions such as fear can modulate epileptic spikes, which may support stressful emotions as triggers for seizures. The slight increase of epileptic spikes during relaxation agrees with the known increase of spikes at sleep onset. Any beneficial effects of meditative relaxation on seizures may be similar to effects of sufficient sleep: both temporarily increase epileptic spikes and could decrease seizures in the long term.

1541 | Evaluating the Utility of Routine Outpatient Electroencephalography: Insights from 18 months

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Purpose: Routine outpatient electroencephalography (EEG) is widely used to diagnose and monitor epilepsy. However, its utility in clinical practice is not consensual, as epilepsy remains a predominantly clinical diagnosis. This study aims to analyze the reasons behind routine EEG requests and to evaluate how the EEG findings influenced clinical decision-making.

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Method: This observational, retrospective, and consecutive study reviewed clinical records and outpatient routine EEG performed between July 2022 and December of 2023 (18 months). An EEG was considered "useful" if in the subsequent appointment a decision was made in line with the EEG findings.

Results: A total of 776 outpatient EEGs were done; 163 were excluded because of insufficient written clinical information on follow-up. A total of 613 EEGs were analyzed; 305 were requested for the differential diagnosis of epilepsy, 287 for follow-up/monitoring of epilepsy, and 21 for other reasons (mainly dementia work-up). Epileptiform activity (EA) was present in 27.7% of the requests for "first epileptic seizure", in 8.5% of non-specific loss of consciousness, and in 5% of focal positive symptoms. EEGs were useful to clinical management in 337 cases (55.0%). When considering the original request, EEGs were useful in 67.9% of diagnostic requests, in 76.6% of the requests related to anti-seizure medication (ASM) reduction, and in 47.5% of requests prompted by an increased frequency of seizures. In follow-up requests without further information, EEGs were considered relevant in only 22.7%. During subsequent appointments 38 patients were diagnosed with epilepsy, of whom only 16 had EEGs with EA.

Conclusion: Routine outpatient EEGs were most effective when ordered to exclude the diagnosis of epilepsy and to assess ASM reduction. Their utility was less pronounced in control/follow-up evaluations and in decision-making for epilepsy patients with seizure aggravation. Clinical history still remains the most important aspect of epilepsy diagnosis and follow-up.

1685 | "Diagnostic Yield of Electroencephalogram in Adults with Epilepsy": A prospective study from South India

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Purpose: To prospectively estimate the diagnostic yield of electroencephalogram in adult patients with epilepsy

Method: Adult patients with a clinical diagnosis of epilepsy were enrolled in this study. Their clinical, radiological, and details of electroencephalography were abstracted. Appropriate statistical methods were applied. EEGs were classified as per the Mayo system of classification

Results: Out of 385 patients, 254(66%) were males. The mean age at presentation was 42.61 ±15.86 years. Focal seizure (n=214, 55.58%) was the most common clinical type of seizure, followed by Focal with Generalized Tonic-Clonic Seizures (22.34 %, n=86) and GTCS (17.93 %, n=69). EEG was found to be abnormal in 304 patients (79 %). 137 patients (35.6 %) were classified as having definite spike-wave discharges (SWD). Among patients with Focal epilepsy (N=300), 32.66 % of patients had SWD. Among patients with Generalized epilepsy (N =77), 50.64 % of patients had SWD, and none in the unclassified epilepsy group. Among 137 (35.56%) patients who showed epileptiform discharges in the awake state, all the patients showed continued activation in sleep. In patients with normal awake EEG, sleep activation of epileptiform discharges was seen in 18.7 % (N=72) of patients. Positive photo paroxysmal response (Grade 3) was seen in 7.5 % (n=29) of the patients. Hyperventilation-activated epileptiform discharges in 1.29 % of patients. Sensitivity was 54.3%.

Conclusion: Epilepsy is a clinical-based diagnosis. The EEG is a key supportive investigation with a reasonable specificity and variable sensitivity. Our study adds information to the evidence that the sensitivity of EEG is variable, and the inclusion of natural sleep-in routine EEG studies can increase the yield of EEG in adult patients with epilepsy.

1706 | Region-specific postictal spreading depolarization observed in LFP microwire recordings from depth-electrode-implanted epilepsy patients

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Purpose: Epilepsy patients face up to three times the risk of premature death compared to the general population, with a particularly vulnerable postictal period—lasting minutes to hours— marked by an increased risk of injury and fatality. Despite its clinical relevance, its underlying mechanisms are still poorly understood. Here, we provide evidence of localized seizure-associated spreading depolarization (sSD) electrographic components recorded from temporomesial structures using implanted Behnke-Fried microwire electrodes. Our results suggest temporomesial sSD as a candidate mechanism driving postictal symptoms.

Method: Data from 16 seizures in four patients with intractable mesiotemporal lobe epilepsy were recorded using bilaterally implanted Behnke-Fried depth electrodes targeting mesiotemporal and neocortical structures.

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These electrodes feature eight high-impedance platinum-iridium microwires extending a few millimeters beyond the tips, enabling simultaneous local field potential (LFP) and intracranial EEG (iEEG) recordings.

Results: We focused on sSD at the end of seizures. Here, sSD was detected in 20% of recorded seizures, affecting 1/5 of all seizure-invaded implanted regions, half of which were hippocampal. Notably, all sSD events were confined to temporomesial structures. These events appeared exclusively in LFP traces recorded from microwires, and were absent in iEEG data from macro-contacts. Frequency analysis revealed a significant reduction in postictal high-gamma band power (80–100 Hz) and a prolonged high-gamma recovery time in regions where sSD was detected. Other frequency-band changes showed no differences between sSD-invaded and non-invaded regions.

Conclusion: Our findings demonstrate that sSD can be detected in epilepsy patients through depth-electrode recordings. We also show that SDs are detectable at the more localized LFP level but not in iEEG traces. We suggest that temporomesial sSD is a distinct pathoclinical entity and a possible postictal biomarker, highlighting the need to reconsider the current clinical EEG standard that includes a 0.5 Hz high-pass signal filter.

1733 | The Contribution of Functional Connectivity and Graph Theory to Anatomo-Electro-Clinical correlation during Pre-Surgical Evaluation

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Purpose: The epileptogenic zone (EZ) is characterized by the onset of low-voltage fast activity, which may be missed in scalp EEG recordings, particularly when the EZ is deeply localized. Scalp EEG typically shows slower, delayed rhythmic activity, reflecting discharge propagation [1]. Investigating functional connectivity prior to the first clinical or EEG changes could help identify the epileptogenic network, aiding in its lateralization and localization [2][3].

Method: We retrospectively analyzed 40- and 64-channel EEG recordings from 10 patients with drug-resistant epilepsy undergoing pre-surgical evaluation, surgery, or Stereo-EEG implantation for EZ definition. Scalp EEG signals were reconstructed in 68 cortical regions (ROIs). We calculated functional connectivity using Granger Causality (GC) in the time-frequency domain and assessed Hubness during the 10 seconds before the first EEG change and the 5 seconds after.

Results: The cohort included 10 patients (6 females, mean age 37, range 20-45) with a mean disease duration of 17 years (range 4-39). Seven had structural epilepsy. EZ localization was confirmed in the temporal lobe (7 patients, 4 right), frontal lobe (2 patients, 1 right), and right temporo-parietal lobe (1). Seven patients underwent surgery, with six achieving favorable outcomes (Engel Ia in 4, Ib in 1, Id in 1) and one having poor outcomes (Engel IIIa). Functional connectivity analysis was performed on 5 patients. In three with good outcomes, Hubness analysis confirmed accurate EZ lateralization and localization. One case was compromised by movement artifacts. Regarding patient with poor outcome, the method revealed a broader epileptic network than the clinically suspected EZ, offering valuable insights beyond traditional electroclinical analysis

Conclusion: Integrating functional connectivity and graph theory with anatomo-electro-clinical correlation enhances the lateralization and localization of the EZ in non-invasive pre-surgical evaluations.

1752 | Pathological finding of EEG in patients with migraine

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Purpose: Electroencephalography (EEG) is an electrophysiological method for assessing the degree of brain function disorders and is important in the diagnosis of epilepsy, migraine encephalopathy, encephalitis, sleep

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disorders, as well as in determining brain death. Migraine is a type of primary headache, a hereditary disease with unilateral localization of pain, usually pulsating, which worsens during physical activity. It is accompanied by nausea, vomiting, photophobia, phonophobia), osmophobia. EEG is the method of choice for assessing the degree of brain function disorders. Pathological findings of EEG have been described in patients with migraine.

Method: A group of 35 patients with migraine was included, while the control group consisted of 96 patients with headache due to sinusitis, febrility, transient hypertension. The patients of both groups had a normal MRI of the brain with MRA. None of the patients of both groups had febrile convulsions in childhood. The pathological finding of the EEG was considered to be the finding of slow alpha activity, the appearance of sharp waves, theta activity, generalized or focal on the side of the hemicrania. The recording was done 48 hours after a headache attack.

Results: In the experimental group, 23 patients (65.7%) had pathological finding, in control group 26 (27.08%). There is a statistically significant number of pathological EEG findings in the group with migraine ($p<0.01$).

Conclusion: EEG is a cheap and non-invasive ectrophysiological diagnostic procedure that is an important diagnostic procedure in the assessment of patients with migraine.

1759 | Music Modulatory Effects on Intracerebral EEG

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Purpose: The objective of our study was to validate the effect of various types of music on epileptic patients by utilizing intracerebral electroencephalography recordings, and to investigate the hypothesis that the act of listening to music with diverse acoustic properties would modulate interictal discharges (IEDs) and high frequency oscillations (HFOs) differently in the epileptic and non-epileptic hippocampus.

Method: A total of thirteen patients who were candidates for epilepsy surgery underwent implantation of depth electrodes, targeting hippocampus. The patients listened to four different types of music: James Horner – 'Bicentennial Man'; Philip Glass – 'Metamorphosis Three'; Camille Saint-Saëns – 'Danse Bacchanale'; Wolfgang Amadeus Mozart – 'Piano Concerto 27' K 595. These compositions were selected based on their different musical features in terms of rhythm, melody, and harmony. Subsequently, we analyzed the effect of listening to music on the IEDs and HFOs occurrence and characteristics in both types of hippocampi, comparing the results statistically. For HFOs detection, we used CS detector, and a Janca detector to detect IEDs.

Results: Intracerebral electroencephalography recordings revealed a significant reduction of normalized HFOs rates in the ripple frequency ranges when subjects listened to any type of music, regardless of the presence of an epileptogenic zone, with a more pronounced reduction in the pathological hippocampus. No significant changes occurred in the fast ripple range. Regarding interictal epileptiform discharges (IEDs), an influential effect was noted specifically while listening to Mozart's music only, showing significant IEDs reduction within the non-epileptic hippocampus and a noticeable trend in the epileptogenic hippocampus.

Conclusion: Our results indicate that music listening selectively impacts interictal electroencephalographic markers by reducing ripples without affecting fast ripples. This was consistent across both epileptogenic and non-epileptogenic hippocampi, regardless of the music type. Interestingly, only Mozart's music had an effect on interictal discharges reduction.

1823 | Neural correlate of the sense of agency in voluntary movement in patients with non-epileptic motor functional paroxysmal events

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Purpose: There are very few studies on neurocognitive alterations and their neurophysiological correlates in Paroxysmal Non-Epileptic Disorder (PNES)
To compare the neural correlate of the sense of agency in its predictive and postdictive signal assessed with a high temporal uncertainty paradigm evaluated with event-related potential (ERP) between patients with Paroxysmal Non-Epileptic Disorder and healthy control subjects.
Method: Case-Control. Cross-sectional study. We included 15 Mexican women aged 18-45 years with a diagnosis of motor Paroxysmal Non-Epileptic Disorders (PNEs) confirmed by video-electroencephalogram (video-EEG) and 15 healthy women aged 18-45 years. Their sociodemographic and clinical variables will be collected. An event-related potential (ERP) analysis was performed in which the neural correlate of the sense of agency (SoA) was explored as part of the voluntary movement process through the recording of ERPs in EEG, implementing a sensorimotor paradigm of high temporal uncertainty that evaluates the phenomenon of intentional binding as an implicit measure of the sense of agency.
Results: We found that there are significant differences between patients with PNES in the signal amplitude in the blocks of high temporal uncertainty in the ERP compared to control subjects.
Conclusion: The differences in the amplitude of potentials observed between neuronal activity in the right inferior parietal lobe and the right superior temporal gyrus in patients with PNES may be related to impairments in the processing of predictive and postdictive signals involved in movement agency.

1828 | An electric source imaging approach demonstrating diagnostic value of nasopharyngeal electrodes in temporal lobe epilepsy

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Purpose: To investigate the different regions covered by nasopharyngeal (NPEs) and anterior temporal (ATEs) electrodes in assessing temporal lobe epilepsy (TLE), to overcome the limitations of the 10-20 electroencephalography (EEG) in diagnosing the basal and mesial temporal regions.
Method: EEG data from 229 patients diagnosed with TLE were simultaneously analyzed with attached NPEs and ATEs. In case of discrepancies in EEG interpretation, a consensus interpretation was reached among three epilepsy experts. Spike detection was conducted using the Curry9® program for secondary analysis of electric source localization, with source location performed using standard brain magnetic resonance imaging data.
Results: In total, 2,721 interictal epileptiform discharges (IEDs) from 175 patients were analyzed. Of these, 734 IEDs from 48 patients were detected exclusively with NPEs, while 1,987 IEDs from 127 patients were detected simultaneously by both NPEs and scalp EEG, respectively. The former IEDs exhibited clustering dipoles in the basal and mesial temporal regions, while the latter were localized solely to the frontotemporal and lateral temporal regions.
Conclusion: NPEs can identify IEDs in the mesial and basal temporal region that cannot be detected by ATEs. NPEs offer additional diagnostic value in regions not confirmed by the existing 10-20 EEG electrode system, including those covered by ATE.

Comorbidities

414 | Predictive factors for developing epilepsy after autoimmune encephalitis in Neurological Institute of Thailand

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Purpose: Autoimmune encephalitis (AE) is a groups of conditions that occur when the immune system mistakenly attacks brain cells, causing swelling and a variety of symptom, including seizure. Post-autoimmune encephalitis epilepsy (PAEE) is defined as having at least one unprovoked seizure that occurs at least six months after the resolution of AE and within one year of the onset of AE. Nevertheless, the risk factor of develop PAEE remain unclear. This study aim to identify risk factors associated with development of PAEE and associated outcome at 6 month follow up.
Method: A retrospective cohort study of adult patients diagnosed with AIE between 1st May 2018 and 31st May 2024 at The Neurological Institute of Thailand. Baseline characteristic, laboratory results, treatment regimens and outcomes were collected. We divided the patient to PAEE group and non-PAEE group. Comparison between groups using the Chi-square test and Fisher's exact test. Data analysis using SPSS for window, version 17.0

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Results: Of 65 AE patients, 8 develops PAEE with median age of 34.5 year[IQR,29.25-54.5], the early seizure present was 100% (8 of 8) and 75% (6 of 8) were treated with IVMP + second line therapy compare to 26 year [20-59], 61.4% (35 of 57), 12.3 % (7 of 57) in non PAEE group respectively. The treatment with IVMP alone increased risk of PAEE (OR 19.047, [2.35-154.56], p=0.006). The poor prognosis outcome associated with nosocomial infection and absence of maintenance immunotherapy.
Conclusion: The treatment with IVMP without second line drug is the predictive factor of development of PAEE in Thai population. A present of nosocomial infection and absence of maintenance immunotherapy associated with poor prognosis at follow up period.

420 | Cognitive impairment in children with epilepsy due to focal cortical dysplasia

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Purpose: To establish the frequency and predictors of cognitive impairment in children with epilepsy due to focal cortical dysplasia (FCD).
Method: 56 children with FCD were analyzed: 27(48.2%) males and 29(51.8%) females. FCD was limited to one lobe in 46(82.1%) cases, to several lobes - in 10(17.9%). In 34(60.7%) cases FCD was localized on the left, in 17(30.4%) – on the right, in 5(8.9%) – in both hemispheres. Epilepsy was diagnosed in 53(94.6%) children. The average age of seizure onset was 2[IQR: 0.5; 4.0] years, the duration of epilepsy – 9.0[IQR: 7.0; 11.0] years. In 36 (64.3%) cases epilepsy was drug-resistant.
Results: Cognitive impairment was identified in 22(39.3%) cases: mild – in 11(19.6%), moderate – in 6(10.7%) and severe – in 5(8.9%). Developmental encephalopathy was diagnosed in 3(5.3%) children, developmental and epileptic encephalopathy – in 5(8.9%) and epileptic encephalopathy – in 14(25.0%). Cognitive impairment was more common in patients with earlier seizure onset (p=0.042), with a history of infantile spasm syndrome (p=0.004, OR=15.4 (95% CI: 1.74; 136.6), with drug-resistant epilepsy (p=0.006, OR=8.38 (95% CI: 1.67; 42.1), and with concomitant motor disability (p=0.020, OR=1.22 (95% CI: 1.00; 1.49). No dependence was established on the duration of epilepsy (p=0.451), the maximum duration of remission (p=0.437), the seizures frequency (p=0.507), the localization in the frontal (p=1.00) and temporal lobe (p=0.401), right (p=0.771) and left (p=0.411) hemisphere, the presence of tonic-clonic seizures (p=1.00), the history of epileptic status (p=0.235), the presence of regional (p=0.573) and diffuse (p=0.133) epileptiform activity.
Conclusion: Every third child with epilepsy due to FCD has cognitive impairment, which is more common in patients with early seizures onset, a history of infantile spasms syndrome, drug-resistant epilepsy and concomitant motor disability.

489 | ISEM: Impact of Sleep referrals in Epilepsy Management

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Purpose: Sleep disturbances, including insomnia, obstructive sleep apnea (OSA), and excessive daytime sleepiness, are prevalent among individuals with epilepsy. These disturbances, influenced by nocturnal seizures, psychosocial stress, and anti-epileptic drug side effects, exacerbate seizure frequency and disease progression. This study aimed to evaluate the prevalence of sleep disorders in epilepsy patients, assess their impact on disease outcomes, and identify opportunities for integrating sleep management into epilepsy care to reduce seizure frequency and improve quality of life.
Method: A systematic review of 107 epilepsy patients was conducted between January and June 2024. Sleep disorders were screened during routine epilepsy clinic visits. Patients with suspected sleep issues were referred to specialized sleep clinics. Data collected included the prevalence of OSA, restless legs syndrome (RLS), nocturnal epilepsy, and referral outcomes. Diagnostic bottlenecks, patient adherence to appointments, and service efficiency were analyzed. Statistical measures, including prevalence rates and referral outcomes, were assessed.
Results: OSA was identified in 50% of patients, RLS in 7%, and nocturnal epilepsy in 3%. Approximately 13% were discharged due to non-attendance, while 10% awaited polysomnography (PSG) and another 10% awaited specialist appointments. Of the cohort, 28% required specialized interventions. Routine sleep disorder screening highlighted a high prevalence of comorbid conditions, emphasizing the necessity of integrated care. The data suggested improved patient outcomes through timely intervention, reduced seizure frequency, and enhanced overall well-being.
Conclusion: This study underscores the critical interplay between sleep and epilepsy. Routine screening for sleep disorders, efficient diagnostic pathways, and patient-centered care strategies are essential for optimal epilepsy management. Addressing sleep disturbances can reduce

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seizure frequency, enhance quality of life, and potentially lower the risk of sudden unexpected death in epilepsy (SUDEP). Establishing integrated sleep clinics within epilepsy services is recommended to streamline care and improve outcomes.

514 | Eslicarbazepine Acetate Ameliorates Hyperactivity and Cognitive Deficits in a Murine Model of Focal Stroke

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Purpose: The incidence of developing epilepsy after stroke is approximately 2-20%, with data varying substantially, depending on the study. Stroke also frequently causes cognitive impairment, observed in up to 70% of acute stroke patients. Here, we hypothesized that focal stroke leads to neuronal hyperexcitability at sites distant from the primary lesion, leading to impaired cognition. We further tested if the anticonvulsant drug eslicarbazepine acetate (ESL) could be useful to curb hyperexcitability and improve cognition.
Method: We induced a very restricted infarct (0.1 mm^3) in the somatosensory cortex using a photothrombotic stroke mouse model. Overall, 140 mice in 5 experimental groups were treated with ESL or vehicle over the course of 5 weeks.
Results: Behavioral assessment revealed a stroke-induced significant reduction of long-term, but not short-term habituation to an open field arena. Moreover, we found a significant impairment of object but not spatial working memory. Importantly, behavioral impairments were completely abolished by ESL treatment. We mapped the activity-dependent immediate early gene c-fos to excitability in areas remote from the stroke site. The number of c-Fos positive neurons was higher in somatosensory cortex contralateral to the infarct site, in medial prefrontal cortex, and the hippocampal CA1 subfield following stroke, suggesting elevated neuronal activity in those regions. Importantly, the numbers of c-Fos-positive neurons was completely normalized by ESL treatment.
Conclusion: We found long-lasting cognitive impairment and hyperexcitability in brain regions remote to the infarct location. We further show that ESL was able to prevent those cognitive conspicuities as well as the increased neuronal activity in cognition-related brain regions. This study provides support for the notion that focal stroke leads to changes in the functional properties of connected regions, a phenomenon termed diaschisis proposed by Monakow in 1914. It further suggests that anticonvulsant drugs may be used to alleviate diaschisis and improve cognition.

544 | A Targeted Literature Review of Comorbidity Burden in Focal Onset Seizures

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Purpose: Epilepsy is associated with high risk of morbidity and mortality; individuals experience high hospitalization rates and reduced quality of life (QoL). A targeted literature review was conducted to understand the comorbidity burden in adults with focal onset seizures (FOS).
Method: Medline and EMBASE were searched (2013 to 2023) for publications focusing on comorbidities in adults with FOS along with a supplementary manual search. A dual-review process assessed citations for quality.
Results: Out of the 13 studies identified, most were retrospective (n=5) or cross-sectional (n=4), with a few prospective (n=2), case-control (n=1), and systematic review (n=1) studies. Studies investigated the impact of comorbidities on seizure frequency (n=5), economic burden (n=4), QoL (n=3), and adherence (n=1), revealing that comorbidities in FOS are linked with increased burden and costs for patients with comorbidities compared to those without. Patients with FOS and depression and/or insomnia also experienced worse QoL, but findings varied on the impact of comorbid anxiety (n=4). Ten of 13 studies reported mental health comorbidities, showing varied effects on seizure outcomes. Depression (n=7), anxiety (n=3), mental health or psychiatric comorbidity/condition (n=3), and suicidality (n=1) were the most commonly reported mental health conditions. Three studies reported that patients with mental health comorbidities, particularly depression, had worse seizure outcomes compared to those without depression. One study reported that depression scored significantly worse on measures of seizure severity, and another reported that the odds of failing to achieve 1-year seizure freedom were significantly higher in patients with depression. One study reported that any mental health comorbidity was associated with significantly increased seizure-related healthcare use.
Conclusion: This review demonstrates that mental health comorbidities in patients with FOS amplify clinical, economic, and humanistic burdens, especially in those with depression. Understanding the association between mental health comorbidities may enable personalized treatment and help in improving patient outcomes.

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557 | Hippocampal calponin-3 is Involved in the comorbidity of AD and epilepsy

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Purpose: Seizure-like activity may begin at the prodromal stage of Alzheimer's disease (AD) and exacerbate disease progression. Calponin-3, encoded by the *CNN3* gene and a regulator of excitatory synapses, is abnormally elevated in serum and brain tissue in epileptic patients and animals. This study aimed to explore the effect of calponin-3 on cognitive function and brain pathology in an APP/PS1 mouse model of AD.

Method: We used stereotaxic adeno-associated virus (AAV) injection to interfere with the expression of calponin-3 in the hippocampus of APP/PS1 mice. Cognitive function and spontaneous seizures were assessed by electroencephalogram (EEG) and behavioral tests, including the Novel Object Recognition (NOR), Morris Water Maze (MWM), and Contextual Fear Conditioning (CFC). Western Blot (WB), Co-Immunoprecipitation (Co-IP), transcriptomic analysis, Mass Spectrometry (MS), and immunofluorescence (IF) were used to detect related pathological molecular changes. All procedures were approved by the Ethics Committee of Kunming Medical University (Approval No. kmmu2021167).

Results: Compared to age-matched wild type (WT) mice, calponin-3 was significantly elevated in APP/PS1 mice aged 4, 6 and 9 months, progressively forming aggregates that co-localized with β-amyloid (Aβ). Overexpression of calponin-3 in the hippocampus, as opposed to knockdown, resulted in cognitive impairments and an increased frequency of spontaneous seizures. In the CoIP-MS, pyruvate kinase M(PKM)was identified as a molecule interacting with calponin-3, and this interaction was confirmed by CoIP-WB. Meanwhile, PKM is a transcriptional coactivator of signal transducerand activator of transcription 1(STAT1). STAT1, as A transcriptional regulator of β-secretase (BACE1), promotes the production of Aβ.

Conclusion: Increased calponin-3 in the hippocampus of APP/PS1 mice aggravated Aβ deposition via the PKM-STAT1-BACE1 pathway, modulating changes in cognitive function and spontaneous seizures. This study provides new evidence for the involvement of calponin-3 in the comorbidity of AD and epilepsy.

660 | Elevated suicide risk in individuals with epilepsy: A systematic review and meta-analysis

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Purpose: Suicide is among the top 10 leading causes of death. Epilepsy is associated with increased diagnoses of psychiatric conditions. Approximately 5% of deaths in people with epilepsy (PwE) are caused by suicide. We aim to compare the suicide incidence in PwE vs. people without epilepsy.

Method: A systematic review was performed looking at suicide incidence among PwE compared to persons without epilepsy. The reporting guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses standards were followed in this study. The search included records until February 2024 in Ovid® MEDLINE, Embase®, and PsycINFO. Abstracts were screened in duplicate and extracted using standard proforma. Data were recorded on the incidence of suicide ideation, attempt, or completed suicide in PwE compared to persons without epilepsy. Meta-analyses were performed along with descriptive analyses.

Results: Out of a total of 7,371 records identified from the systematic search, 13 met the eligibility criteria. Meta-analysis showed a significantly higher incidence proportion of suicide ideation in PwE than those without epilepsy (risk ratio [RR]: 2.06, 95% CI 1.47- 2.89). For suicide attempt, incidence proportion (RR: 3.62, 95% CI 2.88-4.55), incidence rate (incidence rate ratio [IRR]: 4.94, 95% CI 4.44-5.50) and hazard (adjusted hazard ratio [HR]: 2.32, 95% CI 2.17-2.48) were all significantly higher in PwE vs. people without epilepsy. Lastly, incidence proportion (RR: 2.39, 95% CI 1.28-4.47), incidence rate (IRR: 2.26, 95% CI 2.13-2.40), and hazard (adjusted HR: 2.50, 95% CI 1.99-3.16) of completed suicide were all significantly higher in PwE than those without epilepsy.

Conclusion: The incidence of suicide ideation, suicide attempt, and completed suicide were significantly higher in PwE compared to people without epilepsy. Comprehensive support systems to educate, diagnose, and manage epilepsy and concurrent psychiatric conditions in PwE are highly suggested.

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824 | CYP2C19 polymorphism and prevalence of depression in persons with epilepsy on antiseizure drug levetiracetam

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Purpose: CYP2C19 polymorphism has been associated with depression and an increased suicidal intent. In persons with epilepsy (PWE), CYP2C19 along with CYP2C9 have been studied for their influence on toxicity of antiseizure drugs (ASDs). In this study, the prevalence of depression and whether it correlates with the polymorphism of CYP2C19 allele CYP2C19*2 and CYP2C19*17 was determined, in PWE on levetiracetam (LEV) based monotherapy or polytherapy.

Method: After Institute Ethics Committee approval, 60 PWE (≥18yrs, either sex), meeting the inclusion and exclusion criteria, were recruited and evaluated using the MINI, NDDIE and HAM-D, to assess, depressive symptoms, severity of depression and suicide risk. A 5ml blood sample was collected from the antecubital vein, genomic DNA isolated and gene sequencing carried out using 'Sanger Sequencing' by chain termination method. The sequencing data was analyzed using 'BioEdit-Sequence-Alignment-Editor' (version 7.2.5). All data was entered in the MS excel sheet and analysis done using 'STATA' (version 16.1).

Results: The prevalence of *CYP2C19*17* polymorphism in the study population was 3.33%, while that of *CYP2C19*2* polymorphism was 19.04%. However, no significant association was seen between seizure control and the presence of these polymorphisms Prevalence of depression, assessed with different scales ranged from 21.7-39.6 %. The CYP2C19*17 PWE were male with GTCS, childhood onset (<5 years), seizure frequency of 1-2/year and depressed. CYP2C19*2 PWE were predominantly female (75 %), onset (≥14 years), 62.5 % GTCS and 37.5 % focal seizures and higher seizure frequencies. Presence of this allele did not alter the percent depression assessed using MINI, NDDIE or HAM-D.

Conclusion: CYP2C19*2 and CYP2C19*17 polymorphisms are unlikely to affect the outcome of LEV therapy in PWE. It needs to be further validated if CYP2C19*17 is associated with higher risk of depression.

859 | Developing a transition intervention for young people with epilepsy

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Purpose: To identify key aspects of an intervention study for the optimal transition of young people with epilepsy (YPE) to adult healthcare employing Experienced Based Co-Design (EBCD).

Method: EBCD is a structured, yet flexible method of co-designing health interventions with persons affected by the intervention. As a part of this process workshops were held. Adolescents with epilepsy, caregivers, healthcare personnel and managers in healthcare settings attended. The workshops took place in two different hospitals, Queen Silvia Children's Hospital, Sahlgrenska University Hospital, Gothenburg, Sweden, and in Ryhov County Hospital, Jönköping, Sweden. The workshops were brainstorm sessions, focused on questions including: How might we improve the transition process? Which possible strategies/solutions do participants suggest? How might strategies work in reality? What outcomes could be used to assess the interventions?

Results: Thematic analysis of the workshop responses resulted in eight group of ideas for interventions:

1. Empowering YPE.
2. Re-evaluation of medical diagnoses and treatment.
3. Providing information on the transition process.
4. Providing continuous care without gaps.
5. Guiding parents on the transition process.
6. Providing holistic support.
7. Tailoring information to the individual.
8. Coordinate multiple transfers.

Conclusion: EBCD with the stakeholders involved in transition for young people with epilepsy is a feasible way of developing intervention strategies. Our work sets the scene for the development of an intervention for young

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people with epilepsy which can be tested regarding clinical and cost effectiveness.

1058 | Beyond Seizures: Mapping Cognitive Development in Genetic Absence Epilepsy

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Purpose: Absence seizures (ASs) are characterized by brief lapses of consciousness, accompanied by 2.5-4 Hz spike-wave discharges (SWDs) in the thalamocortical network in the EEG. Childhood absence epilepsy is accompanied by neuropsychological comorbidities in 60% of patients. In animal models of ASs, dysfunction of thalamic GABA transporter-1 enhances tonic inhibition, which is crucial for the development of SWDs. Moreover, in adult Genetic Absence Epilepsy Rat from Strasbourg (GAERS), we found impairments in spontaneous alternation, spatial working memory, and cross-modal recognition, as well as a preferential use for egocentric strategies in spatial memory tasks which were not dependent on anxiety-like behavior or neophobia (Neuparth-Sottomayor et al, Neurobiol Dis 2023). This study aims to examine the sensorimotor developmental trajectory and cognitive profile in a model of absence epilepsy.
Method: We investigated the behavior of GAERS and non-epileptic controls (NEC) during key developmental stages: postnatal days (P)8-10 (prior to SWDs), P18-19 (after tonic-inhibition increases), P30 (with immature SWDs), and P40 (with mature SWDs).
Results: Results showed that GAERS exhibited accelerated early development, with earlier eye-opening and better maternal bedding choice (P12, $p<0.05$) and enhanced performance in geotaxis tests (P10-11, $p<0.01$) compared to NEC rats. Spatial learning emerged faster in GAERS P19 compared to NEC, with recognition memory maturing at P21. Recognition and working memory deficits emerged at P28 ($p<0.01$), after the onset of immature SWDs. Spatial memory impairments emerged at P40 ($p<0.01$), following the onset of mature SWDs.
Conclusion: In summary, memory deficits in GAERS emerged after the onset of epileptiform activity, indicating that cognitive impairments develop following immature seizure activity. These findings underscore the need to consider early development and cognition in absence epilepsy and highlight the value of thorough behavioral assessments in animal models. Funding: 2023.01003.BD. Project:ISN Career Development Grant 2021, Open Call 2024 for Drug Discovery, ISN Career Development Grant 2021, Paneris, Gapic, AccelBio.

1088 | Epilepsy and vascular risk: evaluation of the influence of antiseizure medications on atherosclerotic disease

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Purpose: People with epilepsy (PE) have an increased vascular risk, and the use of antiseizure medications (ASM) seems to be one of the culprits. This study aimed to assess if PE being treated with ASM with different interactions with the cytochrome P450 enzyme system also had differing vascular risk profiles.
Method: Longitudinal prospective observational study with 159 participants, 33 controls and 126 PE, subdivided into 4 groups (numbered 1-4) according to their enzyme interactions (strong inducers [1], weak inducers [2], non-inducers [3], and inhibitors [4]). Clinical data was collected, as well as analytical and ultrasound studies assessing cerebral blood flow (CBF), carotid intima-media complex thickness (CA-IMT), pulsatility index (PI) and the presence of atherosclerotic carotid plaques. After one year, ultrasound evaluation was repeated.
Results: Most participants were female (56.0%), with a mean age of 45.57 years. Most patients had focal epilepsy (66.6%) of structural etiology (42.8%), and 64.0% had vascular risk factors. CBF was higher in controls than in PE, both at baseline and at one-year (675 vs 560 mL/100gr/min in group 1, $p<0,001$). PI after one year was higher in groups 1 and 2 than in controls (0.86 and 0.90 vs 0.80, $p=0.037$). At baseline, patients in group 1 had a higher prevalence of carotid plaques compared to group 3 (13 vs

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2, p=0.002). There were no statistically significant differences between the progression of the parameters (CBF, IMT, PI) between groups over a 1-year period. IMT at baseline was correlated with gender (p<0,001), vascular risk factors (p=0,033), age (p<0,001), and Hba1c (p=0,040).
Conclusion: PE had a decrease in CBF, the enzyme-inducing group had a higher prevalence of carotid plaques and a higher PI, which may reflect a higher risk of macro and microvascular disease. These data emphasize the importance of comprehensive intervention in the care of these patients, focusing on vascular risk factors.

1128 | Why does epilepsy develop after predominantly subcortical strokes?

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Purpose: Strokes are the most common cause of epilepsy in individuals over 65 years of age, typically when the stroke affects the cerebral cortex. Nevertheless, up to 30% of poststroke epilepsy cases occur in individuals with predominantly subcortical strokes. We analyzed the factors contributing to the development of epilepsy after predominantly subcortical strokes.
Method: We included patients with predominantly subcortically located ischemic strokes and categorized them based on the development of epilepsy. Using Fisher's Exact Test and Kaplan-Meier curves, we analyzed the impact of clinical and radiological parameters on the risk of developing epilepsy.
Results: Of the 381 participants included, 15 (4%) developed epilepsy. Patients with predominantly subcortical strokes and epilepsy were more likely to have additional involvement of cortical areas (50% with epilepsy vs. 18% without epilepsy, p=0.003) and had more frequently microbleeds (43% vs. 14%, p=0.005) or hemorrhagic transformations (21% vs. 5%, p=0.007). The cumulative risk of developing epilepsy after 5 years was significantly higher in those patients with at least one of these radiological findings compared to those without (11% vs. 1.5%, p<0.001).
Conclusion: The additional involvement of cortical areas, along with the presence of microbleeds, and hemorrhagic transformations increases significantly the risk of developing epilepsy after predominantly subcortical strokes. In the absence of these findings, epilepsy was rarely observed.

1252 | Comorbidities in adult patients with epilepsy: A population-based cross-sectional study

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Purpose: To assess the frequency, types and possible reasons of comorbidities in adult people with epilepsy and evaluate the differences between those with epilepsy and without epilepsy.
Method: We conducted this cross-sectional study using data from National Health and Nutrition Examination Survey (NHANES) 2013-2018. We included adult participants aged 20 and above in these cycles and excluded those with missing variables in epilepsy. During the analysis process, the data was weighted to represent all populations in the United States.
Results: We included 17038 participants in NHANES, of whom 149 [weighted proportion is 0.76% (95%CI 0.61%~0.95%)] reported with epilepsy (taking at least one antiseizure medication (ASM) for epilepsy and recurrent seizures). In participants with epilepsy, 83.26% (95%CI 71.64%-90.74%) (weighted proportion), had at least one comorbidity. The weighted proportions of comorbidities in participants with epilepsy are as follows: stroke (22.43% (95%CI 14.46%-33.08%)), sleep disorders (48.23% (95%CI 37.26%-59.38%)), asthma (21.37% (95%CI 13.65%-31.84%)), emphysema, chronic bronchitis and COPD (20.42% (95%CI 12.61%-31.34%)), heart diseases such as congestive heart failure, angina, heart attack, and coronary heart disease (18.77% (95%CI 11.21%-29.71%)), hypertension (52.65% (95%CI 41.36%-63.68%)), diabetes (18.06% (95%CI 10.85%-28.53%)), failing kidneys (8.42% (95%CI 3.77%-17.75%)), arthritis (41.24% (95%CI 30.82%-52.51%)), thyroid problems (22.49% (95%CI 13.73%-34.60%)), liver conditions (7.92% (95%CI 3.06%-19.00%)), cancer (17.24% (95%CI 10.56%-26.87%)). In participants with epilepsy, only 48.79% (95%CI 57.43%-37.78%) of them had optimal sleep duration (7 to 9 hours). Participants with epilepsy had a higher incidence of stroke (OR=6.50, P<0.001) and sleep disorders (OR=1.66, P=0.027) compared with those without epilepsy, while others had no statistical significance.
Conclusion: Comorbidities in epilepsy are not uncommon, especially neurological comorbidities such as stroke and sleep disorders. The existence of comorbidities may increase the difficulty of treatment of epilepsy. Therefore, in clinical work, while paying attention to epilepsy itself, attention should also be paid to the identification and treatment of comorbidities.

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1275 | When a seizure isn't a seizure ... Or is it a seizure?: Finding functional seizures in an epilepsy monitoring unit

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Purpose: Distinguishing functional from epileptic seizures is challenging. 20-40% of patients admitted to the epilepsy monitoring unit (EMU) are eventually diagnosed with functional seizures. Concurrent epilepsy and affective concerns (17-22% of patients with functional seizures) further complicate treatment. Psychiatric comorbidities (e.g., depression; 36-80%), childhood trauma, and sexual assault (73%) can be affiliated with functional seizures. Complications in etiology and diagnostic clarity are further compounded when up to 8% of patients with functional seizures display interictal epileptiform abnormalities. This case series juxtaposes three patients with functional seizures diagnoses. Various treatment options are examined.

Method: Three patients underwent cvEEG monitoring in the University of Kentucky EMU. Typical events were captured, and diagnoses were discussed prior to discharge.

Results: Patient 1 demonstrated typical spells without ictal EEG correlation. During a functional seizure discussion, they elucidated that the EMU admission was the anniversary of her daughter's murder. She was provided diagnostic psychoeducation and referred for outpatient CBT. Patient 2 demonstrated typical spells without ictal EEG correlation, though interictal EEG showed frequent generalized high-voltage spike-and-slow-wave discharges at 3-4 Hz. They were educated on non-epileptic abnormal EEGs. Given the absence of electroclinical correlation, no antiseizure medication (ASM) was prescribed at discharge (though lamotrigine was initiated to assist with affective concerns), and she continued working with established psychotherapy. Patient 3 has previously demonstrated functional seizures across multiple admissions but presented with a novel semiology. EEG showed independent bilateral temporal sharps and a left temporal focal seizure. She was optimized on ASMs in conjunction with referral for outpatient psychotherapy.

Conclusion: Patient education including diagnostics, treatment options, and prognosis is of paramount importance. Current modalities include myriad psychotherapeutic options and psychiatric management. Despite current treatment options, only 20% of functional seizure remission is reportedly achieved, and mortality rate is 2.5x higher in patients with functional diagnoses.

1285 | Neurodegeneration in Epilepsy: Pilot Study of Risk Biomarkers for Cognitive Decline in Cerebrospinal Fluid of Patients with Temporal Lobe Epilepsy

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Purpose: The relationship between temporal lobe epilepsy (TLE) and biomarkers of neurodegeneration remains controversial. Our aim was to establish distinctive features between patients with and without cognitive impairment (CI).

Method: A cross-sectional study was conducted, including patients with non-lesional TLE (both sexes, aged 40–70 years). Correlations between cerebrospinal fluid (CSF) biomarkers (t-tau, p-tau, beta-amyloid) and neuropsychological and clinical variables were analyzed (Spearman), along with mean comparisons between groups with and without CI (Mann-Whitney U test). The study was approved by the Ethics Committee of the University of Navarra.

Results: N=14 patients with TLE (57% male), 56 ± 3 years of age, disease duration 17.7 ± 4.6 years (64% indeterminate etiology, 43% drug-resistant). 71% (10/14) reported cognitive complaints; (6/10) had CI (p=0.56). Fifty percent (7/14) met CI criteria; 3/7 showed beta-amyloid abnormalities. Correlation was found between beta-amyloid and semantic fluency (0.679; p=0.08), phonological fluency (0.704; p=0.005), naming (0.069; p=0.009), delayed verbal memory (0.657; p=0.011); between t-tau and interference resistance (0.651; p=0.044), delayed verbal memory (0.599; p=0.024), graphomotor speed (-900; p=0.037); and between p-tau and interference resistance (0.678; p=0.008), constructive praxis (0.590; p=0.026), visual memory (0.541; p=0.046), and delayed verbal memory (0.663; p=0.010). Analysis of differences between groups (CI vs. non-CI) showed differences in verbal memory (Z=3.000; p=0.006), visual memory (Z=30.000; p=0.004), semantic fluency (Z=31.500; p=0.007), processing speed (Z=37.000; p=0.047), cognitive flexibility (Z=34.000; p=0.018), and interference resistance (Z=31.000; p=0.006), t-tau (Z=7.000; p=0.048), p-tau (Z=7.000; p=0.025), and beta-amyloid (Z=36.000; p=0.035).

Conclusion: Multidomain CI is frequent in patients with TLE. Cognitive complaints may represent a risk factor. Consistent with previous observations, CI in this population may be associated with amyloidopathy. Longitudinal studies with larger sample sizes are required to clarify its value as a risk biomarker.

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1368 | Theta slowing accompanies the onset of the epileptic and cognitive phenotype in Dravet Syndrome

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Purpose: The causes of cognitive impairment in developmental epileptic encephalopathies are still debated. In a previous study (Salgueiro-Pereira et al 2019) we have demonstrated that the interaction between $Na_V1.1$ mutation and seizures is necessary to induce the typical behavioral alterations in Dravet Syndrome. In this study we leveraged the properties of the *Scn1a*$^{R1648H/+}$ mouse model to investigate possible neural bases underlying this phenotypic switch.
Method: Mice carrying the *Scn1a*$^{R1648H/+}$ mutation display spontaneous phenotypic variability that can be controlled experimentally by the induction of short thermic seizures. These engender a complete epileptic and cognitive phenotype also in mutant mice who were previously indistinguishable from WT littermates. We performed *in vivo* LFP recordings in behaving *Scn1a*$^{R1648H/}$ mice during novelty detection before and after the induction of thermic seizures in parallel with chronic video/LFP recordings to detect spontaneous seizures.
Results: We demonstrated that the onset of the Dravet Syndrome phenotype is accompanied by a reduction of the frequency of the hippocampal theta oscillation that is probably due to an impaired modulation of the theta from external stimuli.
Conclusion: We argue that this can be a fundamental mechanism underlying the cognitive impairment observed in Dravet Syndrome.

1381 | Visual aura and driving

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Purpose: The aim of this study was to determine the prevalence of severe visual disturbances in patients with migraine with visual aura (PWMVA) during a migraine attack. A secondary aim was to document the current approach of the professional community to PWMVA in terms of assessing their ability to drive and compare it with approach to PWE (patient with epilepsy).
Method: PWMVA (n = 56) were enrolled from 2 centers. Semi structured telephone interview was used to assess the severity of visual impairment during visual aura, the type of symptoms and speed of the development of the visual aura, the type and prevalence of the prodromal symptoms and other clinical aspects, which are relevant to the quality of life and to the safe driving in PWMVA. 35 Czech neurologists responded to a questionnaire sent by e-mail (questions regarding the length of neurology practice, average number of treated PWE monthly, average number of treated patients with migraine monthly). It also included questions about restrictions regarding driving, which were used in PWE or in PWMVA.
Results: In twenty, i.e. 35.76% of patients, we found out the combination of the severe visual impairment with rapid (2 minutes or less) onset of visual deficit during visual aura . Frequency of migraine attacks with aura/month in these patients was: (median and IQR): 3, (1-5). None of the 35 neurologists have ever restricted a patient with migraine from driving. All of the neurologists surveyed have at some point restricted driving in PWE.
Conclusion: A significant proportion of PWMVA is disabled by rapid onset of severe visual deficits during aura. This fact is not adequately taken into an account in medical practice, unlike with PWE. This should be discussed within the medical community to improve the assessment of driving ability in PWMVA.

1441 | Prevalence and possible associations of brain-gut axis disorders in children aged 4 to 18 years with epilepsy

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Purpose: The prevalence of epilepsy in Colombia is 1.3%, and worldwide, disorders of gut-brain interaction (DGBI) have a prevalence of 23.0%. The aim of this study was to determine the prevalence of DGBI and its possible associations in children with epilepsy.
Method: A prospective, descriptive, observational study was conducted in children aged 4 to 18 years attending the Pediatric Neurology Outpatient Clinic at the "Evaristo García" University Hospital in Cali, Colombia. The validated Spanish version of the Pediatric Rome IV Questionnaire for Gastrointestinal Symptoms (QPGS-IV) was used to identify

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the presence of DGBI. Sociodemographic, clinical, and dietary variables were included.

Results: A total of 161 children were included (mean age 11.3+/-4.1 years); 55.3% were male and 5.6% were immigrants. Focal epilepsy was more common (66.9%), focal motor seizures predominated (54.3%), and 26.1% had intractable epilepsy. Valproic acid was the most used medication (41%), 1.9% underwent epilepsy surgery, and 1.9% were on a ketogenic diet. 33.8% had malnutrition as a comorbidity. The prevalence of DGBI was 36%, with functional postprandial dyspepsia (16.8%, n=27) and functional constipation (13%, n=21) being the most common diagnoses. 10.6% (n=17) had more than one DGBI, with the most common overlap being functional postprandial dyspepsia + functional constipation. Children with epilepsy attending private schools (40.5% vs. 59.5%, p=0.008) had more DGBI than those attending public schools. The risk of functional dyspepsia was higher in children with epilepsy and cerebral palsy GMFSCIII (7.4% vs. 92.6%, p=0.038). Children with a history of epilepsy surgery had a higher risk of functional constipation (25.2% vs. 74.8%, p=0.005).

Conclusion: More than a third of children with epilepsy had some form of DGBI, with functional dyspepsia being the most common. The most important associated factors were private school attendance, cerebral palsy, and a history of epilepsy surgery, especially DGBI associated with abdominal pain.

1445 | Motor impairment in people with epilepsy persists regardless of seizure control

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Purpose: Although neuroimaging studies have shown cortical atrophy in the precentral gyri and alterations of corticospinal tracts in focal and generalized epilepsies, little is known about motor dysfunction in people with epilepsy (PWE). The purpose here is to investigate motor impairment in PWE and the impact of symptoms of depression and anxiety in this context.

Method: We interviewed and tested 177 people with epilepsy (PWE, median of 35 years of age and 11 years of education) at a Tertiary Centre (before their outpatient appointment) and 252 healthy volunteers (HV, median of 35 years of age and 15 years of education) at the University Campus. Subjects performed 9-hole peg test (9-HOLE), Box and Block Test (BBT), Tower of Hanoi (TH), Block design subtest of the Wechsler Adults Intelligence Scale (BD-WAIS), Generalized Anxiety Disorder Questionnaire (GAD-7) and Neurological Disorders Depression Inventory for Epilepsy (NDDI-E). PWE was separated into seizure-free (76 subjects), lower-frequency (13 subjects), pharmacoresistant (70 subjects) and unknown (17). We used SPSS23 for statistical analyses with non-parametric tests for group comparisons (Mann-Whitney and Spearman correlation). We excluded subjects with intellectual or motor impairment.

Results: Although the groups of PWE and HV were balanced for age (p=0.96), scores of anxiety (GAD-7, p=0.4) and of depression (NDDI, p=0.2), we detected poor performance of 9-HOLE (bimanual, p<0.001), BBT (bimanual, p<0.001), TH (p<0.001) and of BD-WAIS (p<0.001). The PWE performance was 15-22% worse than their age-paired controls. Seizure control was not associated with better motor performance.

Conclusion: Despite similar levels of anxiety and depression, PWE presented poor motor performance on both fine (9-HOLE) and gross tests (BBT) and worse scores for more complex tests (BD-WAIS and the Tower of Hanoi) that demand integration of different cognitive functions. Future analyses of types of epilepsies and their adverse effects are necessary to understand the dysfunction and create specific strategies for rehabilitation.

1500 | Differing Perspectives of Caregivers and Physicians in France on Key Issues in the Management of Patients With Lennox-Gastaut Syndrome: Results From the REFLET Survey

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Purpose: The REFLET survey captured parent/caregiver and physician views in France on the management of patients with Lennox-Gastaut syndrome (LGS).

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Parent/caregiver responses have previously been reported (26èmes journées Française de l'épilepsie, 2024). Here, we describe major aspects identified from each group's perspective, noting areas of alignment or misalignment.

Method: Surveys, completed February 29–May 12, 2024, were designed based on in-depth analysis of the literature and individual interviews with experts, and endorsed during group discussions. The survey complied with MR004 (CNIL declaration 2232699), and all participants gave informed consent.

Results: Overall, 53 parents/caregivers and 36 physicians responded. Both groups reported the same items of importance regarding the management of patients with LGS: seizure outcomes (duration, frequency, type), adverse events (AEs), non-seizure outcomes (sleep, behavior), and quality of life (QoL; autonomy, CG QoL). Of these items identified by both groups, ≥78% of physicians considered all were managed by them. Some items are viewed as managed by them despite physicians considering the items outside their remit (behavior: 14%; QoL: 17%). Notably, whilst parents/caregivers acknowledged seizure impact (frequency and duration of seizures: 92%) and AEs (83%) were well addressed by physicians, contrary to physician perspectives, they felt behavioral issues and QoL are not sufficiently taken into consideration by physicians (38% and 62%, respectively) to the extent they would like.

Conclusion: The REFLET survey helps us to understand perceptions of parents/caregivers on one hand and physicians on the other, regarding how physicians address key aspects of LGS management in France. Results suggest parents/caregivers perceive there are opportunities for physicians to adopt a broader multidisciplinary approach with greater focus on non-seizure outcomes and QoL, as well as seizure outcomes and AEs. Funding: Jazz Pharmaceuticals, Inc.

1518 | A Qualitative Analysis of the Perceptions of Adults with Epilepsy Engaged in an Online Modular Stigma Self-Management Program

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Purpose: Perceived stigma is a prevalent source of distress among people with epilepsy (PWE), often leading to psychosocial challenges and reduced quality of life. Nevertheless, interventions targeting stigma remain limited. Rise Above, a self-paced online program aimed at managing stigma, reduced stigma and improved psychosocial outcomes in a pilot study. The current study examines the perceptions of PWE who completed Rise Above.

Method: Participants (n=20; age M=47.30, SD=14.25, range=22-67; 30% BIPOC; 30% unemployed; 50% female) were recruited from 13 U.S. states. After completing Rise Above, they participated in individual one-hour, semi-structured interviews via Zoom. Participants were asked standardized open-ended questions about their perceptions of Rise Above's impact on their thoughts, feelings, and reactions to stigma, and relationships. They also provided recommendations for program improvement. Interviews were transcribed, double coded, and analyzed in NVivo 12 software. Extracted themes included program facilitators and barriers to psychological benefits, as well as unmet needs and content recommendations.

Results: Thematic analysis found Rise Above improved participants' self-awareness of stigma and strengthened their ability to manage stress and regulate emotions. The program's emphasis on handling interpersonal stigma helped participants progress toward self-acceptance and boosted self-efficacy, with many expecting lasting benefits. Barriers to benefit included emotional discomfort while engaging with stigma-related material, challenges understanding or relating to certain content, and a lack of resources addressing external stigma (e.g., discrimination). Participants suggested enhancing the program content by incorporating greater cultural and demographic diversity.

Conclusion: Rise Above shows potential for improving stigma-related self-awareness, stress management, and interpersonal self-efficacy in PWE. To augment its effectiveness, future versions should incorporate content that helps participants manage emotional discomfort during the learning process, includes resources for addressing external stigma, and tailors content to better reflect diverse experiences and backgrounds. These adjustments could enhance program impact and position it well for larger-scale efficacy trials.

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1524 | Science to Service: Growing Capacity and Impact via an Epilepsy Self-Management Translational Network

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Purpose: Evidence-based epilepsy self-management (ESM) has been challenging to bring to clinical centers. Without infrastructure, ESM programs will continue to be underutilized, accessibility will remain limited and the needs of people with epilepsy (PWE) will continue to be unmet. The current study shares real world outcomes in PWE who engaged in ESM via a hub and spoke model, the Hobscotch Institute Translational Network (HITN), engaging clinicians and PWE from 18 diverse US epilepsy centers.

Method: Targeted clinician education, sharing ease of access to the Hobscotch program, was delivered to all HITN epilepsy center teams. Patients were referred by HITN spoke site clinicians to the Hobscotch Institute hub, prescreened and matched to a Cognitive Coach for 1:1 telehealth delivery of the 8-week program. Pre/post surveys measuring quality of life (QOLIE-10), subjective cognition (Everyday Memory Questionnaire (EMQ)) and post-program satisfaction surveys (Likert scale) were collected; QOLIE-10 and EMQ scores were analyzed using Wilcoxon signed-rank test.

Results: Hobscotch participants (n=89) were connected to the program via clinicians engaged in HITN. Pre-intervention QOLIE-10 ($M = 3.04 \pm 0.08$) was greater than post-intervention ($M = 2.74 \pm 0.08$; $p < .001$), indicating a statistically significant improvement in quality of life. Improvement was also observed in EMQ scores post intervention (n=76; Pre $M=29.99 \pm 1.30$ vs Post $M=24.95 \pm 1.36$; $p<0.001$). Satisfaction surveys revealed 91% strongly/mostly agreed Hobscotch provided useful tools and strategies for everyday life, 96% strongly/mostly agreed they enjoyed working with a Cognitive Coach, and 89% strongly/mostly agreed they were better able to manage memory challenges.

Conclusion: We describe a translational network enhancing real-world ESM program capacity and engagement with potential to facilitate improved patient outcomes broadly. Findings suggest a hub and spoke model can support provider referral augmenting patient access to ESM. Real-world telehealth delivery of ESM through collaborative networks will aid ESM programs to reach their potential for having population health level impact.

1591 | Evaluation of depressive-like effects in an animal model of epilepsy

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Purpose: The presented study aimed to develop an animal model of comorbidity between depression and epilepsy that may be used to understand whether acute stress inducing a depressive-like phenotype may facilitate the development and the progression of mTLE.

Method: Depressive-like behavior was induced in C57BL/6 mice using two protocols. In the Learned Helplessness (LH) paradigm, animals underwent two sessions of unpredictable, unavoidable stress and were tested the next day to assess the % of resilient animals. In the chronic corticosterone protocol, animals received corticosterone in drinking water (350 mg/L) for 28 days. In this case, depressive-like behaviors were evaluated using the forced swimming test (FST) and sucrose preference test (SPT). Before electrode implantation, LH, CORT, and control animals received an intra-hippocampal injection of kainic acid (KA) or vehicle to induce status epilepticus (SE). All mice were monitored for 15 days using a video-EEG system to assess the presence spontaneous recurrent seizures (SRSs).

Results: After the LH procedure, approximately 85% of the animals exhibited depressive-like behavior. Although

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the LH+KA group developed SE later than the KA group, the percentage of LH+KA animals manifesting SRSs was higher compared to the group that had not experienced acute stress before SE. Moreover, higher mortality was observed in the LH+KA group compared to the KA group in the days following SE. On the other hand, chronic corticosterone administration appeared to induce only mild depressive-like behaviors, detectable only in the FST but not in the sucrose preference test SPT. During SE, CORT+KA animals experienced a more severe SE, with a 30% increase in mortality compared to the control group. No video-EEG recordings were obtained.

Conclusion: Overall, these data confirm that acute stress can facilitate the development and worsening of mTLE. These models system may be used for further investigation aimed at better understanding the relationship between depression and epilepsy.

1638 | Somatic comorbidity impact on effectiveness of epilepsy treatment in children

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Purpose: Presence of concomitant somatic disorders found in epilepsy debut on the stage of the first seizure can have impact on effectiveness of initial anticonvulsant therapy in children.

Method: 447 patients were examined who had epilepsy debut at the age of 0 to 18 years old. Effectiveness of initial treatment with following full clinical remission was analyzed with evaluation of presence of chronic somatic pathology in cardiovascular, visual, orthopedic and other systems excluding neurologic and psychic disorders at the stage of the first seizure.

Results: Chronic somatic comorbidity before start of treatment was found in 61.5% patients (N=275). Clinical remission at initial therapy after 6 months was reached in 38.5% cases (N=172). Among patients with somatic comorbidity remission at initial therapy was reached in 30.2% cases (N=83), ineffectiveness of treatment was registered in 69.8% (N=192). Among patients without somatic comorbidity remission at initial therapy was reached in 51.7% cases (N=89), ineffectiveness of treatment was registered in 48.3% cases (N=83).

Conclusion: It was found that in group of children without remission occurrence of somatic comorbidity was indicated 2 times more often that in the group with remission: 69.8% and 30.2% correspondently, p_{Fisher}<0,001. Presence of concomitant chronic somatic diseases raises the chance by 2.5 that the remission at initial therapy will not be reached (OR=2,480; S=0,201; 95% ДИ [1,672; 3,681]).

1746 | Somniloquy: an "underdog" from sleep with important associations in epilepsy

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Purpose: Epilepsy and sleep are known to have many interactions. Somniloquy (sleep-talking) stands out as one of the most prevalent benign sleep phenomena, however it is often left out of attention. Our aim was to study the possible associations between somniloquy and sleep and epilepsy parameters among adults with epilepsy (AWE).

Method: Participants were divided into epilepsy (EG) and healthy control group (HCG). They were also divided into: Non-Sleep-talkers (NST), Sleep-talkers (ST). We used the validated Armenian versions of Pittsburgh Sleep Quality Index (PSQI) and Epworth Sleepiness Scale (ESS) to assess sleep quality, excessive daytime sleepiness respectively. Hamilton depression and anxiety (HAMD, HAMA) scales were used. Participants underwent one-night EEG-PSG. Statistical analysis included Wilcoxon Signed Rank and Chi-squared tests.

Results: Overall, 174 AWE were included in the EG: mean age 35.2±13.5 years (18-71), females=83(47.7%). Of them 24.7% were ST. For the groups NST/ST respective values were: age-35.9/33.3years (p>0.05), BMI-23.6/25.1kg/m2 (p>0.05), number of sleep complaints-3/5.9 (p<0.05), HAMA-13.1/18.7 (p<0.05), HAMD-11.2/16.2 (p<0.05), number of antiseizure medications-0.8/1.2 (p<0.05), daily dosage (DD) of carbamazepine-556.4/726.3mg (p<0.05), valproate DD-916.7/777.9mg (p>0.05), yearly seizure frequency (SF)-30.7/49.7 (p>0.05), monthly SF-3.5/4.5 (p>0.05), total sleep time-423/456.6mins (p=0.06), sleep efficiency-83.2/90.6% (p<0.05), wake during PSG-15.6/9.3% (p<0.05), leg movement index(/h)-11.7/15.7 (p<0.05), periodic leg movements index(/h)-4.6/8.8 (p<0.05), PSQI-7.5/8.9 (p>0.05), ESS-4.6/5.3 (p>0.05). No differences were found in sleep macrostructure between the groups by PSG. Chi-square test results for somniloquy: focal vs generalized epilepsy-21.6%/35% (p>0.05), insomnia-18.3%/32.1% (p<0.05), restless legs syndrome-22.2%/33.3% (p>0.05), periodic leg movements in sleep-20.4%/34.6% (p<0.05), bruxism-17.3%/48.7% (p<0.05), late coffee consumption-9.6%/30.9% (p<0.05), smoking-19.8%/41.4%

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(p<0.05), suicidal tendency-20.9%/50% (p<0.05). None of the above sleep associations were seen in HCG (n=130).
Conclusion: Our findings elucidate interesting links somniloquy may have in AWE. It is associated with more severe epilepsy course, higher antiseizure medication consumption, lower mood, higher anxiety and sleep disturbances, like periodic leg movements in sleep and bruxism.

1784 | Online CO-OP (Cognitive orientation to daily occupational performance) approach applied with parents for improving performance in daily activities of children with Dravet Syndrome

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Purpose: Dravet syndrome (DS) is characterized by drug-resistant seizures and comorbidities that significantly impact the quality of life. Data regarding rehabilitation treatment to improve autonomies is scarce. The Cognitive orientation to daily occupational performance (CO-OP) Approach has been used directly with children across ages and diagnoses. While parent involvement is a key characteristic of CO-OP, no study to date has explored applying it directly with parents for improving their children's performance in daily activities. The objective of this study was to explore the effectiveness of implementing the CO-OP Approach in a telerehabilitation format with parents for improving the performance of daily activities of children with DS.
Method: A pre-post quasi-experimental single group design with 1-month follow-up was used with 9 parents of children with DS (aged 9-18 years) who received eight online intervention sessions. Five goals related to their children's daily activities were identified by the parents, using the Canadian Occupational Performance Measure (COPM), three of which were targeted during the intervention. Children's performance of selected daily activities was rated using the Performance Quality Rating Scale (PQRS) and parents rated their child's performance and satisfaction using the COPM. Parents' sense of competency was also explored. Nonparametric statistics with a Holm-Bonferroni correction were undertaken.
Results: Significant improvement was obtained on the PQRS for children's trained goals at post and follow-up. Untrained goals significantly improved at follow-up. For the COPM of both trained and untrained goals, parents' perceived performance and satisfaction, regarding their child's performance, improved significantly at post and follow-up. Finally, significant improvement at post-test was noted for a total score of the Parenting Sense of Competence Scale.
Conclusion: The results provide preliminary evidence for the use of CO-OP applied directly with parents online, improving children's performance on both trained and untrained goals and positive change in parent self-efficacy.

1838 | Seizure prevention in angioplasty for symptomatic extracranial carotid and vertebral artery stenosis

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Purpose: Seizure is not common during and after carotid angioplasty, the main predictors for seizure are age, degree of stenosis, preexisting cerebral ischemia in the treatment territory has been increasingly reported as a complication of carotid angioplasty and stent placement. the aim of the present study is to evaluate the efficacy of Levetiracetam in prevention of periprocedural seizure disorder.
Method: A retrospective study included files of patient undergoing stenting for carotid or vertebra-basilar arteries stenosis the over 2 years from January 2022 to January 2024. All patients received Levetiracetam 500 mg twice daily orally starting one day before and 14 days following the procedure. all patients undergone angioplasty and stenting. All patients had 3, 6, and 12 months follow-up
Results: Nineteen (19) patients were included. the mean age was 67.6 years (54-80), sex ratio male female was 2.8 (14 male, and 5 female). history of hypertension, diabetes, or dyslipemia was recorded in 89 % (17/19); combination of at least 2 risk factors was recorded in 89 %, and 54 % (10/19) of patients had combinations of the three risk

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factors. The extra-cranial stenosis was symptomatic in 16 patients (84%). it involved carotid arteries in 15 patients (79%), and vertebro-basilar system in the remaining 4 patients (21%). the mean stenosis severity was 79% (50 to 90 %); it was an ulcerated stenosis in 2 patients. All patients received Levetiracetam 500 mg twice daily orally starting one day before and 14 days following the procedure. all patients undergo angiography with stenting, and 18 (95%) of them had additional post stenting angioplasty, the mean duration of hospitalization was 8 days (1 to 28). 52% (10/19 had hospitalization duration less than 7 days. In all patients no seizures were recorded after 3, 6, and 12 months.
Conclusion: Short course of Levetiracetam prevents seizures in angioplasty and stenting.

Drug Therapy

267 | Application of Causal Inference to Identify Determinants of Seizure Reduction and Quality of Life in Patients with Lennox-Gastaut Syndrome, Dravet Syndrome, and Tuberous Sclerosis Complex Treated With Cannabidiol

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Purpose: Causal inference modelling investigates cause-effect relationships between factors within populations eg, outcomes in patients from clinical trials. This *post hoc* analysis explored the relationship between seizure reduction and Caregiver Global Impression of Change (CGIC) in the randomised controlled trials (RCTs) and open-label extension (OLE) studies investigating highly purified cannabidiol (CBD), aiming to contextualise the findings for clinical practice.
Method: Structural Causal Model (SCM) methodology was applied to data from patients with Lennox-Gastaut syndrome (LGS), Dravet syndrome (DS), or tuberous sclerosis complex (TSC) from RCTs and OLE studies investigating CBD, Epidyolex®[EU]/Epidiolex®[US]; 100 mg/mL oral solution. The primary objective was to confirm the causal-effect relationship between end-of-RCT (Weeks 14–16) seizure reduction and Week 24 (Wk24) CGIC considering baseline characteristics, CBD treatment, comorbidities, and adverse events. Mediation analysis estimated direct and indirect effects impacting CGIC. *P*-values were uncontrolled for multiplicity.
Results: Among 371 patients (138 LGS; 86 DS; 147 TSC) aged 1–57 years, a significant causal-effect relationship between seizure reduction and CGIC was confirmed in the overall population, and specifically in patients with LGS or TSC ($P<0.05$), but not DS ($P>0.05$). Direct effects (mean estimate ± standard error) of CBD treatment on reducing end-of-RCT seizure frequency (-0.13 ± 0.051, $P=0.008$) and end-of-RCT seizure frequency on Wk24 CGIC (0.21 ± 0.049, $P<0.0001$) were determined. Data confirmed an indirect effect of CBD treatment on Wk24 CGIC (-0.03 ± 0.013, $P=0.03$), and a direct effect of number of comorbidities on Wk24 CGIC (-0.11 ± 0.050, $P=0.03$) and Wk24 adverse events (0.15 ± 0.051, $P=0.0003$). Seizure reduction and CGIC scores were unaffected by baseline characteristics.
Conclusion: The findings suggested a causal-effect relationship between CBD treatment, seizure reduction, and CGIC, and indicated that seizure frequency reduction correlates with overall CGIC improvement. SCM could help define non-seizure endpoints as key outcomes in future clinical trials. Funding: Jazz Pharmaceuticals, Inc.

277 | Felbamate as a Therapeutic Alternative to Drug-Resistant Genetic Generalized Epilepsy: A Systemic Review and Meta-Analysis

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Purpose: The effect of felbamate (FBM) on genetic generalized epilepsy (GGE) remains largely unknown. The utilization of FBM has been limited due to its potential risk of aplastic anemia and hepatic failure. This study aimed to comprehensively evaluate the efficacy and safety of FBM in the treatment of drug-resistant GGE.
Method: We searched the databases, including PubMed, Web of Science, Embase, and Google Scholar, to identify cases of GGE treated with FBM. Data on outcomes and adverse events were extracted from these studies.
Results: The literature search yielded 9 studies with 166 cases in which FBM was used as an adjunct therapy to treat drug-resistant GGE. The pooled responder rate to FBM was 65% (95% confidence interval CI, 51-80). 17% (95% CI, 3-31) achieved seizure freedom. 81% (95% CI, 60-100) of patients with Epilepsy with myoclonic atonic

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seizures were responders. Adverse events occurred in 40% of patients (95% CI, 26-54). No cases of aplastic anemia or hepatic failure were observed.

Conclusion: Patients with drug-resistant GGE achieved good responses to FBM. The high heterogeneity between studies calls for further research with large-scale, randomized controlled trials. Given the rare reports of idiosyncratic reactions of aplastic anemia and hepatic failure, intense laboratory monitoring and a slower titration schedule are recommended.

283 | Long-Term Safety and Efficacy of Azetukalner, a Novel, Potent K_V7 Potassium Channel Opener in Adults With Focal Epilepsy: Update From the Ongoing 7-Year Open-Label Extension of X-TOLE

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Purpose: In the double-blind period (DBP) of X-TOLE, azetukalner (10, 20, and 25 mg once daily [QD] with food with no titration period) showed dose-dependent, statistically significant, and rapid-onset reductions in focal onset seizure (FOS) frequency. This abstract reports ≥36-month data from the X-TOLE 7-year, open label extension (OLE) study of azetukalner in participants with FOS.

Method: Participants received 20 mg QD with food at start of the OLE. Assessments were performed at week 3 and at 3-month intervals thereafter. Safety assessments included treatment-emergent adverse events (TEAEs), serious adverse events (SAEs), and significant changes in laboratory findings. Primary efficacy outcome was median percentage change (MPC) in monthly (28-day) FOS frequency from DBP baseline.

Results: 285 participants completed the DBP, and 275 (96.5%) enrolled in the OLE. At this interim analysis (datacut October 2024), 182 participants had been treated for ≥12 months and 143 for ≥36 months. 131 (47.6%) are ongoing. TEAEs were reported in 244 (88.7%) participants, and the majority were mild or moderate; 46 participants (16.7%) reported severe TEAEs. The most common TEAEs were dizziness (23.3%), headache (17.5%), coronavirus infection (17.1%), somnolence (16.0%), fall (13.5%), weight increase (10.9%), and memory impairment (10.2%). Mean (SD) weight gain was 0.75 (8.7) kg at 3.2 years in the OLE. SAEs occurred in 40 (14.5%). There was 1 case of SUDEP reported as non-treatment related. MPC was −85.3% at the 36-month time period and seizure freedom for ≥12-month, ≥24-month, and ≥36-month consecutive durations was achieved in 32.7%, 20.4%, and 10.2% of those participants with ≥36 months treatment in the OLE (n=147).

Conclusion: In the ongoing X-TOLE OLE, azetukalner was generally well tolerated with no new safety signals. These promising interim data continue to suggest long-term safety and efficacy of azetukalner in a difficult-to-treat population.

312 | Use of Fenfluramine and Cannabidiol in Daily Practice: A Retrospective Analysis of German Prescription Claims

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Purpose: To describe use of fenfluramine (FFA) versus cannabidiol (CBD) in Germany, based on age/gender distribution, prior anti-seizure medication (ASM) use, dosage, and medication persistence, in patients with Dravet (DS) and Lennox-Gastaut (LGS) syndromes.

Method: This was a retrospective analysis of German prescription claims from 2020/03-2023/10. Patient index was date of first FFA or CBD prescription. Patients with stiripentol (STP) and without felbamate (FLB) or rufinamide (RUF) at any time during study period were assigned to DS group; those with FLB or RUF and without STP were assigned to LGS group. Prior ASMs were analyzed for 9 months prior to index. Persistence was analyzed up to 36 months after index; patients lost to follow-up due to end of database records were censored. Data were extrapolated to the German statutory health-insured population.

Results: 379 FFA (26.1% DS; 10.6% LGS; 63.3% undefined) and 1,918 CBD (4.6% DS; 17.2% LGS; 78.2% undefined) patients were identified in the database (with extrapolation). At index, FFA patients had a mean±SD

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age of 15.0±12.9 years; 40.9% male, 34.3% female, 24.8% unknown. Patients with CBD had a mean±SD age of 19.4±15.7 years; 37.8% male, 34.8% female, and 27.4% unknown. 93.7% of FFA patients and 85.5% of CBD patients received prior ASM(s). Mean±SD FFA dosage/day was 18.2±35.2 mg and mean±SD CBD dosage/day was 559.8±718.2 mg. Persistence after 12, 24, and 34 months was 73.7%, 65.6%, and 61.5% for FFA, and 52.1%, 37.1% and 32% for CBD, respectively. Results by DS or LGS will be presented.

Conclusion: Despite limitations (indication assignment, dosage calculation without patient weight), this analysis suggested that FFA and CBD recommended dosages/day were not exceeded. The proportion of FFA patients with prior ASMs was numerically higher compared to CBD. The overall (not indication-specific) medication persistency was numerically higher for FFA vs CBD. UCB-supported.

383 | Loss of Function *ABCG2 c.421C>A* (rs2231142) Polymorphism Decreases Lamotrigine Trough Concentrations in Adults with Epilepsy

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Purpose: Lamotrigine is a commonly used antiepileptic drug known for a considerable inter-subject variability in systemic exposure due to variable total body clearance. It is a substrate to ATP binding cassette subfamily G member 2 (ABCG2) transporter. The objective of this study was to evaluate the effect of the common loss-of-function polymorphism *ABCG2 c.421C>A* (rs2231142) on the lamotrigine trough concentrations at steady state in adults with epilepsy.

Method: In two consecutive studies (Study 1, Study 2) in patients on lamotrigine monotherapy, carriers of the variant ABCG2 c.421C>A allele (CA/AA) were considered exposed, and wild-type homozygotes (CC) were considered controls. They were mutually balanced on covariates (age, sex, body weight, several polymorphisms in genes encoding other transporter proteins and lamotrigine-metabolizing enzymes that have been suggested to affect exposure to lamotrigine) to estimate the exposure effect (geometric means ratios, GMRs) in each study separately and overall (individual patient data meta-analysis). The overall estimate was evaluated for sensitivity to residual confounding.

Results: In both studies (exposed n = 28 vs. controls n = 103; exposed n = 44 vs. controls n = 153, in Study 1 and Study 2, respectively) and overall (exposed n = 72 vs. controls n = 256), dose-corrected lamotrigine trough concentrations were moderately lower in the exposed patients: frequentist GMR [95% CI] = 0.82 [0.63-1.08]; GMR = 0.69 [0.60-0.81] and GMR = 0.72 [0.63-0.83] in Study 1, Study 2 and overall, respectively; Bayes GMR [95% CrI] = 0.83 [0.68-1.00]; GMR = 0.69 [0.58-0.83] and GMR = 0.75 [0.65-0.86] in Study 1, Study 2 and overall, respectively. Estimates appeared resistant to unmeasured confounding-the E-values for the pooled point estimates were high, and estimates corrected for a strong hypothetical bias were GMR = 0.78 [0.68-0.90] frequentist and GMR = 0.81 [0.70-0.93] Bayes.

Conclusion: *ABCG2 c.421C>A* polymorphism moderately reduces lamotrigine concentrations in adults with epilepsy.

429 | Cenobamate in super-refractory post-stimulation epilepsy after acute viral encephalitis-case report and literature review

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Purpose: To provide preliminary evidence of the use of adjunctive cenobamate in drug- and neuromodulation-resistant epilepsy of an infectious etiology, and to briefly review the literature regarding the treatment of postencephalitic epilepsy.

Method: Results of brain MRI, brain PET scan, long-term video-EEG recordings, and cerebrospinal fluid testing were assessed. Adjunctive cenobamate was introduced with an initial dose of 12.5mg once daily and slowly titrated to 100mg twice daily. The patient was followed up for 12 months for evaluation of safety and effectiveness.

Results: A 19-year-old Chinese girl had daily seizures and significant cognitive impairment due to super-refractory epilepsy after acute viral encephalitis at the age of 5. Brain MR demonstrated bilateral hippocampal sclerosis, cerebral atrophy, and ventricular enlargement. Her pre-surgical evaluation turned out ineligible. Ictal

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EEG revealed focal-onset seizures with a left-temporal predominance which frequently progressed to generalized tonic-clonic seizures. Combined treatment of multiple anti-seizure medications, vagus nerve stimulation, and deep brain stimulation of the anterior nucleus of the thalamus was not effective and incurred serious adverse drug reactions. Adjunctive cenobamate was efficacious in reducing seizure frequency and was generally well-tolerated. A reduction in seizure frequency by > 50% was reported at the dose of 50mg twice daily. At one-year follow-up, this girl was having one focal onset seizure per week without secondary generalization and enjoyed an improved quality of life.

Conclusion: Post-encephalitic epilepsy has a poor prognosis profile. It is often resistant to treatment with traditional anti-seizure medications or resective surgery and has an unclear response to neuromodulation. Cenobamate might serve as a considerable treatment option for refractory postencephalitic epilepsy, especially in developing countries where cerebral infection still accounts for an important cause of epilepsy.

488 | Point of care Lamotrigine monitoring in epilepsy: A Pilot Study Using a Carbon Screen-Printed Electrode

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Purpose: This study evaluates the performance of a novel electrochemical method for direct detection of lamotrigine (LAM) using an in-house carbon screen-printed electrode in biological matrices and compares the results to the gold-standard mass liquid chromatography spectroscopy (LCMS) based blood testing. There is a clear unmet clinical need in epilepsy for a rapid and accurate method of measuring Lamotrigine concentrations. Current lab-based LCMS testing takes approximately two weeks to yield an actionable result. The aim is to provide a foundation for developing a cost-effective, point-of-care (POC) device for therapeutic monitoring of anti-seizure medications.

Method: A prospective non-interventional approach was adopted to assess the sensor's performance in an initial cohort of 20 patients undergoing therapeutic drug monitoring. Eligible and consenting participants had three additional samples (serum, plasma, and whole blood) collected during routine phlebotomy. Samples were processed within two hours and analyzed using the carbon screen-printed electrode. Each sample was tested three times, and the results were compared to those obtained through LCMS.

Results: The sensor demonstrated robust detection capability in complex biological matrices, including commercially available human serum and plasma. Sensitivity, calculated from the concentration vs. charge plot slope, was 2.0964 E^{-08} C/μM, indicating a sensitive response to LAM concentrations. Preliminary findings highlighted the assay's reliability and reproducibility, providing a basis for real-time therapeutic monitoring. Trends associated with variability in assay performance were also explored, informing potential areas for further optimization.

Conclusion: This pilot study underscores the feasibility of a novel electrochemical approach for direct detection of lamotrigine in epilepsy patients. The carbon screen-printed electrode shows promise as a simple, cost-effective, and accurate platform for therapeutic drug monitoring. Future work will focus on miniaturizing the assay for portable POC applications, facilitating improved clinical outcomes through real-time monitoring in routine care settings.

493 | Phase 1 Multiple Ascending Dose Studies Demonstrate Favorable Safety and Tolerability of BHV-7000, a Novel Kv7 Potassium Channel Activator

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Purpose: BHV-7000 is a novel, small molecule, selective activator of Kv7.2/7.3 potassium channels in late-stage clinical development for epilepsy and neuropsychiatric disorders. In preclinical studies, BHV-7000 demonstrated minimal $GABA_A$ receptor activation and exhibited potent anti-seizure efficacy without negative effects on neurobehavior or motor function. A Phase 1 EEG study confirmed CNS target engagement of BHV-7000. The objective of this analysis was to assess safety and tolerability of BHV-7000 across multiple ascending dose (MAD) studies.

Method: Results were pooled from Phase 1 placebo-controlled MAD studies. Healthy adults aged 18-55 years were included, and participants were randomized to oral BHV-7000 immediate release (10, 25, 40, 80, or 120 mg daily), extended-release (25, 50, or 75 mg daily), or matching placebo, and treated for up to 15 days. Safety

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evaluations throughout the studies included AE monitoring, clinical laboratory tests, vital signs, ECGs, physical examinations, and suicidality assessments.

Results: Across the MAD cohorts, 66 participants received BHV-7000 (N=53) or placebo (N=13). Adverse events (BHV-7000 vs placebo) occurring in ≥5% of participants included headache (11.3% vs 23.1%), back pain (11.3% vs 0%), constipation (5.7% vs 23.1%), and dizziness (5.7% vs 15.4%). There were low rates of CNS-related AEs; no somnolence was reported. The majority of AEs were mild and resolved spontaneously. There were no serious AEs, severe AEs, or dose-limiting toxicities. No AEs were reported amongst participants receiving BHV-7000 75 mg extended release (n=12), the highest dose in ongoing Phase 2/3 studies.

Conclusion: BHV-7000 was safe and well tolerated in multiple-dose Phase 1 studies across all doses evaluated for up to 15 days. Adverse events typically associated with other ASMs, such as somnolence and cognitive/mood disturbances, were not reported at equivalent doses to those currently being dosed in Phase 3 trials in focal epilepsy, generalized epilepsy, major depressive disorder, and bipolar disorder.

517 | Cannabidiol administration in patients with Lennox-Gastaut syndrome or other pharmacoresistant epilepsy: a single center's experience

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Purpose: Cannabidiol has been approved as add-on antiseizure therapy in patients with Lennox-Gastaut syndrome (LGS), Dravet syndrome or Tuberous Sclerosis, usually co-administered with clobazam. We describe our experience from four patients that are being treated with cannabidiol in our clinic.

Method: The first patient, a 10 year-old girl with LGS, was started cannabidiol while already administered valproic and clobazam. A month later, seizure frequency and behavior were improved, however parents mentioned drowsiness. Lab tests revealed elevated AST, ALT and valproic in serum. After reducing valproic and cannabidiol dosage, symptoms recessed, serum values returned to normal and seizure frequency continued to improve. The second patient, a 12-year-old girl with LGS, was started cannabidiol while already taking valproic and clobazam. Soon after initiation at the lowest dosage, seizure frequency was remarkably declined. The third patient, a 13-year-old boy with cerebral palsy and pharmacoresistant epilepsy that was already administered levetiracetam, valproic and clobazam without satisfactory seizure control. Thus, cannabidiol was initiated at a low dosage with significant clinical improvement. The fourth patient, a 10-year-old girl with pharmacoresistant epilepsy and continuous spike and wave in sleep EEG, was administered cannabidiol as an add-on therapy. Seizure frequency was slightly improved but behavior improved significantly.

Results: All four patients showed clinical improvement that became more obvious after the first trimester of administration. Unwanted events included drowsiness, elevated AST, ALT, NH3 as well as coadministration issues. All of the events were managed with dosage modification and discontinuation was not necessary.

Conclusion: Cannabidiol is a good option for pharmacoresistant epilepsy, in both seizure control and behavior improvement. Unwanted events are manageable but close monitoring is recommended.

539 | Clinically Meaningful Reduction in Seizure Frequency in Patients with Tuberous Sclerosis Complex Treated with Cannabidiol

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Purpose: In clinical trials, a ≥50% reduction in seizure frequency is often accepted as a primary endpoint for treatment efficacy, but the real-world threshold for a clinically important response (CIR) for patients with tuberous sclerosis complex (TSC) is largely untested. We investigated the CIR in patients with TSC from a randomized controlled trial of plant-derived, highly purified cannabidiol (CBD; Epidyolex® [EU]/Epidiolex® [US] 100 mg/mL oral solution; NCT02544763).

Method: This *post hoc* analysis used receiver operating characteristics (ROC) to quantify the threshold at which monthly seizure reduction could be deemed clinically important in pooled data from patients receiving 25 or 50 mg/kg/day CBD (n=132). For CIR, reduction in seizure frequency was anchored to Caregiver Global Impression of Change (CGIC) ratings of 'slightly improved' or better (scores 1, 2, 3 versus 4, 5, 6, 7), or 'much improved' or better (scores 1, 2 versus 3, 4, 5, 6, 7). The minimal clinically important difference (MCID), defined as the smallest

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change that can be detected beyond random error, was investigated using half standard deviation (SD) and standard error of the mean (SEM).

Results: The best-fit ROC-derived threshold for CIR associated with CGIC of 'slightly improved' or better was a 33% reduction in seizure frequency, and for 'much improved' or better was 52%. Thresholds for MCID (SD [SEM]) were −17.8% (−19.5%) for a CGIC of 'slightly improved' or better, and −17.2% (−18.9%) for 'much improved' or better. Spearman's correlation was 0.54 (P<0.001).

Conclusion: Anchoring between reduction in TSC-associated seizures and CGIC seems appropriate, (Spearman's correlation >0.30). Anchoring to CGIC of 'slightly improved' or better, the threshold for a CIR in seizure reduction was 33%, suggesting that a cut-off of 50% may overlook patients who are achieving meaningful improvements in their overall condition, as perceived by their caregivers. Funding: Jazz Pharmaceuticals, Inc.

540 | Investigating the effect of steady state cannabidiol on the single dose pharmacokinetics of CYP2B6, CYP2C9, UGT2B7, and UGT1A9 substrates

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Purpose: *In vitro* data suggest cannabidiol (CBD; Epidyolex® [EU]/Epidiolex® [US]; 100 mg/mL oral solution) may inhibit or induce (CYP2B6 only) the metabolism of substrates of CYP2B6, CYP2C9, UGT2B7, and UGT1A9. We assessed the effect of steady-state CBD on the pharmacokinetics of probe substrates of these enzymes.

Method: The effect of CBD on metabolism mediated by CYP2B6 (bupropion) or CYP2C9 (tolbutamide), and UGT2B7 (zidovudine) or UGT1A9 (mycophenolate mofetil [MMF]) was investigated in two phase 1 drug-drug interaction studies. Healthy participants received bupropion 150 mg, zidovudine 300 mg, tolbutamide 500 mg, or MMF 1500 mg on Day (D) 1, and CBD 7.5 mg/kg twice daily from D4–10 (D2–6 for zidovudine), with concurrent dosing on D8 (D6 for zidovudine). $AUC_{0-\infty}$ and C_{max} were assessed with geometric least squares mean (GLSM) ratios and associated 90% confidence intervals (CIs) for substrates plus CBD versus substrates alone.

Results: 90% CIs of GLSM ratios were outside the bioequivalence criteria of 0.80 to 1.25 for bupropion (n=16; $AUC_{0-\infty}$: 0.801 [90% CI: 0.717, 0.896] and C_{max}: 0.807 [0.677, 0.962]), zidovudine (n=16; $AUC_{0-\infty}$: 1.19 [1.10, 1.29] and C_{max}: 1.07 [0.898, 1.28]), and MMF (n=11 or 14; $AUC_{0-\infty}$: 1.35 [1.19, 1.54] and C_{max}: 1.16 [0.969, 1.38]). Conversely, 90% CIs of GLSM ratios were within the bioequivalence range for tolbutamide (n=16; $AUC_{0-\infty}$: 1.03 [0.971, 1.10] and C_{max}: 0.947 [0.897, 1.00]).

Conclusion: The observed exposure changes following CBD coadministration for substrates of CYP2B6 and UGT2B7 were not considered clinically meaningful; dose adjustments are not warranted for these or for substrates of CYP2C9 when used with CBD. However, CBD coadministration resulted in weak inhibition of UGT1A9 with increased exposures up to 54%, which was beyond the observed variability (~30%). Consequently, dose reduction of sensitive UGT1A9 substrates may be warranted if adverse reactions occur when administered concomitantly with CBD. Funding: Jazz Pharmaceuticals, Inc.

575 | Freedon study: Real-life outcomes of cenobamate at different lines of treatment

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Purpose: Number of prior ASM has been reported as a key prognostic factor of response in epilepsy. The current study analyzes cenobamate (CNB) outcomes at different lines of treatment

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Method: Multicenter, retrospective, observational study. Inclusion criteria were 1) 18 years; 2) Focal seizures 3) Treated with 2-6 prior ASM (including concomitant) before starting CNB. At this interim analysis effectiveness and safety outcomes were reported for those patients with a minimum follow-up of 12 months. The source of data was patient clinical records and time-points analyzed were baseline, 6 months (6m) and 12 months (12m).
Results: 143 patients (54% female) were included. At baseline, mean age was 44 (18-87), mean epilepsy duration was 18 years and median number of seizures/month was 4 (27,4% focal evolving to bilateral). Cortical malformation was most frequent etiology. Regarding lines of treatment, 17 (11.9%), 21 (14.7%), 31 (21.7%), 37 (25.9%) and 37 (25.9%) had tried 2, 3, 4, 5 and 6 prior ASM. The median dosage of CNB (12m) was 200 mg (100-400) regardless line of treatment. Retention rate at 12m was 95% (6 patients discontinued). Regarding ≥50% responder considering the line of treatment (2, 3, 4, 5, 6 prior ASM) was 70%,73%,48%,62%,37% (6m) and 82%,84%,76%,67%,66% (12m), ≥75% responder was 50%,47%,27%,40%, 21% (6m) and 72%, 68%, 56%, 52%, 51% (12m), ≥90% responder was 30%, 26%,14%, 28%, 15% (6m) and 54%, 36%, 36%, 38%, 15% (12m), seizure-free was 20%, 26%, 13%, 25%, 6% (6m) and 27%, 21%, 20%, 26%,15% (12m). Worsening was reported by 20%,5%,7%,6%,15% (6m) and 9%,5%,10%,14%,9% (12m). Cumulative adverse events (AE) at 12m were reported by 60%. The most frequent AE were somnolence (32%) and dizziness (16%)
Conclusion: Interim outcomes proved sustained effectiveness of CNB over different lines of treatments although outcomes were better after the failure of 2 ASM and 12m of treatment. Somnolence was most frequent AE

591 | Benefits beyond-seizures of optimized seizure control after cenobamate initiation

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Purpose: To establish the clinical impact of seizure control after cenobamate (CNB) initiation in terms of quality of life (QoL), affective and cognitive symptoms.
Method: Observational, longitudinal, prospective study of patients with epilepsy (PWE) in which CNB was introduced. Demographic and clinical characteristics were recorded at baseline. Seizure frequency was recorded as the average monthly seizure count, during the 3 months prior to CNB initiation and at 6-month follow-up. QoL, cognitive status and anxiety/depression were evaluated at baseline and follow-up using the Quality of Life in Epilepsy inventory (QOLIE-31), Short-Form-36 Health Survey physical (SF-36-P) and mental (SF-36-M) components, Montreal Cognitive Assessment (MoCA) and Hospital Anxiety and Depression Scale (HADS).
Results: 45 patients were included, mean age (SD) 41.2 (±16.1) years, 51.1% male. The median (IQR) seizure frequency was 3 (1-8) seizures/month, and the median (IQR) number of antiseizure medications (ASM) at baseline was 2 (1-4). At follow-up, retention and responder rates were 88.9% and 64.4% respectively, and 33.3% of patients were seizure-free. There were no significant differences in global QOLIE-31, SF-36 or HADS scores at follow-up with respect to baseline. Median MoCA score improved at follow-up (16 vs. 17; p=0.022). Reduction of seizure frequency correlated with better scores in QOLIE-31 (r: -0.481; p=0.015), HADS-depression (r: 0.323 p=0.042) and MoCA (r: -0.332; p=0.073). Seizure freedom at follow-up was associated with better QOLIE-31 (median +7 vs. -3.5; p=0.012), HADS-depression (median 0 vs. +2; p=0.021) and MoCA (median +2 vs. 0; p=0.046) scores. Reduction of concomitant ASM occurred in 6 patients during follow-up (13.3%) and was associated with greater improvement in SF-36-P (+5.7 vs, 1.1; p=0.033).
Conclusion: Optimizing seizure control can improve QoL, cognitive and depressive symptoms in PWE after CNB initiation. ASM simplification is associated with better-perceived physical health as measured by SF-36 scale.

606 | Utility and safety of anti-seizure medication withdrawal during long term video-EEG

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Purpose: Anti-seizure medication (ASM) withdrawal in long term video-electroencephalogram (VEEG) is an important tool that facilitates the diagnosis and presurgical evaluation of epilepsy patients. However, faster tapering can cause possible complications. We aim to analyze strategies for withdrawal ASM during VEEG in terms of safety and study utility.
Method: Retrospective and observational study about VEEG recorded on 2023, with a minimal duration of 72hs,

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in patients receiving ASM. We analyzed the study utility (defined as if all patient events were recorded and the study aim was met), complications and clinical features comparing groups with faster(>50), lower <50%) and no ASM tapering. Chi squared and Mann Whitney tests were performed to verify the statistical significance of the results.

Results: 125 VEEG met inclusion criteria. Out of these, 77.6% were adults and 53.6% women, with a median of seizures onset at 13 years (IQR=5-21) and a median age of 29 years (IQR=18-42). VEEG duration was 72 hours on 68.8%, 96 hours on 14.4% and 120 hours on 16.8%. We recorded events in 94 studies, of which 71% were epileptic. The first seizure occurred on day 1 in 52.3%. The VEEG was useful on 64% and 11.7% had complications (most of these were self limited tonic-clonic seizures). There were no statistically significant differences regarding study utility, time to first seizure, history of SE and complications. In patients with epilepsy resistant to ASM and high frequency of seizures we observed a lower tapering of ASM on day 1 (p=0.005 y p=0.04 respectively).

Conclusion: ASM withdrawal is a safe tool in VEEG monitoring. Faster ASM tapering was not associated with a higher rate of complications. The decision between fast vs lower tapering seems to be conditioned by frequency of events and resistant epilepsy. Prospective studies are needed to determine a standardized protocol for an optimal decrease of ASM during VEEG.

623 | Tuberous Sclerosis Complex–Associated Neuropsychiatric Disorders Outcomes Following Add-on Cannabidiol Treatment: 3-Month Analysis of the Open-Label Phase 3b/4 Trial EpiCom

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Purpose: Limited treatment options exist for tuberous sclerosis complex (TSC)-associated neuropsychiatric disorders (TAND), which affect ≈90% of people with TSC. EpiCom (NCT05864846) is evaluating behavioral and other outcomes after add-on cannabidiol (CBD; Epidyolex® [EU]/Epidiolex® [US], 100 mg/mL oral solution) treatment in participants with TSC and epilepsy; we present prespecified 3-month analyses.

Method: Patients with TSC and moderate/severe behavioral challenges are receiving CBD ≤25 mg/kg/day and standard of care (SOC) for 26 weeks; then continuing CBD+SOC or SOC alone for up to 52 weeks overall. Outcomes are change from baseline in most problematic behavior (MPB) on the TAND Self-Report Quantified Checklist (TAND-SQ)/Aberrant Behavior Checklist (ABC) at Week 13, and CareGI-S/CGI-Severity (CGI-S) scales at Weeks 4 and 13.

Results: At 3 months, 24 patients had enrolled and 19 started CBD. In evaluable patients (n=17), median (range) age was 21 (5–42) years. At baseline, nine patients (47%) had seizures, with a mean (SD) of four (7) seizures per 28 days. The median (range) number of antiseizure medications at baseline was 3 (1–5). Most common concomitant medications were lamotrigine (n=6 [32%]), topiramate (n=6 [32%]), and everolimus (n=5 [26%]). Five patients completed Week 13 assessments; mean (95% CI) change from baseline in MPB numerical rating scale was −4.6 (−8.1, −1.1). Of seven TAND-SQ clusters, the greatest changes were in dysregulated behavior and overactive/impulsive scores. In ABC, the greatest changes were in irritability and hyperactive noncompliance. Fewer caregivers and clinicians rated behavioral problems as severe/very severe on CareGI-S and CGI-S at Weeks 4 and 13 versus baseline. Adverse events (AEs) occurred in 12/19 participants (63%); most common was diarrhea (n=8 [42%]). Four participants discontinued due to AEs.

Conclusion: Despite sample size limitations, this planned 3-month analysis reported behavioral improvements across evaluated subscales after initiating CBD. The safety profile is consistent with previous studies. Funding: Jazz Pharmaceuticals, Inc.

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624 | Safety, efficacy and pharmacokinetic analysis of intravenous VAL-1221 treatment in Lafora disease

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Purpose: Lafora Disease (LD) is a progressive myoclonus epilepsy with onset in previously healthy adolescents leading to death in young adulthood, with no effective treatments currently available. This study investigates the safety, efficacy and pharmacokinetics of intravenous VAL-1221, the first potentially disease-modifying treatment administered to LD patients.
Method: Monocentric analysis of a 12-month compassionate use program for VAL-1221 (20 mg/kg every other week) in LD patients. Safety was assessed through adverse events (AE) monitoring. Efficacy was evaluated using clinical scales (including the Lafora disease clinical performance scale-LDPS) and neuroimaging. Pharmacokinetic studies were performed using liquid chromatography-high resolution mass spectrometry (LC-HRMS) to analyze plasma and CSF samples.
Results: Five patients (range: 17-24 years; 3 females) at intermediate to advanced stages of LD received VAL-1221. Four patients completed the 12-month treatment course, while one discontinued after 8 months due to status epilepticus. We observed 5 mild infusion-related AEs (skin rash, n=1; hypotension, n=4) and no other treatment-related AEs. Efficacy analyses showed a trend of deterioration from baseline to 12 months across various measures. The pharmacokinetic of VAL-1221 was characterized by plasma concentrations (Cmax 100-150 ug/mL; T1/2 60 min), but the drug was undetectable in CSF in all three assessed patients.
Conclusion: VAL-1221 demonstrated an acceptable safety and tolerability profile. Evidence of disease progression and the lack of identification of the drug in CSF suggest that intravenous VAL-1221 does not cross the blood-brain barrier and is therefore ineffective for treating LD in this formulation. Further studies are needed to explore alternative administration methods.

628 | Global Seizure Rescue Medication Landscape: Availability & Reimbursement

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Purpose: Perform a global scan of availability and reimbursement coverage of seizure rescue medications (RMs) for use in the outpatient setting. Due diligence was performed to highlight the current environment of seizure RMs, outlining products available in each country, and their reimbursement/coverage.
Method: To conduct the global scan we: (1) identified products currently approved as outpatient seizure RMs across all age groups, focusing on FDA/EMA approvals; (2) leveraged NAVLIN's pricing sources to capture countries where products have public prices; (3) leveraged links/sources for each country's reimbursement decision authority (typically Ministry of Health) to identify if RM was either reimbursed, partially reimbursed, not reimbursed or had no reimbursement information; (4) conducted mapping exercise to highlight countries where analogues are currently available (public list price) and reimbursement status of each product in corresponding countries. Countries that do not publish pricing data were not included.
Results: Overall, the scan identified seven different molecule-routes of administration combinations that qualify as RMs. Reimbursement information from 53

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countries was available with notable gaps within South America, Africa, Asia. The scan identified significant differences in availability and reimbursement of seizure RM types across different regions. Products for rectal-administration of diazepam are the most available/reimbursed RM option, but are not reimbursed everywhere. Products for oromucosal-administration of midazolam are mostly available in Europe; however, reimbursement varies widely across countries and between adult and pediatric patients. Products for nasal-administration of diazepam and midazolam are available and reimbursed in US and India, and are currently not reimbursed in Europe.
Conclusion: Critical differences in availability and reimbursement of seizure RMs were observed across countries, representing significant barriers to access for patients. These findings highlight the need to better understand the evolution of the RM landscape worldwide. Elevating standard-of-care by ensuring equitable access to RMs worldwide, regardless of age, is essential for improving patient-outcomes/quality-of-life. UCB-sponsored

635 | Different effects of structurally similar dibenzazepine family on neuronal networks; Microelectrode array study

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Purpose: Voltage-gated Na^+ channels are critical therapeutic targets of anti-seizure medications (ASMs). The structurally related compounds carbamazepine (CBZ), oxcarbazepine (OXC), eslicarbazepine acetate (ESL), and S-licarbazepine (S-Lic) of the dibenzazepine family are generally presumed to exert similar effects; however, a comparative analysis of its effects on neuronal networks is lacking. We compared these effects using microelectrode array (MEA) recording.
Method: MEA recordings were conducted from primary cortical neurons using a Maestro Edge System. We analyzed activities grouped into four categories: spiking, single-electrode bursting, network bursting, and synchrony by Axion Integrated Studio software for the different ASMs (50 μM; CBZ n = 6, OXC n = 6, ESL n = 5, S-Lic n = 6, Lacosamide (LCM) n = 6).
Results: CBZ, OXC, and ESL exhibited equivalent and strong effects across all categories: spiking, single-electrode bursting, network bursting, and synchrony. In contrast, LCM and S-Lic did not affect mean firing rates. Instead, LCM exerted a pronounced effect on burst duration, similar to CBZ and OXC, while S-Lic induced significant effects only on network bursting, but not any other firing parameters. Overall, CBZ, OXC and ESL had significantly stronger effects than LCM, except for burst duration. In comparison to CBZ and OXC, S-Lic showed consistently smaller effects across parameters.
Conclusion: CBZ, OXC, and ESL produced comparable effects on spiking, single-electrode bursting, neuronal network, and synchrony. In contrast, S-Lic and LCM exhibited distinct effects on neuronal networks compared to CBZ and OXC. While S-Lic demonstrated mild effects only on network burst frequency, LCM notably influenced burst duration. This indicates that these, structurally in part very similar compounds, can exhibit quite pronounced differences in the ways they affect synchronous network activity. This may be rooted in differences in voltage- and use-dependent inhibition of sodium channel isoforms.

639 | Overcoming challenges in epilepsy clinical trials: the role of European Consortium for Epilepsy Trials

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Purpose: The European Consortium for Epilepsy Trials (ECET) was established by the regional Executive Committee of the International League Against Epilepsy (ILAE-Europe) and endorsed by the European Reference Network for Rare and Complex Epilepsies, ERN EpiCARE, in 2021. As a legal entity, ECET Ltd. aims to elevate the standard of epilepsy trials - on medical therapies, devices, epilepsy surgery and natural history studies – in the European region, focusing on both adult and pediatric populations. This mission is driven by fostering collaboration among experts, patient advocates, academia, and industry.
Method: New-onset epilepsy affects annually 130,000 children and adolescents, 96,000 adults (20–64 years), and 85,000 elderly individuals in Europe, with over 30% developing a rare or complex form, often drug-resistant. ECET, under the guidance of a Scientific Advisory Committee, unites 93 experts from reference centers in 32 countries in Europe, offering expertise to optimize trial design and implementation.
Results: Since its creation, ECET has supported the development of high-quality trials through targeted surveys, scientific review of trial designs and site selection. It has contributed to two natural history studies and organized educational activities to enhance the skills of researchers

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and clinicians involved in clinical trials. ECET has identified key shortcomings in epilepsy trials, including inadequate adaptation of methodologies to specific epilepsy types, neglect of comorbidities, and insufficient patient advocacy involvement. ECET addresses these gaps by offering expert advice, standardizing adjudication processes, and fostering international collaboration.

Conclusion: ECET represents a pivotal initiative in transforming epilepsy clinical trials in Europe, addressing the complexities of epilepsy research and fostering collaboration across stakeholders. ECET aims to improve treatment outcomes, enhance patients' quality of life, and reduce the societal impact of epilepsy. ECET emphasizes the necessity for robust, representative trials to drive innovation in epilepsy care.

655 | Efficacy and Safety of Trofinetide for the Treatment of Rett Syndrome: Results From the Pivotal Phase 3 LAVENDER Study

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Purpose: Rett syndrome (RTT) is a debilitating genetic neurodevelopmental disorder that primarily affects females. Trofinetide is a synthetic analog of glycine–proline–glutamate, a naturally occurring tripeptide cleaved from insulin-like growth factor 1. Phase 2 studies in RTT demonstrated a clinical benefit over placebo in clinician- and caregiver-assessed efficacy measures. Here, we present the efficacy and safety results of LAVENDER, a randomized, placebo-controlled, phase 3 study of trofinetide in girls and young women with RTT.

Method: Females with RTT, aged 5–20 years, were randomized 1:1 to twice-daily oral trofinetide or placebo for 12 weeks. Coprimary efficacy endpoints included the caregiver-assessed Rett Syndrome Behaviour Questionnaire (RSBQ) and the clinician-assessed Clinical Global Impression–Improvement (CGI-I) scale. Safety measures included adverse events.

Results: Overall, 187 participants were randomized to trofinetide (n=93) or placebo (n=94). After 12 weeks of treatment, trofinetide demonstrated a statistically significant improvement over placebo for co-primary and key secondary endpoints. Least squares (LS) mean change from baseline to week 12 in the RSBQ for trofinetide vs. placebo was -4.9 vs. -1.7 (p=0.0175; Cohen's d effect size = 0.37). LS mean CGI-I score at week 12 was 3.5 vs. 3.8 (p=0.0030; Cohens' d effect size = 0.47). The most common adverse event in the trofinetide and placebo groups was diarrhea (80.6% and 19.1%, respectively) with 97% of all cases experiencing mild-to-moderate severity.

Conclusion: This study demonstrated that trofinetide is efficacious and has an acceptable safety profile in girls and women with RTT. This study was supported by Acadia Pharmaceuticals Inc.

672 | Long-term Evaluation of the Safety Profile of Highly Purified Cannabidiol: Analysis of Plasma Levels of THC

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Purpose: Highly purified cannabidiol (hpc) (Epidyolex®), is an adjunctive treatment for drug-resistant seizures in Dravet Syndrome (DS), Tuberous Sclerosis Complex (TSC), and Lennox-Gastaut Syndrome (LGS) (Iannone L.F., et al. Front Neurol. 2021;12:673135.2; Thiele E.A., et al. Epilepsia. 2022;63(2)426-439). Although hpc lacks psychotropic effects, some studies suggest an accumulation of tetrahydrocannabinol (THC) in adipose and brain tissue following repeated administrations (Kreuz D.S., et al. Science 1973;179(4071):391-3). We evaluated the long-term plasma levels of THC in patients treated with hpc (Epidyolex®).

Method: Children with drug-resistant epilepsy receiving add-on treatment with hpc (Epidyolex®) underwent baseline blood sampling. Plasma levels of CBD and THC were measured using a validated method based on liquid chromatography coupled with mass spectrometry (Pigliasco F., et al. Front Pharmacol 2022;13:1038754).

Results: Eleven patients (mean age = 14 years) were enrolled. The syndromic classification was DS in 7 (64%) patients, TSC in 3 (27%), and LGS in 1 (9%) patient.

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The median follow-up (FU) was 1.3 years (range, 5-52 months). All patients received incremental doses of hpc (Epidyolex®), with the average dose at the last FU being 12 mg/kg/day. The average plasma concentration of CBD at the last FU was 203.2 µg/L, while that of THC was <0.2 µg/L.

Conclusion: Despite incremental doses and repeated administrations of hpc (Epidyolex®), plasma levels of THC remained below 0.2 µg/L, confirming the absence of accumulation at therapeutic dosages.

677 | Histone deacetylase inhibitors in epilepsy: insights on blood-brain barrier integrity and excitation-inhibition balance

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Purpose: Identify a histone deacetylase inhibitor (HDACi) capable of reinstating blood-brain barrier (BBB) integrity and excitation-inhibition balance.

Method: Three non-pan HDACi (HDACi 1-3) were tested in a human-like triculture BBB model. Lipopolysaccharide (LPS; 10µg/mL) was used to trigger BBB disruption. Six conditions were investigated: no LPS, LPS alone, LPS+valproic acid (VPA; 2mM) and LPS+HDACi (1-3; 100nM). VPA was chosen due to its BBB-repairing effect as HDACi (Wang et al. J. Cereb. Blood Flow Metab., 2011, 31(1), 52-57). Sodium fluorescein (NaF) and FITC-dextran were used as integrity markers (n=3 independent experiments). Then, pharmacokinetic studies were performed in CD-1 mice for HDACi 2 and 3 (n=40; 0.15mmol/kg) by intranasal route. Lastly, the vehicle and HDACi 3 (0.15 mmol/kg) were administered to the intrahippocampal kainic acid (IHKA) model of epilepsy (n=8 for 5 days, starting on day 1 immediately after kainic acid). Brain metabolites [GABA, glutamine+glutamate (Glx)] were measured by ^{1}H-magnetic resonance spectroscopy before kainic acid administration (day 0); 3h (day 1) and 21 days after kainic acid.

Results: *In vitro* all HDACi and VPA elicited BBB-repairing effect compared to LPS alone, for NaF ($p<0.05$) and FITC-dextran ($p<0.0001$). This was more evident for HDACi 2 and HDACi 3 ($p<0.0001$, both markers), selected for pharmacokinetic studies. HDACi 3 demonstrated greater brain exposure (area under the curve of 0.092 vs. 0.029µg/mL.h), remained longer in brain (elimination half-life of 0.55 vs. 0.072h) and yielded higher brain-plasma ratios (0.012 vs. 0.008) than HDACi 2. In the IHKA model, vehicle-dosed mice revealed lower GABA/Glx ratios on day 1 ($p<0.01$) compared to day 0. Conversely, HDACi 3-dosed mice displayed higher GABA/Glx ratios on day 1 ($p<0.01$) compared to vehicle, and identical ratios to day 0.

Conclusion: The results suggest that HDACi 3 restores BBB integrity and excitation-inhibition balance.

681 | Improved Psychiatric and Cognitive Outcomes Following the Switch from Levetiracetam to Brivaracetam

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Purpose: Levetiracetam is an effective treatment for seizures. However, side effects such as aggression, mood disorder and cognitive impairment sometimes necessitate discontinuation. Brivaracetam shares a similar mechanism of action to levetiracetam and is suggested to have improved tolerability. However, data comparing psychiatric and cognitive outcomes between these drugs remains limited. This study aims to evaluate the psychiatric and cognitive outcomes of switching from levetiracetam to brivaracetam.

Method: A retrospective chart review included 23 individuals with epilepsy treated with levetiracetam. Assessments were conducted at baseline and 4–7 months after switching to brivaracetam using validated psychiatric scales and neuropsychological tests. Outcomes included, depression, anxiety, somatization, aggression, emotional regulation and quality of life, together with processing speed, attention, and visuospatial and verbal memory. Before and after means were compared along with clinical impact as measured by category shifts (e.g. from moderate to mild symptoms). Statistical analyses included repeated measures t-tests and Wilcoxon Signed Rank tests with Chi goodness-of-fit applied to evaluate clinical outcomes.

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Results: Switching to brivaracetam led to significantly more positive than negative clinical outcomes in psychiatric and neuropsychological measures (p = 0.01 and p = 0.05). In addition, depression symptoms (p = 0.001), emotional regulation strategies (p = 0.01), anger (p = 0.05) and quality of life (p = 0.001) improved significantly. Cognitive domains including processing speed and attention (p = 0.03) and visuospatial memory (p = 0.005) also improved after switching to brivaracetam. Importantly no significant declines were observed in any other measures suggesting no worsening of symptoms following medication change.
Conclusion: Switching from levetiracetam to brivaracetam improves psychiatric symptoms and cognitive function with no evidence of worsening symptoms. These findings suggest brivaracetam is an alternative for individuals experiencing levetiracetam side effects and are potentially important for clinical practice. Further investigation with a larger sample size is warranted.

692 | Highly purified cannabidiol in highly active genetic developmental and epileptic encephalopathies: a multicenter real-world study

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Purpose: This real-world, retrospective, multicenter study aimed to evaluate the effectiveness of highly purified cannabidiol (CBD) in patients with highly active monogenic developmental and epileptic encephalopathies (DEEs).
Method: The study included patients from 27 epilepsy centers with monogenic DEEs (i.e., caused by monogenic pathogenic or likely pathogenic variants) treated with highly purified CBD for at least 3 months. Patients with ≥20 seizures per month at baseline were classified as 'highly active".
Results: A total of 243 patients (119 females, 49%) with monogenic DEEs were included, with a median age at CBD initiation of 12 years (interquartile range 7-20). The most common genetic variants were SCN1A (32.1%), TSC2 (13.6%), CDKL5 (4.9%), and MECP2 (4.1%). Patients with highly active DEE (n=155, 63.8%) exhibited nominally lower mean seizure reduction (37.4% ±32.3 vs. 41.6% ±35.7, p=0.4), ≥50% seizure reduction rates (46.6% vs. 50.0%, p=0.6), ≥75% seizure reduction rates (19.3% vs. 26.1%, p=0.2), and seizure freedom rates (6.0% vs. 10.2%, p=0.2) compared to those with a lower seizure burden, although these differences were not statistically significant. Patients with highly active DEEs were more frequently prescribed CBD as an off-label medication (47.7% vs. 26.1%, p<0.001), had less frequent use of concomitant clobazam (52.3% vs. 64.8%, p=0.06), and received higher final doses of CBD (15.4 ±7.1 mg/kg/day vs. 11.7 ±5.4 mg/kg/day, p<0.001).
Conclusion: This study demonstrates that highly purified CBD may serve as a viable treatment option for patients with highly active monogenic DEEs, highlighting its potential utility in managing this challenging population.

703 | Use of Phenozanic acid in patients with epileptic seizures and ischemic stroke

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Purpose: To access a recurrence of seizures after acute symptomatic seizures or late focal-onset seizures at different periods of the acute stroke on the background of the combined use of basic anti-seizure medications (ASMs) and phenozanic acid (PA).
Method: A retrospective analysis included 16 patients: 7 patients had seizures or status epilepticus in debut of stroke, 5 patients had late focal-onset seizures (>7 days after stroke), 4 patients had focal onset seizures after hemorrhagic complications of thrombolytic therapy. PA 800 mg per day was prescribed in combination with basic ASMs (valproic acid up to 3000 mg per day–10 patients, levetiracetam at a dose of 2000-3000 mg per day–6 patients).
Results: Video-EEG showed regional epileptiform discharges in 9 patients, only regional slowing in the stroke zone in 7 patients. During the hospitalization 1 patient with the stroke-onset from status epilepticus died. Because of effects of PA the dose of ASMs was redused: valproic acid to 750-1000 mg, levetiracetam to 1000 mg per day. For 6-12 months patients took prescribed therapy, seizures relapsed in 2 patients with the stroke onset with series of epileptic seizures. In 13 patients epileptic seizures didn't relapse.
Conclusion: Phenozanic acid - antiepileptic drug with an antioxidant mechanism of action. It has a

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membrane-stabilizing effect, decreases epileptic system formation and allows to reduce doses of basic ASMs. Acute symptomatic seizures, neurodegenerative processes, edema, neuroinflammation, oxidative stress, metabolic disorders, changes in transcription's regulation occur during the first hours and days after acute brain damage (stroke, trauma). PA according to the literature data has a potentiating effect and may be perspective for combined use with basic ASMs in patients with acute brain injury to prevent the recurrence of epileptic seizures and to reduce the risk of dose-dependent adverse events. The results are primary and require further observation.

708 | Brivaracetam Adjunctive Therapy in Paediatric and Adult Patients With Focal-Onset Seizures in Mid-European Countries: 12-Month, Real-World Outcomes from the BRIVA-REG Study

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Purpose: Evaluate utilization/effectiveness of adjunctive brivaracetam (BRV) in pediatric and adult patients in the clinical standard-of-care setting.
Method: Final analysis from prospective, non-interventional, post-marketing study BRIVA-REG/EP0099. BRIVA-REG included patients aged ≥4 years with focal-onset seizures (FOS) with/without focal to bilateral tonic-clonic seizures in Bulgaria, Czech Republic, Greece, Hungary, Poland, Romania. Selection criteria: no prior BRV treatment, ≥1 antiseizure medication (ASM) at BRV initiation. Data for Safety Set are presented; some pediatric data were analyzed post hoc.
Results: 798 patients received ≥1 BRV dose (Safety Set), including 56 (7.0%) aged <18 years. Baseline characteristics in overall population and pediatric patients, respectively, were median age: 40.0, 13.0 years; median time since diagnosis: 14.41, 7.23 years; median number of lifetime ASMs (prior ASMs/concomitant ASMs at BRV initiation): 3.0 (n=796), 3.0 (n=56). At 12 months, BRV retention-rate (overall population, pediatric patients): 83.8% (n=798), 83.9% (n=56); ≥50% responder-rate: 82.4% (n=612), 87.5% (n=40). Clinical Global Impression of Change at 12 months versus baseline in overall population (n=667): 75.6% of physicians reported any improvement (minimally/much/very much) in their patients, 20.4% no change, 4.0% any worsening (minimally/much/very much). Patient Weighted Quality of Life in Epilepsy Inventory-Form 31 total score reported by patients aged ≥18 years: median 60.11 at baseline (n=131) and 60.88 at 12 months (n=59) (median change from baseline: 0.99 [n=46]). Pediatric Quality of Life Inventory total score reported by patients aged ≥8–<18 years: median 66.33 at baseline (n=8), 80.47 at 6 months (n=4) (median change from baseline: 5.47 [n=3]). Drug-related treatment-emergent adverse events were reported in 7.9% of overall population.
Conclusion: BRV retention- and responder-rates at 12 months suggest adjunctive BRV was effective in pediatric patients with FOS in routine clinical practice; results were similar in overall population. In overall population, >75% of physicians reported improved condition in their patients at 12 months versus baseline; BRV was well-tolerated. UCB-sponsored.

757 | A Phase 1 clinical study of BMB-101 shows linear PK and a reduced rate of somnolescense and GI/Urinary side effects compared to other 5-HT2C agonists

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Purpose: Somnolence is a common side effect seen with 5-HT2C agonists (fenfluramine, lorcaserin, and bexicaserin) used for the treatment of DEE. It can significantly impact patients' quality of life and lead to drug discontinuation. Recent studies have shown that newer 5-HT2C agonists BMB-101 demonstrates a reduced rate of somnolence compared to other agents in this class. The purpose of this abstract is to explore the potential mechanisms behind that and its correlation with the pharmacokinetics (PK) profile.
Method: Randomized, double-blind, placebo-controlled Phase I study of BMB-101 in healthy human subjects. This

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consisted of 3 parts: a single ascending dose, a food effect, and multiple ascending doses (N=76). The primary objective was to investigate the safety and tolerability of BMB-101 following single and multiple oral administration to healthy adult (18-65) subjects.

Results: BMB-101 was well tolerated at all doses, with no serious adverse events reported. The most common side effects were mild and included headaches, nausea, and oral paresthesia, the latter due to excessive sucralose in the formulation. No somnolence was observed over dose range 40-80 mg BID, which is predicted to be the effective dose/exposure range of BMB-101. Evidence of target engagement at the 5-HT2C receptor in the CNS was established based on increased prolactin secretion and quantitative EEG changes. PK was linear and dose-proportional from 40 to 120 mg/70 kg.

Conclusion: The Phase 1 clinical trial of BMB-101 has shown a decreased incidence of somnolescence compared to other 5-HT2C agonists e.g. 27.9% with Bexicaserin in Ph.2, 21% with fenfluramine in the recent Ph.3 trial. Furthermore, BMB-101 demonstrated fewer GI/Urinary side effects than other 5-HT2C agonists, e.g., Bexicaserin 28 % micturition urgency, 24 % constipation, and 20 % diarrhea. This improvement in the side effect profile, coupled with linear PK, could potentially offer a more favorable therapeutic option for patients with epilepsy.

758 | Pyridoxine and brivaracetam adherence in epilepsy

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Purpose: Although many epilepsy patients gain seizure control with antiseizure medications (ASM), side effects can be severe. Compared to its predecessor Levetiracetam (LEV), patients on Brivaracetam (BRV) experience fewer psychiatric side effects. When psychiatric side effects emerge on LEV, Pyridoxine (Vitamin B6) has been used to ameliorate these effects. Given mechanistic similarity between LEV and BRV, this study sought to determine whether B6 can promote BRV adherence in epilepsy patients.

Method: Single-center retrospective review of electronic medical records from epilepsy patients prescribed B6, BRV, or LEV from the time BRV became commercially available for prescription. Primary outcome was time to BRV or LEV discontinuation. We conducted survival analyses of patients taking BRV+B6 vs. BRV, and BRV+B6 vs. LEV+B6.

Results: We identified 107 charts over the 70-month study period. A total of 88 subjects were included. Median age was 37.5 years (IQR 29.25-51.5), 45.5% were male, mean ASM number was 2.43 (SD 1.1), 10% had VNS, and 81% had focal epilepsy. 15 patients were prescribed BRV+B6, 34 were prescribed LEV+B6, and 39 patients took BRV alone. Time to BRV discontinuation was significantly longer in the BRV+B6 group than in the group taking BRV alone (median time to discontinuation 663 vs. 408 days, p=0.0172). There were more males in the BRV+B6 than BRV groups (66.7% vs. 33.3%, p=0.035). Times to discontinuation did not significantly differ between BRV+B6 and LEV+B6 groups (p=0.1876).

Conclusion: This open-label, retrospective study suggests that Vitamin B6 can promote adherence to BRV by prolonging time to BRV discontinuation. Vitamin B6 also worked just as well promoting adherence to BRV as to LEV. These findings set the stage for larger randomized controlled multi-center studies.

764 | Safety and efficacy of vigabatrin add on compared to placebo in Lennox-Gastaut Syndrome (LennoVig): A randomized double-blind placebo-controlled trial

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Purpose: Lennox-Gastaut syndrome (LGS) is a childhood epileptic encephalopathy, and often refractory to ant seizure medication (ASM). We report the safety and efficacy of adjunctive vigabatrin compared to placebo in the patients with LGS.

Method: Children aged 2 to 18 years with LGS were included. After screening, patients were observed for 1 month during which caregivers were trained to maintain a diary noting down the daily seizure frequency, seizure type and drop attacks. The demographic details, clinical details, and the Clinical Global Impression Scale (CGIS) were recorded. Patients were randomized to vigabatrin (25/kg in first week and 50/kg ~4g/day in 2 divided doses) or identical looking placebo using simple 1:1 randomization. Midazolam nasal spray was advised if there was frequent generalized tonic clonic seizure. Outcome was defined at 3-month. The primary outcome was > 50% reduction in drop attacks, and secondary outcomes were 1)

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percentage change in drop attacks, 2) ≥ 50% reductions in all seizure types, 3) number of seizure free days, 4) improvement in the CGI-S and 5) adverse events.

Results: 47 patients received vigabatrin and 45 received placebo. The baseline characteristics were comparable between the groups. Higher proportion of patients in vigabatrin group achieved primary outcome compared to placebo (51.1% vs 8.9%; P <0.01). Vigabatrin resulted in reduction in all types of seizure except generalized tonic-clonic seizure. Vigabatrin reduced total number of seizures (-40.5% vs 2.6%; P= <0.01), and increase seizure free days (4.6 vs 0.53 days; P=0.02) compared to placebo. The CGIS also improved in vigabatrin group. Adverse effects were comparable except sedation was more frequent in vigabatrin group (P<0.01).

Conclusion: In LGS, vigabatrin is effective in reducing drop attacks, and focal, myoclonic and atypical absence seizures along with improvement in the CGIS.

792 | Efficacy of Stiripentol Beyond Generalized Tonic-Clonic Seizures: A Retrospective Analysis of Dravet and Non-Dravet Patient Records

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Purpose: Stiripentol, approved for Dravet syndrome (DS) with clobazam and/or valproate for refractory generalized tonic-clonic seizures, has limited data in other refractory epilepsies.

Method: This retrospective study analyzed stiripentol efficacy and safety in patients ≤15 years with refractory epilepsies (DS and non-DS) treated from 2014 to 2023.

Results: 18 DS and 17 non-DS patients (76.5% of the latter with developmental and epileptic encephalopathy) initiated STP at median ages of 40 [4-179] and 64 [5-180] months, with median doses of 50 [20-100] and 35 [4-100] mg/kg/day (p = 0.032), respectively. Prior to stiripentol, DS patients used a median of 4.5 antiseizure medications (ASMs), and non-DS patients used 9 (p = 0.002). At stiripentol initiation, they were on 2 and 3 concomitant ASMs, respectively. After three months of STP, seizures improved in 76.5% of non-DS and 61.1% of DS patients. Seizure frequency reduced by ≥50% in 44.4% of DS and 58.8% of non-DS patients, and by ≥75% in 38.9% of DS and 41.2% of non-DS patients. 20% achieved seizure freedom. Efficacy was sustained in 90.9% of DS and 69.2% of non-DS patients for a median of 87 and 13 months, respectively (p = 0.052). Sustained STP efficacy was more probable in DS (120 months) than non-DS (16 months; p=0.012). STP reduced all seizure types and resolved status epilepticus in 5 patients (median 0.5 days). STP also improved cognition and Clinical Global Impression scale scores in ~60% of all patients. Adverse events (AEs) occurred in 44.1% of all patients. Severe AEs were only reported in three DS patients, leading to two discontinuations. Six non-DS patients (35.3%) discontinued ≥1 other ASM post-STP.

Conclusion: Add-on STP improved various seizure types in children with refractory epilepsy, including syndromes other than DS. It also positively impacted comorbidities and was effective in terminating status epilepticus. STP is generally well tolerated. Biocodex support

801 | Characterizing Seizure Free Epochs based on Anti-seizure Medications Failed for Patients with Focal Treatment Resistant Epilepsy (FTRE)

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Purpose: Prior studies suggest that after failure of 6 ASMs, there may be futility of trying additional ASMs. The Human Epilepsy Project 2 (HEP2) is a prospective, observational multicenter US study with the goal of identifying treatment response in FTRE. Here, we characterize seizure free epochs in relation to the number of ASMs failed.

Method: All subjects had FTRE, failed ≥4 ASMs, were 16-65 years old, and were followed for 18-36 months. At enrollment, subjects provided data on prior and current ASMs, devices, surgeries. Prospective seizure tracking involved seizure diaries, monthly coordinator check-ins, and medical record review. Subjects who provided sufficient medication and seizure data without surgery/devices placed within 6 months of seizure free epochs were analyzed. Baseline seizure rate was determined from the first 3 months of tracking. Subjects were analyzed in ≥3-month seizure free, ≥6-month, or no seizure free epoch cohorts. Student's t-test was used to analyze differences in ASMs failed between cohorts.

Results: 125/146 subjects met analysis criteria. Average age was 40 ±12, average epilepsy duration was 20 ±13, and 59.5% were female. The average baseline seizure rate

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was 19.5 ±39.2. 16 subjects had seizure free epochs ≥3-month, 9 ≥6-month, 107 no seizure free epochs. Average ASMs failed for the no seizure free epochs cohort was 8 ±3.8, for the ≥3-month cohort 7.4 ±3.2, and for the ≥6-month cohort 7.8 ±3.7 (p=NS).

Conclusion: There were no significant differences in baseline seizure rate or ASMs failed between subjects who had seizure free epochs and those who didn't. The seizure free epoch cohorts also had subjects who failed up to 14 ASMs. These data suggest continued ASM trials for FTRE patients can improve seizure burden even in patients with high ASM failure rates. HEP2 received funding from UCB, who had no role in the design/conduct of study/collection/management/analysis, or interpretation of data.

805 | How could cenobamate influence the plasma lipid levels in epilepsy patients

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Purpose: Epilepsy is a chronic condition requiring long-term treatment with one or more antiseizure medications (ASM). Patients with epilepsy in comparison to the general population have shown a higher incidence of vascular disease. Moreover, the use of certain ASM seems to increase the risk of developing dyslipidemia. So, we aimed to evaluate the influence of cenobamate (CNB) on plasma lipid levels in adult epilepsy patients.

Method: We proceed to an observational and prospective study, including patients with refractory epilepsy who started treatment with CNB. Clinical assessments were performed at baseline, 3, 6 and 12 months. Blood samples for lipid profile were collected at baseline and 12 months of follow-up. As a marker of dyslipidemia, the low-density lipoprotein cholesterol (LDL-C) level was calculated using Friedewald equation.

Results: Twenty three patients (56.5% male) were included with a mean age of 35±10.4 years. Treatment efficacy of CNB at 12 months was 85%, with reduction in seizure frequency greater than 75% in 58.8% and three patients (17.6%) were seizure-free. Three patients discontinued CNB during the follow-up due to a lack of efficacy. At 12 months, 75.0% of patients reported at least one side effect, such as drowsiness or imbalance. At baseline evaluation, three patients (13.0%) had previous history of vascular risk factors (VsRF). The mean LDL-C levels for the non-VsRF and VsRF groups were 117.5±37.0 and 137.3±46.8mg/dL, respectively. One year after the initiation of CNB, the levels in the VsRF group significantly increased to 166.9±12.6mg/dL (p=0.011), while the non-VsRF group remained around 117.6±31.1mg/dL. Also, seven patients (35.0%) increased their body weight with a mean of 3.95±2.0Kg. The LDL-C baseline level was not associated with age, gender or epilepsy duration.

Conclusion: According to our results, routine monitoring of body weight and LDL-C level, especially in patients with previous vascular risk factors, is recommended.

831 | Drug repurposing based on integrated in silico and in vitro approach to find a therapy for KCNA2-related disorders

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Purpose: Variants in *KCNA2* (Kv1.2) causing loss-, gain-of-function (LoF, GoF) and mixed LoF/GoF defects cause rare neurological disorders including developmental and epileptic encephalopathy (DEE) and ataxia, ranging from mild to severe (Masnada et al., Brain 2017,140(9):2337-2354; Imbrici et al., IJMS 2021;22(18):9913). Antiseizure medications have variable effects and drug-resistance occurs in most patients affected by DEE. 4-aminopyridine, a non-selective Kv1 blocker, is the only precision medicine approach trialed in some patients carrying GoF variants (Hedrich et al., Sci Transl Med. 2021;13(609):eaaz4957). Thus, new molecules acting on Kv1.2 need to be developed. This study aims to identify approved drugs to be repurposed in *KCNA2*-related disorders.

Method: Using a homology model of Kv1.2 channel, multiple-grid structure-based virtual screening has been performed by using a collection of about 2000 approved drugs. The automated patch clamp platform, Patchliner (Nanion) has been used to validate in silico data on Kv1.2 channels and E236K mixed LoF/GoF mutant expressed in HEK293 cells.

Results: A pool of repurposed drugs has been identified as promising modulators of Kv1.2 including paroxetine and fluvoxamine, selective serotonin reuptake inhibitors (SSRIs), and cannabidiol, recently approved as add on for rare epilepsies. Fluvoxamine blocked Kv1.2 with IC50 ~8.1±1.9 μM and E236K channels with IC50 ~12.2±4.6

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μM. Similar block has been observed for paroxetine (IC50 ~8.9±4.4 μM for Kv1.2 and ~7.5±3.7 for E236K). Cannabidiol blocked both channels with lower affinity (IC50 ~40.3±15.4 μM for Kv1.2 and ~52.1±26.0 μM for E236K).

Conclusion: Our results suggest that two SSRIs, paroxetine and fluvoxamine, are potential repurposing candidates for children harboring *KCNA2* GoF or mixed variants. These data support previous findings showing the effect of fluoxetine on other potassium channels variants (Ambrosino et al., Epilepsia 2023;64(7):e148-e155). Our data also suggest that cannabidiol, a drug with multitarget activity, may modulate Kv1.2 activity, albeit with a low affinity.

851 | Use of oral cannabis in a drug-resistant epilepsy: A five-year single center experience

YH Kim[1], HJ Kim[2], S Jang[2], H-J Yun[3], JH Cha[1], JM Kim[1], S Lee[1], SY Kim[1], J-H Chae[1], KJ Kim[1], BC Lim[1], W Kim[1]

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Purpose: Purified cannabidiol (CBD) has been approved by the Korean government as a treatment for drug-resistant epilepsy (DRE) since 2019. We aimed to investigate the long-term efficacy, tolerability, and predictors of favorable outcomes in pediatric DRE patient treated with CBD.

Method: We included 96 pediatric patients treated with CBD (including 40 whom tapered-off) who visited the Department of Child Neurology from March 2019 to July 2024. Follow-up data were collected until CBD discontinuation or up to 36 months. CBD efficacy was assessed by seizure frequency (categorized as seizure-free, >50% reduction, <50% reduction, or no effect) and reduction in the number or dosage of anti-seizure medications (ASMs). Adverse effects were monitored to evaluate safety.

Results: The median (Q1, Q3) age at CBD initiation was 9.7 (6.4, 14.7) years, with its median treatment duration of 18.3 (5.1, 37.6) months. The proportions of children who used CBD for more than 12, 24, and 36 months were 57.3%, 41.7%, and 26.0% respectively. The proportion of children who achieved seizure free or a >50% reduction at 12 month was 43.8%, while the proportions at 24 and 36 months were 34.4% and 24.0%, respectively. During the period of CBD use, 10% of the children reduced the number of ASMs, and additional 9.4% reduced the dosage of their ASMs. The most prevalent reasons for tapering off CBD was poor efficacy (26/40), followed by gastrointestinal symptoms (5/40) and somnolence (4/40).

Conclusion: In pediatric patients with DRE, CBD may be a useful treatment option that allows the reduction or reducing concomitant ASMs. CBD was also shown to be able to be used safely long-term. Proper monitoring of adverse effects and tailored dosage modification should be accompanied.

877 | Two-year safety, efficacy, and retention of Cannabidiol (CBD) as add-on therapy in patients with refractory epilepsy

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Purpose: We aimed to assess real-life safety, efficacy, and retention of Cannabidiol (CBD**)** as adjunctive therapy in Cypriot patients with refractory epilepsy of any etiology.

Method: Thirty-three adult patients (including two with Tuberous Sclerosis and three with Lennox-Gastaut Syndrome) followed at a tertiary epilepsy center were studied retrospectively for two years after the addition of CBD in their Antiseizure Medications (ASMs). CBD dose ranged between 5-20 mg/kg/day. Data on seizure frequency, seizure intensity, treatment-emergent Adverse Events (AEs), and overall CBD effect were obtained from medical files and patient and caregiver diaries.

Results: At the time of CBD initiation, the mean illness duration was 26 (9-58) years and patients were experiencing a mean of 14 (1-60) seizures per month. Patients had failed a mean of 8 (3-12) ASMs and combinations thereof. CBD was added to a mean of 4 (1-6) concomitant ASMs. Sixteen patients (48%) were under treatment with Vagus Nerve Stimulation (VNS). Twenty-seven patients (82%) completed two years of treatment. A mean reduction of 25% in monthly seizure frequency was observed compared to baseline (p=0.067). Six patients (18%) discontinued CBD treatment: four due to AEs (transaminase elevation, somnolence, aggression, and sialorrhea), and two patients due to seizure frequency increase. CBD retention rate was 82%. Thirteen patients (39%) responded to CBD treatment achieving seizure reduction of ≥50% sustained for 24 months, whilst one patient (3%) became seizure-free. Subjective sustained improvement in seizure frequency, seizure intensity, and/or patient behavior was reported by 55% of caregivers. None of the baseline characteristics was found to affect the probability of patient response to CBD

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treatment. AEs were reported by nineteen patients (58%). Most frequently reported were somnolence (18%), irritability (15%), and nausea (9% of patients).

Conclusion: Cannabidiol was proven to be a safe and effective addition to anti-seizure medications in our population of highly pharmacoresistant patients.

911 | Post-hoc Analysis of Fenfluramine for Lennox-Gastaut Syndrome by Baseline Frequency Quartiles of Seizures Associated With a Fall

KG Knupp[1], R Nabbout[2], IE Scheffer[3], J Sullivan[4], SM Zuberi[5], KC Nickels[6], L Lagae[7], R Guerrini[8], J Wheless[9], B Ceulemans[10], P Healy[11], M Langlois[12], J Abraham[11], A Lothe[12], A Gil-Nagel[13]

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Purpose: In this post-hoc analysis, baseline frequency of seizures associated with a fall was used as a surrogate marker of disease severity to evaluate efficacy and safety of fenfluramine (FFA) in patients with Lennox-Gastaut syndrome (LGS) who participated in the randomized controlled trial (RCT, NCT03355209).

Method: In the RCT, patients were randomized to FFA 0.2 mg/kg/day or FFA 0.7 mg/kg/day (maximum = 26 mg/day) or placebo. For this analysis, median change from baseline in frequency of seizures associated with a fall and incidence of treatment-emergent adverse events (TEAEs) in ≥10% of patients were reported by quartiles (quartile 1 [Q1], quartile 2 [Q2], quartile 3 [Q3], and quartile 4 [Q4]) of baseline frequency of seizures associated with a fall. Descriptive statistics were used.

Results: Numbers of seizures associated with a fall/28 days per quartile were: Q1: 2-34, Q2: 35-76, Q3: 77-175, Q4: >175 seizures. Over the study, median percent change from baseline in frequency of seizures associated with a fall for placebo (n=87), FFA 0.2 mg/kg/day (n=89), and FFA 0.7 mg/kg/day (n=87), respectively, were: Q1: 7.6%, -39.1%, -27.7%; Q2: -15.7%, -8.8%, -31.6%; Q3: -21.3%, -33.1%, -36.3%; Q4: -11.2%, -7.7%, -13.5%. In each of the four quartiles, decreased appetite and fatigue occurred in ≥10% of patients on FFA 0.7 mg/kg/day. Ratings of clinically meaningful improvement on Clinical Global Impression-Improvement (CGI-I) scale by investigator and caregiver at last visit and additional analyses on change in generalized tonic-clonic seizure (GTCS) by baseline GTCS frequency will be reported.

Conclusion: In this post-hoc analysis, greater median percent reductions in seizures associated with a fall were observed in all quartiles in patients on FFA 0.7 mg/kg/day versus placebo. Additionally, both FFA treatment doses were well tolerated; thus, baseline LGS severity did not impact FFA safety/ tolerability. These results support FFA use across a spectrum of LGS disease severity. UCB-supported.

917 | A Stratified Analysis of Efficacy and Safety of Fenfluramine in Patients With Dravet Syndrome

R Nabbout[1], J Sullivan[2], S Auvin[3], B Ceulemans[4], JH Cross[5], O Devinsky[6], A Gil-Nagel[7], R Guerrini[8], KG Knupp[9], MS Perry[10], R Sanchez-Carpintero[11], IE Scheffer[12], N Specchio[13], A Strzelczyk[14], J Wheless[15], EC Wirrell[16], D Morita[17], M Langlois[18], P Healy[19], A Lothe[18], L Lagae[20]

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Purpose: Three pivotal phase 3, double-blind, placebo-controlled, randomized clinical trials (RCTs) of fenfluramine (FFA) in Dravet syndrome (DS) were pooled and stratified by baseline characteristics not originally reported.

Method: Pooled data from patients (2-18 y) with DS treated with placebo, 0.2 or 0.7 mg/kg/d FFA (0.2FFA, 0.7FFA) without stiripentol (STP), or 0.4 mg/kg/d FFA with STP (0.4FFA+STP) were included across 3 studies (NCT02682927, NCT02826863, NCT02926898). Pooled data were stratified by FFA initiation age (<4y and ≥4y), severity (number of failed antiseizure medications [ASMs]: 1-3, 4-6, and 7+), and *SCN1A* pathogenic variant status (+ or -). Baseline characteristics, safety, median percentage change in monthly convulsive seizure frequency (MCSF), and proportion of patients with clinically meaningful improvement (much or very much improved) on Clinical Global Impression—Improvement (CGI-I) (caregiver and investigator) were assessed.

Results: Across the RCTs, 348 patients were included; 0.2FFA (n=85), 0.4FFA+STP (n=43), 0.7FFA (n=88) and placebo (n=132). Most patients were ≥4y (83.7%-89.4%) and *SCN1A*+ (70.6%-81.4%). Many patients failed 4-6 (31.8%-48.8%) or 7+ ASMs (34.8%-57.6%); however, no patients treated with 0.4FFA+STP failed 7+ ASMs. Treatment-emergent adverse event rates were similar across groups (81.8% [placebo]–97.7% [0.4FFA+STP]). Highest FFA dose groups experienced the greatest percentage MCSF reduction vs placebo. In patients treated with 0.4FFA+STP, MCSF reductions were highest in patients <4y, with 4-6 failed ASMs, or who were *SCN1A*-. Frequency of clinically meaningful improvement on CGI-I was higher with FFA treatment (pooled) vs placebo. CGI-I scores were consistent across stratified groups (detailed data to be presented).

Conclusion: FFA is associated with improved seizure and non-seizure outcomes relative to placebo, regardless of age, severity, or *SCN1A* status. Results are considered nominal due to the post-hoc nature of this analysis. Larger samples of each population of interest may provide a better understanding of benefits seen with different DS populations, concomitant ASM synergies, and FFA doses. UCB-supported.

921 | Tolerability and Safety of Fenfluramine and Global Functioning of Patients in a Combined Open-label Extension Study of Children and Adults With Dravet and Lennox-Gastaut Syndromes

A-S Schoonjans[1], KG Knupp[2], A Gil-Nagel[3], B Gunning[4], EA Thiele[5], IE Scheffer[6], R Sanchez-Carpintero[7], N Specchio[8], R Nabbout[9], N Dickson[10], A-L Schulz[11], L Perrin[12], M Langlois[13], A Lothe[13], J Sullivan[14]

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Purpose: To describe long-term safety of fenfluramine (FFA) and global functioning in children and adults with Dravet syndrome (DS) or Lennox-Gastaut syndrome (LGS).

Method: This open-label extension (OLE) study (NCT03936777) enrolled patients who had participated in FFA open-label studies: NCT02823145 (DS), NCT03355209 (LGS), or NCT03467113 (DS/LGS, FFA+concomitant cannabidiol). Last FFA doses from the previous studies were

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continued (maximum FFA 0.7 mg/kg/day without stiripentol [26 mg/day] or FFA 0.4 mg/kg/day with stiripentol [17 mg/day]). At least 1 concomitant anti-seizure medication (ASM) was required; ASM dose changes or additions were permitted if clinically warranted. Primary objective was assessment of safety and tolerability, including cardiovascular safety. Clinical Global Impression-Improvement (CGI-I) ratings by investigator and caregiver at last visit were used for evaluating global functioning compared with baseline of this OLE study. Descriptive statistics were used.

Results: 412 patients were enrolled (DS: 265 [64.3%], LGS: 147 [35.7%]). Mean±SD age was 14.1±6.8 years (2–<18 y: 69.2%; ≥18 y: 30.8%). 352 patients (85.4%) completed the study, 50 (12.1%) discontinued, 10 (2.4%) are ongoing. Median FFA duration in this OLE: 729.5 days (range, 8-1544). No patient experienced clinically confirmed valvular heart disease or pulmonary arterial hypertension. 311/412 (75.5%) patients reported ≥1 treatment emergent adverse event (TEAE) and 5 (1.2%) reported treatment-related serious TEAEs; 3 patients died (unrelated to FFA). TEAEs occurring in ≥5% of patients: coronavirus infection (20.6%), seizure (15.3%), pyrexia (13.1%), nasopharyngitis (11.9%), diarrhea (7.3%), decreased appetite (6.1%), upper respiratory tract infection (5.8%), somnolence (5.1%). On last visit CGI-I (n=401), investigators and caregivers rated 376 (93.8%) and 373 (93.0%) patients, respectively, as "improved or no change" compared to this OLE baseline.

Conclusion: These data reveal no new or unexpected safety signals and sustained clinical benefit by investigator and caregiver CGI-I ratings, supporting long-term FFA treatment for children and adults with DS or LGS.

UCB-supported.

926 | Impact of Fenfluramine on Convulsive Seizure Frequency in Dose-Capped Patients With Dravet Syndrome

R Nabbout[1], KG Knupp[2], L Lagae[3], JH Cross[4], J Sullivan[5], A Gil-Nagel[6], R Guerrini[7], A Strzelczyk[8], M Langlois[9], P Healy[10], A Lothe[9], IE Scheffer[11]

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Purpose: Dravet syndrome (DS) is a rare treatment-resistant developmental and epileptic encephalopathy characterized by seizure onset within the first year of life and developmental delay. Fenfluramine is approved in the United States, European Union, United Kingdom, Israel, and Japan for seizures associated with DS in patients ≥2 years old. Weight-based fenfluramine dosing and daily fenfluramine maximum dose guidelines may cap heavier patients below their therapeutic dose. Here, we determined fenfluramine effectiveness in dose-capped patients with DS.

Method: Patients with DS who completed any of three randomized controlled trials (RCTs) were eligible to enroll in a 36-month open-label extension (OLE; NCT02823145). At RCT completion, patients were re-initiated with fenfluramine 0.2 mg/kg/day for 4 weeks, and then titrated to effect and tolerability with a maximum dose of 0.7 mg/kg/day (maximum 26 mg/day) or 0.4 mg/kg/day (maximum 17 mg/day) with concomitant stiripentol. Patients weighing ≥37.5 kg were potentially dose-capped if the maximum daily dose was reached before reaching 0.7 mg/kg/day (or 0.4 mg/kg/day with stiripentol). In this post-hoc analysis, median percentage change in monthly convulsive seizure frequency (MCSF) from RCT baseline to OLE Month 2 to end-of-study (EOS) was assessed.

Results: Of 374 patients who received fenfluramine, 93 (24.9%) were dose capped. Mean baseline age (SD) was 13.4 (2.9) years old (range, 7-18 years). Mean (SD) baseline bodyweight was 49.9 (13.2) kg (range, 28.3-99.7 kg). Median percent change in MCSF from Month 2 to EOS was -69.06 (range, -100 to 285.4), -62.80 (range, -100 to 247.5), and -61.56 (range, -99.2 to 90.8) in patients weighing <37.5 kg, ≥37.5 kg, and ≥37.5 kg + dose-capped, respectively (nominal Wilcoxon signed rank $P<0.0001$ for each).

Conclusion: Patients weighing ≥37.5 kg and receiving the maximum daily dose of fenfluramine (i.e., dose-capped) experienced similar MCSF change from RCT baseline as patients who were not dose-capped. UCB-supported.

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942 | Neuropsychiatric symptoms in patients with epilepsy on levetiracetam monotherapy and its correlation with biomarkers levels and neuroimaging findings

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Purpose: This study aimed to investigate the association of adverse events, particularly neuropsychiatric events (NPEs) with biomarkers and neuroimaging findings in persons with epilepsy (PWE) on levetiracetam (LEV) monotherapy.

Method: A cohort of 141 PWE on LEV monotherapy and 20 healthy controls (HC) were recruited for the study. Neuropsychiatric assessments were conducted using MINI and DASS-21. On the basis of MINI, PWE were divided into NPE+ (with neuropsychiatric-events) and NPE- (without neuropsychiatric-events). Neuroendocrine parameters (BDNF and S100B) and neuroimaging analyses (HD-EEG and fMRI) were performed on a subset of LEV patients.

Results: As per MINI scale, 59 were NPE+ among 141 PWE. DASS-21 also revealed significant difference in depression, stress and anxiety between NPE+ and NPE- (p=0.04; 0.045, 0.001 respectively). BDNF levels in NPE+ (n=30) were significantly high compared to the NPE- (n=36) and HC (p=0.023 & p=0.018 respectively). In HD-EEG, NPE- (n=16) showed significantly lower Delta wave activity (linked to deep sleep) in regions like F7, T7, and F3 compared to NPE+ (n=14), and in P7, O1, and F4 compared to HC. Theta activity in the F4 region was lower in NPE+, while Alpha activity in O2 region were higher than HC. Gamma waves were significantly lower in C3 region compared to all LEV patients. In fMRI, comparison of connectivity between region of interests (T-50) between NPE+ (n=14) vs NPE- (n=16) revealed significant difference in Middle Temporal Gyrus posterior division (8.72 vs 7), Parahippocampal Gyrus anterior division (9.52 vs a8.77), Inferior Temporal Gyrus temporooccipital (7.88 vs 7.09), Middle Temporal Gyrus temporooccipital part (6.66 vs 6.89), Inferior Temporal Gyrus, anterior division (5.59 vs 5.98).

Conclusion: About 42% PWE on LEV had neuropsychiatric symptoms, and these subjects were with higher BDNF levels. Similarly, the HDEEG and fMRI revealed significant difference between these two groups suggesting potential association with NPE.

955 | Non-seizure benefits of long-term fenfluramine treatment in pediatric patients with Dravet syndrome

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Purpose: Evaluate the impact of long-term fenfluramine treatment on cognition, adaptive behavior, quality of life (QoL), and caregiver burden in pediatric patients with Dravet syndrome.

Method: Pediatric patients with Dravet syndrome, initiating fenfluramine treatment between February 2017 and October 2023, were assessed by a neuropsychologist. Fenfluramine-related benefits on cognition (via The Bayley Scales of Infant and Toddlers Development (Bayley-IV), or The Wechsler Intelligence Scale adapted to age), adaptive behavior (Vineland Adaptive Behavior Scales (VABS-III)), sleep (using Sleep Disturbance Scale for Children (SDSC)), QoL (using QoL in children with Epilepsy (QOLCE-55)), and other behavioral aspects (Behaviour Rating Inventory of Executive Function (BRIEF), Aberrant Behavior Checklist (ABC), Social Responsiveness Scale (SRS-2), Strength and Difficulties Questionnaire (SDQ)) were measured. Caregiver burden was estimated using (Depression, Anxiety and Stress Scale (DASS-21), Parental Stress Scale (PSS), International Trauma Questionnaire (ITQ) score for post-traumatic stress, and Perceived Control-VAS (PC-VAS)). Seizure outcomes were retrieved from medical records.

Results: All patients (n=20, 10 girls) had a verified pathogenic *SCN1A* variant, with a mean age of 12 years (range 4-23). Fenfluramine treatment lasted a mean of 59 months (range 25-93), at a mean maintenance dose of 0.57 mg/kg/day (range 0.24-0.7). A mean 75% reduction (range 30-100%) in generalized tonic-clonic seizures was observed at the last follow-up. Preliminary cognitive data from 9 children (mean age: 10.8 years, SD: 5.9, range 4-18; mild/moderate/severe: n=4/4/1) were markedly below population norms but appear improved relative to a Swedish fenfluramine-naïve cohort, especially in social functioning (mean (SD) scores: Adaptive behavior composite: 57.9 (11.5); Communication ability: 53.0 (16.3); Daily

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functioning skills: 52.6 (17.7), Social ability: 60.0 (12.3), Motor ability 65.9 (9.5)). Cognitive and caregiver burden evaluations are ongoing.

Conclusion: Findings will provide valuable insights into fenfluramine seizure efficacy in pediatric patients with Dravet syndrome and its impact on daily functioning and caregiver burden

957 | Prospective evaluation of fenfluramine use in a cohort of pediatric and adult patients with Dravet syndrome

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Purpose: Assess whether fenfluramine treatment affects cognition and adaptive behavior in pediatric and adult patients with Dravet syndrome, and if the outcome impacts caregiver burden

Method: We aim to prospectively include 15 patients with Dravet syndrome (verified by pathogenic *SCN1A* variants) starting fenfluramine treatment between August 2023 – August 2025. Generalized tonic-clonic seizure frequency, comprehensive neuropsychologist assessment, and caregiver burden will be measured before and one year after fenfluramine initiation. Outcomes include fenfluramine-related non-seizure benefits, measured in terms of cognition (via Bayley Scales of Infant and Toddler Development (Bayley-IV), or The Wechsler Intelligence Scale adapted to age), adaptive behavior (via Vineland Adaptive Behavior Scales (VABS-III)), sleep (via Sleep Disturbance Scale for Children (SDSC)), quality of life (via Quality of Life in Children with Epilepsy (QOLCE-55)), and additional behavioral aspects (via the Behavior Rating Inventory of Executive Function (BRIEF), Aberrant Behavior Checklist (ABC), Social Responsiveness Scale (SRS-2), and Strengths and Difficulties Questionnaire (SDQ)). EEG data, treatment dosages, and efficacy will be extracted from medical records. Caregiver burden will be assessed via the Depression, Anxiety, and Stress Scale (DASS-21), Parental Stress Scale (PSS), International Trauma Questionnaire (ITQ) for post-traumatic stress, and Perceived Control-VAS (PC-VAS).

Results: To date, 2 pediatric patients (aged 4-6 years, 1 female) and 5 adult patients (aged 24-46 years, 2 females) have been enrolled and completed pre-fenfluramine evaluations. Preliminary cognitive data for 2 children (3-6 years), and 2 adults (32-36 years) (severity: normal (n=1), mild (n=1), severe (n=1), profoundly severe (n=1)) were markedly below population norms, and in line with a Swedish fenfluramine-naïve cohort (mean (SD) scores: Adaptive behavior composite: 46.3 (30.9); Communication ability: 46.8 (31.0); Daily functioning skills: 45.0 (29.6), Social ability: 49.0 (35.4)).

Conclusion: Once assessed overall, findings will provide valuable insights regarding impact of fenfluramine treatment on daily functioning in patients with Dravet syndrome and their caregivers. Study funded by UCB

967 | A time based analysis for Cenobamate use in focal epilepsy

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Purpose: This study aimed to assess the clinical response to add-on cenobamate (CNB) through a time-to-event approach and explore the potential contribution of the concomitant classes of antiseizure medications (ASMs).

Method: A subgroup analysis of a larger retrospective, multicenter study on adults with focal-onset seizures participating in the Italian Expanded Access Program at 5 pre-established centers. The primary endpoint was the time-to-baseline seizure count; secondary endpoints included the rates of seizure response, seizure freedom, treatment discontinuation and adverse events (AEs).

Results: Data on 92 participants were extracted, with a median age of 44 (29.25-50.75) years. Baseline seizure frequency was reached by 59/92 (64.1%) subjects during the 12-month follow-up. A higher, but not statistically significant probability of reaching the number of baseline seizures was shown in the subgroups of subjects taking CNB with sodium channel blockers (SCBs) (HR: 2.75; 95% CI: 0.79-9.61, p=0.112) and both SCBs and GABAergics (HR: 1.48; 95% CI: 0.43-5.09, p=0.536) compared with subjects taking GABAergics without SCBs. At 12 months, the rates of seizure response, seizure-freedom and treatment discontinuation were 42.0%, 13.6% and 23.9%, respectively. A total of 47/92 (51.1%) subjects experienced AEs (mainly

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somnolence, dizziness, and balance disorders) at a median time of 61 (30-101) days. There was a higher, but not statistically significant risk of AEs occurrence in subjects treated with both SCBs and GABAergics and in those taking SCBs without GABAergics (HR: 2.24; 95% CI: 0.51-9.82, p=0.286 and HR: 1.40; 95% CI: 0.31-6.39,p=0.661, respectively) compared with those taking GABAergics without SCBs.

Conclusion: This time-to-event analysis added new insights to the currently available evidence about the real-world effectiveness of add-on CNB. Explorative estimates suggested favorable trends for subjects treated with concomitant GABAergics and without SCBs, who seemed to reach baseline seizure frequency and experience AEs less frequently and later than subjects treated with other concomitant ASMs.

968 | The Bright Side of Drug Load: How Third-Generation Antiseizure Medications Reshape Treatment Strategies in People with Epilepsy

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Purpose: To assess the impact of one-year adjunctive treatment with third-generation antiseizure medications (ASMs) on drug load in adult people with epilepsy. Total and stratified drug load (by concomitant ASM class and therapy response) were analyzed to provide insights for optimizing treatment strategies.

Method: Data were collected in a larger multicenter, retrospective study (Roberti R et al., *Epilepsia* 2024;65:456-472). Total drug load was quantified as the sum of the ratios (daily dose/defined daily dose as provided by the World Health Organization) for each ASM in the individual regimen. Concomitant ASMs were categorized by their main mechanism of action and ability to strongly induce enzyme metabolism. Statistical comparisons were performed using the t-test or nonparametric tests (Wilcoxon matched-pairs signed-rank or Mann-Whitney) depending on the normality distribution of continuous variables.

Results: Complete dosage data were available for 613 patients (51.5% females, median age 44 years), with structural epilepsy (51.7%) and focal seizures (70%), who were previously treated with a median of 3 ASMs. Adjunctive therapies included perampanel (PER; 35.1%), lacosamide (LCM; 29.5%), brivaracetam (BRV; 24.3%), and eslicarbazepine acetate (ESL; 11.1%) added to a median of 2 concomitant ASMs. After one year of treatment, total drug load significantly increased across subgroups (median percentage increases: BRV, 100%; ESL, 67.95%; LCM, 33.33%; PER, 35.71%) and was higher for nonresponders (p=0.0048 in the PER group; p<0.0001 in others). Concomitant drug load decreased significantly, particularly for SV2A ligands and ASMs with multiple mechanisms of action (MoA) in the ESL group, and sodium channel blockers, SV2A ligands, and ASMs with MoAs in the LCM and PER groups.

Conclusion: Adjunctive therapy with third-generation ASMs increased total drug load but allowed redistribution and reductions in specific concomitant ASM classes. Nonresponders exhibited higher total drug loads, highlighting the need for optimizing treatment strategies to enhance efficacy and minimize drug burden.

1009 | An open-label, observational, prospective, multicenter study to evaluate the long-term efficacy and safety of perampanel as monotherapy in subjects age 4 years and older with focal onset seizures: PORTABLE Study

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Purpose: We investigated the efficacy and safety of Perampanel (PER) as a first-line monotherapy over a long period of time, and its impact on quality of life (QOL).

Method: Patients with new-onset/recurrent epilepsy with focal onset seizures starting treatment with PER monotherapy were enrolled. All patient signed an informed consent. The observation period was up to 30 months. During the COVID-19 period, the research was carried out as a semi-virtual clinical study, and the digital technology of eConsent, ePRO (Patient Reported Outcome) was incorporated. The study was carried out as a multi-institutional collaboration of 15 facilities in Japan. The primary endpoint was the rate of seizure freedom at 24 months, and the secondary endpoints were the rates of seizure freedom at 6, 12, 18, and 30 months, the rate of retention of PER, and QOL (EQ-5D etc.). In addition, safety was evaluated based on the number of adverse events reported.

Results: Sixty-one patients (mean age 38 years old, 25 were woman) were enrolled between May 2021 and June 2022. The mean baseline seizure frequency was 2.9 times/month. The starting dose of PER was <2 mg in 26.2% and 2 mg for 72.1%. The modal dose (the dose used for the longest period during observation) was median 3.0 mg/mean 3.2 ± 1.5 mg. At 24 months, the seizure-freedom rate was

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83.3% (95% CI: 67.2-93.6%), the retention rate was 67.2% (95% CI: 53.5 – 77.7%) and QOL was stable. The most common adverse reactions were somnolence (14.8%), dizziness (11.5%), and psychiatric disorders including irritability (8.2%).

Conclusion: The study confirmed efficacy and safety of PER as a first-line therapy in patients with epilepsy who are naïve to anti-seizure medications at 24 months of treatment, suggesting that PER may also be a treatment option for patients with new-onset/recurrent epilepsy. Funded by Eisai Co., Ltd. (Tokyo, Japan)

1022 | Cenobamate treatment for drug-resistant epilepsy: A quality of life and drug utilization study from an Italian pharmacy

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Purpose: Cenobamate is a drug approved by the European Medicines Agency in 2021 as adjunctive therapy for seizures in adults with drug-resistant epilepsy inadequately controlled by at least two antiepileptic drugs. Its exact mechanism of action remains unclear. Cenobamate is prescribed in a titrated dosage, starting at 12.5mg/day and increasing up to 400mg/day. This study aims to evaluate drug utilization, therapeutic adherence and quality of life (QoL) improvements in patients who received cenobamate from an Italian pharmacy, following prescription appropriateness assessments.

Method: Cenobamate disbursements from September 2022 to May 2024 were analyzed to evaluate therapeutic adherence and QoL, using an anonymous questionnaire based on the Morisky scale. Data collected included patient demographics (age, gender, epilepsy type, polytherapy with other antiseizure drugs), compliance and adherence.

Results: The study included 34 patients with focal structural, drug-resistant epilepsy, including one off-label prescription for early childhood epileptic encephalopathy. The cohort was 56% female and 44% male, with a mean age of 38.5 years. Age distribution:59% aged 30–50 years, 20%(18–30 years), 18% >50 years, and 3%(0–18 years), all with childhood-onset conditions. To date, 28 patients remained adherent to therapy; two discontinued due to comorbidities (chemotherapy, kidney problems), three due to ineffectiveness or adverse reactions, and one never initiated treatment. Questionnaire analysis showed that 20 patients had high adherence, 6 intermediate, and 1 low. Polypharmacy data revealed that 9 patients combined one additional antiseizure drug, 12 combined two, 4 combined three, and 2 combined four drugs. Most patients were not autonomous in daily activities. 71.4% reported QoL improvements, including reduced seizure frequency. Conversely, 25% of adherent patients reported no QoL improvement despite treatment.

Conclusion: This study highlights the efficacy and safety of cenobamate, supporting its value as a new therapeutic option for drug-resistant epilepsy. The high prescription appropriateness underlines the critical role of pharmacists in monitoring and optimizing emerging therapies.

1024 | Electrophysiologic, behavioral, molecular and pharmacologic characterization of a prolonged febrile seizure paradigm in the *Scn1a(+/-)^{tm1Kea}* mouse model of Dravet syndrome

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Purpose: The primary cause of the rare, incurable epilepsy known as Dravet Syndrome (DS) is mutations in the *SCN1A* gene. Relevant traits, such as sensitivity to seizures brought on by heat, are displayed by animal models such as young *Scn1a(+/-)^{tm1Kea}* mice. Researchers usually only use heat to induce brief seizures to study effects on outcomes and assess anti-seizure medications. However, febrile seizures are frequently complex and recurrent in DS individuals. The effectiveness of various treatments in DS model mice exposed to prolonged febrile seizures is uncertain. The objective of this work was to evaluate a model of prolonged febrile event (PFE) in *Scn1a(+/-)^{tm1Kea}* mice. We report seizure characteristics and outcomes and benchmark the effects of valproic acid in the model.

Method: Male and female *F1.Scn1a(+/+)* and *F1. Scn1a(+/-)^{tm1Kea}* (n = 10/group) underwent PFE at P17. Pups were placed in a warmed-air chamber and then the chamber temperature was gradually raised, followed by a 30 min holding phase at 41°C before cooling. We tracked behavior changes, SUDEP rates in the mice and tested responses to valproic acid. We used c-FOS mapping to trace brain networks recruited during seizures.

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Results: The PFE resulted in seizure-like behavior in all *F1.Scn1a(+/−)^{tm1kea}* animals at temperatures ranging from 39.1°C to 39.9°C. Seizure count ranged from 1 to 5 with a median duration of ~150s. 62.5% of all seizures occurred during the raising phase. C-FOS mapping revealed the PFE triggered bilateral seizures that involved the hippocampus, cortex and select thalamic nuclei. Pretreatment with valproic acid prevented PFE seizures in mice. Sexual dimorphism was revealed in the behavior and SUDEP analyses at P90, highlighting an extended mortality rate, peaking at 54%.

Conclusion: This study highlights the clinical relevance of the PFE and its utility for testing anti-seizure drugs and gene therapies in *Scn1a(+/−)^{tm1kea}* mice across life stages.

1074 | Cenobamate in Developmental and Epileptic Encephalopathies and Generalized Epilepsies: A Case Report on Epilepsy with Myoclonic-Atonic Seizures and Systematic Review of Current Evidence

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Purpose: Cenobamate (CNB) has demonstrated remarkable efficacy in the treatment of drug-resistant focal epilepsy (FE). However, its role in other epilepsy types - such as drug-resistant generalized epilepsies (GEs), combined generalized and focal epilepsies (CGFEs), and developmental and epileptic encephalopathies (DEEs) - remains underexplored. This article assesses the current evidence of CNB efficacy in these often complex and challenging patient populations.

Method: A case report is presented detailing a 22-year-old male with drug-resistant epilepsy with myoclonic-atonic seizures (EMAtS) who achieved seizure freedom on CNB. To evaluate CNB's efficacy in GEs, CGFEs, and DEEs, a systematic literature review was conducted across major databases. Descriptive statistics and subgroup analyses were employed to summarize seizure outcomes (≥50% reduction and seizure freedom), adverse events (AEs), and dose-response relationships. Statistical analysis and visualizations, including dose-response and subgroup analyses, were performed using R (v4.4.2).

Results: The EMAtS patient achieved seizure freedom sustained for 18 months, with concomitant antiseizure medications (ASMs) tapered without AEs. The systematic review included 32 patients across six studies. Among them, 59.4% achieved a ≥50% seizure reduction, and 9.4% attained seizure freedom. Subgroup analysis showed ≥50% seizure reduction in 50% of Lennox-Gastaut syndrome (LGS) and 80% of Dravet syndrome (DS) cases, with seizure freedom in 20% of DS and 50% of epilepsy with eyelid myoclonia (EEM). Adverse events were reported in 74%, primarily sedation and fatigue. CNB facilitated ASM tapering in 31.25% of patients.

Conclusion: CNB demonstrates potential efficacy in managing seizures across refractory epilepsy syndromes, extending its established use beyond FE. Further prospective trials are needed to validate these findings and optimize dosing strategies.

1076 | Levetiracetam to Brivaracetam : A Mood Swing in Epilepsy Management?

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Purpose: To evaluate the impact of transitioning from levetiracetam to brivaracetam on neuropsychiatric changes in Indian epilepsy patients previously on levetiracetam

Method: Levetiracetam and brivaracetam are newer antiepileptic drugs commonly used in the management of epilepsy. Both drugs exert their antiepileptic effects through selective binding to synaptic vesicle glycoprotein 2A (SV2A) in the brain (Feyissa et al.). While levetiracetam is effective, it has been associated with neuropsychiatric adverse effects such as mood changes, irritability, and anxiety, which can significantly affect the quality of life in epilepsy patients. Brivaracetam, a derivative of levetiracetam, has emerged as an alternative, particularly in cases where levetiracetam causes excessive adverse effects. Previous studies (e.g., Kassoum et al.) suggest that brivaracetam may lead to improved psychiatric outcomes compared to levetiracetam due to its pharmacological properties. However, the effect of switching to brivaracetam from levetiracetam on neuropsychiatric adverse effects, especially in the Indian population, remains understudied. To address this research gap, a prospective cohort study was conducted at GMCH, Chandigarh, involving 42 adult patients (mean age = 42.38 ± 18.35 years) with primary generalized epilepsy. These patients, who were on an average of 2.88 ± 0.77 antiepileptic drugs (including levetiracetam), required a switch due to neuropsychiatric adverse effects. Brivaracetam was introduced as

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an alternative, and mood symptoms were assessed using the abbreviated Profile of Mood States (POMS) scale (JR Grove et al.) at baseline and follow-ups every 15 days until day 45. Statistical significance was evaluated using a two-factor ANOVA without replication.

Results: baseline-POMS=73.43±5.22, day-15-POMS=72.24±6.67, day-30-POMS=75.64±8.80, day-45-POMS=77±10.32, (p-value=0.000527)

Conclusion: The increase in POMS scores over time suggests a possible worsening of mood symptoms after switching from levetiracetam to brivaracetam. This finding challenges the expectation of improved psychiatric-side-effects with brivaracetam and highlights the need for further studies to better understand impact of switch on mood in epilepsy patients.

1079 | ARGUS: A Phase 3 Study of EPX-100 (Clemizole Hydrochloride) in Patients with Dravet Syndrome

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Purpose: To evaluate safety and efficacy of EPX-100 as adjunctive therapy in patients with Dravet Syndrome (DS). EPX-100 is a 5HT2 (serotonin) agonist identified to have antiseizure activity using an innovative and highly predictive zebrafish model for DS and LGS. ARGUS is a multicenter, randomized, double-blind, placebo-controlled, phase 3 study to evaluate the efficacy and safety of EPX-100 as adjunctive therapy in children and adult participants with DS. A prior phase 1 double blinded placebo-controlled study of 24 adults revealed 25 (21 mild, 4 moderate) treatment emergent adverse events (TEAEs) with mild somnolence being the most common TEAE along with a predictable and dose proportional pharmacokinetic profile.

Method: The study will enroll patients aged 2 years and older with a clinical diagnosis of DS, genetic confirmation of *SCN1A* mutation, and ≥4 seizures during the 28-day screening/baseline period. Eligible patients will be randomly assigned (1:1) to receive EPX-100 oral solution (weight-based dosing: 1-4 mg/kg BID, max 80mg BID) or placebo. The 16 week (4 weeks titration, 12 weeks maintenance dose) double-blind period will be followed by an optional 156-week open label extension (OLE).

Results: The primary endpoint will be the mean percent change between EPX-100 vs placebo in countable convulsive seizure frequency in the titration plus maintenance periods relative to baseline. Key secondary endpoints include number of countable convulsive seizure-free days in the T+M period relative to baseline and change in clinical global impression scores for the investigator and parent/caregiver assessments in the T+M period. Preliminary safety and tolerability data from the ongoing OLE will be presented.

Conclusion: ARGUS study is currently enrolling participants in North America and Europe (NCT04462770) and aims to determine the safety and efficacy of EPX-100 in patients with DS. Acknowledgement/Funding: This study is sponsored by Harmony Biosciences.

1081 | Real life experience with cenobamate as monotherapy or part of dual therapy: a Spanish cohort

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Purpose: Cenobamate has shown a high effectiveness in real life experience over the past few years despite its indication only for drug resistant epilepsy patients. We aim to describe its effectiveness, safety and potential to improve adverse effects (AEs) by reducing the overall antiseizure medication (ASM) load in real life experience.

Method: Retrospective observational study. Patients followed at 6 different Spanish Epilepsy Units and treated with cenobamate (after monotherapy conversion from polytherapy, or along with one more ASM) for a minimum of 3 months were assessed. Demographic data, treatment, evolution and AEs were collected from clinical histories. Effectiveness was measured through reduction in seizure frequency, while safety was measured based on AEs. The AEs rate was compared with that shown in previous real life experience studies about cenobamate where patients used more concomitant ASMs.

Results: This series included 125 patients, 18.4% underwent monotherapy conversion. The median age at baseline was 47 years. The median follow-up duration was 11 months. The median daily cenobamate dose was 200 milligrams. The median number of ASMs withdrawn before starting cenobamate was 3. Up to 31.4% reached seizure freedom and 75.8% achieved a seizure reduction ≥50%, while 12.1% did not achieve any change in their seizure frequency and 3.4% experienced an increase. Although 50.4% of patients suffered an AE at some point (always mild or moderate), no patients discontinued cenobamate due to AEs, and AEs rate decreased to 40.8% at last follow-up.

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Conclusion: Cenobamate showed a very high effectiveness for drug resistant epilepsy in this cohort and a safe AEs profile. The AEs rate was lower than seen in prior real life experience studies with cenobamate and more concomitant ASMs.

1085 | A 20-Week Multicenter, Randomized, Double-Blind (DB), Placebo-Controlled, Phase 3 Trial (EPX 100-003) evaluating EPX-100 (Clemizole Hydrochloride) as Adjunctive Therapy in patients with Lennox-Gastaut Syndrome (LGS)

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Purpose: To evaluate safety and efficacy of EPX-100 as adjunctive therapy in patients with Lennox- Gastaut Syndrome (LGS). EPX-100 is a 5HT2 (serotonin) agonist identified as having antiseizure activity using an innovative and highly predictive zebrafish model for Dravet Syndrome (DS) and LGS. Mechanism of action studies suggest antiseizure effects are due to serotonergic agonist activity. A prior phase 1 double-blind, placebo-controlled study of 24 adults revealed 25 (21 mild, 4 moderate) treatment-emergent adverse events (TEAEs), with mild somnolence being the most common TEAE, along with a predictable and dose proportional pharmacokinetic profile.
Method: Study will enroll a total of 260 patients, 2-55 years of age with a diagnosis of LGS. After an initial screening visit, patients will enter a 4-week observational phase to assess baseline seizure frequency based on diary recordings of daily seizure activity. Patients must have at least 4 countable major motor seizures (CMMS-28) during observational phase. Eligible patients enter a subsequent DB period (4-week titration, 12 weeks maintenance) and are randomly assigned to receive EPX-100 or placebo. Patients who complete the DB period can enter an optional 156-week open-label extension.
Results: Primary endpoint is the percentage change in CMMS-28 from Baseline Period through the end of DB Period (titration plus maintenance phase) between EPX-100 vs. placebo. Key secondary endpoints include proportion of participants with ≥50% reduction in CMMS-28 from the Baseline Period to the end of the DB Period, percent change in CMMS-28 seizure-free days during the DB Period relative to the Baseline Period and Clinician Global Impression of Change (CGI-C) score at the end of the DB Period. Safety assessments include incidence and severity of adverse events, clinical laboratory tests.
Conclusion: This is a Phase 3 study to determine effectiveness and safety of EPX-100 in patients with LGS.
Acknowledgement/Funding: This study is sponsored by Harmony Biosciences.

1086 | Hyponatremia in patients on therapy with Carbamazepine, Oxcarbazepine or Eslicarbazepine

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Purpose: To assess the frequency and severity of hyponatremia in patients on therapy with Carbamazepine (CBZ), Oxcarbazepine (OCBZ) or Eslicarbazepine (ESL). These are anti-seizure medications (ASMs) with similar chemical structure and mechanism of action and could lead to a common adverse effect – hyponatremia. Hyponatremia may cause brain edema, weakness, fatigue, headache, nausea, vomiting, qualitative and quantitative disorders of consciousness, seizures and death.
Method: For the period of one year 80 patients on therapy with CBZ, OCBZ or ESL came to our clinic for follow-up or due to worsened seizure control. 34 of the patients were on CBZ, 28 were on OCBZ and 18 patients were on ESL. Full physical and neurological examination, EEG and laboratory tests were performed on every patient.
Results: Hyponatremia was found in 12 (35%) of the patients on CBZ, 14 (50%) of the patients on OCBZ and 8 (44%) of the patients on ESL. Severe hyponatremia (below 125 mEq/L) was registered in 5 patients – 1 on CBZ, 2 on OCBZ, 2 on ESL. Furthermore, hypochloremia was found in 9 of the patients with hyponatremia – 3 on CBZ, 3 on OCBZ, 3 on ESL. After standardization analysis there was statistically significant deference in the number of patients with hyponatremia between the three groups (14.9% in the CBZ group, 17.5% in the OCBZ group, 9.9% in the ESL group). In all patients the electrolyte disturbance was slowly restored by 0.9% or 3% solution of NaCl and limited liquids intake, depending on the severity of the imbalance. Only 3 patients preserved their current therapy, while in the others the ASM was gradually replaced by another one.
Conclusion: Patients taking Carbamazepine, Oxcarbazepine or Eslicarbazepine should be strictly followed for electrolyte disbalance, which may be the reason for not feeling well, seizure control worsening and other potentially severe complications.

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1094 | Early Efficacy, Lasting Impact: Cenobamate Reduces Seizures and Concomitant Medication Use Over 3 Years

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Purpose: To evaluate the long-term efficacy and tolerability of cenobamate (CNB) in a real-world setting, focusing on treatment simplification through co-medication reduction in patients with focal drug-resistant epilepsy (DRE).
Method: We conducted a retrospective observational study of 94 patients with focal DRE treated with CNB in our clinic for at least one year. Treatment outcomes, co-medication adjustments, and adverse effects were assessed over a follow-up period of up to 36 months.
Results: Ninety-four patients were included, 33% initiated CNB after ≤5 prior anti-seizure drugs. Fifty-seven and twelve of them had reached 24 months and 36 months of follow-up by January 2025, respectively. Mean CNB doses increased progressively from 185.9 mg (SD 31.2) at 3 months to 320.8 mg (SD 78.2) at 36 months. Median seizure reduction was 95%, 88.9%, and 98.1% at 1, 2, and 3 years, respectively. At 12 months, response rate (>50% seizure reduction) were 79.57%, with 55.91% achieving >90% seizure reduction and 35.56% achieving seizure freedom. Responder rates were 80% and 75% at 2 and 3 years of follow-up, respectively. Seizure- freedom rates were 30.9% and 41.7% at 2 and 3 years of follow-up, respectively. Patient-reported global impression of improvement was "very much better" or "much better" in 82.98% of cases at 12 months. The defined daily dose (DDD) of co-administered drugs decreased significantly from 3.2 at baseline to 1.2 at 12 months and 1.1 at 36 months ($p<0.001$). Monotherapy was achieved in 13.8% of patients, and 51.1% were on bitherapy at 12 months. Adverse effects decreased over time, from 65.96% at baseline to 33.3% at 36 months. Weight loss occurred in 35.6%, 48.08%, and 33.3% of patients at 1, 2, and 3 years, respectively.
Conclusion: Cenobamate demonstrates outstandingly high and sustained efficacy, improved quality of life and good tolerability, facilitated by a significant co-medication reduction in patients with focal DRE.

1098 | Repurposing approved drugs as a pathway to novel treatments for Lafora Disease

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Purpose: Lafora disease (LD) is a rare, fatal, progressive myoclonic epilepsy that leads to severe cognitive and motor deterioration. Symptoms appear in adolescence and life expectancy of affected individuals is about 10 years. LD is caused by mutations in the *EPM2A* or *EPM2B* genes encoding for proteins laforin and malin, respectively – both of which are involved in regulating glycogen synthesis. Dysfunctions of these proteins lead to the accumulation of insoluble glycogen inclusions in the brain, known as Lafora bodies, which are responsible for neurodegeneration. Currently, there is no therapy that can prevent glycogen accumulation or slow disease progression. Available symptomatic treatments include antiseizure drugs, metformin, ketogenic diet and trehalose (*d'Orsi et al, Front Pharm, 2022*). While enzyme- and oligonucleotide-based therapies are being explored, new therapeutic strategies are needed. Recent studies suggest that gliflozines might offer a promising treatment for LD (*Imbrici et al, Pharmacol Res, 2024*). Thus, identifying new pharmacological targets and drugs is crucial for developing effective treatments. This study aims to repurpose approved drugs by employing computational approaches, followed by validation through in vitro experiments.
Method: Human glycogen synthase (hGYS1) and glucose transporters (GLUT1/3) have been selected as targets. Virtual screening, based on docking simulations, has been performed using 3D structures of hGYS1 and GLUT1/3 to identify potential drug candidates from the ChEMBL database. Drugs identified from the *in silico* screening will be tested in SHSY-5Y cells for their ability to modulate intracellular glucose and glycogen concentration using specific *in vitro* assays.
Results: Computational screening identified several promising drug candidates, including zoledronic acid,

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canagliflozin and nebivolol, as potential binders to the selected targets. In vitro validation assays are currently ongoing.

Conclusion: This study successfully identified approved drugs able to modulate glucose concentration. This integrated research strategy based on the repurposing of commercial drugs could accelerate the discovery of new therapies for LD.

1102 | Bexicaserin Reduces Seizures and Modulates Interictal Spectral Power in the GAERS Absence Epilepsy Model

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Purpose: Absence seizures are common in patients with developmental and epileptic encephalopathies (DEEs). 5-HT_{2C} receptors have been implicated in thalamocortical and corticostriatal circuits that underly absence seizures. Bexicaserin (LP352), a potent and highly selective 5-HT_{2C} receptor superagonist, is an investigational molecule currently in development for seizure treatment in patients with DEEs. The effect of bexicaserin was evaluated in a preclinical model of absence epilepsy to further demonstrate its broad anticonvulsant activity.

Method: Male Genetic Absence Epilepsy Rat from Strasbourg (GAERS) were implanted with cortical electrodes over the frontoparietal cortex. The number and duration of spike-wave discharges (SWDs) were recorded for 10-130 minutes following administration of vehicle, bexicaserin, or positive control valproate. Spectral power analyses, including at classical frequency bands, were conducted for ictal and interictal periods. For statistical comparisons to the vehicle group, data were normalized to average baseline values.

Results: Oral administration of bexicaserin dose-dependently decreased the number and duration of SWDs in the GAERS, reaching peak effect by 30-50 minutes post-dose and lasting 70 minutes post-dose ($p<0.05$). Nearly complete suppression of SWDs (~99%) was observed with the highest dose. Consistent with the reduced average duration of SWDs, bexicaserin increased the principal ictal frequency ($p<0.05$). Bexicaserin also reduced overall interictal power (0.5-130 Hz, $p<0.01$) for 50 minutes post-dose. The reduction in power was prominent in the theta band (4-8 Hz), and low (30-45 Hz) and high (60-130 Hz) gamma bands ($p<0.05$).

Conclusion: Bexicaserin significantly reduced SWDs in the GAERS model of absence epilepsy and modulated interictal spectral power that may be consistent with target engagement and/or inhibition of cortical hyperexcitation. These data support the potential for bexicaserin to treat absence seizures in patients with DEEs exhibiting this seizure type. Acknowledgement: This study was conducted by SynapCell and sponsored by Longboard Pharmaceuticals, Inc., a wholly owned subsidiary of Lundbeck.

1104 | Evaluation of the effectiveness and dosage-relationship of Pirampanel in patients aged ≥12 years with focal epilepsy: a real-world retrospective observational study from southern China

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Purpose: To evaluate the effectiveness and safety of different doses of Perampanel (PER) in southern Chinese patients with focal epilepsy (FE) in a real-world setting, and to analyze the correlation between clinical characteristics and dosage.

Method: We retrospective included patients aged ≥12 years with FE treated with PER at our hospital's Epilepsy Center between July 2020 and August 2023. Follow-up evaluations were conducted at 3, 6, 9 and 12 months. Subgroup analysis of clinical characteristics was performed.

Results: At the baseline, a total of 191 patients were enrolled according to the inclusion and exclusion criteria. At each follow-up time period, patients were divided into three groups based on PER median dose 2 mg, 4 mg, and 6-8 mg. After 6 months, the 50% drug response rates were 58.4% (2 mg), 51.9% (4 mg), and 68.8% (6-8 mg). After 12 months, the rates were 44.6% (2 mg), 50% (4 mg), and 66.8% (6-8 mg). Patients with ≥5 years disease duration and focal seizures responded better to 6-8 mg than 2 mg ($P=0.023$ and 0.044). After 6 months, 2 mg monotherapy or combined with one ASM had a higher response rate than 4 mg with combined ASMs≥2 [$P=0.024$, OR=0.379, 95%CI (0.163-0.880)]. After 12 months, 6-8 mg for patients with disease course ≥5 years had a higher response than 2 mg for those with <5 years course [$P=0.032$, OR=14.718, 95%CI (1.265-171.208)]. Adverse event incidence was 7.4% (2 mg), 10.1% (4 mg), and 5.8% (6-8 mg). Retention rates at 6 and 12 months were 75.1% and 60.5%.

Conclusion: In southern Chinese patients with focal epilepsy, a lower dose of 2-4 mg as PER monotherapy or early added-on therapy may also yields favorable

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short-term outcomes. Patients with shorter disease duration (<5 years) may achieve better long-term seizure control at this lower dosage.

1138 | Seizure Reductions and Tolerability in Participants With Developmental and Epileptic Encephalopathies Newly Exposed to Bexicaserin: Interim Results From the Phase 1b/2a PACIFIC Open-Label Extension

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Purpose: Developmental and epileptic encephalopathies (DEEs) are the most severe group of epilepsies characterized by drug-resistant seizures, electroencephalogram background abnormalities, and developmental plateauing or regression. Bexicaserin is a highly specific and selective 5-HT_{2C} receptor superagonist that demonstrated a favorable safety, tolerability, and efficacy profile in the double-blind Phase 1b/2a PACIFIC trial in participants with Dravet syndrome (DS), Lennox-Gastaut syndrome (LGS), and other DEEs. The open-label extension (OLE) of the PACIFIC trial further assessed the long-term safety, tolerability, and efficacy of bexicaserin in participants newly exposed to bexicaserin.
Method: After completing the PACIFIC trial, participants aged ≥12 and ≤65 years with DS, LGS, and DEE Other were given the option to enroll in the OLE. They underwent a 15-day flexible titration period (maximum dose of 12 mg TID, based on tolerability), followed by up to one year of maintenance treatment.
Results: Forty-one participants (32 bexicaserin, 9 placebo) enrolled in the OLE and received bexicaserin (3 DS, 20 LGS, 18 DEE Other). All 9 placebo participants who then received bexicaserin in the OLE successfully titrated to their maximum tolerated dose and entered the OLE maintenance phase. In this interim analysis of the placebo-to-bexicaserin cohort, at approximately 6 months, no new serious adverse events were reported. Furthermore, a 57.3% reduction in countable motor seizures and a 61.2% reduction in total seizures were observed. Moreover, 55.6% of participants demonstrated a ≥50% reduction in countable motor seizure frequency.
Conclusion: All participants successfully transitioned from placebo to bexicaserin in the OLE with no discontinuations, reinforcing the tolerability of bexicaserin in an inclusive DEE population. The comparable seizure reductions in the double-blind PACIFIC trial and the placebo-to-bexicaserin cohort in the OLE reinforce the consistency of bexicaserin across heterogeneous DEE subgroups and are supportive of Phase 3 development.

1141 | Vormatrigine Demonstrates Potent Antiseizure Activity Across Three Acute Models with Highest Predictive Validity for Focal Onset Seizures

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Purpose: Approximately 3.5 million people in the US are diagnosed with epilepsy, with around 60% classified as focal onset seizures (FOS). Despite the availability of over 30 antiseizure medications (ASMs), 30-40% of patients remain refractory to current treatments. Vormatrigine, a functional state modulator that targets the hyperexcitable state of CNS sodium channels, is currently in development for adult FOS, with emerging preclinical and clinical data pointing to an ideal precision ASM profile. We recently implemented the Praxis Analysis of Concordance (PAC) framework to assess the translational concordance of common preclinical seizure models. Using this framework, we deployed a decision tree for accelerated FOS drug discovery that includes three acute seizure models with high predictive validity: audiogenic, maximal electroshock (MES) and 6-Hz (32mA). Here, we assess vormatrigine's antiseizure efficacy across these models.
Method: Male and female juvenile DBA/2J mice were used to assess the antiseizure activity of vormatrigine in the audiogenic seizure model. MES and 6-Hz experiments were conducted in adult male CD-1 mice. Mice were pretreated with vehicle or vormatrigine by oral gavage 30min prior to audio or electrical stimulus and observed for the presence or absence of full tonic hindlimb extension (audiogenic and MES), or psychomotor seizures defined as stun/immobility, forelimb clonus, Straub tail and lateral head movement (6-Hz).
Results: Mice were completely protected from audiogenic-induced tonic hindlimb extension (ED_{50} 0.55mg/kg). In the MES acute seizure model, vormatrigine completely protected mice from tonic hindlimb extension (ED_{50} 0.42mg/kg). Vormatrigine also significantly reduced incidence of psychomotor seizures induced by 6-Hz (32mA), with an ED_{50} value of 1.9mg/kg.
Conclusion: Vormatrigine exhibited potent antiseizure activity across all three acute seizure models and surpasses thresholds needed to progress development, providing robust support for its accelerated development for FOS.

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1142 | Updates from the First-in-human Phase 1 Clinical Trial Evaluating the Safety, Tolerability, Pharmacokinetics and Food Effect of Vormatrigine in Healthy Participants

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Purpose: PRAX-628-101 was a first-in-human Phase 1 trial evaluating the safety, tolerability and pharmacokinetics of vormatrigine (PRAX-628). Preliminary PK findings from Part A (single ascending doses, SAD) and Part B (multiple ascending doses, MAD) demonstrated a favorable safety and tolerability profile in doses up to 45mg and 30mg, respectively. This update is from the MAD cohort up to 45mg, and includes the food effect data from Part C.
Method: PRAX-628-101 enrolled healthy participants aged 18 to 55 years. Parts A and B were randomized, double-blinded, and placebo-controlled, with participants randomized 3:1 to receive vormatrigine or placebo under fasting conditions. SAD cohorts received single doses starting at 5mg and MAD cohorts received daily doses for 10 days. Part C utilized a randomized, open-label, crossover design with participants receiving two 30mg doses (fasted and fed states) separated by a 7-day washout. Safety and tolerability assessments included adverse events (AEs), vital signs, 12-lead ECGs, physical examinations, clinical laboratory tests, and the Columbia-Suicide Severity Rating Scale (MAD only). Plasma PK parameters were analyzed.
Results: 52 healthy participants completed Parts A (n=18), B (n=18) and C (n=16). Vormatrigine was well tolerated with AEs mostly mild, transient, and self-resolving. PK data showed dose-dependent exposure proportional to dose increases up to 45mg. Food effect analysis revealed no clinically significant impact to C_{max} or AUC at steady state.
Conclusion: Vormatrigine demonstrated consistent safety, tolerability, and PK profiles, with no significant food effect. These results support flexible dosing regimens up to 45mg in the ongoing vormatrigine ENERGY program.

1144 | POWER1 – A Double-Blind, Randomized, Multicenter Phase 2/3 Study Evaluating the Efficacy and Safety of Vormatrigine in Adults with Focal Onset Seizures

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Purpose: Focal onset seizures (FOS) are characterized by localized neuronal hyperexcitability, with current standard-of-care limited by tolerability issues and need for titration to avoid side effects. Vormatrigine, a functional state modulator precisely targeting the hyperexcitable state of sodium channels, is currently in development for adult FOS and generalized epilepsy. Vormatrigine has presented with a superior preclinical profile, with demonstrated favorable tolerability in healthy volunteers, including preliminary evidence of cardiac safety. Notably, emerging preclinical and clinical data demonstrate its ability to significantly exceed therapeutic concentrations while well tolerated. This study evaluates the efficacy, safety, and pharmacokinetics of vormatrigine in adults with FOS.
Method: POWER1 is a global, multicenter, double-blind, randomized, parallel design Phase 2/3 study enrolling ≈230 participants aged 18-75 years with FOS, currently taking 1-3 ASMs. Participants are randomized 1:1 to receive vormatrigine QD, at 20mg for the first 6 weeks and 30mg for the second 6 weeks, or matching placebo for 12 weeks. The study will consist of Screening/Observation (Baseline), Treatment and Follow-up periods.
Results: The primary endpoint will be median percent change in monthly (28 days) focal seizure frequency from the Baseline Period to the Treatment Period for vormatrigine compared to placebo. Key secondary endpoints will include the proportion of subjects experiencing a ≥50% reduction in monthly focal seizure frequency (responder rate) from the Baseline Period to the Treatment Period for vormatrigine compared to placebo. Further secondary and exploratory endpoints will examine the effect of vormatrigine on additional efficacy and safety outcomes, including pharmacokinetic characterization of plasma concentrations of vormatrigine. Enrollment is ongoing with topline data anticipated by year end 2025.
Conclusion: Expanding on preclinical and preliminary clinical data, the POWER1 study will examine the efficacy, safety and pharmacokinetics of vormatrigine as an ideal precision ASM for FOS.

1145 | RADIANT – An Open Label Phase 2 Clinical Trial to Evaluate the Efficacy and Safety of Vormatrigine in Adult Patients with Focal Onset or Primary Generalized Tonic-Clonic Seizures

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Purpose: Epilepsy affects ~3.5 million individuals in the US with at least one-third experiencing uncontrolled seizures. While sodium channel therapy is the most effective approach for treating seizures, currently approved medications suffer from insufficient efficacy or dose-limiting tolerability concerns. Vormatrigine is a functional state modulator precisely targeting the hyperexcitable state of sodium channels in the brain, currently in development for adult focal onset seizures (FOS) and generalized epilepsy. Emerging data point to a superior preclinical profile alongside favorable tolerability in healthy volunteers, with demonstrated ability to significantly exceed therapeutic concentrations while well tolerated. This study evaluates its efficacy, safety, and pharmacokinetics in adult patients with FOS or primary generalized tonic-clonic seizures.

Method: Radiant is a Phase 2, open-label, single-arm, multicenter clinical trial enrolling up to 50 participants aged 18-75 years diagnosed with focal onset or idiopathic generalized tonic-clonic seizures according to the International League Against Epilepsy Classification. Participants will receive vormatrigine 30mg daily for 8 weeks. The study will consist of Screening/Observation (Baseline), Treatment and Follow-up periods.

Results: The primary endpoint will be median percent change in monthly (28 days) focal seizure frequency from the Baseline Period to the Treatment Period for vormatrigine. Secondary endpoints will include the proportion of subjects experiencing a ≥50% reduction in monthly focal seizure frequency (responder rate), as well as the proportion of participants experiencing seizure freedom, 100% reduction in monthly seizure frequency from the Baseline Period to the Treatment Period for vormatrigine. Further secondary and exploratory endpoints will examine the effect of vormatrigine on additional efficacy and safety outcomes, including pharmacokinetic characterization of plasma concentrations of vormatrigine. Enrolment is ongoing with topline data anticipated in 1H2025.

Conclusion: The vormatrigine ENERGY program is advancing, with the Radiant study intended to examine the impact of vormatrigine on seizure burden across patients with FOS and generalized epilepsy.

1146 | Relutrigine Demonstrates Robust Seizure Reduction and Seizure Freedom in DEEs: Results from the EMBOLD Study

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Purpose: Developmental and epileptic encephalopathies (DEEs) are devastating pediatric neurological disorders characterized by severe, frequent seizures and increased early mortality. Relutrigine is a differentiated functional state sodium channel (Na_V) modulator currently in development for DEEs. The EMBOLD study (NCT05818553) was a Phase 2 randomized clinical trial exploring its safety, tolerability, efficacy, and pharmacokinetics in early onset SCN2A-DEE and SCN8A-DEE.

Method: This multicenter, double-blind, placebo-controlled, randomized study, followed by open-label extension (OLE), enrolled 16 eligible male and female participants aged 2-18 years, inclusive, diagnosed with early onset SCN2A-DEE or SCN8A-DEE. Participants were randomized (1:1) to receive relutrigine QD for 16 weeks, or relutrigine QD for 12 weeks and matching placebo QD for 4 weeks, with timing of placebo administration blinded for both participants and investigator. Participants could opt to undergo study assessments in a hybrid fashion (in-clinic and at-home visits) or with at-home visits only (fully decentralized). Key endpoints included TEAE incidence and severity, and efficacy assessments based on changes from baseline in monthly (28-day) motor seizure frequency, seizure freedom and clinician and caregiver-reported outcomes.

Results: Relutrigine was generally well tolerated. AEs were mostly mild to moderate, with no study drug-related SAEs and no dose reduction required. Relutrigine demonstrated 46% placebo-adjusted reduction in motor seizures during the double-blind portion of the study, with significant reductions observed over single 28-day (27%, n=8 vs 1.6% placebo, n=7) and OLE (77%, n=13) periods. 33% of patients were seizure-free, with ~30-70% improvements reported by clinicians and caregivers across multiple domains.

Conclusion: Relutrigine is poised to be a first-line, best-in-class treatment for all DEEs, demonstrating well-tolerated, short- and long-term improvement in motor seizures alongside marked seizure freedom. A registration-enabling Embold cohort extension has been initiated, with future plans for the Emerald study in a broader, pan-DEE patient population.

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1147 | Emergency Use Case of Relutrigine, a Functional State Sodium Channel Modulator, in an Infant with SCN2A-DEE and Refractory Status Epilepticus

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Purpose: Developmental and epileptic encephalopathies (DEEs) are devastating pediatric neurological disorders characterized by severe, frequent seizures and increased mortality. Certain pathogenic variants in voltage-gated sodium channel (Na_V) genes can increase Na_V activity leading to the neuronal hyperexcitability observed in severe DEEs. Relutrigine is precision sodium channel modulator with demonstrated selectivity for disease-state sodium channel hyperexcitability currently in development for DEEs. Here we describe its first emergency use case in an infant with SCN2A-DEE and refractory status epilepticus (SE).

Method: An 11-month-old patient with SCN2A-DEE began receiving relutrigine in February 2024 at age 4 months, on a named patient, emergency-use basis following a medical history of refractory seizures with multiple episodes of SE requiring ICU admissions and IV medications to resolve the clinical status. In the 7 days preceding relutrigine initiation, the patient had been in SE on three separate occasions and was receiving clobazam, lacosamide and phenytoin without any impact on seizure frequency and severity. Several other ASMs were trialed in the first months of life without response.

Results: Following weaning off phenytoin, treatment with relutrigine commenced at a starting dose of 0.5mg/kg/day, with increasing increments of 0.5mg/kg every two to four weeks, up to a dose of 3mg/kg/day as of August 2024. Since treatment initiation, there has been a marked reduction in episodes of SE and hospital admissions, with durable reduction in seizure frequency and a decrease in emergency medications administered. Over the course of treatment, relutrigine has been well-tolerated with no clinically significant findings on biweekly blood draws, urine or ECG analysis, and no drug-related or severe adverse events.

Conclusion: Relutrigine's early clinical experience indicates tolerability and marked seizure reduction, including cessation of previous SE. Ongoing follow up will determine long-term effects on seizure frequency, intensity, and associated comorbidities. Relutrigine made available under an emergency use provision from Praxis Precision Medicines.

1148 | Preclinical Findings of Relutrigine, a Functional State Sodium Channel Modulator, Point to Anticonvulsant Potential in Dravet Syndrome

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Purpose: Dravet syndrome is a severe, intractable developmental epileptic encephalopathy (DEE) largely resulting from *SCN1A* haploinsufficiency and is characterized by frequent seizures, behavioral and developmental delays and increased mortality. While the use of sodium channel blockers in Dravet syndrome remains controversial, emerging preclinical and clinical data suggest that sodium channel modulation may be an appropriate therapeutic strategy in Dravet syndrome. Relutrigine represents a differentiated sodium channel modulator class which exhibits selectivity for disease-state sodium channel hyperexcitability and is currently in development as a first- and best-in-class small molecule for all DEEs. Relutrigine has recently received Rare Pediatric Disease designation for Dravet syndrome, building on encouraging clinical findings from the EMBOLD study demonstrating well-tolerated seizure reduction and freedom in *SCN2A* and *SCN8A*-DEE. Here, we evaluate its effect in a zebrafish preclinical model of Dravet syndrome.

Method: The anticonvulsant potential of relutrigine was assessed in an established zebrafish model of Dravet syndrome with translational validity. Locomotor activity of individual untreated and relutrigine-treated *scn1Lab*$^{s552/s552}$ larvae was tracked with the DanioVision/EthoVision automated tracking system.

Results: Preliminary results in the *scn1Lab*$^{s552/s552}$ zebrafish model of Dravet syndrome show significant reversal of seizure-like behavior with relutrigine (mean velocity and distance travelled).

Conclusion: Preliminary findings in a zebrafish model point to relutrigine's anticonvulsant action in Dravet syndrome and the potential for superior efficacy over current standard-of-care. In combination with recent results from the Embold study in *SCN2A* and *SCN8A*, these findings emphasize its promising potential to address significant unmet needs across the spectrum of DEEs.

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1149 | Clinical Updates from the Elsunersen Emergency Use Program: A Novel ASO for Treatment of Early Onset *SCN2A* Developmental and Epileptic Encephalopathy

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Purpose: Early onset *SCN2A* developmental and epileptic encephalopathy (*SCN2A*-DEE) is a rare, severe disorder caused by gain-of-function (GoF) mutations in the *SCN2A* gene. Elsunersen is an intrathecally administered ASO in development, with emerging clinical data highlighting its disease modifying potential for early onset GoF *SCN2A*-DEE. Here, we provide clinical updates from 4 patients currently receiving Elsunersen under an Emergency Use Program.
Method: Elsunersen has been administered in Germany since March 2023 to treat a preterm infant (29+4 weeks gestation) diagnosed prenatally with a pathogenic *SCN2A* variant. The patient was in constant, life-threatening status epilepticus (SE), with only partial effect of high-dose sodium channel blockers. Elsunersen treatment commenced at age 6 weeks. An 8-year-old patient with GoF *SCN2A*-DEE has been receiving Elsunersen in Australia since December 2023, following a history of refractory seizures, global cerebral atrophy, global developmental delay, frequent oculogyric movement, and severe dystonia while awake. Two *SCN2A*-DEE patients from the completed EMBRAVE study were granted emergency access to continue receiving Elsunersen in the US since April and March 2024, respectively.
Results: There have been no reported drug-related severe or serious AEs following ongoing administration of any dose in any patient, with procedure and dosing well tolerated. In the German patient, early dosing led to SE cessation and revealed a temporal association with seizure reduction. Seizure frequency remains stable with ongoing dosing; maintained after tapering phenytoin at age 14 months. In the Australian patient, 2 weeks after the second dose, a 0.5ml weekly reduction of ethosuximide was achieved, with facial myoclonus subsiding during waking. Significantly fewer clinical and electrographic seizures were noted, alongside notable quality-of-life improvements.
Conclusion: Elsunersen's clinical experience to date demonstrates a well-tolerated, consistent and meaningful therapeutic response. Ongoing follow up will determine long-term effect on seizures and associated comorbidities. Elsunersen made available under emergency use provisions from Praxis Precision Medicines.

1159 | Short-term efficacy of fenfluramine in Lennox-Gastaut syndrome and related intractable epilepsies

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Purpose: Fenfluramine (FFA) is approved as add-on therapy for the treatment of seizures associated with Dravet syndrome (DS) and Lennox–Gastaut syndrome (LGS) in Japan. We aimed to evaluate the efficacy of FFA in LGS and LGS-like pharmacoresistant epilepsy.
Method: Efficacy and adverse effects were retrospectively investigated in patients with intractable epilepsy other than DS who received FFA as add-on therapy from May, 2020 to September, 2024.
Results: A total of 44 patients (24 males [55%]) were enrolled. Median age was 27 (range: 6-52) years and median treatment duration was 4.5 (0-60) months. Ten patients discontinued treatment after less than 3 months because of increased seizure frequency in 4 or adverse effects in 5. Of the 34 patients who continued treatment for at least 3 months, 18 (53%) achieved ≥50% reduction in seizure frequency at final visit. The 50% responder rates for seizure frequency were 54% in generalized tonic seizures (GTS) (n=28), 80% in generalized tonic-clonic seizures (GTCS) (n=5), 100% in myoclonic seizures (n=3), 20% in epileptic spasms (n=5), and there were no responders in atypical absence seizures (n=4) and focal seizures (n=4). The 50% response rates in epilepsy syndromes were higher in LGS (54%, n=26), generalized epilepsy (60%, n=5), and progressive myoclonus epilepsy (PME) (100%, n=1) compared to focal epilepsy (0%, n=2). There was no significant difference in the final dose of FFA between responders and non-responders (0.20 vs. 0.19 mg/kg/day). The common adverse reactions were drowsiness (39%), decreased appetite (23%), and diarrhea (16%); one patient discontinued due to mild aortic regurgitation.
Conclusion: Our study suggests that FFA is effective in reducing GTS, GTCS, and myoclonic seizures associated

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with GE and PME other than LGS and is less effective for atypical absence and focal seizures.

1190 | Association between Antiseizure Medication Therapy and Quality of Life in Patients with Temporal Lobe Epilepsy

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Purpose: Temporal lobe epilepsy (TLE) is one of the most common epilepsy syndromes, with over 50% of patients required multiple antiseizure medication (ASM). The objective of ASM administration should extend beyond seizure-control and minimal adverse effects, rather also to improve patients' quality of life (QoL). This study aims to evaluate the association between ASM administration and QoL in Indonesian TLE cohort.
Method: This cross-sectional study was conducted on April-December 2023 in Cipto Mangunkusumo National Referral Hospital. Inclusion criteria were adult TLE patients (≥18 years) on a stable ASM regimen for at least one month. Exclusion criteria comprised multifocal epilepsy and inability to independently complete the Quality of Life in Epilepsy Inventory-31 (QOLIE-31). Variables collected were demographics, clinical data, ASM characteristics, and QOLIE-31 score. Higher QOLIE-31 score indicated better quality of life. Statistical analysis included one-way ANOVA, independent t-test, Pearson, and Spearman correlation analysis.
Results: A total of 100 subjects were recruited, predominantly female (58%) with median age of 30 (18-65) years. The mean total QOLIE-31 score was 61.46 (±1.63). Polytherapy was used by 70% subjects, with no significant association between the number of ASM used and QOLIE-31 scores. Better total QOLIE-31 score (67.26; p=0.026) was independently associated with carbamazepine administration, specifically in seizure-worry and social function domain. Moreover, positive correlation found between social function score (r=0.428) and clobazam dosage, while inverse correlation found between levetiracetam dosage and seizure worry (r=-0.323). Levetiracetam also significantly associated in lower energy domain score (55.00; p=0.05). Surprisingly, Topiramate administration was associated with lower score in three domains, which were social function (50.28; p=0.03), cognitive (50.54; p=0.04), and medication effect (41.44; p=0.04).
Conclusion: Several factors of ASM administration were associated with patients' overall QoL and several specific domains. It is crucial for clinician to also consider the QoL in selecting the most appropriate ASM for each patient.

1219 | Experience and opinions regarding therapeutic drug monitoring in Irish epilepsy care: a patient perspective survey

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Purpose: This survey explored the experiences and opinions of Irish patients regarding therapeutic drug monitoring. Pharmacological treatment of epilepsy is complex, with many different anti-seizure medications available, each with its side effects and interactions. Therapeutic drug monitoring can help improve seizure control in various ways, including detecting sub-therapeutic drug levels, poor adherence to prescribed therapy, toxicity, and determining individual therapeutic levels. However, guidelines vary regarding its use and patients are not always involved in decision-making regarding its use.
Method: The data was collected using an anonymous online survey built on Microsoft Forms. Patients were recruited through the St James Hospital Dublin epilepsy clinic and promoted online via the Epilepsy Ireland newsletter and website. The survey was open for four months and closed once 100 responses were gathered.
Results: The most reported antiseizure medications were Levetiracetam (25%) and Lamotrigine (21%). About half (48%) of responders had undergone a blood test for an anti-seizure medication level, with the most common reason cited being uncontrolled seizures (29%) followed by dose correct (20%); 67% of responders were women, and pregnancy was only cited as the reason for blood testing in 11%. The reasons for testing and results were only consistently discussed in 36%, while the results took longer than ten days in about half of cases. Most responders (65%) felt strongly that a point-of-care method to measure antiseizure medications would be helpful and felt confident they could perform such a test themselves (80%).
Conclusion: This survey provides interesting insights into the use of therapeutic drug monitoring in Ireland from a patient perspective. We demonstrate widespread utilization, often with poor communication and delays concerning the indication and outcome. However, patients are

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interested in the practice and wish to be more involved. These findings support our ongoing efforts to develop a point-of-care therapeutic drug monitoring platform for epilepsy.

1238 | Glutamate-dependent inhibition and desynchronization of early AMPAergic currents by the anticonvulsant perampanel

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Purpose: Perampanel (PMP) is a widely prescribed antiseizure medication. PMP is unique in terms of the prominent inhibitory effect on AMPA receptors (AMPAR). Molecular dynamics simulation studies suggest that PMP binds to the pre-M1 linker of AMPAR to prevent channel opening. However, gating modification of AMPAR by PMP, such as state-dependent changes in the binding kinetics and affinity, has not been directly measured. It also remains obscure whether and how PMP could selectively inhibit seizure but not normal discharges.
Method: AMPAergic currents in freshly dissociated hippocampal CA1 neurons from C57BL/6 mice were recorded with whole-cell voltage-clamp and rapid exchange of external solutions containing different concentrations of glutamate and PMP (and 50 μM D-AP5 to block NMDAergic currents). Oligo-channel outside-out micropatch recordings were also exercised to investigate the PMP action at the molecular level.
Results: PMP has just a modest effect on the AMPAR activation curve. Consistently, PMP binds to and unbinds from the open-desensitized and closed AMPAR with rather similar kinetics. PMP shows no apparent effect on AMPAR desensitization, but dose-dependently slows activation and thus inhibits peak AMPAergic currents with an apparent dissociation constant of ~90 nM, well within the therapeutic range in human (~26 – 140 nM). PMP also decreases and desynchronizes early AMPAergic currents more in high (e.g. 1 mM) than in low (e.g. 0.3 mM) ambient glutamate, constituting a novel form of use-dependent inhibition of ligand-gated channels.
Conclusion: PMP inhibits AMPAergic currents by activation slowing but unaltered desensitization. The inhibition involves desynchronization of AMPAergic currents, and is glutamate concentration-dependent. PMP may therefore have a selective effect against seizure discharges.

1265 | Analysis of the final medication adjustment leading to seizure freedom in patients treated with cenobamate

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Purpose: To explore the final antiseizure medication (ASM) adjustment that resulted in seizure freedom in patients treated with cenobamate.
Method: We identified patients with previously drug-resistant focal epilepsy who had terminal remission for ≥3 months while taking cenobamate. We identified the final adjustment that preceded seizure freedom. We also recorded age, age at onset, epilepsy duration, baseline seizure frequency, cenobamate dose, concomitant ASMs, and duration of terminal seizure freedom.
Results: Out of 76 patients currently receiving cenobamate, 15 (19.7%) were seizure-free for >3 months at the last visit. Their mean age was 46 years (range 26-71) and mean duration of epilepsy was 31.4 years (range 10-59). The mean seizure frequency at baseline, prior to initiating cenobamate, was 7.6 seizures per month. The duration of terminal seizure freedom ranged from 4 to 73 months (mean 29 months). The cenobamate dose at the time of seizure freedom ranged from 100 mg to 400 mg (mean 262 mg). The most commonly used concomitant ASM was clobazam (13 patients) with a dose range of 2.5-15 mg (mean 8.3 mg). Other commonly used concomitant ASMs were lamotrigine (8 patients), levetiracetam (4 patients), lacosamide (3 patients). The most common last adjustment that led to seizure freedom was addition of cenobamate (4 patients), cenobamate dose increase (4 patients), increasing clobazam dose (4 patients), and addition of clobazam (2 patients). Five of six patients who became seizure-free after addition or titration of clobazam had previously failed clobazam alone.
Conclusion: The findings support evidence for synergy between cenobamate and clobazam and support the strategy of addition/ titration of clobazam in patients who have not become seizure-free on cenobamate. In addition, the study supports continued cenobamate titration until seizure freedom or limit of tolerability.

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1270 | Effectiveness, adherence and safety of cenobamate in patients diagnosed with focal refractory epilepsy: results of the CiFES study

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Purpose: We aimed to assess the effectiveness, adherence and safety of cenobamate (CEN) in a cohort of patients diagnosed with refractory focal epilepsy in clinical practice.
Method: The CiFES (Cenobamate in Focal Epilepsy Study) study is an observational, retrospective study comparing the following variables up to 6 months after initiating CEN: number of monthly epileptic seizures, concomitant antiepileptic drugs (AEDs) compared as the number and as the corresponding Defined Daily Dose (DDD), the retention rate at 6 months and the side effects related with CEN withdrawal or dose adjustment.
Results: 41 patients were included. 27 (65.8%) were male, 71% between 30-50 years of age, 57% diagnosed 10-20 years ago, 48% with focal motor seizures and 4.13±0.52 seizures per month. Treatment with CEN significantly reduced the number of epileptic seizures from baseline (13.12±0.75) at 1 month (9.74±0.42, $t_{1.40}$=4.863; p=0.001), 3 months (1.96±0.57, $t_{1.40}$ =6.810; p=0.001) and at 6 months (1.69±0.48, $t_{1.40}$ =6.938; p=0.001). 5 (12%) patients were seizure-free at 6 months. Furthermore, the number of concomitant AEDs was significantly lower after 6 months with CEN (2.57±0.20 *vs*. 2.91±0.23, $t_{1.40}$ =2.676; p=0.041) and the DDD significantly (p=0.007) decreased from 5.87±0.31 to 4.34±0.29 after 6 months. 5 patients suffered side effects being dizziness the most reported (n=2, 4.8%). Only 1 patient discontinued CEN after 6 months being the retention rate of 97% in the study period.
Conclusion: CEN is an effective and well tolerated antiepileptic treatment for patients with drug-resistant focal epilepsy.

1274 | Clinical Utility of Therapeutic Drug Monitoring of Anti-Seizure Medications Following Breakthrough Seizures

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Purpose: Despite adherence to ASM treatment, many patients experience breakthrough seizures. Therapeutic Drug Monitoring (TDM) is useful in considering possible causes for breakthrough seizures. This study aimed to evaluate the clinical utility of TDM of ASMs following breakthrough seizures through the investigation of patient factors, medication adherence, and the possible relationship between TDM results and these seizures in a group of patients with epilepsy in Malta.
Method: A questionnaire was developed in order to collect demographic data, epilepsy-related information, TDM of ASMs results and the Medication Adherence Reporting Scale (MARS). Patients with epilepsy were recruited from the Neurology Epilepsy Outpatient Clinic at Mater Dei Hospital, main teaching hospital in Malta.
Results: Fourteen participants were recruited: 64% were female. TDM results showed that for the three most common ASMs measured in MDH, sodium valproate levels were evenly distributed across subtherapeutic, therapeutic, and toxic ranges; carbamazepine levels were mostly in the toxic range, and phenytoin levels were all in the therapeutic range. Stress was identified as a major trigger for breakthrough seizures irrespective of range of TDM, with lack of sleep particularly prevalent in the toxic range. There was no statistically significant correlation found between TDM levels and either age or seizure frequency. Despite high adherence to medication regimens, as indicated by MARS questionnaire scores, all participants experienced ASM side effects such as hair loss, weight gain, and drowsiness.
Conclusion: Breakthrough seizures in patients with epilepsy present a significant clinical challenge, and are often of uncertain cause. TDM of ASMs can provide valuable guidance, however in this present study no clear correlation was found between TDM drug levels, patient clinical factors and breakthrough seizures. Despite its limitations, especially due to small sample size and interpatient variability in epilepsy types and ASM treatments, this study highlights the importance of considering individual patient factors when managing epilepsy.

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1287 | Efficacy and Tolerability of Cannabidiol in Adult Patients with Lennox-Gastaut Syndrome: A Retrospective Review

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Purpose: To report our experience of cannabidiol in adults with Lennox-Gastaut Syndrome (LGS).
Method: A retrospective record review was conducted. Seizure control, medication adjustments, side effects, changes in concomitant medication, clobazam dosing, cognitive changes and caregiver feedback at 6 months were noted. Cannabidiol titration and adjustment of concomitant anti-seizure medication (ASM) continued after.
Results: Of 79 (40 male, aged 18–62 years, mean age=30), 67 (86%) continue on cannabidiol with 19 still titrating. Eight withdrew due to side effects/inefficacy. Four died of unrelated comorbidities. Forty-seven had functioning Vagus Nerve Stimulator (VNS). Twenty-five had previously tried ketogenic diet. Most (n=72) had moderate-to-severe intellectual disability and 75 were on ≥3 ASMs. Cannabidiol doses ranged from 100–1100 mg/day (mean=410 mg, median=400 mg) with follow-up up to 72 months (mean=29.3). At six months, 48(60.8%) achieved >50% reduction in overall seizures (50-75% n=26; 75-90% n=17; >90% n=5). Seizure-free days increased from an average of 7 to 11/month. Reduced buccal midazolam use was reported in 32(41%). Hospital attendance decreased from an average of 0.3/year to 0.05/year (21 unknown). In around half, cognitive improvements were reported. Clinically significant drug interactions, mainly with clobazam, valproate, lamotrigine and phenytoin, necessitated dose adjustments in 51 patients. Thirteen were able to withdraw concomitant ASM (1 ASM: n=11; 2 ASMs: n=2). Liver function abnormalities in 12 responded to adjustments in valproate/clobazam. Diarrhoea (n=24) resulted in withdrawal (n=2) or dose reduction/slower titration (often successful), in 17 limiting the dose. Forty-one took regular clobazam before cannabidiol, 37 starting after to satisfy NICE prescribing requirements. Where not tolerated, minimal doses of clobazam were used (≤2.5mg/day (n=29), ≤1mg/day (n=14). Despite fulfilling criteria for continuing cannabidiol, in 24 ongoing seizures required an additional ASM.
Conclusion: Cannabidiol demonstrates good efficacy and tolerability with high retention rates in adults with LGS, improving both seizure and non-seizure outcomes.

1299 | Evaluating the Cognitive Effects of Cenobamate in Real-World Settings: A Literature-Based Analysis

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Purpose: Cenobamate is a novel antiseizure medication (ASM) with proven efficacy in the treatment of focal epilepsy and epileptic syndromes, as demonstrated by both clinical trials and real-world studies. While its therapeutic benefits are well-documented, its impact on cognitive function— a critical factor influencing quality of life in epilepsy patient —remains less explored. This study evaluates the cognitive effects of cenobamate in real-world settings, addressing an important gap in clinical profile.
Method: A comprehensive literature search was conducted in PubMed database for English-language articles published up to January 3, 2025, using terms such as "cenobamate", "cognitive function" and "epilepsy".
Results: The analysis included 256 patients with drug-resistant focal epilepsy (46.1% female; mean age from 27.9-40.9 years, range 18-71 years), evaluating cenobamate doses ranging from 12.5-400 mg/day. Seizure reduction ≥50% was achieved in 42–70%, with seizure freedom in 5%-20.2%. Cognitive outcomes varied across the studies. Two studies reported no significant changes in overall cognitive performance, with no correlation between outcomes and cenobamate dose or total ASM load. One study observed improvements in naming and attention/executive functions, while another reported statistically gains in cognitive test scores, including verbal episodic memory and visuospatial episodic memory, independent of dose or ASM load. However, one study found a decline in executive functions at doses exceeding 300 mg/day, and dose-independent negative effect on verbal memory and retention tests. Some improvements in memory were accompanied by worsening attention scores in one study.
Conclusion: These findings highlight the heterogeneous cognitive effects of cenobamate with potential benefits in memory and executive functions balanced against risks of impairments in attention and verbal memory, particularly at higher doses. Despite these risks, real-world studies demonstrated that cenobamate is a promising option for drug-resistant focal epilepsy, highlight its promise as an option for drug-resistant focal epilepsy, emphasizing the need for personalized dosing and cognitive monitoring.

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1301 | What´s on With Cenobamate? A Portuguese Series of Adult Patients with Generalized Epilepsies and Combined Focal and Generalized Epilepsies

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Purpose: Cenobamate (CNB) is the most recently approved antiseizure medication (ASM) for adjunctive treatment of focal-onset seizures with or without secondary generalization in adult people with epilepsy who did not achieve adequate seizure control despite treatment with at least two ASMs. CNB blockades sodium currents persistently and has positive allosteric modulation of the γ-aminobutyric acid-A receptor. CNB was licensed in Portugal in March 2024.
Method: We evaluated retrospectively the efficacy and tolerability of CNB for 3-10 months follow up in patients with genetic generalized epilepsies(GGE)-cohort 1(n =3)- and combined generalized and focal epilepsies(CGFE)-cohort 2 (n=12)- including symptomatic and epileptic encephalopathies, using a cohort of patients from ULSAS.
Results: 15 patients were included (60% female; median age 40,7 years. The mean age of epilepsy onset ranged from 4 months to 55 years, with 23,5 years of average disease duration. Five patients had moderate/severe intellectual disability. The mean number of prior ASM was 5,8 (between 2-11ASM). When CNB was introduced, the mean number of concomitant ASM was 2,5. In both groups, the mean reduction of all seizure types was ≥50%. Four patients are seizure free for ≥6 months with ≥150mg CNB. 40% of patients experienced side effects, warranting a modification of treatment with CNB or discontinuing other ASMs. Two patients stopped CNB due to side effects. 53,3% patients had mood and behavior improvement.
Conclusion: This retrospective case series shows that CNB has a broad-spectrum efficacy in both generalized and focal-onset seizures, either in genetic or symptomatic epilepsies. Adverse effects were common, but manageable by dose adjustments in CNB and/or of concomitant ASM. This study has limitations due to its retrospective nature, small sample size and relatively short follow up. Nonetheless, most patients experienced seizure reduction, four of them with longer follow-up are seizure free for ≥6 months and most patients experience better quality of life.

1321 | AAV gene therapy at neonatal age in a mouse model of STXBP1 haploinsufficiency

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Purpose: STXBP1 disorders are linked to a loss of function of the syntaxin-binding-protein-1 (STXBP1) and are associated with severe neuronal development delay, intellectual disability and seizures. There are currently not efficacious treatments for the disease and in this study, we evaluated the potential of a gene therapy (GT) approach to modulate STXBP1 haploinsufficiency in a relevant mouse model.
Method: STXBP1 heterozygous (HET) KO mice have been licensed from the University of Amsterdam. AAV9 constructs encode the WT hSTXBP1-HA tag gene under the control of a neuronal promoter. Animals have been injected at post-natal day 1 (PND1) using intra cerebroventricular administration (ICV) with either vehicle or AAV treatment. EEG recordings were performed in group housing video-EEG wireless telemetry platform (24 hours/day). A battery of behavioral tests was performed to evaluate motor and cognitive performances. Biochemical analysis of transgene expression was performed in prefrontal cortex tissue using qPCR, Western Blot and LC-MS. Immunohistochemistry analysis using HA-tag antibodies was performed on fixed sagittal brain slices.
Results: STXBP1 HET mice have reduced STXBP1 protein levels and present a robust disease phenotype with reduced body weight, frequent absence seizures, motor and cognitive deficits. AAV GT administered at PND1 by ICV translates into increased levels of STXBP1 in the prefrontal cortex and to a large brain distribution of the HA-STXBP1 protein. GT treated HET animals showed a robust decrease in SWD after 2 months and a rescue in body weight. Animals have been followed-up for 6 months for behavioral studies and we show that treated mice have gained normal motor behavior (hindlimb clasping, wire hanging) and cognitive performance (fear condition test).
Conclusion: This study shows that AAV GT administered by ICV at PND1 in STXBP1 HET mice provides a therapeutic approach to overexpress STXBP1 across wide brain regions and to rescue disease symptoms.
UCB funded work

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1324 | Thyroid Under Siege: The Impact of Anti-Seizure Medications on Epileptic Patients

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Purpose: Epilepsy is a chronic disease with around 8.2/1000 prevalence in the general population and in developing countries it is more than 10/1000 (1). Anti-seizure medications (ASMs) used to treat epilepsy are known to have many associated effects including endocrine, metabolic and reproductive disturbances (2). We undertook this study to determine thyroid dysfunction in epileptic patients on ASMs. Aim of the study: To determine the incidence of subclinical hypothyroidism in those on ASMs and to determine the effect of older versus newer ASMs on thyroid function

Method: This is an observational, retrospective, cross-sectional study carried out in 203 epileptic patients who were admitted in epilepsy ward between July 2013 and March 2014 at R. Madhavan Nayar Center for Comprehensive Epilepsy Care, Sree Chitra Tirunal Institute for Medical Sciences and Technology (SCTIMST), Thiruvananthapuram, Kerala, southern India.

Detailed data including demographics, seizure type, duration of anti-epileptic therapy and thyroid function including TSH (thyroid stimulating hormone), fT4 (free thyroxine) and fT3 (free tri-iodothyronine) levels are collected from electronic medical records (EMR) and compared between the older and newer ASMs.

Results: Among 203 patients on ASMs, 27 patients (13.3%) developed subclinical hypothyroidism with maximum abnormality seen with valproate and clobazam. 24 patients were associated with low fT4 and low fT3 levels with maximum reduction caused by those on clobazam, oxcarbazepine and valproate. There was no significant difference noted between monotherapy versus polytherapy ASMs and thyroid dysfunction

Conclusion: Thyroid dysfunction in epilepsy on therapy is an important disturbance that has to be diagnosed and followed up while patients are on ASMs. Our data showed older generation drugs had more thyroid dysfunction than the newer ASMs.

1339 | Cardiac Arrest Following Lacosamide Intoxication in an Adolescent

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Purpose: Lacosamide exerts its therapeutic effects by selectively enhancing the slow inactivation of voltage-gated sodium channels. With a favorable safety profile and better tolerability than other anti-seizure medications, lacosamide is often the preferred choice for managing focal epilepsy.

Method: This report describes a case of cardiac arrest following lacosamide overdose in an adolescent girl.

Results: The patient was a 12-year-old girl with no psychiatric history, receiving 200 mg of lacosamide daily for focal epilepsy of unknown etiology. Her medication adherence was poor, resulting in seizures every few months. She attempted suicide by ingesting 3,800 mg of lacosamide and was discovered by her family experiencing seizures. During ambulance transport, she developed pulseless ventricular tachycardia, followed by asystole, requiring cardiopulmonary resuscitation. She was intubated and admitted to the intensive care unit for supportive therapy. On admission, her plasma lacosamide concentration was 106.74 μg/mL, markedly exceeding the therapeutic range and electrocardiography revealed the prolongation of the PR and QRS intervals. She was extubated several days later with full recovery of consciousness, normalized ECG, normal brain MRI and EEG. In overdose situations, lacosamide's sodium channel blocking properties can contribute to significant neurological and cardiac toxicity. Lacosamide inhibits cardiac SCN5A, which could be a potential underlying mechanism for arrhythmias. In this case, ST-segment changes and ventricular arrhythmias observed in the automated external defibrillator recording were attributed to the lacosamide overdose-induced inhibition of cardiac SCN5A. Although cardiac arrest is rare, it represents a severe and potentially fatal complication, with sporadic cases reported in the literature following lacosamide overdose.

Conclusion: This case highlights the severe cardiac complications of lacosamide and emphasizes the importance of recognizing psychiatric conditions and assessing suicide risk in adolescents with epilepsy. Clinicians should remain vigilant when prescribing anti-seizure medications, prioritizing comprehensive monitoring, particularly for patients with poor medication adherence.

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1359 | Identifying antiseizure medications specific association with systemic inflammatory biomarker

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Purpose: Various antiseizure medications (ASMs) have been investigated for their anti-inflammatory effects. However, limited studies have compared these effects among different ASMs within a single large cohort using routine blood tests. This study aimed to elucidate the relationship between specific ASM use and systemic anti-inflammatory effects.
Method: Blood test results were collected from a retrospective epilepsy cohort. Patients who underwent blood tests within three months of their first visit to our clinic were included. The systemic inflammatory index (SII, platelet × neutrophil / lymphocyte), was compared across ASM categories.
Results: A total of 1,782 patients (714 female) with epilepsy were analyzed. At the time of blood testing, 838 patients (47.0%) were drug-naïve. 515 patients were on one ASM, 252 on two, 119 on three, 41 on four, 13 on five, and three on more than four ASMs. The proportion of ASM users with levetiracetam, valproate, oxcarbazepine, topiramate, lamotrigine, and carbamazepine, were 387(21.7%), 297 (16.7%), 189 (10.6%), 188(10.5%), 173 (9.7%), and 155 (8.7%), respectively. Significant differences were observed between ASM users and drug-naïve controls in epilepsy onset age, duration, febrile seizure history, MRI abnormalities, the interval from the last seizure and SII. Stratified multiple linear regression revealed that only valproate showed a significant association with reduced SII levels, whereas no such association was observed with levetiracetam, oxcarbazepine, topiramate, lamotrigine, or carbamazepine. Subgroup analysis of monotherapy cohorts further confirmed that patients on VPA monotherapy exhibited markedly lower adjusted SII levels compared to drug-naïve controls ($p < 0.002$).
Conclusion: Valproate is inversely associated with SII, whereas other ASMs do not exhibit similar effects. This underscores the more distinctive role of valproate in modulating systemic inflammatory responses and highlights its unique potential to influence both neuroinflammation and systemic inflammation. These results may provide valuable insights into the underlying mechanisms of valproate's therapeutic effects.

1364 | Evaluation of psychiatric and behavioral adverse effects in persons with epilepsy on levetiracetam monotherapy versus those on levetiracetam with concomitant clobazam therapy

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Purpose: Clobazam(CLB) is a routinely used benzodiazepine drug. Levetiracetam(LEV), used as a first-line anti-seizure medication is reported to have undesirable psychiatric and behavioral adverse effects. In this study, the evaluation and comparison of the adverse effects profile in persons with epilepsy(PWE) on LEV monotherapy versus those on LEV plus CLB was done in a tertiary health care setting in India.
Method: As part of an ongoing study, the evaluation of PWE on LEV therapy attending the neurology OPD, in AIIMS New Delhi from March 2024 was done. Patients on LEV monotherapy or taking CLB as an add-on medication for seizures were included in the study. Psychiatric and behavioral adverse effects were determined using the Quality of life in epilepsy(QOLIE 1O),Liverpool adverse events profile(LAEP),Generalized anxiety disorder scale(GAD-7) and Neurological disorders depression inventory in epilepsy(NDDI-E)scales. Patients with a prior history of mood disorders were not included in the study.
Results: A total of sixty six adult patients were recruited(35 in LEV group and 31 for LEV + CLB group). Both groups had balanced baseline demographic characteristics. The LAEP scores(34.85±7.4 in LEV group and 33.54±5.89 LEV+CLB group)were lower in the LEV+CLB group, indicating a comparatively better quality of life. Considering a cutoff of 11 in the NDDI-E scale,57.14% patients in the LEV group reported depressive symptoms as compared to the 48.38% in the LEV+CLB group. Fatigue(71.4%v/s41.9%),aggression(60%v/s51%) and agitation(48.5%v/s25.8%)were the most often reported issues according to the LAEP scale, with higher incidences in the LEV group as compared to LEV+CLB. However, the mean QOLIE-10 scores did not reflect any significant differences(26.17±7.96 v/s 27.03±7.42).
Conclusion: Psychiatric and behavioral adverse effects occur frequently in both groups, which can be attributed to LEV. The addition of CLB appears to be associated with a lower incidence of aggression, agitation and depressive

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symptoms. These findings may help guide further treatment decisions.

1365 | Efficacy and safety of cenobamate in adults with uncontrolled focal seizures in the Spanish cohort of a Phase 3 open-label clinical trial: a multicenter retrospective study

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Purpose: This study evaluated the efficacy and safety of cenobamate as adjunctive therapy for the treatment of focal seizures in patients who participated in the Phase 3 open-label clinical trial YKP3089C021 in Spanish centers.
Method: This was a multicenter, retrospective, observational study in 9 Spanish hospitals. Inclusion criteria were age 18–70 years, diagnosis of focal seizures, antiseizure medication (ASM) for uncontrolled seizures in the last 2 years, and 1–3 concomitant ASMs at baseline. Data were sourced from patient clinical records. The primary endpoint was retention rate; secondary endpoints included reductions (100%, ≥90%, ≥75%, ≥50%) in seizure frequency, concomitant ASM management, and safety.
Results: The study included 129 patients with a mean age of 39.8 years; 55.8% were female. Median (range) baseline seizure frequency was 6 (0–180) per month. The mean (SD) numbers of previous ASMs (excluding concomitant ASMs) were 3.6 ± 2.8 and previous/concomitant ASMs at baseline 6.0 ± 2.9. Cumulative retention rates were 71% at 1 year, 60% at 2 years, and 56% at 3 years. At the last visit, 27/94 patients (28.7%) were continuously seizure free for at least 1 year, 15/80 patients (18.8%) for at least 2 years, and 9/76 patients (11.8%) for at least 3 years. At least 1 concomitant ASM was discontinued in 44.9% of patients and the dosage of concomitant ASMs was reduced in 58.3%. The cumulative percentage of patients with treatment-emergent adverse events (TEAEs) and TEAEs leading to discontinuation were 95.3% and 23.3%, respectively. The most frequent TEAEs were CNS-related (somnolence, dizziness).
Conclusion: These data suggest that cenobamate is a safe and effective treatment for patients with drug resistant focal onset seizures, reducing seizure frequency and concomitant ASM usage over the long term.

1388 | Parry-Romberg Syndrome and Epilepsy: Unveiling the Crucial Role of Immunosuppression

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Purpose: Progressive facial hemiatrophy (Parry-Romberg syndrome) is a localized form of scleroderma characterized by unilateral atrophy of the soft tissues and/or bones of the face. These patients can have neurologic complications, such as seizures.
Method: We present a twenty years-old female with Parry-Romberg syndrome diagnosed at four years-old and epilepsy since fifteen years-old. The seizures occurred during awakeness or sleeping, characterized by: (1) ocular supraversion and opening of the mouth, unresponsiveness and fall (if standing) with tonic posture and/or rhythmic movements of the four limbs; (2) same seizure described in 1 but anticipated by déjà-vu sensation; (3) same seizure described in 1 but anticipated by feeling of generalized malaise. Brain MRI showed discrete hypersignal of left amygdala and hippocampus and slight asymmetry of the cerebral hemispheres, with less overall volume on the left. EEG had moderate slow activity in the right temporo-occipital topography and dysfunctional slow activity in the left temporal region. Interictal SPECT revealed evident asymmetry of radiopharmaceutical uptake in the temporal lobes, with relative hypocapture on the right, and left temporo-occipital and right parietal hypocapture.
Results: The patient was initially treated with methotrexate during childhood and it was suspended, because she was seizure-free. With development and growth, her epilepsy became refractory, with several drugs tried – levetiracetam, eslicarbazepine, perampanel, zonisamide and clobazam. Due to drug-resistant seizures, methotrexate was simultaneously added with cenobamate, with reduction of the number of seizures per month and their intensity.
Conclusion: Seizures represent an important component of the burden of the Parry-Romberg syndrome and significantly affect both quality of life and neurodevelopment. Immunosuppressive drugs may have some impact on seizure control in some patients, and should probably be considered as a complement to classic antiepileptic drugs,

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when the seizure control is not achieved with classical antiepileptics.

1395 | Timing Matters: Evaluating the Start of Home Antiseizure Medications After Hospital Admission

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Purpose: This study aims to evaluate delays in restarting home anti-seizure medications (ASMs) upon hospital admission. While the International League Against Epilepsy (ILAE) provides guidelines for the timely management of prolonged seizures and status epilepticus, there are no standardized guidelines or hospital policies for the prompt administration of home ASMs in hospitalized epilepsy patients. In this single-institution quality improvement project, we hypothesize that delays exist between the time patients take their ASMs at home and when treatment is resumed in the hospital.
Method: Retrospective review of the electronic medical records of epilepsy patients admitted over a one-month period to either the General Neurology inpatient service or those for whom primary teams consulted the Neurology service. The study included patients with a prior diagnosis of seizures who were prescribed ASMs. Data collected included demographics, time of arrival to emergency triage, home ASMs, time of home ASMs order and administration, time of intravenous ASMs administration (if applicable), and time of Neurology consult order.
Results: A total of 27 patients were identified during the study period. Ten patients were admitted to the General Neurology service, while 17 were managed by the Neurology Consult team. For patients admitted to the General Neurology service, the average time from arrival to triage to first ASM was 460 minutes (about 7.5 hours), whereas for those managed by the Neurology Consult service, the average time was 764 minutes (about 12.5 hours).
Conclusion: This study highlights significant delays in administering and resuming home ASMs, which may negatively affect seizure control, length of hospitalization and patient outcomes. The variability in treatment initiation across services suggests an opportunity to standardize ASM administration with protocols and improved communication, ensuring timely intervention for all patients. These findings point to a potential area for quality improvement in hospital protocols to enhance patient outcomes.

1399 | Clinical evaluation of reversible visual impairment induced by high-dose antiseizure medication

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Purpose: Occurrence of visual impairment due to antiseizure medication (ASM) is a rare event, and the incidence rate is unknown. Vigabatrin is one of ASM which is known for causing irreversible visual field constriction with long-term high-dose administration, therefore in Japan, regular electroretinography (ERG) is mandated during vigabatrin treatment. In addition to vigabatrin, irreversible visual impairment due to long-term high-dose administration of phenobarbital (PB) and phenytoin were reported previously, indicating that ERG was used to evaluate visual function. In this study, we conducted an ophthalmologic evaluation of a patient with visual impairment during a period of frequent seizures. Notably, symptoms improved following a tapering of ASMs.
Method: The patient was a 10-year-old boy who developed focal onset seizure clusters following a febrile illness. Despite intravenous administration of ASMs, the refractory seizures persisted, leading to a diagnosis of febrile infection-related epilepsy syndrome (FIRES). High-dose PB, continuous intravenous midazolam and thiamylal were administered for suppression of the seizure clusters over one month. After withdrawal of thiamylal, the patient regained consciousness and reported experiencing visual disturbances. Ophthalmologic evaluations were conducted to clarify the pathology.
Results: Central flicker values, retinal three-dimensional imaging, and ERG revealed no significant abnormal findings. However, on the standard color vision test (SPP2), the patient was unable to perform the demonstration at the first time, resulting improvement in test performance with tapering PB.
Conclusion: The visual impairment caused by ASM has been reported to result from damage to retinal epithelial cells, and ERG is useful tools for the evaluation. In our case, with resulting normal ERG, the symptoms have improved with tapering PB, and reversible changes may be expected with early dose reduction of ASM. ERG can be performed on patients under sedation and is expected to assist in the adjustment of ASM based on the evaluation of visual function.

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1405 | Biomarker-Guided Efficacy of Fenofibrate Adjuvant Therapy In Persons With Active Epilepsy: The Randomized, Placebo-Controlled Trial

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Purpose: A pilot clinical study demonstrated fenofibrate's efficacy in nocturnal frontal lobe epilepsy, but no randomized placebo-controlled trial assessed its role in persons with active epilepsy (PWE). This trial investigated the efficacy and safety of adjuvant fenofibrate in PWE.
Method: This single-centric, parallel-group, double-blind, placebo-controlled, randomized trial was conducted in PWE in a tertiary care referral hospital in India with 3 and 6-month follow-ups involving PWE aged 18-50 years with at least 2 seizures in the last 3 months and receiving ≥2 antiseizure medications (ASMs). Participants were randomly assigned to receive concealed fenofibrate (145 mg once daily orally for 6 months) or matched placebo adjuvant to ongoing ASMs. The primary outcome was a percentage change in monthly seizure frequency from baseline to 6 months. Other measures were a 50% responder rate, epileptogenic biomarkers [i.e. total antioxidant capacity (TAC), neurotrophin-3, high mobility group box-1], quality of life, and safety parameters. Trial registered in Clinical trials registry India, CTRI/2021/03/032317.
Results: 80 PWE [24.7 ±6.2 years; 58(72.5%) male] were randomized to fenofibrate (n=40) or placebo group (n=40). The percentage change in monthly seizure frequency was significantly higher in fenofibrate group {median [Inter quartile range] 57.50(4.30 to 75)} compared to the placebo [-40.20(-60.92 to 39.60)]; [median estimate with 95% confidence interval: 70(34.60 to 102.50), (p<0.001)] as per intention to treat analysis. Similarly, the 50% responder rate was significantly higher in fenofibrate group compared to placebo (60% vs. 22.5%, p=0.001). The percentage increase in TAC was significantly higher in fenofibrate group compared to placebo at 6 months (p=0.01). Fenofibrate was well tolerated without any serious adverse events. Adverse events reported in fenofibrate group: decreased appetite (5%), arthralgia (1.25%), and headache (1.25%); in placebo: eructate (1.25%).
Conclusion: Fenofibrate adjuvant therapy had significantly reduced seizures and increased TAC compared to placebo suggesting its potential beneficial role in epilepsy treatment.

1407 | Zonisamide in the practise of an epileptologist: Focus on safety

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Purpose: To evaluate the efficacy and tolerability of the use of zonisamide in daily clinical practice due to clinical guidelines of the decision on the AED regime is at the discretion of the specialist.
Method: The study design was a review of the pharmacokinetic parameters of zonisamide based on the literature and an in-house analysis of a retrospective observational cohort study. The study included patients with epilepsy receiving drug therapy with zonisamide in 2 age groups: 1st group – adults - 37 patients, 2nd group – pediatrics – 13 patients. The age criterion in the pediatric group was chosen taking into account the minimum approved age for the administration of zonisamide.
Results: The average age of the cohort was 29.8±12.5 years. The ratio of men to women was 1:1.2. The duration of disease in the cohort was 16.2±10.8 years (in Gr.1-19.7±10.1, in Gr.2 -6.1±4.4. Zonisamide was used as monotherapy in 12% and as polytherapy in 88%. The average dosage in adults – 301.6mg/d, in children – 182.7mg/d. In the cohort, the combination of zonisamide with levetiracetam dominated polytherapy, followed by valproic acid and lacosamide in descending order. A positive response to therapy was observed in 36 patients (71%). Lack of effect/insufficient efficacy (reduction in seizure frequency <50%) - in 14 patients (29%), but 40% of them noted positive dynamics in reducing the severity and/or duration of seizures. Adverse drug reactions were reported in 1 of the seizures, the average distribution of adverse effects per person was 1.3. Discontinuation of zonisamide due to intolerance occurred in 2 cases (4%).
Conclusion: Zonisamide has been used in a broad spectrum: from idiopathic focal epilepsies to pediatric epileptic encephalopathies and drug-resistant epilepsies in neurosurgical patients. The efficacy of zonisamide was 71%, and side effects of zonisamide of mild to moderate severity occur in less than one third of patients.

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1418 | Prescription patterns of antiseizure medications in Sweden 2007-2023

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Purpose: The aim was to investigate prescription patterns of antiseizure medications (ASMs) during the last 17 years as treatment recommendations have changed and new ASMs have emerged.
Method: Register data of everyone in Sweden with incident epilepsy 2007-2023 and subsequent ASM monotherapy was used (n = 143483, 53% males). Prescription rates of different ASMs as first, second, and third medication were analyzed.
Results: In 2007 Carbamazepine was the most prescribed first ASM (44%, 95%CI: 43-46, n = 1434) followed by Valproate (25%, 95%CI: 24-27, n = 811) and Lamotrigine (15%, 95%CI: 14-16, n = 492). Levetiracetam constituted less than 3% of prescriptions in 2007 but rose quickly and by 2013 it was the most prescribed first ASM. In 2023 63% (95%CI: 62-65) of first ASM prescriptions were Levetiracetam (n = 2507) and 22% (95%CI: 21-23) were Lamotrigine (n = 871). At this point Carbamazepine was prescribed in less than 2% (95%CI: 1-2) of cases (n = 65) and Valproate in 3% (95%CI: 3-4, n = 137). Interestingly, Lacosamide was the only one rising in popularity by 2023, though numbers were still modest (n = 73, 2%, 95%CI: 1-2). Regarding second ASMS, by 2023 Lamotrigine (34%, 95%CI: 32-36) was the most popular followed by Levetiracetam (26%, 95%CI: 25-28) and Lacosamide (10%, 95%CI 9-12). As third Lamotrigine (26%, 95%CI: 23-28), and Levetiracetam (19%, 95%CI: 17-22) were the most common, followed by Valproate 14% (95%CI: 12-16) and Lacosamide 14% (95%CI: 11-16).
Conclusion: There was a clear shift from Carbamazepine and Valproate to Levetiracetam and Lamotrigine as first treatment, in line with changed treatment recommendations. Lacosamide, a relatively new ASM, is gaining popularity. As prescribed medications are subsidized, with a maximum patient cost of 2900 SEK (~260 USD) per year, pricing affecting ASM selection is likely minimal.

1437 | Preliminary results of efficacy and adverse effects of fenfluramine treatment in a tertiary care hospital

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Purpose: Fenfluramine is an anti-crisis medication with a novel mechanism of action, consisting of activity on the serotonergic system, recently approved for patients with developmental epileptic encephalopathies, such as Dravet syndrome (DS) and Lennox-Gastaut syndrome (LGS). Our aim is to characterize patients who benefit from this treatment, in addition to providing preliminary results on efficacy and tolerability.
Method: An analysis of the clinical characteristics of 8 patients under active treatment with fenfluramine in follow-up in the Epilepsy Unit and in the Neuropediatrics Clinic of our hospital was carried out.
Results: Fifty percent are female, with a median age of 17 years (4-43). Of all patients, 5 are diagnosed with LGS: 2 of unknown etiology, 2 of structural etiology (post-infectious encephalopathy and hypoxic-ischemic encephalopathy) and 1 of genetic etiology due to mutation in the SYNGAP1 gene. The other 3 patients were diagnosed with DS due to SCN1A channelopathy. They had a mean of 4.25 anti-crisis medications prior to the start of fenfluramine and 3.25 after the start of fenfluramine. The most frequent types of seizures presented by these patients were tonic-clonic seizures, tonic seizures and atypical absences. 7 of 8 patients (87.5%) showed clinical improvement (reduction in the number or duration of seizures) and no relevant adverse effects.
Conclusion: Fenfluramine has proven to be an effective and safe drug in our patients, simplifying their treatment. However, it is necessary to continue analyzing more data in the future for a better understanding of the drug and its use in real clinical practice.

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1455 | Ethnic Disparities in Pharmacogenetics of Antiseizure Medications: A Systematic Review Subanalysis

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Purpose: Pharmacogenetics aims to optimize antiseizure medication (ASM) therapy by identifying genetic variants associated with drug response and tolerability. However, ethnic disparities in genetic research may limit the applicability of findings to diverse populations. This systematic review sub-analysis explores ethnic differences in pharmacogenetic studies related to epilepsy treatment.
Method: A systematic review was conducted following PRISMA guidelines. We included studies evaluating genetic polymorphisms associated with ASM effectiveness or tolerability. Studies without ethnicity-specific data were excluded. Data were synthesized qualitatively and visualized through heatmaps.
Results: A total of 168 studies were analyzed. Ethnic representation was predominantly Asian (56%) and European (20%), with minimal inclusion of Middle Eastern/North African (8%), Admixed American (2%), and none African/African American populations. Key findings include:

- HLA-B*15:02 and HLA-A*31:01 were extensively studied in Asian populations, confirming their association with severe cutaneous adverse reactions (SCARs) to carbamazepine and phenytoin.
- CYP2C9 polymorphisms (rs1799853, rs1057910), influencing phenytoin metabolism and neurotoxicity, were primarily investigated in Asian and European populations, with limited data in other ethnicities.
- SCN1A (rs3812718) and ABCB1 (rs2032582, rs1045642), linked to ASM resistance, were mainly studied in Asian cohorts, despite their clinical relevance in multiple populations.
- Admixed American and African/African American populations were severely underrepresented, limiting the generalizability of findings to these groups.

Conclusion: Pharmacogenetic research in epilepsy disproportionately focuses on Asian and European populations, leaving significant gaps for underrepresented ethnic groups. Future studies must prioritize diverse cohorts to enhance personalized ASM therapy and ensure equitable healthcare applications.

1488 | Association of metformin use with a reduction in epilepsy related hospital admissions in Wales, United Kingdom

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Purpose: Metformin, a drug traditionally used for diabetes, has demonstrated antiseizure effect in animal models of epilepsy. A hypothesized mechanism of this is action via the AMPK-mTOR pathway, but it also has anti-apoptosis and anti-inflammatory effects. The benefit of metformin over other potential drug re-purposing options is that it is safe in pregnancy, and therefore could be a promising drug to improve seizure burden in pregnant women where antiseizure medication choice is becoming increasingly restricted. The aim of this study was to investigate if metformin use associates with a reduced seizure burden in people with epilepsy (PWE).
Method: We conducted a retrospective database analysis of PWE using the Secure anonymized information linkage databank (SAIL) which contains routinely-collected health data from patients in Wales, UK. Patients > 18 years of age with a diagnosis of epilepsy between Jan 2000—Jan 2020 were included. A logistic regression model was used to assess the probability of PWE on metformin, compared to PWE not on metformin having an epilepsy related hospital admission. We included metformin use, age at epilepsy diagnosis, gender, deprivation quintile and number of other antiseizure medications in the model.
Results: 2283 out of 23,457 PWE were prescribed metformin during the study period. Metformin use was associated with a reduction in epilepsy related hospital admission (adjusted OR [aOR] 0.48, 97.5% CI, 0.43-0.53). Increasing age at diagnosis (aOR 1.01, 97.5% CI 1.00-1.01), increasing number of epilepsy medications (aOR 1.45, 97.5% CI 1.42-1.49) and increasing deprivation (aOR 0.93, 97.5%CI 0.91-0.95) were also associated with an increased risk of epilepsy related hospital admission.
Conclusion: PWE on metformin were 52% less likely to have an epilepsy related hospital admission compared to PWE not on metformin. Although this is a surrogate for seizure control, this analysis suggests that metformin

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use should be further explored as an adjunct therapy in epilepsy.

1493 | TrkB activation as a novel target for drug resistant temporal lobe epilepsy: from animal models to the human epileptic brain

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Purpose: Epilepsy is one of the most common neurological disorders. All pharmacological agents that are currently in use are symptomatic. Furthermore, 30% of patients are drug-resistant. New treatments are needed capable of changing the natural history of the disease. BDNF, activating receptor TrkB, may play a kay role in epilepsy development as well as in the generation and recurrence of seizures. However, BDNF cannot be used as a regular drug because of its poor bioavailability. The aim of this study was to test the effects of a TrkB receptor agonist, 7,8-dihydroxyflavone (7,8-DHF) as a putative anti-epileptogenic and/or anti-epileptic drug.
Method: We used pilocarpine rat model. Subsequently, we administered 7,8 DHF (5 mg/kg or 10 mg/kg), during the latent period (anti-epileptogenic effect) or during the chronic phase of the disease (anti-epileptic effect). We performed behavioral tests for the evaluation of comorbidities. Moreover, rat brains were collected for the evaluation of neuronal death and neuroinflammation. The effect of 7,8 DHF on GABA-current run-down will be evaluated in Xenopus oocytes, incorporated with cell membranes isolated from f TLE patients, or from pilocarpine rats.
Results: Low-, but not high-dose 7,8-DHF can exert strong anti-epileptogenic effects. Low dose of 7,8-DHF also showed an attenuation of epileptic comorbidities. These different effects appear to correlate with differences in TrkB phosphorylation patterns and activation of specific TrkB-dependent signaling pathways. We are now investigating 7,8-DHF as putative anti-epileptic drugs. Therefore, we are testing them in the rat pilocarpine model and in human mesial temporal lobe epilepsy (mTLE) tissue surgically resected from drug-resistant patients.
Conclusion: The animal study provides information on efficacy against seizures, epilepsy-associated comorbidities and induced pathological traits, as well as on the safety of these drugs. This combination of in vivo and ex vivo preclinical data with ex vivo human data will set the ground for future translational and clinical studies.

1509 | Is earlier better? One year cenobamate outcome in a large real world population

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Purpose: CNB is a recently approved antiseizure medication (ASM) for adjunctive treatment of focal drug-resistant epilepsy (DRE).
Method: We conducted a 12-month retrospective study on CNB use in DRE patients, comparing early (EA, ≤5 ASMs before CNB) and late adopters (LA, >5 ASMs).
Results: A total of 281 patients were included (88 EA, 193 LA). EA patients had a later epilepsy onset (15 vs. 6 years, $p < 0.0001$), shorter disease duration (19 vs. 26 years, $p < 0.001$), lower prevalence of intellectual (35% vs. 61%, $p < 0.0001$) and psychiatric disabilities (22% vs. 40%, $p = 0.005$), less prior carbamazepine use (39% vs. 76%, $p < 0.0001$), fewer concomitant ASMs (2 vs. 3, $p < 0.001$), and lower baseline seizure frequency (9.5 vs. 35/month, $p < 0.0001$). At 12 months, the cumulative CNB discontinuation rate was 10.0% (95% CI: 6.5–15.4%). The responder rate ≥75% was consistently higher in EA at all time points (42% vs. 21%, $p = 0.0028$; 75% vs. 36%, $p = 0.0039$). Seizure freedom was achieved at 2- to 3-fold higher rates in EA than LA at 3, 6, 9, and 12 months (32% vs. 12%, $p = 0.0005$; 36% vs. 9%, $p = 0.0039$). Sustained seizure freedom over 12 months was observed in 15% of patients. Most adverse

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events (AEs) occurred within the first three months (34%), mainly somnolence (23%) and fatigue (13%), with no differences between EA and LA. The proportion of patients on a single ASM increased from 14 to 75% in EA and 4 to 30% in LA. Clobazam and lacosamide were the most discontinued or reduced ASMs.

Conclusion: CNB demonstrated sustained high effectiveness over 12 months, with a significantly better overall response and notably higher seizure freedom rates in patients treated earlier. The safety profile was favorable with progressive reduction in total drug burden.

1525 | Clinically relevant pharmacokinetic interactions with cenobamate

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Purpose: Cenobamate is a new antiseizure medication (ASM) used in adults as add-on treatment in focal epilepsy. It is increasingly used in refractory epilepsy as part of complex pharmacotherapy. The purpose of the study was to identify and evaluate clinically relevant pharmacokinetic interactions with cenobamate in patients with refractory epilepsy.

Method: Therapeutic drug monitoring (TDM)-data from January 2022–2025 were analyzed. Serum concentration measurements of all ASMs in use were performed at Section for Clinical Pharmacology, National Center for Epilepsy, Oslo University Hospital. Statistical analyses by pairwise comparisons with Wilcoxen-rank test were performed, $p<0.05$ was considered significant. The study was approved by the Regional Ethics Committee.

Results: Data from 216 patients were included, 120 female/96 male, mean age 39 (SD 14). Mean cenobamate dose and serum concentration based on the most recent measurements for each patient was 175 mg/day (range 12.5-400 mg/day) and 57.3 umol/L (range 5-146 umol/L) (reference range 15-130 umol/L). Cenobamate exposure led to significant changes ($p<0.05$) in the concentration/dose (C/D)-ratios of common combinations: Increase of 88% for desmethylclobazam (n=44) 0.35-0.65 umol/L/mg but not for clobazam, 22% reduction in lamotrigine (n=46) 0.12-0.09 umol/L/mg. There was a tendency towards an increase, although non-significant, of 14% in cannabidiol 0.00034-0.00039 umol/L/mg and 24% in 7-hydroxycannabidiol (n=6) 0.00011-0.00014 umol/L/mg. In 84% of these patients the dose of cenobamate was from 100 mg/day, assumed to be relevant to cause pharmacokinetic interactions. There were no significant changes on a group level for valproate (n=52), levetiracetam (n=29) or lacosamide (n=28), but there were relevant changes in serum concentrations in some individual patients.

Conclusion: The present results demonstrate clinically relevant but unpredictable pharmacokinetic interactions caused by cenobamate in combination with other ASMs, with a need for close follow-up and use of TDM to account for these interactions in patients with refractory epilepsy.

1534 | Efficacy and tolerability of Brivaracetam: preliminary results of a National multicenter prospective audit on a mixed adult and pediatric population

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Purpose: To assess the efficacy and tolerability of Brivaracetam in a real-world pediatric and adult epilepsy population.

Method: A prospective audit across seven tertiary epilepsy centers. Brivaracetam was introduced as an add-on or a switch from Levetiracetam. Data were collected over six-month follow-up, including clinical history, medication dose, seizure frequency, and adverse effects. The methodology was designed to reduce bias from exclusively retrospective data collection.

Results: The audit included 103 patients (55 children, 48 adults), mean age 27.3 years (range 3–83). Epilepsy classification: 63 focal (30 children, 33 adults), 11 Genetic Generalized Epilepsy (8 children, 3 adults), 12 developmental/epileptic encephalopathy (11 children), and 17 unclassified (6 children, 11 adults). The mean epilepsy duration was 15.3 years. Among 31 patients who switched

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from Levetiracetam (11 children, 20 adults), 28 remained on Brivaracetam at six months (8/11 children, 20/20 adults), with 7 seizure-free (1 child, 6 adults). The overall retention rate was 81.5% (84/103)—76.3% in children (42/55) and 87.5% in adults (42/48). At six months, 30% (31/103) of patients had >50% seizure reduction [27.2% (15/55) of children, 33.3% (16/48) of adults], of whom 13.5% (14/103) were seizure free (5 children, 9 adults). Adverse events were reported in 35% (17 children, 19 adults), with behavioral issues, fatigue, and headache being most common. Fifteen percent (15%) of patients discontinued treatment (10 children, 6 adults), mainly due to adverse effects, inefficacy, or seizure worsening.

Conclusion: Brivaracetam is similarly tolerated in pediatric and adult populations, with a high retention rate. Adverse effects are common but often manageable with dose adjustments. Notably, switching from Levetiracetam to Brivaracetam preserves seizure control with good tolerability.

1568 | Re-analysis of trials of brivaracetam using Epilepsy DOOR to holistically account for benefits and harms of anti-seizure medications for people with epilepsy

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Purpose: Clinical trials of new therapies in patients with drug resistant epilepsy are typically designed and powered to detect changes in seizure frequency as the primary endpoint, without integrating other benefits and harms associated with treatments. We previously developed a new consumer codesigned outcome, the Epilepsy-DOOR, which combines seizure frequency with quality of life and adverse event measures. This study evaluated the Epilepsy-DOOR in previously completed phase 3 clinical trials of brivaracetam as an adjunctive therapy in patients with drug resistant epilepsy.

Method: The Epilepsy-DOOR was derived for each participant who completed the main RCT of three phase 3 trials of brivaracetam (N01252, N01253, N01254). Win odds for treatment with brivaracetam over placebo were estimated for each dose in each study. Win odds were estimated for change in seizure frequency, quality of life and adverse event severity and odds ratio estimated for responder rate.

Results: In N01252, the Epilepsy-DOOR demonstrated benefit of 100mg brivaracetam (Win Odds 1.42, 95% CI 1.03, 1.97, p=0.03) but not smaller doses over placebo, in line with the results when using seizure responder rate alone (Odds ratio 1.14, 95% CI 1.02, 1.29, p=0.02). In studies N01253 and N01254 benefit as assessed by Epilepsy-DOOR did not attain statistical significance, despite benefits at some doses when measuring seizure responder rate. Integration of adverse events contributed to lesser benefits of brivaracetam as measured by the Epilepsy-DOOR.

Conclusion: Epilepsy-DOOR showed similar effect sizes but slightly reduced power when compared with seizure responder rate. This reduced power is due to the appropriate reflection of adverse events by the Epilepsy-DOOR. Epilepsy-DOOR provides a more holistic measure of anti-seizure medication treatment, combining relative benefits and harms. It has potential as a future endpoint in clinical trials in epilepsy, including those of potential disease modifying therapies which aim to improve epilepsy co-morbidities and seizure frequency.

1578 | Influence of titration schedules on safety and effectiveness of eslicarbazepine acetate in Asian patients with focal epilepsy

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Purpose: Eslicarbazepine acetate (ESL) is indicated for the management of partial-onset seizures. Given the concerns regarding the safety profile of ESL in Asian populations, it is crucial to determine the most effective titration schedules for this demographic. We evaluated the efficacy of a low-dose initiation and gradual titration approach in comparison to the standard therapy initiation in Asian patients diagnosed with focal-epilepsy.

Method: Asian patients who commenced and adjusted their dosage of ESL in accordance with the manufacturer's guidelines were included. The standard titration protocol involved an initial dosage of 400mg od, with subsequent increases of an additional 400mg od every 1-2 weeks. This was contrasted with a low-dose initiation and gradual titration approach, which started with 200mg once daily and involved increments of 200 to 400mg every 3-4 weeks. After a 12-month period following the initiation of treatment, we compared the discontinuation rates, seizure freedom, response rates (reduction in seizure frequency of 50% or more from baseline), and side effects.

Results: The study involved a total of 194 patients (131 individuals on standard titration and 63 individuals on slow titration). The rate of discontinuation was significantly

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higher in the slow titration group compared to the standard group (40.3% versus 23.8%, p<0.05). Additionally, the responder rate and the rate of seizure freedom were notably lower in the slow titration schedule (61.1% versus 49.2% and 17.6% versus 6.3%, respectively, p<0.05). Furthermore, the slow titration schedule was linked to a reduced incidence of sedation (3.2% versus 4.7%) and dizziness (4.8% versus 9.5%). No significant differences were noted in other adverse effects, including hyponatremia or rash.

Conclusion: The initiation of low doses and the gradual titration schedule of ESL in Asian patients with epilepsy are linked to reduced efficacy and an increased rate of discontinuation, even though there is a marginally lower incidence of sedation and dizziness.

1585 | Outcomes of Adjunctive Cenobamate Therapy in a Large Early Access Cohort of Adult Patients with Drug Refractory Epilepsy with Focal-Onset Seizures

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Purpose: Cenobamate is a new antiseizure medication (ASM) licensed for adjunctive treatment of drug refractory focal-onset epilepsy. Approved in December 2021, studies suggest cenobamate is well-tolerated and highly impactful. We have been prescribing cenobamate since October 2020 as part of the Early Access Programme and aimed to retrospectively analyze tolerability and seizure outcomes for a large patient cohort under long-term follow-up in Newcastle-upon-Tyne.

Method: We collected data on 253 adult participants, including demographics (age at cenobamate initiation, sex), clinical data (epilepsy etiology, presence of intellectual disability), and number of previous ASMs categorized as early(2), mid (3, 4), or late (5+) cenobamate initiation. We explored drug retention and seizure outcomes ('seizure-free' (absolute absence of seizures), 'improved' (reduced seizure frequency/intensity), ongoing, or worse).

Results: Mean cohort age was 39.8 years (range 18-76), 59.7% male. Intellectual disability was present in 19.8%. Etiologies included neurodevelopmental (e.g. schizencephaly, polymicrogyria) in 8.7%; other structural (e.g. FCD, mesial sclerosis) in 18.6%; tumors in 4%. Tuberous sclerosis, Rasmussen's, and mitochondrial disease were present in 6, 3 and 3 patients, respectively. Most patients used cenobamate late (75.1%) (range 5-17 prior drugs), compared to mid (22.1%) and early (2.8%). Mean follow-up was 658 days (range 30-1583). Retention rates (mean 87%) and seizure outcomes were similar between early, mid, and late groups. 37.6% had improved seizures, of which 7.1% remained long-term seizure-free. 51.8% had ongoing seizures. 3.2% reported seizure aggravation. 40 patients(15.8%) concomitantly used VNS, of whom 47.5% had improved seizures and 1 remained long-term seizure-free. Analysis continues, including concomitant treatment discontinuation rates, etiology-specific outcomes, and off-licence prescribing.

Conclusion: Our results support the reputation of cenobamate as a clinically impactful, well-tolerated ASM. There is no evidence of clinical waning, with 30.4% patients reporting improved seizures after long-term follow-up. There appears no outcome benefit from earlier cenobamate use. Synergism of cenobamate use with VNS is apparent.

1597 | Anti-seizure medication prescribing habits in Portugal in stroke patients – a nationalwide survey

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Purpose: To characterize the prescription habits of Portuguese neurologists regarding post-stroke seizures and epilepsy.

Method: A convenience sample of 81 Portuguese neurologists answered an online survey about the management of stroke patients regarding anti-seizure medication (ASM) using different clinical scenarios. A descriptive analysis is reported.

Results: In patients with remote seizures after an ischemic stroke (IS), hemorrhagic stroke (HS) or cerebral venous thrombosis (CVT), most (93,75%, 91,25% and 88,75% respectively) would start an ASM in the acute setting. After

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the follow-up visit, at 6-12 months, without further seizures, the percentage of neurologists who would continue an ASM regardless of workup (EEG and brain-MRI) was 60% for IS and HS and 52,5% for CVT. In the setting of an acute symptomatic seizure after an IS, HS or CVT with or without parenchymal lesion, 51.25%, 61.25%, 83,75% and 70% respectively would start an ASM in the acute setting. After the follow-up visit, at 6-12 months, without further seizures, the percentage of neurologists who would continue an ASM regardless of workup was 11,5%, 15%, 11,25% and 3,75% for IS, HS, CVT with or without parenchymal lesion respectively. After an IS or HS, 1,25% and 3,75% respectively, would start an ASM as primary prophylaxis in the acute setting, and 10% and 5% would continue an ASM after 6-12 months. After a CVT with parenchymal lesion, 91,25% would start an ASM prophylactically and 7,5% would continue it regardless of any workup after 6-12 months.

Conclusion: This study reflects real-life management decisions of Portuguese neurologists. It identifies areas of consensual approach in post-stroke seizure management, but also topics with an heterogenous approach. It underscores the need for more evidence to fill knowledge gaps and guide clinical practice. If current guidelines change in the future, this work may allow the characterization of prescribing trends.

1608 | MicroRNA-134 inhibition attenuates intrinsic and synaptic dysfunction underlying pathophysiologic properties of the hippocampus in mice with Drug-Resistant Epilepsy

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Purpose: Drug resistance affects approximately one-third of the epilepsy population worldwide. MicroRNAs are short noncoding RNAs that regulate the networks of genes that control neuronal structure and function, setting excitability thresholds in the brain. Recent studies have shown that inhibiting miR-134 using antisense oligonucleotides (antimir-134) reduces spontaneous recurrent seizures in mice with drug-resistant epilepsy. However, the mechanism of this network-stabilizing effect is unknown. Previous electrophysiology studies suggested antimir-134 has limited effects on intrinsic properties of principal neurons in the hippocampus, but those studies were in naïve (healthy) animals.

Method: Here, we analyzed CA1 pyramidal neuron intrinsic excitability and network actions after antimir-134 treatment in mice with pre-existing epilepsy. Brain samples were collected 48 hours after injection of antimir-134 or PBS into epileptic mice. Whole-cell patch-clamp experiments were performed on *ex vivo* slices.

Results: CA1 pyramidal neurons from Antimir-134-treated epileptic animals displayed a reduced intrinsic excitability compared to epileptic controls, displaying fewer action potentials following current injections, and exhibiting action potentials with slower repolarization slope and longer widths properties. Antimir-134-exposed CA1 neurons also exhibited a lower voltage-gated potassium channels-dependent A-type current density. Synaptic transmission analysis revealed attenuated pre- and postsynaptic excitatory transmission mechanisms in Ant-134-treated CA1 neurons. We observed lower excitatory post-synaptic potentials (EPSPs) in response to electrical stimulus following antimir-134 treatment, and a restitution of network deficits toward expected levels in the CA3-to-CA1 synapse, indicating a basis for rescue of learning-related synaptic plasticity.

Conclusion: These findings show that inhibition of miR-134 can stabilize multiple aspects of neuronal network performance in the epileptic hippocampus. This may underlie the potent effects of antimir-134 on spontaneous seizures. The results support preclinical development of this novel disease-modifying treatment for temporal lobe and perhaps other epilepsies.

1613 | Evaluation of cognitive impairment in persons with epilepsy (PWE) on levetiracetam (LEV) versus sodium valproate (SV) monotherapy

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Purpose: Studies show that LEV has a better side effect profile than SV. SV is most commonly prescribed as the first-line drug because of its low cost. Multiple studies show PWE on LEV have better cognitive status. The study's main aim is to determine if LEV monotherapy has any significant impact on cognitive status compared to SV monotherapy.

Method: PWE attending the OPD Department of Neurology, AIIMS, New Delhi, were screened for eligibility to participate in the study. After obtaining consent, verbally as well as via Google Forms (This study was conducted during the COVID pandemic from December 2019 to December 2021), we enrolled a total 88 participants-LEV

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monotherapy (n=50) and SV monotherapy (n=38). They were screened for cognitive impairment using Telephone Interview for Cognitive Status(TICS) and the scores were further categorized into various cognitive sub-domains.

Results: Out of 88 patients interviewed, the mean score of TICS was 33.98 with SD of 3.42 and the median was 35 with a range of 22-41. Among the subdomains tested, the scores for memory were normally distributed whereas the scores for orientation, language and executive function did not follow normal distribution. The percentage of patients with no cognitive impairment was approximately 66% (n=58), with half undergoing monotherapy and the other half undergoing SV monotherapy. About 32% (n=28) of patients had ambiguous cognitive status, with over 2/3rd receiving LEV monotherapy (n=19) and the remaining 9 patients receiving SV monotherapy; 2 patients having mild cognitive impairment were receiving LEV monotherapy.

Conclusion: Our study did not show any significant difference in the cognitive status of patients receiving LEV or SV monotherapy. When individual cognitive domains were examined, the SV monotherapy group performed significantly better than LEV monotherapy in terms of orientation. whereas in the rest of the domains including memory, executive function and language skills there was no difference.

1619 | Sodium blockers challenge: the effects of Lacosamide versus Cenobamate on heart rate variability (HRV) in patients with drug-resistant epilepsy

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Purpose: Drug-resistant epilepsy (DRE) is known for yielding worsening changes on cardioautonomic control, mainly evaluated in terms of heart rate variability (HRV). Aside from long-lasting epilepsy, sodium channel blockers are today believed to play a similar role in disrupting HRV balance. Cenobamate (CNB) and Lacosamide (LCS) are both third-generation drugs frequently employed in the treatment of DRE, but their effects on HRV has not been evaluated yet.

Method: We compared two groups (LCS-group and CNB-group) of drug-resistant epileptic patients, each consisting of 20 subjects, matched for sex, age and seizure frequency. All patients underwent EEG and EKG registrations prior to and following the introduction of CNB or LCS as add-on therapies (median EEG time since the start of the new therapy: 6 months). Linear mixed models (LMM) were implemented to ascertain the difference in terms of HRV changes between the aforementioned populations.

Results: At baseline no differences were detected between the CNB group and the LCS group according to time-domain and frequency-domain HRV parameters. At follow-up, a multiplicative effect for the interaction between treatment and time was observed in CNB group for MeanRR (p=0.03), pNN50 (p=0.50), LF n.u. (p=0.02), HF n.u. (p=0.02) and LF/HF (p<0.01), ApEN (p=0.02).

Conclusion: When it comes to the topic of cardioautonomic control and HRV, there is no current solid data concerning the tolerability of novel sodium channel blockers. As gathered from our studied cohorts, Cenobamate appears to stand out among other drugs interfering with sodium currents, on the basis that its lack of disarranging effects on HRV gives it a superior tolerability profile compared to Lacosamide, on top of the emerging evidence about its efficacy on seizure control.

1631 | Cenobamate in Pediatric Patients with Drug Resistant Epilepsy: Real-World Data from a European Multicenter Retrospective Study

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Purpose: Drug-resistant epilepsy (DRE) in pediatric patients presents a significant challenge, necessitating effective and well-tolerated treatments. Cenobamate (CNB), a novel anti-seizure medication (ASM) with established efficacy in adults, is used off-label in children, though data on its safety and efficacy remain limited. This European multicenter retrospective study evaluates CNB outcomes in pediatric patients.

Method: A retrospective analysis was conducted across nine European centers on pediatric patients treated with CNB. Data collection is ongoing.

Results: This preliminarily analysis included 108 pediatric patients with epilepsy, with a mean age of 14.27 ± 3.81 years. The most common epilepsy etiology was structural (n = 61). Focal seizures predominated, with focal (n = 35) or multifocal (n = 39) EEG patterns. Patients had trialed an average of 6.56 ± 4.32 prior ASMs. CNB was initiated at 13.18 ± 3.4 years (mean epilepsy duration: 9.04 ± 4.25 years). Mean CNB dose was 166.67 ± 91.2 mg (3.52 ± 1.64 mg/kg/day). Seizure frequency decreased from a median of 30 to 9 per month ($p < .0001$), with seizure freedom in 20 patients (18.5%) and >50% seizure reduction in 37 (34.3%). At least one ASM was discontinued in 57 patients (54.2%), while dose reductions were achieved in 51 patients (48.5%). Adverse events occurred in 56.4 % (n = 62), most commonly fatigue. Despite this, CNB demonstrated a high retention rate of 84.2%, with a median follow-up duration of 581.5 days.

Conclusion: This study demonstrates CNB potential as an effective and well-tolerated treatment for pediatric DRE, with notable seizure reductions, high seizure freedom rates, and reduced reliance on other ASM. Despite common adverse events like fatigue, its high retention rate supports tolerability. Ongoing subgroup analyses aim to refine its clinical application.

1643 | Highly purified cannabidiol (hpCBD) in CDKL5 deficiency disorder (CDD): open label prospective study

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Purpose: CDKL5 deficiency disorder (CDD) is an early-onset developmental epileptic encephalopathy characterized by high seizure burden and drug-resistance, cerebral visual impairment, motor and sleep disorders. There is preliminary evidence of highly purified cannabidiol (hpCBD) efficacy in CDD in reducing seizures (Devinsky O. et al. EpilepsyBehav. 2018 Sep;86:131-137) but no reported effects on other comorbidities. The aim of this study is to further define efficacy and safety of hpCBD in CDD.

Method: **T**his is a prospective single-center open label study with hpCBD in patients with CDD older than 1 year. We assessed the frequency of countable motor seizures, parental and physician perception of global improvement (CGI), changes in sleep, motor performance and EEG at 3, 6 and 12 months after enrollment.

Results: 8/9 patients (9 females, median age 10 years, range 1-24 years) completed the study, one patient withdrew at 6 months due to skin rash. Seizure reduction >50% at 3 months was achieved by 8/9 subjects at 3 months, 7/9 at 6 months, 3/8 at 12 months. In three patients there was a significant improvement in motor performance and in four patients in sleep quality. All caregivers reported at least a minimal global improvement (CGI 3) throughout the study while in three cases there was a great improvement (CGI 2), with a peak at 6 months. At 12 months, all subjects achieved a minimal global improvement, which was the reason for hpCBD continuation despite relative loss of efficacy on seizure frequency. No severe adverse event was recorded during the study.

Conclusion: hpCBD could be a safe and effective option for CDD although efficacy on seizure tends to decrease over time similarly to what happens with most drugs used in this condition. Results suggest a possible global improvement beyond epilepsy. Future trials should include assessment of non-seizure outcomes and compare long-term efficacy of different ASMs.

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1669 | A single-centre, open-label pilot study to assess the efficacy and safety of Cannabidiol oral solution as an adjunctive treatment for pediatric subjects with Developmental and Epileptic Encephalopathy

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Purpose: This study aims to evaluate the effectiveness, safety, and tolerability of CBD as an add-on treatment in children with Developmental and Epileptic Encephalopathy (DEE) and highly treatment-resistant epilepsies
Method: This single-center, open-label pilot study evaluates the efficacy, safety, and tolerability of CBD as adjunctive therapy in pediatric patients with DEE. Conducted as a non-profit initiative, it includes a 4-week Baseline Period for eligibility screening and seizure monitoring, a 21-day Titration Period reaching 20 mg/kg/day, and a 20-week Maintenance Period. Primary endpoints assess seizure reduction and EEG improvement via blinded evaluation. Secondary endpoints evaluate safety through adverse events, lab tests, ECG, vital signs, and neurological exams. Parents/caregivers record daily seizure frequency. The total study duration, including follow-up, is approximately 30 weeks.
Results: Nineteen patients were enrolled. The study demonstrated that CBD therapy significantly reduced both the number and severity of seizures and improved EEG abnormalities in children with DEE when administered alongside existing AEDs. The treatment was well tolerated, with adverse effects managed through dosage adjustments
Conclusion: This pilot study provides preliminary evidence supporting the efficacy and safety of CBD as an adjunctive treatment for highly treatment-resistant DEE. The findings suggest that CBD can be a valuable therapeutic option for children with this condition, reducing seizure frequency and severity while being generally well-tolerated

1684 | Antiseizure rescue medications use in Epilepsy clinic of a level 4 Epilepsy center

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Purpose: The purpose of this study is to assess the use of Antiseizure rescue medication in adult patients with seizures in the outpatient setting at a level 4 Epilepsy center. The main themes of the recent findings are that rescue medications and seizure action plans (SAPs) are underutilized, particularly in the adult population. This underutilization is seen in academic epilepsy centers as well. The safety and efficacy of intranasal midazolam and intranasal diazepam is comparable with rectal diazepam for the treatment of seizure clusters. Additionally, this intranasal formulation has the benefit of a more socially acceptable route of administration and ease of use.
Method: We reviewed the adult patients with epilepsy seen in our epilepsy clinic over 1 year (January to December 2024). We excluded the patients with one time seizure, spells of unknown nature, psychogenic nonepileptic spells.
Results: Seven epileptologists' patients with epilepsy were reviewed for use of Antiseizure rescue medications; intranasal midazolam, intranasal diazepam, rectal diazepam, lorazepam tablets and diazepam tablets. Total patients with epilepsy seen were 3116 in 2024 and the use of rescue medication among the providers ranged from 3.4% to 9.2% patients.
Conclusion: The use of Antiseizure rescue medication is low even in academic centers and poses a disparity of care and suboptimal treatment. Substantial portion of patients with ongoing seizures did not receive rescue medications. The implication of these findings is greater and points to a need to improve awareness of rescue medications available to our patients.

1688 | Corticosteroids in pharmacoresistant epilepsy: A single-center experience with oral methylprednisolone therapy

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Purpose: Pharmacoresistance to common antiseizure medications affects approximately 20% of pediatric epilepsy cases (Wirrell EC et al. Epilepsia 2013; 54:1056–64). For many years, corticosteroids (CS) and adrenocorticotropic hormone (ACTH) have been used to manage these cases, based on the hypothesis of neuroinflammation in epilepsy. In addition to treating infantile spasms (IS), CS have also been used for other severe forms of epilepsy in children (Bast T et al. Neuropediatrics 2014;45:378–85). We present a retrospective analysis of a group of patients with various forms of severe childhood epilepsy (excluding IS) who were treated with pulsatile oral methylprednisolone

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(MPR) therapy to evaluate the efficacy, safety, and tolerability of this treatment.

Method: This study included 39 children with drug-resistant epilepsy of different etiologies who were seen at a tertiary epilepsy center.

Results: Initially, patients received a median of six MPR pulses (range: 4–9), each consisting of a single oral dose of 20 mg/kg/day of MPR, administered over three consecutive days per week. Following this initial phase, the intervals between pulses were adjusted based on the individual response and other relevant factors. A total of 33 out of 39 patients (85%) showed a positive response, with 22 cases achieving an optimal efficacy outcome based on clinical and electroencephalographic criteria. Response rates were observed in 7 of 10 cases (70%) with a genetic origin, 17 of 20 (85%) with a structural cause, and 100% of those with an unknown etiology. Specifically, all patients with Spike Wave Activation in Sleep (SWAS) responded, as did 4 of 5 patients with Lennox–Gastaut syndrome. Most patients did not experience severe adverse effects.

Conclusion: This study confirms the efficacy, safety, and high tolerability of oral MPR pulse therapy in pediatric patients with epileptic encephalopathies, developmental and epileptic encephalopathies, and other refractory epilepsies.

1692 | High-dose cenobamate in the treatment of drug-resistant epilepsy and the effect on the concomitant medication

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Purpose: Clinical trials and real-world observational studies have shown that cenobamate (CNB) is highly effective in the treatment of focal epilepsy. We investigated real-world outcomes and safety with high-dose cenobamate in patients with drug-resistant epilepsy and the effect on the concomitant medication.

Method: This was a single-center retrospective analysis of adults with drug-resistant epilepsy treated cenobamate between September 2022 and January 2025. Effectiveness endpoints included ≥50%,≥75%, ≥100% reductions in seizure frequency, safety endpoints included rates of adverse events (AEs) and AEs leading to discontinuation. We analyzed the change in concomitant medication.

Results: The analysis included 39 patients (22 men and 17 women) with refractory epilepsy treated cenobamate as add-on therapy. The mean age of patients was 38 years, mean duration of epilepsy 24 years. The mean number of prior antiseizure medications (ASMs) was 8,6 (2 to 17), 14 patients (35,9%) were before cenobamate treated with VNS, 10 patients (25,6%) underwent resective epilepsy surgery, four of them being treated with both. 10/39 patients (25,6%) stopped cenobamate due to adverse events. Among patients who continued cenobamate (29 patients 74,4%), the mean therapeutic dose of CNB was 260mg per day (100 to 400), and 79,3% patients had dose ≥200mg. The mean follow-up was 79 weeks (7 to 124). At the last available visit, the rate of seizure freedom was in 8/29 patients (27,6%), ≥75%, ≥50% were in 5/29, 6/29 (17,24%, 20,7%), and one patient stopped cenobamate due to lack of efficacy. The number of the concomitant ASMs was reduced in 10/29 patients (34,5%), and discontinued in 14/29 patients (48,3%).

Conclusion: Patients with drug-resistant epilepsy experienced meaningful seizure outcomes on cenobamate. High-dose CNB is generally well-tolerated ASM, AEs were frequent but mostly mild or moderate, and few led to discontinuation. Adding cenobamate led to reduced mean concomitant ASM drug loads.

1743 | Efficacy and tolerability of Cenobamate: real-world experience from an Italian tertiary center

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Purpose: To investigate the real-world efficacy and tolerability outcomes of cenobamate (CNB) in a group of people with drug-resistant epilepsy (DRE) in an Italian tertiary center.

Method: We conducted a single-center, retrospective, observational study at Bellaria Hospital between 2022 and 2024. Inclusion criteria were age ≥18 years, focal seizures, DRE and 12 months follow-up. Data were collected from medical records. Primary efficacy endpoints included seizure reduction (≥50-80%, ≥80.1-99%, 100%) at 3, 6 and 12 months. Safety endpoints included rates of adverse events (AEs) at 3, 6 and 12 month visits.

Results: The study included 96 people with DRE, 13.5% of whom had developmental and epileptic encephalopathy (DEE). Etiology was known in 69% (11.5% genetic, 9.4% vascular malformation, 3% autoimmune, 3% infectious, 36.5% structural and 5% genetic and structural). At

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baseline, the median duration of epilepsy was 26 years and the median number of seizures/month was 12.5. The median number of previous antiseizure medications (ASMs) and concomitant ASMs was 6 and 2.5, respectively. Retention rates were 95%, 92% and 88.7% at 3, 6 and 12 months, respectively. The mean CNB dosage/day was 113 mg, 149 mg and 181 mg at 3, 6 and 12 months. At the last available visit, the rate of seizure freedom was 15.9%, while the ≥50-80% and ≥80.1-99% responder rates were 28.6% and 20.6%, respectively; the seizures/month rate did not change in 17.5% and worsened in the remaining 17.5%. There was a significant reduction in the number of seizures per month at all three timepoints considered ($P < 0.001$). The cumulative percentage of people experiencing AEs was 46%, 39.6% and 38.7% at 3, 6 and 12 months, respectively.

Conclusion: In our refractory population, CNB showed good efficacy regardless of etiology, prior and concomitant ASMs, and duration of epilepsy. AEs were common but mostly mild-to-moderate and tended to decrease over time.

1750 | Trends in Antiseizure Medication Prescriptions for Children in France (2014-2023): Shift to Newer Generations, Reduced Teratogenic Risks, and Growing Generic Prescriptions

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Purpose: This study analyzes trends in antiseizure medication (ASM) prescriptions in children in France from 2014 to 2023, focusing on drug evolution, gender disparities, and the use of generics

Method: Data from the French National Health Insurance database (Open Medic) covered all reimbursed ASM prescriptions for patients aged 0–19 years. Trends were analyzed using multivariate logistic regression and LASSO regression to assess factors influencing generic prescriptions and gender differences.

Results: Between 2014 and 2023, 2,013,994 children received an ASM prescription, totaling 15,733,118 medication boxes and 254,374,700 euros in healthcare expenditure. ASM prescriptions increased significantly over time, while overall expenditure remained stable. Third-generation ASMs represented the majority (64.6%), particularly those introduced between 1990 and 2000. Meanwhile, second-generation ASMs declined (-31%), and first-generation ASMs remained stable (+9%). Hospital practitioners issued 66.1% of ASM prescriptions (n = 10,393,970), while prescriptions from general practitioners declined by 28.7% (n = 3,181,162 in 2023) and those of private psychiatrists increased substantially by 251% (n = 74,598 in 2023).

Sodium valproate prescriptions dropped by 37%, with a more pronounced decline in girls (-21% vs. -17% in boys), following regulatory restrictions. Carbamazepine use also decreased (-36%), while lamotrigine (+49%) and levetiracetam (+77%) showed the most significant increases.

The proportion of generic ASM prescriptions doubled from 10.7% (n = 20,181) in 2014 to 20.4% (n = 47,122) in 2023 ($p<10^{-4}$). Increased generic prescribing was associated with later years and psychiatrist prescriptions, whereas sodium valproate use and prescriptions by neurologists and pediatricians correlated with lower generic uptake.

Conclusion: Over the last decade, ASM prescriptions in children increased, with a shift toward newer-generation ASMs, a decline in teratogenic-risk drugs, and a moderate rise in generics. These trends highlight the impact of evolving prescribing practices and regulatory measures on pediatric epilepsy management.

1753 | Long-Term Efficacy, Safety, and Retention of Cannabidiol in Pediatric Drug-Resistant Epilepsy

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Purpose: This study evaluates the efficacy, safety, and long-term retention of cannabidiol (CBD) in a pediatric population with drug-resistant epilepsy, including both approved and off-label conditions.

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Method: We conducted a prospective study in a tertiary pediatric epilepsy center, including consecutive patients who initiated CBD between 2019 and 2021. Seizure and non-seizure outcomes were assessed via caregiver-reported questionnaires at 1, 2, and 6 months. Retention rates were analyzed up to 18 months. Cox proportional hazards models identified factors influencing retention.
Results: A total of 103 patients (52 boys, median age 11.2 years, IQR: 7.1–15.4) were included. CBD was prescribed for conditions covered by its European label in 46.6% of cases (n = 48, Dravet syndrome: 47.9% (n = 23), Lennox-Gastaut syndrome: 31.3% (n = 15), tuberous sclerosis complex: 20.8% (n = 10)), while 53.4% (n = 55) were off-label users. Between M0 and M1, 54% of patients reported reduced seizure frequency, 50% noted an improved global condition, and 45% saw enhancements in communication. Between M1 and M2, seizure duration decreased in 36%, while 43% of patients reported behavioral improvements. By M6, these effects persisted, with 48% maintaining seizure reduction, 60% reporting improved communication, and 58% experiencing global improvement. Retention rates were 97% at M1, 90% at M2, 82% at M6, 66% at 12 months, and 56% at 18 months. Off-label use (p = 0.02), male gender (p = 0.049), and older age at initiation (p = 0.03) were associated with higher retention.
Conclusion: CBD demonstrated sustained efficacy, good tolerability, and high retention rates in pediatric drug-resistant epilepsy, including off-label conditions. Some effects continued to emerge up to 6 months after treatment initiation, particularly in non-seizure-related domains such as communication and behavior. Further research is needed to explore its benefits in orphan epilepsy syndromes.

1770 | Cenobamate early adoption in patients with drug-resistant epilepsy

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Purpose: Drug-resistant epilepsy (DRE) is identified by the failure of two antiseizure medications (ASMs), either in monotherapy or in combination. Cenobamate (CNB) is a novel ASM which can be employed as an add-on therapy in DRE. Data about the effectiveness and tolerability of CNB implemented as third-line ASM (i.e., early adoption) are scarce.
Method: 23 DRE patients treated with CNB as early adoption (EA) treatment (EA-CNB-group) and a sex-, age- and seizure type-matched group of 46 DRE patients treated with other ASM as EA (CNT group) were enrolled. Demographics and clinical data were compared between the two groups. The effectiveness and tolerability of CNB was evaluated at 3-, 6- and 12-months follow-up visits.
Results: At baseline, there was a significant difference in seizure frequency between the two groups, with EA-CNB group experiencing a higher seizure burden (p=0.003). At 3-month, patients in EA-CNB group showed a higher seizure freedom rate compared to CNT group (p=0.01). A sustained seizure freedom rate difference between the two groups was also reported at 6-month and 12-month follow-up visits (p=0.01 and p=0.04, respectively). CNB showed a greater tolerability, with a lower prevalence of side effects at 3-month follow-up compared to CNT group (p=0.04). No differences according to AE occurrence between the two groups were reported at 6- and 12-month.
Conclusion: Our data support the evidence of greater tolerability and effectiveness of CNB as early adoption treatment compared to other third-generation drug classes.

1785 | Stiripentol as an adjunctive therapy for refractory epilepsy caused by SLC6A1-NDD

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Purpose: *SLC6A1*-related neurodevelopmental disorder (*SLC6A1*-NDD) is a rare disease characterized by intellectual disability, epileptic encephalopathy, neurobehavioral and/or psychiatric manifestations. In many cases the epilepsy is refractory. *SLC61A* encodes a GABA transporter, GAT1, which reuptakes GABA into presynaptic neurons and glia. One of the mechanisms of action of Stiripentol is the enhancement of GABAergic transmission by inhibiting GABA transaminase (GABA-T), blocking the GABA transporter (GAT) and acting as a positive allosteric modulator of GABA A receptors. We aimed to investigate Stiripentol as an adjunctive therapy in these cases.
Method: Retrospective review of two patients with SLC6A1-NDD with refractory epilepsy treated with Stiripentol as adjunctive therapy, one from Milan (Italy) and the other one from Basel (Switzerland). Information on family and personal history, psychomotor development, behavioral manifestations, epilepsy, genetic studies, EEG and previous anticonvulsive medications were

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collected. In the Italian case, the Stiripentol was introduced together with sodium valproate, ethosuximide and clobazam. In the Swiss case, it was added to sodium valproate, cannabidiol and clobazam.

Results: In the Italian case, the introduction of Stiripentol led to a freedom of seizures. In the Swiss case, a very significant reduction in the number of seizures was achieved. In both cases, an improvement in cognitive and behavior was showed. No important side effects were reported.

Conclusion: Given these promising results, we can conclude that Stiripentol in adjunctive therapy can be an effective alternative in cases of SL6CA1-NDD with refractory epilepsy.

1793 | Impact of Fenfluramine on Seizure Frequency, Socio-Communicative Skills, Behavior, and Quality of Life in Patients with Dravet Syndrome: Results from a Semi-Structured Interview with Caregivers

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Purpose: Fenfluramine (FFA) has proven to be highly effective in controlling seizures in patients with Dravet syndrome (DS). This single-center longitudinal study aims to evaluate its impact on executive functions, attention, participation, and overall quality of life (QOL) in these patients

Method: We followed a cohort of 33 patients with DS treated with add-on FFA. The median duration of treatment was 44.5 months (range 2-82 months). We assessed both seizure-related and non-seizure-related QOL domains after initiating FFA treatment in 22 of the 33 patients (ages 4–30 years, M = 15.85, SD = 7.02). 23% of the participants underwent pre- and post-treatment cognitive assessments. Raw scores were standardized using normative data ($\mu = 100$; $\sigma = 15$) and analyzed qualitatively. Changes in standardized scores were examined in relation to treatment duration and patient age. Additionally, a semi-structured caregiver interview was conducted to collect insights into the patient's attention, social skills, and overall QOL.

Results: After FFA treatment, seventy-five percent of the patients had a significant reduction in seizure frequency. Of those who completed cognitive assessments, 60% showed significant improvements in standardized scores, while 40% with shorter treatment durations experienced mild declines. Caregiver interviews revealed statistically significant improvements in cognition, attention, speech, social skills, and both patient and caregiver QOL. Patients without side effects demonstrated greater behavioral improvements ($p = 0.019$) and better social communication ($p = 0.046$). Minor improvements were also observed in motor function.

Conclusion: The best outcome of this drug therapy was observed in seizure control. Fenfluramine treatment in DS patients is effective not only in managing seizures but also in improving overall quality of life. Long-term treatment showed more pronounced and statistically significant improvements across various domains. The excellent results in cognitive function are likely due to the reduced negative impact of seizures on this patient cohort.

1794 | Effectiveness of Cenobamate on seizures in focal epilepsy: a single center real-world observation

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Purpose: Cenobamate (CNB) is an anti-seizure medication indicated for drug-resistant focal epilepsy. This study aims to evaluate CNB effectiveness on the number and type of focal seizures.

Method: Twenty patients with focal epilepsy starting CNB according to clinical practice and indication, reaching a dose of 200 mg/daily at the first follow-up visit were enrolled. Patients were evaluated at baseline (T0) and after six (T1) and twelve months of treatment (T2). The type of seizures was classified using ILAE 2017 Classification.

Results: At T0, 4 patients presented focal aware seizures (FAS), 11 had focal impaired awareness seizures (FIAS), and 5 patients presented focal to bilateral tonic-clonic seizures (FBTCS). At T1, 6 patients were seizure free (1 FAS,4 FIAS,1 FBTCS), 6 patients reduced the seizure frequency (1 FAS,4 FIAS,1 FBTCS), 3 patients changed the type of seizures (3 FBTCS to FAS/FIAS), 3 patients (1 FAS,2 FIAS) did not change the seizure frequency and 2 patients (1 FAS,1 FIAS) had more seizures of the same type thus all needing the increase of the dose of cenobamate (4 to 250 mg/day and 1 to 300 mg/day). At T2, 16 patients were seizure free (4 FAS,9 FIAS,3 FBTCS), 1 had less episodes of the same type (1 FIAS), 1 had more events (1 FIAS), 1 patient condition was unchanged (FBTCS to FAS/FIAS) and 1 had a different type of seizure (FBTCS to FAS/FIAS).

Conclusion: This real-world study showed the effectiveness of CNB in treating focal onset drug-resistant seizures

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at the dose range between 200 to 300 mg/day. The main effect was observed at the 12-month follow-up visit. All types of focal seizures responded to CNB treatment (82% FIAS, 80% FAS, 60% FBTCS), and in a few cases seizures changed during the CNB treatment (mainly in case of FBTCS becoming FAS or FIAS).

1813 | Cenobamate and QT Interval: A Prospective Study on Cardiac Safety

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Purpose: Cenobamate (CNB) is a novel antiepileptic drug that may cause dose-dependent QT interval shortening, raising concerns about cardiac safety [Krauss GL et al. Epilepsia 2020;61:1099-1111.]. While QTc values below 300 ms significantly increase the risk of fatal arrhythmias [Viskin S et al. J Am Coll Cardiol 2020;75:2372-2382.], some antiseizure medications affect QT intervals, necessitating thorough evaluation [Schmidt D et al. CNS Drugs 2021;35:537-548.]. This study examines QT interval variations and safety in refractory epilepsy patients.
Method: A prospective observational study was conducted with 40 patients (60% male, mean age 35 ± 10.8 years). Electrocardiograms (ECG) and clinical assessments were performed at baseline and after six months of CNB therapy (≥200 mg/day). Statistical analyses assessed QT/QTc distributions and paired tests for differences between time points. Safety data were collected based on reported adverse events.
Results: QT shortening was observed but remained within safe limits (mean QTc change: -12.2 ms). Baseline QTc was 397.46 ± 22.9 ms, decreasing to 385.29 ± 22.6 ms at six months (p=0.032). No values fell below 340 ms. Adverse effects occurred in 65% of patients, including drowsiness and dizziness, with no arrhythmias reported. However, one patient experienced a cardiorespiratory arrest shortly after initiation and discontinued CNB. Although a direct causal link was not established, the event was reported to INFARMED. Two additional patients discontinued due to inefficacy (one at 200 mg after six months), and one withdrew early due to diarrhea.
Conclusion: Cenobamate demonstrated a dose-dependent but clinically insignificant QTc shortening, supporting its cardiac safety in refractory epilepsy. However, QT monitoring is advisable, particularly in patients with cardiac conditions or those on concomitant QT-shortening drugs. Further studies are needed to assess potential rare cardiac risks.

1814 | Impact of Cenobamate on Sodium Levels and Antiseizure Medication Adjustment: A 12-Month Prospective Study

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Purpose: Cenobamate, a novel antiseizure medication (ASM), has demonstrated high efficacy in epilepsy treatment [Krauss GL et al. Epilepsia 2020;61:1099-1111.]. However, its long-term metabolic effects, particularly on sodium balance and polytherapy adjustments, remain underexplored. Sodium disturbances have been reported with certain ASMs, including sodium channel blockers (SCBs), necessitating further evaluation [Lattanzi S et al. Neurology 2020;95:e2713-e2725.]. This study assesses the impact of cenobamate on serum sodium levels, total ASMs, and SCB usage over 12 months.
Method: A prospective study was conducted with 23 patients with refractory epilepsy initiating cenobamate (mean age: 35 ± 10.4 years; 56.5% male; mean epilepsy duration: 26 ± 10 years). Three patients discontinued treatment, leaving 20 for analysis at 12 months. Serum sodium levels and ASM usage were assessed at baseline, 3, 6, and 12 months. Normality testing guided statistical analyses, including the Wilcoxon signed-rank test for paired sodium comparisons and the Friedman test for ASM count. The McNemar test assessed SCB reduction ($p < 0.05$).
Results: Throughout the study, sodium levels remained stable, with median values ranging from 140.0 to 141.0 mmol/L. No significant variations were observed over time (Wilcoxon test, p>0,05). The total number of ASMs showed minor fluctuations but remained stable over 12 months. The median ASM count remained constant at 4.0 across all time points. SCB usage decreased from 85.0% at baseline to 70.0% at 12 months; however, this reduction was not statistically significant (McNemar test, $p = 0.26$).
Conclusion: Our findings indicate that cenobamate does not significantly impact serum sodium levels or alter the need for SCBs over 12 months. The total number of ASMs remained stable, and sodium homeostasis was preserved. These results support the favorable metabolic profile of cenobamate, with no significant risk of electrolyte

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disturbances. Future studies with larger cohorts and extended follow-up are needed to confirm these findings.

1836 | A case of linear sebaceous nevus syndrome treated with alpelisib

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Purpose: Linear sebaceous nevus syndrome (SLNS) or Schimmelpenning-Feuerstein-Mims syndrome is a mosaic RASopathy characterized by the association of craniofacial sebaceous nevus with variable multisystem alterations, being one of the main ones hemimegalencephaly, which usually causes refractory epilepsy. In many cases, this RASopathy results from a somatic variant in PIK3CA gene. Alpelisib is a PI3K protein inhibitor approved by the FDA for the treatment of patients with PROS (PIK3CA-related overgrowth spectrum) and has shown promising results in pediatric patients, especially with regard to the improvement of neurological symptoms and control of overgrowth.
Method: Retrospective review of a SLNS case with refractory epilepsy secondary to hemimegalencephaly.
Results: We present the case of a 10-month-old girl with hyperkeratosis and discrete congenital hypertrophy of the left lip. At 4 months, he developed marked hypertrophy of the left upper and lower lip, associated with hypertrophy of the gums, tongue, and palate. In addition, she presents a well-defined, yellowish-orange left hemifacial plaque, along with strabismus and seizures consistent in generalized hypertonia or only disconnections. With the suspected diagnosis of SNSL we performed a magnetic resonance imaging (it showed left hemimegalencephaly with diffuse polymicrogyria), an electroencephalogram (compatible with focal epilepsy), biopsy of the skin lesion (compatible with sebaceous nevus) and genetic study in tissue (pathogenic variant in PIK3C). Anticonvulsant treatment (levetiracetam, oxcarbazepine and vigabatrin) was started, with poor seizure control, pending finally surgical evaluation (first one was made with the result of the MRI). In this context we begin treatment with alpesilib, prior obtaining compassionate use (it is only approved in children over two years of age) and in this moment we are waiting for the first results.
Conclusion: We want to highlight the importance of multidisciplinary management (neuropediatricians, dermatologists and anatomopathologists). Furthermore, we conclude that in refractory epilepsies it is important to use drugs directed to the gene variant found

1201 | Pharmacological Evaluation of Anti-Seizure Medications in the Rat Amygdala-Kindling Model

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Purpose: Despite advances in epilepsy treatment, unmet clinical needs persist, particularly in patients who exhibit resistance to Anti-Seizure Medications (ASMs). Preclinical models are crucial for early drug discovery and the development of therapies for symptomatic epilepsy treatment. The rat amygdala-kindling model, characterized by repetitive subconvulsive electrical stimulations, provides valuable insights into epilepsy progression. This model predicts drug efficacy in seizure control, from focal to secondarily generalized convulsive seizures. Purpose: In this study, we evaluated the pharmacological profiles of various ASMs using this model.
Method: Methods: Sprague Dawley rats were implanted with electrodes in the basolateral amygdala (BLA), parietal cortex, and prefrontal cortex. Epileptic activity was assessed via electroencephalogram (EEG) recordings and synchronized video monitoring. After discharges (ADs), defined as EEG spikes and spike-waves following stimulation, were used to determine the AD threshold (ADT) for each rat. The kindling protocol was administered daily until rats reached stage 5 on Racine's scale for three consecutive days. Rats were alternately treated with ASMs (or respective vehicles): diazepam, ethosuximide, carbamazepine, retigabine, and levetiracetam.
Results: Results: Differential pharmacological responses were observed, for instance, diazepam at 3 mg/kg produced seizure control as measured by a reduction in motor components of the seizure and a reduction in after discharge duration (ADD). Conversely, ethosuximide at 100 mg/kg did not show any effect on motor components of the seizure nor on ADD. We reported distinct effects between focal and cortical EEG responses for the remaining three ASMs, which will be described in further detail in the results section.
Conclusion: Conclusions: This study highlights the translational relevance of the rat amygdala-kindling model for identifying novel compounds with improved tolerability and efficacy against focal and secondarily generalized seizures. Combining this model with a cross-over design offers a decision-enabling screening platform for epilepsy treatment, particularly in cases of pharmacoresistant focal seizures.

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1567 | Pharmacokinetics, safety, and efficacy of eslicarbazepine acetate in Asian and Caucasian patients: a comparative observational study

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Purpose: Eslicarbazepine acetate (ESL) received approval for the treatment of partial-onset seizures. However, the underrepresentation of Asian patients in the approval studies has led to uncertainties regarding safety issues in this demographic, which in turn affects clinical decision-making. In this study we present real-world data on the pharmacokinetics, safety, and efficacy of ESL in Asian patients in comparison to their Caucasian counterparts with focal-epilepsy.

Method: Data was gathered from a comprehensive epilepsy registry. Both Asian and Caucasian patients received daily doses of ESL ranging from 400 to 1600 mg. The plasma levels of ESL and (R)-licarbazepine were measured approximately 10 to 12 hours post-administration of ESL. The documentation included, the response rate (reduction in seizure frequency of 50% or more from baseline) seizure freedom after a 12-month period and side effects.

Results: The study involved a cohort of 268 patients diagnosed with focal-epilepsy, evenly divided between Asian and Caucasian ethnicities. Among the 133 Asian participants, the predominant nationalities included Chinese (47.4%), Korean (39.1%), and Thai (6.0%). The average dosage of ESL was not different between the Asian group (780±231mg/d) and the Caucasian group (820±185mg/d, p=0.83). Likewise, the mean plasma concentrations of ESL and (R)-licarbazepine were comparable between the two ethnic groups (ESL: 14.9±5.0µg/ml vs 15.2±4.8µg/ml; (R)-licarbazepine: 0.8±0.4µg/ml vs 0.9±0.3µg/ml, p=0.81). There were no statistically significant differences in response rates (Asian: 60.9% vs Caucasian: 61.7%) or in the rates of seizure freedom (Asian: 17.3% vs Caucasian: 18.0%). The safety profile was also similar, with no notable differences in occurrences of sedation, dizziness, hyponatremia, or rash.

Conclusion: The findings from our real-world study indicate that the efficacy, pharmacokinetics, and safety profile of ESL are comparable between Asian and Caucasian patients. This may motivate Asian epileptologists to adopt the dosing regimen for ESL that has already been established for Caucasian patients.

Epidemiology

311 | Semiology and classification of functional seizures in two public and private hospital settings

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Purpose: At present, no data exists on the semiology of functional seizures (FS) among patients from Sub-Saharan Africa. Additionally, potential differences in FS semiology among patients across varying socioeconomic backgrounds are still unexplored. This study examined how socioeconomic factors may influence FS presentation by comparing seizure manifestations between patients from a private and a public epilepsy monitoring unit (EMU) in Cape Town, South Africa.

Method: Patients diagnosed with FS through video-electroencephalography (video-EEG), without concurrent epilepsy, were included in this retrospective case-control study. Seizure semiology data were extracted from digital patient records, from the earliest available digital record at each hospital until 2022. Descriptive statistics summarized categorical, count, and continuous data, while bivariate analyses used chi-square, Fisher's exact, and Wilcoxon rank-sum tests. Logistic regression models were employed to identify factors independently associated with public hospital status, adjusting for sex, age, and the total number of reported seizure signs.

Results: The study comprised 372 patients, with 305 from a private and 67 from a public hospital. Akinetic and subjective seizure types were more commonly documented in the private hospital cohort. In contrast, public hospital patients were more likely to report emotional triggers (aOR=2.57, 95% CI [1.03, 6.37]), episodes involving loss of consciousness or awareness (aOR=2.58, 95% CI [1.07, 6.24]), and rapid recovery after a seizure (aOR=6.01, 95% CI [2.52, 14.34]). They were less likely, however, to describe seizures lasting under 30 seconds (aOR=0.21, 95% CI [0.08, 0.55]) or over 5 minutes (aOR=0.73, 95% CI [0.13, 0.56]), amnesia associated with the event (aOR=0.19, 95% CI [0.09, 0.43]), ictal aphasia (aOR=0.33, 95% CI [0.14, 0.76]), or falls and drop attacks (aOR=0.43, 95% CI [0.18, 0.996]).

Conclusion: Although seizure semiology was largely comparable between the two socioeconomic groups, some nuanced differences were identified, highlighting the

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need for further investigation into the influence of socioeconomic factors on FS presentation.

612 | Clinical characteristics and antiseizure medication use in people with newly diagnosed epilepsy worldwide: Does money decide?

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Purpose: To summarize characteristics of people with newly diagnosed epilepsy and global patterns in antiseizure medication (ASM) prescribing practices, and to identify their association with national income levels.
Method: We analyzed data from the Epilepsy Cohorts for Artificial Intelligence Research (EpiCFAIR), a multinational collaboration of 13 registries across 10 countries. Newly diagnosed epilepsy patients aged ≥12 years who started ASMs and were followed for at least one year between February 1972 and January 2023 were included. Baseline clinical characteristics and initial ASM treatment were compared between middle- (MICs) and high-income countries (HICs) according to World Bank classification.
Results: Among 6668 patients (46% female, median age 29 years, IQR: 19-46) studied, 46% were from MICs and 54% from HICs. Among them, 69% had focal epilepsy and 31% had generalized/unclassified epilepsy. Across both epilepsy types, patients from MICs had higher rates of febrile seizures and CNS infections, but lower rates of family history of epilepsy, substance and alcohol abuse, cerebrovascular and psychiatric disorders, and learning disabilities compared to HICs. Patients with focal epilepsy from MICs were also younger (median age: 26 vs 40 years, Holm-Bonferroni-corrected [HB]-p<0.001) and had more frequent >5 pre-treatment seizures (53% vs 43%, HB-p<0.001) and epileptiform EEG (64% vs 31%, HB-p<0.001). While the global use of newer ASMs has risen, the use of these was adopted by MICs a decade later than HICs. In the last decade (2013-2023), MICs still predominantly prescribed valproate (32%) for focal epilepsy, while HICs primarily used levetiracetam (57%, p<0.001) as initial monotherapy.
Conclusion: Clinical characteristics and risk factors differ significantly between people with newly diagnosed epilepsy in MICs and HICs, reflecting disparities in healthcare access and socioeconomic conditions. The delayed adoption of newer ASMs in MICs suggests potential inequities in treatment availability and affordability, highlighting the need for strategies to enhance epilepsy care globally.

659 | Predictors of first anti-seizure medication prescribed in a cohort of adults with newly diagnosed epilepsy

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Purpose: Anti-seizure medication (ASM) is the primary treatment modality in epilepsy. There exist evidence-based recommendations for ASM selection in epilepsy, but these medication recommendations are inconsistently followed. We sought to examine predictors of recommended first ASM in newly diagnosed adults with epilepsy.

Method: We conducted a retrospective cohort study of adults (≥18 years) newly diagnosed with epilepsy in New York, identified using validated ICD-CM codes, for the period 2011 to 2019. Primary outcome of interest was the use of an AES/AAN guideline-informed ASM and exposures of interest included patient characteristics (e.g. age), provider characteristics (e.g. specialty) and structural characteristics (e.g., practice setting). Multivariable Poisson regression for risk ratios modeled the probability of being prescribed a neutral/recommended or non-recommended ASM, adjusting for covariates.

Results: 2340 adults with new epilepsy were prescribed an ASM within 1-year. The most frequently prescribed ASM was levetiracetam (45.5%), which aligns with recommendations. However, 40% were prescribed a non-recommended medication. The prescription of a recommended ASM was associated with older age at diagnosis (relative risk (RR) 1.01; 95% confidence interval (CI) 1.00-1.01), Black race (RR 1.12; 95% CI 1.03-1.23), being in a relationship (vs. divorced/separated/single or widowed (RR 1.13; 1.06-1.22)) and a history of stroke (RR 1.19; 1.05-1.34). Prescriptions from physician trainees (vs. non-trainees) were more likely to align with recommended ASMs (RR 1.15; 95% CI 1.06–1.25), but no differences by physician specialty. Inpatient setting was associated with fewer recommended ASM prescriptions (vs. outpatient setting) (RR 0.82; 0.75-0.89). There was no difference between emergency department and outpatient prescriptions.

Conclusion: Understanding where/why less favorable ASM prescription may occur is important to target potential prescribing interventions. In this study, recommended ASM prescriptions were associated with patient, prescriber and setting characteristics. Notably, trainees prescribed recommended/neutral ASM more often, which underscores the importance of prescriber education in improving prescribing practices.

711 | Describing the Population of Patients with Prolonged Seizures: Results from a Global Real-World Point-In-Time Study

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Purpose: People with epilepsy (PwE) can experience prolonged seizures (PS), which may progress to *Status epilepticus* (SE). However, the definition, prevalence, and patient population have not been well characterized.

Method: Data were drawn from Adelphi's PS Disease Specific Programme™ (DSP), a real-world, point-in-time survey conducted in United States, France, Germany, Italy, Spain, United Kingdom, Japan, China, March 2023–February 2024. Neurologists/epileptologists/internal medicine specialists (IMs) completed record forms for consecutively consulting PwE, all receiving a stable regimen of anti-seizure medication and had experienced ≥1 PS (lasting ≥2 minutes and/or longer than normal ["non-PS"]) in prior 12 months. SE: seizure(s) lasting ≥5 minutes. Physicians provided data on demographics, seizure characteristics, treatment including rescue medication (RM), condition burden and healthcare resource utilization. PwE self-reported seizure worry using a 0-10 scale where 10 was "worry all the time". Data presented for overall study population, outcomes for both PS and non-PS.

Results: 251 neurologists, 48 epileptologists, 9 IMs completed records for 2,454 PwE experiencing PS. Median [Q1-Q3] patient age was 35.0 [23.0-51.0] years, 56% male, 41% required caregiver(s). 49% of sample had ever experienced SE, 27% seizure clusters (SC). Prior 12-month reporting of seizure-linked events among sample: SE (36%), SC (PS: 14%; non-PS: 11%), aura (PS: 45%; non-PS 40%), injuries (PS: 26%; non-PS 22%), required emergency services (PS: 27%; non-PS: 22%) – necessitating emergency room (ER) admissions (PS: 71%; non-PS: 58%), intensive care unit (ICU) (PS: 12%; non-PS: 7%) – and hospitalization

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(PS: 26%; non-PS: 14%). 60% of sample were prescribed RM (oftentimes including oral benzodiazepines), 57% had seizure action plans. PS worry (median [Q1-Q3]): 6.5/10 [4.0-8.0]; non-PS: 5.0/10 [3.0-7.0].

Conclusion: PwE experiencing PS regularly encounter progression to SE and/or SC, leading to emergency care, and hospital/ER/ICU admissions, despite best practice. Better options for treating PS are necessary to prevent seizure progression to more severe states. UCB-sponsored.

723 | EPIPORT - Epidemiologic population-based study to assess prevalence of epilepsy in Portugal

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Purpose: Epilepsy is one of the most common neurological diseases, significantly impacting patients' lives, with an estimation of about 50 million patients globally. EpiPort is a population-based epidemiological study in Portugal aimed at estimating the prevalence of epilepsy in children and adults, addressing the lack of recent evidence on these population metrics.

Method: This cross-sectional, population-based study was carried out through a nationwide random-route door-to-door survey among the general population in Portugal from May 2023 to July 2024, screening 10,666 individuals. The sample had a 95% confidence interval (CI) of 0.259 percentage points, and the prevalence was adjusted for age and sex. Trained interviewers visited selected households to recruit and interview participants, using questionnaires to identify undiagnosed epilepsy cases and collect information on positive epilepsy diagnoses and management. Previously diagnosed cases had their diagnosis confirmed by a Neurologist from the study Steering Committee.

Results: In the entire study population, 104 individuals were estimated to have epilepsy. From this data, the crude prevalence rate was determined to be 9.764 cases per 1,000 people, leading to an estimated total of 100,993 epilepsy cases within the Portuguese population. The average age of the prevalent cases was 44.22 years (±21.99). Epilepsy was more common among females (55.8%), adults (~82%), and residents of the North (45.5%), Center (26.6%), and Lisbon Area (15.3%) regions.

Conclusion: The results of the EpiPort study indicate national Epilepsy prevalence estimates highly above the 4.4 per 1,000 people, published in the last national study. It emphasizes that epilepsy significantly affects a large segment of the Portuguese population, particularly females and older adults. However, the study's representativeness in certain regions or age groups should be interpreted with caution due to limitations such as the small number of confirmed epilepsy cases and the low rate of HCP contacts.

763 | Spectrum of the clinical, radiological and electrophysiological profile of Patient with Epilepsy in North East India

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Purpose: To study clinical, radiological and electrophysiological profile at tertiary care hospital of northeast India.

Method: It was a hospital based prospective cross-sectional study of the epilepsy patient coming to neurology department at IGIMS PATNA. All patient of age 1 year and above fulfilling ILAE 2017 criteria for epilepsy were included in study. Patients of age < 1 year of age and not giving consent for study were excluded

Results: Out of 310 patients, most common age group in our study was 18-30 (23.8%) followed by 13-18 yrs age (23.5%) and 6-12 years (19.6%).194 patients (62.5%) were males, and 116 patients (37.5%) were females. Male:Female ratio 1.7:1. Most common type of epilepsy was focal (55.8%) while 45.1% had generalized epilepsy. Most common seizure semiology was focal to secondary generalized (36.4 %) followed by generalized tonic clonic seizures(36%) and

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focal seizure with impaired awareness{13.5%). 43.8% patients had positive findings on MRI while 46.12% patients had normal MRI on 1.5 Tesla MRI. Abnormal EEG was seen in 15.8% patients among which generalized epileptiform discharge was seen most commonly. Etiology was known in 59.7% and remained unknown in 40.3%. Among known etiology, the most common was structural (39.35%) followed by infection (13.5%), genetic and inflammatory/autoimmune causes were present in 3.2 and 2.5% respectively. Among the structural causes of epilepsy, hypoxic ischemic encephalopathy (38.4%) was the most common cause followed by gliotic changes (25.9%) other than HIE, tumors {14.4%) and post-stroke {11%).Among the infective causes, neurocysticercosis (NCC) was the commonest cause followed by tuberculoma and viral encephalitis.

Conclusion: Focal epilepsy is the most common type of epilepsy with focal to secondary generalized being the most common seizure semiology. Among the epilepsy patients with known etiology, structural and infective were the common causes. Abnormal EEG was seen in 15.8% of patient and generalized epileptiform discharges were most common abnormal finding.

837 | Well-being in School-Aged Children with Epilepsy by use of Antiseizure Medication

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Purpose: Antiseizure medications (ASMs) are essential for seizure control in children with epilepsy, but their potential contribution to well-being is unclear. In this nationwide study, we examine the association between ASM treatment and well-being among school-aged children with epilepsy in Danish public schools.

Method: We conducted a cohort study of children in grades 4-9 in Danish public schools (2015-2022) using data from the Annual National Surveys on Well-being. Epilepsy diagnoses (ICD-10: G40) and ASM use were identified through the Danish National Patient and Prescription Registers. Logistic regression models with generalized estimating equations estimated adjusted odds ratios (aORs) for poor well-being across three dimensions (overall, academic, and social), comparing children with epilepsy (grouped by types of recent ASM use) to matched reference children without epilepsy. Recent ASM use was defined as redeeming prescriptions within 90 days before each well-being survey (ATC codes: N03A, N05BA09).

Results: We identified 5,150 children with epilepsy and 58,400 matched reference children (47% girls, mean age at survey: 12.6 years (SD 1.7), mean age at matching: 7 years (SD 3.9)) who completed a total of 15,170 and 179,330 well-being surveys, respectively. Recent ASM was observed in 49% of children with epilepsy. Compared to children without epilepsy, the odds for poor overall well-being in children with epilepsy varied according to ASM treatment (e.g., no ASM treatment: aOR 1.12, 95%CI 1.03-1.22; valproate monotherapy: aOR 1.51, 95%CI 1.18-1.94); lamotrigine monotherapy: aOR 1.24, 95%CI 1.01-1.53; levetiracetam monotherapy: aOR 1.14, 95%CI 0.88-1.49). Odds for poor academic and social well-being were similarly increased, with nominally larger effect sizes seen for academic well-being.

Conclusion: Childhood epilepsy was associated with poor well-being across all well-being dimensions, and this varied by types of ASM use. These variations may be explained by underlying epilepsy, challenges in seizure control, or ASM side effects.

849 | Epilepsy and educational outcomes: A Nationwide Cohort Study in Denmark

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Purpose: Children with epilepsy are thought to be at increased risk of academic difficulties, even when they have normal intelligence and no other major comorbidities. In this study, we explored associations between childhood epilepsy and educational outcomes later in life.

Method: We carried out a register-based nation-wide cohort study of all children born in Denmark 1987-2005 who resided in Denmark on their 15th birthday. Data from population and health registers were utilized to identify children with epilepsy, including psychiatric comorbidities. Educational outcomes included 1) not completing elementary school before age 17 years, 2) average score in 9th grade final exams, and 3) highest educational attainment

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at specific ages from age 15 to 30 years. The associations of epilepsy with these outcomes were estimated using logistic and linear regression models, adjusted for relevant confounders.

Results: From a population of approximately 1.2 million children, we identified a total of 11,760 (0.98%) children with epilepsy before the age of 15. The mean (SD) age of children at the time of epilepsy diagnosis was 7.2 (4.3) years. Among children with epilepsy, 3180 (27%) had psychiatric comorbidity before the age of 15 years. Having epilepsy was significantly associated with the risk of not completing elementary school before the age of 17 (11.9% of children with epilepsy vs. 3.8% of children without epilepsy, adjusted OR 2.95, 95% CI: [2.78-3.13]). This association persisted even among children with epilepsy without psychiatric comorbidity (adjusted OR 2.60 [2.41-2.80]) but was more pronounced in those with psychiatric comorbidity (e.g. epilepsy and comorbid intellectual disability adjusted OR= 4.8 [4.3-5.4]). Further analysis of 9th grade performance and long-term educational attainment is currently ongoing.

Conclusion: Children with epilepsy are at increased risk of experiencing poor long-term educational outcomes, and our findings highlight the need for educational support, even when the epilepsy is not complicated by e.g. psychiatric comorbidity.

1062 | The Value of Rare Disease Registries: insights from an ERN-EpiCARE Center

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Purpose: ERN EpiCARE (European Reference Network for rare and complex epilepsies) successfully obtained a grant to establish a registry employed across the network. This project aims to enhance our understanding of the epidemiology of rare and complex epilepsies among participating centers.

Method: An IT platform, developed on the REDCap system, was created for systematic collection of clinical, instrumental, and genetic data from patients among the EpiCARE members. The platform ensures anonymization, security, and GDPR compliance, supporting both retrospective and prospective data collection.

Results: Since 2022, 667 pediatric patients have been included in our local "Fondazione Mondino" registry, with complete data available for 357 patients. The most common etiology was genetic (46.2%), followed by structural (21.3%), primarily related to brain malformations or acquired lesions. Less frequent causes included metabolic (8%), post-infection epilepsy (2.5%), and immunomediated (2%); while in 20% of cases was unknown. In terms of seizure types, generalized onset seizures were most common (55.2%), followed by focal onset (31.3%); 16% of patients presented a focal to bilateral tonic-clonic evolution. A small percentage had unclassified (2.7%) or unknown (1.1%) seizures onset. Status epilepticus occurred in 14.6% of patients. The age of onset varied, with infantile onset being the most frequent (50.9%), followed by school-age (20.8%), adolescence (10.9%) and neonatal (3.6%). Age-independent onset was documented in 13.8% of patients. A significant proportion of patients (38.5%) were drug-resistant. Pre-surgical evaluation was performed in 5% of cases, and surgical treatment was undertaken in 3.6%. Additionally, 14.3% of patients were treated with ketogenic diet as an alternative for refractory epilepsy.

Conclusion: The establishment of a computerized registry enhances our understanding of rare and complex epilepsies: it ensures secure collection and storage of data, monitors the natural history of these conditions, and strengthens our local epidemiological knowledge. Furthermore, it allows for the rapid identification of eligible patients for clinical studies.

1208 | Information Needs of People Considering Surgery for Epilepsy Management: A Scoping Review

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Purpose: Current guidelines recommend surgery for drug-resistant epilepsy, yet surgery remains underutilized. The underutilization of surgery may be attributed to a lack of high-quality information-based resources to support patients through this decision-making process.

Method: We conducted a scoping review using 12 databases (1990-June 2024). Studies were included if they identified information needs of patients/caregivers considering epilepsy surgery or evaluated resources designed to aid this process. The study was reported according to The PRISMA for Scoping Reviews standards. Screening, data extraction, and charting were completed in duplicate with disagreement resolved through discussion/involvement of a third author.

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Results: We identified 2729 references, of which 17 were included: 11 addressed patients' informational needs, four resources aimed to improve patients/caregivers' knowledge about surgery, and two resource readability. Themes of information needs included risks/benefits discussion, personalized prognostic information, procedure-specific outcomes, and description of medical assessments and process for choosing surgery. Six studies highlighted the value of having clinical data presented by epilepsy specialists while six identified the importance of hearing testimonials from other patients. Most studies indicated current resources lack clarity with two that assessed the average readability of resources to be "difficult" or at/above grade 12 level. Four studies evaluated resources including a mixed reality education tool, a caregiver intensive information program, use of a decision coach, and a patient information program.

Conclusion: This scoping review revealed limited studies addressing information needs of patients considering epilepsy surgery. Our findings provided a good foundation for identifying the specific content needed by patients and highlighted the importance of patient testimonials. However, the lack of clarity and poor readability of existing information suggests greater need for usable and patient-centered resources to support patients considering epilepsy surgery. Future research should address how information should be delivered to patients and adapted to meet the needs of specific socioeconomic populations.

1269 | Optimal Approach to Standardized Documentation in Epilepsy Clinics: A Scoping Review

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Purpose: Clear documentation, communication and transfer of information between different healthcare providers is key to ensuring the delivery of high-quality patient care. How to best optimize and standardize physician documentation in outpatient epilepsy clinics has not yet been reviewed.

Method: We conducted a scoping review of studies implementing standardization and optimization of physician documentation within outpatient epilepsy clinics. The study was reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Extension for Scoping Reviews (Prisma-sCr). Studies were uploaded into Covidence for review. The following databases were searched from inception to September 2024: MEDLINE, Embase, APA PsycInfo, CINAHL, Cochrane Library. All abstracts, full-text reviews, and data charting were completed in duplicate by two authors. Disagreements were resolved through discussion until consensus was reached.

Results: 9,173 studies were identified, including 6,182 after removal of duplicates; 41 were reviewed as full-text and 16 met inclusion criteria. Studies were from the United States (N=13;81.25%) Canada (N=3;18.75%), both United States and Canada (N=2;12.5%), and Ireland (N=2;12.5%). Studies either focused on adult (N=9;56.25%), pediatric practices (N=5;31.25%) or were unspecified (N=2;12.5%). Studies included quality improvement implementations (N=7;43.75%), retrospective chart reviews (N=5;31.25%), observational (N=2;12.5%), quasi-experimental (N=1;6.25%), and mixed-methods (N=1;6.25%) designs. Most clinical notes were in electronic medical records (EMR) (N=15;93.75%) using standardized templates (N=13;81.25%). Common data elements included seizure information (e.g., frequency, severity) and treatment counselling information (e.g., medication management). Outcomes of standardized note implementation included reduced epilepsy-related adverse hospitalizations, better seizure control, and more consistent documentation rates of pertinent patient information (e.g., seizure type, preconception counselling, and medication side effects).

Conclusion: Attempts to develop a standardized format for epilepsy outpatient documentation are associated with fewer adverse epilepsy-related events and better seizure control. Adequate adoption and implementation by physicians were variable. Limitations of implementation included high programming costs and phasing out in-use EMR systems.

1281 | Sociodemographic differences in stroke as an etiology of late onset epilepsy: Results from a multi-center cohort

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Purpose: New-onset epilepsy is common in older adults and this population is expanding as the world ages. Social determinants of health may be associated with development of epilepsy, but this is not well studied in older adults. We examined the relationship between sociodemographic data and ischemic stroke as an etiology of epilepsy in a cohort of older adults with new-onset seizure.
Method: The ELUCID study is a multi-center, prospective cohort study of adults with late-onset unexplained seizures. Using electronic medical records, we retrospectively identified persons aged 55 and older with new seizure between February 1, 2021 and December 31, 2024. Chart review was conducted by trained reviewers and decisions were adjudicated by epileptologists. Sociodemographic, imaging and clinical data were reviewed. We used Chi-squared tests to examine relationships between ischemic stroke as a seizure etiology, and race, ethnicity, sex, and preferred language.
Results: We identified 2010 persons aged 55 or above with new seizure. The sample was comprised of 51.4% male (n=1,013), 17.6% Black (n=346), 2.6% Asian (n=51), 0.4% American Indian, Alaska Native, Hawaiian or Pacific Islander (n=7), 64.8% White (n=1,277), and 9.2% Hispanic or Latino ethnicity (n=180). Non-English language was preferred in 18% (n=361). Ischemic stroke was the seizure etiology for 16.9% (n=339) and was more likely to be the cause of seizure in non-English speakers (23.5% vs. 17.6%, p=0.013), Black (compared to White) (25.1% vs. 12.4%, p<0.001) and Hispanic or Latino (compared to non-Hispanic) (24.4% vs. 15.6%, p=0.003). There was no significant difference by sex.
Conclusion: There are significant differences in the etiology of late-onset epilepsy among sociodemographic groups. Understanding how the etiology of epilepsy varies across groups is important both for planning health care delivery systems and identifying populations where preventive strategies may be most effective.

1290 | Is school performance in children with epilepsy lower than in children with other chronic diseases?

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Purpose: To study school performance in children with epilepsy compared to children with Type-1 diabetes.
Method: This was a register-based nation-wide cohort study of children born in Denmark from 1997-2009, who were living in Denmark at 6 years of age and participated in the Danish National School Test Program between 2010-2019. Epilepsy was defined as having an ICD-10 diagnosis of epilepsy (G40) in the Danish National Patient Register and a filled prescription for antiseizure medication (ATC codes N03A and N05BA09) in the Danish National Prescription Register. Similarly, Type-1 diabetes was defined by an ICD-10 diagnosis of Type-1 diabetes (E10) and a filled prescription for insulin (ATC code A10A). Children with epilepsy and Type-1 diabetes were each matched with 10 reference children without these disorders on age and sex.
Results: Among the 582,970 children with one or more school tests, we identified 3,360 (0.6%) with epilepsy, and 2,400 (0.4%) children with Type-1 diabetes. In children with epilepsy, the mean age at time of diagnosis was 7.7 years (s.d. 4.3) and in Type-1 diabetes it was 9.2 years (s.d. 3.8). Children with epilepsy had poorer test scores compared to their matched references (mean test score 46.4 vs 56.6, adjusted mean difference -9.1 (95% CI: -10.0; -8.3)). In contrast, children with Type-1 diabetes performed at the same level as their matched references (mean test score 56.4 vs 56.7, adjusted mean difference 0.1 (95% CI: -0.9; 1.0)).
Conclusion: Children with epilepsy have much lower test scores in national school tests compared to children with Type-1 diabetes. The results indicate that the academic consequences of having a brain disorder in childhood are much larger than having another chronic disorder such as Type-1 diabetes. The finding suggests a greater need for educational support in children with brain disorders such as epilepsy.

1529 | Prescription patterns of anti-seizure medications for generalized and focal epilepsy in Morocco: A cross-sectional study

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Purpose: Epilepsy is a chronic neurological disorder affecting over 50 million people worldwide, particularly in low- and middle-income countries. Anti-seizure

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medications (ASMs) remain the cornerstone of epilepsy management, aiming to control seizures and improve quality of life. This study examines the prescription patterns of older- and newer-generation ASMs among Moroccan physicians.

Method: We conducted a cross-sectional, descriptive, and analytical study using an anonymous questionnaire over a two-month period. Participants included Moroccan physicians who treat epilepsy and prescribe ASMs. The analysis compared the prescription profiles of older and newer ASMs for generalized and focal epilepsy and explored factors influencing the use of newer ASMs. We used chi-square test for bivariate analysis and logistic regression for multivariate analysis.

Results: 140 physicians responded to the questionnaire, with a majority of neurologists (55.7%). Key factors influencing ASM choice included seizure type (91.4%), patient age (75%), treatment efficacy (74.3%), and cost (67.9%). Valproate (76.4%) was the most prescribed first-line treatment for generalized epilepsy, while carbamazepine (65%) was most used as first-line for focal epilepsy. Newer ASMs were more frequently prescribed as second-line treatment for generalized (68.6%, $p < 0.001$) and focal epilepsy (66.4%, $p = 0.001$). In multivariate analysis, neurologists were significantly more likely to prescribe newer ASMs as second-line treatment for both generalized (OR = 3.58 CI [1.4 – 9.16], $p = 0.008$) and focal epilepsy (OR = 3.36 CI [1.31 – 8.58], $p = 0.01$).

Conclusion: Our study shows that Moroccan physicians predominantly prescribe older ASMs as first-line treatment, influenced by cost and availability. However, newer ASMs are preferred as second-line options due to their improved safety profiles. These findings highlight the need for policies promoting accessibility to newer ASMs to optimize epilepsy management in Morocco.

1629 | Prevalence, comorbidities and mortality of epilepsy in an older Chinese population: The Shanghai Aging Study

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Purpose: To investigate the prevalence, comorbidities and mortality of older adult epilepsy in a community-dwelling Chinese population.

Method: The Shanghai Aging Study (SAS) is a community-based longitudinal cohort study conducted in urban Shanghai, China. From January 1, 2010, through September 30, 2011, community residents aged ≥60 years were recruited. Participants were interviewed for clinical evaluations including demographic and medical history questionnaires, physical and neurologic examinations, neuropsychological testing. Prevalent epilepsy cases at baseline were determined with either diagnosis or anti-seizure medication prescriptions confirmed by medical records. All participants were followed for survival status until Dec. 31, 2023. Deceased cases and dates of death were confirmed by the local mortality surveillance system.

Results: Twenty-six participants were determined as people with epilepsy (PWE) among 3530 enrolled participants, indicating the prevalence (95% confidence interval) of epilepsy was 7.37 (4.80-10.80) per1000 persons. Half of PWE was male, the average age of PWE was 70 (SD 7.0) years, median onset age was 57 (IQR 43.5, 68.3) years, and median duration was 11 (4, 21) years. Epilepsy prevalence rates were 7.68, 8.84, and 4.48 per 1000 persons in participants aged 60-69, 70-79, and ≥80 years, respectively. The major comorbidity of epilepsy was depression, with a significantly higher prevalence than that in participants without epilepsy (29.6% vs. 3.2%, $p<0.001$). Six PWE and 673 without EP died during the 13-year follow-up, demonstrating mortality rates of 2.64 (0.98-5.65) and 2.37 (2.20-2.55) per 100 person-years. Mortality rates in PWE aged 60-69 and 70-79 years were higher than that in non-epilepsy participants (60-69 years: 2.82 (0.59-8.00) vs. 0.67 (0.54-0.82) per 100 person-years; 70-79 years: 3.26 (0.68-9.23) vs. 2.30 (2.02-2.61) per 100 person-years.

Conclusion: This community-based study fills the gap in epidemiological data of older adult epilepsy in China where the population ages dramatically.

1768 | Immune dysfunction, infection risk, and mortality with anti-seizure medications

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Purpose: Some antiseizure medications (ASMs) have been associated with immune dysfunction. We aimed to investigate (i) whether ASM use was associated with markers of immune dysfunction (leukopenias, hypogammaglobulinaemia); (ii) whether ASMs were associated with infections; and (iii) whether markers of immune dysfunction were associated with mortality in ASM use.

Method: We linked routinely collected healthcare datasets from North-East Scotland (2009-2024): community prescribing, laboratories, hospital discharge coding, and death registrations. We excluded those with co-morbidities associated with immune dysfunction. Each case (individual prescribed ASMs) was matched to four controls

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(without ASM prescription) with the same sex, age (+/-1 year) and Charlson Comorbidity Index (CCI). We used logistic regression adjusted for matching variables to assess association between ASMs and number of antibiotic prescriptions; and between any ASM and hospital infection episodes (excluding aspiration pneumonia). We used Cox regression in cases treated with ASMs to investigate associations with mortality adjusted for age, sex, and CCI.
Results: We linked data on 23182 cases (on any ASM) and 92728 controls. ASM use was associated with neutropenia (OR [95%CI]: 1.57 [1.43-1.73], lymphopenia (1.34 [1.28-1.40], hypogammaglobulinaemia (1.23 [1.12-1.35]. Carbamazepine and phenytoin had the highest risk of lymphopenia; carbamazepine, levetiracetam, phenytoin, and valproate had the highest risk of neutropenia; lamotrigine and topiramate had the highest risk of hypogammaglobulinaemia. ASMs were associated linearly with more antibiotic prescriptions per year (>4 vs 0 antibiotics/year OR [95%CI]: 2.18 [1.88-2.53]), with valproate having the strongest association. ASM use was associated with hospital infection episodes (2.11 [2.01-2.2]). In those treated with ASMs, Lymphopenia was associated with increased mortality (hazard ratio [95%CI] =1.32 [1.23-1.42]), whereas neither neutropenia nor hypogammaglobulinaemia were associated with significantly increased mortality.
Conclusion: ASMs are associated with leukopenia, neutropenia, hypogammaglobulinaemia and higher infection risk. ASM-associated lymphopenia was associated with increased mortality. Further work should clarify causation, but the role of ASMs should be considered in those with frequent or unusual infections.

Epilepsy and Reproductive Health

410 | Epilepsy Clinical Support Coordinator Certification System in Japan

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Purpose: The National Liaison Council for Epilepsy Control, consisting of epilepsy regional center organizations, recommended the role and definition of epilepsy clinic support coordinators and launched the epilepsy clinic support coordinator certification system in 2020.
Method: Epilepsy clinic support coordinators must fulfil all of the following requirements They must work at an epilepsy treatment center facility, have basic knowledge of the social insurance system and social welfare system, have basic knowledge of epilepsy, have elementary psychological consultation skills for anxiety and psychological stress on the part of patients, and hold national qualifications in medical and welfare matters. Specific tasks of the epilepsy treatment support coordinators include: providing professional consultation support and advice to epilepsy patients and their families; providing advice and guidance to cooperating medical institutions in the jurisdiction; coordinating and coordinating with relevant organizations (mental health welfare centers, medical institutions in the jurisdiction, health centers, municipalities, welfare offices, public employment security offices, etc.).
Results: The following activities are carried out: training for medical staff, staff of relevant institutions, epileptic patients and their families, and awareness-raising activities for epileptic patients, their families and local residents. A condition for certification as an epilepsy care support coordinator is to attend at least six of the following lectures/training courses on epilepsy of at least three hours in a three-year period. Certified coordinators are renewed every three years, with the first certificates being issued from 2020. A total of 2,000 people have attended training courses organized by the National Epilepsy Support Centre, bringing the total number of certified epilepsy care support coordinators to approximately 200.
Conclusion: Epilepsy care support coordinators, as defined in the Epilepsy Community Care Coordination and Development Project, will play an important role.

836 | Breastfeeding patterns among women with and without epilepsy – A nation-wide study from Denmark

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Purpose: The benefits of breastfeeding are well established, but women with epilepsy may be less likely to initiate or continue breastfeeding over concerns of how treatment with antiseizure medication affects their child. In this study, we compared breastfeeding patterns among women with and without epilepsy on a nation-wide scale.
Method: We carried out a register-based study of all live-born singletons in Denmark between 2012-2018. Mothers with epilepsy were identified by the combination of a hospital-recorded diagnosis of epilepsy and a redeemed prescription for antiseizure medication in a 10-year period before delivery. Using information on breastfeeding collected by child health nurses at routine home visits and recorded in the Danish National Child Health Register,

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we categorized the duration of exclusive breastfeeding (missing or non-initiation (which was indistinguishable); <1 month; 1-4 months; 4-6 months; and >6 months) and reported the proportion of children within each category. The median duration (interquartile range, IQR) of breastfeeding among initiators was furthermore calculated according to maternal characteristics.

Results: Among 321,750 live-born children, we identified 1,920 (0.6%) children of mothers with epilepsy. Children of mothers with epilepsy were more likely to lack information on breastfeeding and have shorter duration of exclusive breastfeeding (44.3% missing; 15.5% <1 month; 13.4% 1-4 months; 19.7% 4-6 months; 7% >6 months) than children of mothers without epilepsy (38.4% missing; 12.3% <1 month; 13.8% 1-4 months; 25.2% 4-6 months; 10.3% >6 months). The median duration of breastfeeding was similar for children of mothers with epilepsy without use of antiseizure medication (119 days (IQR=29-152 days)) and with use of antiseizure medication in monotherapy (120 days (IQR=27-159 days)), but shorter in children of mothers using antiseizure medication in polytherapy (48 days (IQR=16-139 days)).

Conclusion: Women with epilepsy are less likely to exclusively breastfeed than women without epilepsy, particularly if treated with antiseizure medication in polytherapy.

922 | Prevalence of Sexual Dysfunction in Patients with Epilepsy: A Cross-Sectional Study from a Tertiary Care Facility

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Purpose: This study aimed to investigate the prevalence of sexual dysfunction in individuals with epilepsy and its impact on overall quality of life.

Method: One hundred and twenty patients diagnosed with epilepsy and 50 healthy controls were assessed on Changes in Sexual Functioning Questionnaire Short-Form (CSFQ-14) to estimate the prevalence of sexual dysfunction. Epilepsy patients were additionally evaluated for psychiatric morbidity using structured diagnostic interview.

Results: On CSFQ-14, 97.5% of epilepsy patients experienced sexual dysfunction, surpassing controls. CSFQ's suggested cutoff norms revealed prevalence of impaired pleasure/arousal (97.5%) to be the most common dysfunction, followed by reduced desire (93.33%), orgasm dysfunction (89.16%), painful erection (61.7%), and painful orgasm (30%). Compared to healthy subjects, epilepsy patients displayed significantly higher prevalence of sexual dysfunction across all domains ($P < .001$). Patients with psychiatric morbidity had significantly higher prevalence of sexual dysfunction, when compared to those without psychiatric morbidity. Overall, the presence of sexual dysfunction had a significant negative impact on the quality of life.

Conclusion: The present study suggests a very high prevalence of sexual dysfunction in epilepsy patients, and emphasizes the need for holistic care in these patients. Healthcare providers must recognize and address sexual dysfunction to enhance the overall quality of life of patients with epilepsy.

1169 | Clinical practice guidelines for women with epilepsy: A systematic review

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Purpose: To identify and evaluate clinical practice guidelines (CPGs) for the management of women with epilepsy (WWE) worldwide.

Method: A systematic review of CPGs published between 2014 and 2024 in English or Korean was conducted using electronic databases (Medline, Embase, Guideline International Network, and KoreaMed). Two independent reviewers screened abstracts, reviewed full-text articles, and performed data abstraction. The Appraisal of Guidelines for Research and Evaluation (AGREE) II instrument was used to assess guideline quality, and textual syntheses were employed to compare recommendations.

Results: The search identified 956 abstracts, with 62 articles selected for full-text review. Ten guidelines met the eligibility criteria, including six for general epilepsy and four specific to women. Geographic distribution included three from the US, two each from the UK, Scotland, and

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Norway, and one each from Sweden and Spain. Only one CPG addressed catamenial epilepsy and menopause, respectively. The overall quality of the CPGs was moderate (mean 60.1%, SD 7.8%). No guideline achieved high ratings (>75%) across all AGREE-II domains. The highest-rated domain was 'scope and purpose' (82.2%, SD 15.9), while 'applicability' scored lowest (30.6%, SD 15.7).

Conclusion: This review revealed considerable heterogeneity in the methodological quality of CPGs for WWE, with particular weaknesses in applicability. There is a notable lack of comprehensive guidelines addressing catamenial epilepsy and menopause in WWE, indicating areas for future guideline development.

1188 | Contraception for Women with Epilepsy - A Systematic Review of Antiseizure Medication and Hormonal Contraceptive Interactions

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Purpose: Contraceptive counseling is a crucial component of care for women with epilepsy (WWE). Studies show that about 60% of WWE risk unplanned pregnancies, and many do not use effective contraception. Hormonal contraceptive (HC) use is lower among WWE, especially those treated with enzyme-inducing antiseizure medications (ASMs), which can lead to contraceptive failure. HCs can also affect the response to some ASMs by modifying their plasma concentration. Personalized contraception choices are crucial, considering potential interactions between ASMs and contraceptives.

Method: Eligible RCTs, observational studies, case series and case reports (including pharmacokinetic studies) addressing the drug-drug interactions (DDIs) of interest were identified through an electronic search of MEDLINE, Embase, and CENTRAL databases up to 31st December 2024. The titles and abstracts were screened. Selected full texts will be assessed and the risk of bias evaluated independently by two authors. The DRIVE scale to describe study quality criteria and interpretation and GRADE system to indicate quality of evidence and strength of recommendations will also used. Disagreements will be resolved through consensus or by a third reviewer. Data extraction will follow using a pre-established form, designed and pilot-tested by the authors. Thematic coding, summary and descriptive statistical analysis will be conducted.

Results: The search returned 3305 records and 2646 duplicates were removed. After title and abstract screening, the articles included will be assessed for full-text screening. We will synthetize available evidence on interactions between HCs and ASMs affecting pharmacokinetic measures, contraceptive effectiveness, seizure control and adverse events.

Conclusion: Our educational review article aims to provide a practical guide that answers the question: "What counsel should neurologists give about ASMs and HC interactions in WWE?".

1239 | Maternal AEDs now-child development later, what are the results&

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Purpose: The study investigated the neurobehavioral development of children born to mothers with epilepsy.

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Method: Study involved 88 children aged 3-9 years and their mothers. 62 mothers took monotherapy, 13 of them - topiramate, 14 - lamotrigine, 14 – valproic acid, 11 – did not take any AEDs, their children formed the control group. The rest took other AEDs or polytherapy. Clinical history, CBCL (Achenbach), neuropsychological tests by J.M.Glozman (for children aged 3-6 and 7-11), WISC, ADHD scale (by N.N.Zavadenko) were used.
Results: The study found that children whose mothers took valproate had worse development of gnosis (p=0.038), grammar (p=0.015), and performed worse on the "Arithmetic" subtest (p=0.038) compared to the control group. No significant differences were found between the control group and the children whose mothers took lamotrigine. "Lamotrigine group" showed better development in understanding of logic (p=0.033), grammar (p=0.005), emotional gnosis (p=0.064), spontaneous speech (p=0.087) and overall speech development (p=0.027). They performed better on the "Encryption" (p=0.038) and "Arithmetic" subtests (p=0.021) and had better socialization (p=0.094) compared to those whose mothers took valproate. Taking topiramate harms children's understanding of logic more (p=0.033) than lamotrigine. The correlation analysis confirmed that valproate and topiramate had the worst teratogenic effects. Topiramate significantly correlated with problems in children's subject, acoustic gnosis and phonemic hearing and their understanding of logic, logical operations, and intelligence in general. Maternal intake of valproate led to motor awkwardness in children, mental retardation, and functional malformation of the left temporal region. Children whose mothers took valproate had the highest rate of neuropsychological disorders. Their emotional and general understanding of things, as well as their ability to reproduce rhythmic structures, delayed reproduction, spontaneous speech, understanding of reversed speech, logic, grammar, and overall speech development, suffered.
Conclusion: Choosing the safest anti-epileptic drugs (AEDs) for a mother can reduce the risks of neurobehavioral teratogenesis in their children.

1344 | Use of new-generation antiseizure drugs in women with juvenile myoclonic epilepsy

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Purpose: Juvenile Myoclonic Epilepsy (JME) is a common form of idiopathic generalized epilepsy that requires long-term treatment. Traditional first-line treatment with Valproate (VPA) is limited in women of childbearing age due to its adverse effects, therefore the need to explore safer alternatives. This study aimed to describe the use and dosing of new generation antiseizure medications (ASM) in young women with JME. Secondary objectives include identifying the most used ASM, describing the number of patients on monotherapy or polytherapy, and evaluating seizure types and seizure control.
Method: An observational, retrospective, analytical, and cross-sectional study was conducted at the National Institute of Neurology and Neurosurgery in Mexico City. Women aged 15–45 years with JME were included. Data analysis employed descriptive and inferential statistical methods.
Results: The study included 122 patients. Levetiracetam (LEV) was the most used ASM (60%), followed by VPA (43%). LEV use was associated with a significantly longer seizure-free period (3.9 months) compared to non-users (2.36 months, p=0.0017). The relative effectiveness of ASM varied by seizure type, with LEV showing high effectiveness for myoclonic seizures and VPA for generalized tonic-clonic seizures. Average daily doses were 1969 mg for LEV, 177 mg for topiramate (TPM), and 805 mg for VPA.
Conclusion: The findings support the use of LEV as an effective therapeutic option for young women with JME, providing better seizure control and a favorable safety profile compared to traditional ASM and VPA. This study highlights the need to reconsider the use of VPA in this population due to associated risks. Future research should focus on dose-response relationships and other factors influencing seizure-free periods to optimize treatment outcomes in JME patients.

1536 | Utility of Responsive Neurostimulation in Reducing Antiseizure Medication Exposure During Two Pregnancies in a Single Patient

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Purpose: Refractory epilepsy (RE) is characterized by persistent seizures despite adequate trials of two or more

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antiseizure medications (ASMs). Neuromodulation, such as responsive neurostimulation (RNS), offers a promising option for managing RE, particularly in females with epilepsy (FWE), where ASM polytherapy and high doses increase the risk of fetal malformations. This study evaluates the utility of RNS in reducing ASM exposure during pregnancy.

Method: A retrospective review (2015–2025) identified 10 female patients with RNS for RE, including one patient who underwent two pregnancies while receiving RNS therapy. This patient had chronic bitemporal epilepsy secondary to autoimmune encephalitis, confirmed by presurgical evaluation and intracranial EEG monitoring.

Results: Prior to RNS, the patient experienced daily focal aware seizures (FAS), weekly focal impaired awareness seizures (FIAS), and rare focal to bilateral tonic-clonic seizures (FBTC), managed with polytherapy (levetiracetam, lacosamide, topiramate, and perampanel). Following RNS implantation, she reported no change in FAS, >50% reduction in FIAS, and 100% resolution of FBTCs. Improvement enabled tapering of topiramate and perampanel before pregnancy due to teratogenic concerns. During the first pregnancy, RNS settings were adjusted due to increased FIAS, with charge density, frequency, and current ranging from 2.5–3.5 $\mu C/cm^2$, 100–200 Hz, and 4–6 mA, respectively. No RNS adjustments were required in the second pregnancy (3.5 $\mu C/cm^2$, 4 Hz, 12 mA). The first pregnancy was complicated by gestational hypertension and three FIAS during labor, requiring a Caesarean section. The second pregnancy involved a first-trimester subchorionic hemorrhage and FIAS during labor. Both pregnancies resulted in healthy outcomes.

Conclusion: RNS may be a valuable tool for reducing ASM exposure in FWE seeking pregnancy, minimizing teratogenic risks while maintaining seizure control.

Epilepsy in Crisis Settings

449 | Comparison of the course of epilepsy and the provision of medical care to pediatric patients with epilepsy during the COVID-19 pandemic and during the full-scale war in Ukraine

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Purpose: Comparing the situation in which Ukrainians were during the war and COVID-19 pandemic may not seem entirely justified, but many of characteristics of the negative impact of these disasters are common.

Method: Two questionnaires were developed to study impacting these two crises.

"Features of providing medical care to patients with epilepsy during the war in Ukraine." and "Features of providing medical care to patients with epilepsy during the COVID-19 pandemic". Surveys were conducted in March - May 2023 and April - June 2020, respectively.

Results: In both crisis periods, about half of the families faced problems in obtaining ASM under budget programs. Problems in purchasing these and other necessary drugs in the pharmacy network were significantly more common among parents during the war, this can be explained by the closure of many pharmacies, difficulties in the supply of drugs, especially in certain regions and in the first months of the war. In 27.78% of cases, against 70.09% during the pandemic, parents did not record any deviations in mood state of their children. A separate analysis of the appearance of "new", uncharacteristic mental/psychological features of the child revealed the appearance of anxiety during the war in 19.44% of children against 3.74% during the pandemic.

Conclusion: Practicing remote interaction with a doctor during pandemic can be considered positive experience that has become useful, and in some cases, life-saving already during military operations. Medical care pediatrician epilepsy patients can be organized and provided (with adequate compliance) at high level, despite active hostilities in the country, the closing and destruction of medical facilities, and patients changing their place of residence. The realities of the modern world, the experience of Ukraine during a full-scale war prove the need to develop methodological recommendations for the treatment and monitoring of epilepsy patients during hostilities and global disasters.

630 | Understanding and Optimising the Seizure Emergency Pathway

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Purpose: Understand the end-to-end care pathway of an acute seizure emergency event (status epilepticus, seizure

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clusters and prolonged seizure) based on reference guidelines, to identify management care gaps and inform optimization opportunities to improve patient experience and ultimately prevent avoidable seizure escalation, risk of injury and death.

Method: 60-minute in-depth qualitative interviews (four per country) with key stakeholders involved in the seizure emergency pathway across UK, France, Italy, Germany, with 10-minute pre-task prior to interviews. Respondents included a mix of epileptologists, emergency doctors, paramedics, epilepsy nurses and patient association experts (one of each per country). Qualitative research was accompanied by review of publicly available online literature and seizure emergency guidelines.

Results: Each country has both national and specific hospital or regional guidelines that outline seizure emergency care pathways. There are, however, inconsistencies across countries with regards to management recommendations between pre-hospital, paramedic care, emergency and hospital care and discharge. Notably, NICE and German guidelines emphasize strict timing protocols for administering medications and escalating care (5–10 minutes). French and Italian guidelines lack strict timing but highlight rapid escalation. Rapid and Early Seizure Termination (REST) has been proposed as a new management concept for early initiation of rapid treatment to terminate ongoing seizures, preventing seizure progression to status epilepticus. REST has not yet been included in national or regional guidelines.

Conclusion: Pain points identified in current pathways provide opportunities to optimize seizure emergency guidelines. Stronger focus on pre-hospital guidelines could empower patients and caregivers to manage acute seizures in the outpatient-setting, potentially avoiding unnecessary seizure escalation, injury, hospitalization and death. Seizure emergencies affect many stakeholders along the pathway and therefore are systemically burdensome. Inclusion of REST in guidelines could lead to a behavior shift to earlier management and prevention of seizure emergency escalation in the community-setting, preventing negative patient-outcomes and decreasing unnecessary economic burden. UCB-sponsored

806 | Prevalence of Post-Traumatic Epilepsy and Risk Factors Associated with its Development

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Purpose: To analyze the prevalence and risk factors associated with the development of post-traumatic epilepsy (PTE) in adult patients hospitalized for traumatic brain injury (TBI).

Method: A retrospective study was performed on 295 adult patients hospitalized for TBI at the Unidade Local de Saúde do Alto Minho (ULSAM) between January 1, 2017, and December 31, 2023. Patients were selected through convenience sampling. Data on demographic, clinical, imaging, therapeutic, and pathological variables were collected and analyzed. A logistic regression model was used to identify predictors of PTE development.

Results: Among the 295 patients hospitalized for TBI, the prevalence of PTE was 9.83% (n=29). The presence at the time of TBI of loss of consciousness, focal neurological deficits, lower scores on the Glasgow Coma Scale and mass effect on cranial computed tomography scan, along with male sex, acute symptomatic seizures surgical intervention and histories of chronic alcoholism, revealed a statistical significant association ($p<0.05$) with the development of PTE. The logistic regression model demonstrated robust predictive capability (R^2Nagelkerke=0.363; accuracy=91.9%). Acute symptomatic seizures were the strongest predictor of PTE (odds ratio [OR]=15.207; $p<0.001$), followed by chronic alcoholism (OR=3.925; $p=0.006$) and focal neurological deficits (OR=3.769; $p=0.006$).

Conclusion: The prevalence and risk factors identified in this study align with findings from similar research. Acute symptomatic seizures, chronic alcoholism and focal deficits emerged as key predictors of PTE. These results underscore the importance of early risk identification and close monitoring of TBI patients to optimize management and mitigate the potential development of PTE.

1063 | Improving Lives in Dravet Syndrome: Overcoming Challenges in the Family Journey

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Purpose: Dravet Syndrome (DS) is a developmental and epileptic encephalopathy that is primarily characterized by drug-resistant epilepsy, which typically manifests within the first year of life (Cardenal-Muñoz E et al. Epilepsia 2022;7(1):11-26). DS is associated with significant comorbidities, including behavioral, motor, and cognitive disorders, as well as sleep disturbances and feeding cycle disruptions (Dravet C. Epilepsia 2011;Apr;52;Suppl2:3-9). These factors complicate disease management and patient care. This study aims to analyze the present status of DS standard of care in Spain and identify actionable strategies to enhance disease management within the National Health System and the broader community.
Method: The methodology includes the formation of a multidisciplinary team of 14 experts, including healthcare professionals from diverse medical specialties relevant to DS and representatives from patient advocacy organizations. Following individual interviews, a working session was held with the experts to discuss and reach a consensus on the Family Journey of both pediatric and adult DS patients.
Results: The experts and patient advocacy organizations highlighted critical areas for improving DS patient care. Key priorities include facilitating access to genetic testing for early diagnosis and individualized approaches. They also emphasized the importance of training for Emergency and Primary Care professionals, standardizing referral times, and fostering multidisciplinary collaboration. Notably, ensuring a coordinated transition from pediatric to adult care, raising awareness of available social resources, and simplifying benefit access were also highlighted. Additionally, addressing comorbidities through coordinated psychosocial resources and improving accessibility to socio-health institutions are vital. By integrating professional expertise and the voices of families, this multidimensional approach aims to enhance outcomes and align care with patient needs.
Conclusion: Collectively, the proposed Family Journey encompasses not only aspects of the care process but also the emotional, educational, and social support required to improve the quality of life for patients and their families.
Fundings: UCB Pharma

1071 | Lennox-Gastaut Syndrome. Situation analysis and Family Journey

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Purpose: Lennox-Gastaut Syndrome (LGS) is a rare and severe form of developmental and epileptic encephalopathy that typically manifests during childhood. It is characterized by multiple epileptic seizure types, electroencephalogram abnormalities, and neurodevelopmental delays (Wheless J et al. CNS Drugs 2014;28(6);553-573). LGS is associated with cognitive and behavioral problems, nearly always treatment-resistant seizures, and progressive deterioration throughout the patient's life. The objective of this study is to outline the Family Journey of both pediatric and adult LGS patients and their families.
Method: A multidisciplinary team of 8 experts, including clinical professionals (pediatric neurologists, adult neurologists, neuropsychologists, and nurses), patient representatives and family members, participated in a working session. Individual interviews were conducted with the experts, and their insights were discussed and consolidated during the session.
Results: The study highlights the critical burden faced by caregivers of patients with LGS. Key findings include promoting innovative therapies and raising awareness among healthcare professionals, families, and society are crucial for enhancing early diagnosis and access to treatments. Experts emphasized the need for differential diagnosis in childhood epilepsy and re-evaluation of adults with uncontrolled seizures and/or major cognitive and motor impairments. Particular attention is placed on multidisciplinary approaches that integrate specialized medical care, psychosocial support, and access to financial resources. Simplifying processes and ensuring coordinated care aim to ease caregiver strain and enhance patients' and families' quality of life.
Conclusion: This work focuses not only on clinical and therapeutic management but also on enhancing the quality of life of patients and families by means of educational, emotional, and social support. This comprehensive framework aims to address the diverse challenges faced by the

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LGS community while promoting a more integrated and effective approach to care. Fundings: UCB Pharma.

1173 | The "Chapeau de Gendarme (CG) sign: clinical characteristics and medical and surgical outcome

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Purpose: We identified patients who presented with Chapeau de Gendarme (CG)sign and looked into anatomical patterns, clinical characteristics, medical and surgical outcome.
Method: Five patients presenting with the CG sign were identified over the last year. All patients were submitted to interictal and ictal video electroencephalogram (VEEG), magnetic resonance imaging (MRI), neuropsychological evaluation. Stereoelectroencephalography (SEEG) was performed in one patient. Surgery was performed in 3 patients.
Results: All patients had refractory epilepsy. Mean age was 30.4 years. The average age at epilepsy onset was 8.66 years. In 3 patients the CG sign appeared at the onset of the clinical seizure, in the other two, it appeared later. Epileptiform activity was noted over the parasagittal frontal region when CG occurred early in the seizure onset. In those patients in whom CG appeared later after, one had an anterior temporal lobe onset and one had a posterior temporal lobe onset. No patients had auras. Three patients presented with focal impaired awareness seizures and two focal motor seizures. MRI findings showed right hemispheric atrophy in 2 patients, multiple tubers in one, and in two were non-lesional. One patient underwent SEEG and ictal onset was found in the anterior cingulate gyrus. Three patients were submitted to surgery: two underwent hemispheric surgery and one was submitted to cingular and mesial frontal resection. Two patients submitted to surgery were rendered seizure-free and one had at least 95% reduction in seizure frequency. Two patients are waiting surgery.
Conclusion: The functional network associated with CG includes cortical and subcortical structures mainly located the frontal lobe (anterior cingulate cortex, mesial prefrontal/premotor cortex, supplementary motor area, orbito-frontal). In patients in whom CG sign early during seizure onset, a cingular or mesial frontal onset should be suspected. Surgical treatment in well selected patients can yield very good seizure outcome.

1659 | Predictors of outcome in patients with super refractory status epilepticus- a multicentre study

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Purpose: We conducted a multicentric study in ten centers from India to determine the clinical and electrophysiological predictors of outcome in Super Refractory Status Epilepticus (SRSE).
Method: Data was collected from case records of those satisfying the diagnosis of SRSE during 2011 to 2021 from SCTIMST (Data controller) and 9 other centers (Data providers) fulfilling data sharing agreement norms. Functional outcome was measured by Glasgow outcome score (GOS) and was dichotomised into bad outcome (< 2) and good outcome (> 3).
Results: 200 SRSE patients were included. Acute symptomatic (88-44%) was the most common etiology. Focal onset generalized seizures were the most common seizure type in 116 (58%) and 116 (58%) were diagnosed as NORSE and 71 patients had FIRES at presentation. 80(40%) patients had a bad outcome. Univariate analysis showed duration of ICU stay (p-0.0017), acute symptomatic etiology (p- 0.043), 'After Status Epilepticus Discharges' (p -0.030), delay in starting anesthetic agents (p<0.001), need for vasopressors (p-0.001), number of ASMs (p-0.004) and delay in initiating immunotherapy (p<0.001) as independent predictors of outcome. Multivariate analysis showed acute symptomatic etiology (p-0.024) and delay in initiation of anesthetic agents (p<0.001) as predictors of bad outcome. Burst suppression achieved with anesthetics (p 0.036) and the need for vasopressors (p-0.004) were associated with good outcome.
Conclusion: We identified independent therapeutic and electrophysiological prognostic factors for predicting the outcome of SRSE. The etiology, early initiation of anesthetics and immunotherapy, and post-SE discharges were identified as key predictors of independent outcomes. Only one-third (40%) will have a bad outcome in SRSE if treated promptly and aggressively, one of the very sinister neurologic emergencies.

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Epilepsy in Older People

411 | A study of characteristics of acute symptomatic seizure related to acute ischemic stroke compared to poststroke epilepsy

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Purpose: Acute symptomatic seizure (ASS) is known as one of major early complications occurring in close temporal association with acute ischemic stroke. The mechanism of this symptom has not been made sufficiently clear. The purpose of our study is to identify the characteristics of ASS patients from the perspective of cerebral infarction characteristics.

Method: We selected retrospectively both patients who showed ASS while presenting an acute cardioembolic cerebral infarction, and post stroke epilepsy (PSE) while presenting an old one matching age and sex who taken to our hospital from January 2014 to December 2023. ASS group was brought to our hospital by ambulance showing clinical epileptic seizure induced by acute cerebral infarction. The PSE group had no seizures for at least three years from onset of first stroke. Patients were investigated with vital signs, laboratory data, neurological findings and MRI findings. These two groups were compared using statistical analysis.

Results: 10 ASS and 43 PSE patients were finally analyzed in this study. The ASS group showed 85.5 [80-90] years old, 21.5 [11-27] points of National Institutes of Health Stroke Scale (NIHSS) and 60.0% of the males (*median [interquartile range]). The PSE group showed 79.0 [71-86] years old, 10.0 [5-16] points of NIHSS and 48.8% of the males. Both groups did not show statistical differences in age, sex, past history and laboratory data. Most of them showed generalized tonic-clonic convulsions and cerebral infarctions occupying several cortices. However, volume of infarctions at the frontal lobe, elevation of points of NIHSS were significantly more conspicuous in the ASS group than the PSE group.

Conclusion: Details of ASS related to ischemic stroke are quite different from PSE. Prefrontal cortices have a quite strong relationship with limbic systems. ASS might be related to the severe destruction of prefrontal cortices compared to PSE, inducing hyperactivity of limbic systems.

549 | Risk Factors Associated with Late-Onset Epilepsy in Persons with Dementia and Mild Cognitive Impairment

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Purpose: The risk of developing epilepsy substantially increases after 60(late-onset epilepsy [LOE]), particularly in people with cognitive decline(PWCD, i.e., dementia and/or mild cognitive impairment). Epilepsy is associated with worse cognitive and mortality outcomes in PWCD. Identifying PWCD at risk for LOE can facilitate early screening and treatment of epilepsy. Our study investigated factors associated with LOE in PWCD.

Method: This longitudinal, multicenter study is based on 39 US Alzheimer's Disease Research Centers from 9/2005–12/2021. We investigated the association between various factors and LOE development, which is defined as seizures starting at or after 60 in PWCD. Those who did not develop LOE but were $\geq$60 at follow-up served as controls. A multivariable Cox regression analyzed the association between various factors and LOE. Independent variables included age, sex, and socio-economic factors (education, race, ethnicity), cardiovascular risks (hypertension, diabetes, hyperlipidemia), cerebrovascular disease (stroke or transient ischemic attack[TIA]), other neurologic comorbidities (Parkinson's disease[PD], traumatic brain injury), cognition (age of dementia-onset, dementia severity, dementia type: Alzheimer's disease [AD] vs. non-AD), genetics (APOE4 status), lifestyle (alcohol abuse, smoking), and depression.

Results: Of the 14,685 participants (7,355(50%) female; mean age=73.82$\pm$8.5years) who met the inclusion criteria, 221(1.5%) developed LOE during follow-up. After adjusting for covariates, the following were associated with a higher risk of LOE: APOE4 allele (aHR:1.39, 95%CI:[1.04,1.86],p=0.03), dementia-onset before 60 (adjusted hazard ratio(aHR):2.46, 95% confidence interval[CI]:[1.53,3.95],p<0.001), worse cognition (aHR:2.35, 95%CI:[1.97,2.79],p<0.001), AD dementia subtype (aHR:1.68, 95%CI:[1.13,2.49],p=0.01), stroke/TIA [aHR:2.03, 95%CI:[1.37,3.01],p<0.001]), and PD (aHR:2.53, 95%CI:[1.08,5.95],p=0.03). In sensitivity analysis, using alternative LOE definition of epilepsy-onset after 65 revealed the same factors associated with LOE.

Conclusion: Our study showed that the APOE4 allele, dementia-onset before 60, AD dementia subtype, worse cognition, stroke/TIA, and PD are associated with LOE

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development in PWCD. PWCD with these risk factors may be considered for routine screening with an EEG for early identification of LOE.

701 | Use of perampanel in elderly patients with focal epilepsy and atherosclerotic lesions of brachiocephalic arteries

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Purpose: To assess the effectiveness of Perampanel in patients with cognitive impairment, stenosis of brachiocephalic arteries and hypercholesterolemia.
Method: We examined 55 patients (age 55-79 years) with focal epilepsy, complaints of cognitive impairment, clinically significant stenosis of brachiocephalic arteries (>70%) and hypercholesterolemia (cholesterol more than > 6.1 mmol/l, LDL > 3.3 mmol/l). MoCA score <26 registered in 76.4% (42) patients. 26 patients with ongoing seizures take antiseizure medications (ASM) in monotherapy (carbamazepine 8, levetiracetam 12, valproic acid 6). 18 patients were on duotherapy (carbamazepine+levetiracetam 9, oxcarbazepine+levetiracetam 4, lamotrigine+levetiracetam 5). In 18 cases Peramanel was added as early (primary) duotherapy, in 13 cases enzyme inducers were replaced on Perampanel. The seizure frequency, MoCA test, and QOLIE10 were analyzed.
Results: In analysis group were included 31 patients who take Perampanel in a dose 6-10 mg per day. Seizure frequency after 6-12 months of therapy significantly decreased compared 6 months before adding Perampanel (3.75 ±4.8 vs. 8.2 ±6.1, p=0.036). 15 patients had 6 months seizure remission. MoCA test results before and after adding Perampanel were 23.75 ± 5.74 vs 24.25 ± 2.54 (p=0.06). An improvement in the quality of life was noted (possibly because the number of seizures decreased). QOLIE10 showed significant improvement in the cognitive functioning and seizure worry sections.
Conclusion: Risk of cognitive impairment increases in patients with focal epilepsy who takes antiepileptic drugs affecting lipid metabolism. Correction of ASM is an important step in patients with high cardiovascular risk. Perampanel can be the drug of choice in this group of patients. It's effective in older patients with epilepsy, has minimal drug interactions and doesn't increase risk factors of cerebrovascular diseases. Perampanel showed a trend of improving cognitive functions and quality of life after adding or replacing other ASM.

1174 | What is new in New onset Seizures in Octogenarians?

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Purpose: To analyze the clinical characteristics of patients with new onset seizures >85 years of age and compare the characteristics between seizure recurrence and non-recurrence group. The occurrence of new seizure(s) in older adults is two to three-fold higher as compared to younger population and previous studies have characterized the clinical features of seizures in patients beyond 60 or 65 years. Following the recent ILAE task force on Epilepsy in Elderly (2023), this study has evaluated the clinical characteristics in old-old adults (>85 years).
Method: Data was collected from prospectively maintained electronic medical records and the participants were divided into seizure free and seizures recurrence group. Independent t test was used to compare the data between both the groups. p<0.05 was considered statistically significant
Results: We included a total of 40 patients with a mean age of 88.7 + 2.79 years and 77.5% males over a 30-year lengthy period at a single comprehensive epilepsy care center. Generalized tonic-clonic seizure (45%) was the most common seizure type and the positive yield of neuroimaging was 42.5%, while EEG showed specific abnormalities in 50%. Etiology was unidentified in 50%, while stroke was the most common among identified etiologies (27.5%). 62.5% were well controlled on mono therapy and 47.5% had recurrence during a mean follow-up of 1.4 [0.2 - 5.8] years. A history of prior stroke [47.3% versus 23.8%, p=0.031], use of phenytoin [68.4% versus 33.3%, p=0.056] and clobazam [42.1% vs 19%, p=0.049] were found to be the significant risk factors for seizure recurrence when compared to non-recurrence group.
Conclusion: This study contributes to better identification and improved characterization of late onset seizures and adds that appropriate timely management results in better outcomes.

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1257 | Comprehensive Profiling of Late-Onset Epilepsy: Demographics, Clinical Features, Diagnostic Patterns, and Treatment Approaches

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Purpose: To enhance understanding and management strategies for Late-Onset Epilepsy (LOE), a condition that is increasingly prevalent as the population ages, yet comprehensive data on its clinical and diagnostic aspects remain limited.
Method: A retrospective analysis of 3192 epilepsy patients identified 265 individuals with LOE (seizure onset at age ≥60 years). Clinical and demographic data were collected.
Results: The mean seizure onset age was 69.18 ± 7.56 years, with a mean current age of 73.79 ± 8.85 years. Male patients comprised 136(51.3%). Most were white 218(82.3%), followed by black 14(5.2%), Asian 2(0.8%), and others 31(11.6%). Epilepsy types included focal 189(71.3%), generalized 36(13.5%), and unknown 27(10.2%). Auras were reported in 25(9.4%), and status epilepticus in 12(4.5%). Comorbidities included stroke 38(14.3%), dementia 12(4.5%), brain tumor 10(3.8%), and traumatic brain injury 3(1.1%). 34(12.8%) had depression and 26(9.8) had anxiety. Family history of epilepsy was documented in 6(2.3%) patients. Structural etiologies were identified in 32(12.1%), with stroke being the most frequent (9 ischemic, 4 hemorrhagic). No cause was identified in 130(49%). EEG abnormalities were found in 114(68.3%) of 167(63%) patients, with epileptiform discharges in 38(33.3%) and background slowing in 49(42.9%) focal slowing 27(23.6%). MRI abnormalities were found in 98(79.7%) of 123(46.4%) patients, primarily chronic ischemic changes 32(32.6%). Treatment included monotherapy in 153(57.7%) and polytherapy in 61(23%). Levetiracetam was used in 148(55.8%) and phenytoin in 41(15.4%). LOE patients had higher prevalence of comorbidities ($p = 0.001$), structural etiologies ($p = 0.001$), MRI abnormalities ($p < 0.001$), EEG abnormalities ($p = 0.096$), levetiracetam ($p < 0.001$), and phenytoin ($p = 0.001$) usage, and lower rates of family history of epilepsy ($p < 0.001$) and distinct epilepsy types ($p < 0.001$) compared to early-onset epilepsy.
Conclusion: In our cohort LOE is more likely to be focal onset associated with structural abnormalities in the brain. Levetiracetam is the most common anti-seizure medication utilized initially.

1280 | DeRitis ratio as a novel biomarker for post-stroke seizures

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Purpose: Post-stroke seizures (PSS) occur in approximately 3%–15% of ischemic stroke and 10%–16% of patients with intracerebral hemorrhage. Despite the relatively high incidence, the factors that predict which patients will develop PSS remain unclear. Our study aimed to investigate the incidence of PSS and evaluate the De Ritis (AST/ALT) ratio as a potential biomarker for PSS.
Method: We included 602 patients with ischemic or hemorrhagic stroke, of whom 528 presented with acute stroke and 74 had a history of stroke-related seizures. Serum biomarkers were analyzed, and all patients underwent EEG evaluations. The De Ritis ratio was calculated for each patient, and the mean ratio was compared across three patient groups: seizure-free, early-onset PSS, and late-onset PSS. Descriptive statistics and ANOVA were performed.
Results: Early-onset PSS occurred in 40 patients (7.5%), while late-onset PSS was observed in 27 (4.8%). The groups had no significant differences in age or stroke severity, as measured by the NIH Stroke Scale (NIHSS). The mean De Ritis ratio was significantly lower in the seizure-free group (0.999 [SD 0.58]) compared to the early-onset PSS group (1.187 [SD 0.459]) and the late-onset PSS group (1.318 [SD 0.541]) ($p < 0.001$ for both comparisons). No significant difference in the De Ritis ratio was found between the early- and late-onset PSS groups.
Conclusion: The incidence of PSS in this study aligns with previously reported rates. The elevated De Ritis ratio observed in patients with PSS may reflect systemic stress in late-onset PSS and systemic inflammatory responses or metabolic dysfunction in early-onset PSS. These findings suggest the De Ritis ratio could serve as a predictive biomarker for PSS, though further research is required to validate this hypothesis

1283 | Assessing the Risk of Early Post- Stroke Seizures After Thrombectomy: A Retrospective study

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Purpose: This study investigates the risk of early post-stroke seizures after mechanical thrombectomy compared to the general risk and examines the relationship between reperfusion and infarct demarcation on seizure development.
Method: We conducted a retrospective analysis of 208 patients who underwent thrombectomy for intracranial emboli between June 2023 and December 2024. Patients with pre-existing epilepsy, prior ischemic lesions, or severe hyponatremia were excluded. We identified patients with early seizures, analyzing seizure types and occurrence time. The relationship between infarct size (measured by ASPECTS and modified pc-ASPECT/ac-ASPECT) and post-thrombectomy perfusion (TICI classification) with seizure development was examined.
Results: The median age was 78.6 years, with a median observation time of 16 days. Fifteen patients (7.2%) developed early seizures, with 13 occurring within the first 24 hours. Focal to bilateral tonic-clonic seizures were most common (80%). While 93% of patients in both groups achieved successful recanalization (≥ TICI 2b), those with early seizures had larger infarct sizes (mean ASPECTS/pc-ASPECT 5/10 vs. 7.3/10 without seizures; ac-ASPECT 2/3 vs. 3/3 for anterior circulation).
Conclusion: Mechanical thrombectomy does not appear to increase the risk of early seizures compared to the general risk (7.2% vs. 2-20%). Recanalization seems unrelated to seizure risk, but larger infarcts may increase it. Future research aims to develop a predictive score for early seizures by validating additional risk factors and exploring preventive pre-treatment for at-risk patients.

1284 | Late onset epilepsy in cerebral small vessel diseases

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Purpose: The aim of this study was to assess the burden of leukoaraiosis, cortical atrophy, and particularly medial temporal lobe atrophy in patients with late-onset epilepsy.
Method: One case report involved a 64-year-old female patient who was hospitalized in our neurological department between November 2024 and December 2024. The extent and spatial distribution of white matter hyperintensities, along with medial temporal lobe atrophy, were analyzed using 3 Tesla magnetic resonance imaging (MRI). The Fazekas scale was applied to assess the degree of microangiopathy, and nocturnal video-EEG monitoring was conducted.
Results: Patient A.M., 66 years old, has been suffering from small vessel disease – Binswanger's disease, since 2010. The first signs of the disease manifested with mild cognitive and behavioral impairments. Over the last 4 years, the patient's condition has significantly worsened, with the development of speech and movement disorders, as well as severe cognitive impairments. After 14 years from the onset of the disease, focal seizures began in March 2024. To date, 7 unprovoked epileptic seizures have been noted. According to the MRI findings, there are signs of pronounced atrophy of the cerebral hemispheres - a neurodegenerative process. The mesial temporal areas are symmetrical, with a significantly reduced volume. Cerebral microangiopathy according to the Fazekas scale, is graded as III. Additionally, communicating hydrocephalus ex vacuo is observed . On the EEG: During sleep, a prolonged asynchronous arrhythmic regional slowing is recorded in the rhythm, predominantly in the delta range, in the frontal-central-temporal regions, more on the right, with an amplitude of up to 50 μV.
Conclusion: In summary, epilepsy was linked to reduced cortical volume and atrophy of the hippocampus or temporal lobe. However, further cohort studies are necessary to determine whether, and to what extent, vascular comorbidity and late-onset seizures share a common underlying basis.

1367 | Sleep quality and sleep-wake cycle dysregulation in late onset epilepsy of unknown origin: an actigraphic study

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Purpose: Sleep disturbances frequently occur in people with epilepsy and may be more pronounced in older adults (Lee SK J epilepsy Research 2019;9(1):27). Late-onset epilepsy of unknown etiology (LOEU) accounts for 15–20% of LOE cases (van Golde EGA et al. Sleep Med Rev. 2011;15(6):357-368), however, sleep disturbances objectively assessed in LOEU remain insufficiently explored. This study aimed to evaluate sleep-wake cycle in LOEU patients compared to healthy older controls (HC) using actigraphy and self-reported sleep assessments.
Method: Thirty-eight LOEU patients (38.9% males, mean age of 67.1±7.75) and 16 HC (14.8% males; mean age of 64.4±9.59) underwent 7-day actigraphic recording to evaluate sleep-wake rhythm. Participants completed self-report questionnaires assessing excessive daytime

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sleepiness (Epworth Sleepiness Scale, ESS), subjective sleep quality (Pittsburgh Sleep Quality Index, PSQI), and chronotype (Morningness-Eveningness Questionnaire, MEQ). Exclusion criteria included concomitant unstable medical conditions, psychiatric or neurological diseases, and shiftwork. Patients presenting seizures during the actigraphic recording were excluded.

Results: Considering the actigraphic recording, LOEU patients exhibited longer sleep latency (p=0.044), lower sleep efficiency (p=0.012), higher sleep fragmentation (p=0.028), and increased sleep fragmentation (p=0.015) than HC. Considering both objective and subjective circadian rhythm parameters, no significant differences were observed in relative amplitude, interdaily stability, intradaily variability, the day-night activity ratio and MEQ scores. Subjective sleep quality, as measured by PSQI, was significantly worse in LOEU patients (p=0.006). while excessive daytime sleepiness did not differ between groups (p=0.955).

Conclusion: LOEU patients present poorer sleep quality, lower sleep efficiency and increased sleep fragmentation compared to healthy older individuals, but no circadian rhythm alterations or excessive daytime sleepiness were found. These findings suggest that sleep disturbances in LOEU may be related to sleep disruption rather than circadian rhythm misalignment or daytime wakefulness impairment., highlighting the need of assessing sleep problems in epilepsy, particularly in LOEU.

1496 | Comparison of Standard and Extended 3-Hour EEG in Elderly with Acute Confusion

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Purpose: Several studies have been conducted to ascertain the efficacy of continuous EEG (cEEG) in elderly patients presenting with acute confusion state (ACS). These studies have yielded preliminary evidence suggesting that cEEG may offer superior detection of NCSz and NCSE compared to standard EEG. The objective was to assess whether a 3-hour EEG could yield more data than a 20-minute standard EEG, particularly in terms of identifying epileptiform discharges (ED) and other pathological findings in elderly individuals with acute confusion of unknown origin at the onset of their symptoms in resource – restricted settings.

Method: Prospective observational study of 40 elderly patients presenting with ACS of unknown etiology underwent 20-minute, 30-minute and 3-hour EEG recording.

Results: There were no statistically significant differences in EEG patterns between the 20-minute, 30-minute, and 3-hour EEG groups ($p > 0.05$). No clinical, laboratory, or neuroimaging markers were identified as prognostic indicators of epileptic EEG patterns.

Conclusion: A prolonged 3-hour EEG does not provide additional benefits for the older patient population with an acute confusional state of unknown etiology. When present, specific EEG changes suggestive of non-convulsive seizures (NCSz) or non-convulsive status epilepticus (NCSE) can be identified within the standard 20-minute EEG recording period.

1711 | Stability in Cognitive Functioning, Psychological and Lifestyle-Related Factors in Older Adults with Focal Epilepsy

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Purpose: Cognitive complaints are common in older persons with focal epilepsy (PWE), yet little is known how remediable lifestyle-related or psychological factors affect progression in cognitive functioning over time. The present study investigated the role of depression, anxiety, stress, and sleep problems over two years in older PWE (≥50 age).

Method: Participants were older adults with focal epilepsy (n = 21), recruited from the Karolinska University Hospital Epilepsy Team. All participants completed neuropsychological tests of memory, attention, processing speed, executive functioning, and filled out self-report questionnaires about depression, anxiety, stress, and sleep problems at baseline and at a two-year follow-up.

Results: The results indicated that there was no significant difference in verbal learning (M±sd T1=48.2±10.4; T2 =49.5±13.0, p>0.05) and delayed recall (T1= 48.1±11.7, T2 = 50.57±13.4, p>0.05) as measured by the Rey Auditory Verbal Learning test (RAVLT) across two years. There was a significant correlation ($r > 0.61$, $p < 0.01$) between baseline performance and T2 for the same variables. There was a significant correlation between T1 and T2 scores for sleep, depression, and generalized anxiety (r>0.58, $p < 0.01$), but not for perceived stress. Correlation analyses indicated no significant associations between cognitive and lifestyle- or psychological variables. Similar results were observed for

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measures of visual memory, working memory, processing speed, and executive function.

Conclusion: Cognitive performance and lifestyle- and psychological variables remained stable across a two-year follow-up, and there were no significant associations between the two sets of variables. This may have clinical relevance when discussing progression of cognitive functioning over time in older adults with focal epilepsy. The study highlights the importance of a neuropsychological evaluation to accurately capture cognitive, psychological, and lifestyle-related functioning in older PWE and allow for targeted interventions. Supported by a grant from the Swedish Association for Epilepsy.

Epilepsy in Resource-restricted Settings

561 | The Electroencephalography Federal University of Rio de Janeiro/Democratic Republic of Congo/University of Oxford Study Group: results of a two-year collaboration

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Purpose: The Democratic Republic of Congo (DRC) has a population of around 105 million people, with a minimum prevalence of 1% suffering with epilepsy [Kazadi P et al. World Neurology 2023;38:8.]. The country has few neurologists and lacks equipment, such as electroencephalograms (EEGs), leading to a lack of training in performing and interpreting EEGs, compromising the diagnosis and management of epilepsy. Here we evaluate the results of a two-year collaboration between Federal University of Rio de Janeiro (UFRJ/Brazil), DRC and University of Oxford (United Kingdom) designed to improve EEG learning in the DRC.

Method: In 2023, a group of doctors from the Global Epilepsy Foundation in the DRC (ASLEK) requested collaboration for training in EEG to improve their practice in resource-restricted settings. A Study Group of UFRJ Professors (Neurology and Clinical Neurophysiology), UFRJ medical students and Adult Epilepsy Specialists from University of Oxford was formed. An EEG Course was delivered remotely (workload 24 hours). In 2024, the Congolese Group underwent an in-person hands-on EEG training at the Deolindo Couto Institute of Neurology/UFRJ (workload 140 hours).

Results: Over these two years, the Study Group has provided sustainable education in EEG. An EEG machine was donated by a Brazilian manufacturer to the DRC group. More UFRJ medical students, from low-resource countries, including Angola, Benin, Congo-Brazzaville, Gabon, Haiti and Kenya, have joined us thereby having the opportunity to learn EEG and take this knowledge to their countries when appropriate. Cultural exchanges are being strengthened by support from the Centre for Afro-Brazilian and Indigenous Studies (NEABI/UFRJ), a dedicated UFRJ Librarian and The Centre for Global Epilepsy in Oxford.

Conclusion: Our expanding Study Group has effectively collaborated with Medical Education in EEG and the DRC. We offer a template for how upper middle- and high-income countries can work together to deliver better epilepsy care in resource underprivileged settings.

773 | Knowledge, attitudes, and perceptions of epilepsy among school teachers in Georgia

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Purpose: The stigma of epilepsy among school teachers often creates significant problems for children and adolescents with epilepsy in relationships with their teachers, which hinders the educational process and reduces the quality of life of individuals with epilepsy. In order to implement the proper intervention measures in this group of society, it is necessary to assess the level of awareness on epilepsy-related issues among teachers.

To study knowledge, attitudes and perceptions of epilepsy among secondary school teachers.

Method: The study was carried from 1st September to 30th November, 2024 in three secondary schools located in different parts of Tbilisi, Georgia. We used the Georgian version of the "Questionnaire for Knowledge, Attitudes, and Perceptions (KAP) on epilepsy", which was adapted from the original Chinese version and previously was used in Georgia (Gzirishvili et al, 2013). The KAP questionnaires were distributed among school teachers; study subjects had the opportunity to fill them out anonymously and return to the researchers.

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Results: 180 questionnaires were distributed, 141 were returned, and 135 of them were appropriately completed, on the basis of which the data analysis was performed. Out of the 135 participants, aged between 27 and 66 years (SD 45 years), 78 (57.7%) were male. Almost all respondents (n=132; 97.7%) had heard of epilepsy and less than half of them (n=60, 44.4%) believed that epilepsy is a form of mental illness, or psychiatric disease (n=23; 17%). 40 (29.6%) schoolteachers would not allow their children to marry a person with epilepsy.
Conclusion: There is a serious lack of knowledge about epilepsy among school teachers; more action is needed to raise their awareness and create an adequate social and learning environment for children with epilepsy in schools. Acknowledgements: The study was conducted within the grant of the Shota Rustaveli National Science Foundation (PHDF-24-271) and internal scientific grant of CIU (# CIU-FR).

826 | Patient Experience with Telephonic Consultations in Korean Epilepsy Care: A Survey Study

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Purpose: Patients with epilepsy often face challenges in visiting hospitals due to mobility issues, concerns about seizure occurrences, work-related constraints, or the social stigma associated with epilepsy. In South Korea, telemedicine is largely prohibited, but telephonic consultations were temporarily permitted during the COVID-19 pandemic. This study aimed to evaluate the experiences and satisfaction of epilepsy patients with telephonic consultations.
Method: A survey was conducted among epilepsy patients receiving care at the neurology department of a tertiary university hospital. Patients who had experienced at least one telephonic consultation were included. Surveys were administered either in-person during hospital visits or via phone calls by research staff. Participants were allowed to select multiple options when identifying the aspects of telephonic consultations they were most satisfied with. Other responses were rated on a 5-point Likert scale, with 1 indicating strong disagreement and 5 indicating strong agreement.
Results: Of the 248 patients who received telephonic consultations, 200 provided consent and completed the survey. The cohort included 104 males and 96 females, with a mean age of 43 years (range: 21–71 years). Overall satisfaction with telephonic consultations was high, with a mean score of 4.2 (SD: 0.7). Satisfaction did not significantly differ based on epilepsy duration, seizure type, seizure frequency, or the number of medications taken. The most satisfying aspects of telephonic consultations were 'saving time' (83%) and 'avoiding waiting at the hospital' (74%). Patients rated 'the physician's understanding of their condition' and 'adherence to the scheduled appointment time' both at 4.3 points. The lowest satisfaction score was for 'ease of receiving medication,' which was rated at 1.7 points.
Conclusion: Epilepsy patients reported high satisfaction with telephonic consultations, suggesting that remote evaluations and education can be effective for non-emergency care. These findings underscore the potential benefits of expanding telemedicine options for epilepsy patients to enhance accessibility and convenience.

1035 | Comparison of epilepsy diagnosis and management in rural Indian populations with and without a smartphone application (Epilepsy Treatment Aid)

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Purpose: That many people with epilepsy (PWE) remain untreated is an issue not only for them and their families, but also for their country's economy, since they are mostly young and either often miss education or are unemployed. Apart from cost and availability of antiseizure medicines (ASMs), lack of access to doctors experienced in epilepsy is a major cause of this treatment gap. One solution to this is to train primary care doctors (PCDs) in epilepsy, and another would be to make available to them a smartphone application (app) which suggests a personalized treatment based on their symptoms and available ASMs. We compared the accuracy of treatment appropriateness compared with an experienced epilepsy specialist in two groups of PCDs, one trained and using the app and the other trained and not using the app, studied prospectively.
Method: Two blocks in Chhattisgarh were selected for study. PCDs were trained on epilepsy in-person for two days, with two hours for app training. PWE were identified from community engagement. The Epilepsy Treatment Aid (NetProphets Cyberworks Pvt) was used; this was an extension of previous apps to include treatment suggestions. Patients in both treatment arms were assessed face-to-face after six months and the original treatment graded as correct, partially correct, or incorrect.

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Results: Forty-eight PWE were seen with the app and 40 without. Follow-up rates were 27% and 40% respectively. Agreement (full or partial) occurred in 85 % (app) and 71% non-app.

Conclusion: Although these numbers are small, they suggest that first, a treatment app is at least as safe as trained PCDs in managing epilepsy in community settings, and second, is worthy of further study. Acknowledgement: This study was supported by the Indian Council of Medical Research (ICMR) grant number I-1321.

1090 | Quantitative EEG biomarkers for post-malarial epilepsy

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Purpose: Severe malaria with neurologic involvement contributes significantly to the global burden of acquired pediatric epilepsy. Limited literature indicates a role for quantitative EEG (QEEG) in predicting epileptogenesis after brain injury. We examined the relationship between QEEG measures and post-malarial epilepsy, hypothesizing a role for gamma based on prior work from our group.

Method: 186 patients, aged 6 months to 11 years, with cerebral malaria (CM, P. falciparum infection and coma defined as GCS ≤10 or BCS ≤2) or CNS malaria (prolonged seizures or impaired consciousness without coma) were enrolled in a prospective observational study conducted in Chipata, Zambia. Admission EEG (obtained within 48h of admission) were available for 179 patients. Follow-up EEGs are being obtained at regular intervals for 2 years (ongoing), for whom 154 participants have currently completed 1-month studies. Out of this cohort, 30 have developed epilepsy to date. We examined the early phase of illness using EEGs at admission (n = 179) and 1-month follow-up (n = 154) to identify differences between patients who developed epilepsy and those who did not. For each recording, we computed relative power and magnitude-squared coherence (MSC) in the traditional EEG frequency bands, and sample entropy (SampEn).

Results: At admission, we found a significant increase in relative delta, theta, and gamma power, and alpha, beta, and gamma MSC in the epilepsy group. At 1-month, we found significantly increased delta MSC and decreased relative beta and gamma power, gamma MSC, and SampEn in the epilepsy group ($p < 0.01$ for all measures).

Conclusion: Measures of relative power and MSC, particularly in the gamma band, likely have utility in predicting post-malarial epilepsy and suggest underlying network remodeling that can be tracked quantitatively during the early phase of illness. We aim to incorporate these measures in identifying patients at high risk of epilepsy for follow up and intervention.

1259 | Home-Based vs. Clinic-Based Care for Epilepsy: A Cost-Effectiveness Study

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Purpose: To evaluate the cost-effectiveness of home-based epilepsy care (HBC) and routine clinic-based (CBC) among people with epilepsy (PWE).

Method: The societal perspective of cost estimation and a bottom-up approach were used to conduct a prospective cost-effectiveness analysis (CEA) on 173 PWE receiving home-based and clinic-based epilepsy care. The study involved consenting individuals with active epilepsy who were identified through a population survey conducted in underserved communities for 24 months (Singh G. et al., 2022). The cost data was collected, including direct medical costs, direct non-medical costs, and indirect costs, for 24 months by researchers and field workers. The EQ-5D-3L scale was used to calculate QALYs. The primary outcome was the total cost involved in both groups and the cost-effectiveness in terms of QALYs gained.

Results: A total of 24 clusters, each made up of ten people with epilepsy, were randomly allocated to either home-based care or clinic-based epilepsy care. The mean total cost in USD was $285.6 per patient in CBC, and the QALY's gained in 2 years were 0.03, while the mean total cost in HBC care was $297.4 per patient, and the QALY's gained in 2 years were 0.11. The ICER was found to be $ 47.9/QALY, which is lower than the threshold value (willingness to pay)

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for the gain of 1 QALY for India, i.e., $542.7 (Pichon-Riviere A., 2023). Thus, showing HBC is cost-effective as compared to CBC. The costs were converted to USD during the financial year 2021-22 (74.5 Rs per USD).

Conclusion: Home-based care presents a marginal increase in costs compared to clinic-based care, but cost-effectiveness is evident when considering the substantial QALYs gained. It is critical to promote the integration of home-based epilepsy care into India's current healthcare system.

1360 | Superstitions and beliefs related to the outcomes of epilepsy treatment in Thailand

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Purpose: To investigate the relationship between superstitions or beliefs and epilepsy treatment outcomes in Thailand.

Method: The study included adult outpatients with an epilepsy diagnosis. Questionnaires were used to collect epilepsy information, which included demographic data, beliefs about the cause of epilepsy, ideas about seizure triggers, and opinions about epilepsy and its treatment.

Results: The responses to questions about superstitions and beliefs about the cause of epilepsy, trigger factors, superstitions and traditional treatments, knowledge and attitudes about epilepsy, ideas about taking ASM, and alternative treatments revealed no significant difference in the number of patients in the seizure-free group versus the ongoing seizure group. Patients who lived in rural areas had a significantly higher rate of ongoing seizures than those living in Bangkok ($p = 0.035$). Patients with less than a higher degree have a significantly higher rate of ongoing seizures ($p = 0.007$).

Conclusion: The outcomes of epilepsy therapy in Thailand were unaffected by superstitions or beliefs. Poor epilepsy treatment outcomes have been linked to lower levels of education and living further away from the country's center.

1361 | How Much Training is Required to Diagnose and Treat Epilepsy? A Serendipitous Study

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Purpose: The World Health Organisation has suggested that non-physicians have an important role in managing people with suspected epilepsy (PWSE). This unplanned study provides an example.

Method: It happened at epilepsy outreach clinics at two blocks in Chhattisgarh, India. VP, a UK-based neurologist was helping see PWSE and required a translator. SC, a health economist with no previous clinical experience of epilepsy, volunteered. At the first block, 10 patients were seen by VP. VP explained to SC how best to ask relevant questions, including using gestures to define seizure semiology. A smartphone application (app) [Epilepsy Treatment Aid, Netprophets Cyberworks Pvt] was being evaluated by MS in this clinic and SC expressed an interest in seeing this. VP demonstrated this to SC on a simulated patient. At the second block, it was decided that SC could test the app to generate diagnoses, and suggest appropriate treatment as proposed by the app. VP clarified any uncertainty about the app questions, reviewed the suggested treatment, and gave appropriate information which was translated by SC. Prescriptions were signed off by MS.

Results: Twelve PWSE were seen. Age range was 5-64 years, median 32. Five were female. Three were taking anti-seizure medication. SC with the app diagnosed 11 with focal epilepsy and one with non-epilepsy. VP concurred in all, further diagnosing the latter as syncope. VP altered the app-suggested treatment in two PWSE, phenytoin being prescribed instead of carbamazepine in one, and carbamazepine instead of phenytoin in the other.

Conclusion: Even though this study has potential biases – VP developed the app, and was with SC when she evaluated the patients – it is remarkable that a non-physician with little training in epilepsy should perform so well in both diagnosis and treatment of PWSE. Therefore, non-physicians may not require as much training as previously thought if a suitable app is provided.

1409 | Epidemiological Profile and Treatment Status of Epilepsy Patients in Chhattisgarh, India: A Baseline Analysis

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Purpose: India is committed to achieving IGAP targets by 2030, but significant treatment gaps persist in rural areas like Chhattisgarh, exposing patients to stigma and poor outcomes[1]. This study examines the demographic and clinical profiles of epilepsy patients at outreach clinics

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to identify barriers to care. The findings aim to propose actionable solutions to improve access to treatment in resource-limited settings.

Method: This study analyzed data from four epilepsy outreach clinics in Nagri and Ambagarh Chowki, Chhattisgarh, India, from September 2023 to July 2024. Participants were diagnosed by a neurologist and prescribed antiseizure medications. Using convenience sampling and standardized questionnaires on demographics and treatment adherence, the study employed t-tests, Chi-square tests, and multivariate logistic regression for statistical analysis, with significance set at $p < 0.05$.

Results: Of the 437 participants (mean age: 25.8 years, 55% male), 63% were untreated. Significant differences were observed between treated and untreated groups in age (median 23 vs. 27 years, p=0.007), age of epilepsy onset (median 9 vs. 13 years, p<0.001), monthly family income (median ₹5000 vs. ₹3000, p<0.001), and cultural identity (non-tribal vs. tribal, AOR: 2.6, 95% CI: 1.7–4.0, p<0.001). Barriers included stigma, cultural beliefs, and financial constraints, particularly among tribal populations. Younger age at onset was associated with higher treatment uptake, suggesting early intervention benefits.

Conclusion: A significant treatment gap exists in rural Chhattisgarh, especially among tribal and low-income communities. Cultural stigma, financial barriers, and limited healthcare access worsen these disparities. To address these issues, it's crucial to focus on community education, diagnosis, affordable medications, and improving the epilepsy primary care processes and systems.

Acknowledgement This study was supported by the Indian Council of Medical Research (ICMR) grant number I-1321

Reference: 1. Singh MB, Suri A. Is achieving IGAP targets realistically possible without a major change in strategy? A view from India. Seizure. 2022 Dec;103:151–2.

1417 | A community-based model for bridging Epilepsy treatment gap in resource limited setting: An Observational Study

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Purpose: Although epilepsy being highly treatable condition, 50–90% treatment gap exists in India. Given the importance of implementing the Intersectoral Global Action Plan (IGAP) for epilepsy, this study aims to illustrate how a community-based model focused on conducting epilepsy outreach camps and training healthcare workers can help address the treatment gap and strengthen epilepsy primary care in a resource limited setting.

Method: This is an observational, community-based study being conducted in Gumla district of Jharkhand, a tribal-dominated district in India with a population of 1.4 million. Training sessions were conducted for primary care doctors and community health workers to improve epilepsy case identification and follow-up. Community outreach activities, such as miking, poster campaigns, and educational discussions, were conducted to encourage treatment-seeking behavior. Thereafter, we conducted epilepsy outreach camps to provide clinical evaluations and initiate treatment. Data on injuries, self-reported addiction and comorbidities were also collected.

Results: A total of 795 patients attended six epilepsy camps in Gumla district, with 70% being male. Of these, 95% had never received prior treatment and were started on medication during the camps, with 74% receiving monotherapy. The prevalence of comorbid conditions included hypertension in 5% (36/795), self-reported addiction in 34% (267/795), and injuries in 14% (111/795) of patients. Additionally, 33 primary care doctors and 103 community health workers were trained for follow up care during the initiative.

Conclusion: Community-based outreach camps, combined with training primary care providers, can effectively address the treatment gap for epilepsy. This approach provides a scalable model for improving epilepsy care in resource-limited settings.

This research was supported by District administration, Gumla, Jharkhand, India and Wellcome DBT Clinical Research Training Program Fellowship.

1460 | Multidisciplinary Management of Adult Patients with Tuberous Sclerosis Complex: Insights from an Epilepsy Clinic Cohort

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Purpose: Tuberous sclerosis complex (TSC) is a multisystemic disease. Neurological manifestations affect up to 95% of cases, positioning neurologists as primary care providers. Ensuring multidisciplinary follow-up may present significant challenges. This study aims to characterize adult TSC patients, focusing on multidisciplinary care.

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Method: Retrospective observational study including adult TSC patients (Northrup *et al*, 2021 criteria), followed in an epilepsy clinic at a tertiary hospital in the northern Portugal. Data were collected from medical records and interviews.

Results: Among 41 patients (51% female; mean age 36±16 years; mean age at diagnosis 12.3±17 years), 87.8% had epilepsy, and 33.3% were drug-resistant (DRE). Treatments for DRE included Everolimus (26.8%, 17.7% ongoing), neurosurgery (14.6%), and vagus nerve stimulation or ketogenic diet (9.7%). Cognitive deficits were identified in 73.2%. Genetic studies were available for 17 patients: 64.7% were TSC2+, 5.9% TSC1+, and 35.3% were negative.

Regular follow-up in at least one specialty beyond neurology was provided to 80.5% of patients, mostly in one or two fields. The most common were nephrology (51.2%), dermatology (36.5%), and cardiology (24.4%). Despite adequate monitoring of neurological symptoms, gaps in recommended screenings for other organs and systems (Northrup et al., 2021; Direção-Geral da Saúde, 2019) were identified. Specifically, 31.8% of patients did not undergo abdominal/renal imaging, 46.4% missed renal function assessments, and 53.6% did not have an ECG as recommended. Among women, 61.9% had not undergone an abdominal CT. Patients without multidisciplinary follow-up exhibited significantly more gaps in screenings. Furthermore, annual evaluations by dermatology, ophthalmology, and dentistry, as recommended, were not conducted in 63.4%, 78%, and 90.2% of patients, respectively.

Conclusion: This cohort highlights the critical role of multidisciplinary protocols in optimizing care for adult TSC patients, particularly those with more severe disease and multisystemic manifestations. Improving coordination across specialties and addressing screening gaps could enhance outcomes and quality of life.

1728 | Challenges and gaps in epilepsy care in the Republic of Moldova

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Purpose: This study aims to assess the current state of epilepsy care in Moldova, identify key barriers to treatment, and propose strategies to improve epilepsy outcomes.

Method: Data from the National Bureau of Statistics and healthcare institutions were analyzed to evaluate epilepsy prevalence, access to specialized care, treatment availability, and referral pathways. A comparative analysis with international standards was performed in order to identify deficiencies in epilepsy care system.

Results: In 2023, epilepsy prevalence in Moldova was 29.6 per 10,000 people, with rural areas more affected (33.1 vs. 20.1 per 10,000 in urban settings). Specialized care access was limited, as 58.5% of patients received treatment from psychiatrists instead of neurologists or epileptologists. Shortages of EEG and MRI facilities contributed to delayed diagnoses, particularly in rural regions. Only 5.5 per 10,000 rural patients were referred to specialized epilepsy center, compared to 14.4 per 10,000 in urban areas ($p<0.05$), reflecting disparities in care. Treatment availability remains a major issue, with newer antiseizure medications either inaccessible or not covered by national insurance. The lack of newer drugs for drug-resistant epilepsy forces many patients to seek treatment abroad.

Conclusion: Epilepsy care in Moldova is hampered by specialist shortages, inadequate diagnostic tools, limited treatment options, and geographic disparities. The high cost of treatment and insufficient government prioritization exacerbate the situation. Strengthening national epilepsy care policies and improving access to specialized treatment are essential for better disease outcomes and reducing epilepsy burden.

1741 | Evaluating Clinician Engagement and Gain of Knowledge in Online Educational Modules on Epilepsy Self-Management

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Purpose: Epilepsy self-management (ESM) has been defined as the steps or behaviors people with epilepsy (PWE)

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use to manage their seizures, treatments, and the impact of epilepsy on their daily lives. Evidence-based ESM is a critical part of patient-centered care. This pilot study aims to quantify the impact of educational interventions targeted towards multidisciplinary health care professionals inclusive of epilepsy specialists and non-specialists, concerning knowledge of ESM and identifying appropriate ESM programs for PWE.

Method: Two interactive, on-demand educational eLearning modules were developed by the American Epilepsy Society (AES) in collaboration with the Dartmouth Health ESM team target to epilepsy specialists ("Empowering Epilepsy Patients: Self-Management Programs in Your Clinic") and non-specialists ("Epilepsy Self-Management: A Learning Module for Multilevel Primary and Behavioral Care Providers"). Recruitment of participants included distribution to AES membership and to non-specialist professional organizations and community-based epilepsy organizations that are representatives on a standing AES advisory committee. We evaluated knowledge gains as demonstrated by the differences in pre- and post-course assessments for a 13-month period (10/2023–11/2024).

Results: A significant increase in knowledge was observed for the non-specialist module (n=18; 8 states and 4 international locations) (baseline M=57, SD=19.2; post-module M=75, SD=20.0; p=.006). A trend towards improvement was observed in the specialist module (n=14; across 9 states) (baseline M=80, SD=13.1; post-module M=81, SD 21.8; p=.5). Module evaluations across both courses (n=55) shared 89% of respondents agreed/strongly agreed that the course helped them recognize the benefits of ESM for PWE; and 90% agreed or strongly agreed that they have more confidence in identifying appropriate EMS programs.

Conclusion: A population health-based approach to improving outcomes in epilepsy requires building a healthcare workforce with knowledge around the multiple aspects of epilepsy and inclusive of evidence-based ESM. Our study demonstrates that participants of targeted educational interventions experience increased knowledge about ESM.

1754 | Knowledge Gains in Epilepsy Specialist and Non-Specialist Clinicians Following Online Educational Modules

SL Strickland[1], AD Griffith[1], SJ Kaden[2], A Gramiak[1], BC Jobst[2,3], M Ball[1], EY Zhang[3], T McKenzie[2,3], ET Kiriakopoulos[2,3]

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Purpose: People with epilepsy (PWE) face significant healthcare disparities, including limited access to specialized care, challenges in managing comorbid mental and physical health conditions, socioeconomic barriers, and insufficient social support. In the United States, PWE seek care across clinical settings, with approximately 80% consulting general practitioners and 60% visiting neurologists or epileptologists annually. This study identifies the impact of online educational interventions targeting areas of insufficient knowledge and confidence in epilepsy care with both epilepsy specialist clinicians (ESC) and non-specialist clinicians (NSC).

Method: National needs assessment data gathered from ESC (n=167) and NSC (n=109) informed the development of six on-demand courses. The three ESC courses focused on advanced epilepsy treatment, genetic testing, and social determinants of health (SDOH). The three NSC courses addressed living with epilepsy; therapeutic considerations of anti-seizure medications, and nonpharmacologic treatments. We evaluated knowledge gains as demonstrated by the differences in pre- and post-course knowledge assessments between 10/2023–11/2024.

Results: Significant increases in knowledge were observed across courses. 425 participants from 39 states and 28 international locations completed one or more of six courses. For ESC, the greatest increase in test scores was observed in advances in treatment (baseline M=66, SD=15.2, post-module M=88, SD=10.2, p<.001); genetic testing (baseline M=60, SD=12.2, post-module M=77, SD=13.2, p<.001) and SDOH courses (baseline M=76, SD=13.5, post-module M=86, SD=9.9, p<.001) also improved knowledge. For NSC, the anti-seizure medication course showed the most improvement (baseline M=49, SD=14.3, post-module M=80, SD=12.9, p<.001), followed by living with epilepsy (baseline M=55, SD=13.1, post-module M=85, SD=11.3, p<.001) and nonpharmacological treatments (baseline M=54, SD=15.0, post-module M=78, SD=14.6, p<.001).

Conclusion: Healthcare providers — both ESC and NSC — caring for PWE desire easily accessible online educational resources to improve their knowledge of facets of epilepsy care. Our study demonstrates that participants of targeted educational interventions experienced increased knowledge, and provider satisfaction with the course materials.

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1799 | Advancements in Epilepsy Surgery in Chile: A Review of National Program Outcomes During and Post-Pandemic (2019-2024)

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Purpose: Chile, a developing country, has established a national epilepsy program aligned with IGAP policies, promoting timely diagnosis and treatment for epilepsy patients. One of the major areas of advancement has been epilepsy surgery. This study presents the key developments during the pandemic and the subsequent recovery period.

Method: A retrospective review was conducted of all epilepsy surgery cases performed in Chile's public health network from 2019 to 2024. The annual frequency, type of surgery, and postoperative outcomes were analyzed.

Results: We identified 403 patients who underwent epilepsy surgery, mainly in four hospitals that are national referral centers for this condition. Most surgeries were curative (294 surgeries, 73%). The number of surgeries increased by 1.69 times in the post-pandemic period (2022 to 2024) compared to 2019 to 2021. Approximately 75% of curative-intent surgeries achieved Engel I outcomes.

Conclusion: Despite the significant resource constraints in developing countries like ours, an organized national program that prioritizes the needs of epilepsy surgery can enhance access to this treatment for the population.

Epilepsy Infection and Inflammation

477 | The seizure outcomes of pediatric probable antibody-negative autoimmune encephalitis: a retrospective case series

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Purpose: Children with probable antibody-negative (Ab-negative) autoimmune encephalitis (AE) may present with seizures, and some develop epilepsy. As these seizures are potentially treatable with immunotherapy, we investigated the clinical manifestations, laboratory/imaging findings, and treatment outcomes of pediatric probable Ab-negative AE.

Method: A retrospective study was performed on probable Ab-negative AE patients who were hospitalized in the Department of Pediatrics and Adolescent Medicine, Queen Mary Hospital, Hong Kong, from July 2019 to August 2024. Probable Ab-negative AE were defined as: i) symptom onset of less than 3 months; ii) 2 or more of seizures, altered mental status, psychiatric symptoms, cognitive difficulties, or focal neurological deficits; iii) CSF pleocytosis and/or MRI features of encephalitis; iv) negative serum antibody tests (Ant-GAD, Anti MOG, Anti-NDMAR, Anti-CASPR2, Anti-AMPA1/2, Anti-LGI1, Anti-DPPX, Anti-GABAR B1/B2, anti-thyroglobulin, anti-thyroid peroxidase, Anti-TSHR, ANCA, ANA, Anti-Ro, Anti-La, Ant-Sm, Anti-RNP), and CSF antibody tests (Anti-NDMAR, Anti-CASPR2, Anti-AMPA1/2, Anti-LGI1, Anti-DPPX, Anti-GABAR B1/B2); v) excluded other alternative etiologies.

Results: 9 patients were identified as probable Ab-negative AE; 5 were females, and the median age of onset was 8.0 years (range 1.7 – 17.5 years). 5 patients (55%) presented with seizures. All patients showed improvement after receiving immunotherapy (intravenous immunoglobulin, high-dose corticosteroids, and/or plasma exchange). The median duration of follow-up was 27 months (range 6 – 66 months). 3 patients (33%) developed epilepsy as their seizures persisted more than 6 months after onset. When compared to our local case series on antibody-positive AE, 14 (93%) out of 15 pediatric patients with Anti-NMDAR encephalitis presented with seizures, yet only 1 patient (6%) developed epilepsy after a double-hit with HSV and anti-NMDAR encephalitis (Ho AC et al. Brain Dev. 2018 Jun;40(6):473-479).

Conclusion: Seizure is a common presentation in both pediatric Ab-positive and probable Ab-negative AE, and

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they could develop epilepsy. CSF and serum testing in research laboratories may identify unknown antibodies contributing to AE.

726 | Temporal Dynamics of TNF-α and IL-1β Levels in Relation to Epileptiform Activity in a 4-AP Rat Model of Epilepsy

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Purpose: This study investigates the acute time course of the proinflammatory cytokines TNF-α and IL-1β levels in cerebrospinal fluid (CSF) with a temporal resolution of one minute. As well as their relationship with epileptiform activity in a 4-aminopyridine (4-AP)-induced rat model of epilepsy.
Method: Male Wistar rats (250-300 gr) were implanted with superficial electrodes and a cannula to the right lateral ventricle. Following a 5–10-day post-surgical recovery period, time course experiments took place. Either 4-aminopyridine (75 mM for 10 min at 314 nL/min, ICV, n=6) or NaCl (NaCl 0.9% for 10 min at 314 nL/min, ICV, n=6) were administered and cerebrospinal fluid samples were collected simultaneously with EEG during 30 min (baseline), 10 min of drug administration and 6-h post-administration periods. Cytokine concentrations were determined by enhanced chemiluminescence, and epileptiform discharge trains were identified and quantified.
Results: Baseline cytokine levels were nearly undetectable. Following 4-AP administration, epileptiform discharge trains began at 11 min post-administration and persisted for 90 min. TNF-α exhibited a rapid increase peaking at 11 min (147±65 ng/mL) which preceded the onset of epileptiform activity; IL-1β followed with a peak at 14 min (220±24 ng/mL). TNF-α remained elevated for 10 minutes and IL-1β for 50 minutes (both $p<0.05$), then cytokine levels returned to baseline. Control animals displayed cytokine levels comparable to baseline across all timepoints.
Conclusion: Our findings demonstrate that the administration of 4-AP induces a rapid, transient elevation of TNF-α and IL-1β. Both exhibit distinct temporal dynamics, suggesting differential roles in the early neuroinflammatory response. These results underscore the potential contribution of cytokine release to the initiation and propagation of epileptiform activity and provide a foundation for investigating targeted interventions in acute neuroinflammation. This work was supported by funding from the University of Guadalajara (PROSNI 2022-2023 and Programa Fortalecimiento 2023-2024) and COECyTJAL (Fodecijal, 2022) for LMC.

731 | Pharmacological inhibition of the RNA demethylase FTO increases seizure resilience

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Purpose: Epileptogenesis is characterized by extensive epigenetic and gene dysregulation. N6-methyladenosine (m6A) is a recently described post-transcriptional RNA modification which alters mRNA fate has been linked to neurological diseases however its role in epilepsy is only beginning to emerge. We previously reported that m6A is extensively dysregulated in both experimental and human temporal lobe epilepsy. Hypothesis: Here we determine whether modulation of the m6A demethylase enzyme FTO impacts seizure dynamics and/or improves status epilepticus-induced pathology.
Method: FTO was inhibited using a specific FTO inhibitor (FB23-2) administered intracerebroventricularly (20 μM). To test the effect of the drug on seizure threshold and dynamics we used the pentylenetetrazol (PTZ) model (80 mg/kg) in male C57Bl/6 mice using an adapted Racine scale. The intra-amygdala kainic acid model was used to test the effect of FTO inhibition on seizure-induced hippocampal cell death and glial activation by quantifying Fluorojade B (degenerating neuronal marker) and IBA1 (microglia) and GFAP (astrocyte) immunoreactivity respectively. Animal group sizes were determined using power analysis and based on previous studies.
Results: FTO-treated animals displayed no difference in the latency to seizure onset compared to vehicle treated PTZ controls however they did display significantly fewer and less severe seizures. FjB staining revealed that FTO-inhibitor treated animals displayed significantly fewer degenerating neurons in area CA3 of the hippocampus compared to vehicle-treated controls. Similarly, FTO-inhibitor-treated mice had fewer GFAP and IBA1 positive cells compared to vehicle-treated controls throughout the hippocampus.
Conclusion: Our data shows that FTO inhibition reduces seizure severity and frequency in the PTZ model and protects against seizure-induced cell death in mice. These findings suggest that increasing m6A levels with an FTO inhibitor may confer cellular adaptation and protect from

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pathomechanisms of epileptogenesis triggered by status epilepticus.

732 | Cytokines expression in blood plasma from drug resistance epilepsy patients

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Purpose: Drug-resistant epilepsy (DRE) is a multifactorial and complex condition. It has been considered that activation of immune cells and increased cytokine production could contribute to DRE pathogenesis and progression. We aimed to investigate 27 plasma cytokines as possible biomarkers in DRE.
Method: This was a case-control study. We obtained plasma from 41 patients with DRE, 13 drug-controlled epilepsy patients (DCE), 11 drug-resistant post-operated patients (DRO), and 11 control (C) patients. We measured 27 cytokines profile in DRE: FGF, Eotaxin, G-CSF, GM-CSF, IFN-gamma, IL-1beta, IL-1ra, IL-2, IL-4, IL-5, IL-6, IL-7, IL-8, IL-9, IL-10, IL-12, IL-13, IL-15, IL-17A, IP-10, MCP-1, MIP-1alpha, MIP-1beta, PDGF-BB, RANTES, TNF-alpha, and VEGF by Bio-Plex Pro Human Cytokine 27-plex Assay.
Results: 27 cytokines (ng/ml) of the peripheral blood of the patients in the four groups were detected. We found the following cytokines were significantly decreased: IL-5, IL-7, IL-13, FGF, G-CSF, IFN, MIP-1alpha, RANTES, and TNF-alpha. Whereas, MIP1alpha and VEGF were significantly higher compared to the control patients. No significant differences were found in the other cytokines. The Kolmogorov-Smirnov test was applied to verify the normality of data distribution. We used ANOVA and post hoc Dunnet´s Test. Data were expressed as mean ±error standard.
Conclusion: Inflammatory cytokines have been implicated in epilepsy pathogenesis despite their complex association with multiple regulatory pathways. This cohort confirmed that patients with DRE have different levels of plasma inflammatory, anti-inflammatory, and proinflammatory markers independent of the underlying etiology. MIP1beta and VEGF were detected in blood plasma; this assessment may be easily achieved in clinical practice without the invasiveness of a spinal tap. It could be possible to propose as potential biomarkers of DRE. However, due to the complexity of neuroinflammation in epilepsy, further studies are warranted to confirm our findings.

852 | The role of early introduction of rituximab in an adult patient with FIRES: a pathway to improved outcomes

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Purpose: New-onset refractory status epilepticus (NORSE) is defined as a first episode of refractory status epilepticus without an active structural, toxic, or metabolic cause. Febrile infection-related epilepsy syndrome (FIRES) is a subtype of NORSE that occurs 24 hours to 2 weeks after a febrile illness. FIRES frequently presents as super-refractory status epilepticus and the prognosis is usually poor. Early treatment with first-line immunotherapy, antiseizure medications (ASM), and ketogenic diet is recommended. In refractory cases, evidence supports the early use of second-line immunosuppressants. The authors describe a case of early introduction of rituximab in an adult patients with FIRES.
Method: Case report. Data retrospectively collected.
Results: A 44-year-old woman, with no known history of seizures, was brought to the ER after a bilateral tonic-clonic seizure. She had a febrile illness one week earlier. She developed convulsive status epilepticus, requiring treatment with ASM and anesthetics. Investigations included: CSF with 7 mononuclear cells, negative viral PCR and cultures, negative autoimmune and neuronal antibody panels. Brain MRI revealed claustrum sign. Whole-body CT and transvaginal ultrasound were unremarkable. EEG showed focal extreme delta brushes. The diagnosis of idiopathic NORSE/FIRES prompted treatment with methylprednisolone, intravenous immunoglobulin, ketogenic diet and ASM titration; however, no improvement was seen. Rituximab was introduced on day 22, leading to the discontinuation of anesthetic treatment one week later. She remained in the ICU for 53 days and was discharged to a rehabilitation center about a month later,

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seizure-free. At six-month follow-up, she was autonomous with preserved cognition but experienced frequent seizures, which persisted despite treatment with three ASM. Following the introduction of cenobamate, seizure control was achieved.

Conclusion: Cenobamate has shown potential in the treatment of immune-mediated epilepsies such as this case. Despite a negative autoimmune panel, rituximab proved beneficial for both epilepsy control and cognition, suggesting mechanism potentially mediated by a yet unidentified pathogenic antibody.

973 | Zolpidem prevents cognitive impairment and reduces ictal activity in a rat model of $GABA_AR$ antibody-mediated encephalitis

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Purpose: $GABA_A$ receptor ($GABA_AR$) autoantibodies are found in autoimmune encephalitis (AE) presenting with frequent seizures and neuropsychiatric manifestations. Our previous study demonstrated intra-cerebroventricular infusion of patient-derived $GABA_AR$ monoclonal-antibodies (mAbs) into rodents induced a severe epileptic phenotype, similar to patient symptoms (Kreye et al., 2021). We studied the in-vivo treatment effect of zolpidem, a positive allosteric modulator at the $GABA_AR$.

Method: Patient-derived $GABA_AR$ mAbs targeting the α1 subunit were infused for 7 days in juvenile male Wistar rats (n=13) via osmotic-pumps (Alzet,USA) connected to cannula placed in both cerebral lateral ventricles. Rats were treated with subcutaneous saline (n=7; GABA-saline group) or zolpidem (n=6; 1 mg/kg; GABA-zolpidem group) 24 hours after start of antibody infusion. Wireless EEG transmitters (Opensource Instruments) were used to record EEG from a hippocampal CA3 depth electrode for 9 days. EEG was analyzed using automated ictal event detection (Neuroarchiver, OpenSource Instruments) and custom-code for powerband analysis. On day 2, 6 and 9 PSBB (post-seizure behavioral battery) and NOR (novel objection recognition) tests were performed as measures of hyperexcitability and cognitive function.

Results: The 9-day total ictal count was significantly decreased in the GABA-zolpidem treatment group (27±24 vs. 246±95;p=0.01) compared to GABA-saline. The overall EEG delta power was significantly increased in the GABA-saline group compared to the zolpidem-treated (7512±522 vs. 3437±104;p<0.0001). The GABA-zolpidem group did not show any hyperexcitability in behavioral testing as compared to the GABA-saline (4.8±2.1 vs. 13.7±2.2;p<0.05). GABA-saline group showed significantly impaired cognitive function as measured by NOR index on Day6 (0.54±0.03 vs. 0.83±0.06;p<0.001) and Day9 (0.56±0.04 vs. 0.81±0.02;p<0.01) compared to zolpidem-treated animals.

Conclusion: Overall, this preliminary study demonstrates that zolpidem reduces ictal activity in a $GABA_AR$-Ab AE animal model and prevents cognitive dysfunction. This proof-of-concept study highlights the potential use of receptor specific treatments in antibody mediated epileptic encephalopathy.

1083 | Epileptogenesis disrupts diurnal molecular dynamics of key extracellular matrix components in the mouse hippocampus

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Purpose: Epileptogenesis is the process of developing epilepsy, defined as the period between a precipitating injury and the onset of the first clinical seizure. Our previous research found that epileptogenesis triggered a molecular remapping of the transcriptome and disruption of circadian rhythms, identifying extracellular matrix (ECM) proteoglycans as a significantly enriched pathway. Here, I hypothesize that the disruption of circadian rhythms plays a key role in epileptogenesis by altering the ECM. Critically, this mechanism may happen via perineuronal net (PNN) disturbances.

Method: Male adult C57BL/6 mice (n=5/group) underwent intra-amygdala kainic acid-induced (i.a. KA) status epilepticus (SE) or vehicle (i.a. PBS) injection. From 24 h after SE, mice were euthanized and the ipsilateral hippocampi were collected at 6 time points (Zeitgeber times, ZT), every 4 h over 24 h, starting at 8 am, for RNA sequencing or qPCR. ECM-related genes were identified using the GO database, followed by differential gene expression (DGE) analysis across ZTs and validation via qPCR. Rhythmicity analysis was performed using the R software and the MetaCycle package.

Results: Based on the RNA sequencing dataset, I found 10 dysregulated genes associated with the ECM (7 upregulated and 3 downregulated) in epileptogenesis group mice comparison to control group. The qPCR analyses confirmed the changes in *Adamts1, Tlr2, Bcan*, and *Col4a1* were consistent with the DEG analysis. The rhythmicity

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analysis showed that *CD44, Col4a1, Tlr2, Bcan*, and *Hapln1* did not exhibit KA-induced circadian rhythmicity, whereas *Adamts1* and *Cspg4* gained rhythmicity, while *Tnc* lost its rhythmicity during epileptogenesis.

Conclusion: Our study revealed that epileptogenesis alters the relative expression of ECM genes at specific timepoints and disrupts the oscillatory profile of relevant ECM components. This sheds light on a previously unknown, novel mechanism of epilepsy pathogenesis. Further *in vivo* and *in vitro* studies are required to uncover the underlying molecular mechanisms of ECM dysregulation.

1107 | Relationship between febrile seizures in children and complete blood count inflammatory indices

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Purpose: To investigate the applicability of red blood cell distribution width (RDW), neutrophil-to-lymphocyte ratio (NLR), mean platelet volume (MPV) and mean platelet count ratio (MPR) in children with febrile seizures (FS).

Method: A sample of 50 children with FS and 50 age-matched and sex-matched controls (had a febrile illness without seizures) were sequentially enrolled in this work. Venous samples for complete blood count were obtained within 2h of FS, and then the values of RDW, NLR, MPV, and MPR were calculated, tabulated, and statistically analyzed in both groups.

Results: We noted that the raised NLR and MPR values were linked with the raised likelihood of FS. The optimum cutoff values of NLR and MPR for FS probability were 1.25 and 0.024, whereas the area under the curve was 0.664 and 0.822, successively. The mean values of MPV statistically significantly decreased in complex febrile seizures (CFS) compared to simple febrile seizures (SFS). However, there was no significant statistical difference between CFS and SFS regarding NLR and MPR mean values. Furthermore, we found no significant statistical difference regarding the mean values of RDW either between FS and controls or between CFS and SFS.

Conclusion: Increased NLR and MPR values in FS support the hypothesis of white cell subset implication in FS generation, and our study guaranteed that MPV is a simple, but limited, indicator in distinguishing CFS from SFS.

1237 | Electroencephalography features in children exhibiting neurological manifestations of SARS-CoV-2 infection

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Purpose: To describe the electroencephalography (EEG) features of children who presented with primary neurological manifestations (NM) caused by SARS-CoV-2 infection and to assess the relationship between COVID-19-related EEG features and NM.

Method: A total of 100 children aged 29 days - 3 years old were enrolled in this prospective study, divided into two groups according to the EEG characteristics: normal and abnormal EEG. Inclusion criteria included NM, acute SARS-CoV-2 period (positive PCR), and the absence of a prior history of neurological disorder; all patients had their EEG recorded. Additionally blood markers of inflammation, cerebrospinal fluid (CSF) test, and imaging findings were collected. Statistical analysis included descriptive statistics of continuous variables, and the proportion of categorical variables; p-value <0.05 was considered statistically significant.

Results: EEG showed epileptiform abnormalities in 20% of the studied patients. Background abnormalities (generalized/focal slow activity) (42.72%) were the most common EEG abnormality, followed by abnormal discharges: frontal intermittent rhythmic discharges (39.49%). The percentage of patients diagnosed with status epilepticus (SE) and encephalopathy/encephalitis was higher in the abnormal EEG group than in the normal EEG group ($p=0.015$; $p=0.003$), while the opposite was true for febrile seizures ($p=0.002$). Regarding age, a higher percentage ($p<0.001$) detected in the abnormal EEG group were less than 12 months and compared to the normal EEG group ($p=0.005$). Patients with abnormal EEG had a higher hospitalization rate, and longer stay ($p=0.002$, $p<0.001$). Concerning blood markers of inflammation, patients with abnormal EEG presented frequently pathological values ($p<0.05$). Five patients with NM underwent a lumbar puncture (LP): three exhibited normal CSF results, and two displayed elevated glucose and protein levels. Brain CT was performed on seven patients, with only two showing findings.

Conclusion: Our study reported that children with NM may exhibit abnormal EEG, with the most common pattern being background wave slowing or slow waves.

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1267 | Kappa Free Light Chain index as biomarker in autoimmune encephalitis presenting with seizures

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Purpose: The presence of high levels of free light chains (FLC) in cerebrospinal fluid reflect an imbalance in immunoglobulin synthesis, signaling inflammatory processes associated with various neurological conditions. Particularly, the relevance of an elevated kappa FLC (kFLC) index has been established in neuroinflammatory disorders such as multiple sclerosis. This study investigates the diagnostic and prognostic utility of the kFLC index in autoimmune encephalitis (AIE) with seizures.
Method: A single-center retrospective study was designed, and 94 patients were included. Patients were categorized into the following groups: seronegative AIE (AIE-, n=27), seropositive AIE (AIE+, n=23), Rasmussen's Encephalitis (RE, n=8), and two control groups - hydrocephalus (HC, n=13), and neurodegenerative diseases (Ndeg, n=23).
Results: Medians values of the kFLC index differed significantly across all five groups (P<0.001, Kruskal-Wallis test; CI of 95%). AIE+ and RE patients exhibited higher values (3.68 – IQR 2.53-2.83; and 11.11 – IQR 2.51-30.70, respectively) compared to both control groups (HC 1.68 – IQR 1.63-2.65; Ndeg 1.76 – IQR 1.57-2.22), and AIE- patients (1.92 – IQR 1.52-2.73). Such differences amongst groups persisted in patients with a negative oligoclonal bands profile (P<0.001, Kruskal-Wallis test; CI of 95%). Based on ROC curve analysis, a kFLC index cut-off of 2.48 demonstrated 86.1% specificity and 53.4% sensitivity for AIE diagnosis (AUC of 0.614). Upon evaluation of response to treatment with high-dose steroids, higher kFLC index values were associated with a trend toward greater seizure frequency reduction.
Conclusion: The kFLC index shows to be a promising biomarker for diagnosing and managing AIE with epileptic features. Its ability to differentiate encephalitic conditions and predict treatment response requires further validation in larger studies. Future research should refine disease-specific cut-offs and investigate kFLC production mechanisms in AIE.

1370 | Reading-induced seizures secondary to autoimmune encephalitis

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Purpose: To describe the first documented case of reading-induced seizures (RIS) as an acute symptomatic manifestation of autoimmune encephalitis (AE) mediated by anti-NMDA receptor antibodies.
Method: A 10-year-old boy with no prior medical history presented with self-limiting events triggered only by reading, characterized by visual symptoms, expressive aphasia, and cognitive impairment. Diagnostic workup included brain MRI, cerebrospinal fluid (CSF) analysis, and EEG studies. An autoimmune encephalitis panel tested positive for anti-NMDA receptor antibodies. Video-EEG monitoring during a reading activation maneuver confirmed RIS.
Results: RIS were identified as focal impaired awareness seizures. MRI findings were normal, and CSF analysis showed a type 2 oligoclonal band pattern. Following immunotherapy with intravenous immunoglobulin and methylprednisolone, the patient showed complete resolution of seizures. One month later, a follow-up EEG revealed only left temporal slowing, with no epileptiform activity induced by reading.
Conclusion: This case highlights the rare presentation of RIS as an acute symptomatic seizure secondary to AE. Immunotherapy effectively resolved seizures, confirming the autoimmune etiology. Early recognition and tailored treatment are crucial in managing AE-related seizures, as they respond poorly to antiepileptic drugs but favorably to immunotherapy.

1560 | Plasma Inflammatory Markers May Assist Early Diagnosis of Pharmacoresistance

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Purpose: Epilepsy is one of the commonest chronic diseases and incurs a high cost for patients and society.

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One third of patients present pharmacoresistance, the diagnosis of which is based on a failed attempt to use successive medicines, which takes time. A set of biomarkers present in peripheral blood would be useful in diagnosing pharmacoresistance.

Method: This was a cross-sectional observational study, approved by the local Ethics Committee under number CAAE 74772917.0.0000.5258. Participants were recruited from the Epilepsy outpatient clinic of the Gaffrée and Guinle University Hospital after informed consent, as follows: 10 patients with pharmacoresistant (PR) mesial temporal epilepsy, 10 patients with pharmacosensitive (PS) mesial temporal epilepsy, mean age 44.25 ±10.94 years diagnosed according to ILAE, free of comorbidities, as well as control group (C) integrating 20 healthy volunteers belonging to patients' families or the hospital staff aged 39.5 ±10.3 years. We aimed at quantifying inflammatory markers (interferon) IFN-gamma, (interleukin) IL-1beta, IL-2, IL-4, IL-5, IL-6, IL-8, IL-10, TNF-alpha and M-CSF in the plasma samples using a multiplex/Luminex immunoassay with the ProcartaPlex Human Cytokine Magnetic 10-plex panel, catalog LHC0001M (Thermo Fisher/Vienna, Austria). Biomarkers concentrations were expressed as average values and standard deviations for each group. Comparisons between groups were performed using the Mann-Whitney test, $p<0.05$.

Results: IL-6 values differentiated pharmacoresistant patients from controls and from pharmacosensitive patients: C: 2.88 ±0.21 pg/ml; PS: 2.97 ±0.31 pg/ml PR: 3.30 ±0.24 pg/ml; C x PS $p=0.44$; C x PR $p<0.0001$; PS x PR $p<0.0001$. IFN-gamma values differentiated controls from patients, but not pharmacoresistant from pharmacosensitive patients: C: 1.31 ±0.46; PS: 1.52 ±0.41; PR:1.78 ±0.79; C x PS $p=0.03$; C x PR $p=0.01$; PS x PR $p=0.99$. Other markers were not useful in discriminating the groups.

Conclusion: Early detection of epilepsy and pharmacoresistance may be assisted by combined plasma IL-6 and INF-gamma assays.

1584 | Exploring the long-term effects of COVID-19 in patients with epilepsy: a multicenter Italian observational study

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Purpose: COVID-19, caused by SARS-CoV-2, has resulted in a global pandemic since its emergence in December 2019. People with epilepsy (PwE) are at higher risk for severe outcomes from SARS-CoV-2 infection and may be more vulnerable to long-term neurological and psychiatric sequelae. This study aims to evaluate the long-term neurological and psychiatric effects of COVID-19 in PwE.

Method: This multicenter, retrospective cohort study reviewed the medical records of adults with epilepsy and confirmed SARS-CoV-2 infection (COVID+ group) from four Italian hospitals (March 2020–December 2021). A control group (COVID- group) consisted of age- and sex-matched patients without SARS-CoV-2. Demographics, epilepsy features, COVID-19 severity, and neurological/psychiatric outcomes were assessed at baseline, 6 months, and 12 months. Statistical analyses included regression and linear mixed model (LMM) to examine changes in outcomes over time.

Results: A total of 130 patients (39 COVID+ and 91 COVID-) were included. At baseline, no significant differences were observed between groups in demographics, epilepsy characteristics, or comorbidities. At 6 months, the COVID+ group exhibited increased seizure frequency ($p=0.03$) and higher rates of new psychiatric ($p<0.01$) and neurological symptoms ($p<0.01$), with specific treatment needed for neurological symptoms ($p=0.01$). At 12 months, new psychiatric and neurological disorders persisted in the COVID+ group ($p<0.01$), with a higher prevalence of treated neurological symptoms ($p<0.01$). LMM analysis revealed no significant difference in seizure frequency over time ($p=0.47$), but changes in focal-to-bilateral tonic-clonic seizures showed a time-dependent interaction ($p=0.025$).

Conclusion: This study highlights the persistent neurological and psychiatric effects of SARS-CoV-2 infection in PwE. While acute seizure frequency effects are transient, long-term symptoms, such as cognitive impairment, insomnia, and depression, persist, emphasizing the need for continuous monitoring and personalized care.

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1693 | Improving understanding of Febrile Infection Related Epilepsy Syndrome (FIRES) in children and young people

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Purpose: FIRES and New-Onset Refractory Status Epilepticus (NORSE) are super-refractory epilepsy syndromes that cause excessive morbidity and mortality in children and adults. No defined treatment pathway is universally effective, and no disease models have yet recapitulated the clinical features. Pro-inflammatory molecules are considered the main causative agents. Aims: 1. Undertake a pediatric surveillance study using the new accepted clinical definition of FIRES/NORSE to identify cases, current treatments, and outcomes in conjunction with British Paediatric Neurological Surveillance Unit (BPNSU). 2. Establish *in vitro* and *in vivo* models to facilitate testing of novel and existing drugs and understand disease pathogenesis using patient cerebrospinal fluid (CSF) samples.
Method: BPNSU is the major surveillance, research, and disease registry portal for UK pediatric neurologists and will provide a rapid-response online notification portal for retrospective and prospective FIRES cases. We will use our existing laboratory protocols to create *in vitro* and *in vivo* FIRES models and use them to assess effectiveness of current treatments.
Results: To date, 15 retrospective patients have been recruited: Six are female, median age is 8,5 yo [4-16]. 4/15 had a preceding upper respiratory tract infection,1 had confirmed HSV(+) viral swab,1 had MOG-Ab(+). Three had normal acute MRI, 6/15 had basal ganglia involvement. In follow-up MRIs, all developed parenchymal loss. All patients developed neurodisability and refractory epilepsy. In preliminary *in vivo* experiments, using CSF from 5 patients (from NORSE biorepository, Yale, USA), ictal activity was recorded in 1/5 rats during intracerebroventricular infusion. This was the only CSF sample obtained pre-treatment. Further analysis of EEG and behavioral tests is underway.
Conclusion: This research project aims to enhance understanding of FIRES/NORSE by collating clinical data on the natural history and establishing *in vivo* models with translational potential. Future work will concentrate on analyzing further patient clinical and paraclinical data (EEG, MRI) and developing *in vitro* models for drug testing.

Epilepsy Surgery

302 | Outcomes of Epilepsy Surgery over 25 Years: Insights from an Epilepsy Referral Center

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Purpose: Despite pharmacological advances, approximately one-third of patients have refractory epilepsy. High-quality studies about surgical outcomes with follow-up longer than 5 years are rare. Our goal was to analyze the factors influencing the outcomes of patients who underwent epilepsy surgery with a minimum follow-up period of 15 years.
Method: We designed a retrospective longitudinal study conducted at the Refractory Epilepsy Center of our center (Unidade Local de Saúde de Coimbra, Coimbra, Portugal). We included all patients who underwent resective and non resective epilepsy surgery between January 1997 and December 2009 and evaluated their postoperative outcomes. We used the Engel's classification to assess seizure freedom and applied correlation tests between the variables with a statistical significance level set at 0.05.
Results: We included a total of 160 patients with a minimum follow-up of 15 years. The mean age was 31.94 years (SD 12.76). More than half of the patients (57.5%) were considered seizure-free at 15 years, and most of the remaining patients (63,2%) had rare disabling seizures. The majority discontinued at least one ASM (65%). Temporal surgeries ($\chi^2(1) = 8.444$, $p < 0.05$), left-sided surgeries ($\chi^2(1) = 6.436$, $p = 0.04$), mesial sclerosis ($\chi^2(1) = 50.870$, $p = 0.024$), and the use of intraoperative ECOG ($\chi^2(1) = 23.235$, p-value < 0.001) were associated with better prognosis. No differences in outcome were found between the different temporal lobe surgeries (Fisher's exact test value $= 0.859$, $p = 0.659$).
Conclusion: Referrral to a refractory epilepsy center can lead to a multidisciplinary approach that results in seizure-free outcomes for most patients undergoing surgery. This conclusion is especially valid for left-temporal lobe epilepsies with the aid of intraoperative monitoring techniques.

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437 | Voxel-based morphometric analysis for perforating artery injury and postoperative motor deficit in peri-rolandic epilepsy

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Purpose: Surgery for peri-rolandic epilepsy could cause postoperative motor complications. We hypothesized that surgery-related ischemic subcortical damage, as well as eloquent cortical damage, affected postoperative motor deterioration.

Method: This retrospective, single-center study included 16 cases with peri-rolandic epilepsy who underwent resection surgery. Data on imaging studies, postoperative seizure outcomes, and the presence and duration of postoperative motor deterioration were investigated. In all cases, voxel data of the resected cortex and subcortical ischemic areas were analyzed with voxel-based morphometry. Postoperative motor deterioration in the orofacial, upper and lower limb, and their duration of "no", "transient", and "permanent" were assessed.

Results: During a mean follow-up period of 28 months, 10 cases (62.5%) achieved Engel class I. Fourteen cases (87.5%) experienced postoperative motor deterioration in the following regions (no/transient/permanent): orofacial (11/5/0), upper limb (9/5/2), and lower limb (9/3/4). Orofacial motor deterioration was associated with cortical resection of the inferior third of the peri-rolandic cortex. Cortical resection associated with permanent upper and/or lower limb motor deterioration was not significant in cases undergoing the resection of precentral gyrus ($p = 0.26$) but that of postcentral gyrus ($p < 0.01$). Ischemic subcortical damage to the corticospinal tract tended to be located more posteriorly in the cases with permanent upper and/or lower limb motor deterioration than that in the cases with no or transient upper and/or lower limb motor deterioration.

Conclusion: Both resected cortex and ischemic subcortical damage were responsible for postoperative motor deterioration in resection surgery for cases with peri-rolandic epilepsy. Cortical resection of postcentral gyrus might lead to injury of the vasculature critical for the descending motor pathway in the corticospinal tract, resulting in permanent motor deterioration. In contrast, cortical resection of precentral gyrus might not lead to permanent motor deterioration due to compensation by functional reserves.

468 | Stereo-EEG guided radiofrequency thermocoagulation for drug-resistant focal epilepsy: Initial results from 15 patients at a tertiary Epilepsy Center

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Purpose: Radiofrequency thermocoagulation (RFTC), as a minimally invasive treatment method, can serve as an alternative to resective epilepsy surgery for drug-resistant focal epilepsy. Here, we present our experiences and preliminary results following the implementation of this treatment method in our epilepsy center with a cohort of 15 patients. The aim was to analyze the treated population with regard to technical aspects, underlying pathologies, treatment-associated complications, and seizure outcomes.

Method: A retrospective observational study was conducted on 15 consecutive patients with pharmacoresistant focal epilepsy over 24 months. Dixi Medical depth electrodes (DE) were used for RFTC. Thermal ablation was performed by applying bipolar voltage between adjacent contacts. Seizure outcomes were evaluated using the ILAE classification. Patients were divided into two groups (seizure-free [SF] vs. non-seizure-free [non-SF]) for analysis.

Results: The study included 15 patients (8 male) with an average age of 31.8 years and a mean follow-up of 6.8 months (range: 1–20 months). A median of 9 DEs (4–16) were implanted per patient, and RFTC was performed on a median of 2.5 DEs (1–8), generating a median of 9.5 lesions (1–22). At the last follow-up, 7 patients (46.7%) were seizure-free. The responder rate, defined as ≥50% reduction in seizures, was 80%. Two patients (13%) with ILAE Class 3 outcomes after RFTC underwent lesionectomy at 9 and 6 months, respectively, resulting in postoperative seizure freedom. The proportion of patients with distinct localized lesions (FCD, PVNH, and HH) was significantly

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higher in the SF group compared to the non-SF group (100% vs. 37.5%; p=0.01). No complications or neurological deficits were observed in any patient following RFTC.
Conclusion: Our initial experiences suggest that SEEG-guided RFTC is a promising and safe treatment option for carefully selected patients. In particular, patients with localized, well-defined lesions appear to have a higher likelihood of achieving seizure freedom.

494 | Developing a New Endovascular Electroencephalogram Electrode (EP-01) for a Minimally Invasive Method for Seizure Localization: Clinical Feasibility Trial

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Purpose: A minimally invasive endovascular intracranial electrode (EP-01) has been developed, enabling the simultaneous recording from multiple locations within the brain. The purpose of this study was to evaluate the feasibility, technical performance, and safety of the EP-01 in short-term recordings.
Method: This was a single-center, prospective, exploratory trial conducted in five patients with drug-resistant focal epilepsy undergoing the Wada test. Up to 6 EP-01 electrodes, equipped with a platinum monopolar tip, was introduced into major venous sinuses using a microcatheter. Simultaneous recordings of eEEG and scalp electroencephalogram (EEG) were performed. The primary endpoint was the feasibility of eEEG signal acquisition. Secondary endpoints included a comparison of eEEG and scalp EEG signal sensitivity, technical success, and safety assessment.
Results: In all cases, multiple (an average of 4.5) EP01 electrodes were implanted in the brain and EEG simultaneously was recorded. The EP-01 electrode successfully captured interictal epileptiform discharges (IEDs) in all five patients, with a total of 157 IEDs recorded. The amplitude of IEDs were significantly higher in EP-01 (median 130.9 μV) compared to scalp EEG (median 0 μV), with 57.3% of IEDs undetectable by scalp EEG (p<0.001). Electrode tip displacement during neck rotation was minimal (median 3.45 mm). No adverse events, including hemorrhagic or thrombotic complications, occurred during or after the procedure, and all devices were safely removed.
Conclusion: The EP-01 can be implanted in the brain in multiple locations and simultaneously measure EEG. It has been demonstrated to detect epileptic discharges that could not be detected by scalp EEG. It showed superior sensitivity for detecting IEDs compared to scalp EEG. These results suggest that EP-01 may offer a less invasive alternative to traditional methods. Further multicenter studies are necessary to validate its clinical utility and long-term safety.

597 | Prognostic factors and outcomes in patients with TLE

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Purpose: To evaluate surgery outcomes in patients with drug-resistant structural temporal lobe epilepsy (PTLE).
Method: 244 patients with drug-resistant TLE were prospectively followed from surgeries (from 01.01.2014 till 31.12.2022). The results were evaluated 12-84 months after surgery according to the scale of results of surgical treatment by J. Engel (1993).
Results: Two hundred and twenty-four (124 females) and 120 males PTLE were followed. The mean age at surgery was 32.06 years, and the mean duration of the disease from the beginning to surgery - 17.96 years. The results after 12 months were assessed in 197 (80%) PTLE, 118 (60%) out of whom had Engel I: Engel Ia - 102 (52%), Engel Ib - 10 (5%), Engel Ic/Id - 6 (2%). The proportion of PTLE with Engel II was 15%: 7 (3%) had Engel IIa, 19 (10%) - Engel IIb, 4 (2%) - Engel IIc/IId. Eighteen (9%) PTLE had Engel IIIa, 4 PTLE (2%) - Engel IVa, 22 (11%) - Engel IVb, 5 PTLE (3%) - Engel IVc. After 60 months, 112 (45%) PTLE were analyzed, 62 (55%) of whom had Engel I, 23 (20.5%) - Engel II, 13 (12%) - Engel III, 14 (12.5%) - Engel IV. After 84 months, 56 (23%) PTLE were analyzed, 35 (62%) of whom had Engel I, 13 (23%) - Engel II, 6 (10%) - Engel III, and 2 (5%) - Engel IV. The prognostic factor for unsatisfactory results after 24 months was earlier age of seizure onset

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(mean age 10.6, median 7 years) (p=0.02). At 24 and 72 months, the risk for unfavorable outcome was the presence of bilateral-tonic-clonic seizures(BTCS) (p=0.02).
Conclusion: The rate of outcomes after temporal lobe epilepsy surgery confirms data from large epilepsy centers. Presence of BTCS and earlier age of seizure onset were prognostically unfavorable risk factors in our cohort.

599 | Neuropathological spectrum of drug-resistant TLE in Russian Federation

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Purpose: To analyze histopathologic data of patients with temporal lobe drug-resistant epilepsy (PTLE).
Method: We report the histopathological spectrum of 244 PTLE, operated by the neurosurgery team of Russian University of Medicine from 01.01.2014 to 31.12.2022 using the classification of I. Blumcke (2011).
Results: There were 244 PTLE (124 females) with the mean age 32.06 years and the mean duration of the disease 17.96 years. Unilateral temporal form of epilepsy was found in 184 patients (75%), and bilateral form in 60 patients (25%). MRI-positive form was diagnosed in 215 (88%) PTLE, while 29 (12%) had MRI-negative form. AMTLE was performed in 233 cases, tailored resection – in 10, SAH – in 1. Histopathological findings after surgery were: FCD Ia – 5 (2%) patients, FCD Ic– 25 (10%), FCD IIa – 34 (14%), FCD IIb –7 (3%), FCD IIIa – 139 (57%), FCD IIIb – 10 (4%), FCD IIIc – 5 (2%), FCD IIId – 10 (4%), LGG-8 (3%), HS-1 (<1%). In group of patients with FCD IIIa, the accompanying pathology with HS was: FCD Ia – in 7 patients (5%), FCD Ib – 2, FCD Ic – 26 (19%), FCD IIa – 50 (36%), FCD IIb – 54 (39%).The main type of histopathology detected in MRI negative form was FCD I (48%) of which 78% had FCD Ic type, in MRI positive form - FCD III (71%) and among this group 87% had FCD IIIa type (p<0.001).
Conclusion: The proportion of PTLE with FCD IIIa was significantly higher compared to other studies, that requires further research.

614 | Cortical hypometabolism partially reflects local atrophy in temporal lobe epilepsy and enhanced performance in predicting postoperative seizure outcomes with multiparametric MRI radiomics

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Purpose: To investigate regional distribution of grey matter atrophy and hypometabolism in temporal lobe epilepsy (TLE) and evaluate enhanced prediction value in postoperative seizure outcomes with multiparametric MRI radiomics.
Method: The T1-weighted MRI, ^{18}F-FDG-PET, and postoperative CT scans were retrospectively collected. Spatial patterns of decreased cortical thickness and standardized uptake value ratio were compared using age- and gender-adjusted W-score maps based on an open-access database of 20 healthy controls. Regional relationship of atrophy and hypometabolism were assessed using bivariate correlations and multiple regression analyses. Laterality of seizure onset, proportion of (extra-)temporal atrophy/hypometabolism, and resection volume were selected as predictors to predict seizure freedom 1 year after surgery using logistic regression and support vector machines algorithms.
Results: 101 patients with drug-resistant TLE and confirmed/suspected hippocampal sclerosis (48 left, LHS; 53 right, RHS) were enrolled, 72 of whom underwent standard anterior temporal lobectomy. Hypometabolism was significantly higher than local atrophy in the left temporal lobe and insula in TLE-LHS, while atrophy exceeded hypometabolism in bilateral occipital regions in TLE-RHS. Positive correlations between local atrophy and hypometabolism were more robust in ipsilateral temporal lobe in TLE-LHS. The full model performed best (area under the curve, AUC = 0.66-0.81) with all predictors input. Combined model trained with preoperative atrophy and hypometabolism features showed significantly higher AUC (0.6-0.76) and accuracy (0.57-0.72) than models using single-modality data alone.
Conclusion: Grey matter atrophy and hypometabolism exhibit distinct patterns in drug-resistant TLE that may

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characterize the epileptogenic network from different perspectives. Combined PET and structural pattern improve prediction of postoperative seizure freedom in TLE. Further prospective and external validation of our findings seems warranted to enable individualized prognosis and guide preoperative decision-making.

617 | Late seizure recurrence after anterior temporal lobectomy in patients with mesial temporal sclerosis: The prevalence and its prognostic factors

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Purpose: Late recurrence after initial seizure freedom in patients who underwent anterior temporal lobectomy (ATL) was not uncommon, but risk factors associated with such recurrence are unclear. Therefore, we investigated the proportion of late seizure recurrence (LSR) and its prognostic factors after ATL in patients with mesial temporal sclerosis (MTS).
Method: This retrospective study recruited 121 adults who underwent ATL in patients with MTS. We excluded if they had seizure recurrence in the first two years after surgery and if they had less than 3 years of post-surgical follow-up. Finally, 71 patients were included. Seizure freedom was defined as ILAE outcome class 1 and 2. LSR was defined as seizure recurrence after initial 2-year seizure freedom. The logistic regression with backward elimination was performed. Age, sex, and the potential variables exhibiting a p-value of <0.2 in the univariate analysis were entered in the initial model.
Results: The follow-up period after surgery ranged 36 to 181 months. Hippocampal sclerosis was confirmed pathologically in all patients. The rate of LSR was 25.4% (n=18) and its timing was mean 44.3±16.0 months after surgery. Univariate analyses showed that extratemporal interictal epileptiform discharges (IEDs) during video-EEG monitoring (p=0.048), ATL without invasive presurgical evaluation (p=0.053), and the presence of a history of febrile convulsion (p=0.192) had a p-value of <0.2 in association with LSR. The logistic regression showed that LSR tended to be independently predicted by the presence of extratemporal IEDs (odds ratio 7.714, p=0.088) and ATL without invasive presurgical evaluation (odds ratio 6.222, p=0.090).
Conclusion: About one fourth of MTS patient who had initial 2-year seizure freedom after ATL may have LSR. Patients with MTS who had extratemporal IEDs or ATL without invasive presurgical evaluation may be at high risk for LSR after ATL.

646 | Hippocampal transections for mesial temporal lobe epilepsy

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Purpose: The purpose of this study was to evaluate the effectiveness of multiple hippocampal transections (MHT) in the treatment of drug-resistant mesial temporal lobe epilepsy.
Method: Six patients underwent MHT at Burdenko Neurosurgery Center in 2018. The age of the patients varied from 18 to 43 years. All patients suffered from refractory epilepsy caused by focal lesions of the mesial temporal complex or temporal pole in dominant side. Postoperative pathology revealed neuronal-glial tumors in two patients, focal cortical dysplasia (FCD) of the temporal pole - in two patients, cavernous angioma - in one patient, and encephalocele of the preuncal area - in one patient.
Results: All patients underwent surgery satisfactorily. There were no postoperative complications except for homonymous superior quadrantanopia. This kind of visual field loss was noted in four cases out of six. During the follow-up period five patients out of six had Engel Class I outcome (83.3%). In one case, seizures developed after 1 month in a patient with FCD in the uncus (Engel IVA). After surgery, three out of six patients developed significant nominative aphasia. Two patients relative to the preoperative level demonstrated improvement in delayed verbal memory after MHT. Two patients showed a decrease level in delayed verbal memory. In preoperative period, visual memory was below the normal in one patient. Delayed visual memory in two cases impaired compared to the preoperative level.
Conclusion: MHT can be considered as an effective method of drug-resistant mesial temporal lobe epilepsy caused by tumors of the medial temporal complex. At the same time, MHT makes it possible to preserve memory in patients with structurally preserved hippocampus. However, MHT do not guarantee the preservation of memory after surgery.

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679 | Clinicopathological characteristics of patients surgically treated for focal epilepsy and generalized seizures

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Purpose: Patients with focal epilepsy may exhibit generalized seizures; however, the underlying mechanisms remain unclear. This study aimed to elucidate the clinicopathological characteristics of patients with focal epilepsy presenting with generalized seizures.
Method: We analyzed 233 patients who underwent curative epilepsy surgery at our institution and had confirmed pathological diagnoses. Clinical and pathological indicators were extracted and compared between the generalized and focal seizure groups using the Mann–Whitney U test and Fisher's exact test.
Results: Preoperative seizure types included 30 cases (13%) of generalized seizures and 203 cases of focal seizures. The mean age at surgery was 8.1 years in the generalized seizure group and 18.9 years in the focal seizure group, while the mean ages at onset were 2.7 years and 3.8 years, respectively, both of which were significantly lower in the generalized seizure group. The incidence of generalized seizures according to lesion location was as follows: frontal lobe, 19%; occipital lobe, 0%; parietal lobe, 11%; and temporal lobe, 7%, indicating a higher tendency in the frontal lobe. The incidence of generalized seizures according to the clinicopathological classification was as follows: focal cortical dysplasia (FCD) type I and mild malformation of cortical development with oligodendroglial hyperplasia (MOGHE), 45%; FCD type II, 0%; hippocampal sclerosis, 0%; tumors, 13%; and others, 14%. The incidence was significantly higher in FCD type I and MOGHE than in other clinicopathological groups, with SLC35A2 mutations identified in three cases.
Conclusion: Generalized seizures were associated with younger age of onset and a pathological diagnosis of MOGHE or FCD I. These findings suggest that immature neural circuits and pathological conditions contribute to the occurrence of generalized seizures in focal epilepsy. In young patients presenting with generalized seizures, careful evaluation to detect subtle MRI findings corresponding to FCD type I or MOGHE is crucial for selecting appropriate treatment strategies.

686 | Optimizing Seizure Outcomes with Vagus Nerve Stimulation: Analysis of Programming Parameters in Drug-Refractory Epilepsy

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Purpose: Vagus nerve stimulation (VNS) has emerged as a promising adjunctive therapy for drug-refractory epilepsy (DRE), particularly in patients with multifocal or generalized seizure onset. Advances in device programming have demonstrated potential for improved outcomes, necessitating a systematic evaluation of optimal stimulation parameters to enhance efficacy across varied clinical conditions. This study aims to evaluate the efficacy of VNS programming parameters in reducing seizure frequency in patients with DRE.
Method: This retrospective study analyzed clinical data from patients with DRE treated with VNS at a tertiary care center over a seven-year period. Implantations included devices with and without auto-stimulation capabilities. Programming parameters assessed included output current, frequency, pulse width, On/Off times, and duty cycles. Seizure frequency was documented through patient-reported histories and device use (auto-stimulation/magnet application). Treatment response was defined as a ≥50% reduction in seizure frequency (McHugh ≥2B).
Results: A total of 26 patients (19 male; mean epilepsy onset age: 5 years) were included, of whom three had prior resective or ablative surgeries. Lennox-Gastaut syndrome was present in 35% of cases. At 12 months post-implantation, 55% of patients achieved a favorable response. Poorer outcomes were observed in patients with epilepsy onset ≤1 year of age (33% vs. 64%) and those with perinatal hypoxic-ischemic imaging findings (46% vs. 71%), though these differences were not statistically significant. Patients with atonic seizures had positive outcomes in 50% of cases, compared to 67% in those without atonic seizures. Positive outcomes were associated with higher duty cycles (≥16%: 75% vs. 10%: 53%) and higher output currents (>1.5 mA: 62.5% vs. ≤1.5 mA: 33.3%).
Conclusion: VNS is an effective treatment modality for patients with DRE, offering a favorable seizure reduction in appropriately selected patients. Optimizing VNS programming parameters, particularly duty cycles and output currents, may enhance therapeutic outcomes over time.

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688 | Results of screening diagnosis of cognitive impairment in neurosurgical patients with drug-resistant epilepsy using MoCA

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Purpose: To determine the effect on cognitive functions of resective and destructive surgeries in drug-resistant epilepsy (DRE) in dynamic assessment using the Montreal Cognitive Assessment Scale (MoCA).
Method: The research was carried out within the state assignment of the Ministry of Health of the Russian Federation (№123021000127-7). Object of the study - neurosurgical patients with a verified diagnosis of focal DRE. The subject of the study - cognitive impairment using the MoCA. Cognitive functions were assessed preoperatively and from 6 months to 5 years after surgery. Methods of descriptive statistics were used. The study included data of 109 patients hospitalized in the Russian epileptology center with electrophysiology laboratory of the Polenov Neurosurgical Institute: 58 men and 51 women. The mean age in the cohort was 32.3±9.13 years. The distribution of the epileptic focus in the cohort was as follows: temporal – 86 (78.9%), frontal – 15 (13.8%), and frontotemporal – 8 (7.3%).
Results: Normal scores (≥26 points) on the MoCA scale were achieved by 21.1% of the cohort preoperatively and in 25.7% after surgical treatment. The mean score in the cohort was 23.3 points preoperatively and 23.2 points postoperatively. The study of the structure of cognitive deficit in patients with reduced MoCA scores showed a statistically significant predominance of deterioration in the cognitive domains 'Memory' and 'Speech', while the domains 'Attention' and 'Executive functions' showed less pronounced impairment. The most preserved functions were 'Naming', 'Orientation' and 'Abstraction'. The significant memory impairment observed is probably related to the localization of brain damage, namely the prevalence of temporal lobe epilepsy in the cohort.
Conclusion: The majority of patients with DRE admitted for surgical treatment to a neurosurgical hospital show significant cognitive decline, which is predominantly in the 'Memory' and 'Speech' domains. There is no evidence for significant cognitive decline after resective and destructive interventions.

695 | Surgical outcome in patients with mesial temporal lobe epilepsy and unilateral hippocampal sclerosis associated with calcified neurocysticercosis

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Purpose: Introduction: Calcified neurocysticercosis (cNCC) is considered a frequent etiology of epilepsy in developing countries. Objective: To evaluate if co-existent cNCC affects surgical outcomes in mesial temporal lobe epilepsy with unilateral HS (MTLE-HS).
Method: We analyzed 82 patients with MTLE-HS operated between 1997 and 2020 at the University of Campinas, Brazil. All patients had ictal semiology indicating MTLE and EEG findings concordant with the side of HS diagnosed with high-resolution 3T-MRI epilepsy protocol. We determined the presence of cNCC with CT scans or SWI MRIs. We analyzed the postoperative outcomes according to the Engel classification. We used Fisher´s exact test to analyze differences in proportions.
Results: The median age was 42.15 years, and 54.87% were women. Thirty-three (40.2%) had multiple cNCC lesions in addition to HS, and 49 (59.8%) did not. Fewer patients with cNCC reported a history of febrile seizures compared to those without cNCC (2 [6.1%] vs. 7 [14.3%]), but without statistical significance (p=0.3). The mean postoperative follow-up was 12.5 years for those with cNCC and 5.5 years for those without. Overall, 58/82 (70.72%) achieved Engel IA. At the last follow-up, 27/33 patients (81.8%) with cNCC were categorized as Engel IA compared to 31/49 (63.3%) in those without cNCC; however, this difference was not significant (p=0.086).
Conclusion: Our results confirm previous studies showing that in patients with refractory unilateral MTLE-HS with concordant ictal semiology and EEG findings, cNCC does not change the probability of excellent postoperative seizure control and does not contraindicate surgery. These findings also indicate that the real cause of ongoing seizures in these patients who became seizure-free after surgery was not the cNCC but the HS. Therefore, the finding of cNCC on CT or MRI does not necessarily indicate the etiology of epilepsy, and perhaps neurocysticercosis acts as a precipitating insult in some patients with MTLE-HS.

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707 | Epicenters of postoperative atrophies are associated with seizure outcomes in temporal lobe epilepsy

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Purpose: Anterior temporal lobectomy (ATL) is a recommended surgery for drug-resistant temporal lobe epilepsy (TLE), offering seizure freedom in about 70% of patients by disconnecting the presumed epileptogenic zone from the brain. However, the impact of this disconnection on the remaining brain and its role in seizure control or recurrence remains unclear. We use an individualized network diffusion model (NDM) to simulate postoperative atrophies in TLE patients, identifying epicenters of these changes and their relevance to outcomes.
Method: Forty-four TLE patients underwent T1 scans before and ~1 year after ATL, categorized into seizure free (SF: Engel I, L/R=14/15) and seizure recurrence (SR: Engel II-IV, L/R=7/8) groups. Regional volumes and postsurgical changes were estimated with FreeSurfer. An individualized resection mask was applied to generate preserved structural connectome (pSC) for each patient, used for NDM simulation of postoperative atrophy progression. Epicenter probability was determined by correlating simulated and actual atrophy patterns. The same analyses were performed on a replicate cohort of 38 TLE patients (SF: L/R=11/10; SR: L/R=8/9).
Results: Postoperative atrophy progression may originate from regions with epicenter probabilities greater than zero ($P<0.05$, FWE-corrected), primarily in the ipsilateral frontal lobe, extending to multiple contralateral regions. The SR group showed higher probabilities, especially in the bilateral frontal lobes and contralateral thalamus ($P<0.05$, FWE-corrected). For each patient, we compared their regional epicenter probabilities to null distributions generated from 1000 randomized pSC simulations. Regions exceeding the 95th percentile were designated as individual epicenters. We found a significant interaction effect ($F(1,42)=4.9$, $P=0.03$), whereas SR patients showed higher proportion of epicenters located within the areas disconnected by ATL, compared to SF patients. Similar results were also observed in the replication cohort ($F(1,35)=5.9$, $P=0.02$).
Conclusion: Postoperative atrophies in TLE patients after ATL may follow a specific progression trajectory. SR Patients tend to have more epicenters, primarily emerging from areas disconnected by resection.

720 | Usefulness of stereoelectroencephalography (SEEG) in patients with bitemporal epilepsy diagnosed by video electroencephalogram (VEEG): Experience in high complexity center in Argentina

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Purpose: To evaluate the usefulness of stereoelectroencephalography (SEEG) in determining the lateralization of the epileptogenic zone (EZ) in patients with epilepsy when lateralization cannot be established through noninvasive studies
Method: We conducted an observational study of adult patients with focal drug-resistant temporal lobe epilepsy (DR-TLE) and suspected bilateral epileptogenic zone (EZ), as indicated by surface recording (VEEG). All patients underwent bilateral intracerebral SEEG recordings targeting temporal and extratemporal areas at El Cruce Hospital, Buenos Aires Argentina, between 2014 and 2023. The study also included patients with lesional and non-lesional findings on neuroimaging or those with discrepancies between VEEG and MRI results.
Results: Twenty patients were included, 55% of whom were male, with a mean age of 25 years (range: 18-49 years). Eight patients (40%) had lesional findings, with hippocampal sclerosis being the most common pathology. SEEG demonstrated unilateral laterality of the EZ in 11 patients (55%): 7 (35%) on the left and 4 (20%) on the right. In 8 patients (40%), the ictal onset zone (IOZ) was bilateral, and in 1 patient (5%), the IOZ was extratemporal. Among the 11 cases with unilateral lateralization, 7 patients underwent surgical intervention, achieving Engel I to III/ILAE 1 to 4 outcomes after up to 10 years of follow-up. Four additional patients are currently on the surgical waiting list.
Conclusion: SEEG is a critical tool for identifying the ictal onset zone and determining the lateralization of the EZ in patients with drug-resistant bilateral TLE. This facilitates surgical decision-making and improves patient outcomes. In our study, SEEG established lateralization in 55% of cases, consistent with findings reported in the literature.

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722 | Morphometric analysis of oligodendroglial cells in the cerebral white matter of surgical specimens from epilepsy patients

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Purpose: The presence of oligodendrocytes exceeding 2,200/mm 2 in the cerebral white matter from epilepsy surgery is one of the histopathological features suggesting mild malformation of cortical development with oligodendroglial hyperplasia in epilepsy (MOGHE). However, our preliminary study revealed that non-specific reactive oligodendroglial accumulation or MOGHE-like oligodendrogliosis (OG) can also occur with the number of olig2-immunoreactive oligodendrocytes (olig2/mm2) over 2,200 in patients with temporal lobe epilepsy without hippocampal sclerosis (HS). We investigated olig2/mm 2 in various epileptogenic conditions to clarify the clinicopathological relevance and differences from genetically confirmed MOGHE.

Method: Archival paraffin blocks from 135 epilepsy surgical cases (median age: 29 years, range: 1-74), including HS (56 cases), FCD type I (7), mild malformation of cortical development (mMCD) (25), MOGHE with SLC35A2 mutation (2), vascular malformation (VM) (4), destructive lesion (16), and no lesion (25) were subjected to olig2 immunohistochemistry. The highest number of olig2/mm 2 in the cerebral white matter was counted on TIFF images using ImageJ software. The mean values of olig2/mm 2 were statistically compared by analysis of variance followed by Bonferroni test for multiple comparisons (p-value < 0.05).

Results: Significant differences in the mean olig2/mm 2 were observed between MOGHE (3,940±512) and HS (1,829±497), FCD type I (1,850±413), mMCD (1,981±719), VM (2,437±506), destructive lesion (1,807±556), and no lesion (2,215±670). MOGHE-like OG was identified in 41 cases (30%), with the mean olig2/mm2 (2,451±495) being significantly larger compared to HS, FCD type I, mMCD, and destructive lesion, but not different from VM, and smaller than MOGHE ($p < 0.05$).

Conclusion: MOGHE-like OG can be observed in association with various epileptogenic lesions. To clarify the clinicopathological relationship and differences between MOGHE and MOGHE-like OG, detailed morphometric analyses involving more cases and genetic testing will be necessary.

725 | Clinical Utilization of High Frequency Oscillation Rate and Network Properties in Epilepsy Surgical Decisions: A Pilot Study

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Purpose: Only 35-80% of patients achieve seizure freedom after epilepsy surgery despite best clinical practice. There is thus great interest in finding additional biomarkers of the epileptogenic zone (EZ). High frequency oscillations (HFO) are a promising biomarker, but it is unclear how they affect clinical decision-making during surgery planning.

Method: Deidentified EEG data from four past patients who underwent intracranial EEG implantation and surgical resection were presented to six epileptologists retrospectively. The following were presented incrementally, each step adding to the previous information: 1. Standard clinical presentation of EEG and imaging data, 2. HFO rates for each channel, 3. HFO network properties for each channel. Clinicians labeled which channels they would choose to resect (EZ) after each step. We used linear mixed models to compare the number of selected channels, resection volumes calculated from 3D channel coordinates, and confidence scores at different steps. Patient and clinician were considered random effect variables.

Results: We observed a significant increase in the average number of selected channels at steps 2 (3.1±1.8, $p < 0.01$) and 3 (4.6 ±1.8, $p < 0.001$) compared to step 1, and in the average resection volume at steps 2 (89%, $p < 0.01$) and 3 (133%, $p < 0.001$) compared to step 1. On average, epileptologists' confidence score increased by 0.5 ±0.5 (from step 1 to 3), but this change was not significant. Average Fleiss's Kappa (measure of agreement between clinicians) for step 1,2, and 3 was 0.65, 0.61, and 0.73, respectively. Clinicians overwhelmingly reported that they would like to have HFO data available to them during surgical decision-making.

Conclusion: Clinicians tend to increase potential resections when presented with HFO data. HFO rates along with network properties may point out epileptogenic areas that are otherwise unidentifiable by epileptologists and could be used to inform clinical decisions in the future.

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730 | Analyzing Barriers and Challenges in a Specialized Epilepsy Surgery Center in Chile: Working Towards Access and Opportunity

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Purpose: A proportion of patients with drug-resistant epilepsy (DRE) can achieve seizure freedom through epilepsy surgery (ES). Early identification of ES candidates enhances seizure control and improves post-surgical quality of life. This study aims to identify barriers to access in a national referral center within Chile's public health system and propose strategies to optimize the pathway to ES.
Method: We conducted a descriptive, observational, and retrospective study analyzing patient records at the Instituto de Neurocirugía Dr. Asenjo (INCA) from 2015 to 2024. The data reviewed included demographic characteristics, duration of presurgical evaluations, types of surgeries
Results: From 2015 to 2024, 206 ES procedures were performed at INCA: 109 in patients under 17 years old (mean age: 8.6; SD: 4.4) and 97 in adults over 18 years old (mean age: 34.1; SD: 12.7). These procedures included 131 resective and 75 palliative surgeries. The most common etiologies were malformations of cortical development, tumors, and hippocampal sclerosis. The average hospitalization duration was 12.3 days, including 3.6 days in the intensive care unit (ICU) and 8.8 days in intermediate care. The average waiting time between long-term EEG monitoring (LTM) and surgery was 383 days. Identified barriers included prolonged presurgical evaluation times, regional disparities in access to care, and resource limitations, both technical and human.
Conclusion: This study highlights the clinical and epidemiological features of patients with DRE who underwent ES in a specialized center in Chile. The findings underscore significant challenges within the public health system, including delays from diagnosis to surgery. These insights may inform strategies to streamline presurgical evaluations, address regional disparities, and improve patient outcomes

747 | Electrical, metabolic, and genetic cascades in focal epilepsy

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Purpose: Focal cortical dysplasia type II (FCDII) is a leading cause of drug-resistant—yet often surgically remediable—epilepsy. Despite their small size, these lesions can provoke widespread seizure activity. Using cortex-wide maps of electrical stimulation, glucose metabolism, and gene expression, we hypothesized that the potent epileptogenicity of FCDII stems from their strategic positions within brain networks susceptible to the excitatory cascades driving seizure onset and propagation.
Method: We studied 400 patients with FCDII-related focal epilepsy (median age=10 years) who underwent MRI and fluorodeoxyglucose (FDG)-PET. FCDII were manually segmented and mapped to a template brain surface (*fsaverage*). Using data from the F-TRACT project (an atlas of intracranial EEG from ~600 individuals; doi:10.1093/brain/awab362), we generated cortex-wide maps of evoked responses to electrical stimulation at FCDII sites. Linear mixed-effects models assessed spatial correlations between evoked response patterns and (i) control-normalized hypometabolism on patients' FDG-PET scans and (ii) regional expression of >15,000 genes from the Allen Human Brain Atlas (doi:10.1038/nature11405). Gene-set enrichment analyses identified biological processes linked to transcriptomic signatures mediating the evoked response patterns of FCDII sites.
Results: 284/400 (71%) underwent surgery; 86% were seizure-free 1 year post-operatively. Histopathology was IIA in 36% and IIB in 64%. FCDII predominated in frontal and insular cortex and were less common in temporal and occipital lobes. They were preferentially located in regions with higher probability of evoking responses elsewhere ($p<6.8e^{-16}$). Connected areas with higher response amplitude showed greater FDG-PET hypometabolism ($p<3.2e^{-75}$) and expression of genes implicated in vesicle-mediated transport, glutamatergic synaptic transmission, and vasculature development ($p<0.01$).

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Conclusion: FCDII occur in areas with heightened potential to cause widespread electrical and metabolic dysfunction, likely by exploiting the genetic architecture governing excitatory neurotransmission. These findings clarify the network and molecular mechanisms by which targeted therapies, such as ablation or resection, can achieve seizure freedom by addressing the localized origin of these diffuse effects.

749 | Emergent lesionectomy with Electrocorticography in focal status epilepticus: a case report

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Purpose: To describe a case report highlighting the benefit of electrocorticography (ECoG) during tumor resection in a patient with previously controlled seizures presenting with focal status epilepticus, resulting in subsequent seizure freedom.
Method: Details of the case were retrospectively reviewed and reported.
Results: Here we present a 38-year-old right-handed female with history of focal epilepsy related to a known right frontal lesion who presented with focal status epilepticus. This patient was well-controlled with carbamazepine for nearly 10 years. However, over the past three years she began experiencing occasional focal impaired awareness seizures consistent with giggling while fumbling with both hands. An adjustment to her antiseizure medication was attempted, but due to weight gain and the patient's concerns about developing additional side effects, carbamazepine was switched to levetiracetam. The patient initially responded well to levetiracetam monotherapy at a therapeutic dose for several weeks. Unfortunately, she began presenting focal impaired awareness seizures that rapidly escalated to focal status epilepticus. The scalp EEG pattern revealed diffuse fast activity, that evolved maximum over the right frontocentral head region, concordant with the region containing the lesion. This was refractory to multiple medication trials with levetiracetam, valproic acid, lacosamide, phenobarbital, and perampanel as well as transcranial direct current stimulation (tDCS). Emergent lesionectomy was planned with intraoperative ECoG. Pre-resection ECoG revealed multiple seizures characterized by paroxysmal fast activity. After initial resection, the post-ECoG revealed abundant multifocal polyspike and wave activity. This prompted further resection, that resulted in marked improvement of epileptiform activity on the final ECoG. The pathology from the resected tissue revealed Polymorphous Low-grade Neuroepithelial Tumor of the Young (PLNTY), CNS WHO grade 1. The patient has remained seizure free since (Engel class 1A).
Conclusion: Emergent lesionectomy can be beneficial in focal SE. ECoG can help tailor resections in these cases.

774 | Passive Auditory fMRI for Language Lateralization in Presurgical Evaluation of Temporal Lobe Epilepsy: A Retrospective Single-Center Study

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Purpose: Preoperative assessment of potential language impairment risk is crucial in temporal lobe epilepsy (TLE) surgery. Functional MRI (fMRI) is widely recognized as the most useful non-invasive method for determining language lateralization. However, standardized language fMRI protocols are lacking, and several challenges persist, especially for Japanese-speaking patients. Notably, commonly employed language tasks primarily involve active paradigms requiring explicit patient participation, which can be challenging for pediatric patients or those with cognitive impairments. This research employed task-based fMRI with passive narrative listening to assess speech comprehension and estimate language function in Japanese-speaking patients with medically refractory TLE.
Method: The study included 21 patients, six of whom had cognitive impairments. The participants were exposed to passive auditory stimuli comprising combinations of forward and silent playback, as well as forward and backward playback. Activation patterns were extracted using a block design, and lateralization indices were computed. The fMRI findings were then compared with the results of Wada test.
Results: The agreement rate between fMRI and Wada test results was 95.2%. Notably, meaningful responses were successfully elicited even from participants with cognitive impairments.
Conclusion: This passive fMRI paradigm offers a safe and accessible method for preoperative language evaluation, particularly beneficial for individuals who may struggle with active paradigms.

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779 | Mastery in Anatomy: The Most Effective Surgical Technique in Patients with Recurrent Temporal Lobe Epilepsy

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Purpose: Resective epilepsy surgery is the most efficacious therapeutic modality for patients with intractable focal epilepsies; however, surgical failures remain a challenge. Even with the availability of advanced surgical equipment and technology, achieving optimal surgical outcomes may be challenging without a thorough understanding of the temporal region's anatomy. This study aimed to evaluate the causes and risk factors for seizure recurrence, and reoperation outcomes for patients who had insufficient seizure control following surgery on mesial temporal lobe epilepsy.
Method: This is a retrospective single center study comprising clinical data, surgical failure causes, long-term seizure outcomes and postoperative complications of patients, who had undergone a second or further resective epilepsy surgery from 1990 to 2024.
Results: A total of 240 patients (127 females and 113 males) with medically refractory mesial temporal lobe epilepsy underwent resective epilepsy surgery. The overall seizure-free (Engel grade 1) rate at the last follow-up was 90.8% (218/240). Of the 240 patients, 12 (5%) underwent reoperation owing to seizure recurrence after the initial surgical treatment; however, of these 12 patients, 6 had incomplete data, and were excluded from this study. All the 6 patients (100%) improved and were completely seizure-free after reoperation (median follow-up 15 years, range 3–19 years). The patient age at reoperation ranged from 17 to 59 years. All patients, except one (patient 6), had "early" seizure recurrence within the first 6 months postoperatively. Following the last surgery, there were no serious complications.
Conclusion: Reoperation can considerably improve the operative outcome of the previous failed epilepsy surgeries. If the mastery of the mesial temporal lobe anatomy is not very high, it would be advisable to avoid performing surgery and instead refer patients to advanced centers. An experienced epilepsy team evaluation and more effective surgical technique would achieve seizure freedom for these patients as a last hope.

787 | Successful resective surgery for posttraumatic extratemporal epilepsy: Six case reports

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Purpose: Reports of surgery for posttraumatic epilepsy are relatively rare. We report six cases of posttraumatic epilepsy successfully treated with resective surgery
Method: Among 491 patients who underwent curative epilepsy surgery since 2014 April, patients who were diagnosed with posttraumatic epilepsy are included. Clinical characteristics, results of presurgical evaluation, surgical procedure, and postoperative seizure outcomes are examined
Results: Six patients were included. The causes of trauma were traffic accidents in three patients, and the accident during skiing in one. Other two patients were diagnosed with growing skull fractures. Latency between the trauma and the epilepsy onset ranged 1-6 (mean 3) years. In all six patients, MRI revealed scar lesions due to trauma (frontal 3, fronto-temporal one, and hemispheric 2). Semiology and EEG findings were concordant with the location of MRI lesion. No patients underwent intracranial EEG. The procedure performed was hemispherotomy in 2 patients, and lesionectomy in four. Three of four patients followed-up more than 2 years became completely seizure-free (Engel class-Ia). Another patient has only nocturnal seizures (class-IId). Two patients with less than 1-year follow-up are seizure-free. No patients had unexpected neurological deficits postoperatively
Conclusion: Non-invasive data were concordant with the location of MRI lesions, and all patients proceeded to surgery without intracranial EEG, and achieved favorable outcomes. The lesion-oriented strategy may be justified in cases with MRI abnormality.

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908 | Development of the Pretrained Resnet for surgical Outcome prediction using PET Hypometabolism and Excised Tissue (PROPHET): a deep learning tool to predict surgical outcome in patients undergoing epilepsy surgery

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Purpose: Despite rigorous selection processes, fewer than 70% patients who undergo epilepsy surgery become seizure free. Neuroimaging provides prognostic information about the chance of seizure freedom following epilepsy surgery, however in clinical practice, imaging cannot give an individualized prediction of risk. The aim of this study was to develop and validate a deep learning model to predict seizure freedom following epilepsy surgery.

Method: We conducted a retrospective, multi-center study of adults who underwent epilepsy surgery across 9 centers worldwide. We collected pre- and post-operative T1-weighted MRI, pre-operative FDG-PET and 12 month surgical outcome. Imaging data were pre-processed using SPM-12. A mask of the resection region was generated using EPIC-CHOP. The dataset was used to train (80%) and validate (20%) 3 convolutional neural network (CNN) models (early fusion, late fusion and Resnet10), to predict seizure freedom (Engel class 1) at 12 months following epilepsy surgery. We repeated this process using CNNs that had been pretrained using data (n=416) from the Alzheimer's Disease Neuroimaging Initiative database.

Results: 515 subjects were included, of whom 336 (65.2%) were seizure free at 12 months. 373 subjects (72.4%) underwent temporal epilepsy surgery, and 142 (27.6%) underwent extratemporal epilepsy surgery. Of the 3 CNN models, Resnet10 performed better (best AUC=0.68, accuracy=0.62, PPV=0.73, NPV=0.46) than late fusion (best AUC=0.63, accuracy=0.62, PPV=0.71, NPV=0.46) and early fusion (best AUC=0.62, accuracy=0.64, PPV=0.69, NPV=0.68). The Resnet10 model performance was improved with pretraining (best AUC=0.75, accuracy=0.69, PPV=0.83, NPV=0.54). Interrogation of the "learning curves" indicated that "early-stopping" was invoked for all models at early epochs, and were overfitting to the training set, whilst poorly fitting the validation set.

Conclusion: Our models demonstrated poor-fair classification of seizure freedom. Future work will attempt to prevent overfitting by introducing L2-regularisation, feature-extraction (hypometabolism estimation, asymmetry mapping), and introducing salient information including laterality and lobe of hypothesized epileptogenic zone.

937 | SEEG-guided thermocoagulation outcome in drug-resistant focal epilepsy

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Purpose: To evaluate the utility and safety of thermocoagulation in drug-resistant focal epilepsy

Method: We retrospectively reviewed the patient with drug-resistant focal epilepsy who performed stereoencephalography [SEEG] and treatment with thermocoagulation at the Neurological Institute of Thailand from January 2019 to December 2023. We evaluated the postoperative seizure outcome using the ILAE criteria and also analyzed the epilepsy history and postoperative adverse events.

Results: Seven patients were identified. We found that 42.83% [3/7] patients achieved seizure-free status after thermocoagulation, with the longest period being 42 months. One patient with a history of post-encephalitis became seizure-free after thermocoagulation at twelve electrodes in three ictal foci. The mean seizure-free period for all patients was 19.21 ±17.49 months, and the mean seizure-free period for the seizure-free group was 37.33 ±4.16 months. Three patients did not improve in their seizure outcome, leading to further resective surgery; two of these patients were seizure-free after the operation. All pathology in the resective group indicated FCD. The most common reason for performing thermocoagulation was the proximity of the epileptogenic zone to an eloquent area. One patient, whose epileptogenic lesion was located near the facial motor area, experienced right facial palsy, while another patient experienced speech problems that eventually improved. There were no serious adverse events related to SEEG-guided thermocoagulation.

Conclusion: Thermocoagulation in drug-resistant epilepsy was safe. It could also be used as a treatment option or as a step before resection surgery in people who had an epileptogenic zone close to an eloquent area or multiple foci.

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954 | The Correlation of Cortical Mapping and Neuroimaging Findings in Patients with Epilepsy

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Purpose: Accurate determination of the epileptogenic zone (EZ) is crucial for successful epilepsy surgery. Invasive EEG should be considered when EZ localization is uncertain, when there is discordance among noninvasive methods, or when EZ is near eloquent cortex. This study highlights the importance of correlating cortical mapping and functional magnetic resonance imaging (fMRI) with 18-fluorodeoxyglucose (FDG) positron emission tomography – computed tomography (PET-CT) findings in preoperative evaluation.
Method: We enrolled a retrospective study with patients who had undergone invasive video EEG monitorization. Subjects with invasive EEG, imaging data allowing to re-evaluation, eloquent cortex which was adjacent to the EZ as determined by cortical mapping were included. Cortical mapping done by direct electrical cortical stimulation (DECS) was compared with fMRI for motor functions, and the impact of FDG PET-CT findings on this comparison was evaluated.
Results: Three out of 69 patients who underwent invasive EEG met the criteria, and all of these patients had focal cortical dysplasia on their MRI scans. There was discordance between cortical mapping and fMRI in two cases and concordance in one. Discordant fMRI findings were considered false negatives, as the DCES is the gold standard. The study also examined how PET findings influenced the agreement between cortical mapping and fMRI, revealing hypometabolism in all patients' FDG PET-CT scans.
Conclusion: In patients with epilepsy who are candidates for surgery, when evaluating epileptogenic lesions near eloquent cortex, the possibility that metabolic changes in this area may affect fMRI findings should be considered, and compared with the gold standard method, DECS. It must be kept in mind that the false positive or false negative fMRI results that may arise due to these metabolic changes, which can be evaluated with PET-CT, could influence the decision-making process.

1000 | Psychosocial impact of pediatric epilepsy surgery - a single center experience

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Purpose: The psychosocial impact of childhood epilepsy is high for most families, and undergoing brain surgery is further stressful and may affect the overall mental health of caregivers. Understanding these factors better can support pre- and rehabilitation.
Method: Caregivers of children enrolled in the surgical programme at the Danish Epilepsy Centre during 2017-2023 were approached with an online questionnaire.
Results: Caregivers of 42 pediatric patients participated in the survey, of whom 38 children had undergone epilepsy surgery at least once. 63% of the children who had surgery were seizure-free, and three out of four were rated as having better functioning in daily life. Symptoms of psychopathology were present in 25% of caregivers, with a lower prevalence in caregivers of operated children and children awaiting surgery than in caregivers who did not know if their child would be offered surgery. In addition, caregivers of children with better daily functioning after surgery had a significantly lower prevalence of psychopathology than caregivers of children with the same or worse functioning. Caregiver perceived stress was significantly associated with child behavior problems and symptoms of child depression. There were no differences in symptoms of psychopathology between caregivers of children with and without seizures, and symptomatology was not related to the length of time the child had been in the surgical programme.
Conclusion: Results suggest that child psychosocial factors and daily functioning affect carers' mental health more than epilepsy-related factors. An awareness of this impact may guide health care professionals to provide better support to caregivers throughout the programme.

1004 | Awake craniotomy in pediatric epilepsy patients – feasibility and safety

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Purpose: Awake craniotomy (AC) with direct electrical cortical or subcortical stimulation is the gold standard for surgical treatment when the resection area is adjacent to structures considered being involved in cognitive or motor functions. While often well tolerated in adults, AC has been considered challenging in children due to necessity of intraoperative cooperation. We aimed to evaluate feasibility, safety and postoperative outcomes after AC in pediatric patients.
Method: We analyzed results of AC performed in 10 pediatric epilepsy patients between 2013 and 2023. Outcomes were defined as: 1) Feasibility – proportion of patients able to undergo AC; 2) Safety – occurrence of intraoperative complications or permanent deficits; 3) Seizure outcomes – based on Engel classification; 4) Cognitive and fine motor outcomes – based on neuropsychological evaluation.
Results: Median age at surgery was 14 years (range 11-18). Main histopathological findings were focal cortical dysplasia, gliosis and tumors. In all patients, the epileptic zone was localized near motor or language areas. All patients managed AC well, one experienced easily interrupted seizures and none needed conversion to general anesthesia. Neuropsychological assessment demonstrated better or unchanged postoperative; verbal IQ in 7 (70%), non-verbal IQ in 8 (80%); attention and executive functions inn all (100%); and fine motor skills in 8 (80%). Seizure freedom (Engel IA or B) was achieved in 6 (60%) patients. None reported the AC as traumatic.
Conclusion: Our data suggest that AC can be performed safely in pediatric patients evaluated as good candidates for the procedure, with low risk for intraoperative seizures or need for conversion to general anesthesia. This type of surgery requires a close cooperation with neuropsychologists monitoring cognitive and/or motor functions and the patient's well-being. Despite surgery in eloquent cortex, our results indicate that the risk of postoperative cognitive or fine motor deficits is small. In our sample, the seizure outcome is acceptable.

1021 | From Subdural Grids to Stereo-EEG. A single center experience of the first 100 Stereo EEG cases

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Purpose: The methodology of Stereo EEG requires a thorough understanding of the anatamo-electro-clinical correlations. While subdural grids and Stereo-EEG are both intracranial procedures to assist patients with drug resistant epilepsy, the insertion, understanding and interpretation of both procedures are very different. King Faisal Specialist Hospital & Research Centre in Riyadh, commenced their epilepsy surgery program using subdural grids in 1996. The first implantation of Stereo-EEG was in February 2023. Since that time, we have routinely implanted 2 cases per week, increasing to 4 cases per week with the expansion of our Epilepsy Monitoring Unit. Here the Epilepsy team present our experiences from three decades of subdural grids to recently moving to Stereo-EEG and implanting our first 100 cases.
Method: The first 100 Stereo EEG cases were reviewed from February 2023 to January 2025. We reviewed the total number of electrodes, the method to implant electrodes, the patients undergoing surgery, no surgery or neuromodulation and complication rates
Results: In total 1497 electrodes were implanted, on average 14.97 per case. The first six months of Stereo EEG were implanted using frame based technology, before moving to robotic assisted implantations. 75% of patients were candidates for surgical resection and radiofrequency thermocoagulation, 15% underwent neuromodulation (including VNS & DBS) and 10% did not undergo any procedure. 2 patients were completely seizure free after Stereo-EEG implantation. All Stereo EEG cases underwent routine high and low frequency cortical stimulation. Intermediate frequency stimulation has been introduced more recently for language and memory testing.
Conclusion: In keeping with international publications, Stereo-EEG is a safe procedure, with no major complications occurring. Team challenges that had to be overcome through education and exposure have included developing an understanding for the SEEG methodology, being comfortable with sampling of networks rather than contiguous areas (such as in subdural grids) and the interpretation of the StereoEEG waveforms.

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1047 | Phenotype and genotype of pediatric epileptic patients with focal cortical dysplasia type II and brain somatic mutation in *MTOR* gene

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Purpose: Brain somatic mutations in *MTOR* (MIM 607341) are the predominant cause (57%) of focal cortical dysplasia type II (FCDII). FCDII subtype b is the most frequently observed, and hemimegaencephaly (HME) is more rarely detected. The aim of this study is to determine the frequency of the *MTOR* gene somatic mutations in patients with FCDII, and to describe their phenotype-genotype.
Method: Thirty-one children with drug-resistant focal epilepsy with a postsurgical histological diagnosis of FCDII were included. Targeted gene sequencing (≥2000X read depth) was performed on matched blood-brain samples to search for low-allele frequency variants in mTOR pathway and FCD genes. Brain somatic mutations in mTOR pathway related genes were identified and further validated using long-PCR and NGS sequencing.
Results: Brain somatic mutations in *MTOR* gene were the most frequent mutation detected (5/31, 16%), with no associated germline mutation. Two recurrently-mutated regions were identified: c.5930C>A/(p.Thr1977Lysc) in two subjects, and c.6644C>T (p.Ser2215Phe) in others two; c.7498A>T (p.Ile2500Phe) was detected in another subject. The mean mosaic level was 3.9 % (range 2.5% to 7.57%). One c.5930C>A/p.Thr1977Lys variant was associated with HME. The others four patients presented FCDIIb in frontal location(1/4) fronto-basal (2/4) and peri-central sulcus (2/4). Motor focal seizures, mainly tonic (4/5), were described in all patients, A more extensive resection than the lesion visible on MRI was required to achieve Engel Ia in 3/5 patients.
Conclusion: *Variants in MTOR* gene are the most frequent somatic mutation in FCD type II and predominantly associated with subtype IIb. Some phenotype aspects are frequently common in these patients, such as frontal FCD location, focal motor tonic seizures, and a FCD extension larger than the MRI lesion.

1078 | Intermediate 3 Hz frequency stimulations to induce seizures during S-EEG in 3 pediatric patients

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Purpose: When necessary, S-EEG is the gold standard for defining the epileptogenic zone in drug-resistant focal epilepsies. Stimulations during S-EEG provide information about the excitability threshold and functionality of the stimulated cortex. The occurrence of a typical seizure during low-frequency 1 Hz stimulations is correlated with a good post-surgical prognosis. However, these stimulations sometimes remain negative. We report three pediatric patients in whom 3 Hz stimulations induced seizures.
Method: In the absence of seizures during 1 Hz stimulations, we performed 3 Hz stimulations in cortical areas showing interictal activity suspected to originate from a dysplastic cortex.
Results: Three patients, whose 1 Hz stimulations were ineffective, experienced seizures triggered by 3 Hz stimulations. The first patient is a 5-year-old boy with left frontal epilepsy and a poorly demarcated lesion in the left apical frontopolar region. PET imaging revealed hypometabolism in the left lateral frontopolar region. The second patient is an 8-year-old girl with right frontal epilepsy and a lesion compatible with a suspected dysplasia in the right anterior cingulate gyrus. The third patient, a 17-year-old boy carrying an *NPRL3* variant, presented with a dysplasia located on the right lateral temporo-occipital junction, along with an extensive hypometabolism in the lesion and in the two temporal lobes.
Conclusion: These three clinical cases highlight the effectiveness of 3 Hz stimulations during S-EEG exploration in generating patients' habitual seizures, underscoring the importance of exploring these intermediate frequencies in pediatric patients. The prognostic value of this approach remains to be demonstrated in this population following an analysis of surgical outcomes after taylored resections of these excitable cortical areas.

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1095 | A Tale of Two Modalities: Discordance between MRI and Histopathology in Epilepsy

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Purpose: Patients with MRI negative epilepsy may have significant findings on the postoperative histopathological report. Similarly, patients may have significant MRI findings but may not have significant findings on the postoperative histopathological report. Identifying the cause of discordance between these two modalities is important to optimize patient outcomes and ensure that the correct epileptogenic foci undergo surgical intervention.
Method: We reviewed the electronic medical records of 234 refractory epilepsy patients who underwent surgical intervention over 20 years from 2003 to 2023 and selected those with discordant MRI and histopathology findings.
Results: A total of 51 patients in our cohort had no significant findings on MRI out of which ten had a significant histopathological report. One of these patients underwent a right temporal lobectomy due to PET showing decreased metabolism in the mesial temporal lobe and histopathology demonstrated Focal Cortical Dysplasia (FCD) grade 1 in this case, he had ILAE grade 1 on one-year follow up. The nine remaining patients demonstrated non-lesional histopathology, with two patients having meningeal inflammation, one having arterial inflammation, one having an organizing infarct, one with an edematous cortical tissue, one having non-dysplastic gyral thickening, one with polymicrogyria, and two with features of dysgenesis. In contrast, 23 patients who had prior MRI findings demonstrated no remarkable findings on histopathology. Three of these patients had demonstrated T2 hyperintensity with features concerning for FCD, eight had shown evidence of Hippocampal Sclerosis (HS), two had demonstrated evidence of a tumor, two had shown vascular malformations, and eight had shown unspecified lesional changes in the area of interest. One patient demonstrated both HS and tumor on MRI.
Conclusion: Surgical epilepsy necessitates robust identification of epileptogenic foci with concordant modalities. Understanding the reason behind discordant findings in cases can be key to realizing limitations within investigational modalities and supplement shortcomings as needed.

1118 | Epileptic Seizures in Brain Metastases: Treatment Approaches and Disease Progression

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Purpose: Understanding the prevalence and impact of epileptic seizures in patients with brain metastases is crucial yet remains inadequately explored. This study aims to investigate the frequency of seizures in this cohort and assess the efficacy of treatments for brain metastases in mitigating seizure occurrence. Additionally, it seeks to evaluate the consistency of seizure evaluation practices at the initial diagnosis of brain metastases, aiming to enhance patient care and outcomes.
Method: In this retrospective monocentric cohort study, data was analyzed from 293 consecutive patients diagnosed with brain metastases from solid tumors. These patients underwent either tumor resection and/or radiation therapy between September 2015 and September 2023.
Results: More than half of all patients (median age 64 yrs, range 30-86, 49% male) harbored brain metastasis from lung cancer and 23% experienced at least one seizure. First line treatment was Levetiracetam in most patients as monotherapy (77%). Whole-brain radiation was applied in 139 patients, 200 received stereotactic radiosurgery for brain metastases, and 27 underwent hippocampal sparing radiation therapy. Resection of brain metastasis was done in 36% of the patients. Interestingly, there was no standardized evaluation of seizures in more than ¾ of the patients with brain metastasis in the initial diagnostic work up.
Conclusion: More than 20% of the patients in our retrospective monocentric study experienced at least one seizure. The origin of brain metastasis in our cohort was lung cancer in most cases. It can be assumed that the number of unreported cases is higher and that a systematic evaluation will further increase the incidence. Taken into account that epileptic seizures are a strong and additional negative factor for the overall quality of life of cancer patients, this data shows the urgent need of further research and the development of interventions to improve the outcome of these patients.

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1156 | Impact of initial seizure semiology on seizure free outcome after temporal lobe epilepsy surgery

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Purpose: Epilepsy surgery is an effective treatment for many patients with medically refractory epilepsy. Several factors have been studied in the past to predict postsurgical seizure free outcome. Seizure semiology has been studied with regard to its lateralizing or localizing value, but not yet to predict postsurgical seizure freedom. Here we investigate the impact of initial seizure semiology on postsurgical outcome in temporal lobe epilepsy (TLE).
Method: A retrospective analysis of 213 operated adults with TLE was conducted at a tertiary epilepsy center. Patients with less than 12 months follow-up (n=31), psychogenic non-epileptic seizures (n=2), prior epilepsy surgery (n=18), or high-grade tumors (n=2) were excluded. Patients underwent individualized temporal lobe resections of variable extent. The study analyzed the number of different initial seizure semiologies based on patient history and video-EEG monitoring.
Results: 160 patients were included (57% female; mean age 40 years, range 18-73). At last follow-up (mean 7.1 years, range 1-19) 78% (n=125) were seizure-free (Engel I).
The most frequent initial semiologies in TLE were: epigastric aura, psychic aura and dialeptic seizures. Initial automotor, aphasic or hypnopompic seizures and olfactory, acoustic or vegetative auras were rare.
A trend was observed, where patients with one or two initial semiologies achieved a good outcome in 80%, those with three or four semiologies in 75%, and those with five or more in only 60%.
Conclusion: Seizure semiology contributes relevant information to predict postsurgical seizure freedom. Multiple different initial seizure semiologies seem to reflect a more widespread, probably multifocal epileptogenic network, associated with a less favorable outcome. The limited sample size warrants larger studies to confirm these findings, and also to identify specific initial semiologies associated with unfavorable outcome.

1187 | Spectral factorization-based identification of seizure onset zone by the Janashia-Lagvilava algorithm – preliminary data

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Purpose: Accurate localization of the epileptic seizure onset zones (SOZ) and their propagations, which usually depends on the information obtained from EEGs, is crucial for successful epilepsy surgery. For this reason, the analysis of high-frequency (>80 Hz) oscillations by nonparametric Granger Causality (GC) has been reported to be successful. The GC method, which uses heavy mathematical computations, relies on Matrix Spectral Factorization (MSF). So far, the Wilson algorithm (WA) for MSF dominated in neuroscience applications, however, an alternative Janashia-Lagvilava algorithm (JLA) was also found to be effective and accurate for noisy data in two pilot study cases. The aim of the study was to test capacities of JLA on real data obtained from ictal EEG recordings in patient with drug-resistant epilepsy.
Method: Two regions (*X* and Y) of interest and a time epochs were isolated in eight people referred for presurgical evaluation. In order to apply GC estimation for these regions, cross power spectral density matrix *S(f)* was constructed in frequency domain by the multitaper method. The factorization $S(f)=H^*(f)EH^*(f)$, where *H(f)* is a transfer function and *E* is a noise covariances matrix, was performed by JLA. The GC estimations $I_{y\text{-}x}(f)$ and $I_{x\text{-}y}(f)$ were computed for high frequency values by the standard formula using *H(f)* and *E*. These estimations were used to confirm the visually suspected seizure onset region and its propagation.
Results: Instead of WA, JLA was successfully used for identification the precise localization of the SOZ and its propagation by GC based on real EEG data analyses, which was also confirmed by the effective outcome in four epilepsy surgery cases (Engel I).
Conclusion: The new JLA has the potential to substitute the WA which is widely used in computational neuroscience at present. Acknowledgments: The study is ongoing in a frame of the Shota Rustaveli National Science Foundation of Georgia (#FR-23-18000).

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1199 | Intraoperative ultrasonography (IoUS) in surgical epilepsy management; an underutilized cost effective tool

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Purpose: The outcome of epilepsy surgery depends on correct localization and complete resection of the epileptogenic lesion. Even with extensive pre-surgical workup, on-table identification of the epileptogenic lesion especially cortical dysplasia remains a challenge. Intraoperative Ultrasonography (IoUS) is readily available, inexpensive under-utilized and underreported in the field of epilepsy surgery. We describe the usefulness of IoUS in epilepsy surgery.

Method: We retrospectively collected thirty-five cases from 2016 to 2024 who had IoUS during surgery. Mean age was 18.2years(2-40years) with male: female ratio of 1.9. IoUS was performed by the Neurosurgeon before and after opening of dura, post resection for cavity exploration and for directing the insertion of depth-electrodes during electrocorticography (ECoG). Cases were analyzed for the ability of IoUS to identify the lesion and its margins, it's aid in placing intraoperative depth electrode to obtain 3D electrophysiological boundaries, identify residual lesion and analyze sonographic features and its correlate with MRI /histopathology. Engel's classification was used for seizure outcome.

Results: Epileptogenic lesion was identified by IoUS in 34/35 cases. Histopathology included FCD-2a(n=5), FCD-2b(n=13), tumor(n=4), Ganglioglioma(n=3), FCD-3(n=2), gliosis(n=2), Tuberous-sclerosis(n=1), Rasmussen-encephalitis(n=1), DNET(n=1), polymicrogyria(n=1), cysticercosis(n=2). Margins of the lesions were clearly seen in 26/35 cases. Thirteen patients had IoUS guided depth electrode placement adding useful 3D electrophysiological information. Four patients had SEEG and in these cases electrode trajectories were visible on IoUS helping identify the lesion and plan resection. One patient was post-thermocoagulation in whom the THC lesions visible on IoUS helped localize the lesion. Eight patients had extended resection based on IoUS. Post surgical outcome was Engel-I in 32 patients and Engel-II in 2patients and is not known for one patient.

Conclusion: In our series, IoUS was useful in identifying epileptogenic lesions and aided with 3D electrocorticographic information. Larger studies are required to understand the sonographic features of epileptogenic lesions to improve surgical outcomes.

1260 | Late onset epilepsy and epilepsy surgery: clinical characteristics and long-term postsurgical outcomes

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Purpose: Epilepsy surgery is rarely performed in patients with late onset (after 40 years of age) epilepsy. Observations on long-term postsurgical outcomes are, therefore, scarce. We aimed at evaluating histopathologic entities, and postsurgical seizure as well as neuropsychological outcomes in this patient group.

Method: Clinical records of patients undergoing epilepsy surgery between 2003 and 2022 in our tertiary center were screened, and patients with late onset epilepsy selected accordingly. Demographic variables, histopathologic findings, postsurgical seizure and neuropsychological outcomes (where available) were extracted and analyzed further.

Results: We identified 52 patients fulfilling the criteria. Median age at epilepsy onset was 46 years (quartiles: 43 and 49 years), median age at surgery 54.5 years (quartiles: 49.5 and 59 years). Forty-eight patients were operated on the temporal lobe, four patients on the frontal lobe and/or central region. Most frequent histopathologic findings were hippocampal sclerosis or astrogliosis (27 cases), cavernous or arteriovenous malformations (13 cases) and neuroglial tumors (9 cases). Focal cortical dysplasia was found in two cases only. Lymphocytic infiltrations were found coexistent with other hippocampal pathologies in four cases. At 12 months 63.4% of patients attained complete seizure freedom (Engel class IA), and altogether 68.3% displayed an excellent (Engel class I) outcome. At the longest follow-up (FU, median 39 months) 50% of patients were completely seizure free, and 70% had an Engel class I outcome. Cavernous malformations were associated with the best postsurgical outcomes (however, in many cases only shorter FUs were available). Patients with hippocampal pathologies (hippocampal sclerosis or astrogliosis) achieved complete seizure freedom in 50%, and an excellent long-term seizure outcome in 68.2% of cases. Neuropsychological tests indicated a remarkably significant postoperative worsening in certain cognitive domains in 12 patients.

Conclusion: Postsurgical seizure outcomes are favorable in patients with late onset epilepsy. The risk of worsening neuropsychological functions, however, is not negligible.

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1320 | De novo psychogenic non-epileptic seizures in neurosurgical patients with drug-resistant epilepsy

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Purpose: To investigate the prevalence and semiology of de novo PNES in neurosurgical patients with drug-resistant epilepsy (DRE).
Method: A single-center observational study was conducted as part of the State assignment No. 122011900530-8. All patients with a referral diagnosis of DRE from 2017 to 2023 were included, the PNES cohort of patients was allocated, divided into 2 groups in terms of surgical intervention. The clinical and demographic characteristics of de novo PNES were analyzed.
Results: We analyzed 369 patients with DRE and identified a cohort of 29 patients with PNES (8%). The incidence of de novo PNES was 2.8%.The mean age was 32.25±3.1 years, male: female = 1:1.25. The mean duration of epilepsy before surgical treatment was 27.4 years and the age at onset of epilepsy was 9.4 years. Temporal lobe epilepsy was observed in the majority of cases, left lateralization of the epileptic focus was two times more frequent, and the frequency of anxiety-related depressive disorders was 22.2%.The mean MoCa score was 21 and corresponded to the norm in 3 individuals. Social adjustment in the group of patients with de novo PNES was altered in 44%. Resection surgery was performed in eight cases and stereotactic radiofrequency ablation in one case. De novo PNES was diagnosed one year after surgery, and in the post-seizure period there was a change in seizure semiology with a predominance of focal non-motor seizures accompanied by sensory or autonomic disturbances, but without disturbances of consciousness.
Conclusion: The problem of psychogenic non-epileptic seizures is important in neurosurgical epileptology. Psychogenic non-epileptic seizures occur in every 12th patient in the epilepsy surgery department and the frequency of de novo psychogenic non-epileptic seizures was 2.8% in operated patients. Early diagnosis of psychogenic non-epileptic seizures in the postoperative phase (early or remote) during surgical treatment of epilepsy significantly reduces the efficiency of epilepsy surgery.

1351 | Long-term outcome of temporal lobe epilepsy surgery in adults - a single centre experience

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Purpose: We aimed to assess the correlation between long-term outcomes of surgical resections in temporal lobe with underlying pathology, extent of resection and risk factors for epilepsy.
Method: We performed a retrospective monocentric longitudinal study. We selected adult patients after temporal lobe epilepsy surgery investigated at the epilepsy surgery program of the Motol University Hospital between 1999 and 2024. Collected data included sex, age of onset and epilepsy duration, side and type of procedure. The full text of the neuropathology report was retrieved for all patients. Outcomes were traced and evaluated according to the Engel scale.
Results: Between 1999 and 2024, 291 temporal lobe procedures were performed. These included 273 primooperations and 18 reoperations. We were able to evaluate the five-years outcome in 199 patients. The most common procedure was anteromedial temporal lobe resection (AMTR, 149 patients), followed by lesionectomy (25), temporopolar resection (22), and corticectomy (3). The most common pathological finding was hippocampal sclerosis (HS, 54 patients), followed by focal cortical dysplasia (FCD) type 3A (50), tumors and cavernomas (35), FCD type 1 (24), gliosis (14), FCD type 2 (13), normal tissue (5) and non-diagnostic sample (2). At the five-years follow-up 88% of lesionectomy, 62% of AMTR and 63% of temporopolar resection patients were free from disabling seizures (Engel I). With respect to etiology, freedom from disabling seizures was observed in 83% tumors and cavernomas, in 70% of FCD type 2, in 67% HS, in 54 % FCD 3A, in 64% gliosis, in 57% normal tissue and in 54% FCD type 1 patients.
Conclusion: Long-term outcome of temporal lobe epilepsy surgery is influenced by etiology of epilepsy and 54 to 83% of patients are free from disabling seizures.

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1373 | Seizure outcomes in patients with burned-out hippocampus syndrome operated after noninvasive investigation

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Purpose: To evaluate the postoperative outcome of patients with BHS operated with noninvasive investigation.
Method: We retrospectively reviewed the medical records of patients with MTLE who underwent surgery at the Hospital das Clínicas of Unicamp from 2011 to 2024 with the following criteria: a) unilateral HS and b) surface electroencephalogram with onset of the majority of ictal activity in the contralateral side and few or none on the side of hippocampal atrophy
Results: Of all patients with MTLE-HS who underwent surgery at this time, 5 met the diagnostic criteria for BHS, four women and one man, with a mean age onset of epilepsy of 21.2 years, mean epilepsy duration of 26.4 years, and mean seizure frequency prior to surgery of 8.9 seizures per month. Four patients had right, and one had left HS. Ictal activity was discordant with hippocampal atrophy in 75% of the records. The unilateral interictal activity was discordant in 28.9% of the records, and bilateral interictal EEG activity was predominantly contralateral to the affected hippocampus in 50% of the cases. FDG-PET/SPECT scans showed hypometabolism or ictal hyperperfusion lateralizing to the side of the hippocampal sclerosis in all patients. The surgical decision was based on all noninvasive investigations. At the last postoperative follow-up (mean 5,8 years) 3 (60%) were classified as Engel Ia, one (20%) as Engel Ib, and one (20%) as Engel IIb.
Conclusion: In this series, all patients had excellent postoperative outcomes, becoming seizure-free or almost seizure-free. Some patients with MRI signs of unilateral hippocampal sclerosis have scalp ictal activity that is falsely lateralizing (BHS), which does not contraindicate surgical management when other studies are congruent. These patients may not need intracranial EEG recordings when semiology, neuropsychological investigation, and other noninvasive techniques for localizing the epileptogenic zone, such as FDG-PET and ictal SPECT, lateralize to the side of the HS.

1408 | Epilepsy surgery improves postoperative developmental rates in children with drug-resistant

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Purpose: Symptoms of epilepsy are seizures and brain dysfunction. In the developmental stage, progressive brain dysfunction due to the epileptic encephalopathic effect is larger than the adult stage. The primary purpose of surgical treatments is controlling seizures, but is it effective for this encephalopathic effect on brain functions? In this study, we reported that the postoperative developmental rate (DR, the value obtained by dividing the difference in developmental age before and after surgery by the follow-up period) in addition to the developmental quotient was used to evaluate the postoperative changes in behavioral and cognitive development.
Method: We analyzed 64 children who underwent resective surgery before the age of 6 years, and total DR and its subscales were calculated in each patient.
Results: Total DR of the first year after surgery (1st year) was significantly higher than that of the second-to-final years (2nd-final years). Verbal DR of the 1st year was also significantly higher than that of 2nd-final years. However, there was no difference in motor DR between the two periods.
Conclusion: Results of this study suggest that recovery of the brain function by epilepsy surgery appears as early as less than 1 year after surgery, especially language functions in pediatric patients with drug-resistant epilepsy. On the other hand, the developmental rate decreased after the second year. It was also considered that the pathological condition probably due to the etiology was large in addition to the encephalopathic effect of epilepsy itself (developmental and epileptic encephalopathy).

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1415 | The vigilance state influences the connectivity of the epileptogenic networks: an SEEG study allowing to better define the epileptogenic zone

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Purpose: How sleep modulates connectivity in epileptic patients has not been deeply investigated, despite evidence of his role in alter others interictal markers. This study aims to clarify how vigilances states influence the epileptogenic network dynamic, and its relations with thalamus during ictal/pre-ictal periods

Method: 36 patients with SEEG implantation presenting seizures during sleep (S) and wakefulness (W), characterized by low voltage fast activity pattern (LVFA) and thalamic electrode, were selected. EI was used to identify contacts belonging to 3 network zones (EZN, PZN, NIZ) and to assess S/W's epileptogenicity variations. Nonlinear correlation coefficient (h^2) evaluated functional connectivity (FC) differences, comparing S/W, within zones and between zones and the thalamus. FC analysis was performed across four periods: Background (BG, before seizure), Pre-LVFA, LVFA, and Post-LVFA, based on their relationship to rapid discharge

Results: No differences were found in the number of contacts across the different zones between S/W. During the preictal period, FC in the EZN between S/W is stable, while a significant increase in FC during S was detected during BG and Pre-LVFA in the PZN ($p<0.001$, $p=0.028$) and in the NIZ ($p<0.001$). Inter-zone analysis revealed increased FC during sleep in (BG and Pre-LVFA across all comparisons performed ($p<0.001$). An increase in FC during S was observed only in BG for EZN-thalamus and PZN-thalamus ($p=0.004$, $p=0.001$), and in BG and Pre-LVFA for NIZ-thalamus ($p<0.001$, $p<0.001$). No FC alterations between S/W were observed during ictal periods (LVFA and post-LVFA)

Conclusion: Sleep does not appear to modulate epileptogenicity and FC during ictal periods. However, EZN exhibits a distinct FC profile that remains unaffected by vigilance state, unlike PZN. This may be a new biomarker to differentiating it during pre-surgical evaluation (Epilepsia Lambert et alia 2018; Brain, Lagarde et alia 2018, Annals of Neurology, Hannan et alia 2023)

1424 | Translating abnormality metrics to clinical end-users with Z-Brains

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Purpose: Recent advances in surgical target definition using magnetic resonance imaging (MRI) have contributed to improving outcomes for individuals with drug-resistant seizures. Despite this progress, many algorithms for lateralizing hippocampal sclerosis (HS) and for detecting focal cortical dysplasia (FCD) remain underutilized in clinical settings. This gap is partially due to challenges in translating tools developed in research settings into formats compatible with surgical navigation software. We present Z-Brains, an open-source Python-based platform that addresses that performs abnormality detection on MRI data and generates outputs compatible with a range of modern surgical planning and neuronavigation software.

Method: Z-Brains leverages Brain Imaging Data Structure (BIDS) compatible data and utilizes a normative data generation based on either z-scoring or age-and sex-corrected w-scoring against a reference set of healthy controls. The control dataset currently includes 506 individuals scanned at 3T (252 F; mean age=30.2 +/- 9.7) aggregated across several multisite cohorts. To capture the pathological features of FCD and HS, the normative data includes neocortical and hippocampal surface maps of cortical thickness, intensity gradient, FLAIR intensity, and diffusion-derived microstructural metrics. The dataset also includes 30 participants (19 F; mean age=27.8 +/- 4.3) scanned at 7T.

Results: This large normative sample allows mapping measurements deviations. Based on significant surface deviation maps in individual patients with FCD and HS, Z-Brains can readily generate DICOM-formatted outputs in the native voxel space. These outputs are compliant with and successfully tested on different neurosurgical software platforms, including the ROSA ONE Brain neurosurgical robot, the Medtronic StealthStation, and Brainlab's Cranial software.

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Conclusion: Normative mapping of multicontrast MRI alterations may provide improved definition of prevalent surgical targets. By interfacing with common neurosurgical planning platforms, our approach is a key step towards bridging the gap between research and clinical practice.

1438 | [^{18}F]FDG PET/MRI in the presurgical evaluation of Pediatric Focal Epilepsies

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Purpose: To evaluate the role of hybrid [^{18}F]FDG PET/MR in the presurgical assessment of pediatric patients with focal epilepsy
Method: Multicentric retrospective study on pediatric patients (<18 years old) with inconclusive or negative prior MRI results, who underwent hybrid [^{18}F]FDG PET/MR for presurgical evaluation of focal epilepsy (2017–2021). Previous MRI data were re-evaluated (Phase 0), PET/MR MRI sequences independently reviewed (Phase 1), combined PET/MR findings assessed for grading and extension of metabolic abnormalities (Phase 2). Periprocedural EEG abnormalities were classified by type and frequency. Concordance with hypothesized epileptogenic zones (EZ) was analyzed, using SEEG and surgical outcomes where available (Phase 3).
Results: 79 patients (62% M), mean age 9.48 $\pm$ 5.42 years; epilepsy duration 4.39 $\pm$ 4.31 years; 83% drug-resistant. Initial MRI was inconclusive in 26/79 (32.9%) and negative in 53/79 (67.1%). Hypothesized EZs were primarily the frontal (40%) and temporal (26%) lobes, 48% on the left. Blinded 3T MRI identified lesions in 36/79 (46%), improving prior MRI accuracy in 10 patients. PET/MR detected metabolic abnormalities in 89% of cases (96% hypometabolism), without correlation with seizure frequency, EEG abnormalities and sedation. Subtle hypometabolism showed significant positive correlation with single sulcus/gyrus extension ($p<0.05$), revealing FCD in 67% of cases. PET+/MRI+ cases (46/79) showed greater concordance with electroclinical hypotheses and higher surgical rates than PET+/MRI- cases (24/79) (98%vs62%; 54%vs17%; $p<0.05$). Between the 29 operated patients, 76% achieved Engel IA (mean follow-up 2.1 years); FCD II was the most common diagnosis.
Conclusion: We demonstrated that [^{18}F]FDG PET/MR enhances detection accuracy, as already reported in literature (Guo et al, Eur Radiol 2021;31(9):6974-6982). Studies focused on presurgical evaluation of pediatric cohorts, including extratemporal epilepsies, are still lacking (Courtney et al, Neurology. 2024 14;102(9):e209304). Our study highlights the role of PET+/MRI+ and PET+/MRI- cases, demonstrating that hybrid [^{18}F]FDG PET/MR improves presurgical evaluations and guides treatment in pediatric epilepsy surgery.

1443 | Do classical semiology predict the post-operative outcome in patients with temporal lobe epilepsy?

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Purpose: TLE accounts for about 50-73% of cases being referred for epilepsy surgery. The objective is to find, whether the classical semiology in TLE has a role in predicting the post-operative outcome in patients with refractory epilepsy.
Method: We included 684 patients who underwent a detailed clinical evaluation, neuropsychological assessment, 1.5T/3T MRI, VEEG monitoring, followed by a standard anterior temporal lobectomy from a single tertiary care epilepsy Centre. They were followed up at 3 months,12

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months and yearly with EEG. The outcome was classified in to good, if they don't have either seizure or aura irrespective of the drugs and as bad, even if single seizure occurred postoperatively

Results: Of the 684 patients, 93.7% had behavioral arrest; 88.6% had automatisms,86.7% had amnesia for the events,74.6% had auras and 63.6% had antecedents. All the classical semiology features were present in 37.7% of the whole cohort. 47.8% of the study population had good outcomes till the last follow-up. The mean follow-up period was 75.6 months with a maximum follow-up of 14 years. Cases with antecedents had a lesser probability of seizures at last follow-up (p=0.009). Febrile seizures as a separate variable were found protective (p=0.021) and encephalitis was a risk factor(p=0.026). Behavioral arrest was associated with poor seizure outcomes following surgery(p=0.006). No significant association with outcome was found for auras, automatisms, or amnesia. When the patients with varying combinations of semiological features were compared, we found no significant difference between the seizure outcome in any of the groups

Conclusion: The presence of antecedents, especially febrile seizures was associated with favorable surgical outcomes. The mere presence of auras, automatisms or amnesia does not affect outcome after TLE surgery. Arrest was associated with a worse outcome. Presence or absence of any combination of classical semiological features had no significant bearing on surgical outcome after anterior temporal lobectomy

1465 | How epilepsy etiology, focal cortical dysplasia *versus* a low-grade epilepsy associated tumor, impacts neurocognitive and behavioral outcome after early frontal lobe surgery

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Purpose: Frontal lobe epilepsy accounts for 1/3 of pediatric epilepsy surgery spectrum. Focal cortical dysplasia (FCD) or low-grade epilepsy associated tumor (LEAT) are the main etiologies and are often associated with neurodevelopmental difficulties. We investigate the cognitive and behavioral outcome of 37 patients with FCD (n=25) or LEAT (n=12) who underwent frontal lobe resection (FLR) with excellent or good seizure outcome (Engel 1 or 2).

Method: Cognitive outcomes included the WISC, tests of executive function and Achenbach's Child Behaviour Inventory. Clinical characteristics for FCD or LEAT were as follows (mean in years ± SD): age at seizure onset (2.5±2.4 and 5.4±3.3, p=.001), age at surgery (6.9±3.6 and 8.7±3.4, ns), preoperative delay (4.4±2.5 and 2.94±1.1, p=.03), postoperative follow-up (6±3 and 3.2±1.7, p=.0008), age at assessment (13±2.9 and 11.9±3.3, ns), Engel 1 (76% and 92%, ns).

Results: Children with FCD scored lower than children with LEAT in terms of IQ (ITQ: 85±13.7 vs 106±16.9, p= .0006), verbal comprehension (95.6± 17.7 vs 108.7±20.4, p= .03) and non-verbal index (82.8±13.3 vs 105±17.5, p = .0005), working memory (85.6 ±16.7 vs 104.6 ±8.5, p= .0001) and information processing speed (86.6±10.9 vs 99.3±14.9; p= .007). Children with FCD were slower at TMT B (1.5±2.6 vs .07±.4, p = .02) and needed more trials to identify the first category on the WCST (.58±.25 vs .19±.3, p = .02). On the Achenbach questionnaire, they had more social problems (p= .008) and more externalized behavioral problems (p= .03).

Conclusion: Our study is the first to show an effect of etiology on neuropsychological and behavioral follow-up and highlights the need for long-term cognitive follow-up in this population.

1530 | Stereotactic radiofrequency ablation for treatment of epilepsy

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Purpose: ver the last decade, the role of minimally invasive neurosurgical interventions in the treatment of medication-resistant epilepsy has significantly increased. Currently, techniques such as gamma knife, MRI–guided laser interstitial thermal therapy, and focused ultrasound ablation are widely utilized alongside the classic radiofrequency (RF) lesioning technology. Moreover, RF ablations are favored in many neurosurgical units due to their relative straightforwardness and financial accessibility, which is particularly relevant for the countries with low or middle incomes. The purpose of the report is to demonstrate our experience with the stereotactic RF ablation for the treatment of epilepsy.

Method: t the Romodanov Neurosurgery Institute, 30 patients with drug-resistant epilepsy underwent stereotactic RF ablation. There were 13 (43%) adult and 17 (57%) children. Among them, 21 patients underwent stereotactic callosotomy, 5 patients underwent stereotactic hippocampotomy, 2 patients received RF lesioning of hypothalamic hamartoma, and 2 patients underwent bilateral RF

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ablation of the anterior thalamic nuclei. All patients were evaluated one year after the operation, and 29 (97%) four years postoperatively.

Results: Bilateral or multiple epileptogenic discharges within one hemisphere were detected in 25 (83%) patients, focuses discharges within one hemisphere observed in rest 5 (17%). MRI-negative epilepsy with bilateral discharges – in 11 (37%) patients. After surgery 6 (20%) patients became seizures free (Engel Class IA), in 15 (50%) cases seizures frequency reduced over 75% (Engel Class II-III), and in rest 9 (30%) seizures frequency did not reduce significantly. After callosotomy drop-attacks stopped in 12 out of 16 (75%) patients who had them before. There were no postoperative complications and mortality.

Conclusion: Despite the limited sample size of our study and the variability in epilepsy types and surgical interventions, our results suggest that stereotactic ablations remain a safe and palliative treatment option for medication-resistant epilepsy, particularly in cases where resective surgery is not feasible

1550 | Surgical outcomes in 90 patients with drug-resistant temporal lobe epilepsy secondary to cerebral cavernous malformations: case series

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Purpose: Cerebral Cavernous Malformations (CCMs) are known for their high epileptogenic potential. These are low-flow sinusoidal malformations with relatively low risk of clinically significant bleeding (0.46/100.000 persons/year), but high risk of developing epilepsy (up to 70% of symptomatic CCMs) and drug-resistant epilepsy (40%). We present the largest case series of CCM-related drug-resistant temporal lobe epilepsy (CRETLE) to our knowledge and discuss our diagnostic and treatment protocol.

Method: We analyzed a case series of patients with CRETLE who underwent surgical treatment at the International Center for Epilepsy Surgery in Mexico City from 1997 to 2022 with a minimum follow-up of 12 months. Preoperative evaluation included detailed semiological classification, high resolution magnetic resonance imaging, and video-electroencephalography. All surgeries were performed by a single surgeon. Intraoperative electrocorticography was consistently utilized to define the irritative zone and guide tailored resections.

Results: A total of 90 patients met the inclusion criteria, of whom 52% were male. The median age at epilepsy diagnosis was 32 years, with a mean time to surgery of 4.2 years and a median postoperative follow-up of 28 months. The most common procedure was tailored corticectomy in 71,1%, followed by anteromesial lobectomy (16.6%), selective amygdalo-hippocampectomy (10%) and lesionectomy alone (2,2%). Additional to the CCM, histopathology found 6 hippocampal sclerosis and 5 cortical dysplasias. Transient neurological deficits, primarily in verbal memory, were observed in 6 patients, but all recovered fully while maintaining or improving preoperative functionality. Engel I outcomes were achieved in 87% of patients and Engel II in 13%.

Conclusion: Surgical treatment for CRETLE is both safe and highly effective, aligning with outcomes reported in the international literature. Given the excellent surgical outcomes, we recommend considering early surgical evaluation for CRETLE patients, even prior to meeting drug-resistance criteria.

1580 | Trends in epilepsy surgery – single center experience over 20 years

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Purpose: Epilepsy surgery is an effective treatment option for patients with medically refractory epilepsy. The landscape of epilepsy surgery is constantly changing, but a lot of data is still based on patients and procedures, that have become rare today. Here we report changes over the past 20 years in patients, diagnoses, methods and results from one tertiary epilepsy center.

Method: Data from 402 patients, operated between 2003 and 2023 was analyzed, with a mean follow up of 6.6 years. Demographic, clinical, neuroimaging, neurophysiology, surgical and histological data was taken into account and changes over time were analyzed. We report changes from the first 5 years of the observation period to the last 5 years.

Results: The time from epilepsy onset to surgery shortened significantly, from 19.6 to 11.4 years. The utilization of PET examinations increased from 42% to 73%, the use of sEEG evaluation before surgery increased from 8% to 39%. Multilobar resections increased from 8% to 21%. The incidence of mild malformations of cortical development in surgical specimen increased from 0 to 17%. Engel class I outcome increased from 52% to 72%.

Conclusion: Significant changes could be seen in the last 20 years of epilepsy surgery. Patients are referred to surgery earlier, but the patient population has become more challenging. An increasing use of complementary diagnostic methods such as PET and SPECT imaging, as

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well as invasive EEG recordings and individually tailored surgical strategies are necessary for successful treatment of patients with more widespread epileptogenic networks. However, with a comprehensive presurgical evaluation, good outcome can also be achieved in these complex patients.

1599 | Relevance of the Wada Test in the Pre-Surgical Evaluation of Patients with Temporal Epilepsy Due to Hippocampal Sclerosis

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Purpose: Introduction: Wada test (WT) is used in the pre-surgical evaluation of patients with drug-resistant epilepsy. No reliable alternative to WT has emerged so far. In mesial temporal lobe epilepsy with hippocampal sclerosis (MTLE-HS) it prevents the risk of amnesic syndromes when neuropsychological assessment (NPA) suggests bilateral or contralateral memory deficits relative to the HS. A high concordance between NPA and the invasive WT could make the latter unnecessary. Purpose: To assess the concordance between NPA and WT in patients with MTLE-HS and determine the proportion of these patients who proceeded to surgery.
Method: Patients who underwent WT in the epilepsy surgery program of a tertiary center were reviewed, and those diagnosed with MTLE-HS were selected. NPA results related to visual and verbal memory deficits were considered. WT followed the same protocol and was conducted using amobarbital or, when unavailable, propofol.
Results: A total of 46 WTs were performed, 36 (78.3%) in patients with MTLE-HS. The median age was 44 years (IQR 32–50.75). The HS was on the right in 44.4% of patients, on the left in 52.8%, and bilaterally in 2.8%. NPA showed visual memory deficits in 25% of patients, verbal memory deficits in 30.6%, both in 36.1%, and no deficits in 8.3%. WT validated surgery in 80% of MTLE-HS cases with right-sided sclerosis and verbal memory dysfunction, bilateral memory dysfunction, or no dysfunction. In left-sided MTLE-HS cases, WT validated surgery in 84.6% of patients with visual memory dysfunction, bilateral memory dysfunction or no dysfunction. The WT of the patient with bilateral sclerosis did not validate surgery.
Conclusion: In this series, WT enabled surgery in nearly 80% of patients who initially would not have been surgical candidates based solely on NPA results. WT remains relevant in the evaluation of MTLE-HS patients with visual and/or verbal memory impairment.

1644 | Social cognition in temporal lobe epilepsy patients: long-term outcome after epilepsy surgery

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Purpose: Social cognition is an important skill for integration and interaction within community and society. Deficits in this domain can lead to lower quality of life in people with epilepsy despite achieving seizure freedom.
Method: The study included 24 patients with temporal lobe epilepsy (TLE); 15 left TLE (53.3% male), 9 right TLE (66.7% male). Participants were examined at three timepoints: before surgery (mean age left TLE 34.4 ±10.9; right TLE 42.0 ±8.5), 12 months and 11.6 ±2.2 years after surgery. Social cognition was assessed using the Emotion Recognition Test (ERT) and the Faux Pas Test (FPT), which have been proven to detect social cognition deficits. All participants provided informed consent approved by the institutional ethics committee.
Results: Post-surgery, both groups showed a reduction in seizure frequency (83.3% patients being seizure free). At the long-term follow up, seizure control persisted in both groups. Median score for ERT remained stable over the years (22 points preoperatively; 21 points 12 months after surgery for both TLE groups; 21 in left TLE, 22 in right TLE in long term follow up). Before surgery, the FPT score was lower in the right TLE group (median 13) compared to left TLE (median 15) and declined in long term follow up to the median score of 11 in the left and to 10 in the right TLE group.
Conclusion: Our results highlight frequently overlooked impairment in social cognition that may handicap people with epilepsy in everyday life. These deficits may partly explain why some patients do not experience an increase in quality of life after epilepsy surgery.

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1648 | The Epilepsy Surgery Satisfaction Questionnaire (ESSQ-19): Introducing the Russian Version

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Purpose: Satisfaction with epilepsy surgery is an important measure of patient-reported outcomes that provides a patient-centered view of the effects of surgery. We aimed to validate the Russian version of the Epilepsy Surgery Satisfaction Questionnaire (ESSQ-19).
Method: Patients with focal drug-resistant epilepsy (PDRE) who underwent epilepsy surgery between January 2014 and January 2023 were recruited at least 1 year after operation. Clinical and demographic data were collected. PDRE completed the Russian version of the ESSQ-19 and a set of other questionnaires to assess construct validity. Spearman's rank correlation and ROC-analysis were used to evaluate the validity. Internal consistency analysis was performed calculating Cronbach's α for each of the four domains. Multiple linear regression model was developed to identify the predictors of satisfaction with surgery.
Results: Sixty-six of the 119 eligible patients residing in Moscow participated in the study. The mean summary score was 74.6 (SD 18), which indicates high satisfaction with the surgery in our patients. The questionnaire demonstrated high internal consistency in the four domains (Cronbach's α=0.74–0.93). The ESSQ-19 domains significantly correlated with other measures, such as the QOLIE-31 and GADS, which supports its convergent validity. The questionnaire also demonstrated good discriminant validity for predicting 1-year seizure freedom (AUC=0.78, 95% CI =0.67-0.88) and self-rating epilepsy as disabling (AUC=0.85, 95% CI=0.74-0.93). Seizure-related disability and number of anti-seizure medications were the main predictors of satisfaction with epilepsy surgery.
Conclusion: The Russian version of the ESSQ-19 is a reliable and valid self-reported questionnaire for assessing patient satisfaction with epilepsy surgery. The use of this tool could greatly enhance the ability to evaluate surgical outcomes globally, providing a deeper understanding of surgical procedures and facilitating communication between doctors and patients. This study is the first to provide insights into the level of satisfaction with epilepsy surgery in Russian patients.

1667 | Mesial Temporal Lobe Epilepsy: A Ten-Year Retrospective Cohort Study of Challenges, Treatment and Outcomes

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Purpose: Mesial temporal lobe epilepsy with hippocampal sclerosis (MTLE-HS) is a frequent focal drug-resistant epilepsy (DRE) in adults. The emergence of cognitive problems and psychiatric comorbidities bring an additional burden to these patients throughout life. We aimed to characterize long-term outcomes in this population.
Method: A retrospective cohort analysis was conducted in patients diagnosed with MTLE-HS, managed at a tertiary epilepsy center (January 2010-December 2014), and minimum follow-up of 10 years. Data on demographics, comorbidities, antiseizure medications (ASMs), and treatment outcomes were analyzed.
Results: The cohort included 187 patients, 59.4% female, median age 56 years (range 24-87), seizure onset at 11 years (0.5-65) and 76.9% reporting aura. Risk factors included febrile seizures (45.5%) and family history (30.9%). Over the 10-year follow-up, psychiatric comorbidities were reported in 72% (mood disorders 46.3%, anxiety 42.3%, psychosis 26.1%). Cognitive and functional impairments emerged with memory (52.5%), sleep (41.1%), language difficulties (15.3%), and dementia (23%). Initially, patients were taking 2.9 ASMs, decreasing to 2.3 currently. During the follow-up period, 78.8% had DRE, 26.2% of them achieved seizure control, 74% due to surgery. Among the patients that were initially controlled 10,5% became refractory. At the end of the follow-up, overall, 37.6% of patients underwent surgery and 62.0% remained refractory. Mortality was 7.6% (including 1 SUDEP). Status epilepticus occurred in two patients, 39.7% were functionally independent.
Conclusion: MTLE-HS seems to be a progressive disease, with these patients experiencing the appearance of comorbidities throughout life. Surgery is the best way to control seizures, very few patients achieved control with ASM.

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1714 | Combining tractography and intracranial EEG to define the structural epileptic network

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Purpose: One-third of epileptic patients are resistant to medication, with surgery as a potential solution. However, 25–35% of operated patients continue to experience disabling seizures, showing the need for better surgical targeting. A network-based perspective has improved our understanding of seizure generation, yet the role of white matter (WM) connections in these networks remains underexplored. While intracranial EEG (icEEG) localizes cortical nodes, it omits WM pathways. Here, we integrate diffusion MRI tractography with icEEG to visualize and quantify the WM edges of epileptic networks.
Method: High-resolution T1 and diffusion MRI scans were acquired from 20 patients having undergone an icEEG and from 49 healthy controls (HC). A comprehensive structural connectivity pipeline (Tractoflow, Surface-Enhanced Tractography, and Connectoflow) generated tractograms while correcting for the gyral bias, parcellated the cortex into 246 Brainnetome atlas regions, and computed connectivity strength(CS) using streamline counts and COMMIT weights(a microstructure-informed CS metric). Expert epileptologists classified icEEG contacts of patients into seizure onset (SOZ), propagation (SPZ), irritative (IZ), or non-involved zones (NIZ). Each parcel was assigned to the same zone as the contact within it. Tracts connecting parcels were then grouped into intrazonal (SOZ↔SOZ...IZ↔IZ) and interzonal (SOZ↔SPZ... IZ↔NIZ) networks. CS of analogous networks in HCs were also computed. Across-group, within-network and within-group, across-network differences were assessed using FDR-corrected nonparametric tests.
Results: Across-group FDR-corrected comparisons revealed that patients exhibited increased streamline counts in IZ↔NIZ and decreased COMMIT weights in NIZ↔NIZ. Across-network FDR-corrected comparisons revealed higher streamline counts in SOZ↔SOZ compared to SOZ↔SPZ, SOZ↔NIZ, SPZ↔IZ, SPZ↔NIZ, and IZ↔NIZ. Although COMMIT weights showed overall network differences, no comparisons remained significant after FDR.
Conclusion: These findings underscore the potential of diffusion MRI tractography to complement icEEG by delineating the WM architecture of epileptic networks. Combining icEEG-derived zone definitions with tractography metrics may refine surgical targets and improve seizure outcomes.

1769 | Selective Amygdalohippocampectomy (sAHE) by Stereotactic Laser Thermoablation (sL-TA) results in Functional Shift in Non-Verbal Memory

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Purpose: sL-TA is a minimally invasive and effective procedure for treating drug-resistant epilepsy (1). It is increasingly used in the treatment of mesial temporal lobe epilepsy (mTLE) through sAHE. However, the clinical extent and the network changes of postoperative cognitive function remains unclear. Functional mapping before and after sAHE allows for the evaluation of shifts in cognitive networks, particularly in non-verbal memory processing. This study investigates postoperative changes in non-verbal memory function using a validated fMRI memory paradigm nine patients with right-sided ablations.
Method: Pre- and postoperative assessments were conducted within two weeks before and after surgery, respectively. A non-verbal memory task was employed, where patients viewed 132 black-and-white images of indoor and outdoor scenes during an MRI scan. After a 70-minute interval, a recall-task was administered, combining previously shown images with novel ones. Patients rated image familiarity on a scale from 1 to 5. Functional-MRI data were preprocessed and analyzed using SPM. Postoperative changes in hippocampal and amygdala activations are shown in a maps normalized into MNI space and after using a paired- t-test.
Results: The left superior temporal gyrus (Fig 1a) and the left anterior parahippocampal region (Fig 1b) showed a significant ($p < 0.001$) increase in activation.

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Conclusion: These findings indicate functional reorganization, with a prominent novelty effect observed in brain activity associated with non-verbal memory processing and suggests a shift in memory function networks following sAHE.The applied method offers valuable insights into the interaction between surgical interventions and cognitive network reorganization, supporting further prospective studies in larger cohorts and with comparison to resective sAHE or anterior temporal lobectomy.

1777 | Predictive Value of Preoperative FDG-PET Hypometabolism for Postoperative Visual Field Defects in Temporal Lobe Epilepsy Surgery

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Purpose: Although contralateral quadrant visual field defects (VFD) may occur after surgical treatment of temporal lobe epilepsy (TLE), there are few reports on the quantitative evaluation of VFD and its long-term course. In addition, the association between hypometabolic areas on preoperative FDG-PET and postoperative VFD is unclear. To evaluate the effect of posteromedial temporal (PMT) and medial occipital (MO) cortical hypometabolism on postoperative VFD on FDG-PET before TLE surgery.
Method: A retrospective observational study was conducted on 40 TLE surgery cases from 2007 to 2022. PMT and MO hypometabolism and VFD incidence on preoperative FDG-PET were compared. Humphrey Field Analyzer was used for visual field evaluation, and pattern deviation probability plots (PDPP) of VFD were analyzed preoperatively and at 3 months and 2 years postoperatively.
Results: The incidence of VFD at 3 months postoperatively was 87.5%, and 42.5% were severe. Patients with preoperative PMT and MO hypometabolism had a higher complication rate of severe VFD postoperatively. Most patients with PMT hypometabolism also had mild visual field improvement 2 years postoperatively. In the group with poor postoperative seizure outcome, VFD remained the same 2 years postoperatively.
Conclusion: FDG hypometabolism in PMT and MO suggests a risk of worsening postoperative VFD. Preoperative FDG-PET may be beneficial in terms of predicting postoperative VFD.

1817 | Temporal lobe epilepsy (TLE) patients perform better in vestibulo-dependent spatial orientation after Stereotactic Laser-Thermoablation (sL-TA) compared to "classical" resective surgery and to non-operated patients

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Purpose: Although open surgical approaches, such as temporal lobectomy, have been method of choice for almost a century, minimally invasive sL-TA demonstrated promising results concerning postoperative seizure outcome (1). Postoperatively some memory functions seem to be better after sL-TA in comparison to the "classical" resective procedures (2). However, it remains unknown whether patients who underwent one of these two approaches would show better performance on vestibulo-spatial tasks.
Method: Twenty seven patients were included and divided in three evenly sized different groups: group I: after sL-TA (37.0 ± 15.1 years; 2 females), group II: resective surgery (44 ± 15.7 years, 5 females) and group III: no surgery (43 ± 11.2 years, 3 females) with no significant differences in age, disease duration and number of antiseizure medication (ASM). Groups were compared on their performance in three vestibular-dependent tests: 1. the clinical balance test (CBT), 2. triangle completion test (TCT) for vestibular-dependent spatial orientation and 3. rotational memory (RM) test.
Results: Significantly better performance was found in Group 1 (sL-TA), in comparison to the other two groups (resective surgery and no surgery) on TCT (figure 1). Other tests revealed no significant differences between groups.
Conclusion: Even if the minimal-invasiveness with less removed tissue and collateral damage appear an evident explanation for the better performance in the sL-TA group compared to the resective group, the postsurgical increase in function compared to the non-operated patients remains intriguing. The reasons for these findings could be

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assessed in detail in a larger-scale prospective longitudinal study, so that confounding factors such as influence of operated side, timing of surgery, quantitative and or qualitative drug load in respect to the vestibulo-spatial functions (etc.).

1819 | Seizure Outcome after Selective Amygdalohippocampectomy (sAHE) – 5 years after the introduction of Stereotactic Laser Thermoablation (sL-TA) in combination with Radiofrequency Thermoablation

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Purpose: Inspite a seizure free outcome of 70-80% after 2 years, craniotomy hinders increasing number of temporal lobe epilepsy (TLE) patients to undergo resective surgery. Because of the minimal-invasiveness sL-TA and RF-TA are attractive alternatives. While RF-TA produces too small lesions, sL-TA usually requires only one trajectory for an sAHE. Single center data with early usage of sL-TA for sAHE achieved Engel class I outcome in 53.4% of 58 patients (60.5% to 33% depending on etiology); sL-TA reablation due to failure of seizure freedom was performed in 15.5% (1). Seizure outcome, usage of additional RF-TA and number of re-operations of patients with mTLE from our cohort are presented.

Method: From March 2019 to May 2024 all consecutive patients had follow-up (FU) 4 weeks, 3 months, 6 months, 12 months and then every 12 months for seizure frequency and antiseizure medication (ASM). Surgical and clinical data sheets were assessed for usage of ablation and etiology.

Results: 21 patients underwent sAHE (1 lost for FU with death of unknown cause), two needed additional RF-TA which was assessed preoperatively. Seizure remission required sl-TA reablation in 2 patients. Etiology was in 13 patients HS, in 5 different non-HS lesions and 3 were only SPECT-positive. Seizure outcomes for 1-year-FU and 2-year-FU are shown in table 1a, for last FU in table 1b and for etiology in table 1c.

Conclusion: In our – only on European standard numerous - cohort Engel Class I was achieved in 70 to 72 %. The combination of sL-TA and RF-TA was beneficial in two (i.e. 10%) of the patients and 10% had to be reablated with sL—TA due to seizure remission. Outcome seems to be etiology-dependent: the best outcome for mTLE with HS (88%), the worst for non-lesional mTLE (33%). Whether late sL-TA further improves outcome needs to redetermined in a larger cohort.

1831 | Collapse of interictal suppressive networks precedes seizure spread

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Purpose: How do brain networks limit seizure activity? In the Interictal Suppression Hypothesis, we recently postulated that high inward connectivity to seizure onset zones (SOZs) from non-involved zones (NIZs) is a sign of broader network suppression. If broad networks appear to be responsible for interictal SOZ suppression, what changes during seizure initiation, spread, and termination?

Method: Peri-ictal network dynamics were derived from stereo electroencephalography (SEEG) recordings from 75 patients with drug-resistant epilepsy undergoing presurgical evaluation at Vanderbilt University Medical Center. We computed directed connectivity from 5-second windows in the periods between, immediately before, during, and after 668 seizures.

We aligned connectivity matrices across seizures and patients, then calculated net connectivity changes from the SOZ, propagative zone, and NIZ.

Results: Across all seizure types, we observed two phases: a rapid increase in directed communication towards the SOZ followed by a collapse in network connectivity. During this first phase, SOZs could be distinguished from all other regions (One-Way ANOVA, p=8.32x10-19

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-2.22x10-7). In the second phase and post-ictal period, SOZ inward connectivity decreased yet remained distinct (One-Way ANOVA, p=2.58x10-10-1.66x10-2). NIZs appeared to drive increased SOZ connectivity while intra-NIZ connectivity concordantly decreased. Stratifying by seizure subtype, we found that consciousness-impairing seizures decrease inward connectivity from the NIZ earlier than consciousness-impairing seizures (one-way ANOVA, p<0.01 after false discovery correction). Tracking network reorganization against a surrogate for seizure involvement highlighted a possible antagonism between seizure propagation and the NIZ's ability to maintain high connectivity to the SOZ.

Conclusion: Overall, NIZs appear to actively respond to seizure onset and increase inhibitory signaling towards the SOZ, possibly to thwart seizure activity. While inhibition appears insufficient to prevent seizure onset, the inability to restrict seizure propagation may contribute to loss of consciousness during larger seizures.

Genetics

406 | Focal refractory epilepsy associated to 15q13.3 microduplication

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Purpose: The 15q11-q13 chromosomal region is prone to copy number variations (CNVs), linked to complex neurological phenotypes. CNVs at 15q13.3, involving the CHRNA7 gene, are associated with epilepsy, intellectual disability, and ADHD. Their role in drug-resistant epilepsy (DRE) remains unclear

Method: We report a male in his early 20s with DRE and a maternal history of epilepsy and psychiatric disorders. Seizures began after mild head trauma at age five, progressing to frequent generalized and focal seizures despite treatment with carbamazepine, levetiracetam, and gabapentin. Genetic testing revealed a 440.5 Kb microduplication at 15q13.3 involving CHRNA7, with normal brain MRI.

Results: This case underscores the phenotypic variability and incomplete penetrance of 15q13.3 microduplications, complicating management. Data on effective treatments remain sparse.

Conclusion: 15q13.3 microduplications challenge diagnosis and treatment. Comprehensive genetic testing and personalized strategies are crucial. Further research is needed to refine therapeutic approaches.

480 | *PPP2R1A*-Related Neurodevelopmental Disorder: The First Korean Case with a Novel Variant of *PPP2R1A* and Literature Review

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Purpose: The *PPP2R1A* gene, located on chromosome 19q13.41, encodes the scaffolding Aα subunit of protein phosphatase 2A, which is highly expressed in the developing and adult brain. To date, fewer than 50 cases of *PPP2R1A*-related neurodevelopmental disorders (NDDs) have been reported with various phenotypes. Here, we report the first Korean case of *PPP2R1A*-related NDD harboring a novel *de novo* missense *PPP2R1A* variant.

Method: The proband, a 12-month-old female, presented with developmental delay, intractable epilepsy, and microcephaly. Brain magnetic resonance imaging (MRI), karyotyping, chromosomal microarray, metabolic screening test, and next-generation sequencing (NGS)-based targeted gene panel testing for NDDs were performed.

Results: Karyotyping, chromosomal microarray, and metabolic screening test results were normal. Brain MRI showed a Dandy-Walker continuum with corpus callosum hypoplasia. NGS-based targeted gene panel testing for NDDs revealed a novel heterozygous missense variant of *PPP2R1A*:c.650A>G, p.(Gln217Arg). Sanger sequencing confirmed it as *de novo*. While our case shares similar clinical features with previously reported cases, it stands out owing to a more severe manifestation of the phenotypes. Notably, the patient presented with seizures that did not respond well to medications. In addition, neuroimaging phenotypes not previously associated with the *PPP2R1A* variant, which included the Dandy-Walker continuum, were identified in the patient.

Conclusion: We report the first Korean case of *PPP2R1A*-related NDD harboring a novel *de novo* missense *PPP2R1A* variant with previously unreported clinical and radiologic characteristics. This study significantly expands the phenotypic and genotypic spectrum of *PPP2R1A* variants and emphasizes the importance of careful scrutiny of clinical presentations to achieve a timely diagnosis of *PPP2R1A*-related NDDs.

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650 | The Genetic and clinical phenotype of PCDH19-related epilepsy

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Purpose: PCDH19-related epilepsy is an X-linked epilepsy syndrome characterized by infant onset, clustered and fever-induced seizures, often associated with intellectual disability and autistic features. This study aims to delineate genetic and clinical phenotype of the patients with PCDH19-related epilepsy.
Method: Seventeen female patients of PCDH19-related epilepsy were included in the study. Characteristics of *PCDH19* mutations, electroclinical features, clinical course, and response to the treatment, neuropsychiatric test results were analyzed.
Results: The onset of seizures were ranged from 4 months to 33 months (median 13.0 months). All patients had history of febrile convulsion, except for 1 patient. EEG showed background slowing only or background slowing with focal epileptic discharges. Twelve patients had intellectual disability or developmental delay. Five patients were normal development. Four patients became seizure-free with medication including levetiracetam, phenobarbital, topiramate and valproic acid. Steroid is effective for two patients, Ketogenic diet was effective in two patients, and VNS was effective in one patient.
Conclusion: PCDH19 mutations are involved in infantile onset developmental and epileptic encephalopathy in female patients. As the patients grow, seizures decrease in frequency and cognitive and behavioral disturbances remain the main problems.

653 | Novel risk alleles for Familial Focal Epilepsy with Variable Foci (FFEVF) identified from whole exome sequencing of a small nuclear family

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Purpose: FFEVF is a rare inherited epilepsy syndrome in which mutations in *DEPDC5*, *NPRL2* and *NPRL3* have been identified as being causal in ~10% of patients. Our goal was to identify genetic variations linked to suspected FFEVF in three affected members of a small nuclear family of eight.
Method: Subjects were consented and blood drawn for DNA isolation and whole exome sequencing (WES). WES data were analyzed using DRAGEN germline and joint genotyping pipelines and the Integrative Genomics Viewer (IGV) to align sequences and identify variants. Based on pedigree analysis, we assumed an autosomal dominant inheritance with incomplete penetrance and modeled accordingly. Variants were annotated using dbSNP and ClinVar databases.
Results: We identified 390 SNPs in 272 genes that fit the assumed mode of inheritance. We found no evidence for a causative variation in *DEPDEC5*, *NPRL2*, or *NPRL3*. There is one *de novo* mutation in *COL24A1* which fits the genetic model as well as germline variants in 15 genes linked to epilepsy phenotypes from prior work including *EED, FUT8, FXYD2, GLE1, L2HGDH, MTR, PDE2A, PIBF1, RYR2, SET, SLC28A1, STT3A, STXBP1, TRNT1*, and *ZFYVE26*. None of the variations analyzed thus far are known to be definitively pathological as defined by ClinVar or dbSNP.
Conclusion: Results of this study support a monogenic cause from the *de novo* mutation in the *COL24A1* gene. Mutations in *COL4A1* and *COL4A2* individually lead to neurological phenotypes that include epilepsy. Mutations in *COL5A* and other collagen genes cause Ehlers-Danlos syndrome (EDS) and ~10% or more of EDS patients experience seizures. It remains possible that the cause of FFEVF in this family is polygenic and involves combinations of alleles. Further analyses will focus on more complex genetic models and complete annotation of all variants to identify new risk factors contributing to FFEVF.

680 | Low-level mosaic *SCN2A* variant causing early infantile onset epileptic encephalopathy: characterization using heterologous cell expression and neurons from iPSC cells

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Purpose: Haploinsufficiency in *SCN2A* is involved in a wide range of epileptic phenotypes [Wolff M., et al. Epilepsia 2019;60 Suppl 3:S59-S67]. Pathogenic *SCN2A* variants are generally *de novo* germline mutations and only one case of mosaicism has been described [Zerem A., et al. Eur J Paediatr Neurol 2014;18(5):567-71]. We evaluated the expression and functional effect of a *SCN2A*: c.4976C>T (p.A1659V) pathogenic variant found at a mosaic state in two infants, by virtue of heterologous cell expression and induced pluripotent stem cells (iPSC)-derived neuronal models.

Method: Two patients with seizure onset within the first three days of life and resistant to multiple anti-seizure medications were subjected to next-generation sequencing from blood. The analysis identified a *SCN2A*: c.4976C >T; p.Ala1659Val with a low-level mosaicism (15%), confirmed on both patients' fibroblasts. The p.Ala1659Val variant was inserted in a stabilized SCN2A plasmid by site-directed mutagenesis. Expression and functional characterization of the p.Ala1659Val variant were performed in Hek293 cells by western blotting, confocal microscopy, and patch clamp. Patients' fibroblasts were cultured to reprogram them into iPSCs.

Results: No effect of the p.Ala1659Val variant on channel expression was noted, whilst a reduction of the peak current and a shift of half activation voltage towards more negative values was observed. To get iPSC clones derived from patients, fibroblasts were transduced with Sendai Virus to induce pluripotency. Around 50 iPSC clones were obtained. Each clone was characterized to discern between wild-type (WT) and heterozygous ones. The best clones, both WT and mutated, were differentiated into glutamatergic neurons through neurogenic protocol to test them on MicroElectrode Assay (MEA). Mutated and isogenic neurons will be plated alone and with different grades of mosaicism on MEA.

Conclusion: This study provides valuable insights into the *SCN2A* p.Ala1659Val variant's functional consequences, highlighting the utility of heterologous cell and iPSC-derived neuronal models in understanding complex neurological disorders.

790 | In vitro electrophysiological study of hippocampal network activity in a mouse model of STXBP1 haploinsufficiency

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Purpose: STXBP1 haploinsufficiency disorders are associated with neurodevelopmental delay, seizures and intellectual disability. We evaluated the hippocampal neuronal network activity in STXBP1 heterozygous KO (HET) and WT mice to determine potential changes in excitability and plasticity related to STXBP1 haploinsufficiency.

Method: Local field potential (LFP) recordings were performed in hippocampal slices (n=10 slices/ group) from adult male STXBP1 HET mice and WT littermate mice for comparison. Spontaneous activity was recorded in the slices before evoking field excitatory postsynaptic potentials (fEPSPs) by axonal stimulation. fEPSPs were evoked in CA3, CA1 and dentate gyrus (DG) by electrical stimulation of fimbria, Schaeffer collaterals and perforant path, respectively. The number of population spikes (PSs) per fEPSP and the amplitude of PS1 (first population spike) were measured from input-output (I/O) relationships. Short-term plasticity (STP) was evaluated by applying a series of paired-pulse stimulations.

Results: No spontaneous postsynaptic events were detected in investigated hippocampal regions. In CA1 and DG, I/O curves showed no difference in PS threshold, PS1 amplitude and PSs number (1 PS max) for STXBP1 HET vs WT littermates suggesting no change in excitability. A weak decrease of PS1 amplitude was observed in CA3 responses from STXBP1 HET whilst the PSs number remained unchanged (1 PS max). For STP experiments, paired-pulse ratios (PPRs) based on PS1 amplitude were measured in the three hippocampal regions. An increase of paired-pulse facilitation (PPF) was observed at CA3-to-CA1 synapse whilst PPRs were unchanged in the other hippocampal synapses. PPF reflecting the release probability of the presynaptic cells, an increase of PPF suggests therefore a reduced release probability at the presynaptic cells.

Conclusion: Overall excitability, synaptic transmission, and short-term plasticity remain unchanged in the hippocampal regions of STXBP1 HET, except in CA3 and CA3-to-CA1 synapse, where slight hypo-excitability and potential dysfunction in presynaptic vesicular release were noticed, respectively. UCB funded work

811 | Adult-Onset Drug Resistant Progressive Epilepsy in a Patient with MECP2 Mutation

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Purpose: The aim of this study is to present a novel case of adult-onset progressive epilepsy in a patient with Methyl-CpG-binding protein 2 (MECP2) dysfunction.

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Method: Here we describe a case of a female patient with normal developmental history who first presented at age 27 with refractory epilepsy. Seizure types included focal-to-bilateral-tonic-clonic, atonic, and behavioral arrest. EEG noted frequent generalized spike and polyspike discharges. Brain MRI 3T and sleep testing showed no abnormalities.

Results: Patient was trialed on numerous ASMs with continued daily seizure clusters (up to 20 a day), with longest seizure-free period of one month. Over the next decade, the patient developed a constellation of new symptoms, including cognitive and speech decline, ataxia, autonomic instability (sinus tachycardia, hypotension), weight gain and left eye exotropia. Ambry genetic testing showed a pathogenic variant in exon 4 of the MECP2 gene: c.1059_1190del132ins24. Given this variant, she was seen by a Rett syndrome (RTT) specialist who did not feel that she fit the clinical criteria for classic or atypical Rett. The patient continued to have multiple daily seizures on her current ASM regimen of clobazam, cenobamate, and felbamate. Recent Whole Exome Sequencing confirmed the Ambry genetic test results and was otherwise negative for other variants that are associated with the clinical phenotype.

Conclusion: Mutations in the MECP2 gene are associated with a spectrum of neurologic disorders, the most common of which is RTT, but can range from mild intellectual disability to severe neonatal encephalopathy and premature death. As these mutations occur in germ cells, onset of neurologic symptoms usually occurs in early childhood. Seizures, another common feature of MECP2-related disorders, often occur later in childhood or early adolescence. However, there has never been a documented case of progressive epilepsy and cognitive decline with onset in adulthood. This report expands the phenotypic spectrum of MECP2-related epilepsy.

817 | Genotype-phenotype correlation in *GABRB3* loss-of-function

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Purpose: Pathogenic variants in the *GABRB3* gene, encoding the β-3 subunit of the GABA_A receptor, are associated with a spectrum of epilepsy syndromes, neurodevelopment disorders, and neuropsychiatric conditions. Variants can be divided into Gain-of-Function (GoF) and Loss-of-Function (LoF). LoF variants are found in structurally significant locations, including the GABA-binding-site, coupling-loops and transmembrane-domains. This retrospective cohort study aimed to identify subgroups of patients and uncover genotype-phenotype correlations in GABRB3 LoF.

Method: Patients were recruited through international collaborations and literature review. Clinical data were collected or confirmed by in person interview when possible, otherwise by contact with referring physician or author. Data included genetic findings, family history, EEG, MRI, age of seizure onset and offset, seizure semiology, medical history, developmental trajectory, behavior, and psychiatric comorbidities. EEGs were reviewed by an epileptologist when possible. Developmental and cognitive levels were classified according to DSM-5. Seizure semiology and epilepsy syndromes were classified per the ILAE criteria. Studies on the electrophysiology and structural mapping of each variant were included.

Results: 77 patients, 17 of which are novel, were included. Inheritance was *de novo in 71.4% of patients* (n=55/77). Ninety-seven percent had epilepsy, with a median age of onset of nine months. Forty-nine percent were seizure free at follow up, while 73.3% had developmental delay or intellectual disability. Sixty percent met criteria for a Developmental Epileptic Encephalopathy (DEE). We found no significant risk of refractory epilepsy or comorbidities based on early clinical presentation or any higher comorbidity risk in those with refractory epilepsy. GABA-binding-site variants had a significantly lower GABA-sensitivity and were significantly associated with DEE.

Conclusion: This study found a significant correlation between impaired electrophysiological phenotype, GABA-binding-site variants and DEE. However, the phenotypical presentation remained disparate within distinct protein location and there was no coherent phenotype for any recurring variants. This highlights a requisite for further research into underlying biological mechanisms.

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847 | Genetic causes of malformation of cortical development in children undergoing epilepsy surgery in Norway: Characterization of germline and somatic mutations

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Purpose: Malformation of cortical development (MCD) may arise from early germline or somatic mutations in neurodevelopment. Detecting somatic mutations is challenging due to low-grade mosaicism. This study aimed to improve detection of somatic mutations by applying an improved workflow and bioinformatic pipeline for analyzing affected brain tissue.
Method: A retro- and prospective cohort study, at Oslo University Hospital from 2015 to 2024, including 50 pediatric epilepsy surgery patients with suspect MCD. Pre- and postsurgical data from multidisciplinary investigation, histopathology, and genetic diagnostics were collected. DNA from fresh-frozen brain tissue underwent three investigational steps: 1) Routine diagnostic whole-exome analysis with a gene panel for migration disorders, 2) Data reanalysis using an in-house bioinformatic pipeline with Mutect2, and 3) Variant verification with droplet digital PCR (ddPCR). Paired blood and brain samples were compared for 20 patients.
Results: Radiological findings indicated MCD in 90% (45/50) of cases. Histopathology confirmed focal cortical dysplasia type II or hemimegalencephaly in 67% (33/50). Nine cases with radiological MCD findings had non-specific histopathology: among these, three hemimegalencephaly, and one re-evaluated as mild MCD after detecting a somatic variant in SLC35A. Preliminary genetic results showed a 16% diagnostic yield (6/37) after step 1, and 35% (13/37) after step 2. Additionally, somatic class IV-V variants were detected in MTOR, TSC2, AKT3, PIK3CA, KRAS, and germline variants in DEPDC5 and NPRL2. Variants with allele frequencies below 10% were verified with ddPCR. Notable variation in the number of putative mosaic variants classified as deleterious or in candidate genes was observed but reduced with paired samples. While gene variants known to cause MCD were identified, preliminary results suggest additional novel genetic causes pending verification.
Conclusion: In MCD, routine genetic diagnostics is challenging due to low-grade mosaicism. Results from our improved pipeline suggest enhanced sensitivity. Increased genetic diagnostic yield could facilitate improved, targeted treatment for these patients.

882 | Association of *GSTM1 gene* deletion with therapeutic response in epilepsy

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Purpose: Epilepsy affects millions of people worldwide. Several factors have been associated with treatment outcome in epilepsy including the type of epilepsy and etiology. Identification of the gene mutations involved in epilepsy pathogenesis is expected to enable more effective treatment of this condition.
Method: We have evaluated the presence of GSTM1 gene deletion in 182 people with epilepsy (PWE), 96 of whom classified as idiopathic generalized epilepsy and 86 as focal epilepsy and determined the therapeutic response towards antiepileptics.
Results: To determine the presence of genetic association between GSTM1 gene deletion and therapeutic response towards antiepileptic drugs, patients were divided in two groups: 1. with therapeutic response and 2. resistant to pharmacotherapy. Carriers of the homozygous deletion or null genotype (GSTM1*0) is more frequent (64.23%) in group who respond to medicamentous therapy than the carriers of heterozygous or homozygous genotype with at least one allele (GSTM1*1) at this locus. Evaluation of the frequencies by Chi-squared test showed that these genotype differences are statistically significant ($p<0.05$) and calculated odds ratio (OR=0.470) indicates that carriers of GSTM1*0 genotype have 0, 470 times less chances to develop pharmacoresistancy no matter the type of epilepsy.
Conclusion: Homozygous deletion, null genotype (GSTM1*0) is more frequently represented (64,23%) in patients who respond to medicamentous therapy than genotype in which at least one allele is present (GSTM1*1) in heterozygous or two alleles in homozygous state on this locus. Statistical evaluation showed that these differences are statistically significant with calculated odds

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ratio (OR=0.470; 95% CI 0.250-0.883; p<0.05) indicating that the carriers of GSTM1*0 genotype have 0,470 times reduced odds to develop resistance regardless the epilepsy type. The calculated reduction of the chance is (1-0.470=0.530), so these carriers have 53% lower likelihood to develop resistance to pharmacotherapy.

884 | Diagnostic yield and copy number variants findings in 220 adult patients with developmental and epileptic encephalopathies

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Purpose: Most monogenic Developmental and epileptic encephalopathies (DEE) are caused by pathogenic *de novo* SNV in genes, each contributing to a limited proportion of cases[1]. Thus, WES is considered the most convenient approach for DEE[2], although chromosomal microarray (CMA) for copy number variants (CNVs) detection would be the first-tier genetic test for patients with epilepsy, intellectual disability and/or dysmorphisms, according to diagnostic algorithms[3]. Most of the studies on CNVs focused on pediatric cohorts[4], whereas data on adults are scant. We investigate the role of CNVs in the etiology of DEE in an adult cohort.
Method: All patients with undiagnosed DEE referred to the tertiary epilepsy center of our Institute underwent accurate electro-clinical assessment. CNV analysis was performed by (i) the Agilent Technologies array-CGH 8x60K platform and Cytogenomics software (Agilent technologies) or (ii) SNP-array from Epi25 data using PennCNV for variant calling and AnnotSV software for variant annotation.
Results: 220 unrelated DEE patients (M/F:104/116, mean age at seizures onset: 9.3±5.04 years) underwent array-CGH or SNP-array at a mean age of 35.13±14.95 years. We identified causative CNVs in 18 patients (8.2%), 8 of whom *de novo* (44.4%): del1p36.33-p36.23, dup1q21.1q21.2, del2p16.3, mosaic del2q23, del2q23.3q24.2, del2q37.3, del3p14.2p14.1, del3q29, del6q27, del13q13.2q13.3, del15q11.2q13.1 compatible with Angelman syndrome, dup15q11.2q13, 15q13.2q13.3x3+15q11.2q13.2x4 compatible with an inv-dup (15) syndrome, dup16p13.1, del 17q21.31, del 19q12-q13.11, del 22q11.2, del 22q13.33. The mean age at diagnosis was 32.4±13 years. Of the remaining, 24 (10.9%) had VUS, 178 (80.9%) were negative.
Conclusion: We identified causative CNVs in 8.2% of our adult DEE patients, with a diagnostic delay of 23 years. The diagnostic yield aligns with published data on pediatric series. Although WES is recommended as the initial approach to reduce diagnostic costs and time, incorporating CNV analysis is recommended in the diagnostic workflow for adult patients with DEE as well.

893 | It is a rare cause of West syndrome. SLC38A3 mutation

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Purpose: Developmental and epileptic encephalopathies can arise due to mutations in genes encoding proteins responsible for ion channels and synaptic transmission. Mutations in genes encoding SLC proteins can lead to developmental and epileptic encephalopathies. Here, we present the case of a patient with developmental delay and refractory epilepsy who was found to have a pathogenic variant in the SLC38A3 gene during genetic analysis.
Method: Case Report: The patient was a 2-year-and-7-month-old boy with a history of term delivery. He first experienced myoclonic seizures at the age of 3 months. Physical examination revealed microcephaly (, lack of head control, absence of visual tracking, central hypotonia, and absent DTR. The patient had no speech. EEG showed generalized epileptic discharges. Brain MRI reported thinning of the corpus callosum and mild volume loss in the thalamus and brainstem. The family history included parental consanguinity and a sibling with similar clinical findings who had passed away. Advanced genetic testing revealed a mutation in the SLC38A3 gene (NM_006841.6: c.964_965del, p.(Ser322GlnfsTer41)). Unfortunately, the patient passed away.
Results: The SLC38A3 gene encodes sodium-coupled neutral amino acid transporter 3 (SNAT3), a crucial homeostatic regulator of the glutamate/GABA-glutamine cycle in the brain and a transporter of asparagine, histidine, and glutamine. This explains the diverse clinical findings associated with SLC38A3 mutations. A study identified 10 individuals with biallelic pathogenic variants in SLC38A3 from seven unrelated families across

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six different countries, all presenting with developmental delay and epilepsy. Similar to our case, all reported cases had axial hypotonia and an absence of speech, while nine cases exhibited microcephaly. Some cases also reported vision loss, consistent with our patient, who lacked visual tracking and sight.

Conclusion: SLC38A3 is a rare genetic cause of developmental epileptic encephalopathies. In patients with a family history and accompanying clinical findings, advanced genetic analysis is crucial for accurate diagnosis.

897 | The GABAA-Receptor Portal: A Comprehensive Online Database and Webtool of Homologous Variants

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Purpose: Variants in the GABAA-receptor (GABAAR) are associated with phenotypes ranging from mild to very severe epilepsy syndromes and neurodevelopmental disorders, making the path to accurate diagnosis, prognosis and treatment difficult for many. We are creating an online database and webtool comprising all known GABAAR variants, the GABAAR Portal (the Portal), to better equip clinicians and researchers in their efforts to improve patient care.

Method: Clinical and genetic data were collected and curated for >900 patients using an in-house REDCap database at the Danish Epilepsy Centre. Functional annotations were integrated using the Ensembl Variant Effect Predictor (VEP), and variant pathogenicity was determined according to expert-calibrated ACMG guidelines. Control variant data were sourced from gnomAD (v4), UK Biobank, All of US and the Regeneron Million Exome browser. The processed data were analyzed using R and the platform was deployed as a Shiny web application.

Results: The Portal leverages sequence homology between the GABAAR subunits to locate paralogous variants in a sequence alignment table, allowing users to evaluate clinical features associated with each site. Users are also able to identify regions enriched in variants causing a gain, loss or mixed effect via an interactive distribution plot displaying data from both patient and control populations.

Conclusion: The Portal will benefit the GABAAR community by providing a comprehensive and free resource for variant analysis. Sequence- and structure-based homology modelling of open and closed states, incorporating various protein subunit compositions, will be performed for in silico variant clustering. The results thereof will support pathogenicity predictions, functional analyses, and genotype–phenotype correlation studies. Future updates to the Portal will incorporate pathogenicity- and functional effect prediction tools to facilitate diagnostics, genetic counselling and treatment of novel cases of GABAAR-related epilepsies. The work was funded by the Lundbeck Foundation.

901 | Spatial distribution of brain somatic variants and affected cell types in focal epilepsy

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Purpose: Somatic variants in brain cells, arising during fetal development and unique to brain tissue, are implicated in epilepsy. Pathogenic variants exhibit a distinct gradient in variant allele frequency (VAF) between the seizure onset zone (SOZ) and surrounding tissue. Stereoelectroencephalography (SEEG) electrodes were implanted into multiple brain regions according to clinical need, thus allowing access to region- and cell type-specific brain DNA. This study aimed to map the spatial distribution of brain somatic variants and affected cell types in epilepsy using SEEG electrodes.

Method: SEEG electrode tips of 17 patients were pooled by brain region and seizure onset zone for nuclei isolation, sorting, and DNA amplification. Somatic variants were identified in neuronal DNA via exome sequencing and validated using ddPCR in 8 patients including 4 previously published (PMIDs 38587282, 39751777) and 4 new variants. The spatial and cell type-specific distribution was determined using ddPCR in all available electrode pools and neuronal, astrocyte, and microglia DNA separately.

Results: For the 8 validated variants, neuronal VAF in the electrode pool including the SOZ was 0.46-12.6%. All were

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absent in the electrode pool selected as unaffected control brain region and blood/saliva. So far, 5/8 variants were evaluated in all available electrode pools and other cell types. 4/5 variants displayed clear mosaic gradients (i.e., absence in all unaffected neuronal pools), consistent with pathogenicity. One variant was present in an unaffected pool (1.2%) arguing against pathogenicity. The variants were absent in astrocyte- and microglia-derived DNA.

Conclusion: Our findings confirm that SEEG electrodes can identify mosaic gradients and cell type specificity, providing additional support for the pathogenicity of identified somatic variants. This is a significant advantage over variant identification from resected tissue which typically does not include clearly unaffected brain tissue. Our approach may enhance the possibility for future precision medicine treatments based on the identified variants.

984 | Novel variants and high diagnostic yield of Whole Exome Sequencing analysis in young epilepsy patients

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Purpose: The present study aims to determine the diagnostic yield of Whole Exome Sequencing (WES) in patients with epilepsy.

Method: A total of 34 patients with epilepsy, comorbid with various conditions, were included. All participants signed a written informed consent and WES was performed using the DNA Prep Exome2.0 Plus Enrichment and Mitochondrial DNA, Illumina, following the manufacturer's recommendations. The resulting libraries were subjected to paired-end sequencing on Illumina NextSeq 1000 system. Bioinformatic analysis was conducted using the GATK and ExomeDepth algorithms, in R. Variant interpretation was carried out using Franklin by Genoox software, and variants were classified using standards and guidelines established by the American College of Medical Genetics and Genomics (ACMG).

Results: Out of the 34 participants that underwent WES, 26 (76%) were under the age of 18 (mean age: 8±4.6) and 8 (24%) over the age of 18 (mean age: 33.5±10.3), while 19 (56%) were males. Among those patients, 12 were found to carry a Single Nucleotide Variant (SNV) and one a single Copy Number Variant (CNV) that confirmed their clinical phenotypes. Specifically, out of the 26 pediatric patients analyzed, variants were identified in 8 (31%), while out of the 8 adults, variants were identified in 5 (63%). The overall diagnostic yield was 38% (13/34). Notably, 23% of the identified variants were novel and had not been previously reported in any public database.

Conclusion: The diagnostic yield of WES is quite high in both children and adults with epilepsy without a definitive diagnosis. Therefore, WES is an important clinical tool in Medical Genetics, with high clinical utility in cases of epilepsy in both pediatric and adult populations.

985 | Radiologic findings of patients with sodium channelopathies

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Purpose: We aimed to collect and analyze MRI data from patients with sodium channelopathies.

Method: We reviewed medical records, and MRI findings of 161 patients who were diagnosed with epileptic encephalopathy and sodium channelopathies at Severance Children's Hospital, South Korea, between 2003 and 2023.

Results: Among 161 subjects, brain MRI images were available for 153 patients, and MRI reports were obtainable for 139 patients. Fourteen patients whose MRI were of poor quality were excluded from the study. Of 114 patients with SCN1A channelopathies, 36 patients had normal MRI findings. Of 17 patients with SCN2A channelopathies, only 29.4% of patients with SCN2A mutations had normal MRI results. A significant proportion of patients with SCN2A channelopathies showed brain atrophy (58.8%), and/or malformations (29.4%). White matter abnormalities (23.5%), and findings suggestive of hypoxic-ischemic encephalopathy (11.6%) were also commonly seen. There was only one patient with an SCN3A-channelopathy this patient presented with a subdural hematoma (SDH). Of 7, 57.1% of patients with SCN8A channelopathies had normal MRI findings. However, hippocampal anomalies (14.3%) and white matter abnormalities (14.3%) were occasionally found in patients with SCN8A channelopathies.

Conclusion: Patients with sodium channelopathies can show abnormal MRI features. It is crucial to conduct a comprehensive analysis to understand patients with genetic abnormalities.

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987 | Epileptic seizures and 2q23.1 microdeletion syndrome in pediatric patient – case report

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Purpose: The aim of this report is to highlight the importance of genetic testing in children who present epileptic seizures in association with craniofacial dysmorphism, as well as cognitive impairment.
Method: The authors present the case of a young boy who is evaluated for the first time at the age of 5 years and 4 months for generalized tonic-clonic epileptic seizures. This evaluation consisted of general clinical and neurological examinations, psychiatric interview, electroencephalogram (EEG) recordings, cerebral magnetic resonance imaging (MRI), and genetic testing.
Results: The clinical examination revealed facial dysmorphia. No signs of motor impairment were noticed at the neurological examination. The first EEG showed no pathological modifications; However, the following recordings revealed generalized spike-slow wave discharges. MRI revealed lateral ventricular asymmetry. The psychiatrist's diagnosis was atypical autism and expressive language disorder. DNA microarray analysis identified a small deletion of the chromosomal region 2q23.1 including exon 1 of the MBD 5 gene. Treatment with valproic acid was initiated successfully, seizures being kept under control. 2q23.1 microdeletion syndrome is a chromosomal aberration characterized by psychiatric disorders, craniofacial dysmorphism, and epileptic seizures. The onset age and type of the epileptic seizures may vary. The presented patient had generalized tonic-clonic seizures with an onset after the age of 4. With monotherapy antiseizure medication, the boy had no relapses in 10 months. However, literature data report cases of epileptic seizures resistant to medication.
Conclusion: Even though the clinical manifestations of 2q23.1 microdeletion are non-specific, this syndrome should be taken into consideration in children with neuropsychomotor developmental delays, components of the autistic spectrum, facial dysmorphia, and epileptic seizures. Early diagnosis is important for genetic counselling because of the possibility of autosomal dominant inheritance.

1006 | Characterising Epilepsy Phenotype Heterogeneity in Biobank-Derived Disease Cases

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Purpose: Epilepsy is a heterogeneous neurological disorder with diverse genetic and clinical characteristics. This complicates genome-wide association studies (GWAS) on biobank data, where diagnoses rely on the International Classification of Diseases system rather than detailed clinical characterization. We both explore the scope of this problem by estimating genetic correlations between biobank-derived and clinically validated samples, and whether family history can improve diagnostic accuracy.
Method: We conducted a GWAS within the Lundbeck Foundation Initiative for Integrative Psychiatric Research (iPSYCH) cohort (n=4,409) combining family history with the phenotype using LT-FH++. Genetic correlations between the biobank summary statistics – iPSYCH, FinnGen (n=15,645), and UK Biobank (n=3,500) – and the most recent International League Against Epilepsy (ILAE) GWAS of clinically validated samples (n=29,944) were calculated using linkage disequilibrium score regression (LDSC).
Results: The biobanks were highly genetically correlated with the broadest ILAE GWAS phenotype (iPSYCH rg = 0.96, 95%CI 0.53-1.39, FinnGen rg = 0.78, 95%CI 0.59-0.97, UK Biobank rg = 0.84, 95%CI 0.49-1.19), suggesting consistent overall genetic architectures. Especially the UK Biobank summary statistics were highly genetically correlated with the genetic generalized subtype from the ILAE GWAS (rg = 0.92, 95%CI 0.56-1.27). Conversely, the focal ILAE GWAS subtypes resulted in higher estimates for iPSYCH (rg = 0.99, 95%CI 0.43-1.45) and FinnGen (rg = 0.74, 95%CI 0.45-1.03). Combing family history with the phenotype improved the iPSYCH-ILAE genetic correlations.
Conclusion: This study shows, that non-validated biobank-derived epilepsy cases are highly genetically correlated with clinical cohorts, and combining family history with the phenotype can improve diagnostic accuracy. This improves the outlook of their inclusion in genetic meta-analyses.

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1026 | Circulating microRNAs as Biomarkers of juvenile myoclonic epilepsy

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Purpose: to analysis hsa-miR-134-5p, hsa-miR-106b-5p, hsa-miR-122-5p, hsa-miR132-3p, hsa-miR-155-5p, and hsa-miR-206 as diagnostic biomarkers in patients with juvenile myoclonic epilepsy (JME).
Method: We examined blood plasma with 42 patients (15 males and 27 females) at the age of 27 [20; 33] years with JME, comparison group - 52 patients (27 males and 26 females) at the age of 36 [28,5; 42,5] years with temporal lobe epilepsy, control group – 41 healthy volunteers (14 males and 27 females) at the age of 27 [26; 34,75] years. An inclusion criterion is as follows: confirmed diagnosis of TLE or JME; age 18–55 years; absence of signs of infectious disease during the sampling of biomaterial. The control group included healthy volunteers, without neurological diseases and signs of infectious diseases, without chronic somatic pathologies in the stage of decompensation. The expression analysis was carried out using RT-PCR. Mathematical processing of the data was carried out according to the 2^{-DDCt} method. Receiver operating characteristic curve analysis was performed to assess diagnostic value (ROC analysis).
Results: The analysis revealed statistically significant changes ($p < 0,05$) in the increased expression of the miRNAs in the JME group compared to the control: hsa-miR132-3p, 3,42-fold, and in case of hsa-miR-106b-5p, 3,80-fold. In patients with JME, hsa-miR132-3p circulating levels was –1,966418419 ±4,191636 vs. –1,32194E–15 ±3,359457688 in the control group (U0,05-criterion, p=0,026); hsa-miR-106b-5p levels was ––1,926966184 ±4,096325692 vs. 1,71714E–15 ±1,644399909 in the control group(U0,05-criterion, p=0,025). ROC analysis showed hsa-miR132-3: AUC=0,622, CI [0,50-0,74;p<0,05]; hsa-miR-106b-5p: AUC=0,619, CI [0,49–0,74; p<0,05]. The analysis hsa-miR-134-5p, hsa-miR-122-5p, hsa-miR-155-5p, and hsa-miR-206 did not show statistically significant changes in expression pattern.
Conclusion: The study allows us to propose these microRNAs as plasma biomarkers of JME.

1059 | Peri-ictal respiratory disfunction in focal epilepsy due to mTOR pathway disorders

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Purpose: GATOR1 complex gene mutations leading to mTORC1 upregulation are important causes of focal epilepsy with or without malformations of cortical development. NPLR3, together with NPLR2 and DEPDC5, make the GATOR1 complex, which regulates mTORC1 signaling. Hyperactivation of this pathway induces an alteration in cellular morphology, altered synaptogenesis, and an imbalance between excitation/inhibition. Recently there are growing evidence that ictal and post ictal central apnea are common findings in mTOR-related epilepsy, conferring a significantly higher risk for SUDEP.
Method: We reviewed data of 115 patients collected in two independent cohorts of focal epilepsy patients who prospectively underwent long-term video-EEG monitoring (LTVM) with cardiorespiratory polygraphy. Genetic testing by next-generation sequencing (NGS) was offered according to clinical practice in patients without structural etiology.
Results: 64 patients showed seizures with ictal central apnea (ICA) and 50 out of them had ICA in the context of epilepsy of unknown etiology. NGS was carried out in 33 patients resulting in nine with mTOR pathway pathogenic mutations (one with mTOR, five with DEPDC5 and three with NPRL3). They showed ICA and oxygen desaturation in all recorded seizures with apnea duration ranging from 15 seconds to over 1 minute. Overall, the incidence of mTOR pathway mutation in patients with ICA was 14% and no pathogenic mutations were found in the patients without ICA.
Conclusion: Our findings confirm that ictal central apnea is a common finding in mTOR pathway alterations and highlight their potential role in the mechanisms involved in SUDEP risk. Furthermore, our results support: (i) the need of respiratory polygraphy during LTVM in MRI-negative focal epilepsy to detect peri-ictal breathing alterations, (ii) the potential relevance of genetic testing in these patients.

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1065 | Dynamic analysis of diagnostics and management of monogenic epilepsies and developmental and epileptic encephalopathies

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Purpose: To compare the spectrum of detected gene mutations in patients with epilepsies and developmental and epileptic encephalopathies (DEE) over the past 3 years of clinical practice of specialists in epilepsy, including: analysis of diagnosed epileptic syndromes, methods of defining etiological diagnosis, treatment options and effectiveness.
Method: A multicenter retrospective study including patients of any age and gender with epilepsy or DEE (with mandatory presence of epileptic seizures) and verified gene mutations. The data set started in 2018 and was analyzed as of 2020 and 2023. As a result, the number of patients admitted to the checkpoints was 100 and 205, respectively, 87-90% of whom were children under 18 years of age.
Results: Over a three-year period, the number of patients with a confirmed monogenic disease increased by 2 times, and the number of genes with mutations increased from 67 to 98 variants. Mutations in the SCN1A gene (15%) remain the clear leader. Also, in the practice of epileptologists, patients with mutations in the genes CDKL5, PCDH19, KCNQ2, MECP2 (4-5% each) are consistently encountered. The number of referrals for whole exome sequencing increased from 9 to 18.6% (p=0.026) and the proportion of patients with mutation confirmation by Sanger sequencing increased from 32% to 50.7% (p=0.003). Up to 68% of patients with a confirmed gene mutation are patients with one or another DEE variant. Approaches to ASM therapy have not undergone significant changes. However, the volume of alternative methods (steroids, ketogenic diet, surgical methods, etc.) has slightly decreased from 52 to 45% (p=0.277), with an emerging trend towards increased therapy effectiveness (an increase in the proportion of patients without seizures was from 46 to 54%, p=0.09).
Conclusion: Regular analysis and expansion of practical experience in the etiological diagnosis of monogenic epilepsies and DEE has a positive effect on the targeted selection and therapy effectiveness.

1087 | 4-phenylbutyrate use and efficacy in *SLC6A1*-related neurodevelopmental disorders

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Purpose: *SLC6A1*-related neurodevelopmental disorders (*SLC6A1*-NDDs) are a group of genetic disorders characterized by intellectual disability, behavioral disturbances, and seizures. Some patients benefit from regular antiseizure medication (ASM) such as valproate and lamotrigine, but treatment options are still limited. Development of novel therapies is a tedious process, which is why drug repurposing has gained increased interest. 4-phenylbutyrate (4-PB) is a drug used to treat urea cycle disorders; however, studies have shown a positive effect in both animal models and patients with *SLC6A1*-NDDs. Here, we reviewed ASM use, including 4-PB, in a large cohort of patients with *SLC6A1*-NDDs.
Method: Data from patients with *SLC6A1*-NDDs is continuously collected internationally and stored in a local RedCap database. Clinical information includes genetic, clinical and treatment. Inclusion is aided by the patient advocacy groups (*SLC6A1* connect and *SLC6A1* Connect UK-AQ).

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Results: Data from 244 patients were available. 15.2% are unpublished. Epilepsy was observed in 84.7% of patients, 33.9% were seizure free, while 28.4% had ongoing seizures. The most used ASM was valproate (60 patients, 53% seizure free), lamotrigine (30 patients, 43% seizure free) and levetiracetam (22 patients, 36% seizure free). 42 patients were treated with 4-PB; 30 reported a positive outcome (seizure freedom/reduction, improved cognitive capabilities and/or improved behavior), while 8 reported adverse reactions (acidosis or severe anorexia). One patient became seizure free with a normalized EEG but regressed in behavior and cognition. Three patients reported no effect and no adverse reactions.

Conclusion: In *SLC6A1*-NDDs treatment options are limited, but drug repurposing shows promise for finding novel therapies. This includes 4-PB. While 4-PB has only been used for treatment in a small number of patients with SLC6A1-NDDs it is worth noting that 71% report a positive outcome, however the 19% that report adverse effects should be taken into consideration when counselling patients on treatment options.

1089 | Variants in *FLNB* gene associated with epilepsy in the Drosophila model

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Purpose: The protein encoded by the *FLNB* gene exhibits the ability to regulate cytoskeleton-dependent cell proliferation, differentiation and migration. *FLNB* variants have previously been demonstrated to be associated with skeletal system diseases. This study was aiming to investigate the relationship between *FLNB* and epilepsy, as well as to the potential epileptogenic mechanisms.

Method: Trios-based whole-exome sequencing was performed in a cohort of 298 patients with epilepsy (PWE) without acquired causes. A variety of bioinformatics approaches were employed to assess the pathogenicity of identified *FLNB* variants. The Gal4/UAS system in conjunction with RNAi techniques were utilized to develop Drosophila *cher* knockdown strains. Seizure-like behavior was monitored, brain neuronal activity was assessed via patch-clamp recordings, and brain morphological development was examined under the immunofluorescent staining.

Results: Nine *FLNB* variants, comprising five pairs of complex heterozygous variants and one homozygous variant, were identified in six unrelated PWE. Phenotypic heterogeneity was observed in these patients: two had generalized seizures, one of them had intellectual disability, and four had focal seizures, two of which presented cranial MRI abnormalities. All variants were predicted to potentially deleterious by various silico tools. Compared to the control flies *UAS-cher-RNAi*, the incidence of seizure-like behavior in Drosophila with whole-body cell knockdown *tub-GAL4>cher-RNAi* was significantly elevated (7.64 ±1.67% [n=6] vs 21.87 ±2.23% [n=7], p=0.0004). The frequency of spontaneous excitatory postsynaptic potentials (sEPSPs) was significantly higher in the knockdown group (0.88 ±0.19 Hz [n=5] vs 0.14 ±0.06 Hz [n=3], p=0.0279), as was the amplitude of sEPSPs (0.94 ±0.06 mV [n=5] vs 0.67 ±0.03 mV [n=3], p=0.0156). No significant differences were observed in brain structure.

Conclusion: *FLNB* mutations may potentially be associated with epilepsy. However, its epileptogenicity does not seem to be related to the abnormal neruon proliferation and migration, which needs further study.

1105 | Genotype-phenotype correlation of novel *SCN1A* variants selected from the Italian Registry of Dravet Syndrome Residras

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Purpose: Variants in the *SCN1A* gene, encoding the Nav1.1 sodium channel, are linked to a range of neurological disorders from mild genetic epilepsy with febrile seizures plus (GEFS+) to severe Dravet syndrome (DS). These variants may lead to loss-of-function (LoF), gain-of-function (GoF), or mixed LoF/GoF effects, resulting in significant phenotypic variability and diverse treatment responses (Guerrini et al., *Physiol. Rev*., 103, 433–513, 2023). Therefore, functional studies are critical to establish genotype-phenotype correlations and support therapeutic choices, especially to avoid contraindicated drugs. From the Italian Registry of Dravet Syndrome (Residras), novel *SCN1A* variants associated with DS (R1634Q, F984L) and GEFS+ (V1339A, A1940S, F773L) were selected (Balestrini et al., *Epilepsia Open*, 8(2):517-534, 2023). Except for A1940S, variants were predicted to cause pathogenic LoF or GoF effects using a machine learning model (Heyne et al., *Sci Transl Med*, 12(556):eaay6848, 2020). This study aimed to characterize Nav1.1 mutant channels and guide treatment strategies.

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Method: Nav1.1 wild-type (WT) and mutant channels were expressed in HEK293 cells, and sodium currents were recorded via whole-cell patch-clamp.
Results: Mutant channels displayed normal current amplitude and voltage-dependent activation. R1634Q, F984L, and V1339A negatively shifted voltage-dependent fast inactivation by +16, +10, and +7 mV, respectively, compared with WT. R1634Q also slowed recovery from fast inactivation. F773L accelerated both inactivation kinetics and recovery, while A1940S had no impact on Nav1.1 activity.
Conclusion: R1634Q and F984L cause LoF defects consistent with DS, emphasizing the need to avoid sodium channel blockers. V1339A correlates with mild GEFS+, while F773L exhibits mixed LoF/GoF behavior atypical for GEFS+. These results underline the importance of functional studies to personalize treatment for *SCN1A*-related epilepsies. (PNRR: M6/C2_CALL 2022, Project Code: PNRR-MR1-2022-12376642)

1177 | Genetic Alterations in Pediatric Patients with Cerebral Palsy and Epilepsy

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Purpose: Cerebral palsy (CP) is defined as a group of permanent disorders that affect the development of movement and posture, leading to activity limitations. Patients with CP often have coexisting neurodevelopmental disorders, such as intellectual disability in 27% to 45% of cases, epilepsy in 38%, speech disorders in 33% to 82%, and autism spectrum disorders in 3% to 9%. In this report, we share our experience with the genetic findings of a group of patients evaluated at our institution for CP and epilepsy.
Method: Clinical exome sequencing (CES) after routine karyotyping and chromosomal microarray was performed to identify causative variants and expand the spectrum of mutations associated with CP and epilepsy.
Results: Ten patients with CP and epilepsy were included in the study, comprising 6 males (60%) and 4 females (40%). Regarding the type of CP, 7 patients (70%) had spastic quadriplegia, 2 (20%) had spastic diplegia, and 1 (10%) had the athetoid type. In terms of comorbidities, 6 patients (60%) had a profound degree of intellectual disability (ID), 2 (20%) had a severe degree, 1 (10%) had a mild degree, and 1 (10%) had no ID. Additionally, 3 patients (30%) exhibited hypotonia during the neonatal period, 2 (20%) presented with congenital anomalies, and 1 (10%) had sensorineural hearing loss. Genetic testing revealed that 3 patients (30%) had copy number variants, including 15q11.2 deletion, 17p11.2 duplication, and 18p11.32 deletion. Another 3 patients (30%) were identified to have single nucleotide variants: SLC2A1, c.277C>T (p.Arg93Trp); CDC42BPB, c.4049G>A (p.Arg1350Gln); and GABRA1, c.962A>G (p.Tyr321Cys). Notably, 60% of patients with CP and epilepsy were diagnosed through clinical exome sequencing.
Conclusion: Genetic testing is considered useful for patients with coexisting cerebral palsy and epilepsy, as it enables rational treatment approaches that align with precision medicine.

1179 | Can non convulsive status epilepticus lead to the diagnosis of a genetic syndrome? Case report

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Purpose: Cloves syndrome (Congenital Lipomatous Overgrowth, Vascular Malformations, Epidermal Nevus, Spinal/Skeletal Anomalies/Scoliosis) is a very rare congenital disorder characterized by a combination of vascular, cutaneous, spinal, and bone or joint abnormalities.
Method: A 43-year-old female patient with a known history of intellectual disability was admitted with complaints of slurred speech, dull gaze, and urinary incontinence that began a day prior to presentation. She had a congenital asymmetric deformity affecting the left side of her body, with a longer left leg compared to the right. A prominent "sandal gap" between the first and second toes was noted on the left side. An electroencephalogram (EEG) showed electroclinical seizure activity. Differential diagnoses included nonconvulsive status epilepticus, prolonged postictal state and encephalitis. Findings were compatible with nonconvulsive status epilepticus, and intravenous diazepam was administered, suppressing epileptic activity. A subsequent EEG revealed sharp-slow wave paroxysms, most prominent over the left hemisphere. Levetiracetam was initiated at a dose of 3000 mg, followed by a maintenance dose of 1000 mg twice daily. Despite therapy, the patient experienced recurrent episodes of blank staring and urinary incontinence. A repeat EEG showed a background alpha rhythm with theta slow waves. The levetiracetam dose was increased, and no further seizures were observed. Brain MRI revealed multiple T2 and FLAIR hyperintense foci in the left frontoparietal white matter. The patient was referred for genetic testing to investigate a potential neurodevelopmental disorder, with results pending.
Results: Cloves syndrome is part of PIK3CA-related overgrowth syndromes, caused by somatic mutations in the

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PIK3CA gene. Phenotypic variations depend on the developmental stage of the mutation. Lipomatous masses are present at birth and may accompany capillary malformations. Most cases are reported in patients born to nonconsanguineous parents.
Conclusion: Diagnosis is based on clinical examination of vascular, cutaneous, spinal, and limb abnormalities. Genetic testing is necessary to differentiate from Proteus syndrome.

1296 | Antiseizure Medication Management for Dravet Syndrome: A Retrospective Analysis

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Purpose: Antiseizure medication recommendations for Dravet Syndrome (DS) have evolved over the past decade, particularly following the FDA approval of three new antiseizure medications. This study aims to evaluate the changes in clinical practice regarding antiseizure medication management in DS.
Method: We conducted a study involving patients with DS and confirmed *SCN1A* pathogenic or likely pathogenic variants between 2014 and 2023. The study was approved by the Boston Children's Hospital Institutional Review Board. Antiseizure medications and intervals from genetic testing to the initiation of the first-line therapies were recorded. Valproic acid, clobazam, fenfluramine, stiripentol, and cannabidiol were considered first-line therapies [1, 2]. We analyzed the difference in intervals between patients who received their genetic diagnosis in 2018 or later and those diagnosed before 2018.

Results: This study included 45 patients with Dravet syndrome, with a mean age of 84 ±28 months (range: 24 to 136 months). The interval from genetic testing to initiating one of the first-line therapies was 2.8 ±2.9 months (range: 0 to 8.8 months) in patients diagnosed in 2018 or later (n=21), and 10.2 ±14.3 months (range: 0 to 61 months) in patients diagnosed before 2018 (n=24). There was no statistically significant difference between the two groups regarding the time interval from genetic testing to the initiation of first-line therapy (p=0.068). Among the five first-line therapies, 28 patients (62%) were treated with clobazam, 12 patients (27%) with valproic acid, and 5 patients (11%) with cannabidiol. None of the patients received fenfluramine or stiripentol as first-line therapies. There was no difference between the two groups regarding initial first-line therapy (p=0.7).
Conclusion: First-line therapies were initiated sooner in patients with DS diagnosed in 2018 or later compared to those diagnosed before 2018. Among the first-line antiseizure medications, clobazam was the most frequently used, followed by valproic acid and cannabidiol.

1317 | ODLURO Syndrome: A Recently Identified Cause of Neurodevelopmental Delay and Epilepsy - expanding the phenotype

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Purpose: The O'Donnell-Luria-Rodan (ODLURO) syndrome is an autosomal-dominant neurodevelopmental disorder caused by pathogenic variants in the *KMT2E* gene. Its clinical presentation is heterogeneous, including neurodevelopmental delay, dysmorphism, and epilepsy, which has been reported in 30% of patients. Since its initial description in 2019, the growing recognition of ODLURO syndrome as a cause of epilepsy has led to its inclusion in routine genetic testing panels, enabling diagnoses in patients with long-standing epilepsy of previously unknown etiology. With this case report, we aim to contribute to the characterization of epilepsy in these patients.
Method: We present a clinical case of a patient with refractory epilepsy associated with ODLURO syndrome.
Results: A 43-year-old male was evaluated in a Neurology clinic for infantile-onset refractory epilepsy, characterized by generalized tonic-clonic seizures and focal left hemispheric seizures. His epilepsy is currently controlled with carbamazepine, levetiracetam and topiramate, with seizure freedom since 2022. His prior medical history was notable for macrocephaly and psychomotor developmental delay. Sleep-deprived electroencephalogram revealed identification of basal activity (theta rhythm) with paroxysmal multifocal discharges over the anterior bilateral and left temporal regions. Brain MRI showed diffuse cortical atrophy and atrophy of the left mammillary body and posterior column of the fornix with ipsilateral mesial temporal sclerosis. Neuropsychological assessment revealed severe intellectual disability (IQ = 36). Given the combination of infantile-onset epilepsy, history of neurodevelopmental delay and dysmorphic features, genetic testing was performed, revealing a previously undescribed pathogenic nonsense mutation in the *KMT2E* gene in heterozygosity (c.901C>T(p.(Gin301*)) and supporting the diagnosis of ODLURO syndrome.
Conclusion: This case underscores the role of genetic testing in establishing a definitive diagnosis in patients with

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long-standing epilepsy and neurodevelopmental delay, even in those with focal seizures and structural lesion. As ODLURO syndrome was only recently described, many cases likely remain undiagnosed, highlighting the potential for further identification in adult epilepsy clinics.

1336 | A Case Report of Lafora Disease Associated with NHLRC1 Gene Mutation

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Purpose: Lafora Disease (LD), which is classified among the group of progressive myoclonic epilepsies, follows an autosomal recessive inheritance pattern. This article aims to present a case in which eyelid myoclonus and progressive mental deterioration are prominent features and presenting with non-convulsive status epilepticus.
Method: A 39-year-old female patient presented to our emergency department with complaints of constant drowsiness, decreased communication with her surroundings, inability to walk, and continuous blinking for the past week. Neurological examination revealed open consciousness with impaired orientation, limited cooperation, dysarthric speech, and frequent eyelid myoclonus during the examination. Her medical history revealed that she had started experiencing myoclonus in her hands and involuntary eye blinking at the age of 13, and generalized tonic clonic seizures began at the age of 15. The routine EEG showed frequent generalized sharp slow-wave paroxysms on a background of severe bioelectric slowing, and the patient, who was considered to be in nonconvulsive status epilepticus, was admitted to the intensive care unit. Pentothal infusion was started. After 24 hours clinical and EEG improvements were observed. Five of her 8 siblings also had myoclonus in their hands and eye blinking. No significant findings were observed in laboratory tests. Based on the clinical presentation and history, a diagnosis of LD was suspected, and genetic analysis was performed. A homozygous mutation in the NHLRC1 gene was detected.
Results: Lafora Disease (LD) can be associated with fatal forms related to genetic heterogeneity, but there are also late-onset, slow-progressing, and more variable forms. It is known that cases with an NHLRC1 gene mutation, such as in our case, tend to follow a more favorable course.
Conclusion: Our case is noteworthy as it is a rare presentation of this disease in adulthood, and the identification of the genetic mutation adds value to this report.

1380 | CADASIL and epilepsy: a rare yet significant association

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Purpose: Epileptic seizures are rare in cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL), affecting approximately 10% of patients, and they seldom appear as the first or as an early sign of the disease. Although often associated with ischemic lesions, the underlying cause of the seizures may remain uncertain.
Method: We reviewed a cohort of 19 patients diagnosed with CADASIL at our institution and described the cases with epilepsy.
Results: Four patients (21%), two women and two men, aged between 43 and 70, were identified. All had a diagnosis of genetically confirmed CADASIL, with pathogenic *NOTCH3* gene mutations. Brain MRI revealed extensive white matter hyperintensities in all cases, with no ischemic cortical lesions or microhemorrhages. Epileptic seizures were the initial clinical presentation of CADASIL in two cases. Two patients experienced transient episodes of aphasia and right-arm paresthesia, with EEG revealing left temporal slow activity associated with epileptic activity. Another patient had recurrent seizures described as episodes of impaired awareness, some with right head version, and EEG showed focal left temporal slow activity. The fourth patient had an unprovoked bilateral tonic-clonic seizure, without epileptic activity in routine EEG; this patient was also diagnosed with type 1 neurofibromatosis exclusively with cutaneous involvement. There was no clear vascular event preceding the onset of epilepsy in any of the cases. The patients were started on antiseizure medication, with good control of seizures. Cognitive complaints were reported in three cases, and two progressed to dementia.
Conclusion: We present four clinically heterogeneous patients with CADASIL and associated epilepsy, which was the initial disease manifestation in two cases. We found a higher frequency of epilepsy in our series compared to previous reports. The occurrence of epileptic seizures in the absence of cortical lesions challenges the understanding of the pathophysiology underlying CADASIL-related epileptogenesis.

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1386 | DDC c.1357C>T Variant in a Patient from Uzbekistan with Aromatic L-Amino Acid Decarboxylase Deficiency and Seizures

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Purpose: The clinical spectrum of Aromatic L-Amino Acid Decarboxylase Deficiency ranges from severe to mild forms, including early-onset hypotonia, movement disorders, developmental delay, dysautonomia, pseudomyasthenic signs, sleep disturbances, behavioral abnormalities, and gastrointestinal dysfunction (Rizzi S et al. Behav Neurol. 2022;2022:2210555.). Seizure manifestations in Aromatic L-Amino Acid Decarboxylase Deficiency remain insufficiently documented and are considered rare. This clinical case, one of the first reported in Uzbekistan, expands the phenotypic spectrum of the disorder and may challenge current assumptions regarding seizure prevalence.
Method: A male patient, 5 years old, with developmental delay and hypotonia, presents with generalized tonic-clonic seizures, atonic seizures and focal tonic seizures, as well as non-epileptic attacks. According to clinical data, we performed video-EEG-monitoring, brain MRI (HARNESS protocol), and Whole Exome Sequencing (WES). Identified variants were verified according to ACMG standards (Richards S et al. Genet Med. 2015 May;17(5):405–424.) followed by Sanger sequencing in the proband and parents.
Results: Video EEG-monitoring revealed pathologic EEG findings, interhemispheric asymmetry of EEG recording of more than 70%, an EEG pattern of focal tonic seizure, and multifocal epileptiform discharges. Brain MRI scans showed left-sided cerebral hemiatrophy, areas of demyelination in the white matter of both hemispheres, and subdural hygroma in the fronto-temporal region on the left. WES analysis identified a pathogenic DDC c.1357C>T variant (PM3, PP3,PM2, PP2, PP5). Sanger sequencing in a proband and parents confirmed a homozygous DDC c.1357C>T variant in the proband, with both parents identified as carriers.
Conclusion: The DDC c.1357C>T variant is associated not only with movement disorders and oculogyric crises but also with a spectrum of seizure types, necessitating tailored therapeutic approaches. Further research is essential to elucidate the natural history of seizures in patients with Aromatic L-Amino Acid Decarboxylase Deficiency, ultimately improving clinical management and patient outcomes.

1394 | Evidence of causality of metabolic and lipid species in epilepsy disease risk, with strongest signals in genetic generalized epilepsies

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Purpose: 1) To analyze the overlap between metabolic syndrome genes and epilepsy genes. 2) To investigate the causal relationship between metabolites and lipids with the risk of epilepsy. 3) To identify epilepsy patient subgroups with unusual metabolite or lipid genetic profiles.
Method: Recent published large-scale metabolite and lipid GWAS have identified hundreds of associated genetic loci demonstrating that these quantitative traits have high SNP-heritability (median = 29%) and thus can be explained by genetic variation with strong genetic predictors. To investigate the potential causality of these traits on epilepsy risk, we used Mendelian Randomization. Specifically, the 2-sample MR framework, subject to meeting assumptions, was used to test 233 lipid and metabolic traits based on the GWAS by Karjalainen et al (2024) in conjunction with the most recent ILAE GWAS (2023) for epilepsy risk. Multiple testing was corrected for using the False Discovery Rate method.
Results: Four traits, all lipids, achieved significance for causality for genetic generalized epilepsy (GGE; $p<0.00056$). These are unsaturated fats, Omega3 percentage, MUFA percentage and PUFA by MUFA. No metabolic of lipid traits survived multiple testing correction for focal epilepsy or the 'all' epilepsy group, suggesting that the lipid signal is specific to GGE.
Conclusion: There is known overlap between metabolic disorders and epilepsy risk genes, e.g. GLUT1 deficiency - caused by mutations in *SLC2A1*. This, and anecdotal evidence of dietary impacts on seizure frequency, has led to expanded use of the ketogenic diet. The GLUT1 phenotypic spectrum is broad, ranging from severe developmental and epileptical encephalopathies to relatively mild GGEs. We provide statistical evidence that lipid-metabolites contribute to epilepsy risk. However, given the genetic and clinical heterogeneity of epilepsy it is crucial to determine which patients specifically are affected

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and whether metabolic background may be playing a disease modifying role that could be therapeutically targeted.

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1462 | Identification of the ABCB1 gene in pediatric epilepsy patients of Kazakhstan

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Purpose: Epilepsy is a chronic neurodegenerative disorder, affecting all people, despite of age and ethnicity. Among the six epilepsy causing factors, genetics plays a significant role. With the development of next-generation sequencing (NGS), numerous novel genetic variants associated with epilepsy have been discovered. The genetic basis of the disease is highly important, as specific genetic forms require different anti-epileptic drugs (AED) and treatment strategies. Nowadays, drug resistance is one of the challenges in management of epilepsy. This study aims to explore the genetic variants present in children epilepsy patients using NGS.
Method: Whole blood samples were collected from 10 pediatric epilepsy patients of Asian descent to perform whole-genome sequencing. The sequencing data was further analyzed using bioinformatic tools and annotated using ANNOVAR and public variants databases, such as ClinVar and Franklin Genoox. Identified variants were classified according to the American College of Medical Genetics and Genomics (ACMG) criteria: benign; likely benign; likely pathogenic; pathogenic and variant of unknown significance.
Results: The rs2032582 polymorphism of ABCB1 gene encoding P-glycoprotein, a transporter protein was identified among our pediatric epilepsy patients. 5 patients carried the T/T genotype, while 2 patients carried heterozygous (A/T) genotype. According to previous studies, ABCB1 gene is known to be involved in medication response and located in blood brain barrier endothelial cells. Suggested to play a role in AED response. However, database searches identified rs2032582 polymorphism as variant of uncertain significance (VUS). The direct contribution to epilepsy is still unclear.
Conclusion: Our findings indicate the high importance of the NGS in the genetic profiling and management of epilepsy. The identification of ABCB1 rs2032582 polymorphism in epilepsy patients of Kazakhstan highlights the need for further research to determine the clinical significance. This research has been funded by the

1472 | Beyond Seizures: Deep Phenotyping of $GABA_A$ Receptor Variants Reveals Functional Segregation and Predicts Risk of Gross Motor Dysfunction

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Purpose: This study aimed to investigate the motor, and cognitive outcomes as well as the epilepsy trajectories associated with gain-of-function (GoF) and loss-of-function (LoF) variants in the *GABRB2* and *GABRB3* genes. By employing a standardized phenotyping approach, we sought to investigate differences in cognitive and motor functions between and develop a risk prediction model for gross motor dysfunction
Method: Clinical information was collected through patient advocacy groups, international collaborations, and literature reviews. Gross motor function was classified using the Gross Motor Function Classification System, and functional assessments of variants were performed using electrophysiological recordings. Statistical analyses included Kruskal-Wallis tests, Dunn's post-hoc tests, and logistic ordinal regression.
Results: We analyzed data from 120 individuals for which functional characterization had been performed. Forty-nine individuals carried a *GABRB2* (25 GoF 24 LoF) and 71 individuals a *GABRB3* variant (31 GoF, 40 LoF). Substantial differences in epilepsy syndromes,

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age of seizure onset, and severity of motor and cognitive impairments were observed between the GoF and LoF groups. GoF variants were associated with earlier seizure onset ($p = 6.2x10^{-7}$, Kruskal-Wallis Test) and more severe gross motor dysfunction ($p = 4.1x10^{-4}$) and cognitive impairments ($p = 2.7x10^{-12}$) compared to LoF variants ($p = 4.1x10^{-4}$ and $2.7x10^{-12}$respectively, Kruskal-Wallis test with Dunn's post-hoc test). A strong correlation was found between the age of seizure onset and the severity of gross motor dysfunction in GoF variants, leading to the development of a risk prediction model.

Conclusion: This study highlights the distinct clinical trajectories associated with GoF and LoF variants in the *GABRB2* and *GABRB3* genes. Our findings underscore the importance of seizure onset and its relation to the risk of severe motor impairment. Lastly, the risk prediction model for gross motor dysfunction provides a valuable tool for clinicians in predicting outcomes and evaluating treatment efficacy.

1474 | An integrated single-cell and spatial transcriptomic atlas of human hippocampus in patients with temporal lobe epilepsy and hippocampal sclerosis

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Purpose: Hippocampal sclerosis (HS) is the most common neuropathology in patients with temporal lobe epilepsy (TLE). The spatial and cellular heterogeneity of epilepsy-associated alterations in the hippocampus remains unknown. Our study integrated spatial enhanced resolution omics-sequencing (Stereo-seq) and single-nucleus RNA sequencing (snRNA-seq) to obtain a single-cell and spatial transcriptomic atlas of hippocampus from patients with TLE-HS and controls.

Method: SnRNA-seq was performed on 19 hippocampal samples from 13 patients and 6 controls. Stereo-seq was performed on 9 hippocampal samples from 6 patients and 3 controls. Other data from 11 controls were obtained from two published snRNA-seq datasets. UMAP was used for cluster identification. Cellchat and COMMOT were applied to infer cell-cell communications. scDRS was applied to evaluate the enrichment of putative disease genes from genome-wide association studies in individual cells. SCENIC analysis was performed to identify regulons. DGIdb database was used to predict potential drugs.

Results: Diverse neuronal and glial subpopulations were systematically defined, including pyramidal cell subtypes from hippocampal subfields (subiculum, CA1, CA2, and CA3/CA4), two granule cell subtypes in dentate gyrus, and four astrocyte subtypes. The two granule cell subtypes exhibited different molecular characteristics and vulnerability to epilepsy. Astrocyte subtypes underwent distinct subregion-specific hyperplasia or loss and displayed molecular heterogeneity in the epileptic hippocampus. We further identified major epilepsy-related neuron-glia communications (e.g., NTS-NTSR signaling), key transcription factors (e.g., SOX2), and potential therapeutic drugs (e.g., metformin). Significant enrichment of epilepsy risk genes in ExN-CA1 subtype was observed. We also generated an interactive website (http://shiny.decodelife.net/epilepsy.human/) for data sharing and exploration.

Conclusion: We present an accurate and comprehensive view of the spatial and molecular heterogeneity of neuronal and glial subtypes in the human hippocampus under normal and epileptic conditions. Our study provides a cellular and molecular basis for an in-depth understanding of the mechanisms underlying TLE-HS and may facilitate the development of novel therapeutic strategies.

1477 | Single-Nucleus RNA Sequencing Reveals Cell-specific Dysregulation in the Hippocampus of a Mouse Model of CDKL5 Deficiency Disorder

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Purpose: CDKL5 Deficiency Disorder (CDD) is a devastating neurodevelopmental condition caused by mutations in the *CDKL5* gene, leading to early-onset seizures and intellectual disabilities. The molecular mechanisms underlying these symptoms remain poorly understood. This study aimed to characterize the transcriptional landscape of the

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hippocampus in a murine CDD model using single-nucleus RNA sequencing (snRNA-seq) to identify cell-specific dysregulations and potential therapeutic targets.

Method: Hippocampal tissues from wildtype (WT) and heterozygous (HET) female mice (B6.129(FVB)-Cdkl5$^{tm1.1Joez}$/J) were processed for snRNA-seq using the 10x Genomics Chromium platform. Nuclei were isolated, purified, and encapsulated into nanoliter-scale Gel Bead-In-Emulsions for barcoded transcriptomic profiling. Sequencing libraries were prepared and sequenced on an Illumina platform. Data processing included quality control, normalization, and differential gene expression analysis using Seurat v5, MapMyCells, and clusterProfiler. Gene Ontology (GO) enrichment analysis was performed to explore functional consequences of transcriptional changes in specific neuronal populations.

Results: Analysis revealed distinct transcriptional profiles across neuronal and glial cell types, with significant differential expression in glutamatergic neurons (intratelencephalic/extratelencephalic and dentate gyrus subtypes), GABAergic neurons, and oligodendrocyte progenitor cells (OPCs). GO analysis highlighted dysregulated kinase signaling pathways in glutamatergic neurons, providing insights into cell-specific mechanisms of dysfunction. Enrichment analysis suggested potential compensatory signaling mechanisms and identified novel therapeutic targets.

Conclusion: This study represents the first application of snRNA-seq to CDD providing a comprehensive transcriptional map of hippocampal cells in CDD, identifying distinct molecular changes in neuronal and glial subtypes and new insights into how loss of CDKL5 contributes to transcriptional heterogeneity. The findings highlight the effects of kinase signaling dysregulation, identifying novel genes as a potential driver of pathology and opening avenues for targeted therapies. Future research will focus on these findings and exploring therapeutic interventions to restore kinase function and mitigate disease impact.

1480 | Acetazolamide response in a UK cohort of adults and children with CHD2 associated epilepsy

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Purpose: CHD2 associated developmental and epileptic encephalopathy is most commonly drug refractory and there are no precision medicine approaches. A recent case series of 12 patients identified the potential for acetazolamide in the management of this condition, with some patients reporting complete seizure resolution. Our first adult on low dose acetazolamide went from weekly convulsive seizures to none for six months. For patients and families, it is important that this work is replicated in children and adults.

Method: We set up an observational study in the United Kingdom to report the outcomes of children and adults newly prescribed acetazolamide, in partnership with a CHD2 family group. We are collecting data from families by way of survey and interview, supplemented by information acquired from their clinicians. Data pre and post starting the acetazolamide will be analyzed to identify whether there was a significant change in their epileptic control. Secondary outcomes include changes in behavioral control or functional ability. We also provide videos displaying the types of seizures experienced by these patients.

Results: We will report on how many adults and children in the UK have started acetazolamide in 2025, from a CHD2 group of forty families, and we will present the long term follow-up of our first patient. We will look for side effects of acetazolamide and the potential for withdrawal of other anti-seizure medicines.

Conclusion: It is unclear whether the remarkable reports of acetazolamide response teach us something about CHD2 biology, or whether repurposing older anti-seizure medicines is an attractive strategy for developmental and epileptic encephalopathies. The emergence of a characteristic methylation profile for CHD2 may well lead to further biological insights.

1486 | Genetic and Clinical Characterization of Adult Patients with GABAA-receptor related disorders

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Purpose: Several studies describe the disease course of children with GABAA-receptor related disorders, however knowledge on the outcomes in adulthood are limited. This study aims to investigate the genetic and clinical characteristics of adult patients with variants in the *GABRA1, GABRB2*, and *GABRB3* genes.
Method: Through an international network and patient advocacy groups, we collected data from 54 adults with pathogenic variants in *GABRA1* (22 patients), *GABRB2* (8 patients), and *GABRB3* (24 patients) genes.

Results: The age at last data collection ranged from 18 to 62 years. Intellectual disability (ID) was common, with 66.6% (32/48) of patients exhibiting mild to severe ID. Language impairment was observed in 2/3 of the patients. Neuropsychiatric features, such as autism spectrum disorder, anxiety, and aggressive behavior, were observed in 57.8% (22/38). Epilepsy was present in 98.1% (53/54) of individuals, with a wide range of initial epilepsy syndromes including Dravet Syndrome, Lennox-Gastaut Syndrome, and Generalized Epilepsy with Febrile Seizures Plus (GEFS+). Seizure onset varied widely from day 1 to 16 years (median age – 15 months). Seizure frequency ranged from daily to seizure-free, with 58.5 % (24/41) of patients achieving seizure freedom. Age of seizure offset, ranged between 2-44 years (median age – 17.5 years). The majority of variants occurred *de novo*. The functional effects of the variants were known in 76.9% (30/39): 86.6% (26/30) being loss of function, and 13.3% (4/30) – gain of function.
Conclusion: Half of our cohort with GABAA receptor variants achieve seizure freedom. However, a significant number of patients will continue to experience comorbidities such as ID, language impairment, and behavioral disorders, ranging from mild to severe. Understanding these characteristics will enhance diagnosis, treatment, and outcomes in the adult GABAA cohort.

1487 | *SLC6A1*-related neurodevelopmental disorders: prevalence and characterization of non-epileptic findings

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Purpose: *SLC6A1*-related neurodevelopmental disorders (*SLC6A1*-NDDs) are a group of genetic disorders characterized by epilepsy and intellectual disability (ID) in particular. Several smaller cohorts of *SLC6A1* patients have been published, however only recently the focus has shifted from the epileptic phenotype to the broader concept of SLC6A1-NDDs that also includes behavioral and neurological challenges, such as movement disorders. As the community prepares for clinical trial readiness it is important to uncover all aspects of SLC6A1-NDDs. Here, we sought to delineate the phenotypic spectrum and provide novel details on non-epileptic findings in a large cohort.
Method: Data from patients with *SLC6A1*-NDDs is continuously collected internationally and stored in a local RedCap database. Clinical information includes genetic, clinical and treatment. Inclusion is aided by the patient advocacy groups (*SLC6A1* connect and *SLC6A1* Connect UK).
Results: Data from 244 patients were available. 46% of variants arose de novo, 9% were inherited from a (mildly) affected parent, while inheritance was unknown for 45%. Motor development was normal in 70%. 85% had epilepsy. ID before seizure onset was reported in 31% (mild to moderate) and in 65% after epilepsy onset (mild to severe). Other observations included neurological abnormalities (71%), movement disorders (29%), language impairment (75%), sleep disorders (29%) and behavioral disorders (62%).
Conclusion: As evident from our findings in this the largest cohort published, *SLC6A1*-NDDs implicate much

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more than seizures. In fact, issues such as behavioral challenges and language impairment are findings that have a prominent impact on patient and family quality of life and needs further attention as the *SLC6A1* community prepares for clinical trials.

1489 | A *LAMC3* mutation linked with lissencephaly associated with pachygyria in different cortical lobes

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Purpose: Malformations of cortical development (MCD) include several disorders characterized by the disruption of the cortex formation during development, like focal cortical dysplasia (FCD), polymicrogyria and lissencephaly. Patients usually present pharmacoresistant epileptic seizures, intellectual disability and other symptoms. Important findings support that MCD results from germline, somatic or both "two hit" mutations of genes. In this project, we analyzed the whole exome sequencing (WES) genetic data of patients diagnosed with MCD and associated them with their phenotypic data.
Method: Nine patients (n = 9) with a clinical diagnosis of FCD or MCD with intractable epilepsy were included in this study. They underwent WES and a comprehensive DNA variant analysis was performed using the Nextflow nf-core/Sarek pipeline following filtering with the VarFish software. A gene panel was searched for germline variants in genes associated with MCD or epilepsy.
Results: Clinical data were collected from eight patients with MRI-positive FCD and one with lissencephaly. WES analysis identified a homozygous *LAMC3* pathogenic variant (p.D1061Tfs*20) in a male patient diagnosed with lissencephaly associated with pachygyria, involving the occipital, posterior temporal and parietal lobes. The patient has intellectual disability and has been experiencing frequent focal dyscognitive seizures since 6-years old. The variant was validated with Sanger sequencing. The patient carries also a *TSC2* missense variant of uncertain significance (VUS) and two missense VUS in two MCD-associated genes (*PEX10, TSEN34*). A novel missense *PIK3R2* variant was identified in an FCD patient. The other patients had missense VUS in genes associated with MCD and/or epilepsy.
Conclusion: The unpublished pathogenic germline *LAMC3* variant detected in a patient with *lissencephaly* enhances the findings of similar published *LAMC3*-associated phenotypes. It could provide a possible framework for efficient *LAMC3* testing in patients with comparable phenotypes. The non-existing pathological germline variants in mTOR pathway genes enhance the possibility of the somatic second-hit hypothesis in FCD cases.

1512 | Clinical Heterogeneity in Genetic Sleep-Related Hypermotor Epilepsy – A Systematic Review of Published Cases

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Purpose: Sleep-related Hypermotor Epilepsy (SHE) can be caused by genetic variants in nicotinic acetylcholine receptors (nAChRs), KCNT1, and GATOR1 subunits. We aimed to ascertain the impact of genetic etiology on clinical presentation and treatment responses, as all evidence regarding phenotypic heterogeneity within the syndrome has so far been anecdotal.
Method: We conducted a systematic review following PRISMA guidelines, identifying 345 patients with genetic SHE: 151 featured variants in the three nAChR genes (CHRNA4, CHRNB2, CHRNA2)), 65 in KCNT1, and 129 in the three GATOR1 genes (DEPDC5, NRPRL2, NPRL3). Extracted data included age at seizure onset, semiology, clustering, and frequency of seizures, treatment responses, and cognitive/psychiatric comorbidities. Statistical analyses included the chi squared test for comparison of categorical variables and the z and t-tests for comparison of continuous variables.
Results: The average age of seizure onset for KCNT1 was lower (5.85 years, SD ±4.7) compared to nAChRs (8.66 years, SD ±5.28, P=0.0021). Treatment resistance was more frequent in KCNT1 (71%, X2=13.105, P=0.0003) and GATOR1 (65%, X2=11.5237, P=0.0007), and remission rates lower, compared to nAChRs (43%). Some level of response to sodium channel-blockers was seen in about 42% of all patients with genetic SHE. Seizure semiology seemed to differ between the groups, with KCNT1 patients presenting with tonic asymmetric seizures more

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frequently and nAChR displaying a higher prevalence of seizures lacking hypermotor features. Cognitive and psychiatric comorbidities, particularly intellectual disability, appeared more frequent in patients with KCNT1 variants (82%) compared to nAChRs (51%, X2=15.2489, P=0.0001) and GATOR1 (44%, X2=23.0475, P<0.0001), as was status epilepticus.

Conclusion: Current evidence hints at significant differences in clinical presentation between the three genotypic groups associated with SHE, however, future studies need to address possible biases introduced by inconsistent reporting of relevant data and lack of longitudinal follow-up.

1548 | Germline genetic signatures of epilepsy surgery response: an individual-case meta-analysis

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Purpose: While traditionally considered for focal structural epilepsies, an increasing number of germline genetic epilepsies exhibit focal or lateralized features, making surgical intervention a viable option. However, the impact of genetic etiology on surgical outcomes remains poorly understood.

Method: We systematically reviewed Scopus and PubMed through November 2024, identifying observational and interventional studies reporting seizure outcomes in individuals with pathogenic/likely pathogenic variants in epilepsy-associated genes who underwent resective surgery. Exclusions included tuberous sclerosis, callosotomy, and neuromodulation cases. Additionally, we identified cases from the Cleveland Clinic and Mayo Clinic healthcare systems following the same criteria. Genetic categories were assigned using the PANTHER classification system. Kruskal-Wallis and Fisher tests were used for comparisons, with Bonferroni correction applied (α=0.05).

Results: We analyzed 206 literature cases from 61 publications and 28 in-house cases. Post-surgical seizure freedom at a median follow-up of 24 months (IQR 12–42.5) was recorded in 82/118 mTORopathy (70%), 9/36 channelopathy (25%), 17/28 copy number variant (CNVs; 61%), 4/17 synaptopathy (23.5%), 8/11 vascular disorder (73%), 5/9 overgrowth disorder (56%), and 6/18 other disorder cases (33.3%; p<0.001). Over 80% of cases in all categories were MRI-lesional with the exception of channelopathies (64%) and synaptopathies (76.5%; p=0.008). mTORopathies had higher odds of seizure freedom (OR 3.24, 95% CI 1.84–5.77), while synaptopathies (OR 0.23, 95% CI 0.05–0.76) and channelopathies (OR 0.22, 95% CI 0.09–0.51) had significantly lower odds compared to other genetic categories. This also applied to lesional cases (mTORopathies: OR 3.06, 95% CI 1.61–5.91; synaptopathies: OR 0.24, 95% CI: 0.06-0.57; channelopathies: OR 0.2, 95% CI 0.06–0.57).

Conclusion: Resective epilepsy surgery may benefit individuals with germline genetic epilepsies across various etiologies, though outcomes vary. Channelopathies are associated with particularly unfavorable outcomes, highlighting the need for further research into the role of presurgical genetic testing and informing individualized outcome prediction for surgical candidates.

1589 | SEEG data in two patients with temporal epilepsy of genetic origin with NPRL2 and NPRL3 variants

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Purpose: The *NPRL2* and *NPRL3* genes, together with the *DEPDC5* gene, encode the GATOR1 complex of the mTOR pathway. Variants in these genes are often responsible for focal epilepsy phenotypes (frontal or temporal), sometimes associated with cortical malformations such as focal cortical dysplasia, particularly type 2. These conditions may lead to surgical resection; however, outcomes can be variable.

Method: We performed an SEEG in two pediatric patients with drug-resistant temporal focal epilepsy, each carrying pathogenic variants in *NPRL2* and *NPRL3*, respectively.

Results: The first patient, a 13-year-old girl with an inherited *NPRL2* variant (p.Met1), presented with a left temporal epilepsy and negative MRI findings. However, FDG-PET revealed extensive left temporal hypometabolism affecting the temporal pole, the mesial and basal temporal structures, and the anterior lateral neocortex. SEEG demonstrated an extensive epileptogenic zone involving the mesial, basal, and lateral temporal regions, extending posteriorly to the temporo-parietal, and the temporo-occipital junction. Due to the significant functional risks, surgery was not recommended for this right-handed patient.

The second patient, a 17-year-old boy with an inherited *NPRL3* variant (p.Asn133ThrfsTer6), suffered from lesional right temporal epilepsy with a large lesion compatible with a focal cortical dysplasia on FLAIR imaging, located at the right lateral temporo-occipital junction. FDG-PET showed hypometabolism within the lesion, extending to both temporal lobes, with more extensive hypometabolism on the left. SEEG revealed a unique seizure pattern originating from the right lateral posterior dysplasia, spreading to both temporal lobes, and ending asynchronously in the left temporal lobe.

Conclusion: These two cases illustrate the importance of performing SEEG in patients with *NPRL2* and *NPRL3* variants prior to any surgical procedure, even in patients with focal lesions suggestive of dysplasia. SEEG findings can reveal more complex and extensive epileptogenic networks, which likely explain the moderate success rates of surgery reported in the literature.

1600 | Developing minimum reporting standards for research articles on the treatment of genetic epilepsies

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Purpose: Advancements in next-generation sequencing have accelerated gene discovery in the epilepsies over the past decade. The Genomics England epilepsy panel now includes over 600 genes with well-established links to epilepsy. This growing body of genetic discoveries has significantly increased research into genetically-mediated epilepsies, yet progress in developing targeted therapies has been slow. A key challenge in epilepsy genomics research is the lack of standardized reporting of phenotypic, genomic, and therapeutic data. Without consistent data-sharing practices, research findings remain difficult to compare or translate into clinical applications. Furthermore, no expert consensus exists on best practices for reporting research in this field.

Method: To address this, we conducted a comprehensive PubMed literature search for research articles on monogenic epilepsies published between June 2022 and June 2024, focusing on genotype-phenotype correlations. Our search retrieved 2,610 articles, of which 1,009 met our inclusion criteria. Using a structured questionnaire, we evaluated how comprehensively these studies reported phenotypic, genomic, and therapeutic information. Further, we will conduct a modified Delphi survey, engaging experts in epilepsy genomics to establish key elements are required in research articles.

Results: The results will provide insights into the consistency and quality of current research practices. Preliminary findings indicate significant variability in how phenotypic, genomic, and therapeutic information are reported. The Delphi process will define core reporting elements through expert consensus. The final Delphi survey findings will inform the development of a consensus guideline for minimum reporting standards in epilepsy genomics research.

Conclusion: Adopting standardized reporting will improve data usability, harmonization across studies, and clinical translation. Greater consistency will enable more effective data integration, allowing for better meta-analyses, reproducibility, and clearer genotype-phenotype correlations. Structured clinical and genomic reporting will better equip researchers and clinicians to translate findings into real-world applications. This initiative will bridge the gap between gene discovery and therapy development, advancing personalized epilepsy medicine.

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1604 | Mitochondrial dysfunction in monogenic epilepsies

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Purpose: Differentiating monogenic and chromosomal developmental and epileptic encephalopathies (DEEs) from mitochondrial disorders (MDs) with epilepsy can be difficult based on clinical and biochemical features alone. Assessing muscle functional assays in patients with epilepsy with a genetic diagnosis offers a unique opportunity to examine patterns of mitochondrial dysfunction in monogenic/chromosomal DEEs compared to genetically confirmed MDs.
Method: Clinical and biochemical data were reviewed for patients with suspected MD and epilepsy who underwent a muscle biopsy between 2005 and 2015. Patients were categorized into four groups based on their final diagnosis. The Mitochondrial Disease Criteria (MDC) were scored for every participant. Group differences were calculated using Fisher's Exact, ANOVA, and Kruskal-Wallis tests.
Results: The cohort included 27 patients: 11 (40.7%) with a DEE, 4 (14.8%) with a genetically confirmed MD (2 with and 2 without respiratory chain defects), 8 (29.6%) with a suspected MD without genetic confirmation, and 4 (14.8%) with a non-mitochondrial metabolic disease. Mitochondrial dysfunction was prevalent across all groups; 85% met probable or definite MD criteria on the MDC, over 70% had elevated plasma lactate (>2.5 mmol/L), and 92% showed impaired ATP production in muscle functional assays. Surprisingly, moderate-to-severe complex dysfunction was observed in all groups except the confirmed MDs.
Conclusion: This study demonstrates that significant mitochondrial dysfunction occurs in non-mitochondrial DEEs, the underlying mechanism is most likely multifaceted and patient specific. Patients previously diagnosed with MDs based on clinical criteria may benefit from whole exome sequencing (WES), which could identify pathogenic variants responsive to targeted therapy. Future steps may involve exploring whether treatment or prognosis of non-mitochondrial DEEs should be tailored to mitochondrial function.

1624 | Whole genome sequencing insights in child epilepsy in Kazakhstan

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Purpose: Epilepsy is a multifactorial disease. However, approximately 70-80% of epilepsy cases have genetic etiology. Breakthrough in next-generation sequencing allowed us to understand the genetic basis of the disease and identified over 1000 genes correlated with monogenic forms of the disease. The main aim of this study was to examine the genetic landscape of children with epilepsy in Kazakhstan using whole-genome sequencing
Method: The study involved 10 Kazakh children with epilepsy of unknown cause. Patients were recruited and hospitalized at the Department of Pediatric Neurology of the University Medical Center, Nazarbayev University. All samples were screened on whole genome sequencing using NovaSeq6000 high throughput platform. Identified variants were classified using public variant databases. ACMG criteria were implemented for variant classification
Results: Our study identified ten pathogenic, three likely pathogenic and eight variants of unknown significance. Several genes are associated with epilepsy and neurodegenerative disorders. Pathogenic variant in KCNT1 (rs397515404) and likely pathogenic variant in ARX (rs1064794843) correlated with infantile epileptic encephalopathy and developmental delay. Both variants have a minor allele frequency less than 1%. Additionally, other mutations in genes ABCA4, GJB2, HFE and SLC6A4, which are not associated with epilepsy were identified
Conclusion: This study provides insights into the genetic landscape of epilepsy in Kazakhstani patients. These findings shed light on the importance of genetic screening for further personalized treatment suggestions. Future research focused on the validation of genomic findings is required

1627 | Epilepsy-Associated Chromatin Conformation and Structural Variants Revealed by Hi-C

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Purpose: Epilepsy is a heterogeneous neurological condition influenced by an array of genetic and epigenetic factors. While prior studies have underscored the epigenetic regulation, the contribution of higher-order chromatin structure remains insufficiently characterized. This study seeks to address this knowledge gap by applying Hi-C analysis to an expanded cohort of epilepsy samples—including MOGHE (malformations of cortical development with oligodendroglial hyperplasia and epilepsy), polymicrogyria (PMG) case, and glioneuronal tumors —alongside no-epilepsy autopsy controls.
Method: We performed high-throughput Hi-C to investigate 3D genome organization. We examined compartmentalization (A/B compartments), topologically associating domains (TADs), and potential structural rearrangements such as translocations. Additionally, we correlated these chromatin architectural features with clinical and cytogenetic findings, including instances of Y chromosome abnormalities.
Results: Our expanded Hi-C analysis demonstrates consistent patterns of denser chromatin in MOGHE samples alongside pronounced TAD domain shuffling compared to controls. MOGHE samples showed commonalities matching their overall phenotype but also differences according to their distinct genotypes. HiC sequencing confirmed somatic Y chromosome gain in some MOGHE cases both male and female. PMG showed a recurrent translocation on chromosome 1q, whereas the tumor sample exhibited widespread structural rearrangements that could affect gene regulation. Collectively, these findings highlight diverse chromatin architecture disruptions across multiple epilepsy subtypes and associated with chromosomal imbalances.
Conclusion: These findings expand our understanding of the 3D genomic landscape in epilepsy, highlighting how chromatin conformation may drive or modulate disease progression across diverse subtypes. The identified translocations and TAD disruptions underscore the importance of structural genome variations in epilepsy's etiology. Future investigations targeting these chromatin alterations hold promise for novel diagnostic markers and therapeutic approaches, potentially improving patient outcomes.

1634 | Genetic Susceptibility for Attention-Deficit/Hyperactivity Disorder and Autism Spectrum Disorders in Children Born to Women with Epilepsy

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Purpose: Children of women with epilepsy have a higher prevalence of Attention-Deficit/Hyperactivity Disorder (ADHD) and Autism Spectrum Disorder (ASD), compared to the general population. The contributions of genetic and environmental factors such as *in utero* antiseizure medication (ASM) exposure, remain unclear. This study assessed whether polygenic risk scores (PRSs) for ADHD and ASD are elevated in these children and explored associations with neurodevelopmental traits.
Method: We included children of women with epilepsy (n=422) and without epilepsy (n=73,300) from the Norwegian Mother, Father and Child Cohort Study (MoBa). PRSs for ADHD and ASD in children were calculated to assess genetic susceptibility. Neurodevelopmental traits such as hyperactivity, inattention, social difficulties, language difficulties, repetitive behavior, and motor difficulties were measured using questionnaire-derived z scores at age 0.5, 1.5, 3, 5 and 8 years.
Results: Children of women with epilepsy had higher PRSs for ADHD, not ASD, compared to children of women without epilepsy. ADHD PRSs showed a stronger association with hyperactivity and inattention in children of women with epilepsy, particularly at 8 years (β=0.18, 95%CI=0.04-0.31 and β=0.21, 95%CI=0.07-0.34, respectively) compared to the general population (β=0.13, 95%CI=0.11-0.14 and β=0.12, 95%CI=0.10-0.13, respectively). ASD PRSs showed stronger associations with motor difficulties at 5 years and language difficulties at 8 years in children born to women with epilepsy (β=0.13, 95%CI=-0.06-0.28 and β=0.10, 95%CI=-0.04-0.24, respectively), compared to the general population (β=0.03, 95%CI=0.02-0.0 and β=0.02, 95%CI=0.00-0.03, respectively). Adjusted R^2 values were small indicating limited variance explained by the models.

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Conclusion: Genetic susceptibility to ADHD measured by PRSs, is higher in children of women with epilepsy, likely contributing to their increased risk for neurodevelopmental disorders. However, the limited predictive power of PRSs underscores the need to integrate genetic, epigenetic, and environmental factors for improved risk prediction and preventive strategies.

1661 | Mega-corpus-callosum syndrome with cerebellar hypoplasia and cortical malformations (MCC-CH-CM) related to MAST1 gene: an accurate electroclinical case description

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Purpose: To describe the clinical presentation, diagnosis, and long-term follow-up of a patient with MCC-CH-CM syndromeassociated with a MAST1 gene variant. As a very rare condition with only 16 reported cases, seizures are frequently noted, but few reports have described the epileptic features of this syndrome. This study focuses on the electro-clinical characteristics, emphasizing their relevance for diagnosis and treatment.
Method: We present the case of a 16-year-old patient diagnosed with MCC-CH-CM, who has been followed at our center since his 22 months. The patient's clinical progression, electroencephalogram (EEG) patterns, MRI findings, and genetic analysis are reviewed.
Results: The patient exhibited focal seizures beginning at 3 months. He underwent treatment with Valproic Acid, with partial response, and subsequently was started on Levetiracetam and Clobazam. Seizures, including tonic-clonic ones, increased in frequency and varied in semiology during childhood, often triggered by fever or strong emotions. The patient's EEG revealed interictal abnormalities, including theta alfa-like activity with medium-high voltage on the anterior and vertex regions associated with spike-and-wave patterns, that activate during sleep. MRI showed mega-corpus callosum with cerebellar hypoplasia and abnormalities of the posterior cranial fossa. Genetic analysis identified a de novo MAST1 variant (c.1549G>A, p.Gly517Ser). The patient's phenotype is consistent with the previously described characteristics of MAST1 mutations, which include hypotonia, developmental delay, and varying degrees of motor and cognitive impairment. Seizures are also common in these patients; however, due to the limited number of reported cases, it is not possible to define a typical semiology.
Conclusion: This case underscores the complexity of MAST1-related disorders, emphasizing the need for further research on their electroclinical profile, therapeutic prospects, and the diagnostic role of MRI. Investigating clinical variability and potential electroclinical markers remains crucial.

1751 | Genes and Epilepsy

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Purpose: To characterise the local population of patients with clinical suspicion of genetic epilepsy.
Method: This observational retrospective study reviewed genetic tests performed between 2020 and 2024 in patients with suspected genetic epilepsy. Data was retrieved from electronic clinical records. Patients with mitochondrial diseases or chromosomal abnormalities were excluded.
Results: A total of 27 patients were included, 9 male and 18 female, with a mean age of 30 years. The median age of the first seizure was 11 years. A positive family history of epilepsy was reported in 11 patients, while only two patients reported a history of febrile seizures in childhood. 20 cases were classified as generalized epilepsy, 6 as focal epilepsy, and one as of unknown classification. Cerebral imaging revealed abnormalities in 13 patients, while 12 showed no abnormalities; two imaging results were unavailable. 16 patients were noted to have persistent EEG abnormalities, and in 12 of these patients these were epileptiform. Eight of the genetic tests were classified as variants of uncertain significance or were awaiting feedback from the collaborating genetics team or further testing. 19 patients obtained a definitive molecular diagnosis. Six of these were related to core epilepsy genes (CEGs), another six to developmental and epileptic encephalopathy genes (DEEGs), and seven to seizure-related genes (SRGs), suggesting a combination of structural and genetic etiologies. Among the nine cases classified as refractory epilepsy, two were associated with CEGs, two with DEEGs, one with

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an SRG, and the remainder with variants of uncertain significance.

Conclusion: Genetic testing in epilepsy is clinically relevant, not only for diagnosis but also for its potential in predictive testing, but remains challenging, since known mutations currently explain only a small proportion of epilepsy cases.

1806 | Delta Power Analysis in EEG of Patients with Mitochondrial DNA Depletion Disorders

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Purpose: To evaluate delta power in the EEG of patients with mitochondrial DNA depletion disorders and assess the future potential of this measure as a biomarker in mitochondrial disease.

Method: We analyzed EEGs of patients with mitochondrial DNA depletion disorders. Patients were primarily identified from an ongoing therapeutic clinical trial using pyrimidine deoxynucleosides to treat individuals with these conditions (registered at https://clinicaltrials.gov/study/NCT04802707). In the trial, all patients have a baseline EEG prior to starting the investigational product; this was the EEG used for analysis. We assessed delta power as the primary outcome measure, using relative delta power and power of other frequency ranges as secondary outcomes.

Results: We included 30 patients with mitochondrial DNA depletion disorders due to pathogenic variants in genes including *POLG*, *FBXL4*, *SUCLG1*, *SUCLA2*, and *RRM2B*. Sample sizes were too small to make meaningful statistical comparisons between different genetic etiologies; however, some trends were identified that suggested delta power could be useful in differentiating phenotypes of patients with POLG-related disorders.

Conclusion: Delta power and other frequency analyses have potential as biomarkers in mitochondrial disease, but data from larger cohorts, as well as sequential data from individual patients, are necessary to clarify the clinical utility.

1808 | Identification of potential microRNA biomarkers in pediatric patients with refractory epilepsy

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Purpose: This study aims to identify novel differentially expressed microRNAs (miRNAs) in pediatric patients with refractory epilepsy (RE), assessing their potential as biomarkers for prognosis. By analyzing a preliminary cohort of patients, we seek to contribute to the understanding of the molecular mechanisms underlying epilepsy refractoriness.

Method: 23 patients with RE treated in the reference hospital "Fundación Hospital Pediátrico La Misericordia (HOMI)", located in Bogotá, were sampled for whole peripheral blood to extract miRNA for further sequencing. As a preliminary analysis, data obtained from three patients was processed, performing quality filtering with FastP, miRNA quantification using Bowtie2-EdgeR, mirTRace, and mirDeep2, and differential expression analysis with DESeq2. Additionally, publicly available miRNA sequencing data from epilepsy patients was reanalyzed for comparison.

Results: The analysis identified 73 differentially expressed miRNAs, with 110 overexpressed and 63 under expressed in RE patients compared to controls. Four miRNAs (hsa-miR-3613-5p, hsa-miR-15a-5p, hsa-miR-194-5p, and hsa-miR-153) showed significant overexpression and have been previously associated as potential epilepsy biomarkers. These results suggest a possible role of these miRNAs in the pathophysiology of RE.

Conclusion: These preliminary findings highlight the potential of specific miRNAs as biomarkers for RE. The study is currently being expanded to include data of pending 20 RE patients and 30 control individuals with drug-sensitive epilepsy (DSE) to validate these results and explore the potential clinical implications. This research will provide valuable information for the development of personalized treatment strategies for RE patients. This work has been supported by the Colombian Ministry of Science through the project with contract number 760-2021, awarded to Universidad de los Andes, HOMI, and Biotecgen.

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1824 | Electro-clinical and molecular characterization of patients with SYNGAP1-associated encephalopathy in Argentina

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Purpose: To describe the electro-clinical and molecular characteristics of 18 patients with clinically relevant variants in SYNGAP1.

Method: Descriptive observational work on a series of cases of patients diagnosed with SYNGAP1 encephalopathy. SYNGAP1 gene encodes a synaptic Ras-GTPase activating protein, expressed in excitatory neurons. Loss of function due to deleterious variants in the SYNGAP1 gene is associated with epileptic and developmental encephalopathy.

Results: We present 18 patients, with an average age at molecular diagnosis of 10.4 years (range 1.6 years-28 years). All presented moderate to severe developmental impairment and epilepsy. The initial manifestations were central hypotonia (80%) and absence seizures (20%). Epileptic seizures began at 3.1 years (range 0.75-18 years); eyelid myoclonus with absences, and myoclonic absences were the most frequent seizures (57%). Other types of seizures were myoclonus and atonic myoclonus (50%), atypical absences (42.85%), atonic seizures (35.7%), febrile seizures (28.57%), reflex seizures with swallowing (42.85%). %). All presented uncoordinated walking, achieving ambulation at 2.3 years (range 1.7-6 years). A patient at 10 years old still does not walk. Acquisition of first words at 2.6 years; 3 patients are non-verbal. The most frequent interictal pattern was generalized spike and polyspike wave paroxysms. 92.8% presented autism and high pain threshold, sleep problems (57%) and compromised sucking/swallowing/chewing (28.5%) All presented clinically relevant variants (11 pathogenic/7 probably pathogenic) in SYNGAP1: missense (12.5%), nonsense (43.7%), frameshift (25%).

Conclusion: The presence of global developmental delay, eyelid myoclonus with absences, myoclonic and atypical absences, with reflex seizures are characteristics suggestive of SYNGAP1 encephalopathy. Taking into account that it is an EED with distinctive characteristics, it could be considered a syndrome of specific etiology.

1013 | ATP1A3 related status epilepticus: the potential benefit of early treatment with ketogenic diet

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Purpose: Mutations in the ATP1A3 gene, encoding Na/K ATPase alpha3 catalytic subunit, have been implicated in the pathophysiology of several neurological conditions, such as alternating hemiplegia of infancy and rapid-onset dystonia-parkinsonism. There is growing evidence of their role in the genesis and progression of epileptic seizures and predisposition to status epilepticus. This case illustrates the therapeutic challenge of ATP1A3 related epilepsy.

Method: Case report.

Results: 18-year-old female patient with generalized choreodystonia associated with ATP1A3 gene mutation and early onset epilepsy medicated with levetiracetam 1000mg 12/12h and clonazepam 2.5mg daily. The patient developed refractory convulsive status epilepticus with bilateral frontal and frontotemporal epileptic activity on electroencephalogram. Despite fever, there was no definite infectious focus. MRI showed left temporal mesial sclerosis. The condition was managed with 4 anti-epileptic drugs (AEDs) and a week of sedation. Two weeks later, new bilateral tonic-clonic seizures were witnessed, with progression to super-refractory status epilepticus. A urinary infectious focus was identified and treated. The patient underwent treatment with 5 AEDs and sedation with propofol, midazolam and ketamine. As status epilepticus persisted, a barbiturate coma was induced and ketogenic diet with a 4:1 ketogenic ratio was started. Significant ketonemia was achieved 9 days after diet onset and, given neurophysiological improvement and absence of seizures, sedation was slowly weaned off, without recurrence of status epilepticus.

Conclusion: Epilepsy and status epilepticus associated with ATP1A3 gene mutations have a high rate of

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pharmacoresistance and are associated with worse prognosis. Ketogenic diet is emerging as an effective therapeutic alternative. In this case, it was the only strategy that allowed for status epilepticus resolution. Further investigation is needed to clarify the potential benefits of an early implementation of this adjuvant strategy.

IGAP Implementation

691 | Access and visibility of International League Against Epilepsy Young Epilepsy Section (ILAE-YES) members within ILAE chapters: Global survey 2023

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Purpose: The Young Epilepsy Section of the International League Against Epilepsy (YES-ILAE) is a group of early career professionals from medical and non-medical backgrounds with an interest in epilepsy. YES-ILAE relies on ILAE national chapters for support. Although we expect all YES members to be members of an ILAE chapter, there is anecdotal evidence that some YES members have struggled with finding and joining an ILAE chapter. We designed this questionnaire to investigate whether problems with access exist for ILAE-YES members.
Method: We devised a questionnaire that investigated pre-requisites for chapter membership, costs of membership, and chapter awareness/support of YES ILAE. We distributed the questionnaire in the December 2023 ILAE chapter newsletter and collected data until the end of January 2024.
Results: We have collected responses from thirty-six out of 128 chapters (28.9 %). Except for Africa, we had responses from all ILAE regions. All chapters allow members under the age of 40 years and thirty-one (86.1%) chapters did not have medical education as a pre-requisite. Around 66% of chapters charge fees between 0 and 25 USD per annum. Only a third of chapters have YES representation on their board, and half knew of YES members in their chapter.
Conclusion: The response rate was adequate, but our insights are guarded. We have data that suggests that ILAE chapters are open to younger members in medical training, and membership fees are affordable. The lack of YES representation in chapter boards and clarity about the number of YES members in ILAE chapters may be why membership for non-medical professionals has not been considered. This may have implications in future development of the ILAE and the implementation of the Intersectoral global action plan on epilepsy (IGAP). We propose that this questionnaire should be repeated in a year's time to re-assess the situation.

748 | Access to diagnosis and treatment for epileptic people in Argentina: survey within the framework of the Intersectorial Global Action Plan (IGAP)

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Purpose: Following the aims of the Intersectorial Global Action Plan (IGAP) from World Health Organization (WHO) about epilepsy and other Neurological Disorders 2022-2030, the Argentine League Against Epilepsy (LACE) analyzed access to both diagnostic methods and treatments available to professionals assessing people with epilepsy in all Argentine provinces.
Method: Observational, prospective, cross-sectional study using clustered and stratified samples obtained through a structured questionnaire. Between March-April 2024 an emailed survey was sent to neurologists, child neurologists and clinical/family specialists in charge of people with epilepsy. Information about resources, diagnosis methods, treatment access, and instruction level on epilepsy in both rural and urban areas was gathered. The country was divided into 6 areas: northwest (NOA), northeast (NEA), Cuyo, Patagonia, Pampas and Buenos Aires City (CABA). Statistical analysis was through SPSS28 expressed on absolute frequency and percentage for qualitative variables and media, standard deviation, median, percentile 25- 75 and confidence interval of 95% for quantitative variables.

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Results: 395 responses from all provinces. More than 40% of professionals work in the second-third level of healthcare. CABA/Pampas/Cuyo regions have the highest percentage (≥64%) of training in epilepsy. CABA/Patagonia 70% work in the private system, while in Cuyo/NEA/NOA more than 50% work in the public system. 70% of patients always or almost always have adequate coverage for diagnostic methods/treatments, except for NEA where ≥50% never or almost never have it. Access to antiseizure medication is uneven, 70% (CABA) vs 49% (NOA). This gap is larger for the availability of diagnostic methods.
Conclusion: Survey showed asymmetrical access to diagnosis, treatment and follow-up in the different regions. Many professionals do not have basic training in epilepsy and those trained are concentrated in large cities. A report will be issued to the Ministry of Health. Strategies for education and implementation of telehealth will be promoted by LACE.

874 | Fostering Effective Community-Based Collaborative Research

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Purpose: One of the six guiding principles of the IGAP is that people living with neurological disorders, their families, local communities, and organizations that represent them should be empowered through engagement and consultative mechanisms in care planning, service delivery, policy and legislation development, program implementation, advocacy, research, monitoring, and evaluation. The purpose of this research is to highlight the benefits and barriers that were encountered by a community-based organization in their efforts to conduct research to improve care.
Method: Our research partnership was initiated by a grassroots community-based organization who identified that parents of children with epilepsy wanted a low-cost stress reduction program. We collaborated with a multisector team to identify an intervention and together conducted a randomized control trial (RCT). After the trial we conducted a focus group and administered a questionnaire to collect feedback on the benefits/challenges of our research collaboration.
Results: The community epilepsy agency surveyed parents to understand their needs prior to recruiting a team of experts (psychologists, epidemiologists, university researchers and community-based epilepsy educators) to develop, implement and evaluate an intervention. After completing our RCT we invited thirty-seven stakeholders including our program facilitators and research team to complete an online questionnaire or participate in a focus group to evaluate the benefits and challenges of our collaborative. Our final study sample included nineteen participants who identified the importance of relationship building, shared goal, shared decision-making, acknowledging power differentials and addressing systemic barriers as key to IGAP implementation.
Conclusion: The IGAP framework underscores the critical role of local communities in health research, care planning, and service delivery. Despite their pivotal role in supporting people with epilepsy, community-based organizations are often overlooked or under-compensated in research collaborations. Our research aims to identify ways community-based stakeholders and IBE chapters can participate as equal partners in undertaking research to improve care.

1430 | Empowering Community Health Workers: A Multistate Evaluation of Epilepsy Training Outcomes in India's Primary Care System

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Purpose: A single seizure can trigger cascade of social isolation, missed opportunities, and healthcare barriers for 12 million People with Epilepsy (PWE) in India. Despite India's commitment to the IGAP for epilepsy by 2030, challenges remain in healthcare access, provider knowledge, and available resources. This study assesses a training program for Accredited Social Health Activists (ASHAs) and Community Health Officers (CHOs) to improve epilepsy care and outcomes for PWE.
Method: We implemented a comprehensive training intervention for 1,420 healthcare workers (992 ASHAs and 428 CHOs) across three states: Chhattisgarh, Jharkhand and Uttarakhand. The training sessions covered epilepsy

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diagnosis, management, and follow-up care. Effectiveness was assessed using pre- and post-training questionnaires analyzed with the McNemar chi-square test.

Results: CHOs had diverse educational backgrounds: high school (36.2%), diploma (18.9%), bachelor's (28.0%), and postgraduates (12.7%). ASHA were from Chhattisgarh (77.3%), Jharkhand (13.1%), and Uttarakhand (4.5%), while CHOs were from Chhattisgarh (44.5%), Jharkhand (23.3%), and Uttarakhand (13.3%). Training among ASHAs improved recognition of seizure warning signs from 79.3% to 96.9%, epilepsy being non-contagious awareness from 85.5% to 97.3%, and seizure pattern identification from 64.2% to 90.8%. First aid competency increased from 85.9% to 97.9%. CHOs showed gains in epilepsy knowledge, with awareness about causes rising from 61.0% to 88.3% and importance of treatment compliance from 93.9% to 98.6%. Understanding of follow-up protocol increased from 94.6% to 99.1%. Overall, 94.7% rated the training as highly useful. All improvements were statistically significant with $p<0.05$.

Conclusion: This study demonstrates the effectiveness of targeted training in improving epilepsy care, supporting scalability, bridging knowledge gaps, and contributing to IGAP 2030 targets while enhancing care quality for PWE.

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1663 | Establishing inclusive teaching in medical education: development of a new and innovative curriculum

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Purpose: The prevalence of epilepsy among persons with intellectual disability and vice versa is high. Affected persons have special needs which are frequently not catered for by healthcare professionals and institutions. An important aspect of inclusion in medicine is communication, for instance the use of easy language. Lifestyles, specific needs and perspectives, but also ways of communicating and interacting with people with disabilities can best be taught by themselves. Involvement of experts with lived experience should be able to improve knowledge and attitudes among medical students.

Method: An inclusive team of persons with different types of disability and professional scientific fellows has developed a curriculum for the training of experts-by-experience to be involved into medical education. Inclusion criteria are broad and include persons with epilepsy in association with additional disabilities.

Results: A curriculum of 10 teaching days has been developed. The range spans from reflections on acquiring a new role as assistant teacher and theoretical and practical aspects of barriers and inclusion in medicine to practical aspects of teaching. An exam concludes the course.

Conclusion: We present a curriculum that enables persons with different forms of disability to act as assistant teachers in university training for medical students. An issue of high importance is to alleviate the change of role for the future assistant teachers. The development of this curriculum and the implementation into medical teaching enable students to understand the specific needs of persons with disabilities. This is in accordance with the UN Convention of Rights of Persons with Disabilities (UN General Assembly, Convention on the Rights of Persons with Disabilities: resolution / adopted by the General Assembly, A/RES/61/106, 24 January 2007) and the Intersectoral Global Action Plan on Epilepsy and other Neurological Disorders 2022-2031 (Geneva: World Health Organization; 2023).

1730 | IGAP: Challenges for its implementation in Latin America

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Purpose: To report the results of the first Latin American IGAP workshop organized by the 2 existing PAHO/WHO Epilepsy Collaborating Centers to learn about IGAP, identify priorities and exchange ideas to promote IGAP in the region.

Method: In the context of the XIII Latin ILAE/IBE Latin American Epilepsy Congress stakeholders related to epilepsy were invited to attend: neurologists, PWE, families, health personal, government representatives. 46 participants were divided in 4 groups. Bibliography was sent before and coordinators were selected. The groups had to respond and discuss specific questions that afterwards were presented to the audience, recorded and collected at the end of the day.

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Results: I: IGAP strategic objective 2: To increase prioritization in public policies and strengthen governance: not all countries have national epilepsy programs and diagnostic gaps still exist. There are multiple models of care: public, private, mixed, community based, and inequities are high among access to ASM. II: IGAP strategic objective 3: Implement strategies for promotion and prevention: There is a need to stablish which other pathologies need to be prioritized in each country while education and addressing stigma in epilepsy are essential. Passing specific laws may be a good strategy to improve management of epilepsies. III: IGAP strategic objective 1: Raise policy prioritization and strengthen governance: It is fundamental to involve key stakeholders and actors to reduce the treatment gap.

Conclusion: IGAP is a strong tool to promote the comprehensive care of epilepsies in the world and to work with the governments to fulfill the commitment signed at WHO. The workshop proved to be a good strategy as it has been replicated by some attendees and boosted regional epilepsy advocacy. Financing: Chilean League against Epilepsy - IBE Grant, Endorsement: ILAE -IBE - PAHO

1833 | Strengthening Epilepsy Care in Kazakhstan Through Telemedicine: Policy Challenges and IGAP Implementation

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Purpose: Epilepsy remains a significant health challenge in Kazakhstan, with a shortage of specialized neurologists and limited access to epilepsy care, especially in rural regions. The WHO's Intersectoral Global Action Plan on Epilepsy and Other Neurological Disorders (IGAP) 2022–2031 calls for improved access to care through digital health solutions. Despite Kazakhstan's regulatory framework for telemedicine (Order of the Minister of Health No. KR DSM-158/2020), current telemedicine services remain underutilized due to policy constraints, technological gaps, and reimbursement issues. This study examines how telemedicine can enhance epilepsy care and what regulatory adjustments are needed for its effective implementation.

Method: We analyzed telemedicine utilization in epilepsy care across Kazakhstan from 2023 to 2025, assessing its impact on access to specialists, diagnostic accuracy, and treatment outcomes. Data were collected from the Unified National Electronic Health System (UNEHS), teleconsultation records, and patient-reported outcomes. Additionally, we reviewed existing regulations, including telemedicine licensing, reimbursement policies, and cross-regional specialist consultations.

Results: Telemedicine has expanded access to epilepsy specialists, particularly in remote areas, with a 40% increase in consultations via the UNEHS platform. However, challenges remain: the absence of clear reimbursement policies for tele-epileptology services restricts the financial sustainability of digital consultations. Additionally, remote EEG interpretation is not yet fully integrated into telemedicine workflows due to a lack of standardized protocols.

Aligning with IGAP objectives, we propose policy reforms, including (1) allowing direct-to-patient teleconsultations for epilepsy care, (2) integrating tele-EEG services into the UNEHS platform, and (3) establishing reimbursement mechanisms for remote epilepsy management. These changes would enhance care accessibility, improve early diagnosis, and optimize treatment strategies.

Conclusion: Kazakhstan has the regulatory foundation for telemedicine, but targeted policy modifications are essential to fully leverage its potential in epilepsy care. Implementing these reforms will contribute to IGAP's goal of improving access to epilepsy services and reducing the treatment gap.

Neuroimaging

305 | Seizure Laterality on EEG is Associated with Thalamic SPECT Lateralization

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Purpose: This study explores whether seizure laterality recorded on scalp EEG is related to ictal thalamic perfusion as measured by ictal SPECT imaging.

Method: Patients with intractable epilepsy who underwent ictal and interictal SPECT and were processed with SISCOM during presurgical epilepsy evaluation between 2021 and 2024 at Mayo Clinic Rochester were included. Seizure laterality on EEG, MRI abnormalities, and ictal and interictal SPECT including SISCOM modality were obtained. Thalamic SPECT discordant increased ictal uptake was assessed visually in SISCOM images and categorized as unilateral left or right, bilateral, or absent. Chi-squared and Fisher's exact tests compared categorical variables.

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Results: In total 107 patients were identified. Of these patients, 70 (65%) exhibited either unilateral or bilateral discordant thalamic uptake on SISCOM, with 30 patients having left-sided seizures and 28 having right-sided seizures on EEG. Unilateral left thalamic SPECT increased uptake was observed in 19 patients (63%) with ipsilateral EEG seizures during Neurolite injection, while unilateral right thalamic SPECT uptake was increased in 18 (64%) patients with right-sided seizures (p=0.0005). The overall predominance of the patient's EEG seizure laterality was also associated with thalamic ictal SPECT uptake lateralization: 20 patients (60%) with predominantly left-sided seizures and 15 patients (70%) with predominantly right-sided seizures had ipsilateral thalamic increased uptake (p= 0.0004). Right-sided EEG onset seizures were significantly more likely to have no increased SPECT thalamic activity than left-sided onset seizures (p<0.05). No significant association was observed between thalamic SPECT uptake and age, injection timing, seizure duration, seizure semiology, and the presence and laterality of MRI abnormalities.

Conclusion: The laterality of thalamic SPECT uptake is significantly associated with seizure laterality on scalp EEG and may provide a lateralizing indicator in difficult to localize presurgical cases.

404 | Clinical Relevance of Interictal PET and SPECT in Localizing Epileptogenic Foci for Surgical Planning

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Purpose: Drug-resistant epilepsy (DRE) affects 20–40% of individuals with epilepsy, with mesial temporal sclerosis (MTS) being a leading cause. Surgical treatment is a potential option for MTS, but its success relies heavily on accurate identification of the seizure onset zone (SOZ). This study examines how interictal PET and SPECT imaging contribute to improving SOZ localization and surgical outcomes.

Method: A retrospective review was conducted, including 60 patients who underwent SPECT and 49 who underwent PET. Imaging results were compared against VEEG and MRI findings. Variables assessed included seizure type, SOZ localization via PET and SPECT, and Engel classification at follow-up. Agreement between imaging modalities was evaluated using Kendall's tau-c and Krippendorf's alpha, while logistic regression identified factors associated with SOZ localization and Engel I outcomes.

Results: PET detected epileptogenic regions in 87.8% of patients, slightly outperforming SPECT (85%). PET correlated more strongly with VEEG and MRI ($\tau b = 0.713$, $p < 0.001$) and achieved higher concordance ($\alpha = 0.8171$; 95% CI 0.6762–0.9300) compared to SPECT ($\tau b = 0.536$, $p < 0.001$; $\alpha = 0.6999$; 95% CI 0.5360–0.8421). Extending the ictal phase on VEEG by one second increased the odds of SOZ detection by 1.02 times when using PET/SPECT (p = 0.009). Agreement across PET, SPECT, and MRI significantly raised the likelihood of achieving an Engel I outcome by eight times (p = 0.041).

Conclusion: Interictal PET and SPECT enhance SOZ localization in patients with MTS, aiding in better surgical outcomes. PET demonstrated slightly greater sensitivity, correlation, and agreement compared to SPECT.

413 | Alternations in morphometric similarity network in temporal lobe epilepsy correlated to neuroinflammation pathway gene transcriptions

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Purpose: Morphometric similarity network (MSN) analysis was used to investigate structural changes between TLE and healthy controls and their correlation with inflammation-related gene expression.

Method: The current study population was recruited from the West China Hospital of Sichuan University from 2021/09/01 to 2024/08/31.Structural 3D T1weighted was acquired using a Siemens Trio 3.0T MRI scanner. The cortical surfaces were divided into 308 equal-sized regions (~500 mm^2) based on the Desikan Killiany atlas. For each region, morphometric features from the T1-weighted MRI scan were extracted to construct the morphometric similarity network (MSN) value, including cortical thickness(CT), gray matter volume(GM), surface area(SA), Gaussian curvature(GC), mean curvature(MC) presenting the morphometric features in gray matter and curvature. The above morphometric feature vectors were *z*-normalized across regions to account for variation in value distributions. Pearson's correlation analysis

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was then performed on the morphometric feature vector between each paired cortical region, forming a 308 × 308 MSN for each participants. The regional MSN was then calculated by using the sum of weighted correlation coefficients between a given region and its correlations to all other regions. The comparison was made using generalized linear model (GLM).

Results: We identified widespread alterations across the frontal lobe, parietal lobe, and cingulate cortex, linked to neuroinflammatory genes like PRR5, SMAD3, and IRF3. This correlation was even more pronounced observed when compared between TLE with and without hippocampal sclerosis (HS). Enrichment analysis highlighted pathways related to neurodevelopment and neurodegeneration, supporting a bidirectional link between TLE and neurodegenerative diseases.

Conclusion: These findings revealed the brain wide macroscopic morphometric alternation in TLE correlated to neuroinflammation process. It gave evidence from a new perspective to support the bio-direction link between TLE with the neurodegeneration diseases.

430 | Functional Connectivity Abnormalities Mediating Verbal Fluency Deficits in Newly Diagnosed Epilepsy Patients

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Purpose: Impaired verbal fluency is a common cognitive deficit in patients with epilepsy, but its underlying neural mechanisms remain unclear. Newly diagnosed epilepsy (NDE) patients, who are not yet affected by antiseizure medications, provide an ideal model for investigating the direct impact of epilepsy on language function. This study aims to explore brain network abnormalities and their relationship with verbal fluency deficits in NDE patients.

Method: We recruited 100 NDE patients and 154 healthy controls matched for age, sex, and educational level. Resting-state functional magnetic resonance imaging (fMRI) was used to assess brain networks. Intra- and between-network functional connectivity (FC) was analyzed using dual regression and FSLnets. Verbal fluency was evaluated using character and semantic Verbal Fluency Test (VFT). Correlation and mediation analyses were conducted to examine the relationships among seizure frequency, verbal fluency, and FC.

Results: Compared with healthy controls, NDE patients exhibited significantly reduced intra-network FC in the medial visual, auditory, and lateral sensorimotor networks. Between-network FC involving the language network and the lateral sensorimotor network was also significantly reduced. Correlation analysis showed that seizure frequency was negatively associated with character and semantic VFT scores, while these scores were positively associated with FC in the left auditory network, including the left inferior frontal gyrus (IFG) and superior temporal gyrus (STG). Mediation analysis further revealed that FC in the left IFG and STG partially mediated the relationship between seizure frequency and verbal fluency deficits.

Conclusion: NDE patients exhibit widespread primary sensory dysfunction. Notably, impaired FC in the left IFG and STG within the auditory network plays a critical mediating role in the association between seizure frequency and verbal fluency decline. These findings suggest that primary sensory dysfunction may underlie higher-order cognitive deficits, providing important insights into the neural mechanisms of language impairment in NDE patients.

522 | Connectivity-based activity flow mapping predicts altered declarative memory states in drug-resistant epilepsy

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Purpose: Temporal lobe epilepsy (TLE) patients often exhibit marked episodic and mild semantic memory difficulties, while frontal lobe epilepsy (FLE) patients may present mild declarative memory impairments (Della-Rocchetta et al. Neuropsychologia 1993;*31*(6), 503-524; Helmstaedter et al. Progress in Brain Research 2002;135,439-453). Functional imaging reveals differential activation and connectivity patterns in the medio-temporal and fronto-limbic networks in TLE and FLE, respectively, but these

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patterns have not been systematically assessed across these syndromes. This study used activity flow mapping (AFM; Cole et al. Nature Neuroscience 2016;*19*(12), 1718-1726) to explore the synergy between intrinsic connectivity and functional activation patterns during declarative states and how they relate to cognitive alterations.

Method: All participants (TLE=34, left/right=20/14, age=36±12years, F/M: 17/17; FLE=20, left/right=10/10, 31±11, F/M:11/9; healthy controls=87, HC age=32±9, F/M: 40/47) underwent resting-state, episodic and semantic retrieval tasks. Task activation of each brain regions were first predicted in a HC_1 subgroup (n=45) using the rest-FC and task-activation of its connected regions. AFM predictions were benchmarked as the overlap between predicted and actual activations and were significant in both tasks (r=0.80, p<0.0001). This analysis was repeated in a second subgroup (HC_2, n=42), and in patients groups, with models trained on HC_1 data (Mill et al. NeuroImage 2020; *221*, 117167).

Results: Both tasks activated medio-lateral temporal and posterior-parietal regions, with broader activation in patients. AFM predictions were significant for both tasks (episodic: HC_2=0.61, TLE=0.51, FLE=0.33; semantic HC_2=0.58, TLE=0.53, FLE=0.41; p<0.001), but lower in patients. Prediction accuracies correlated with hippocampal volume in the episodic task, highlighting its role in episodic over semantic processes. Higher prediction accuracies correlated with better behavioral performance, while longer seizure duration reduced accuracy, suggesting that prolonged epilepsy worsens cognitive deficits through network disruptions.

Conclusion: AFM framework accurately predicts task activations, correlating to behavioral performance and may effectively assess cognitive function in patients unable to complete memory tasks.

529 | Thalamic Nuclei Alterations in Pediatric Focal Epilepsy: A Quantitative MRI Study

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Purpose: The role of the thalamus in pediatric treatment-resistant focal epilepsy (trFE) is poorly understood. Using quantitative MRI (T1 and T2 relaxation times at 3T), we investigated the volume and microstructure of thalamic nuclei in children and adolescents with trFE.

Method: 66 children and young people with focal epilepsy (mean age: 12.3 years, mean age-of-onset: 6.86 years) and 44 children without epilepsy (mean age: 10.9 years) took part. 37 patients had a left-lateralized focus and 27 had a right-lateralized focus. Most patients had temporal lobe involvement (n=28), followed by frontal (n=21) and parietal (n=9). Thalamic nuclei segmentation was conducted using THOMAS (Su et al. Neuroimage 2019;194:272-282.). Volume, T1 and T2 relaxation times in the ipsilateral thalamus of patients were compared to controls (who were randomized to match laterality). Nuclei previously implicated in epilepsy and targeted in trFE, notably anteroventral, centromedian, mediodorsal and pulvinar (Fisher RS. Neurobiol Dis 2023;179:106045), were assessed. Robust linear regression was used to assess the effects of group, nucleus, and the interaction between group and nucleus, on volume, qT1 and qT2, controlling for sex and age. Correlations of volume, qT1 and qT2, with disease duration and seizure frequency were assessed using Pearson's correlation. Analyses were repeated for patients with temporal involvement only.

Results: The effect of age and sex was significant (p<0.05) across all measures and analyses, except sex on qT2. Group and interaction effects between group and thalamic nuclei were not significant and investigating temporal lobe patients only did not affect the results. There were no significant associations between MRI measures and clinical variables in patients.

Conclusion: The lack of significant group differences in nuclei volume and microstructure between patients and controls may be due to the heterogeneity or shorter disease durations, and therefore, reduced opportunity for potential disease-related damage, in this group of children.

531 | Sex-related structural abnormalities across different epilepsies: a worldwide ENIGMA study

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Purpose: Epilepsy is a chronic neurological disorder and is increasingly regarded as a network disorder (Larivière et al., 2020). Structural alterations are commonly observed in MRI studies of epilepsy (Whelan CD et al., 2018; Galovic et al., 2019; Kemmotsu et al., 2011). However, the role of sex differences in these structural abnormalities is still under investigation. Here, we analyzed structural MRI data from multiple international sites via the ENIGMA Epilepsy Consortium to assess whether sex influences structural alterations in common epilepsies.
Method: We included 1927 epilepsy patients (881 males, 1044 females) and 639 healthy controls (275 males, 364 females). We applied general linear models to evaluate the influence of (self-reported) sex in cortical biomarkers in temporal lobe epilepsy (TLE) and idiopathic generalized epilepsy (IGE), whether sex differences were different between epilepsy and controls, and to explore the interaction effects between sex and clinical variables, including age of onset and disease duration within these subgroups.
Results: Our analysis revealed that male patients exhibit greater atrophy than female patients in the bilateral frontal cortex and temporal lobes in IGE. However, no significant sex-related differences were identified when comparing epilepsy and control groups. Furthermore, no interaction effects were observed between self-reported sex and clinical factors such as age of onset or duration of epilepsy in cortical thickness. Similarly, interaction effects were absent in subcortical volume and cortical surface area measurements.
Conclusion: Our findings revealed that self-reported sex does not have significant interaction effects with diagnosis, age of onset, or duration of epilepsy in brain structural biomarkers, suggesting that these structural features may not be systematically influenced by sex in the context of epilepsy. However, our results observed potential sex-specific vulnerabilities to structural brain changes in IGE, highlighting the need for further exploration to reveal the underlying neurobiological substrates.

620 | Unveiling Variability in MRI-Negative Temporal Lobe Epilepsy: Distinct Phenotypes from a Multicentric Study

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Purpose: Temporal lobe epilepsy (TLE) is commonly associated with mesial temporal sclerosis (MTS) affecting hippocampal structures, yet ~30% of patients show no detectable MRI lesions (TLE-MRIneg). Despite this, TLE with MTS and TLE-MRIneg are often treated as a single population. This study classified a multicentric TLE cohort based on hippocampal atrophy (HA) to examine TLE-MRIneg variability relative to TLE with HA (TLE-HA).
Method: A total of 172 TLE patients with no MRI lesions other than MTS underwent video-EEG and 3T MRI. Cortical thickness and subcortical volumes were estimated using FreeSurfer, alongside clinical, anamnestic, and demographic data collection. Patients were grouped by HA presence (-1.5 SD from controls) in at least one of the hippocampal subfields (head, body, tail), yielding 69 TLE-HA, 103 TLE-MRIneg, and 102 matched healthy controls. Clinical/demographic comparisons were made between TLE-HA and TLE-MRIneg, and cortico-subcortical features were compared to controls. Finally, cluster analysis was performed on TLE-MRIneg.
Results: Significant differences emerged between TLE-HA and TLE-MRIneg. TLE-HA patients had a younger age of onset ($p<.001$), longer disease duration ($p<.001$), higher antiseizure medication intake ($p<.001$), higher rates of MTS ($p<.001$), drug-resistance ($p=.010$), febrile seizures during childhood ($p<.001$), and epigastric auras ($p=.003$). HA was more frequent in women ($p=.016$). TLE-HA exhibited widespread bilateral cortical thinning, bilateral HA, and ipsilateral thalamic and amygdala atrophy. Conversely, TLE-MRIneg showed mild cortical thinning but a strong ipsilateral amygdala enlargement. Clustering TLE-MRIneg revealed three profiles: (1) 34 with significant bilateral posterior atrophy, (2) 43 with no significant changes, and (3) 26 with sporadic cortical hypertrophy. Clusters differed mainly by MRI age ($p=.003$), with Cluster 3 being the youngest.
Conclusion: These results reveal significant differences between TLE-HA and TLE-MRIneg. While TLE-HA appeared as a homogenous group, TLE-MRIneg is characterized by distinct profiles. This highlights the importance of subgroup identification to address variability and improve diagnostic and therapeutic approaches in TLE.

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661 | Assessing the Consistency and Reliability of Hub Metrics Across Parcellations in Temporal Lobe Epilepsy

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Purpose: An increasing number of studies suggest large-scale network disruptions in focal epilepsy syndromes (Royer J et al. Epilepsia 2022;63:537-550). While hubs, regions crucial for long-range and inter-network communication, are key candidates of investigation (Van Den Heuvel MP et al, Trends Cogn Sci 2013;17:683-696), there has been no heterogeneity regarding their formulation or scale in temporal lobe epilepsy (TLE) versus controls.
Method: 53 TLE patients and 126 healthy controls underwent 3T resting-state functional magnetic resonance imaging. Data were parcellated using Schaefer100, 300, 600, and 900 parcellations (Schaefer A et al. Cereb Cortex 2018;28:3095–3114). Connectivity matrices were computed and thresholded at 10% across participants. Cohen's *d* indexed the TLE-versus-control differences for strength (degree centrality, eigenvector centrality) and integrative (betweenness centrality, participation coefficient) nodes. Dice coefficient and Pearson's correlation assessed consistency between metrics and parcellations.
Results: Positive and negative effects were evenly distributed when comparing TLE and controls, indicating large-scale network reorganization. Strength nodes displayed more consistent patterns ($<r> = 0.88$) across the four parcellations than integrative nodes ($<r> = 0.58$). The 100-node parcellation was least correlated with other parcellations across node types. Dice overlaps were stronger for positive effects ($d > 0.2$, max dice = 0.85 for 100/900 strength parcellations) than negative effects ($d < -0.2$, max dice = 0.73 for 600 strength parcellation). Strength and efficiency nodes were strongly coupled within each parcellation ($<r> = 0.73$), with the 300 and 600 parcellations showing the strongest inter-parcellation coupling across metrics.
Conclusion: Results indicate large-scale hub reorganization in TLE relative to healthy controls, varying across hub metrics and scales. Overall, strength nodes were more consistently reorganized than integrative nodes. Stronger dice coefficients for positive Cohen's *d* indicated more reliability in regions with increased connectivity in TLE. These findings highlight the importance of parcellation schemes and hub metric selection when interpreting TLE-related hub disruptions.

664 | Bilateral precentral gyri and caudate nuclei atrophy in epilepsy patients with postictal generalized EEG suppression

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Purpose: The aim was to investigate the volumes of cortical regions and subcortical nuclei in epilepsy patients with postictal generalized electroencephalographic suppression (PGES).
Method: According to the video-electroencephalography records of epilepsy patients with generalized convulsive seizures, 58 patients with PGES (PGES+) and 51 patients without PGES (PGES−) were recruited. High-resolution T1-weighted images were acquired from each patient and 60 matched healthy control subjects. Cortical gyrus and subcortical nuclei volume were compared among the three groups using FreeSurfer software. The correlations were analyzed between cortical and subcortical volume alterations and against the age of seizure onset, duration of epilepsy, seizure frequency, generalized convulsive seizure (GCS) frequency and number of medications.
Results: Patients with PGES showed reduced cortical volume in the bilateral precentral gyrus (PCG) and bilateral caudates, accompanied by a relatively smaller reduced volume in the left thalamus compared with patients without PGES. In relation to healthy control subjects, the PGES+ group presented atrophy in bilateral precentral gyrus (PCG), left caudal middle frontal gyrus (CMG), bilateral cerebellum, bilateral thalamus, left accumbens and brain stem, while the PGES− group presented reduced volume in the left CMG, bilateral cerebellum, bilateral thalamus, left accumbens and brain stem. There was no significant association between age at seizure onset, duration of epilepsy, seizure frequency, GCS frequency and number of medications with PGES-related cortical and subcortical volume alterations.
Conclusion: Patients with PGES suggest widespread cortical-subcortical network changes and multiple brain regions atrophy. These changes may be related to the generation and spread of seizure activity, underlying the possible physiopathology of PGES.

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716 | Brain perfusion imaging by arterial spin labelling predicts postsurgical seizure freedom in pediatric focal lesional epilepsy: a pilot study

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Purpose: To determine whether integrating arterial spin labeling (ASL) perfusion imaging into presurgical planning improves postsurgical seizure outcomes in children with pharmacoresistant focal lesional epilepsy associated with focal cortical dysplasia (FCD) or low-grade epilepsy-associated tumors (LEAT).

Method: We retrospectively analyzed MRI scans from 18 children (median age 4.8 years, IQR 1.9–11.5) who underwent resection for FCD- or LEAT-associated pharmacoresistant epilepsy, with at least one year of follow-up. All patients underwent presurgical ASL imaging along with pre- and postsurgical structural MRI. Image postprocessing, including segmentation and coregistration, assessed the completeness of resection of the anatomical lesion and ASL-derived perfusion changes. DICE similarity scores measured the alignment of pre- to postsurgical segmentations, and the resection ratio assessed the percentage of presurgical segmentation remaining post-resection. These metrics were then correlated with postsurgical seizure outcomes.

Results: Fourteen (78%) patients achieved seizure freedom, and 13 (72%) had complete lesion resection. Qualitative analysis showed that complete inclusion of the perfusion changes within the resection cavity significantly correlated with seizure freedom (p=0.009), while complete resection of the anatomical lesion did not (p=0.57). Quantitative analysis indicated that higher alignment of the perfusion changes with the resection cavity, measured by the DICE score, was significantly associated with seizure freedom (p=0.043), whereas alignment between lesion and resection was not (p=0.44). Larger residual perfusion volumes significantly correlated with seizure recurrence (p=0.008).

Conclusion: Incorporating ASL perfusion imaging into presurgical evaluation may better delineate the epileptogenic zone, potentially improving postsurgical seizure outcomes. These findings support ASL as a valuable complementary tool in surgical planning for pharmacoresistant pediatric focal lesional epilepsy.

742 | Distributed hypometabolism associated with focal cortical dysplasia reflects structural connectivity of the human brain

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Purpose: Focal cortical dysplasia type II (FCDII), an important cause of surgically remediable epilepsy, are associated with both localized (lesional) and distributed hypometabolism on fluorodeoxyglucose (FDG)-PET. Reasons for distributed hypometabolism are poorly understood, this potentially contributing to excessive or erroneous cortical resection, unnecessary intracranial EEG, or exclusion from surgery. We hypothesized that distributed FDG-PET hypometabolism would recapitulate expected patterns of structural connectivity in patients with FCDII.

Method: We studied 151 patients with focal epilepsy and FCDII who underwent T1-weighted MRI and FDG-PET (median age at scan=10 years). FCDII were manually segmented, mapped to template brain space (*fsaverage*) and assigned to parcels of the HCPMMP1 "Glasser" atlas (doi: 10.1038/nature18933). FDG-PET maps were parcellated using the same atlas and normalized using healthy controls (doi: 10.1186/s13550-021-00830-6) with negative z-scores indicating hypometabolism relative to normal brain. Diffusion MRI structural connectivity of each FCD parcel was calculated using 1200 healthy controls from the Human Connectome Project (doi: 10.1016/j.neuroimage.2013.05.041). A linear mixed-effects model was then used to assess the relationship between control-normalized FDG-PET metabolism and the structural connectivity of each patient's lesion with significance assessed using spin-permutation testing (10,000 spins) (doi: 10.1016/j.neuroimage.2018.05.070).

Results: Median age at seizure onset was 5 years old with FDG-PET being performed at a median of 4 years following

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seizure onset. FCDII preferentially occurred in the frontal lobe (66%). 97 (64%) of patients underwent surgery, 83% remaining seizure-free 12 months follow-up. Brain areas showing greater FDG-PET hypometabolism had stronger structural connectivity with the locations of FCDII (β = -0.373, p=4.3e^{-290} [spin-p = 0.01], 95% CI [− 0.39, − 0.35]).
Conclusion: Distributed FDG-PET hypometabolism in patients with FCDII mirrors expected patterns of lesion-related structural network connectivity. These findings add further support to the idea that distributed cortical hypometabolism seen in patients with FCD reflects expected propagation pathways, rather than being indicative of intrinsically epileptogenic or abnormal tissue.

753 | Metabolic machine learning for temporal lobe epilepsy lateralization

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Purpose: [18F]fluorodeoxyglucose positron emission tomography (FDG PET) is a widely used modality across epilepsy surgery centers worldwide. In this work, we used a support vector machine (SVM) to explore the utility of [18F]FDG PET for temporal lobe epilepsy (TLE) lateralization.
Method: We recruited 41 unilateral drug-resistant TLE patients (37.1±10.5 years, 22 female, 22 left TLE) admitted for presurgical work-up and who had undergone both 3T magnetic resonance imaging (MRI) and [18F]FDG PET. Lateralization was based on clinical consensus of the presurgical workup. [18F]FDG PET was pre-processed and projected to a surface-based cortical model. To lateralize the epileptic focus, an SVM classifier was trained on whole brain [18F]FDG PET data. We evaluated performance using a five-fold cross validation (70% training/30% testing split, 100 iterations). Additionally, we assessed performance of the classifier on those patients who had visually non-localizing clinical MRI (MRI-, n=21), [18]FDG PET (PET-, n=23), and both MRI/[18F]FDG PET (MRI-/PET-, n=12).
Results: The classifier achieved a mean accuracy of 79.6±9.8%, with an area under the curve of 0.83±0.10. Upon interrogation of the model coefficients, mesial temporal regions and temporal poles were the most consistent predictive features. Expert visual assessment of MRI and [18F]FDG PET was able to correctly lateralize only 19/41 patients (46%; 21 non-localizing, 1 lateralization contralateral to consensus) and 16/41 patients (39%; 23 non-localizing, 2 lateralization contralateral to consensus), respectively. On average, the SVM algorithm correctly lateralized 91.6±4.8% of PET- cases, 91.7±4.6% of MRI- cases, and 87.6±7.2% of MRI-/PET- cases.
Conclusion: Machine learning [18F]FDG PET data has excellent lateralizing capability in drug-resistant TLE. The translational value of this method is supported by its application to widely available clinical data. Future work will validate these findings in larger patient subgroups and incorporate multimodal MRI data.

755 | Association between gray matter volume changes and SEEG-defined epileptogenicity

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Purpose: We explore whether alterations in gray matter volume (GMV) are associated with stereo-electroencephalography (SEEG) epileptogenicity biomarkers.
Method: We included 3T non-contrast T1 scans from MRI-positive and MRI-negative drug-resistant focal epilepsy patients admitted for SEEG and age-sex-matched non-epileptic controls. We segmented the GMV map for each subject using CAT12. We then conducted a non-parametric voxel-based comparison on the SnPM toolbox resulting in pseudo-t-maps reflecting GMV differences between patients and controls (adjusted for age, sex, and total intracranial volumes). We classified SEEG contacts as (i) epileptogenic zone (EZ), defined as contacts proposed for primary EZ radio-frequency thermocoagulation, and (ii) contacts generating the top 10% of interictal epileptogenicity biomarkers (spikes, fast ripples, and cross-rates of HFO*spikes) for each patient. We calculated the GMV differences around each SEEG contact and then performed mixed-effect logistic regression.
Results: We included 50 patients (mean age 33.7±10.1 years, female 52.0%, MRI-negative 76.0%) and 68 controls (mean age 34.90±9.86 years, female 55.9%). EZ analysis: Among all contacts (n=4,878), increased GMV was associated with epileptogenic contacts in the whole cohort ($p<0.001$) and MRI-positive group ($p<0.001$), but not within the MRI-negative subgroup ($p=0.051$). In neocortical contacts, increased GMV was associated with the EZ in the whole cohort ($p<0.001$) and the MRI-positive subgroup ($p<0.001$). In contrast, reduced GMV was linked to the EZ across the whole cohort ($p=0.036$) and the MRI-positive subgroup ($p=0.007$) for mesial temporal contacts. Interictal epileptogenicity biomarkers analysis: Increased

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GMV was linked to neocortical contacts exhibiting the top 10% of spikes (p=0.023) and fast ripples (p=0.003). Reduced GMV correlated with mesial temporal contacts showing the top 10% of spikes (p=0.015), fast ripples (p=0.030), and cross-rates of HFO*spikes (p=0.033) in MRI-positive patients.

Conclusion: In MRI-positive cases, GMV was increased in neocortical and decreased in mesial temporal epileptogenic regions. Further research into epileptogenicity biomarkers in MRI-negative cases is required.

759 | Distinct Brain Connectivity Patterns in Autoimmune Limbic Encephalitis and Mesial Temporal Lobe Epilepsy with Hippocampal Sclerosis: Insights from Graph Theory

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Purpose: Diagnosing autoimmune limbic encephalitis in adults with newly-onset seizures presents significant challenges, particularly when seizures are the primary manifestation of temporal lobe epilepsy (TLE) and MRI findings are inconclusive. This study leverages graph theory to analyze brain connectivity patterns, offering a novel approach to differentiate between various etiologies of TLE, including mesial temporal lobe epilepsy with and without hippocampal sclerosis (MTLE-HS).

Method: Brain networks were constructed for 29 patients with a leucine-rich glioma-inactivated 1 (LGI-1) antibody encephalitis, 19 patients with non-lesional TLE, 17 patients with TLE-HS, and 29 age-matched healthy controls. Brain connectivity and structural differences were assessed using T1-weighted structural MRI and diffusion tensor imaging. A within-subject paired comparison was performed between the acute and remission phases in LGI-1 patients. Memory performance was evaluated using the Wechsler Memory Scale-Revised.

Results: The TLE group exhibited an earlier age of onset (44 years [26-51], P = 0.004) and longer disease duration (7 years [2-24], P < 0.001) compared to the LGI-1 group (50.00 ± 12.28 years; 2 years [1-2], P < 0.001), with more pronounced differences in the TLE-HS subgroup (32.82 ± 14.47 years, P = 0.002; 18.59 ± 12.52 years, P < 0.001). The LGI-1 group demonstrated better memory performance than the TLE group (93.07 ± 20.15 vs 81.58 ± 25.04, P = 0.001). LGI-1 patients, exhibited higher local efficiency compared to TLE patients (P = 0.01). No significant difference was found between acute and remission phases in LGI-1 patients (P = 0.94). In contrast, TLE patients showed reduced degree centrality in the contralateral orbital inferior frontal gyrus ($P_{FDR\ corrected} = 0.0048$), with greater reductions observed in the TLE-HS group ($P_{FDR\ corrected} = 0.0078$).

Conclusion: These findings support the utility of graph theory-based analysis for identifying etiology-specific features in seizure disorders with inconclusive MRI results.

794 | Ictal SPECT success rate using a single SPECT session protocol

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Purpose: Ictal SPECT is labor-intensive and expensive. We have developed a more affordable protocol with a single SPECT radiotracer session during a 48-hour video-EEG monitoring (VEM). This study aimed to determine the success rate of ictal SPECT with a single SPECT session (HMPAO or ECD).

Method: This retrospective observational study included all VEM cases performed in the University Malaya Medical Centre, Kuala Lumpur, Malaysia from 1st January 2011 to 30th April 2024, with SPECT as part of the presurgical evaluation.

Results: A total of 189 cases were included. The mean age was 33.3 years old (range 9-68), and 105 (55.6%) were male. The mean baseline seizure frequency before VEM was 21.8 per month. The mean number of seizures recorded during a 48-hour VEM was 10.9. A total of 44 (23.3%) patients had ictal SPECT with a single SPECT session. Ictal SPECT was significantly associated with a higher number of seizures during 48-hour VEM (31.5±58.7 vs 4.4±6.3, $p<0.001$) and younger age (29.9±11.8 vs 34.2±11.9, $p<0.05$). On multivariate analysis, only the number of seizures during 48-hour VEM was a significant predictor for ictal SPECT (95% CI, 1.03-1.12; odds ratio, 1.073; $p=0.002$). Those with at least three seizures during VEM had a ≥30% chance of having ictal SPECT and ≥40% in those with six or more seizures.

Conclusion: A single SPECT session on day 3 of VEM can be a cost-effective option, particularly in those patients with multiple seizures in the first 48 hours of monitoring following a fast medication taper.

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825 | Are peri-ictal MRI abnormalities markers of seizure duration? Insights from a prospective study on status epilepticus and single seizures

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Purpose: Peri-ictal MRI abnormalities (PMA) are more commonly observed in status epilepticus (SE) than in single seizures, suggesting a potential relationship between their occurrence and the duration of ictal activity. This prospective MRI study aimed comparing the occurrence of PMA in patients with SE and those with single seizures.
Method: Patients with a definitive SE who underwent an MRI within 48 hours of SE onset were included. Patients with single seizures also underwent an MRI with the same protocol and timeframe. Convulsive seizures required a witnessed duration of ≥5 minutes, and non-convulsive seizures required an EEG confirmation. Patients were recruited in either the Video-EEG Monitoring Unit, the EEG Laboratory, or the Emergency Unit at the Christian Doppler University Hospital, Salzburg, Austria. Among other sequences, an MRI protocol included diffusion weighted imaging (DWI), fluid-attenuated inversion recovery (FLAIR) and arterial spin labeling (ASL).
Results: From February 2019 to April 2023, we prospectively recruited 352 patients with a SE who underwent an MRI if clinically indicated. Eventually, 149 patients with a SE were included into this analysis after excluding those with an ictal-interictal continuum (N=55), patients with MRI without complete protocol or if it was performed 48hours after the SE onset (N=148). Between October 2019 and June 2022, 243 patients with single seizures were screened, 69 of them met the inclusion criteria and the following patients were excluded: those with non-epileptic seizures (N=38), late MRI (>48 hours post-seizure) (N=62), missing ASL (N=20), and unknown seizure duration (N=54). PMA were detected in 70/149 (47%) of SE patients compared to 7/69 (11%) of patients with single seizures (odds ratio: 9.47, 95% CI: 4.06–22.05; p<0.01).
Conclusion: In this cohort, PMA were significantly more frequent in patients with SE compared to those with single seizures, suggesting that PMA may be a hallmark of a prolonged seizure activity.

846 | Evaluate Tau Distribution Using [^{18}F] PI-2620 PET/CT to Predict Traumatic Brain Injury and Post-Traumatic Epilepsy Outcomes in Sprague Dawley Rat

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Purpose: Traumatic brain injury (TBI) is a heterogenous conditions that can result in debilitating neurological disorders such as post-traumatic epilepsy (PTE). Unfortunately, there are not no effective way to predict the occurrence of PTE. Growing body of evidence has shown that dysregulation of tau protein is relevant to the development of PTE. In this study, we aim to characterize the distribution of tau using PET/CT scanning with a novel tau radiotracer [18F] PI-2620 and investigate whether the change of tau brain distribution can be used a marker of PTE development.
Method: TBI was induced using the lateral fluid percussion injury model (LFP) in 11-week-old (n = 9) Sprague-Dawley rats. Age-matched Sham surgery group (n = 6) was used as control. After LFPI, neuromotor function was assessed on day 2, day 7, day 14 and day 21 post-TBI. Seven days after surgery, all animals underwent T2-weighted MRI and dynamic PET/CT scanning of tau distribution using the radiotracer [18F] PI-2620. Time activity curve (TAC) and standardized uptake value ratio (SUVr) were used for the analysis of the regions of interests (ROI). Seven months post-TBI, epidural video-EEG was recorded to identify the development of post-traumatic epilepsy (PTE).
Results: SUVr in visual cortex, somatosensory cortex and association cortex are significantly higher in the ipsilateral (left) hemisphere compared to the contralateral (left) hemisphere ($p < 0.05$); while SUVr in hippocampus, thalamus and accumbens in TBI animals are significantly lower than Sham animals ($p < 0.05$). In addition, the increase of SUVr in association cortex and visual cortex might be relevant to the decrease of neuromotor functions ($p < 0.05$).
Conclusion: There is an increase of tau level in cortical regions immediately adjacent to the LFPI impact, while there might be a decrease of tau in areas underneath the cortex, which suggests a re-distribution of tau after TBI.

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853 | Determining the Computed Tomography Perfusion Changes in Patients Presenting with Acute Seizures of Different Etiologies – A Case-control Study

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Purpose: It can be challenging at times to differentiate between seizure and acute stroke clinically. This study aimed to compare the computed tomography perfusion (CTP) changes in patients presenting with acute seizures of different etiologies to those with acute cortical stroke.
Method: We conducted a single-center cross-sectional case-control study on the CTP pattern changes of 31 patients presenting with seizures of different causes and compared them with 31 patients of acute cortical stroke patients (n=31) as the control group.
Results: 58.1% had increased time to peak (TTP) in the seizure group. None of the patients in the stroke group had reduced TTP compared to 25.8% in the seizure group. The majority of patients in the seizure group had normal to reduced relative cerebral blood flow (rCBF) (38.7% and 35.5%, respectively). 35.5% and 38.7% of the patients presenting with acute seizures had normal and reduced relative cerebral blood volume (rCBV), respectively. The association between the perfusion parameters and etiology of the seizures, presence of underlying epilepsy, and presence of postictal neurological deficits were not statistically significant. The perfusion patterns among the seizures group included cortical ribbon (51.6%), holo-hemispheric (32.3%), multi-lobar (9.7%), and normal (6.5%).
Conclusion: The majority of the patients in the acute seizure group had normal to hypoperfusion patterns. Seizure-related hypoperfusion was not restricted to vascular territories, and cortical ribbon pattern was found to be predominant in our study.

898 | Quantitative brain T1 relaxometry in Mesial Temporal Lobe Epilepsy

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Purpose: Normative atlases for T1 relaxation times have been proposed for individualized quantification of brain tissue abnormalities, providing deeper insights into pathophysiological processes[1]. Mesial temporal lobe epilepsy (MTLE) is the most common adult form of epilepsy and evidences suggest that pathophysiological changes may extend beyond temporal lobe[2]. In this study we used normative atlases of T1 to identify tissue alterations in patients with MTLE.
Method: Thirty-seven individuals with MTLE (29 females; 36.7±14.6 years) underwent 3T-brain MRI. Twenty-two out of 37 subjects were drug-responsive and treated with one or more anti-seizure medications (ASMs), while 12/37 patients were drug-resistant to ASMs polytherapy. Protocol included high resolution T1-weighted MPRAGE (TR=2300 ms, TE=2.34 ms, voxel size 1.0x1.0x1.0 mm, FOV 256×256 mm) and MP2RAGE (TI1/TI2/TE/TR=700/2500/2.96/5000 ms; flip angles 4/5 deg; 1x1x1 mm^3; GRAPPAx3) sequences. Individual T1 maps were co-registered onto reference atlases established using linear regression models[1]. For each voxel, deviations were evaluated as z-scores and a threshold was applied to maintain only voxels exceeding 2 standard deviations from corresponding normative value[1].
Results: All individuals with MTLE showed positive T1 deviations from the normative population (z>2) in the hippocampus and temporal lobe, as well as diffusely in white matter and subcortical structures, as striatum and thalamus. Drug-resistant MTLE subjects demonstrated larger and more diffuse deviations compared to drug-responsive patients.
Conclusion: T1 z-score maps of patients with MTLE identified alterations of tissue properties with respect to normative atlases[2]. Our findings support the hypothesis that MTLE-related pathophysiological changes extend beyond the temporal lobe and involve different brain regions. Furthermore, MRI alterations appear to align with clinical severity, as subjects with drug-resistant epilepsy exhibited more diffuse changes compared to those with drug-responsive MTLE.

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907 | Exploring the influence of clinical and video-EEG topography on the diagnostic yield of 7 Tesla MRI in epilepsy

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Purpose: Lesion detection in drug resistant focal epilepsy (DRFE) is crucial for surgical planning that increases the likelihood of postoperative seizure control. Due to enhanced spatial-to-noise resolution, 7 Tesla MRI (7T-MRI) is being increasingly used to identify lesions in previously "MRI-negative" patients. 7T-MRI is still not widely available. Establishing patient characteristics that have a higher probability of benefiting could allow better resource allocation.

Method: Single-institution retrospective study, in a Brazilian tertiary hospital, with MRI-negative DRFE patients who underwent 7T-MRI. Outpatient seizure semiology was assessed by two independent neurologists and probable epileptogenic topography was defined. All patients had undergone inpatient video-EEG monitoring, reviewed by an independent epileptologist. Seizure onset zone (SOZ) was classified as localized or regionalized. Epileptogenic topography was defined by combined seizure semiology and video-EEG findings. Disagreement was resolved by consensus. 7T-MRI exams were viewed by two neuro-radiologists.

Results: Eleven patients with DRFE underwent 7T-MRI (72,7% men; median age onset: 8 years IQR 3-14; median number of antiepileptic drugs: 3 IQR 3-4; median interval between MRIs 3 years, IQR 1-8). Video-EEG SOZ was extratemporal frontal (9/11, 82%), temporal (1/11, 9%) or both (1/11, 9%). New potentially epileptogenic lesions were identified in 4/11 (36%) of patients: focal cortical dysplasia (3/4, 75%); other malformations of cortical development (1/4, 25%). Two patients had previously detected lesions unrelated to SOZ (one hippocampal sclerosis and one traumatic lesion). All cases with localized SOZ and concordant semiology had a positive 7T MRI ($p = 0.003$, Fisher's exact test).

Conclusion: Convergent clinical semiology and ictal EEG findings increased the likelihood of identification of a potentially epileptogenic lesion on 7-T MRI. This finding may help optimize patient selection.

975 | Enhancing Seizure Onset Zone Detection Through Combined Neuroimaging Data Features and sEEG Signal Analysis in Pediatric Epilepsy

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Purpose: Accurate spatio-temporal characterization of the seizure onset is critical for the effective surgical treatment of drug-resistant epilepsy. Traditional approaches heavily rely on stereotactic electroencephalographic (sEEG) signal analysis, yet integrating neuroimaging data into these frameworks remains underexplored. This study aims to evaluate the added value of combining structural and diffusion neuroimaging analysis with advanced signal processing techniques for automatic seizure onset zone and time determination.

Method: Pediatric sEEG data from patients at Hospital Sant Joan de Déu were analyzed. Structural and diffusion neuroimaging data were processed to (1) obtain 3D electrode locations from pre- and post-implantation MRI co-registration and relate them to brain atlases and subcortical segmentations (Freesurfer) to incorporate spatial information to the sEEG analysis algorithm, and (2) obtain diffusion-based metrics (such as Mean/Axial/Radial Diffusivity, Fractional Anisotropy) from raw pre-implantation DWI tensors as a proxy of structural connectivity to enhance the functional connectivity sEEG analysis algorithm. sEEG signals were analyzed using Python-based frameworks (e.g., MNE), with power and connectivity biomarkers computed for seizure onset zone (SOZ) prediction. Automated SOZ detection algorithms were developed based on the combination of sEEG power and functional connectivity biomarkers, and neuroimaging data features including inter-contact distance and diffusivity.

Results: Preliminary results on ictal episodes within a retrospective cohort of 50 patients show that the integration of structural and diffusion neuroimaging data with sEEG algorithms substantially improves SOZ localization accuracy in patients with good post-surgical outcome. Additionally, for seizure onset time detection alone,

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preliminary analyses suggest that analyzing features such as signal contact power distribution shifts enhances detection reliability across patients.

Conclusion: This study underscores the potential of combining neuroimaging and sEEG data for SOZ detection and demonstrates promising results in developing automated measures for seizure onset time identification. Future work will validate these findings on larger datasets and refine algorithms to improve clinical applicability.

996 | Atrophy network mapping of clinical symptoms in temporal lobe epilepsy

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Purpose: Numerous studies have established that temporal lobe epilepsy (TLE) is a disease of high clinical heterogeneity. Traditional neuroimaging analysis has limitations in elucidating the network localization due to individual clinical and neuroanatomical variability. This study aims to identify the brain network localization of gray matter atrophy and clinical symptoms in TLE and determine the transcriptomic profiles related to the atrophy network mapping.

Method: We initially defined single-subject atrophy maps by comparing cortical thickness in each TLE patient versus a group of age-matched healthy subjects across two independent datasets (total TLE patients = 182, HC = 1147). Next, we identified the network of brain regions functionally connected to the atrophy locations in each TLE patient in a large normative connectome (n = 1537). We computed the time-course correlations between the mean signal from each single-subject atrophy map and each ROI to determine functional connectivity strength. Additionally, logistic regression was employed to predict the clinical prognosis of TLE patients, using nested cross-validation to determine the network distribution of relevant brain regions. Finally, transcriptomic profiles associated with the case-control differences in the atrophy network mapping were analyzed.

Results: The gray matter atrophy network of TLE comprised a broadly distributed set of brain areas predominantly implicating the limbic, somatomotor, and visual networks. The atrophy network of refractory TLE consisted of circumscribed brain regions mainly implicating the frontoparietal and default networks. The atrophy network mapping was spatially correlated with the brain-wide expression of genes enriched for neurobiologically relevant pathways, and the functional connectivity strength within these networks is closely related to the patients' disease course.

Conclusion: These results demonstrated alterations of the brain network localization of gray matter atrophy in TLE patients and suggested the molecular mechanisms for structural alternations underlying TLE.

1038 | Tuberous Sclerosis Complex: Exploring the Relationship Between Epilepsy, Cognitive Outcomes, and Tuber Burden

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Purpose: This study aims to describe a series of adult patients with tuberous sclerosis complex (TSC), focusing on the relationship between epilepsy, functional outcomes and the number of tubers.

Method: We reviewed clinical and imaging data from patients diagnosed with TSC and epilepsy. Patients were grouped into those with refractory and controlled epilepsy, with or without intellectual disability, with or without ASMs.

Results: We included eight patients (4 female, median age 29.5 years[JNR1] , IQR 19.5). The median age of onset of seizures was 20 months (IQR 36.5). Five had intellectual disability (mild to moderate) and the remaining were cognitively normal. Two patients had refractory epilepsy, using a median of 4.5 ASMs, and six were controlled: four were seizure-free using a median of 1 ASMs (for a mean of 7 years, IQR 5.75), and two maintained seizure control without ASMs (for a median of 32 years). The refractory group had a median of 15.5 tubers (IQR 2.5) on MRI, while the controlled group had a median of 9 tubers (IQR 14), with no statistically significant difference between the two groups (p=0.75). The intellectual disabled group had a median of 19 tubers (IQR 5.25) and the cognitively normal group had a median of 6 tubers (IQR 1.5), which was statistically significant (p=0.02).

Conclusion: This case series highlights that the number of tubers may not correlate with epilepsy refractoriness in patients with TSC but appears associated with cognitive outcomes. Notably, our findings show it is possible for patients with TSC to achieve long-term seizure freedom without ASM, emphasizing the heterogeneity of epilepsy

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in this condition. While the sample size is limited, these observations suggest factors beyond tuber burden likely influence seizure control. Further studies with larger cohorts are needed to develop a prediction model for long term epilepsy outcome and better understand these variations in TSC.

1043 | Altered Seizure Dynamics and Cortical Oscillations in a Mouse Model of Cyclin-Dependent Kinase-Like 5 Deficiency Disorder

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Purpose: Cyclin-Dependent Kinase-Like 5 (CDKL5) Deficiency Disorder is a rare X-linked neurodevelopmental condition characterized by early-onset, intractable seizures and severe neurodevelopmental impairment. The objective of this study was to investigate seizure susceptibility and cortical oscillatory dynamics in a mouse model of CDKL5 deficiency, with a particular focus on cross-frequency analysis.

Method: Male B6.129(FVB)-*Cdkl5*$^{tm1.1Joez}$/J knockout mice (n=6) and wild-type littermate controls (n=6) were implanted with dual-channel telemetry devices for electroencephalography (EEG) recordings (sampling rate of 1000 Hz) over the dorsal hippocampus and visual cortex. Continuous recordings were obtained for at least seven days. Power spectral analyses were conducted for the delta (0.5–4 Hz), theta (4–8 Hz), alpha (8–12 Hz), beta (12–30 Hz), and gamma (30–80 Hz) frequency bands using Fast Fourier Transformation. Phase-amplitude coupling between theta and gamma was quantified using Hilbert transformation. Seizure events were identified by automated detection scripts and manually confirmed.

Results: Two of six knockout mice (33%) developed spontaneous recurrent seizures culminating in sudden unexpected death in epilepsy, whereas no seizures were observed in controls. Seizures were observed exclusively during the light phase. Knockout mice demonstrated abnormal diurnal oscillatory rhythms, including increased delta and theta band power. Phase-amplitude coupling analysis showed a dynamic pattern: theta-gamma coupling heightened in the pre-ictal period, disappeared during seizures, and rebounded post-ictally with enhanced intensity. Interictal phases were characterized by bilateral high-amplitude delta discharges.

Conclusion: These findings highlight altered cortical oscillations and heightened seizure risk in CDKL5-deficient mice, mirroring key clinical features of human CDKL5 Deficiency Disorder. The observed diurnal patterns and distinct changes in phase-amplitude coupling suggest novel targets for therapeutic intervention and warrant further investigation with expanded electrophysiological and behavioral assessments.

1052 | The Role Of Perfusion Head CT In Defining Non-Convulsive Status Epilepticus: A Review

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Purpose: To define the role of perfusion head computed tomography (CT) in diagnosing non-convulsive status epilepticus (NCSE).

Method: Literature review, using electronic databases (PubMed, Scopus, GoogleScholar) to identify articles on the role of perfusion head CT in diagnosing NCSE. Keywords "NCSE", "perfusion head CT", "neuroimaging" were used.

Results: NCSE is a neurologic emergency characterized by continuous/recurrent epileptic activity without motor symptoms. Early and accurate diagnosis is crucial, as NCSE often presents with subtle clinical signs, such as altered mental status, which can be easily mistaken for other conditions. Electroencephalogram (EEG) may not provide conclusive results, as certain patterns of lateralized periodic discharges (LPD) can be challenging to interpret within the ictal-interictal continuum. Perfusion head CT has emerged as a valuable diagnostic tool, enabling the detection of regional cerebral blood flow (CBF) abnormalities linked to seizure activity. NCSE induces localized or generalized changes in CBF due to sustained neuronal excitation, which can be visualized on perfusion CT. Hyperperfusion in specific cortical regions often correlates with ictal activity, while hypoperfusion indicates post-ictal states. Compared to conventional imaging, perfusion CT provides functional insights that complement EEG, which remains the gold standard for NCSE diagnosis. Studies demonstrated perfusion CT's ability to localize seizure foci in patients with ambiguous clinical presentations, enhancing diagnostic confidence and guiding

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therapeutic interventions. Additionally, perfusion CT is rapid and accessible in emergency settings. Limitations include the need for iodinated contrast, radiation exposure, and its lower sensitivity in detecting subtle or widespread NCSE.

Conclusion: Perfusion head CT is a promising technique for rapidly evaluating suspected NCSE, particularly in cases where EEG is unavailable or inconclusive. While it does not replace EEG, it improves diagnostic accuracy by detecting CBF abnormalities associated with seizure activity. Future research focusing on standardizing perfusion thresholds and integrating multimodal approaches may further enhance its role in NCSE management.

1053 | Antiseizure Medications Serial Levels and Quantitative MRI Analysis in Mesial Temporal Lobe Epilepsy

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Purpose: Effects of antiseizure medications (ASMs) on the brain structure of patients with mesial temporal lobe epilepsy (mTLE) are still under investigation. We hypothesized that ASM concentrations may be related to brain structural changes. The aim of this study was to investigate whether areas of structural abnormalities are correlated with serial concentrations of ASMs.

Method: Twenty-four patients with mTLE (mean age of 55±12 years) and twenty-four control subjects were enrolled. All subjects underwent 3T MRI scans. ASMs were dosed on the same day as the MRI. For each patient, the relative position of the medication was calculated according to the concentration range, where a score of 0 corresponded to the lower therapeutic limit and 1 to the upper limit. For patients under politherapy, an overall ASM ratio was calculated by summing the individual medication scores. Image processing was conducted using SPM12. T1 images were automatically segmented, normalized, and smoothed using the DARTEL algorithm. Modulated gray matter (GM) maps were used for the analysis. Statistical analysis was performed using a general linear model (GLM). Comparisons between patients and controls and correlations between GM volume and the overall ASM ratio were performed.

Results: Patients were using an average of two medications, with carbamazepine (n=14) and clobazam (n=12) being the most frequently used. The mean serial dose ratio was 0.9±1.1 (range: -0.3 to 5). Extensive areas of GM atrophy were detected (135,393 mm^3, $p<0.001$ FWE), involving the left precuneus, gyrus rectus, thalamus, insula, superior temporal gyrus, and the right planum temporale, middle occipital gyrus, and posterior cingulate. A weak positive correlation with ASM scores was observed (3,368 mm^3, $p<0.01$ unc), involving the bilateral calcarine cortex, right thalamus, and hippocampus.

Conclusion: ASMs levels were mainly positively correlated with brain structures, particularly in more preserved, non-atrophic areas. This observation may indicate areas influenced by ASMs in mTLE.

1054 | High-Resolution Imaging of Epilepsy: HARNESS MRI Compared to Conventional Protocols

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Purpose: To evaluate the effectiveness of the Harness-MRI protocol in enhancing the diagnostic accuracy of structural brain abnormalities in patients with drug-resistant epilepsy, with a focus on its impact on treatment decisions and long-term clinical outcomes.

Method: A total of 84 patients with epilepsy were assessed. Data were collected and analyzed by reviewing MRI scans and documenting findings related to epileptogenic lesions and forms of hippocampal sclerosis.55 of patients diagnosed using Harness MRI protocol and they included in first group. Second group included 29 patients whose brain scanned using standard MRI protocol. The following MRI scan modes were used in the study T1 TSE - sagittal; T2 FLAIR ISO 3D - axial, T2 FSE Thin - oblique coronal; DWI - axial; T1 IR - oblique coronal. Mean age was 34.5 ±12.3 and 52% of them were female. Data were analyzed to compare the types and frequencies of lesions detected.

Results: The Harness -MRI protocol detected 25 patients with various epileptogenic lesions, achieving a 46% detection rate. In contrast, the standard MRI protocol found only 4 patients, resulting in a 14% rate ($p<0.01$). Statistical analysis showed a significant difference in the detection rates ($\chi^2(1) = 16.35$, $p<0.01$), indicating Harness -MRI's superior effectiveness. Lesion Identification: Harness -MRI (25 patients): Hippocampal Sclerosis: 17. Focal Cortical Dysplasia: 2, Nodular Heterotopia: 3, Cavernoma: 2, Tumor in Hippocampus: 1, Standard MRI (4 patients): Hippocampal Sclerosis: 2, - Nodular Heterotopia: 1, Tumor in Prechiasmal Area: 1

Conclusion: The Harness -MRI protocol offers improved sensitivity for detecting epileptogenic lesions, thereby

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potentially altering the diagnostic and therapeutic approaches for epilepsy.

1119 | Differences in Functional Connectivity Patterns in Temporal Lobe Epilepsy with Hippocampal Sclerosis: A Resting-State fMRI Study

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Purpose: Investigate the differences in functional brain connectivity between Temporal Lobe Epilepsy (TLE) with left hippocampal sclerosis (LHS) and right hippocampal sclerosis (RHS), exploring the role of lateralization in connectivity patterns. Additionally, the study aims to compare these findings with two control groups: patients with focal epilepsy secondary to focal cortical dysplasia (FCD) and healthy controls (HC)

Method: This study included 186 participants: 90 with TLE-HS (LHS: 51; RHS: 39), 68 HC, and 28 with FCD. Static functional brain connectivity was analyzed using resting-state functional Magnetic Resonance Imaging (fMRI). Data were acquired in a 3T MRI scanner (TR 3s, 213 timepoints) and preprocessed using DPABI. Freesurfer atlas including 80 cortical and subcortical regions of interest (ROI) was used. Connectivity matrices were generated by calculating normalized Pearson correlation coefficients between regions in MNI space. Group differences were assessed with Network-Based Statistic (NBS), controlling for family-wise error rate (FWER). Sex, age, and epilepsy duration were included as covariates, with both increases and decreases in connectivity explored across HC, TLE-LHS, TLE-RHS, and FCD groups (two independent sample T Test, alpha 0.05)

Results: TLE-HS exhibited a global reduction in functional connectivity compared to HC ($p<0.02$), affecting both intra- and interhemispheric regions. TLE-LHS showed significant reductions in connectivity mostly within left temporal, pericentral, and insular regions ($p<0.04$). Conversely, TLE-RHS demonstrated diffuse interhemispheric disconnection compared to controls ($p<0.05$). No significant differences in static connectivity were observed between TLE-LHS and TLE-RHS nor between FCD and HC

Conclusion: We identified a global reduction in functional connectivity in TLE-HS (56 connections, 35 nodes, $p<0.02$), with distinct patterns based on lateralization. TLE-LHS exhibited more lateralized disconnection (60 connections, 42 nodes, $p<0.04$), whereas TLE-RHS showed diffuse interhemispheric disconnection. These findings emphasize the role of lateralization in TLE-HS, which remains controversial in the literature, but could help understand cognitive deficits or specific impairments associated with lateralization

1152 | Late-Onset Rasmussen Encephalitis

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Purpose: To analyze the clinical, diagnostic, and therapeutic features of three patients with late-onset Rasmussen Encephalitis (RE).

Method: This retrospective descriptive study included RE cases that met the diagnostic criteria proposed by Bien et al. (2005). Only patients with symptom onset during adolescence or adulthood were included.

Results: Three patients with drug-resistant epilepsy and initially normal neurological examinations were identified. Over time, they developed slowly progressive focal deficits. The mean age of seizure onset was 13 years (range: 11–15 years), and the mean age at diagnosis was 18 years (range: 16–22 years).

Initial MRI findings:

- Patient 1: Right hippocampal sclerosis (HS).
- Patient 2: Left occipital hyperintensity, initially interpreted as focal cortical dysplasia.
- Patient 3: Confluent cortico-subcortical hyperintensities in the right temporal, frontal, insular, and parieto-occipital regions.

All patients exhibited progressive regional cortical atrophy on follow-up MRIs. Based on an initial diagnosis of

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focal drug-resistant epilepsy, temporal lobectomy (Patient 1) and lesionectomy (Patient 2) were performed, with limited clinical improvement. Histopathological confirmation of RE was achieved in both cases, with HS also identified in Patient 1. Treatment included corticosteroids, immunoglobulin, and eventual hemispherotomy. Patient 3 underwent functional disconnection surgery after poor responses to immunoglobulin and rituximab, achieving seizure freedom but with residual hemiplegia.
Conclusion: These cases underscore the importance of considering late-onset RE in adolescents and adults presenting with drug-resistant epilepsy, focal neurological deficits, and slowly progressive unilateral hemispheric atrophy. Prompt recognition is crucial for initiating appropriate treatment and mitigating disease progression.

1168 | Neuroimaging Findings in Patients with Focal Cortical Dysplasia and Secondary Bilateral Synchrony on Interictal EEG

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Purpose: To describe structural brain alterations beyond the epileptogenic lesion in patients with epilepsy associated with focal cortical dysplasia (FCD) presenting secondary bilateral synchrony (SBS) on interictal EEGs.
Method: We selected consecutive patients with pharmacoresistant epilepsy associated with FCD and SBS on routine EEGs. Grey matter (GM) atrophy maps were estimated using an in-house toolbox for single-subject voxel-based morphometry analysis. Normalized GM maps derived from post-processed T1-weighted MRIs were compared to a custom control database comprising 44 subjects, matched by age (±5 years) to each patient (four controls per year of age). Z-tests were applied to compare individual maps. Group analysis was performed using one-sample T-tests (voxel-level $p<0.05$, FWE-corrected; cluster-level $p<0.05$, FDR-corrected) to identify general GM atrophies associated with SBS.
Results: We analyzed 22 patients with FCD, distributed as follows: right frontal (9), left frontal (4), left temporal (6), right temporal (1), right parieto-occipital (1), and right parietal (1). Group analysis revealed GM atrophy in the bilateral thalamus, predominantly in the ventral lateral nucleus (VLN), and bilateral parahippocampal gyrus.
Conclusion: The thalamic atrophy observed in patients with FCD and SBS aligns with the thalamus's established role in generalized epilepsy. The VLN serves as a critical hub in reciprocal loops, enabling the integration of feedback from cortical and subcortical regions. The parahippocampal gyrus and thalamus are interconnected through multiple pathways, facilitating communication within cortical-subcortical networks. These findings highlight the essential role of thalamic involvement in the pathophysiology of focal epilepsies with SBS.

1196 | *In-vivo* evidence for increased tau deposition in temporal lobe epilepsy

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Purpose: Temporal lobe epilepsy (TLE), the most common drug-resistant epilepsy in adults, is associated with structural abnormalities beyond the mesiotemporal lobe. Although traditionally not classified as a neurodegenerative disorder, evidence from *ex-vivo* studies suggest elevated misfolded tau protein in TLE, a hallmark of neurodegeneration. This longitudinal study assessed in-vivo tau deposits in TLE using *^{18}F-MK6240*, a PET tracer validated for tau imaging.
Method: We included 18 drug-resistant TLE patients and 20 age- and sex-matched healthy controls (7 and 10 longitudinally, respectively). 18F-MK6240 PET uptake was registered to 3T T1-weighted MRI, partial volume corrected, normalized to cerebellar grey matter uptake (SUVR), and projected onto cortical surfaces. Vertex-wise MK6240 uptake maps were analyzed using a mixed-effects model, controlling for age and sex, with random field theory correction ($p<0.025$). Group differences in MK6240 uptake were correlated with MRI-derived structural and functional connectivity. Associations with clinical measures (disease duration, Epitrack, semantic memory, episodic memory) were also evaluated.
Results: TLE patients showed significantly increased MK6240 uptake in the superior and medial temporal regions and parietal-occipital areas, bilaterally, with higher abnormalities in the ipsilateral temporal lobe. No significant longitudinal changes were observed within one year.

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MK6240 group differences were mildly related to functional connectivity and strongly associated with structural connectivity. Disease duration but not age correlated with mean MK6240 SUVR in TLE (r=0.5, p=0.03). Higher tau deposits negatively impacted Epitrack and episodic memory performance, while semantic memory was unaffected.
Conclusion: Our findings show *in-vivo* evidence for elevated phosphorylated tau in TLE, which correlated with decline in executive function and episodic memory, but not semantic memory. These findings highlight tau's potential role in TLE progression, warranting larger studies to confirm its role in neurodegenerative aspects of the condition.

1197 | Preoperative Seizures Correlate with Elevated ^11C-Methionine PET Uptake in Oligodendroglioma Patients

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Purpose: Epileptic seizures are a common complication in patients with low-grade gliomas (LGGs). ^{11}C-methionine (MET), a radiolabeled amino acid tracer used in positron emission tomography (PET), provides valuable insights into glioma characterization. This study aimed to investigate the factors associated with MET uptake in LGG patients and to specifically examine its relationship with epilepsy.
Method: MET uptake was retrospectively analyzed in preoperative MET-PET images from 40 patients with an initial diagnosis of LGG, identified by the absence of gadolinium enhancement on MRI. All patients underwent surgical resection and pathological confirmation. The study evaluated correlations between MET uptake and seizure occurrence. The lesion-to-normal tissue ratio (L/N ratio) was calculated by measuring the maximum standardized uptake value (SUV) in the lesion and the contralateral normal brain region.
Results: The cohort had a mean age of 48 years (range: 21–90 years) and comprised 26 males and 14 females. Preoperative seizures and 1p/19q codeletion were significantly associated with higher MET uptake. WHO grade 2 oligodendrogliomas exhibited significantly higher MET uptake compared to grade 2 astrocytomas and glioblastomas. Notably, grade 2 oligodendrogliomas with preoperative seizures demonstrated nearly double the MET uptake compared to those without seizures (L/N ratio: 2.01 vs. 1.20). Receiver operating characteristic analysis determined an optimal L/N ratio cutoff of 2.13 for predicting preoperative seizures. In contrast, MET uptake in grade 2 astrocytomas and glioblastomas, irrespective of seizure status (L/N ratios: 1.44 vs. 1.09 and 1.40 vs. 1.34, respectively), as well as oligodendrogliomas without seizures (L/N ratio: 1.33), remained comparable.
Conclusion: The findings suggest that increased MET uptake in oligodendrogliomas may be linked to epileptogenic mechanisms.

1231 | Crossed Cerebellar Diaschisis in Status Epilepticus: a Systematic Review of the Literature

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Purpose: Crossed cerebellar diaschisis (CCD) is a condition observed in various neurological disorders, including status epilepticus (SE). This systematic review aimed to analyze cases of CCD associated with SE to provide a comprehensive radiological overview of this rare condition.
Method: A systematic literature search was conducted from inception to November 2023 using MEDLINE, Embase, Web of Science, and CENTRAL. Inclusion criteria were: 1) patients with SE and 2) CCD confirmed by neuroimaging (MRI, PET, SPECT). CCD was defined as any observable alteration affecting one cerebral hemisphere and the contralateral cerebellar hemisphere.
Results: Among 1703 initial results, 47 studies comprising 53 patients (mean age: 43.7 years; 27 females) met the inclusion criteria. CCD was identified as alterations in diffusion weighted imaging (DWI) in 40 cases and fluid attenuated inversion recovery (FLAIR)/T2-weighted sequence changes in 29 patients. MR-angiography revealed no cerebellar abnormalities. Arterial spin labeling (5 studies) showed hyperperfusion in the affected cerebral hemisphere and contralateral cerebellum. PET scans (5 patients) demonstrated hypermetabolism in the acute phase or hypometabolism after resolution of a SE. SPECT (6 patients) showed CCD in 5 cases, with cerebral hyperperfusion and contralateral cerebellar hypoperfusion observed 3 to 34 days post-SE onset. Cerebellar atrophy occurred in 4 patients,

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and cortical laminar necrosis was reported in 1 case. Three patients exhibited cerebellar symptoms, persisting in 2 cases at follow-up (3 months and 3 years).

Conclusion: This review challenges the traditional definition of CCD, highlighting its dynamic pathophysiology, including both hyperperfusion and hypoperfusion. CCD may have long-term consequences like cerebellar atrophy or persistent symptoms, underscoring the need for further research into its mechanisms and clinical significance.

1300 | Total gray matter in adults with epilepsy and associations with drug resistant epilepsy, ASM side effects, tonic-clonic seizures and valproic acid

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Purpose: Regional gray matter volume reductions have been observed in selected cohorts with epilepsy. This study aimed to investigate associations between total gray matter (GM) volume and clinical outcomes in a large regional cohort of adults with epilepsy.

Method: A total of n=212 adults with epilepsy were included from a regional cohort study (PREDICT, clinicaltrials.gov, NCT04559919). Clinical data and MRI-investigations were collected from medical records and patient questionnaires. GM volumes were segmented from MRI T1 sequences with SPM12 for MATLAB. GM was corrected for intracranial volume (GM/ICV) and analyzed across groups with drug resistant epilepsy (DRE) and no-DRE, and groups with CNS-related side effects from ASM and no side effects, using Mann-Whitney U test. Associations between GM/ICV and other clinical variables were analyzed in univariable and multivariable linear regression models. Significant associations were analyzed in interaction analysis with age.

Results: In the total cohort of n=212, 112 (52.8%) were female, median (IQR) age at MRI was 37(28) years and GM/ICV% was 51.22(9.78)%. There was no significant difference in GM/ICV% between the groups with DRE(n=51) and no-DRE(n=161), (52.1(46.6-54.1) versus 51.0(45.2-55.3), Mann-Whitney U test, p=0.42), The group reporting CNS side effects (n=70) had higher GM/ICV% compared with no side effects(n=110), (52.9(47.7-55.2) versus 50.3(42.3-55.0), p=0.02). This difference remained significant when adjusting for age, sex, epilepsy duration, epilepsy diagnose, epileptogenic lesion, number of ASM, type of ASM and tonic-clonic seizures. Occurrence of tonic-clonic seizures (p<0.01) and exposure to valproic acid (p=0.04) were negatively associated with GM/ICV with a significant interaction with age.

Conclusion: Total GM/ICV is not associated with DRE, but merits further investigation in association with tonic-clonic seizures and ASM exposure in longitudinal studies. Patients with higher GM/ICV may be more susceptible to experience ASM side effects.

1358 | Multisite validation of a patient-specific MRI-based lesion mapping tool for clinical decision-making in drug-resistant temporal lobe epilepsy

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Purpose: The majority of drug-refractory patients are diagnosed with temporal lobe epilepsy (TLE) and will need surgery for curative treatment. However, lesion detection, surgical candidacy and surgical outcome prediction remain challenging in many cases due to inter-subject variability. Here, we present a patient-specific multicontrast MRI lesion mapping system designed to 1) localize the spatial distribution of structural alterations in neocortical and hippocampal subregions, 2) evaluate the efficacy for seizure focus lateralization, and 3) predict post-surgical outcome.

Method: A total of 493 individuals from four independent sites comprising of 221 TLE patients (123F; mean±SD: 33.8±10.3 years) and 272 healthy individuals (131F; age: 29.8±8.2 years) underwent 3T T1-weighted (T1w) and diffusion MRI. Age and sex were adjusted using w-scores, and $|w|^{3}$ 1.96 were considered altered. Probability of altered cortical thickness, fractional anisotropy (FA), and

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apparent diffusion coefficient (ADC) were mapped on cortical and hippocampal surfaces. Logistic regression (LR) and support vector machine (SVM) algorithms were trained on vertex-wise data using 10-fold cross-validation and bootstrapping to lateralize TLE and predict post-surgical seizure-freedom.

Results: The temporal region was most likely to be altered. Over 40% of patients had altered ADC, less than 30% had altered FA, and less than 20% exhibited significant cortical atrophy. Hippocampal probability maps showed greater atrophy and highly increased ADC, with an anterior-posterior gradient. SVM models trained on neocortical and hippocampal ADC maps showed higher accuracy than models trained on FA and/or atrophy for lateralizing patients (78.7±0.5%) and for predicting post-surgical seizure freedom (74.4±0.1%).

Conclusion: In TLE, ADC signal, the most consistently altered feature within the disease epicenter, achieved highest accuracies in predicting TLE laterality and seizure outcome prognosis after surgery, making it a particularly effective in clinically-applicable decision-support systems.

1398 | Visual and verbal memory networks in temporal lobe epilepsy

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Purpose: Temporal lobe epilepsy (TLE) is increasingly considered a network disorder, with affected networks extending beyond the seizure onset zone. In addition to seizures, TLE often leads to cognitive impairments, particularly in language and memory, significantly affecting patients' quality of life. While approximately 70% of surgically treated therapy-refractory TLE patients achieve seizure freedom, surgery can further impact cognitive function. This study aimed to characterize verbal and visual memory networks in left- and right-sided TLE patients using connectome analyses and to identify predictive markers by correlating functional connectivity with neuropsychological test results.

Method: Sixty-one TLE patients (35 left, 26 right) underwent presurgical neuropsychological assessment and functional MRI (fMRI) at 3 Tesla. A memory paradigm was performed alongside language paradigms, allowing simultaneous assessment of verbal and visual memory. During a 12-minute task, patients viewed faces, objects, and words, followed by a memory test outside the scanner. Data were preprocessed using fMRIprep and analyzed with Statistical Parametric Mapping 12 (SPM12) and the CONN toolbox. Multiple regression analyses examined correlations between functional connectivity and neuropsychological performance.

Results: Preliminary findings revealed significant differences in memory networks between left- and right-sided TLE patients. Verbal memory network connectivity was particularly impaired in left-sided TLE, whereas right-sided TLE showed more disruption in visual memory networks. Increased connectivity between the ipsilateral hippocampus and the contralateral hemisphere correlated with better memory performance in both groups.

Conclusion: Connectivity analyses help characterize memory network differences in TLE and identify vulnerable regions before temporal lobe resections. Network reorganization in epilepsy extends beyond the seizure onset zone. Understanding these memory networks could improve the prediction and mitigation of cognitive impairments in TLE patients pre- and postoperatively.

1422 | Automated whole-brain segmentation with MAPER in refractory temporal lobe epilepsy: a multicenter international validation study

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Purpose: Temporal lobe epilepsy (TLE) is a network disease. Volumetric techniques assessing morphological

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deviations of brain structures are usually specific for the scanner used for image acquisition. This international multicenter study aims to evaluate performance of multi-atlas label propagation with enhanced registration (MAPER) for detecting volumetric deviations on preoperative MRI in TLE patients compared to healthy controls.
Method: Preoperative T1 volumetric MRI of 95 patients with refractory TLE and hippocampal sclerosis from four tertiary centers (Gothenburg, Lund, Uppsala, Prague) were included. As a reference group, we used T1-weighted MR images of 581 healthy participants from the IXI dataset. All images of both patient and reference groups were processed using a MAPER model trained on the Hammers Adult Atlas Database (a prerelease version defining 120 regions). For each input image, MAPER output consisted of an anatomical label map, a crisp tissue class map, and a binary intracranial mask. Using our MATLAB framework, region volumes were calculated and statistically analyzed.
Results: 44 patients underwent surgery for left- and 51 for right TLE. As expected, left and right hippocampus showed atrophy exceeding 2SD in each respective patient group. Other structures with z-score less than -2 were, in left TLE: left thalamus, right thalamus; in right TLE: left amygdala, right hippocampus, left thalamus. The pattern of morphometric deviations was identical between the centers, although the extent of individual changes varied.
Conclusion: MAPER is a robust and scanner-independent method. Volumetric patterns of left- and right-TLE patients differed, suggesting different network derangements. Thalami were the most clearly involved subcortical structure. In our next study, we aim to correlate MAPER findings with clinical variables and patient outcome.

1428 | Validation of the FlaT1 Analysis for Detecting Focal Cortical Dysplasia in Epilepsy Surgery

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Purpose: To evaluate the performance of the FlaT1 analysis, an exclusive module of the SWANe software (Genovese et al., SoftwareX, Volume 26, May 2024), in detecting focal cortical dysplasia (FCD) in patients who underwent epilepsy surgery. FlaT1, based on voxel-based morphometric approaches, employs the ratio between FLAIR and T1-weighted images to enhance contrast between gray and white matter, highlighting areas of abnormal cortical-subcortical junction and extension. This study aims to validate the FlaT1 program for detecting FCD.
Method: This study included 43 patients with histopathologically confirmed FCD, retrospectively recruited from multiple Italian hospitals (Modena, Bologna, Milan, Genoa). Preoperative MRIs were processed with SWANe, utilizing its FlaT1 module. Input data included coregistered FLAIR and 3D-T1W sequences. The FlaT1 analysis generated junction and extension maps and provided an estimation of deviation from a control population using z-scores. The FlaT1 module was validated in a blinded manner, without access to patients' clinical information. The clinical relevance of FlaT1-detected areas was confirmed by correlation with surgical outcomes and histopathology. Additionally, we assessed the concordance between the surgical cavity segmented from postoperative MRIs and the FlaT1 findings using the Sørensen-Dice index.
Results: FlaT1 detected FCD in 70% of cases, with a sensitivity of 0.8 and specificity of 0.45. The overlap between FlaT1+ regions and the postsurgical cavity yielded an average Dice score of 0.7. Patients in whom the FlaT1+ region was completely resected had the best seizure outcomes.
Conclusion: The FlaT1 analysis demonstrates promising utility in identifying FCD on preoperative MRIs, with a Dice score of 0.7 indicating good agreement with surgically resected areas. These findings support the potential of the SWANe software as a tool for improving the detection of FCD, thereby enhancing epilepsy surgery planning and outcomes.

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1478 | Preoperative diffusion tensor imaging (DTI) and neurite dispersion and density imaging (NODDI) in IDH-mutant grade 2 and 3 gliomas: definition of tumor-related epilepsy and predictive factors of seizure outcomes based on a single-center retrospective case series

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Purpose: Understanding and managing seizure activity are crucial in neuro-oncology, especially for highly epileptogenic lesions like IDH-mutant gliomas. Advanced MRI techniques such as diffusion tensor imaging (DTI) and neurite orientation dispersion and density imaging (NODDI) have been employed to describe microstructural changes associated with epilepsy. However, their role in tumor-related epilepsy (TRE) remains unclear. This study aims to investigate the role of DTI and NODDI tumor-derived metrics in defining TRE and predicting postoperative seizure outcomes in patients undergoing surgical resection for IDH-mutant grade 2 and 3 gliomas.
Method: This was a single-center retrospective study. Preoperative DTI parameters included fractional anisotropy (FA) and mean diffusivity (MD). NODDI parameters included neurite density index (NDI), orientation dispersion index (ODI), and free-water fraction (FWF). These metrics were calculated within three volumes of interest [FLAIR tumor volume (Ftv), FLAIR peripheral zone (Fpz), and FLAIR central zone (Fcz)] and correlated with seizure presentation, type, and postoperative control, which was reported according to the Engel classification system.
Results: 57 patients were included in this study. Increased NODDI-derived FWF-Fcz (*p=0.031)* and NDI-Fcz (*p=0.046)* values correlated with preoperative generalized seizure presentation, although only the FWF-Fcz confirmed its statistical significance (*p=0.047)* in the multivariate analysis. Lower MD-Ftv correlated with poor postoperative seizure control both in the univariate (*p=0.015*, *p=0.026)* and multivariate analyses (*p=0.024, p=0.036*), while a trend towards significance was found between higher NDI-Fpz and worse seizure control (*p=0.055*).
Conclusion: DTI and NODDI tumor-derived quantitative parameters may define TRE and predict postoperative seizure outcomes in patients with IDH-mutant gliomas. Notably, DTI metrics were found to be independent predictors of postoperative seizure outcomes, while preoperative NODDI parameters correlated with seizure presentation. Further research is warranted to validate our findings and to better understand the underlying mechanisms driving TRE.

1502 | Examining 'neural soma' compartments to support focal cortical dysplasia lesion detection in paediatric epilepsy

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Purpose: Focal cortical dysplasia (FCD) is often difficult to detect on conventional structural MRI due to their small size and subtle features. Automated machine learning (ML) FCD detection methods, such as the Multi-center Epilepsy Lesion Detection (MELD) project (Spitzer et al.,Brain 2022,145:11,3859-3872), are promising but often output false positives. Here, we examine whether 'neural soma' (NS) parameters (Gyori et al.,Neuroimage 2019,239:118303*)* can help differentiate between true lesions and false positives in pediatric FCD cases, thus improving specificity. We apply this to data acquired in a clinical setting using tensor-valued diffusion encoding (Szczepankiewicz et al.,J Neurosci Methods 2021,15:348:109007), an advanced diffusion MRI technique.
Method: Four pediatric epilepsy patients (Ages 14–16), two histopathologically confirmed (Type IIa and IIb) and two suspected FCD cases, were scanned on a 3T Prisma using a prototype tensor-valued diffusion encoding sequence (scan time ~14 mins). High resolution structural images were also acquired. An expert pediatric neuroradiologist (10+ years) delineated regions-of-interest (ROIs) for identifiable FCDs, contralateral grey and white matter, and the MELD classifier also predicted clusters. Diffusion data was preprocessed and fitted with the NS model. NS parameter maps and ROI distributions were qualitatively compared. Average parameters were compared between FCD, MELD, GM & WM ROIs using Wilcoxon Signed-Rank Tests, with Bonferonni correction.
Results: NS parameters are sensitive to signal changes related to the presence of FCD lesions. In FCD ROI

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distributions, there are higher fractions of spherical than cylindrical compartments. The initial data suggests combining information from NS parameters can be used to identify false positives by contrasting with 'healthy' homotopic regions (i.e., observing distributions of parameters in each ROI). This may support selection of surgical targets when multiple clusters are predicted by ML algorithms.

Conclusion: The 'neural soma' model can potentially support FCD lesion detection by improving specificity between true lesions and false positive ROIs. Funding: GOSH CHR-CIO.

1522 | Evaluating PET Metabolic Activity in Hippocampal Sclerosis: Concordance Between Visual and Quantitative Analyses

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Purpose: Positron emission tomography (PET) scans, reflecting cerebral metabolism, have become critical in guiding epilepsy surgery, particularly when MRI results are inconclusive or when discrepancies exist between neuroimaging and electrophysiology. This study aimed to assess the concordance between subjective visual analysis (VA) grading and quantitative standardized uptake value (SUV) ratios in evaluating metabolic activity in patients with histopathologically confirmed hippocampal sclerosis (HS).

Method: Sixty-two patients (32 females, 30 males) with histopathological HS diagnoses underwent standard preoperative evaluations, including video-electroencephalography, MRI, PET, and neuropsychological assessments. PET scans were analyzed qualitatively through VA and quantitatively by region of interest (ROI) placement. SUV mean values were normalized using the pons, contralateral anterior cingulate gyrus, and contralateral temporal lobe as reference regions. HS subtypes were classified based on the ILAE 2013 criteria: HS-1 (CA1 and CA4 involvement), HS-2 (predominantly CA1), and HS-3 (predominantly CA4).

Results: Among the 62 patients, 45 were classified as HS-1, 8 as HS-2, and 9 as HS-3. VA grading predominantly indicated reduced metabolic activity in the lesion relative to the contralateral side (SUV mean L/Contralateral ratio). Younger age of seizure onset correlated with more pronounced lesion hypometabolism. HS-1 subtypes had significantly lower SUV mean ratios (lesion-to-contralateral and lesion-to-pons) compared to non-HS-1 subtypes, though overall metabolic activity did not significantly differ between HS subtypes.

Conclusion: VA and SUV ratio analyses both demonstrated the clinical utility of PET scans in evaluating metabolic activity in HS, with notable hypometabolism in younger patients and HS-1 subtypes. However, metabolic differences between HS subtypes require further investigation for clinical significance.

1544 | Distinct Phases of Hub Reorganization and Their Association with Post-Surgical Outcomes in Temporal Lobe Epilepsy: A Multimodal Connectivity Analysis

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Purpose: Temporal lobe epilepsy (TLE) disrupts the functional and structural connectivity of brain hubs — highly connected and influential regions — contributing to non-seizure-free (NSF) post-surgical outcomes [Royer et al., Epilepsia, 2022; Gleichgerrcht et al., Ann Neurol, 2020]. While most studies focus on the spatial distribution of hubs, we have examined their dynamic reorganization, specifically hub overload (increased connectivity) and hub failure (decreased connectivity) [Stam, Netw Neurosci, 2024]. In this multi-center study, we investigate how these phases relate to post-surgical outcomes at one year (outcome-1) and two years (outcome-2) after surgery.

Method: We collected resting-state fMRI and diffusion-weighted MRI (dMRI) data from 74 patients with TLE. We calculated hubness metrics — eigenvector centrality (EC), betweenness centrality (BC), and participation coefficient (PC) — for 58 temporal lobe regions using the AICHA atlas. We built separate logistic regression models for each

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hubness metric within each modality to predict outcome-1 and outcome-2, incorporating epilepsy duration as an independent variable. We adjusted outcome-2 models for outcome-1. To mitigate multicollinearity, we pre-selected regions using Elastic Net regression.

Results: We found that increased fMRI EC in the ipsilateral fusiform gyrus was associated with NSF outcome-1. Lower fMRI BC and PC in the ipsilateral inferior temporal gyrus (ITG) were linked to NSF outcome-2. Lower dMRI EC in the ipsilateral hippocampus and contralateral superior temporal sulcus (STS), along with higher dMRI EC in the ipsilateral STS and contralateral middle temporal gyrus (MTG), were associated with NSF outcome-2.

Conclusion: Our findings demonstrate that hub overload, reflected by increased fMRI EC, is specifically associated with NSF outcome-1, whereas hub failure — indicated by decreased connectivity across both modalities — is linked to NSF outcome-2. These results enhance our understanding of hub reorganization and its role in post-surgical outcomes in TLE.

1559 | Neurodegenerative Biomarkers and Cognitive Impairment in Temporal Lobe Epilepsy: Insights from PET Imaging

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Purpose: Cognitive impairment is a common comorbidity of temporal lobe epilepsy (TLE), but its underlying mechanism remains unclear. Neuropathological and neuroimaging studies have revealed that neurodegeneration might play a significant role in it, but the pattern of neurodegeneration and its correlation with cognitive function still need further study. This study aims to localize and quantify hyperphosphorylated tau (pTau) and amyloid-β (Aβ) burden in TLE patients using PET imaging and investigate their correlation with cognitive function.

Method: Our study included 21 TLE patients (13 with cognitive impairment and 8 without) and 11 healthy volunteers. All participants underwent neuropsychological tests, ^{18}F-fluorodeoxyglucose PET, ^{18}F-MK6240 PET (tau-PET), and ^{11}C-PIB PET (Aβ-PET). PET data were processed using PMOD software, and standardized uptake ratios (SUVR) were calculated with the cerebellar cortex as the reference area. Correlations between SUVR in each brain region and neuropsychological testing/clinical factors were assessed.

Results: Compared to healthy controls, TLE patients showed reduced glucose metabolism in the temporal lobe and hippocampus ipsilateral to the epileptic focus. MK6240 SUVR was significantly higher in TLE patients with cognitive deficits, particularly in the hippocampus, heschl gyrus, superior temporal gyrus, middle temporal gyrus, fusiform gyrus, and cingulate gyrus ($p<0.01$). Verbal fluency and MoCA scores were negatively correlated with MK6240 SUVR in these regions ($p<0.05$). PIB SUVR tended to decrease in TLE patients, with a negative correlation observed between PIB SUVR and digit-symbol dubstitution test scores in some regions ($p<0.05$). Both MK6240 and PIB SUVR showed positive correlation with focal impaired awareness seizure frequency in individual brain regions.

Conclusion: High pTau loads were detected in TLE patients with cognitive deficits, correlating with cognitive function. Aβ loading showed an opposite trend, distinct from classical neurodegenerative disorders like Alzheimer's disease. Our findings suggest that neurodegeneration through pTau plays a role in cognitive dysfunction in TLE.

1586 | Are enlarged perivascular space a predictor of acute early post-traumatic seizures after traumatic brain injury?

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Purpose: Post-traumatic epilepsy (PTE) poses a major risk following traumatic brain injury (TBI), particularly with the occurrence of early post-traumatic seizures (EPTS)

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within the first week. Timely identification of patients at high risk for EPTS is crucial to prevent complications and progression to PTE. This study reexamines prior research on using MRI-based perivascular space (PVS) analysis as a biomarker for EPTS, emphasizing the glymphatic system.
Method: In this study, 40 patients with early post-traumatic seizures (EPTS+) (32.5% female, median age 52) and 88 patients without EPTS (EPTS-) (35.2% female, median age 53) were assessed, with controls matched for age and gender using data from Oslo University Hospital's head injury database. Brain MRIs taken within a month post-TBI were processed using PINGU, an enhanced algorithm for automated PVS segmentation. The analysis included PVS count, volume, and asymmetry index (AI) across hemispheres, categorized by vascular territories with the 3D Brain MRI Arterial Territories Atlas. Brain volume analysis was conducted using Freesurfer, and PVS characteristics were compared between EPTS+ and EPTS- patients using non-parametric tests and generalized linear models.
Results: Earlier analysis showed significant differences in the median AI of PVS between hemispheres ((M=0.250, IQR=0.295) vs (M=0.162, IQR=0.227), p=0.022) and in white matter ((M=0.427, IQR=0.371) vs (M=0.222, IQR=0.407), p=0.023). However, upon reevaluation with an improved algorithm, no differences were found in PVS asymmetry between hemispheres or sides (lesional or non-lesional). Sub analysis by vascular territories (ACA, MCA, PCA) revealed no variations in PVS number, volume, or asymmetry between EPTS+ and EPTS- patients.
Conclusion: Contrary to previous findings, this reevaluation does not support PVS as a predictor for EPTS. This highlights the need for model improvements. Longitudinal follow-up studies may further clarify the relationship between PVS and PTE development.

1610 | Estimation of patient head movement during FDG-PET scanning

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Purpose: The surgical treatment of focal drug-resistant epilepsy involves the resection of the epileptogenic regions. Despite the advances in MRI to identify structural abnormalities, more than 20% of cases remain with normal findings. The use of additional glucose metabolic neuroimaging using positron emission tomography (FDG-PET) can reveal hypometabolic epileptogenic tissue. However, technical properties of FDG-PET limit effective image resolution (4-6 mm), resulting in 'blurring' by partial volume effect (PVE), which makes subtle lesions difficult to see. Image post-processing of FDG-PET with registered MRI allows PVE correction to refocus metabolic activity to the cortex. The requirement for patient head stability in neuroimaging is well-documented, though less stringent in FDG-PET due to its lower spatial resolution. Consequently, PVE-correction post-processing is susceptible to movement artefacts.
Method: We analyzed FDG-PET images (Siemens Biograph mCT and Vision600) of 31 patients who were standardly fixed. Low dose CT was acquired prior to the PET scanning for attenuation correction. The PET scanning session was divided into five two-minute blocks. Initially, patient's 3T-MRI scan was registered to the low-dose CT. Subsequently, each PET block was registered to the grey matter mask of the segmented MRI. The obtained rigid transformations reflect the movements of the patient during scanning (three rotations, three translations).
Results: The results demonstrated continuous patient movement, predominantly in the superior-inferior direction, and rotation around the right-left axis (head tilt), likely resulting from neck muscle relaxation. The measured maximal brain displacement was 2.7 (IQR 1.7-4.5, max. 8.9) mm. Despite the scanner operator employing sinograms to control patient movement, slow continuous shifts resulting in movement >4mm were not identified in 11/31 cases.
Conclusion: Despite the fact that the movement was usually under effective PET scanner resolution, inaccuracies in image reconstruction gave rise to artefacts in additional PET post-processing. Consequently, greater emphasis should be placed on ensuring optimal fixation of the patient's head.

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1623 | Increased hippocampal T2 relaxation is associated with differential functional pathways expression in temporal lobe epilepsy patients

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Purpose: Hippocampal atrophy and increased T2 signal are hallmarks of hippocampal sclerosis, the most frequent etiology of focal drug-resistant epilepsy. While previous studies associated astrogliosis with the changes in T2 relaxation, some patients with gliosis and even with neuron loss present normal T2 relaxation. Our aim was to evaluate expression differences related to T2 relaxation.

Method: Patients with mesial temporal lobe epilepsy and hippocampal sclerosis were classified according to presurgical hippocampal T2 relaxation time into those without increase in T2 relaxation ($T2^-$, n=3) and those with increased T2 relaxation ($T2^+$, n=6). Hippocampal relaxation time was measured in T2-weighted images (5 echo times, TE=20-100 ms; TR=3 s, voxel=1x1x3 mm) in a 3T Philips machine. Frozen samples from CA1 subfield were homogenized and digested for *Shotgun* proteomics, and peptides were evaluated with an Orbitrap Exploris 480 Mass Spectrometer and analyzed with data-independent acquisition evaluation in DIA-NN software. All statistical analysis was done in RStudio.

Results: Patients from both groups were similar in several clinical characteristics, including seizure frequency (p=0.87). One patient from the $T2^-$ group had HS type 2, and all of the remaining had HS type 1. $T2^+$ patients had increased T2 relaxation time (p=0.02) and higher heterogeneity in T2 relaxation (p=0.04) compared to $T2^-$. Proteome evaluation revealed 396 proteins detected only in $T2^+$ group, 498 only in $T2^-$, and 3975 found in both groups. The top 10 most expressed proteins were GFAP, HBA1, ACTB, HBB, TUBA1C, MBP, TUBB4B, GAPDH, PLP1, S100B, none of which were differentially expressed between the groups ($p \geq 0.1$). Of all proteins detected in both groups, 38 were over-expressed and 20 under-expressed in $T2^+$ compared to $T2^-$. Pathways with differential expression in $T2^+$ included peptide transport, macromolecules localization, cellular metabolic process, and cellular catabolic process.

Conclusion: Functional changes were more associated with T2 relaxation increase than structural pathways.

1626 | Integration of Diffusion Metrics for Enhanced Detection of Focal Cortical Dysplasia

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Purpose: Traditional MRI often fails to detect subtle microstructural abnormalities in focal cortical dysplasia (FCD). Advanced diffusion MRI (dMRI) techniques provide various microstructural metrics, but their individual diagnostic utility remains limited. This study assesses an integrated diffusion metric (IDM) to improve lesion detection and characterization.

Method: Sixteen patients with histologically confirmed FCD (12 type II, 4 type I) were analyzed using multiple diffusion MRI techniques, including Diffusion Kurtosis Imaging (DKI), Neurite Orientation Dispersion and Density Imaging (NODDI), Fixel-Based Analysis (FBA), and Diffusion Basis Spectrum Imaging (DBSI). Logistic regression was employed to combine diffusion metrics into an Integrated Diffusion Metric (IDM). Lesion visibility was evaluated by experienced neuroradiologists before and after the application of IDM.

Results: The initial spatial overlap between radiologically defined lesions and the epileptogenic zone was low, with a median Dice score of 0.38 (IQR 0.36). The median perilesional volume was 6.5 mL (IQR 13.3 mL). Visual assessment of diffusion metrics showed that most lesions were either not visible or only mildly visible on diffusion metrics, while structural MRI sequences (T1w, T2w, FLAIR) provided clearer lesion visibility. IDM significantly improved lesion contrast compared to individual diffusion metrics. The Dice score for lesion delineation increased from 0.37 (IQR 0.31) to 0.42 (IQR 0.34) ($p = 0.03$). Key contributors to IDM included FA, NDI, FISO, logFC, MK, and WF. IDM also enhanced the contrast between epileptogenic and contralateral healthy tissue, reducing the perilesional volume from 6.5 mL (IQR 25 mL) to 5.1 mL (IQR 18 mL) ($p < 0.001$).

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Conclusion: Integrating diffusion metrics improves FCD lesion detection and delineation. IDM offers a comprehensive representation of tissue abnormalities, potentially aiding pre-surgical planning and reducing MRI-negative diagnoses. Further validation is required to optimize clinical application. Supported by project no.LX22NPO5107 from the MEYS of the Czech Republic: Financed by EU – Next Generation EU

1637 | Role of 18F-FDG-PET/CT in a non-surgical epilepsy center: enhancing diagnostic accuracy

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Purpose: To evaluate the usefulness of 18F-FDG-PET/CT in real clinical practice at an epilepsy clinic without a surgical program.
Method: Retrospective study in adult epilepsy patients who underwent 18F-FDG-PET/CT as part of their diagnostic work-up at our epilepsy clinic. Demographic and clinical data, including MRI and EEG recordings, were collected. The rationale for requesting the 18F-FDG-PET/CT and the subsequent management based on the results obtained were retrospectively analyzed.
Results: Forty-nine epilepsy patients (mean age 41.6±17.6 years; 44.9% women) were enrolled. Mean epilepsy duration was 21.9±16.8 years and 24 patients (49%) had drug-resistant epilepsy. Most patients had focal epilepsy (83.7%; temporal in 53.7%, frontal in 14.6% and indeterminate in 31.7%), whereas the remaining 8 patients had unknown epilepsy with unknown onset tonic-clonic seizures. The etiology of epilepsy was unknown in most cases (73.5%), followed by structural etiology (22.3%; hippocampal sclerosis in 4 patients, focal cortical dysplasia in 3 patients, and other causes). Two patients had DEPDC5-related epilepsy with a normal MRI. The main reason for requesting the test was to increase diagnostic precision in patients with focal EEG or semiology findings and a normal or inconclusive MRI (27 patients; 55.1%), followed by reinforcing diagnostic findings in patients with structural epilepsy (10 patients; 20.4%) and using it as a differential diagnosis tool in patients with suspected frontal versus generalized seizures (8 patients; 16.3%). In 4 patients (8.1%), 18F-FDG-PET/CT was requested as a study for neurodegeneration or autoimmune epilepsy. 18F-FDG-PET/CT showed significant hypometabolism in 51% patients, was inconclusive in 12.2% patients and normal in the remaining 36.7% patients. In 16 patients (32.6%), 18F-FDG-PET/CT findings supported the hypothesized epileptogenic zone despite normal neuroimaging, guiding a targeted review of the MRI.
Conclusion: 18F-FDG-PET/CT, when used rationally, can significantly increase diagnostic accuracy in focal epilepsy, favoring early access to advanced therapies for epilepsy patients.

1651 | Arterial Spin Labeling (ASL) perfusion imaging in Rasmussen Syndrome

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Purpose: The study evaluated the prevalence of cerebral blood flow abnormalities on ASL perfusion images and their relationship with structural abnormalities in patients with Rasmussen Syndrome (RS)
Method: A descriptive-retrospective analysis was performed by searching the electronic database, 47 patients between 2017 and 2024 with definitive diagnosis of RS. The diagnosis of RS was based on Bien's criteria (Bien et al., 2005,) with the ILAE update for epileptic encephalopathy and/or progressive neurological deterioration of variable age. Patients with 1.5T MRI images (Philips Achieva) who had a Pulsed-Pseudo-Continuous ASL sequence in the epilepsy MRI protocol (HARNESS) were included. Cerebral blood flow maps at the 1st available MRI were qualitatively-visually evaluated, looking for asymmetries between cerebral hemispheres and their relationship with structural abnormalities (T2-FLAIR hypersignal and/or atrophy). Demographic data, clinical characteristics, electrophysiological findings, pathology results and therapeutic response were obtained.
Results: Twenty patients were included in the study, of which 16 (80%) were female. The onset of the seizures ranged from 18 months to 13 years (mean 5y). 19 of 20 patients (95%) asymmetry was found in the ASL perfusion, 15 (75%) presented unilateral atrophy and 16 (80%) presented

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brain hyperintensity signal in T2-FLAIR images. 18 (90%) presented hypoperfusion, of these 8 (40%) with hypoperfusion in more than one lobe. 14 (78%) showed simultaneous hypoperfusion and hypersignal on T2-FLAIR. Areas of hyperperfusion were identified in 8 (40%) of the patients, in 3 (15%) of these hyperperfusion affected more than one lobe. All patients with increased perfusion had associated hypersignal on T2-FLAIR images. Four patients (2%) who did not present cerebral atrophy on initial MRI showed asymmetry in cerebral perfusion, 2 with hypoperfusion, 1 with hyperperfusion and another with a mixed pattern.
Conclusion: Cerebral blood flow abnormalities are common in patients with RS; these cerebral perfusion abnormalities can be detected by qualitative visual analysis of ASL sequences.

1720 | Metabolic heterogeneity of mesial Temporal Lobe Epilepsy and functional correlates. Preliminary data

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Purpose: To explore and phenotype cerebral glucose metabolism using [^{18}F]FDG-PET in a heterogeneous group of patients with mesial temporal lobe epilepsy (mTLE) by evaluating regional metabolism and functional connectivity.
Method: We enrolled patients with mTLE who underwent [^{18}F]FDG-PET between 2019 and 2024. Diagnosis was carried out by evaluating the anatomo-electro-clinical correlation and, when feasible, epilepsy surgery outcome. Patients' etiology was classified based on the presence of hippocampal sclerosis (HS), enlarged amygdala (EA), or the absence of a clear etiological/structural cause (cryptogenic). For comparison, a group of healthy subjects (controls) was enrolled. Given the small sample size, [^{18}F]FDG-PET scans were flipped to ensure that the affected side was on the left. Patients and controls' [^{18}F]FDG-PET scans were compared using a t-test (SPM12) to define a region of interest (mTLE-ROI). mTLE-ROI's uptake was measured and normalized to the whole brain. Normalized mTLE-ROI was compared across the three subgroups of patients using ANOVA. Finally, the ROI was used as a seed to assess functional connectivity through "InterRegional Correlation Analysis" and anatomical disconnectivity using a validated atlas (BCB-toolkit).
Results: We enrolled 15 mTLE patients (37±11 years, 8 females, 7 HS, 4 EA, 4 cryptogenic) and 14 controls (35±10 years, 8 females). [^{18}F]FDG-PET analysis identified a mTLE-ROI involving left hippocampus, fusiform gyrus, and basal/polar temporal lobe($p<0.001$). Compared to controls, brain glucose metabolism in the mTLE-ROI was lower in patients with HS and EA($p<0.01$), but not in the cryptogenic group($p=0.09$). Connectivity analysis revealed that the mTLE-ROI metabolism of controls was functionally and anatomically correlated with homologous regions, both ipsilaterally and contralaterally. On the contrary, patients mTLE-ROI metabolism was more extensively correlated with adjacent ipsilateral regions($p<0.001$), while no functional connections with the contralateral lobe were disclosed.
Conclusion: Patients with mTLE exhibit metabolic heterogeneity depending on etiology. Functional connectivity analysis is altered in patients compared to controls.

1735 | Structural and functional connectome-based predictive models (CPM) for temporal lobe epilepsy with hippocampal sclerosis (TLE-HS)

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Purpose: Technical advances and large-scale data sets have allowed for the construction of models capable of classify individual differences for clinical diagnosis using brain connectivity measures derived from neuroimaging data. Here we report the models performance using different automatic machine learning classifiers to differentiate healthy controls from TLE-HS solely based on structural (DTI) or functional (fMRI) connectomes.
Method: We calculated structural (S-conn) and functional (F-conn) connectomes from DTI and fMRI images

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respectively form a cohort of 49 (23 right) TLE-HS patients and 47 healthy controls scanned at a 3T Magnet. We used freesurfer v6.0 (Desikan) atlas to build weighted connectivity matrices including 80 cortical and subcortical regions for each participant and method. For S-conn; each pair of regions were linked using normalized mean FA values and Pearson correlation scores of BOLD signal at rest (fisher transformed) for F-conn. Connectome models for classification were constructed and tested using three algorithms: SVMc, LogReg and LDA implemented with NBS_predict toolbox. We used a cross validation approach (10 K-fold, 10 repeated CV, P-val. 0.01, seed 42 and hyperparameter optimization steps of 5 and 500 permutations).
Results: Mean age in patients was 35,2 (±8y) [22-60y] and 37,5 (±11) [18-61y] in healthy controls, no differences were found in gender between groups (p>.05). Epilepsy evolution time (5-50y) and seizure frequency was similar (p>-.05) between HS side in patients. Classification results for F-conn: LDA (Best performance) Accuracy 0.670 (CI: 0.65-0.68), AUC: 0.679, sens-spec: 0.65-0.70. LogReg (Acc:0.50) and SVMc: (0.47) Classification results for S-conn: LDA (Best performance) Accuracy 0.680 (CI: 0.65-0.70), AUC: 0.682, sens-spec: 0.69-0.67. LogReg (Acc:0.43 and SVMc: (0.43)
Conclusion: Connectome-based predictive models using LDA (linear discrimination analysis) algorithm were consistent to detect TLE-HS patients in our cohort, with implication for diagnosis. Results are constrained by small sample size and needs to be validated on external-bigger databases.

1766 | Value of 7T MRI versus 3T MRI with post-processing in patients with non-lesional focal epilepsy (NLFE)

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Purpose: To evaluate diagnostic yield of 7T-MRI with post-processing compared to presurgical 3T-MRI with post-processing in patients for NLFE-patients, prospectively. Also, MP2RAGE-sequences with morphometric analysis in 3T-MRI were compared to 7T-MRI under a consistent protocol.
Method: 16 presurgical NLFE-patients (evaluated by standard presurgical 3T-MRI) were enrolled. Imaging was performed at 3T Siemens Magnetom Prisma and 7T Siemens Magnetom Terra scanner. The acquisition protocols for 3T-MRI and the 7T-MRI matched as closely as possible. Visual analysis was conducted by two expert neuroradiologists with previous disclosure of seizure onset hypothesis. Morphometric analysis of MP2RAGE-sequence performed with the MAP-18 Toolbox based on SPM-12.
Results: In 18.8% (3/16) of cases, lesions only either suspected or less extensive on 3T-MRI were identified by 7T-MRI combined analysis. Statistical analysis demonstrated significant improvement in lesion detection with MAP-7T-MRI compared to visual 7T-MRI analysis (Z=2.46, p=0.014) and MAP-7T MRI sequences compared to MAP-3T-MRI sequences (Z=2.0, p=0.046).
Conclusion: 7T-MRI with post-processing provides significant diagnostic advantage compared to standard 3T-MRI with or without post-processing in NLFE-patients. Also, MAP-analysis offers a promising approach for better presurgical evaluation. Future studies with larger cohort and with postsurgical outcome are needed to confirm these findings.

1790 | Analysis of Resting-State Functional Brain MRI Connectivity and Clinical Outcomes on Mesial Temporal Lobe Epilepsy with Hippocampal Sclerosis

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Purpose: Mesial Temporal Lobe Epilepsy with hippocampal sclerosis (mTLE-HS) frequently presents pharmacoresistance. Many brain connectivity networks might be negatively affected, with significant impact on functional performance. This study aims to determine the impact of pharmacoresponse on connectivity networks, through resting state functional brain magnetic resonance imaging in TLE-HS.

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Method: Medical charts from tertiary epilepsy service at UNICAMP were reviewed to obtain type of seizure, seizure onset, seizure frequency, febrile seizure, family history, epilepsy duration, follow-up period and antiseizure drugs (ASD). 139 TLE-HS patients (diagnosed according to ILAE 2017 criteria) were divided into three groups: Seizure-free (n=34), defined as absence of seizures for at least two years or more; Fluctuating (n=40), defined as seizure-freedom periods of one year or longer; and Pharmacoresistant (n=65), defined as no seizure-free period of more than one year. Resting-state fMRI were analyzed with SPM/UF2C, seeding the Hippocampus and Thalamus to whole brain networks. Patients were compared to 117 age-matched controls by using General Linear Model in SPSS 22, with $p<0.05$ as significant. Post-processing imaging data were analyzed with SPM.

Results: Seizure-free, fluctuating and pharmacoresistant patients were analyzed according to age (in years, mean age ± SD): 54 ±11,4, 53.3 ±12.7 and 49.1 ±12.3, respectively. The younger epilepsy duration was from seizure-free group (40.9 ±15.5). Number of ASD were also considered (mean 3.4 ASD at seizure-free group and 4.13 ASD at pharmacorresistant group), as well as occurrence of tonic-clonic seizure throughout life (55%, 80% and 55%, respectively). All three subgroups showed reduced connectivity in the hippocampus and thalamus networks when compared to controls, but it was not found among mTLE-HS subgroups cross correlation.

Conclusion: mTLE-HS is correlated with specific cerebral connectivity changes. Our study showed reduced thalamic and hippocampal networks connectivity compared to controls, but not among subgroups, regardless of clinical response profile.

Neuropsychology

276 | The impact of postoperative residual seizures on long-term intellectual outcomes after epilepsy surgery

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Purpose: Intellectual regression caused by seizures in adult patients with epilepsy is controversial. Also there have been very few reports on the long-term intellectual prognosis after epilepsy surgery. We aimed to clarify the clinical characteristics of patients who had long-term intellectual regression following epilepsy surgery.

Method: A retrospective study was conducted on adult patients who underwent epilepsy surgery and who got long-term (4 years or more) intellectual evaluations following surgery (n = 94). Logistic regression analyses with forward selection were performed to extract factors among clinical characteristics, such as diagnosis and seizure prognosis, that were significantly associated with long-term decline in scores of Wechsler Adult Intelligence Scale.

Results: Forty-six of the 94 patients had residual seizures after surgery: 38 had residual impaired consciousness seizures, and 15 had residual focal to bilateral or generalized onset tonic-clonic seizures. Five patients of the 94 patients showed a significant long-term decline in the Full-Scale intelligence quotient (FIQ). However, there were no clinical characteristics significantly associated with the FIQ decline. As for the indexes, a significant decline in the Working Memory Index was observed in 13 of 94 patients, and the presence of focal to bilateral or generalized onset tonic-clonic seizures after surgery was associated with this decline [P = 0.005, Odds ratio (OR) = 11.2]. A significant decline in the Processing Speed Index was observed in 8 of 94 patients, and the presence of seizures with impaired awareness after surgery was significantly associated with this decline (P = 0.006, OR = 43.3).

Conclusion: Considering that almost all patients had severe intractable seizures with impaired awareness or more before surgery, we believe that the results of this study strongly suggest that suppressing seizures with impaired awareness or more by epilepsy surgery can prevent the long-term decline in some intellectual functions like working memory and processing speed.

350 | How much difference does depression make to the outcome of neuropsychological assessment of patients with epilepsy

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Purpose: Cognitive assessment is crucial for the individualized patient care in epilepsy. Depression, a common comorbidity of epilepsy, is a factor that can affect cognition dependent or independent of epilepsy and its treatment. Here, we investigated the extent to which depression affects key cognitive domains in epilepsy and the extent to which a difference in depression makes a significant difference in regard to cognition and quality of life.

Method: In 732 patients with epilepsy (age 18 - 82 years, 49% female, mean age at onset of epilepsy 20 years), Beck Depression Inventory (BDI-I) scores were correlated

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with cognitive outcomes in attention/executive function, motor function, verbal and figural memory, language and visuo-construction, and quality of life (German QOLIE-10 analogue). Regression analysis was used to calculate minimum difference values in the BDI for significant differences in the dependent variables.

Results: 55% of PWE were found to have no depression, 26%, 15% and 4% mild, moderate or severe depression. BDI-scores correlated highly with quality of life (r=0.65). Correlations with cognition were significantly lower and ranged from r=0.17 (p<0.001) for attention to r=0.07 (p>0.05) for verbal memory. The maximum variance in cognition explained by the depression scores was below 3%. Calculating the minimum differences in depression for a significant difference in cognition (>1SD), BDI scores between 6 points for attention/executive functions and 13 points for language and visuo-construction made significant differences. For quality of life (scores 10-63) 16 BDI points made a significant difference

Conclusion: Depression, as measured by the BDI, primarily makes a major difference to quality of life. It appears to play a minor role in cognition, explaining less than 3% of the variance. If it does, then hypofrontality is to be assumed in depression with regard to attention/executive functions and motor skills, and this in those most severely affected with BDI values > 29 points.

508 | Novel tasks to assess material-specific memory impairments in patients with focal epilepsy: preliminary data with pre-surgical patients

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Purpose: Episodic memory tasks employing verbal material are generally sensitive to material-specific memory impairments in individuals with left mesial temporal lobe epilepsy (LmTLE), whereas visuospatial memory tasks are less consistently failed by individuals with right mesial temporal lobe epilepsy (RmTLE). A limitation of these tasks is the possibility for the examinee to use verbalization strategies when tested with visuospatial stimuli, and visualization strategies with verbal material. We recently developed two new analogous computerized recognition tasks aimed to assess material-specific impairments to address these limitations, one using pseudo-words (verbal) and the other using pictures of landscapes displaying mountains, trees, and a lake (visuospatial), and validated these tasks in a sample of patients who had surgery for temporal lobe epilepsy (Landry et al. submitted). The aim of the present study is to examine the ability of these novel tasks to predict the location of the epileptogenic zone prior to surgery among adult patients with drug-resistant epilepsy.

Method: Patients (18-55 yrs) with drug-resistant focal epilepsy referred for a pre-surgical neuropsychological assessment are invited to perform the two novel tasks as part of a research project. Memory performance is compared to data obtained from heathy control participants (*N*=124), and is then examined in relation to the location and the lateralization of the epileptogenic zone among patients.

Results: Similar to what was found in post-surgical patients, preliminary data (*N*=30) tend to indicate that patients with LmTLE show impairments on both the verbal and the visuospatial tasks, whereas RmTLE patients display specific impairments on the visuospatial task, in comparison to patients with extra-mesial temporal lobe epilepsy and to healthy controls.

Conclusion: These novel tasks offer promising tools to predict the location of the epileptogenic zone in patients with drug-resistant epilepsy, and have the advantage of not relying on motor responses and allowing remote testing.

553 | Theta bursts and impaired inhibitory control in sleep-related hypermotor epilepsy

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Purpose: Sleep-related hypermotor epilepsy (SHE) is a rare form of epilepsy linked to impaired inhibitory control[1, 2]. This study aimed to analyze various pathophysiological markers of impaired inhibitory control and identified some that improved after music therapy.

Method: We assessed cognitive performance in 41 patients with SHE using the Go/NoGo task, measuring reaction time, accuracy, and electroencephalographic (EEG) activity before and after a single exposure to Mozart's Sonata K. 448. Similar assessments were performed in two control groups: 41 patients with nocturnal epilepsy (NE) and 40 healthy controls (HC).

Results: SHE showed significantly longer reaction time (($Z_{SHE\ vs\ NE} = 2.46$, $P = 0.041$; $Z_{SHE\ vs\ HCs} = 2.69$, $P = 0.021$), lower accuracy ($Z_{SHE\ vs\ HCs} = 2.27$, $P = 0.031$), later onset of theta bursts in the mid-frontal region ($Z_{SHE\ vs\ NE} = 3.97$, $P < 0.001$; $Z_{SHE\ vs\ HCs} = 5.65$, $P < 0.001$) , later peaking of those bursts ($Z_{SHE\ vs\ NE} = 4.53$, $P < 0.001$; $Z_{SHE\ vs\ HCs} = 3.22$, $P = 0.0038$), and greater amplitude of those peaks ($Z_{SHE\ vs}$

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$_{NE}$ = 2.49, P = 0.038; $Z_{SHE\ vs\ HCs}$ = 10.44, P < 0.001). Severity of them correlated positively with reaction timer (r = 0.37, P = 0.017) . During music exposure, theta activity synchronized with the rhythm of the music. Music therapy significantly shortened reaction time (Z = -3.01, P = 0.0021) and increased accuracy (Z_{NoGo} = 2.09, P = 0.037) in patients with sleep-related hypermotor epilepsy, while also shortening the interval until the onset (Z = -2.72, P = 0.0066) and end of theta bursts (Z = -2.11, P = 0.035) .

Conclusion: SHE involves frontal network damage affecting inhibitory control, and that music therapy can mitigate this damage by facilitating onset of theta bursts and dampening their amplitude.

601 | Intellectual Functioning in Individuals with Developmental and Epileptic Encephalopathies: A Systematic Review

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Purpose: Developmental and Epileptic Encephalopathies (DEE) encompass a group of severe disorders characterized by drug-resistant epilepsy and developmental impairments, often leading to significant cognitive deficits. The variability in intellectual functioning across different DEE syndromes, however, is not well-documented. This systematic review aims to synthesize findings on intellectual functioning in individuals with various DEE syndromes, as measured by standardized intellectual or developmental assessments.

Method: A systematic review protocol was registered with Open Science Framework. Comprehensive searches were performed according to the pre-determined criteria in Medline, PsycInfo, Embase via Ovid and Scopus. Two independent reviewers (i) screened abstracts, titles, and full-texts, (ii) assessed the methodological quality of included studies using The National Institutes of Health's Quality Assessment Tool, and (iii) extracted predefined variables. Discrepancies were resolved through consensus to ensure accuracy and reliability.

Results: Of the 10,942 studies identified in the searches, 165 studies with 6513 patients diagnosed with DEE met the inclusion criteria. The majority focused on pediatric populations, and only 2 were adults-only samples. Intellectual functioning showed significant variability across DEE syndromes, and the Wechsler Intelligence Scale was the most commonly used instrument. Overall, 67.23% of individuals had intellectual disability (ID; Intellectual Quotient (IQ) <70). Nevertheless, 4.24% had very high intellectual functioning (IQ >=130). Syndrome-specific differences were evident; for example, Lennox-Gastaut Syndrome had the highest proportion of individuals with Intellectual Disability, affecting more than 94% of cases.

Conclusion: This systematic review provides the first comprehensive synthesis of intellectual functioning across different DEE syndromes. The findings confirmed a high prevalence of ID and substantial variability in intellectual functioning, emphasizing the importance of syndrome-specific assessments and interventions. Furthermore, gaps in understanding the developmental trajectory into adulthood call for longitudinal studies to better inform clinical management and support tailored interventions for individuals with DEE.

768 | Meta-analysis of neurodevelopmental outcomes following prenatal exposure to monotherapy antiseizure medications

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Purpose: A Cochrane Systematic Review was undertaken to investigate offspring neurodevelopmental outcomes following prenatal exposure to antiseizure medications (ASMs).

Method: Searches were undertaken in MEDLINE (Ovid), SCOPUS, and the Cochrane Central Register of Controlled Trials (December 2024). Predetermined inclusion criteria were defined by population, ASM type and control group. Data were analyzed in RevManWeb. The primary outcomes were global cognitive functioning and neurodevelopmental disorders. Verbal Intelligence Quotient (VIQ) outcomes for key comparisons, including sodium valproate (VPA), lamotrigine (LTG) and levetiracetam (LEV), are reported here due to its known sensitivity to teratogenic effects.

Results: Nine cohort studies were identified to include pregnancies exposed to VPA, six for LTG, and three for

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LEV. VIQ was reduced in children exposed to VPA versus offspring of untreated women with epilepsy (WWE) (n=156 vs n=149, MD = -8.10, CI -11.34, -4.87) and untreated women without epilepsy (WWoE) (n=81 vs n=401, MD = -12.22, CI 15.23, -9.21). Comparable VIQ was observed for children exposed to LEV and children of both WWE (n=101 vs n=55, MD = -0.70, CI -5.52, 4.12) and WWoE (n = 72 vs n=80, MD = -1.00, CI -4.81, 2.81). Similar, non-significant differences were reported between LTG and offspring of WWE (n=29 vs n=25, MD = -0.30, CI -6.79, 6.19) and WWoE (n=123 vs n=340, MD = -2.22, CI -4.87, 0.42). VIQ was significantly poorer for VPA in comparison to LEV (n=74 vs n=60, MD = -8.76, CI -13.28, 4.34) and to LTG (n=141 vs n=176, MD = -6.70, CI -9.36, -4.03). VIQ was comparable for LEV and LTG exposures (n=90 vs n=169, MD = -0.44, CI -3.72, 2.85).

Conclusion: Data for LEV and LTG are broadly reassuring in relation both unexposed control groups and other ASM-exposed comparators. However, data remain limited, for these and other ASMs, particularly at higher doses, and further research is urgently required.

786 | Very long-term cognitive outcomes in generalized epilepsies: a 20-year follow-up study

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Purpose: Subtle cognitive impairment, including one of longer-term memory, has been reported among adults with generalized epilepsies (GE). We aimed to assess whether cognitive dysfunction in this population tends to resolve over time.

Method: A sample of adults with GE underwent neuropsychological re-evaluation 20 years after baseline. Memory was assessed by free recall of a 15-word list, a verbal-logical story and a complex figure over three timepoints: fifth learning trial, immediate recall and copy results as baseline, respectively, and after 30 minutes and 4 weeks. Memory decay was calculated as the percentage recalled in relation to the previous testing point. Digit span and block tapping tasks were used to assess working memory, the trail making task – to assess executive functions. Paired sample t-tests or Wilcoxon rank tests were applied for comparison of performance at follow-up and 20 years ago.

Results: Nineteen PWE (14, 73.7% female, aged 25.7±7.3 years) were included at baseline. Over 20 years, monthly seizure reduction was seen (mean 11.6±30.2 to 3.7±14.5, p=0.002) with a group-level reduction in the number of antiseizure medications. Improvements in longer-term (4 week) but not delayed (30 min) memory were observed for word (90.1±12.7% to 94.8±7.6%, p=0.081 (30 min) and 39.2±26.7% to 67.6±18.5%, p=0.001 (4 week)) and verbal story recall (85.4±17.7% to 93.0±12.3%, p=0.059 (30 min) and 71.1±24.7% to 88.0±20.2%, p=0.004 (4 week)). Both delayed and longer-term visuospatial memory improved (64.0±19.1% to 74.5±21.5%, p=0.046 and 58.6±27.2% to 78.3±24.6%, p=0.005, accordingly). Working memory improvement was seen in the block-tapping (p=0.006) but not digit span tasks. Results of the trail-making test part A (p<0.001), but not part B, improved as well.

Conclusion: Cognitive abilities of adults with GE have improved over 20 years. Controlling seizures and reducing medication is very important for cognitive performance.

804 | The development and implementation of an evidence-based psychosocial intervention for children and young people with epilepsy

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Purpose: We describe an early intervention group therapy for young people with epilepsy that promotes mental wellbeing and resilience, and condition self-management. Building on a successful RCT (Dorris et al, *Epilepsy Behav.* 2017, (72), 89-98), we describe the revised version of our psychosocial intervention for epilepsy (PIE-r) and its implementation across a national healthcare system.

Method: The revised Psychosocial Intervention for Epilepsy (PIE-r) consists of six two-hour sessions delivered by a Clinical Psychologist and Specialist Epilepsy Nurse. Sessions cover epilepsy education, condition self-management, and mental health components using CBT and third wave therapies such as ACT. We updated the digital resources, including the addition of videos from a UK partner charity (Epilepsy Action), and made the intervention more accessible for young people with neurodiversity. We provided a range of training and consultation events before offering the intervention materials to sites delivering PIE-r around the UK.

Results: We describe our experience of adapting an effective RCT-backed intervention to a model of care that can be delivered flexibly by a range of health professionals within specialist epilepsy centers and consider whether it could be used in other settings. We also report findings from the initial 15 UK centers delivering PIE-r and discuss the feasibility, challenges and opportunities for epilepsy

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professionals to deliver low-cost effective psychosocial interventions as a routine part of epilepsy care.
Conclusion: Given the significantly increased incidence of lifespan psychiatric disorders in people with epilepsy, delivering early interventions promoting mental wellbeing and resilience could mitigate some of these later more severe mental health disorders. PIE-r is a brief group intervention with proven efficacy in increasing participants' condition management and confidence in discussing their epilepsy with others. We believe PIE-r provides a cost-effective model that could be used in different healthcare settings to improve epilepsy education, self-management and mental health resilience.

875 | Accelerated long-term forgetting – are we missing it? Evidence from the Crimes and Four Doors Tests

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Purpose: To detect accelerated long-term forgetting in the clinic.
Method: Experimental design
Results: Subjective self-reports of difficulties with memory are relatively common in people with epilepsy, but these do not always align with performance on objective memory tasks. The current study addressed this by gathering qualitative and quantitative subjective reports of memory function in a broad community sample of people with epilepsy who were recruited via the charity Epilepsy Action, along with healthy controls. Participants also carried out one of two recently developed experimental tasks (Crimes or Four Doors) that provide objective measures of long-term memory and forgetting, along with an additional verbal learning and recall task, each of which assess retention over a one-week period. These measures of objective memory were carried out remotely over Zoom. Relative to controls, people with epilepsy reported memory problems across all our subjective measures. They also showed more objective forgetting on Crimes and Four Doors tests over the one-week delay between tests, a difference that was not attributable to level of initial learning performance. These findings indicate atypical and accelerated forgetting in at least some people with epilepsy, and that such difficulties are detectable using remotely administered versions of the Crimes and Four Doors tests, thus showing promise for potential future use in clinical contexts.
Conclusion: We have developed two tests (one verbal and one non-verbal) to detect ALF.

906 | Epilepsy Surgery During the Golden Years – Five Year Neuropsychological Outcomes of an Elderly Patient with Refractory Left Temporal Lobe Epilepsy

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Purpose: The incidence of new-onset epilepsy is higher in the elderly (defined as those aged 60 or 65 and older) than in any other age group. However, epilepsy surgery – particularly resective surgery - is less prominent in elderly patients. While studies have shown that epilepsy surgery, especially temporal lobectomy, can be performed in older patients with good results, general seizure outcomes tend to be less favorable, and the rate of post-operative complications a little higher, than in younger patients.
Method: We present the case of an elderly man who began experiencing focal seizures of left temporal lobe origin at the age of 63. His seizures became refractory to medication, and he was ultimately referred to our National Association of Epilepsy Centers (NAEC) Level 4 program at the age of 66. After extensive pre-surgical evaluation, he was deemed to be an ideal candidate for resective surgery, which he underwent at the age of 67 in November 2019.
Results: He participated in serial neuropsychological evaluation, beginning prior to his left anterior temporal lobectomy, and at one, four, and five-year follow-up appointments. Initial changes (one-year post-surgery) included declines associated with verbal/auditory learning, memory, and recognition (attenuation anticipated as a potential surgical consequence, and discussed with him preoperatively). Over time, improvement was seen on these domains (most notably with regard to initial learning and both short- and long-delayed free recall). Additional longitudinal improvements were seen on some trials of language. This finding is noteworthy, given the surgical proximity with regard to eloquent skill areas. Areas of decline over time not affiliated with epileptogenic findings may be attributable to parallel decline factors associated with aging.
Conclusion: This case demonstrates overall improvement in cognition and quality of life of an elderly patient status post epilepsy surgery and supports the idea that epilepsy surgery may provide long-term benefits for elderly patients.

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932 | Comparing the Classification of Cognitive Function by The International Classification of Cognitive Disorders in Epilepsy, IC-CoDE and The Bonn Code

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Purpose: Two taxonomies independent of the specific tests used, has been proposed to improve data collection across centers: The IC-CoDE (McDonald, C.R. et al. Neuropsychology 2023; 37:301-314) and the Bonn Code (Helmstaedter, C. et al. 2012; 53: 1765-1773; Delev, D., et al. Seizure 2020; 79: 112-119). To our knowledge, a direct comparison of these two taxonomies at an individual level has not been published. This study compares these two taxonomies.
Method: Neuropsychological test results from 97 participants were converted into age corrected z-scores and classified by the Bonn Code and the IC-CoDE (1 SD and 1,5 SD below average).
Results: The Bonn Code classified 10% of participants as unimpaired, whereas the IC-CoDE classified 60% (at -1 SD) and 32% (at -1.5 SD) as unimpaired (Table 2). Correlations between the two taxonomies were moderate to strong (r = 0.66–0.72). See Table 3. The lowest concordance rate (51%) occurred when the Bonn Code's "borderline" category was considered impaired and compared to IC-CoDE at -1.5 SD, yielding slight agreement (Kappa = 0.14). When "borderline" was considered unimpaired, concordance increased to 64%, with fair agreement (Kappa = 0.35). The highest concordance rate (88%) was observed between the Bonn Code (with "borderline" as unimpaired) and IC-CoDE at -1 SD, showing substantial agreement (Kappa = 0.70).
Conclusion: Our findings indicate a moderate to strong correlation between the Bonn Code and the IC-CoDE. The Bonn Code might appear more likely to classify patients as cognitively impaired compared to the IC-CoDE. Classifying the "borderline" category as unimpaired in the Bonn Code increases concordance with the IC-CoDE. Understanding these differences is crucial when comparing studies utilizing different taxonomies and in selecting the appropriate system for clinical or research purposes. Future research should explore these differences in larger, cross-center studies, including associations between cognitive phenotypes and biomarkers. This study was not supported.

939 | Trackognize: A Smartphone-Based Tool for Monitoring Mental Fitness – Willingness of People with Epilepsy to Use It

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Purpose: In the run-up to a clinical validation study, we assessed the willingness of epilepsy patients to use Trackognize, a smartphone application monitoring typing behavior to assess cognition and mental fitness. The objectives included identifying factors influencing the willingness to use the app and exploring patients' concerns regarding such technology.
Method: This cross-sectional study included 349 patients from the Department of Epileptology, University Hospital Bonn. Participants completed a structured questionnaire assessing demographic and epilepsy-related variables, subjective complaints on cognition and behavior, openness to technological solutions, and willingness to use an app-based monitoring. Statistical analyses included chi-square tests and Kendall's tau correlations.
Results: Overall, 68.5% of participants expressed a willingness to use Trackognize. Key factors correlated with a positive attitude included higher educational attainment (>10 years, $\chi^2(1, N = 349) = 13.80$, $p < .001$), not being seizure-free ($\chi^2(1, N = 330) = 5.33$, $p = .021$), and regular use of a seizure diary, particularly smartphone-based ($\chi^2(2, N = 128) = 8.12$, $p = .015$). Technical affinity ($\tau = .24$, $p < .001$) as well as openness to technological solutions ($\chi^2(1, N = 335) = 122.02$, $p < .001$) were further positively associated factors. Qualitative responses highlighted concerns related to data privacy (40.9%), data security (29.5%), and skepticism about the app's validity (18.9%). Surprisingly, cognitive or emotional impairments and the perceived impact of epilepsy on cognition did not significantly affect willingness.
Conclusion: A substantial proportion of participants expressed willingness to engage in app-based cognitive monitoring, especially those with uncontrolled seizures, technical affinity, openness to technology, and seizure diary use. Concerns about privacy, security, and validity are essential and need to be considered when implementing such an app in patients. The findings highlight the potential of mobile health technologies in epilepsy care, especially for patients seeking innovative tools for symptom and cognitive management.

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947 | Correlation between subclinical seizures and cognitive impairment in adult epilepsy patients – a retrospective observational study

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Purpose: Cognitive impairment is highly prevalent and detrimental to the quality of life of people with epilepsy. We aimed to evaluate whether variability in neuropsychology scores among adult epilepsy patients is significantly associated with the presence of subclinical seizures (SCSs) and their characteristics.

Method: A retrospective observational study was conducted, including a cohort consecutive adult patients from a single center, admitted for presurgical scalp or intracranial video-EEG monitoring and neuropsychological assessment within a 12-month period. Video-EEG was reviewed to note SCSs during monitoring, as well as their characteristics (lateralization/localization relative to clinical seizures, estimated daily frequency). Each category was analyzed for a significant association with neuropsychological scores Verbal Comprehension Index (VCI), Perceptual Reasoning Index (PRI) and Auditory Memory Index (AMI), controlling for relevant clinical variables.

Results: Of 140 patients included in the analysis, SCSs were recorded in forty-three patients (31%). On univariate analysis, the presence of SCSs alone was not significantly associated with variation in neuropsychology scores. However, patients with SCSs not colocalised to clinical seizures had significantly lower VCI (t=-2.6647, p=0.029) and patients with more than one SCS per day had significantly lower scores in AMI (t=-3.355, p=0.021). On backward multivariate linear regression models, the presence of non-colocalized SCS was a significant factor associated with VCI, while the presence of more than one SCS per day was associated with both PRI and AMI scores.

Conclusion: Further analysis in larger cohorts is needed to confirm these findings and understand the underlying reason for this association. It is possible SCS characteristics could aid diagnostic processes by fitting profiles of complex drug-resistant epilepsies or that distinctive SCS onset zones may indicate separate epileptogenic networks to be considered for treatment. Our study corroborates the potential usefulness of monitoring and treating frequent SCSs over time.

1036 | Cognitive phenotype of patients with juvenile myoclonic epilepsy

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Purpose: to assess cognitive functions and cognitive impairment of patients with juvenile myoclonic epilepsy (JME) and determine its relation to different clinical epilepsy-related characteristics.

Method: We examined with 42 patients (15 males and 27 females) at the age of 27 [20; 33] years with JME and control group - healthy volunteers 41 (14 males and 27 females) at the age of 27 [26; 34,75] years. Cognitive functions were examined using a full set of specific tests included: WAIS III, FAB, Trail making Test A and B, Munsterberg test, Luria Memory Words Test, Benton Visual Retention Test, Clock-Drawing Test, verbal fluency test, The Schulte table. Anxiety and depression were examined of HADS and Beck Depression Inventory. Adult with intellectual disability were not included in the sample.

Results: IQ levels of patients with JME high average – 100,3 ±2,42 (p <0,001). The duration of the disease is more than 10 years, the pharmacoresistance was influenced by IQ – 90.3 ±3.60 (p = 0.035). In patients with JME, compared with the control group, a decrease was found: TMT–A – 42,3 ±3,76 (p = 0,001), Munsterberg test – 15,3 ±1,05 (p = 0,026), Digit Sumbol-Codingd – 10,8 ±1,52 (p = 0,003), Arithmetic 8,0 ±0,52 (p = 0,001), Information – 9,5 ±0,45 (p = 0,037), Block Design 9,8 ±0,52 (p = 0,001), Matrix Reasoning – 8,4 ±0,41 (p=0,001), Similarities –12,3 ±0,59 (p=0,007), verbal fluency test –10,5 ±0,97 (p = 0,001).

Conclusion: The cognitive phenotype of patients with JME is characterized by an average norm of intelligence, decreased concentration of attention, impaired executive functions related to control and planning, declined concentration of attention, perceptual-motor function, which is manifested by a reduction in visual perception, visual-constructive reasoning, impaired verbal fluency, and decreased memory and learning.

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1243 | Neuropsychological and linguistic evaluation of patients with Dravet syndrome: a systematic review

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Purpose: Dravet Syndrome (DS) is characterized by various manifestations and alterations in neurodevelopment. Initially, the cognitive development of patients with DS is normal, , but cognitive decline typically begins between the second and third year of life, when most patients develop moderate to severe intellectual disability. As for linguistic skills, there is a delay in the development of expressive language, while receptive skills and comprehension are relatively preserved. However, the neuropsychological and linguistic profile of patients with DS has not been thoroughly characterized, nor how it evolves over time.
Method: To gain a broader understanding of the neuropsychological and linguistic characteristics of individuals with DS, a systematic review of the existing literature was conducted. The bibliographic search related to the study's objective was carried out using five databases: PsicoDOC, Scopus, Web of Science, PubMed, and PsycINFO. An analysis of the obtained data was conducted, and the average sample size was calculated.
Results: The studies published to date suggest considerable variability in the profiles of individuals with DS. Some patients show early global deterioration and others a more gradual decline, but in all cases, neuropsychological, communication, and language development are severely compromised throughout their development. This profile suggests a complex pattern of deficits with individual variability, but a general trend toward progressive deterioration.
Conclusion: Currently, there is a lack of scientific literature that identifies these characteristics in order to suggest specific intervention programs targeting the associated pattern of characteristics.

1310 | Executive Functioning Improvement with Behavioral Psychotherapy, but not with Sertraline, in Persons with Mesial Temporal Lobe Epilepsy due to Hippocampal Sclerosis and Major Depressive Disorder: a pilot, randomized and controlled study

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Purpose: This study aimed to compare a non-pharmacological intervention - Behavioral Activation (BA) with a pharmacological treatment for major depressive disorder (MDD) in an etiologically homogeneous sample of persons with in Mesial temporal lobe epilepsy due to hippocampal sclerosis (MTLE-HS) considering depressive symptoms, quality of life, and executive functioning,
Method: Twenty-one persons with MTLE-HS and MDD were randomly allocated in: (1) Experimental Psychotherapy Group (PG) or (2) Active Control Sertraline Group (SG). The outcome measures were assessed by Beck Depression Inventory-II, Quality of Life Inventory in Epilepsy – 31 and Behavior Rating Inventory of Executive Function. Outcomes were systematically assessed with valid and reliable instruments at the following time intervals: (T0)=baseline; (T1)=after the 6th week (middle of treatment); (T2)=immediately after the end of treatment (12th week); (T3)=three months after the end of treatment; (T4)=six months after the end of treatment.
Results: There were no differences between groups concerning any variables at baseline. Longitudinally, there were no differences between groups in the outcome measures at any time interval. In the within-group analysis, compared to baseline: SG showed a reduction in depressive symptoms at T3 (p=0.007) and T4 (p=0.034); PG showed a reduction in depressive symptoms at T1 (p=0.004), T2 (p=0.015) and T3 (p=0.027). The PG also showed an improvement in executive functioning and quality of life at T2 (p=0.027 and p=0.014, respectively).
Conclusion: There was a comparable efficacy of BA and sertraline in reducing depressive symptoms, treatment response, and MDD remission. However, BA also improved executive functioning and QoL. Future research with a more comprehensive assessment of cognitive improvement after BA in persons with epilepsy Is needed due to the impact in patient's social functioning.

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1392 | Emotion recognition across visual and auditory modalities in temporal lobe epilepsy

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Purpose: To explore emotion recognition abilities in patients with temporal lobe epilepsy (TLE) and compare their performance across the visual and auditory domains.
Method: Nineteen patients with TLE (68.4% female; 24-63 years old) from the Department for Epilepsy and Clinical Neurophysiology of The Institute of Mental Health in Belgrade were included. The control group consisted of nineteen healthy subjects (52.6% female; 23-62 years old) without neurological or psychiatric illness history. Facial emotion recognition was assessed through pictures from the Karolinska Directed Emotional Faces Database (Lundqvist D et al, 1998). Five images were used for each emotion (neutral, happiness, sadness, fear, surprise, anger, disgust) for 35 trials. The prosody task test developed in our department evaluated affective prosody recognition (Lalatovic et al, 2023) and consisted of 21 trials, 3 for each emotion.
Results: Patients with TLE performed worse than controls on both tasks (visual domain: $t(36) = 3.32$, $p = .003$; auditory domain: $t(36) = 4.67$, $p = .000$). TLE patients showed deficits in recognition of fearful ($t(36) = 2.15$, $p < .05$) and sad ($t(36) = 2.87$, $p < .01$) faces compared to controls. On the prosody recognition task, patients with TLE had more difficulty recognizing fear ($t(36) = 2.82$, $p < .01$), sadness ($t(36) = 3.41$, $p < .01$), disgust ($t(36) = 2.70$, $p = .01$), and surprise ($t(36) = 2.55$, $p < .05$) than control group. In the visual domain, patients most frequently confused fear with surprise (35.8%) and sadness with neutral (14.1%) expressions. On the prosody task, patients had difficulty discriminating sadness from neutral (45.6%) and fear from sadness (21%).
Conclusion: Emotion recognition accuracy in the TLE group was significantly lower than healthy subjects in both the visual and auditory modalities. Results suggest a more pronounced deficit for 'negative' emotions in TLE patients, mainly fear and sadness.

1412 | Cognitive and Emotional profiles in Children with new-onset Epilepsy: a longitudinal Cohort study 5 years follow-up (EpilETRE)

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Purpose: Epilepsy is frequently associated with an increased risk for social and emotional regulation disorders in children. Our study was designed to detect and assess the risk of appearance of mood disorders in children with new onset epilepsies, aged 6 to 16 years old, using a prospective and longitudinal design. Epileptic encephalopathies were excluded.
Method: We have enrolled 65 children between years 2017 and 2020 with new onset epilepsies from a tertiary medical center in Barcelona. A comprehensive evaluation including standardized assessment tools (MDI-C, CDI, R-CMAS and Akiskal scales), scales for executive functions (EpiTrack) were conducted six months following the first seizure (T0), nine months later (T9), 18 months (T18) from inclusion and finally 5 years follow up (T5).
Results: FSIQ did not changed between T0 and T18 (103,02 /101,13) but verbal coefficient index did (107,05/100,91) p=0,014. Statistically significant differences were found per epilepsy category between T0 and T18 ($p < 0.001$), higher in focal structural epilepsies than in focal genetic or generalized epilepsies. Also higher in left side epilepsies (p=0,001). Patients treated with two antiseizure medications (ASMs) showed a greater decrease in VCI (p=0,001). MDI showed significant results in older patients at T0 but not in T9 or T18. We found less cyclothymia on T9 or T18 than in T0 (p=0,099) on patients treated with 2 ASMs. We also found a higher incidence of depression symptoms in girls than in boys. Generalized epilepsies obtain higher scores in Social problems and Thought problems (p=0,039) especially those with left side focus epilepsies or bilateral ones (p= 0,061).
Conclusion: Our results could guide clinicians to an earlier diagnosis for those children with increased risk of developing psychiatric disorders, thus improving optimal care standards with an impact on quality of life, social functioning and school adaptation.

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1456 | The volume of particular brain regions and working memory performance in patients with left mesial temporal lobe epilepsy

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Purpose: Patients with temporal lobe epilepsy may exhibit a wide range of cognitive impairments, not only directly associated with the location of the epileptic focus. Even though the working memory network mostly includes areas located outside the temporal lobes, it is one of the cognitive areas that is often affected in those patients. The aim of the present study was to compare working memory in patients with left-MTLE and healthy subjects and to correlate their performance with the volume of particular brain structures.

Method: The study included twenty-one patients with left-MTLE and twenty-eight demographically matched healthy individuals. Each patient completed neuropsychological assessment, which included two subtests of Wechsler Memory Scale IV (WMS-IV): Symbol Span and Spatial Addition. Moreover, participants underwent a magnetic resonance imaging (MRI) 3T, which allowed for volumetric evaluation of particular brain parts.

Results: Intergroup comparisons revealed that patients with left MTLE achieved significantly lower scores than healthy participants in *Symbol Span ($p < 0.001$)* and *Spatial Addition ($p < 0.001$)*. It has been shown that in patients with epilepsy working memory performance negatively correlated with: right posterior cingulate ($r = -0.583$; $p = 0.006$), left cerebellum cortex ($r = -0.455$; $p = 0.038$) and right cerebellum cortex ($r = -0.509$; $p = 0.019$). On the contrary left superior parietal cortex ($r = 0.493$; $p = 0.023$) and right cuneus ($r = 0.442$; $p = 0.045$) have shown a negative correlation with working memory indicators.

Conclusion: Patients with left-MTLE experienced significant impairments in working memory. Specific grey matter changes associated with the level of performance in this cognitive domain have also been observed. These alterations include both atrophy in specific brain regions as well as pathological enlargement in other regions and illustrates the complex network of relationships between the brain, epilepsy and cognitive functioning.

1497 | Cognitive profile and family dynamics of patients with psychogenic non-epileptic, epileptic, and coexisting seizure: A comparative study in India

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Purpose: Despite significant advancements in epileptology, understanding the interplay between family environment and cognitive functioning among individuals with epileptic seizures, psychogenic non-epileptic seizures and coexisting seizure disorders remain limited, particularly in south Asian countries like India. This study aims to assess the family environment, a crucial factor that shapes perceptions and treatment approaches, alongside cognitive profiles of affected individuals.

Method: In this cross-sectional; observational study, 31 patients (16 with epilepsy, 10 with PNES, and 5 with coexisting seizures), aged 18-60 years and diagnosed by neurologists with supporting EEG findings, were selected. Participants were compared across various domains including demographics, clinical features, visual and auditory learning and memory, planning abilities, working memory.

Results: Results indicated that patients with epilepsy performed significantly worse than both groups on the porteus maze test, taking longer time and making more errors (mean errors: 4.38; $p = 0.001$). in learning and memory tests, the epilepsy group had the lowest scores on immediate recall, immediate recall after interference and delayed recall ($p = 0.017$, $p = 0.015$ and $p = 0.004$ respectively). A significant difference was also observed in family environment, where high conflict was more prevalent in PNES families ($p = 0.015$).

Conclusion: The study highlights the importance of integrating family dynamics into the clinical evaluations process as interpersonal relationships, emotional and social dynamics play an important role in countries like India. By addressing these gaps in knowledge, we can aim to contribute more effective and culturally sensitive management strategies, cognitive rehabilitation for individuals experiencing both epileptic and non-epileptic seizures.

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1499 | Epilepsy beyond seizures: Exploring psychosocial determinants of treatment adherence in patients with epilepsy

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Purpose: Epilepsy is a chronic neurological condition with substantial psychosocial implications affecting treatment adherence. Psychological distress, stigma, and social stressors further complicate disease management. The cross-sectional study explores the effects of this on adherence by both epilepsy patients and their caregivers.
Method: In total, 43 epilepsy patients and their caregivers participated. Patients completed the Generalized Anxiety Disorder Scale (GAD-7) and Patient Health Questionnaire (PHQ-9) to determine anxiety and depression, while caregivers completed the same together with the Caregiver Burden Scale. Structured interviews explored stigma-related problems, including financial, marital, academic, and employment difficulties. Both patients and caregivers received supportive sessions in order to address psychosocial stressors and enhance coping mechanisms.
Results: Moderate adherence (mean=3.3, scale 1-5) was reported, with 20% of participants classified as high adherence and the remaining 20% as low adherence. Anxiety and depression were associated negatively with adherence (r = -0.43, p<0.01; r = -0.51, p<0.001 respectively), with social stressors (r = -0.38, p<0.05) and caregiver burden (r = -0.34, p<0.05) being correlates with low adherence. The regression analysis revealed depression (β = -0.32, p<0.01), social stressors (β = -0.28, p<0.05), and support systems (β = +0.25, p<0.05) to be significant predictors of adherence.
Conclusion: Integrated mental health support is advocated along epilepsy care against the background of this study's finding. These findings suggest that addressing stigma, financial stress, and caregiver burden with structured interventions can assist in improving adherence and overall well-being. Targeted psychosocial support for both the patients and caregivers ought to be implemented.

1511 | Pre-Surgical Neuropsychological Evaluations for Epilepsy Patients in Mongolia

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Purpose: Neuropsychological evaluations as part of a pre-surgical workup for individuals with drug resistant epilepsy (DRE) has been well established. We depend on appropriate test stimuli and normative data, and well researched outcomes within our population to make clinical judgments. When treating patients in other countries without established neuropsychological measures, we must strive to provide thorough pre-surgical evaluations while acknowledging the limits of our tools and research. The current study aims to establish the clinical utility of a translated neuropsychological measure as part of a pre-surgical workup in Ulaanbaatar, Mongolia. The clinical work was completed as part of a surgical mission with the Virtue Foundation. Specifically, we analyze if the Repeatable Battery for the Assessment of Neuropsychological Status Update (RBANS; Randolph, 2009) can help localize and lateralize cognitive dysfunction associated with the epileptogenic region.
Method: 17 patients (ages 15-53) with focal epilepsy underwent brief neuropsychological testing as part of a pre-surgical workup. Through the use of an interpreter and a translation that focused on both accurate language and the cultural appropriateness of the testing materials, patients were administered the RBANS.
Results: Patients with left sided epileptiform abnormalities performed significantly worse on List Recall [t(12)=-6.315, p <0.001] and List Recognition [t(12)=-2.502, p=0.028] compared to those with right EEG abnormalities. Similarly, there were significant differences in List Recall [t(10) = -6.543 p <0.001] and List Recognition [t(10)=-2.087 p=0.032] performances between those with left versus right abnormalities seen on MRI. Regarding localization, Digit Span scores were significantly higher in those with the temporal versus extratemporal EEG onsets [t(15)=2.359, p=0.11]. The Attention Index did not quite reach significance but was stronger in those with temporal versus extratemporal epilepsy [t(15)=2.108 p=.052].
Conclusion: Neuropsychological testing using a translated RBANS has utility for pre-surgical evaluations in patients with DRE in Mongolia.

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1513 | Influence of epilepsy on neuropsychiatric symptoms and cognitive profile in patients with tuberous sclerosis complex

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Purpose: Tuberous Sclerosis Complex (TSC) is a neurocutaneous disorder associated with epilepsy (70-90% of cases) and neuropsychiatric symptoms (NPS). However, the influence of epilepsy on NPS remains unclear. This study aimed to describe the presence of NPS in a cohort of patients with TSC and to establish their relationship with epilepsy severity and other clinical characteristics such as genetics, neuroimaging, and EEG findings.
Method: Descriptive, cross-sectional, single-center study that included adults (18-65 years) with TSC, without significant intellectual disability. Patients underwent a comprehensive neurological and neuropsychological assessment, which included the TAND-checklist (TAND-L), as well as, the following scales: MoCA (Montreal Cognitive Assessment), the HADS-A (Hospital Anxiety and Depression Scale-Anxiety), HADS-D (Hospital Anxiety and Depression Scale-Depression), EQ5d5l (EuroQol 5-Dimensions 5-Levels), QOLIE-10 (Quality of Life in Epilepsy Inventory-10), TERMO (thermometer Test) and WAIS-IV (Weschler Adult Intelligence Scale-Fourth Edition).
Results: Twenty-eight patients with TSC were included (19 women, 44.7±14.4 years). Seven patients had *TSC1* variants and 11 had *TSC2* variants. Nineteen (67.86%) patients had epilepsy, 7(36.84%) of them exhibiting drug-resistant epilepsy. Five (17.86%) had presented infantile spasms in the past. Regarding TAND-L, the most frequent NPS were: mood swings (80%), excessive shyness (70%), sleep/attention disorders (60%) and low self-esteem (50%). A longer duration of epilepsy and a higher number of anti-seizure medications (ASM) trials correlated with a poorer total Intelligence Quotient (Pearson correlation= -0.53, significant at 0.007 and -0.45, significant at 0.03, respectively). Patients carrying a *TSC2* variant or with a history of infantile spasms had higher intellectual disability and worse TAND scores ($p<0.05$). Despite the high prevalence of NPS, only 4 (14.28%) patients had received specific psychiatric care.
Conclusion: Patients with TSC and severe epilepsy showed worse neuropsychiatric outcomes. The high prevalence of NPS underscores the need for specific protocols for early detection and intervention

1653 | Understanding Caregiver Stress in Pediatric Epilepsy: The Mitigation of Cognitive Level, Education, and Treatment

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Purpose: The aim of this study was to develop a predictive model to identify factors influencing stress levels in caregivers of children with epilepsy. Understanding these factors can help design targeted interventions to support caregivers and improve their well-being.
Method: A cross-sectional study was conducted involving caregivers of children diagnosed with epilepsy. Stress levels were assessed using the Parenting Stress Index (PSI). A multiple linear regression model (MRM) was computed to examine the impact of independent variables: child's age at PSI assessment, caregiver's age, education level, and pharmacological treatment. Non-parametric tests were conducted to study the correlation between stress levels and cognitive impairment, educational level, and pharmacoresistance.
Results: The MRM didn't show significant results ($p>0.05$). The child's age at PSI assessment was significantly associated with Difficult Child (DC)($p=0.011$), indicating a positive relationship. Caregiver age showed no significant effects. Post-hoc analysis revealed significant differences in TSS and Parent-Child Dysfunctional Interaction (PCDI) based on the child's cognitive level, particularly between normal and moderate groups (p-adjusted <0.05). Education level was also a significant factor; caregivers having lower educational attainment reported higher stress levels compared to those with a university degree (p-adjusted = 0.014). About medication type, polytherapy was associated with higher perceived stress in parent-child relationships (p-adjusted = 0.020 for PCDI).

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Conclusion: The findings suggest that factors such as the child's cognitive level, caregiver's educational background, and polytherapy significantly influence caregiver stress levels. Although the overall model explained a limited portion of the variance, these results highlight potential targets for tailored interventions to support caregivers of children with epilepsy. Future studies should explore additional psychosocial and contextual factors to better understand and address caregiver stress. This project was funded from the European Union's Horizon Europe research and innovation programme (grant agreement N° 101136835)

1654 | Neurocognitive Characterization and Clinical Aspects of Glioma-Related Epilepsy: Insights from a Surgical Cohort

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Purpose: Gliomas are a heterogeneous group of brain tumors, often presenting with epilepsy as the first clinical manifestation, leading to surgical intervention. This study provides a descriptive analysis of patients with glioma and epilepsy who underwent surgery in our Unit, focusing on demographic, histological, surgical, and cognitive characteristics.

Method: A retrospective analysis was conducted on 113 patients with gliomas and epilepsy who underwent surgical treatment. Demographic and clinical data were described.

Results: The cohort included 47 females (41.59%) and 66 males (58.41%). The median age at seizure onset was 8.5 years (SD=5.16, range 0.2–24), and the median age at surgery was 11.3 years (SD=6.83, range 0.5–41.4). The median time from seizure onset to surgery was 1.4 years (SD=3.63, range 0–17.4). Regarding histology (N=113), the most common tumor type was glio-neuronal (59.65%), followed by low-grade glial tumors (29.82%), high-grade glial tumors (1.75%), and mixed forms with focal cortical dysplasia. The most frequent surgical site was the temporal lobe (50.88%), followed by the frontal (17.54%) and parietal (15.79%) lobes. Cognitive assessment (N=97) revealed a median IQ of 99 (SD=17.19). Most patients (75.26%) scored in the normal range, while 22.68% exhibited mild impairment and 1.03% moderate/severe impairment. Digit span (N=58) showed median scores of 89.65 (direct) and 93.80 (inverse), with 75.86% and 81.48% performing within the normal range. Visual-spatial memory (N=46) had a median score of 98.2 (SD=19.79), with 89.13% showing normal performance. Behavioral assessment (CBCL, N=36) showed no clinical symptoms in 75% of patients, while 19.44% were in the clinical range.

Conclusion: Most patients performed within normal cognitive levels possibly due to the minimal impact of seizure activity and its pharmacological treatment, showing preserved cognitive functions. This project has received funding from the European Union's Horizon Europe research and innovation programme under grant agreement N° 101136835

1732 | Frontal lobe lesion and overeating/mocking seizures: a case-report

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Purpose: Growing space-occupying brain lesions can manifest with seizures and focal deficits but sometimes progressive changes in personality that may go unrecognized.

Method: Case-report

Results: A 52-year-old healthy male went running in hot weather. Upon returning home he had an inaugural overeating (full rice plate) and endless verbal joking episode followed by left eye and head turning and bilateral tonic-clonic seizure with no full recovery of consciousness. Status epilepticus diagnosis prompted admission in an intensive medical care unit. Family mentioned a 6-month-long personality shift consisting of more disinhibited and confrontational behavior. He required IV antiseizure medication (maximum doses of levetiracetam, valproic acid, lacosamide), sedation and ventilation. EEGs showed diffuse slow activity with right frontal spikes and spike-and-wave complexes, with later resolution. Brain MRI showed a 2-mm right non-contrast enhanced orbitofrontal lesion with vasogenic oedema. He was discharged under all ASM, later suspending lacosamide. However, his behavior changes persisted with added more frequent and maintained joking ("Witzelsucht" cognitive phenomenon). Repeat BMRI showed significant lesion enlargement, enhancement and other atypical characteristics. Repeat routine EEGs did not show epileptiform activity. Brain biopsy confirmed grade IV glioma. He underwent surgery with maximal resection of the lesion and chemotherapy. Ten months later he had another overindulgent

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and more compulsory joking episode followed by a generalized seizure. Lacosamide was reinitiated alongside steroids with resolution, and repeat BMRI showed tumor recurrence and oedema. Though mild joking persisted, his appetite was fairly normal between all these episodes. Repeat routine EEGs showed only right frontal slowed activity. He developed more apathetic behavior 6 months before passing away.

Conclusion: This case describes a rare type of focal seizure with magnification of cognitive changes classically attributed to (mainly right) frontal lobe lesions, before generalization. More persistent behavior changes did not correlate with EEG activity in the initial stage, though post-surgery EEGs showed right slow-wave activity.

1779 | Social Cognition and Epilepsy: A Pilot Study on Happé Strange Stories and Baron-Cohen Reading The Mind in The Eyes Tests

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Purpose: Social cognition is the capacity to build representations of the relationship between onself and others. (Ochsner,K.2008, BiolPsychiatry 64:48-61). It is extensively discussed for autism, but little is known about social cognition in people with epilepsy. We aimed at studying the ability to identify emotions by interpreting the look of others and to interpret the non-litteral meaning of stories (irony, joke, etc.)

Method: We perfomed a pilot cross-sectional observational study approved by local ethics comittee (# 3.900.015). We applied the Brazilian modified version of the Happé Strange Stories Test (12 items) (Happé F. 1994, J Autism Develop Disorders, 24:129-164) and the Brazilian modified version of the Baron-Cohen Reading the Mind in the Eyes Test (Baron-Cohen et al. 1997, J Child Psychol Psychiatry,38(7):813-22) (32 items). Cut offs for impairment were respectively under 8 and 18 righteous answers. Patients were randomly selected from our outpatient Epilepsy service. To infer the influence of global cognition, anxiety, depression and sleepiness, the Mini-Mental State Examination (MMSE), Montreal Cognitive Assessment (MoCA), Beck Anxiety Inventory (BAI), Beck Depression Inventory (BDI) and Epworth Sleepiness Scale (ESS) were performed. Results were expressed as averages and standard deviation. The Spearman test was used to search for correlations between either Happé or Baron-Cohen test and the other scales applied, ($p<0.05$).

Results: Fourteen patients participated, 10 women, aged 37.9, SD=14.41 years, 3 with generalized epilepsy and 11 with focal epilepsy. Participants scores for the Happé Test ranged 2-7, Average= 4.42, SD=1.84 and for the Baron-Cohen ranged 12-26, Average= 20, SD=4.04. There was a moderate positive correlation between MMSE and Baron-Cohen (rS=0.5231; P=0.05) and a tendency for correlation between Moca and Baron-Cohen (rS=0.5078; P=0.06).

Conclusion: A decline in social cognition was detected among our patients. The interpretation of stories was more affected than eyes expression recognition, but the latter was in accordance with other cognitive tests.

1827 | Theory of mind in patients with juvenile myoclonic epilepsy

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Purpose: People who suffer from epilepsy have been shown to present different degrees of deficit in Theory of Mind (ToM). This would result in difficulties in coping, stigma, personal achievements as well as work and social integration. The aim of this study was to explore and characterize the cognitive functions involved in ToM in patients with Juvenile Myoclonic Epilepsy (JME).

Method: A cross-sectional study was carried out including adult patients (18-50 years) with JME at the Hospital de Clínicas, with a control group of healthy individuals matched by sex, age and education. ToM was assessed with validated tests (Reading the Mind in the Eyes and Faux Pas) and global cognitive screening tests were applied (Addenbrook's Cognitive Examination III -ACE III-) with emphasis on executive functions (Trail Making A and B, spatial anticipation tests). Performance was compared with normal standards and between groups, exploring a possible association with different demographic and clinical variables of epilepsy.

Results: 15 patients and 12 controls were included. Lower performance in global cognitive batteries and in Faux Pas tests were found in cases compared to controls. The main difficulties that patients had included recognizing the unintentionality of the character who made the mistake, the inadequacy of what was said and which character was

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saying something inappropriate. Four patients and no control failed in the Reading the Mind in the Eyes test. Patients with less education and longer duration of the disease showed greater difficulty in performing the Faux Pas tasks, without reaching statistical significance.

Conclusion: We conclude that in some patients with JME, alterations in ToM may be present. Its early identification would facilitate a specific approach with potential impact on personal development and social integration, which are often affected by epilepsy.

374 | Early neurocognitive recovery following stereo-EEG

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Purpose: The early neuropsychological recovery following stereo-EEG has not been investigated. This is essential to guide recovery expectations including return to work, study, and caregiving. As such, the current study aims to characterize the early neurocognitive sequalae following stereo-EEG.

Method: Consecutive patients undergoing stereo-EEG were prospectively recruited from two Australian centers. Patients completed the Repeatable Battery for the Assessment of Neuropsychological Status (RBANS) via telehealth before and 3-weeks after stereo-EEG (M=19.69 days, SD=4.41). To evaluate group changes, paired sample t-tests were undertaken. Reliable change indices were undertaken to explore clinically meaningful individual level changes. Person's correlations were conducted to evaluate relationships between change in global cognitive function and stereo-EEG admission variables. Repeated measures ANOVAs compared outcomes across cognitive domains according to whether dominant mesial temporal lobe (mTL) structures were coagulated.

Results: Of the 28 patients (M=37.89 years, SD=9.72, range=17-56 years, 54% female), 11(39%) had a dominant epileptogenic zone (EZ), 13(46%) a nondominant EZ and 4(14%) a bilateral EZ. All patients underwent radiofrequency thermocoagulation (RFTHC) with a mean of 11.43(SD=6.87, range=2-28) coagulation sites. At a group level, RFTHC was not associated with global nor domain specific cognitive change ($p>.05$). Reliable change indices revealed only 4%(1/28) of patients declined on two measures and 10%(3/28) improved. Pearson's correlational coefficients showed no statistically significant association between change in global cognitive function with any stereo-EEG admission factors including length of admission, number of spontaneous or stimulated seizures, number of electrodes, or number of RFTHC sites ($p>.05$). Subgroup analysis revealed a decline in delayed memory following RFTHC of dominant mTL structures, ($F(1,26)=11.53, p=0.002, \eta^2_p=0.21$ large effect).

Conclusion: By three weeks, broad cognitive functioning tends to be in keeping with pre stereo-EEG performances. RFTHC within the dominant mTL, however, appears to be associated with a decline in delayed memory. These findings have direct clinical implications for pre stereo-EEG neuropsychological counselling.

Neurostimulation

524 | Vagus Nerve Stimulator in Genetic Epilepsies: A Single Center Experience

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Purpose: To evaluate the use of the vagus nerve stimulator (VNS) in pediatric patients that have a known genetic etiology of epilepsy.

Method: This was a retrospective chart review of a single epilepsy center program in southern Florida. Included were patients seen in the clinic from 1/1/2020 - 12/31/2024 that had a VNS implanted and had a known pathogenic mutation consistent with epilepsy presentation.

Results: There were 47 patients with a VNS seen during this time period, and 11 of the 47 patients (23%) had a known pathogenic mutation associated with epilepsy presentation. Five patients (45%) had a SCN1A mutation and Dravet syndrome diagnosis. Six patients (55%) had a Lennox Gastaut Syndrome diagnosis associated with a known genetic mutation. The age of the patients when the VNS was initially implanted was between 2 to 18 years old, and all were at a therapeutic setting at time of analysis. The median output current was 2.34 mA with a range of 1.75 mA to 3.25 mA. Nine patients (81%) had auto-stimulation detection set at 20%. All patients had output of 30 seconds, and 7/11 (64%) had a 35% duty cycle and 4/11 (36%) had a 25% duty cycle. All patients had a positive response to VNS. Responses to VNS included 7/11 (64%) had decrease in seizure burden > 50%, 8/11 (73%)

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had decrease in seizure emergencies/rescue medication/hospitalizations, and 11/11 (100%) had improved quality of life reported by caretaker.

Conclusion: The vagus nerve stimulator is an effective treatment for numerous genetic epilepsies. Children with a genetic etiology of intractable epilepsy can require higher output settings and duty cycles than other epilepsy etiologies. Positive responses to the device includes seizure reduction, decrease in seizure duration, decrease use of rescue medication, decrease in seizure emergencies, and improved quality of life.

647 | Effect of intensity and frequency on vagus nerve stimulation-induced pupil dilation response in refractory epilepsy

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Purpose: Vagus nerve stimulation (VNS) has been employed for over 30 years as an adjunctive treatment for drug-resistant epilepsy, which represent one-third of the epilepsy patients worldwide. However, its mechanisms of action are not yet well known and lack optimization. Current evidence states that the modulation of the locus coeruleus (LC)-noradrenergic system is a key pathway supporting the antiepileptic effect of VNS. Moreover, LC activity influences pupil dilation response (PDR), the latter emerging as a potential biomarker for personalized titration. Therefore, this study aims at investigating the effect of intensity and frequency parameters on VNS-induced pupillary dilation.

Method: PDR recordings were collected from five refractory epilepsy patients, responders to VNS therapy, under various stimulation conditions combined into 9 distinct blocks: high (routine+0.25mA), mid (routine), and low (routine–0.5mA) intensities, and high (30Hz), mid (25Hz), and low (20Hz) frequencies. In each block, four stimulation trains of 7 seconds were delivered, followed by 18-second OFF periods. Then, the mean PDR was computed and analyzed in two distinct time windows: early PDR (0 to 2.5s after VNS onset) and late PDR (2.5 to 5s after VNS onset). These values were compared for the left eye (ipsilateral to the VNS) across the tested stimulation conditions using paired t-tests.

Results: No significant differences in the early PDR were observed across distinct stimulation frequencies, whilst differences in late PDR were significant (p=0.03) between 20Hz and 30Hz. Regarding the intensity, no significant differences in early PDR were observed along the three conditions, however, late PDR is significantly different (p=0.04) between low, mid and high intensities.

Conclusion: Results suggest that late PDR may serve as a potential biomarker to optimize VNS therapy. Nevertheless, a larger cohort is further necessary to validate the findings and to correlate these with responsiveness.

729 | Neurophysiological markers and predictors of effectiveness of vagus nerve stimulation (VNS) in people with drug resistant epilepsy

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Purpose: Vagal nerve stimulation (VNS) is an adjunctive treatment for drug resistant epilepsy (DRE) with highly variable efficacy. While its mechanisms of action remain partially understood, VNS is supposed to exert a desynchronization effect on hypersynchronous neural activity. Several neurophysiological metrics have been proposed to predict the therapeutic response to VNS by exploring synchronization dynamics, though evidence is limited and often tied to specific frequency bands. This study aimed to identify potential EEG markers of VNS efficacy using a connectivity and graph-theory approach.

Method: Consecutive adults with DRE who underwent VNS implantation at our Epilepsy Center between 2007 and 2023 were retrospectively enrolled. Participants were required to have at least one EEG recording prior to implantation (T0) and another 6-12 months post-implantation (T1). EEG data were analyzed during resting and hyperventilation (HV) states using phase transfer entropy to estimate effective connectivity and graph theory to evaluate network organization. Statistical tests assessed the ability of these metrics to distinguish responders

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– defined as individuals achieving a seizure frequency reduction of at least one category - from non-responders.
Results: EEG recordings were available for 21 individuals at T0 (12 responders, 9 non-responders) and for 6 subjects at both T0 and T1 (4 responders, 2 non-responders). At T0, responders exhibited lower initial phase entropy in the beta frequency band during HV (p=0.02) and distinct network properties, including higher in-degree (p=0.09), lower eccentricity (p=0.02), and lower diameter (p=0.04). At T1, responders presented reduced in-degree (p=0.04), increased eccentricity (p=0.03), and increased diameter (p=0.04). Non-responders displayed parallel but opposite trends.
Conclusion: Responders demonstrated higher beta-band synchronization and more efficient network organization prior to implantation, which VNS subsequently modulated toward desynchronization. Although based on a small sample size and requiring further validation, these findings underscore the potential for EEG-based markers in predicting outcomes and optimizing candidate selection for VNS treatment.

772 | Unlocking the gut-brain connection: The role of vagus nerve stimulation in epilepsy and depression

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Purpose: Vagus nerve stimulation (VNS) is an effective treatment to reduce seizure frequency in individuals with drug-resistant epilepsy (DRE) and also has a proven antidepressant effect in this population. Traditionally, the positive effects of VNS on seizure frequency have been thought to result from direct, afferent effects. However, the efferent effects of VNS on the intestinal microbiome and the gut-brain axis have received little research attention and could explain the antidepressant effect of VNS. We aim to study the effects of VNS on the gut-brain axis in relation to seizure frequency and depression.
Method: We conducted a review of the current literature on the effects of VNS on the gut microbiome.
Results: In multiple rodent studies, VNS was shown to have a positive effect on intestinal permeability. In addition, VNS was found to be an effective treatment in a small sample of human patients with Crohn's disease, suggesting an effect on intestinal health. More indirect evidence includes several studies in epileptic patients that found increased intestinal permeability and inflammation in a significant patient subset. In addition, the effectiveness of a ketogenic diet at reducing seizure frequency in mice was found to depend on presence of a gut microbiome, and probiotics supplementation in epileptic patients was shown to significantly reduce seizure frequency. These findings suggests an important role for the gut microbiome in epilepsy, potentially targetable by VNS.
Conclusion: The evidence highlights the potential for VNS to influence seizure and depressive symptoms via the gut-brain axis. However, direct evidence in human studies remains limited. Our ongoing E-GUT-VNS study aims to address this gap by investigating the physiological effects of VNS on intestinal permeability, gut microbiota, and immunological parameters in DRE patients. Expanded knowledge in this area could yield predictive biomarkers for treatment outcomes and enhance therapeutic efficacy for DRE and comorbid depression.

776 | Vagus Nerve Stimulation (VNS): Who Benefits most in the Long Run?

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Purpose: VNS is indicated for refractory epilepsy in whom epilepsy surgery has either failed or contraindicated. In this single-center study, our aims were to analyze the long-term outcome of VNS and elucidate predictors of good outcome.
Method: The study was conducted in a tertiary-level teaching hospital in North America. Data was collected retrospectively from chart review and data related to seizure frequency, ASM, and VNS parameters were recorded annually. Subjects were considered VNS responder if they had at least 50% reduction in seizure frequency. Responder rate on annual follow-up and predictors of good outcome were analyzed. IBM SPSS version 29 was used for statistical analysis
Results: 67 subjects were included out which 29 were male. Seizure freedom was attained in 7 (10.4%)

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subjects. Mean age of seizure onset and VNS insertion were 10.08±9.09 years and 33.35±10.71 years respectively. Mean seizure frequency at the time of VNS insertion was 4.25±7.5 per day (95% CI 2.39-6.11). Commonest seizure types were tonic (38.8%) and focal to bilateral tonic clonic [FTBTC] (37.3%). More than 60% of subjects were VNS responder at 1 year which persisted till 10-year follow-up. There was a significant reduction in the number of seizures per day at 1 year and it persisted till 8 years ($p<.05$). Among seizure semiologies, FTBTC showed a significant reduction per day from 1 year till 5 year ($p<.05$) and tonic seizure at 1 year ($p<.05$). Non-lesional MRI, no prior surgery, generalized seizure, focal epileptiform discharges and device with auto-stimulation were associated with significant reduction in number of seizure per day ($p<.05$).
Conclusion: More than 60% subjects were VNS responder at 1 year follow up and the effect persisted for 10 years. Predictive factors can be helpful in guiding optimal patient selection and prognostication and newer devices with auto-stimulation should be preferred over older devices

838 | Feasibility of transcranial direct current stimulation for focal onset seizures using a novel device at Ghent University Hospital in Belgium

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Purpose: Transcranial direct current stimulation (tDCS) is under investigation as a treatment for drug-resistant epilepsy (DRE). Randomized controlled trials are required to evaluate the efficacy, safety and tolerability of novel tDCS devices. We present our preliminary clinical experience in patients with focal onset seizures (FOS).
Method: Three patients (one male, two females) were enrolled at Ghent University Hospital in Belgium, as part of a multicenter, randomized, double-blind, parallel-group controlled trial registered at ClinicalTrials.gov (NCT04770337). Participants were randomized 1:1 to receive either daily active 20 minutes tDCS with the STARSTIM device or sham treatment targeting the epileptogenic focus for 10 consecutive weekdays. A neoprene headcap and electrode montage was tailored for each patient's treatment protocol based on EEG and MRI data. Electrically conductive gel was applied to minimize impedance. A 10-week follow-up phase included three visits to assess feasibility and seizure outcomes. Adverse events (AEs) were monitored. Following the controlled phase, patients were offered the option to participate in an open-label extension (OLE) phase, consisting of active tDCS treatment sessions only.
Results: The protocol was straightforward, feasible and user-friendly and can be completed in less than one hour. Achieving low electrode impedance was unproblematic. AEs were minimal across all three patients. One patient reported a brief episode of transient dizziness and fatigue after a treatment session. All three patients consented to the OLE phase of the trial. Preliminary results indicate that 1/3 patient classifies as a responder, while 2/3 patients had an increase in seizure frequency. Unblinding has not yet been performed.
Conclusion: tDCS using an novel device to treat FOS was well-tolerated, with all three patients opting to participate in the OLE phase. Unblinding will provide insights into the intervention's efficacy and its potential association with the increased seizure frequency observed in two patients *(This study was supported by Neuroelectrics, Barcelona, Spain).*

844 | Non-invasive Temporal Interference Stimulation of the Hippocampus Suppresses Epileptic Biomarkers in Patients with Epilepsy

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Purpose: Medication-refractory focal epilepsy presents a significant challenge, with approximately 30% of patients ineligible for surgery due to the involvement of eloquent cortex in the epileptogenic network. For such patients with limited surgical options, electrical neuromodulation offers a promising alternative therapy. This study evaluates the potential of non-invasive temporal interference (TI) electrical stimulation to reduce epileptic biomarkers in patients with epilepsy by comparing intracerebral recordings obtained before, during, and after TI stimulation, with recordings during low and high kHz frequency (HF) sham stimulation.
Method: Thirteen patients with symptoms of mesiotemporal epilepsy (MTLE) and implanted with

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stereoelectroencephalography (sEEG) depth electrodes received TI stimulation with an amplitude modulation (AM) frequency of 130Hz (Δf), delivered via lower frequency kHz carriers (1kHz + 1.13kHz) or higher frequency carriers (9kHz + 9.13kHz). Stimulation targeted the hippocampus, a common epileptic focus in MTLE. Comparisons were made to sham stimulation at 1, 2, 5, and 9kHz carrier frequencies to evaluate the effects on interictal epileptiform discharges (IEDs) and high-frequency oscillations (HFOs).

Results: TI stimulation resulted in a statistically significant reduction in IEDs and pathological HFOs, specifically fast-ripples (FR), with suppression observed in the hippocampal focus and propagation reduced brain-wide. HF sham stimulation at 1kHz affected IED rates in the cortex but did not impact the hippocampal focus. The effects of HF sham diminished as frequencies increased to 2, 5, and 9kHz, showing a depth-dependent effect that was not observed with TI stimulation, regardless of carrier frequency. A strong carry-over effect was noted with TI, as suppression of epileptic biomarkers persisted after stimulation ended, which was not observed with HF sham stimulation.

Conclusion: Our findings highlight the potential of TI as a non-invasive brain stimulation tool for epilepsy, offering an opportunity to evaluate brain region responses to neuromodulation prior to considering deep brain stimulation (DBS) or responsive neurostimulation (RNS) implants. C*linicaltrials.gov (NCT06716866)*.

998 | Is VNS-CBD combined therapy effective in DEEs? Results from a small group of pediatric patients

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Purpose: To share our experience in treating pediatric patients with Lennox-Gastaut Syndrome (LGS) or Dravet Syndrome using p-Cannabidiol (CBD) in addition to Vagus Nerve Stimulation (VNS) to reduce seizure burden.

Method: We reviewed LGS or Dravet patients who were either implanted with a VNS or receiving CBD. The focus was on those who underwent the combined VNS-CBD treatment and had a follow-up (FU) duration of more than one year.

Results: We identified two patient samples: Sample A (11 patients, CBD after VNS) and Sample B (2 patients, VNS after CBD).

Sample A: The mean age at VNS implant was 9.2 years (SD 2.5 years). McHugh scoring after VNS were as follows: Class I: 0, Class II: 2, Class III: 8, Class IV: 0, and Class V: 1. After adding CBD, the McHugh scores were: Class I: 2, Class II: 8, Class III: 1, and Class IV/V: 0. The mean VNS current was 1.7 mA (range 1-2.0) and the mean duty cycle was 12.4% (range 10-16). The mean CBD dosage was 7,2 mg twice daily (range 5,8-9.1). Prior to VNS implantation, 10/11 patients had experienced at least one episode of Status Epilepticus (SE). After VNS, SE recurrence decreased to 5/11 patients, and with the CBD addition, SE occurred in only 1/11 patients. The mean number of antiseizure medications (ASMs) other than CBD was 2 (range 1-3). The mean FU after p-CBD was 2 years (range 1-7). Sample B: Due to the small sample size, the results lack statistical significance.

Conclusion: Although none of the patients became seizure-free, the majority showed: an improvement in outcome, with most patients moving to a higher McHugh class and a reduction in the frequency of SE. The combination of VNS and p-CBD appears to be a promising therapeutic strategy for improving outcomes and reducing SE recurrence in pediatric LGS/Dravet patients.

1165 | Clinical Profile of Pediatric and Adult Patients Treated with Deep Brain Stimulation for Drug-Resistant Epilepsy in a Public Referral Hospital in Mexico City

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Purpose: To describe the clinical characteristics and outcomes of pediatric and adult patients with drug-resistant epilepsy (DRE) treated with deep brain stimulation (DBS).

Method: A descriptive analysis was conducted on the clinical characteristics and diagnostic approach of four pediatric and adult patients selected by a multidisciplinary team for DBS placement as a treatment for DRE.

Results: Case 1: A 16-year-old male with epilepsy onset at 3 years of age underwent resective surgery at age 3, resulting in a reduction in the frequency of focal seizures. However, he continued to experience hypermotor seizures, predominantly nocturnal, despite treatment with four antiseizure medications (ASMs). DBS was implanted in the bilateral anterior nucleus of the thalamus (ATN), resulting in a seizure reduction of over 50%. Case 2: A 15-year-old male with seizure onset at 20 days

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of life underwent resective surgery at age 13 but continued to experience daily seizures despite treatment with five ASMs. DBS was implanted in the ATN, achieving a 50% reduction in seizure frequency. Case 3: A 36-year-old female with epilepsy onset at age 32 was treated with three ASMs and experienced two seizures per week. Stereoelectroencephalography (SEEG) revealed bilateral spontaneous temporal seizures. DBS was implanted in the bilateral ATN, resulting in a seizure reduction of over 50%. Case 4: A 46-year-old female with epilepsy onset at age 12 initially presented with absence seizures, which evolved into bilateral tonic-clonic seizures. She experienced daily seizures despite treatment with three ASMs. Video electroencephalography (VEEG) revealed generalized epileptiform activity. DBS was implanted in the centromedian nucleus, resulting in a seizure reduction of over 50%.

Conclusion: DBS proved to be effective and safe in reducing seizure frequency and severity in both pediatric and adult patients with drug-resistant epilepsy.

1223 | Patient-controlled neurostimulation using the epicranial EASEE device

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Purpose: To assess the usage, safety and efficacy of patient-controlled neurostimulation (PCN) of a newly available neurostimulation device for epicranial focal cortex stimulation (FCS). The recently certified EASEE® device uses two types of pre-programmed stimulation types, DC-like stimulation and AC stimulation. Additionally, there was an option for patients to trigger an additional bolus of AC stimulation (10-60 seconds) when they experienced an ongoing seizure. Here, data on the usage, safety and efficacy of PCN are reported based on results from the clinical trial PIMIDES I.

Method: 18 patients (mean age 35.7 years, range 22-75 years, 11 female) with focal medically refractory epilepsy participated in the PIMIDES I clinical trial, 17/18 underwent stimulation. Frequency of usage, safety and efficacy of PCN were analyzed based on readouts from the implanted EASEE® devices, on patient reporting concerning adverse effects, and subjective experiences of ictal stimulation on seizure severity as assessed by a questionnaire.

Results: All but one (16/17) patient triggered ictal neurostimulation with a mean and median PCN usage of 0.51 and 0.1/day, respectively. At the 24-month follow-up, 12/16 patients continued to use PCN. There were no adverse events reported considered to result from ictal stimulation, in particular no seizure aggravation; 57% of patients applying PCN reported that ictal stimulation interrupted / shortened seizures or resulted in less severe seizures. Reasons for not using PCN were no or too few seizures, too brief seizure duration and inability to trigger PCN during a seizure, unavailability of the handheld device, and no subjective benefit.

Conclusion: Patient-controlled neurostimulation was applied by the majority of patients. Ictal stimulation was safe and frequently accompanied by a subjective decrease in seizure severity or duration. Further studies using larger patient cohorts and objective data on seizure duration and severity are needed to identify clinical significance of PCN.

1337 | Modulation of Global Neuronal Network Metrics in Patients Undergoing Focal Neurostimulation Therapy by a Novel Implantable Device

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Purpose: Reduction of seizures achieved by open-loop neurostimulation beyond the stimulation intervals is attributed to adaptations in brain network dynamics. This study investigates whether global network characteristics derived from high-density EEG, change over the first months of a novel focal neurostimulation therapy and whether these changes differentiate between responders and non-responders.

Method: The study included 7 patients implanted with an epicranial stimulation device. High-frequency or direct current (DC)-like components were applied via electrode arrays placed epicranially above the individual epileptic focus region. Four of these patients achieved a seizure reduction of at least 50%. High-density EEG recordings were performed immediately before the initiation of neurostimulation and either 7 months later or, in one case, 15 months later. From 10 minutes of resting-state EEG,

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10 artefact-free segments of equal length were selected for the analysis. Global graph metrics, including average path length, average cluster coefficient, synchronizability, assortativity, a measure, which reflects the tendency of edges to connect vertices with similar properties, and average degree, were estimated from these segments.
Results: Due to the small sample size, no statistical tests were applied between the groups or across the two time points. On a qualitative level, responders showed lower assortativity prior to neurostimulation as non-responders (mean non-responder: 0.65; mean responder: 0.46), and a higher average degree after 8-16 months of neurostimulation (mean non-responder: 45; mean responder: 75.1).
Conclusion: Patients with lower assortativity prior to neurostimulation tended to be responders compared to those with higher assortativity. After 8–16 months of stimulation, responder patients exhibited a higher average degree than non-responder. The analysis of epileptic network properties in epilepsy patients may help identify suitable candidates for focal neurostimulation therapy and provide deeper insights into its effects on the neuronal network. These findings require validation in larger cohorts of epilepsy patients.

1491 | Long-Term Outcomes in Patients with Generalized Tonic-Clonic Seizures Following VNS Therapy: Interim CORE-VNS 36 Months

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Purpose: Evaluate long-term outcomes of VNS in patients with generalized tonic-clonic seizures (GTCs).
Method: Patients were enrolled in the prospective, multicenter CORE-VNS study (NCT03529045). Those with primary GTCs were included, while individuals with focal seizures or Lennox-Gastaut Syndrome were excluded. A 3-month retrospective baseline period documented seizure frequency and patient-reported outcomes before VNS implantation. Participants were followed for up to 36 months post-implant. For analysis, patients were categorized by time from diagnosis: within 5 years or more than 5 years. Seizure diaries and adverse events were collected at 3, 6, 12, 24, and 36 months.
Results: Fifty-nine (N=59) participants received a VNS implant: 12 within 5 years of diagnosis and 47 after 5 years. Those implanted earlier were younger (median 9.7 vs. 25.9 years). Patients had failed a median of six antiseizure medications. At 36 months, the GTC responder rate (≥50% seizure reduction) was 70% (N=28, 95% CI: 56%–81.7%), with a median seizure frequency change (MSFC) of -83.2% (95% CI: -100% to -53.3%). Those implanted earlier had a higher responder rate (83.3% vs. 67.7%) and MSFC (-94.3% vs. -76.4%). Quality of life improved in 27% (N=10). Adverse events occurred in 35.6% (N=21), with the most common being dysphonia (11.9%, N=7), dyspnea (6.8%, N=4), implant site pain (5.1%, N=3), and cough, oropharyngeal pain, or infection (3.4%, N=2 each).
Conclusion: Adjunctive VNS was well tolerated and reduced GTC frequency, with a 70% responder rate and MSFC of -94.3% at 36 months. Outcomes were favorable regardless of time since diagnosis, reflecting modern VNS use in GTCs.

1494 | CORE-VNS: Dosing and Titration of VNS Therapy in Contemporary Clinical Practice

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Purpose: Little evidence-based guidance has been made available to characterize appropriate dosing and titration of VNS therapy. In 2022, investigators leveraged a large database of existing VNS clinical evidence to identify a population-level target dose and titration method for VNS. The present work attempts to validate those retrospective findings using contemporary clinical data in a prospective observational study of VNS called CORE-VNS.

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Method: CORE-VNS (NCT03529045) is a global, multicenter, observational study of VNS in patients with drug-resistant epilepsy. Participants in the study who were implanted with their first VNS device and attended at least one of either the 6- or 12-month follow-up were selected for this analysis. Statistical models (generalized linear mixed models, weighted Cox regression, Kaplan-Meier, and Poisson regression) were used to assess the relationship between VNS titration and clinical response. Manually titrated patients were separated from those who were predominantly titrated using automated programming ("Scheduled Programming (SP)").

Results: 499 participants met inclusion criteria. The majority of participants were titrated manually (n=385), with few titrated predominantly using the SP feature (n=46). 68 participants had a mix of manual and scheduled titration events such that the programming process did not appear to be heavily influenced by SP. There were no significant clinical or demographic differences between groups. Participants titrated with SP for 3 or more steps achieved the target dose range (per product labeling) faster than those who used less SP or not at all ($p<0.001$). These same SP-titrated patients had numerically shorter time-to-response (≥50% reduction from baseline in seizure frequency) compared to others, but this effect was non-significant.

Conclusion: SP is a driver of consistent and expedient titration of VNS, and these factors are associated with superior clinical outcomes.

1498 | Long-Term Adjunctive VNS Therapy Use in Patients with Genetic Epilepsy - 24 M CORE-VNS Outcomes

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Purpose: This analysis assesses the effectiveness of adjunctive vagus nerve stimulation (VNS) Therapy in reducing seizures and improving quality of life (QoL) in patients with genetic epilepsies.

Method: Participants with confirmed genetic epilepsy (CGE) who received VNS Therapy were selected from the CORE-VNS Study. Seizure frequency and patient-reported outcomes, including QoL, were assessed at baseline and 3, 6, 12, 24, and 36 months. The 24-month outcomes in neuromodulation implant naïve (NIN) patients were compared to baseline.

Results: Of 252 participants suspected of genetic epilepsy, 114 (45%) were confirmed, including 82 NIN. Median age at VNS implant was 8.33 years for CGE versus 27.93 years for untested patients. CGE patients had a median epilepsy duration, and informed consent was 6.5 and 12.5 years with a median of 7 ASMs. Moderate cognitive impairment was present in 76.8%. At 24 months, 57.9% of CGE patients were responders (>50% seizure reduction) versus 50.9% of untested patients. The median seizure reduction in CGE was -60% (95% CI: -74.8% to -43.6%) overall, -70.5% (95% CI: -93.3% to -57.1%) for focal seizures, and -60% (95% CI: -100% to -10%) for generalized seizures. In CGE patients with generalized tonic-clonic seizures (GTCs), seizure reduction was -85.7% (-110 to -10). QoL ratings improved from 24.4% to 48.4%, with reduced seizure frequency and ASM burden impacting QoL less at 24 months. The most common treatment-emergent adverse event was cough (6.1%).

Conclusion: Genetic testing was associated with earlier VNS use. VNS response was robust and comparable in CGE and untested patients. VNS Therapy improved QoL in patients with confirmed genetic epilepsy.

1543 | First-in-Human Study for Drug-Resistant Epilepsy: Usability and Efficacy of a Novel Optoelectronic Vagus Nerve Stimulation Device Over a 3-Month Follow-Up

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Purpose: Drug-resistant epilepsy (DRE) affects nearly 30% of epilepsy patients. For those ineligible for resective surgery, Vagus Nerve Stimulation (VNS) is a viable add-on treatment. However, current VNS systems face challenges, particularly regarding MRI safety and device longevity. To address these limitations, a novel optoelectronic VNS system was developed, integrating breakthrough technologies to ensure unconditional MRI access and extend device lifespan. The AURORA study, an open-label, interventional, prospective first-in-human trial, aims to assess the safety, device performance, and usability of this system in DRE patients.

Method: Patients will be recruited from three clinical sites: Cliniques Universitaires Saint-Luc (CUSL), Ghent University Hospital (UZ Gent) and Universitätsklinikum Freiburg. Eligible patients are adults diagnosed with DRE and are candidates for VNS treatment. The primary endpoints focus on the incidence rate of procedure and/or device related adverse events up to 3 months after implantation. Secondary endpoints are long-term overall safety, changes in seizure frequency and severity, quality of life and mood over a 24-month follow-up period.

Results: The first five patients were successfully implanted at CUSL and UZ Gent. Postoperative recovery was uneventful, stimulation therapy started 2 weeks later followed by a 10 week titration. By 3 months, therapy was well tolerated by all patients, with initial therapy efficacy observed across patients through either seizure frequency (seizure diary), severity (SSQ questionnaire), quality of life (QOLIE questionnaire), or depression (BDI questionnaire). Additionally, patients and caregivers noted benefits from the controller, which allowed for triggering additional stimulation during seizures to help manage ongoing or upcoming episodes. Over the first 3 months, recharging was efficient, with patients opting for either daily or weekly sessions, requiring only 7 minutes of total recharge time per week.

Conclusion: Initial results demonstrates promising therapeutic outcomes, and positive user feedback, and the potential for the optoelectronic VNS system to transform the treatment landscape for DRE.

1552 | The Journey of Medicaid Enrollees with Drug-Resistant Epilepsy {DRE) to Neuromodulation

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Purpose: Individuals with epilepsy who do not respond to two different anti-seizure medication (ASM) regimens are considered to have drug-resistant epilepsy (DRE). Guidelines recommend neurostimulators (vagal nerve stimulation, deep-brain stimulation, responsive neurostimulation) and other non-pharmacologic alternatives for DRE patients instead of continued ASM trials. However, available data suggest these treatments are often delayed for years after DRE onset. We aimed to characterize the healthcare "journey" of Medicaid enrollees with DRE in the two years before neuromodulator implantation.

Method: Using US Centers for Medicare and Medicaid Services (CMS) data, we identified Medicaid enrollees with DRE who received neuromodulator implantation (2011–2020). The earliest implantation date was the index date. Patients without an epilepsy diagnosis on the index date, ASM claims in the prior year, or continuous enrollment in the two-year pre-index period were excluded. We assessed demographic and clinical characteristics, healthcare utilization, and costs using both all-cause and epilepsy-related perspectives.

Results: A total of 2,469 DRE patients met selection criteria. Mean (SD) age was 20.8 (14.1) years (52% <18 years); 53% were male; 49% non-Hispanic White. Comorbidities included learning disabilities (41%), hemiplegia/paraplegia (32%), anxiety (20%), and depression (17%). Nearly half (45%) received >5 unique ASMs in the pre-index period; 57% had >1 hospitalization, and 83% had >1 emergency department (ED) visit. Most hospitalizations (97%) and ED visits (80%) were epilepsy-related. Median monthly all-cause healthcare costs rose by 61% over two years ($4,184 to $6,727); epilepsy-related costs increased 155% ($1,486 to $3,782).

Conclusion: Medicaid patients with DRE experience substantial healthcare utilization and cost increases before neuromodulator implantation, along with high comorbidity burdens, including mental health disorders. Further research is needed to assess whether earlier neuromodulator implantation and/or non-ASM interventions can reduce the burden of DRE in this vulnerable population.

1553 | Comparison of Healthcare Services and Cost Over the 2-Year Periods Immediately Before and After Vagus Nerve Stimulation (VNS) Implantation Among Medicaid Enrollees with Drug-Resistant Epilepsy {DRE)

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Purpose: DRE leads to poor health outcomes and high healthcare use. VNS is indicated for DRE, reducing seizure frequency and potentially improving quality of life.

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We previously showed in commercially insured and Medicare patients that VNS significantly lowers admissions, ED visits, and healthcare costs compared to expected levels without implantation. While this research highlights VNS's economic and health benefits, its impact on Medicaid enrollees with DRE remains unexplored.

Method: We used CMS healthcare claims to identify Medicaid enrollees with DRE who underwent VNS implantation (2011–2020), defining the earliest implantation date as the index date. Exclusions included patients without an epilepsy diagnosis on index, ASM claims in the prior year, or ≥2 years of continuous pre-index enrollment. Healthcare use and pharmacotherapy during the 2-year pre-index period, excluding pre-implantation preparations, informed regression models estimating expected values for 24 months post-index. Observed follow-up outcomes were compared to expected values on both an all-cause and epilepsy-related basis, the latter including epilepsy-related claims and ASM dispenses.

Results: A total of 2,283 patients met selection criteria. Expected hospitalization and ED visit rates exceeded observed rates for all-cause (37.84 vs. 25.84 per 100 person-months, $P < 0.001$) and epilepsy-related (29.78 vs. 13.87, $P < 0.001$) outcomes. In the 23 months post-implantation, observed all-cause and epilepsy-related monthly costs were $1,177 and $1,621 lower than expected, respectively. Cumulative cost differences aligned by month 18.

Conclusion: For the two years post-implantation, VNS significantly reduced hospitalizations and ED visits, both all-cause and epilepsy-related. Surgery was projected to break even financially in under two years. These findings suggest that, as with commercially insured and Medicare beneficiaries, VNS reduces DRE burden in Medicaid patients. Further research is needed to quantify its physiological and mental benefits in this population.

1556 | Sleep Quality in Children with Confirmed Genetic Epilepsy undergoing Vagus Nerve Stimulation

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Purpose: Many drug-resistant genetic epilepsy syndromes are associated with sleep problems in children leading to additional stress for the patients themselves and caregivers. . This analysis aims to assess sleep quality in children with confirmed genetic epilepsy undergoing VNS Therapy in the CORE-VNS study.

Method: Participants were enrolled in a prospective, multicenter, multinational observational study- CORE-VNS (NCT03529045). Those with confirmed genetic epilepsy (CGE) who received VNS Therapy were selected. Changes in the global score and subdomains of the Children's Sleep Habits Questionnaire (CSHQ) were analyzed for children.

Results: Full CSHQ data was available from 48 patients with CGE at baseline and from 29 patients at 24 months. At baseline the mean global CSHQ score was 54.21 (5.1) above the abnormality cut-off points of 41. CSHQ scores were lower at all follow-up visits after initiation of VNS Therapy, and this reached statistical significance at three months ($p=0.005$) and at six months ($p=0.028$) of VNS Therapy. This improvement was no longer significant at subsequent visits. At three months ($p=0.041$) and 12 months ($p=0.019$), the domain of morning waking and daytime sleepiness was improved compared to baseline. However, this improvement was no longer significant at 24 months. The only domain that showed significant change at 24 months of VNS Therapy compared to baseline was "waking during the night": scores improved from 3.87 (1.4) at baseline to 3.33 (1.4) at 24 months ($p=0.002$).

Conclusion: Children with genetically confirmed epilepsy in CORE-VNS displayed abnormal sleep habits as reported by their parents prior to VNS implantation. Global sleep habits did not show significant change in the course of 24 months of VNS Therapy. However, an improvement of certain sleep behaviors, like waking during the night in children with genetically confirmed epilepsy was seen.

1690 | Forecasting epileptic seizures by monitoring the cortical response to electrical stimulation

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Purpose: Seizure unpredictability is considered the most impactful aspect in the lives of people with epilepsy. Earlier studies on seizure forecasting analyzed intracranial EEG recordings (iEEG) and demonstrated that seizures could be predicted above chance levels. While passive brain observation may offer some insights, actively stimulating the cortex and measuring its response could provide more direct information about cortical excitability. In this study, we explore whether seizures can be predicted by

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stimulating the cortex through intracranial electrodes and assessing the cortical response from the iEEG signal.

Method: We analyze eight patients who were admitted to King's College Hospital for presurgical intracranial implantation. During their stay, they underwent prolonged single pulse electrical stimulation for 19 hours (mean; range 14-25 hours). Stimuli were delivered every 5 minutes to a constant pair of electrodes. All patients experienced at least one clinical seizure. We extracted quantitative features from the iEEG post-stimulus response and developed a logistic regression algorithm to estimate the seizure likelihood at each stimulus. To evaluate the algorithm's performance, we used Improvement over chance, sensitivity, time spent in warning and Brier Skill score.

Results: In seven out of eight patients, seizures could be forecasted above chance levels. The average Improvement over Chance was 0.74 (standard deviation: 0.3), average sensitivity was 0.88 (standard deviation: 0.35), average time spent in warning was 0.14 (standard deviation: 0.09), average Brier Skill Score was 0.33 (standard deviation: 0.22) and average forecasting horizon was 73.86min (standard deviation: 36.41min). In comparison, the seizure forecasting performance based on passive (unstimulated) iEEG was less good (average IoC:0.54; sensitivity:0.64; time spent in warning:0.08; BSS:0.33; forecasting horizon:78.4min).

Conclusion: These results suggest that cortical response to electrical stimulation may aid in the development of seizure forecasting algorithms as well as in the design of novel implantable devices that deliver electrical stimulation to control seizures.

1795 | Autonomic nervous system modulation and cardiac instability evaluation in drug-resistant epilepsy patients submitted to VNS Therapy™

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Purpose: Vagus nerve stimulation (VNS) is an established adjunctive therapy for drug-resistant epilepsy (DRE)[1](Morris GL, et al. Epilepsy Curr. 2013;13(6):297-303), influencing the autonomic nervous system (ANS)[2](Nearing BD,et al. J Cardiovasc Electrophysiol. 2016;27(9):1072-1077). Heart rate variability (HRV), derived from electrocardiographic (ECG) recordings, is a common tool to assess ANS balance[3] (Malik M, et al. Eur Heart J. 1996;17:354-381) while T-wave alternans (TWA) reflects cardiac electrical instability[4] (Verrier RL, et al. J Am Coll Cardiol. 2011;58(13):1309-1324). This study evaluates how VNS affects ANS function by analyzing pre- and post-implant HRV and TWA changes.

Method: We conducted a retrospective, observational analysis of demographic and clinical data for all DRE patients implanted with VNS in our center between 2002 and 2024. EEG recordings with simultaneous ECG, collected at rest, awake, and outside activation maneuvers, were analyzed. HRV parameters included both frequency- and time-domain measures. We compared HRV and TWA changes between VNS responders and non-responders, as well as between patients with and without generalized tonic-clonic seizures (GTCS). Statistical analysis includes normality testing using the Kolmogorov-Smirnov test, and Levene's test assessed variance homogeneity. Group comparisons performed using repeated-measures ANOVA with Bonferroni correction ($p<0.05$).

Results: Data from 25 patients (15 adults, 10 pediatric) with adequate pre- and post-VNS ECG recordings are analyzed. Literature suggests potential autonomic modulation with trends in HRV[5] (H, Yang Z, et al. Epilepsia. 2017;58(6):1015-1022) and TWA changes[6] (Schomer AC, et al. Epilepsia. 2014;55(12):1996-2002). Full statistical analysis is ongoing.

Conclusion: These findings will clarify the impact of VNS on ANS and cardiac function, potentially informing treatment response predictions and patient management in DRE.

Nursing

281 | Assessing the impact of e-learning in caregiver training on pediatric epilepsy awareness and buccal Midazolam administration: a Scottish quality improvement study

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Purpose: Training for carers to administer emergency medication is vital for managing conditions like diabetes, epilepsy, and adrenal insufficiency. In the UK, caregiver training for pediatric epilepsy is carried out by epilepsy nurse specialists and covers epilepsy awareness and administration of buccal midazolam, the drug of choice for

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the management of pediatric status epilepticus. Training is predominately delivered face-to-face due to limited evidence supporting online methods. This project aimed to provide an overview of e-learning use in caregiver training on pediatric administration of emergency medications and to assess the effectiveness of e-learning for pediatric epilepsy awareness and administration of buccal Midazolam.
Method: Pediatric epilepsy nurse specialists from SPEN (Scottish Pediatric Epilepsy Network) and NeSCANN (North East of Scotland Child and Adolescent Neurology Network) developed a standardized online training module, accessible to health, social, and educational services staff. Participants' knowledge was tested via a post-module quiz, requiring at least a 90% score to pass, with three attempts allowed. A Likert scale questionnaire and written feedback were used to evaluate engagement, quality of the module content and delivery method. Average response per question and standard deviation was calculated for the entire cohort and using occupation as an independent variable.
Results: Over 24 months, 3244 learners accessed the module; 83% passed, 1% failed, and 16% are still progressing. Participants came from across Scotland and most were in a teaching or educational support role. Learners felt that the module increased their confidence in seizure first aid and their understanding of appropriate Midazolam administration. Module content, structure, and delivery were all highly rated, independently of learner occupation.
Conclusion: The module improved access to learning, standardizing knowledge across professions and regions and reduced the carbon footprint of training. This e-learning module has potential to become part of clinical practice and for its principles be applied to other clinical areas.

498 | 10 years of educational and recreation camps for children with epilepsy in Croatia

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Purpose: Educational-recreational camps for children and adolescents with epilepsy are organized around the world and have proven to be extremely useful both for the children themselves and for the family, as well as for their education and independence. In Croatia, epilepsy as a chronic disease is a big unknown for children suffering from this disease and their parents. Insufficient information about the existence of educational and recreational camps for children with epilepsy was also expressed. The aim of this work is to show the purpose of holding educational and recreational camps in the Republic of Croatia over ten years and how much this type of activity contributes to the destigmatization of epilepsy in children and adolescents. The main purpose of the camps is to enable interaction with peers in a safe environment, in which sick children strengthen their sense of self-confidence by discovering what can be achieved despite their illness.
Method: The general goal of the action is long-term and includes accepting the disease, supporting the person and family, improving our daily work and experience.
Results: Specific goals relate to solving the most common dilemmas regarding therapy and schooling, organizing continuous support via hotlines and electronic media, inclusion in kindergartens, schools and educational institutions.
Conclusion: This work shows the existence of educational and recreational camps for children with epilepsy in Croatia, as an excellent professional, volunteer way of working for the health team, for the purpose of destigmatizing epilepsy in children and adolescents.

499 | Febrile seizures - education of educators, professional teams and parents - project of the Croatian Epilepsy Association

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Purpose: The Croatian Epilepsy Association in cooperation with the Department of Child Neurology and Epileptology, the Pediatric Clinic, Sestre milosrdnice UHC and the City Health Office of the City of Zagreb, and the City Office for Education of the City of Zagreb has been since 2018. conducting project "Febrile seizures - education of educators, professional team and parents". The goal of the work is to present through the project a model of good team cooperation of all participants in the care of a child with febrile seizures through the education of parents, educators and the professional team.
Method: Educators, health managers from the City of Zagreb Daycare centers, Hospital, the Zagreb County Daycare centers, and parents of children who had febrile seizures and were hospitalized at our clinic participate in the project. The education was divided into 8 workshops in a cycle, lasting 1.5 hours, with 25 participants in each workshop.
Results: In accordance with the national strategy and programs of continuous education, we conducted education for kindergarten teachers and health managers on

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the topic of febrile convulsions. We succeeded in training the participants of the education to know how to define what febrile seizures are, the cause, clinical picture, treatment, prevention of a repeat attack; define the difference between febrile seizures and epilepsy; enumerate and perform procedures during and after febrile seizures; enumerate and perform procedures for lowering elevated body temperature.

Conclusion: With this, we reduced the possibility of more serious consequences for a sick child and reduced the level of stress and disorganization for educators and health managers. Finally, the parents of sick children are calmer knowing that the educators are trained for these very dramatic situations. This project proved to be a model of good team cooperation of all participants in the care of a child with febrile seizures.

869 | Building bridges: A dedicated ERN EpiCARE working group for nurses and vEEG technicians

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Purpose: Rare and low-prevalence epilepsies require a multidisciplinary approach to ensure optimal patient care. Nurses and video-EEG (vEEG) technicians play pivotal roles in these efforts. Therefore, to enhance collaboration and education, ERN EpiCARE established a dedicated working group for these professionals, aiming to bridge clinical expertise, patient advocacy, and operational efficiency.

Method: A survey was distributed to ERN-EpiCARE clinical centers, targeting nurses and vEEG technicians. It assessed their roles, duties, and available educational opportunities across European countries. Based on these insights, a one-day workshop was conducted to exchange practices and deliver targeted educational content.

Results: The survey received 114 responses from 39 different ERN-EpiCARE Health Care Providers, with 53% identifying as vEEG technicians and 47% as nurses across four nursing roles. Most respondents (66%) worked in epilepsy monitoring units, and over 40% had more than 10 years of experience. Awareness of educational opportunities was limited, with 60% either unaware of or unable to confirm the existence of relevant programs in their respective country. While almost all respondents performed EEGs, only 55% drafted reports for review. These findings informed the workshop agenda, which focused on exchanging local practices for seizure testing, pre-interpretation of EEGs, and advanced epilepsy care. Discussions included guiding families on rescue medications and adapting antiepileptic drug prescriptions based on side effects.

Conclusion: The survey and subsequent workshop underscored the importance and diverse expertise of nurses and vEEG technicians in managing epilepsies across ERN-EpiCARE Health Care Providers, revealing educational gaps and a need for improved knowledge-sharing. Therefore, establishing a dedicated working group within ERN EpiCARE facilitates this exchange and collaboration, improves access to tailored educational programs, and enhances clinical and operational practices across European centers.

923 | Implementing and evaluating a novel model of care for patients with developmental and epileptic encephalopathies

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Purpose: The most severe epilepsies, Developmental and Epileptic Encephalopathies (DEEs), are typically characterized by uncontrolled seizures and complex comorbidities. Patients with DEEs have profound healthcare needs, resulting in pervasive negative impacts on caregivers. Dedicated DEE clinical nurse consultants (CNCs) may ease demands on caregivers by coordinating patients' care, providing psychosocial support, and liaising with local clinicians, among many other duties. In a world-first, our team implemented two DEE CNCs and qualitatively assessed their efficacy from the perspectives of caregivers, clinicians, and nurses.

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Method: We co-developed interview and focus group questions with consumer-advocates. We analyzed data with content analysis, using the Knowledge-to-Action Framework to *identify the problem*, *evaluate outcomes*, and identify *barriers to implementation*.

Results: 13 nurses, 15 clinicians, and 9 caregivers participated in interviews/focus groups. Participants *identified the following problems*: families need a single, knowledgeable person to be their 'first-point-of-call' to provide timely answers and advice (otherwise they present to emergency departments), caring for patients with DEEs is extremely time-consuming for neurologists, participants perceived that primary healthcare professionals (HCPs) feel overwhelmed and lack knowledge and confidence in DEEs, and patients are particularly vulnerable during transition from pediatric to adult care. *Evaluation of outcomes*: with access to DEE CNCs, families receive vital psychosocial support, neurologists can delegate tasks (leaving more time for other patients), therapies and transition services are better managed, equitable healthcare for First Nations families is facilitated, and HCPs are better supported meaning that more care can take place within primary care settings instead of hospitals. *Barriers to implementation* are that DEE nurses need to be highly experienced and knowledgeable in seizures and co-morbidities and require sustainable funding.

Conclusion: Government investment in DEE CNCs is urgently needed to facilitate higher value healthcare for patients with DEEs and their families, better support families and HCPs, and potentially reduce unwarranted emergency department presentations and hospitalizations.

1160 | Promoting health literacy in people with epilepsy: recent advances and future directions

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Purpose: Epilepsy is a growing global source of disability raising the need for demanding support (1). Health literacy (HL) is associated with significant gains in chronic diseases' management (2). Parallel to the boom in scientific production on people with epilepsy (PwE), reviews aimed at promoting HL in this population are lacking. Our aim is to identify recent evidence on the promotion of HL in PwE and their caregivers in the health sector.

Method: A rapid review (3) was performed in the Scopus® database with the expression *("health literacy") AND (epilepsy OR "tonic-clonic epilepsy" OR "generalized epilepsy" OR "epilepsy management" OR seizure)* considering articles published between 2019 and 2024, written in English. The selection process was undertaken according to the PRISMA methodology (4).

Results: 25 articles, mainly quantitative (n=19, 76%) were included, highlighting potential predictors of HL of PwE and their caregivers, such as educational level, length of diagnosis and disease severity. The development of educational programmes focusing on self-management and training on clinical and non-clinical issues using digital-based wearables and interactive platforms is recommended to promote HL, greater quality of life and reduced stigma. Co-developing these resources with PwE and caregivers is vital to ensuring tailored, understandable and highly reliable content. There is a clear gap about the promotion of HL in resource-limited settings and on interdisciplinary approaches to address this matter.

Conclusion: Promoting HL in this population is key to foster equitable and sustainable health. Nurses shall use scientific knowledge to provide personalized interventions, aiming to prevent complications. Greater investment in integrated, interdisciplinary and technological approaches is needed for clinical practice to meet the challenges of PwE. More research is urgently needed for this population, particularly in pediatrics and in resource-limited settings, preferably with larger sample sizes.

1571 | Try it, adopt it: Appreciative Inquiry in a French Pediatric Epileptology Department

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Purpose: Appreciative inquiry is defined by mobilizing collective intelligence for the benefit of the group, with a particular focus on what is already working well. The need to refocus the caregivers of the Lyon Pediatric Epileptic Unit on common goals and values led us to contact the members of the I.Care project (Collective Intelligence and Support for Leaders and Teams). The I.Care project is proposed by the French National Association for the Continuing Education of Hospital Staff (ANFH) and

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enables the deployment of an appreciative mindset and approach within hospital departments.

Method: After contacting I.Care and attending a half-day introduction to the appreciative approach, a project group was constituted. An invitation to participate to appreciative inquiry interviews was extended to all members of the department at the end of September 2024 and the interviews began shortly thereafter. A questionnaire assessing the sense of well-being at work was proposed beforehand and will be administered again after the completion of these interviews.

Results: Within the project group, this appreciative approach and vision are being implemented and are beginning to spread throughout the team. The appreciative inquiry interviews, aimed at uncovering the resources and values already present within the unit and fostering reconnection between professionals in pairs, have begun (43% of the staff have already participated in a paired interview).

Conclusion: After gaining an initial understanding of the appreciative mindset, the way professionals perceive one another within the Lyon Pediatric Epilepsy Unit has begun to shift. Following this initial Discovery phase, we will be ready to move forward to the next stages: Dream, Design and Destiny.

1593 | The Epilepsy Specialist Nurse (ESN) 360 Academy – Transforming Nurse Education and Training in Epilepsy

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Purpose: Annually the National Health Service (NHS) spends ~£1.5 billion on epilepsy care. However, there are only ~500 Epilepsy Specialist Nurses (ESNs) supporting the ~675,000 people living with epilepsy in the UK and Ireland (UK-I). Described as 'the glue that connects services to people with epilepsy,' ESNs have repeatedly highlighted the urgent need for high-quality, professional education and training. Here we describe the ESN360 Academy, an annual in-person event for ESNs across the UK-I.

Method: Supported by Angelini Pharma UK-I, the ESN360 Academy was launched in 2022 as a bespoke programme developed for nurses, by nurses, to provide education, training, and practical guidance. The programme was developed by an Expert Committee supporting findings from "Epilepsy Specialist Nurses: The Evidence (ESPENTE): a Systematic Mapping Review" conducted by Epilepsy Action and endorsed by the Epilepsy Nurses Association (ESNA), following a modified Delphi Consensus process.

Results: Now in its third year, this event has been held at the Royal College of Nursing, London, UK, delivering an engaging agenda of plenary sessions, case studies, workshops and live Q&As. Attendance has significantly increased year-on-year demonstrating demand for such content. In 2024, we secured attendance from 144 nurses, 12 speakers and received outstanding feedback: 99% of attendees would recommend the event to a colleague, 98% would like to participate in the next event and 99% agreed the content was relevant to their clinical practice.

Conclusion: The ESN360 Academy is delivering a highly valued, first-in-class educational programme for ESNs in UK-I. Planning for the fourth event in 2025 is currently underway. Disclosures: The ESN360 Academy is a non-promotional activity organized and funded by Angelini Pharma UK-I for UK and Ireland Healthcare Professionals.

Pediatric Epileptology

326 | Genetic movement disorders with epilepsy

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Purpose: Paroxysmal dyskinesia (PD) is a rare heterogenous group of movement disorders manifesting as abnormal involuntary movements that recur episodically and last only a brief time, and sometimes co-occurs with epilepsy. PD includes paroxysmal kinesigenic dyskinesia

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(PKD), paroxysmal non-kinesigenic dyskinesia (PNKD), paroxysmal exertion-induced dyskinesia (PED), and a variant form of PKD, infantile convulsion and choreoathetosis (ICCA syndrome). The causes of PD are multifactorial, but several genes have been associated with different forms of PD, namely: *PNKD* (2q35) mutations have been found to cause PNKD in families whose attacks can be triggered by caffeine and alcohol, *PRRT2* (16p11.2) mutations account for some families with PKD or ICCA syndrome, and *SLC2A1* (solute carrier family 2 (facilitated glucose transporter), member 1) (1p34.2) mutations have been identified to cause PED.

Method: We present clinical history with EEG findings and therapeutical trials of three patients with PNKD, PRRT2, and SLC2A1 mutations. Before genetic testing, we relied on medical history and clinical examination which included recordings of dystonia, abnormal postures and tremor, electroencephalogram, brain imaging (computed tomography or magnetic resonance imaging), and blood chemistry. The detection of known pathogenic mutations confirmed the diagnosis. As a differential diagnosis, we excluded disorders such as multiple sclerosis, Aicardi-Goutières syndrome, myelopathy, cerebral palsy, cerebral infarcts and hemorrhages, focal seizures, encephalitis, radiculopathy, hypoparathyroidism, hypoglycemia, and reflex sympathetic dystrophy.

Results: Upon genetic confirmation, we were able to slowly wean off antiseizure medication in one patient and plan repeated video EEG monitoring to confirm the need for it in the other two.

Conclusion: Genetic counseling should be offered to all patients and families. It is very important to differentiate between movement disorders and pharmacoresistant epilepsy. The frequency of attacks typically diminishes with age in the familial cases and the disease often completely remits.

334 | Intrahippocampal sleep spindles in pediatric epilepsy patients

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Purpose: Pediatric patients are at an increased risk of developing epileptic encephalopathy, a condition characterized by cognitive and behavioral impairments. In adults, intrahippocampal spindles are considered to serve as potential physiological biomarkers for cognitive functioning, an evoked response to afferent epileptic discharges, or even the expression of an epileptic manifestation. This study aims to pave the way to investigate intrahippocampal sleep spindles as a biomarker for epileptic encephalopathy and brain development.

Method: Our study retrospectively analyzed 31 EEG recordings from depth electrodes implanted in the hippocampi of pediatric patients undergoing evaluation for epilepsy surgery at Alberta Children's Hospital between 2015 and 2023. Spindles were marked visually in 1 h of intrahippocampal recording, preferably chosen during the first sleep cycle of the night, at least 6 h apart from seizures and 72 h after the implantation.

Results: Our study cohort consisted of children between 3 and 18 years of age. We detected intrahippocampal spindles in 28 out of 31 patients (90%), with a median rate of 0.4 spindles/minute (range: 0.2–3.7 spindles/min). Spindles were equally distributed across the anterior and posterior hippocampus and left and right hemisphere. Spindle rates increased with age (Spearman's Rho=0.355; p=0.034). No significant difference was seen between spindle rates across the number of ASMs or epilepsy duration.

Conclusion: To our knowledge, this is the first study to investigate intrahippocampal sleep spindles via depth electrodes in a pediatric population. In comparison, a similar study in adults reported spindles in 64% of patients (n=25), with a median spindle rate of 0.6 spindles/min (range: 0.1–8.6 spindles/min) (Frauscher et al., Sleep 2015; 38:1927–1933). Our work shows that intrahippocampal spindles can be used as a biomarker for age dependent brain development in patients with therapy refractory epilepsy. Further investigations are needed to examine detailed effects of epileptic encephalopathy on local spindle rates.

341 | Results of a Long-Term Post-Marketing Surveillance Study on Stiripentol Safety and Efficacy in a Large Cohort of Japanese Patients

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Purpose: After its market authorization in Japan (November 2012), a post-marketing surveillance study in

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all Dravet syndrome (DS) patients that initiated stiripentol was conducted.

Method: Data up to 156 weeks post-stiripentol initiation were analyzed. Stiripentol's safety and efficacy were prospectively investigated in all Japanese DS patients that received the drug from November 2012 to August 2017. Patients initiated with stiripentol were defined as "new patients," while those continuing stiripentol post-domestic clinical studies were named "continuous patients." Treating physicians assessed patient's conditions before and after stiripentol initiation: seizure frequency (SF) and duration, intensity, and daily activities for improvements (rated on as marked, moderate, mild, unchanged, worsened or undetermined), and adverse reactions. The SF percentage change was calculated.

Results: Data were collected from 521 patients (520 safety analysis set (SAS), 515 effectiveness analysis set (EAS)). Adverse drug reactions (ADRs) occurred in 69% of SAS patients, most commonly somnolence (37%), decreased appetite (27%), dizziness (13%), weight decreased (9%), and drug level increased (6%). No new safety concerns were identified. Twelve deaths were reported. After 156 weeks or at drug discontinuation, 38% of new patients showed marked or moderate improvement, and 60% with at least mild improvement. No continuous patients worsened. Median percent change from baseline in tonico-clonic (TCS) and/or clonic seizure (CS) frequency ranged from -46% to -75% after 156 weeks. After 4 weeks of treatment, median SF was -64% for focal impaired awareness seizures and -61% for generalized myoclonic (MS) and/or generalized atypical absence seizures (AAS). SF gradually decreased, reaching -100% after 57 and 49 weeks, respectively.

Conclusion: This analysis reports the largest real-world cohort followed for 3 years. No safety concerns were identified, and long-term stiripentol efficacy in reducing TCS/CS was confirmed. Stiripentol efficacy on focal impaired awareness seizures and MS/AAS is also reported.

Disclosure: supported by Biocodex

358 | Effectiveness of benzodiazepines based on seizure frequency in benign convulsions with mild gastroenteritis

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Purpose: Benign convulsions with mild gastroenteritis (CwG) typically resolve spontaneously without the need for antiseizure medication in most cases. However, recurrent or prolonged seizures may require pharmacological intervention. Previous studies have shown limited efficacy of benzodiazepines in such cases. This study aimed to evaluate the effectiveness of antiseizure medications in relation to seizure frequency.

Method: Patients diagnosed with CwG at our hospital between March 2005 and February 2024 were retrospectively analyzed. They were categorized into three groups based on seizure frequency: group I (single seizure), group II (two seizures), and group III (≥3 seizures). Medical data were compared among the three groups as well as between redefined groups (group I vs. groups II/III; groups I/II vs. group III).

Results: Among 178 patients, 50 (28.1%) were classified into group I, 46 (25.8%) into group II, and 82 (46.1%) into group III. Antiseizure medications were administered to 4%, 43.5%, and 81.7% of patients in groups I, II, and III, respectively ($P=0.000$). Benzodiazepines were used in 2%, 43.5%, and 74.4% of groups I, II, and III, respectively ($P=0.000$). Benzodiazepines achieved >95% efficacy in groups I and II, but 47.5% of patients in group III required second-line therapies. Phenytoin and fosphenytoin were predominantly used in group III (93.9% of 33 trials), primarily as second-line treatments (80.1% of 31 trials). Their efficacy was 83.3% as first-line treatments (N = 6) and 96% as second-line treatments (N = 25). Intravenous phenobarbital (N = 6) and oral carbamazepine (N = 2) were exclusively used in group III.

Conclusion: Benzodiazepines were effective in patients with one or two seizures but showed reduced efficacy in those with ≥3 seizures. Phenytoin or fosphenytoin is recommended as the first-line treatment for CwG patients experiencing ≥3 seizures.

402 | Investigation of the actual status of febrile seizures plus

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Purpose: We report a retrospective study to confirm the incidence of pediatric epilepsy in children with febrile seizures plus (FS+) in our hospital.

Method: Among children who visited our hospital between 2015 and 2024, we extracted those who were diagnosed with FS+. FS+ is a condition in which children have multiple febrile seizures before the age of 6, and also afebrile epileptic seizures occur, or febrile seizures continue after the age of 6. For patients who were subsequently diagnosed with epilepsy and treated with anti-seizure drugs,

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we investigated the age at onset of epilepsy, seizure type, final age of febrile seizures, presence or absence of afebrile seizures, EEG findings, brain imaging abnormalities, family history of febrile seizures and epilepsy, neuronal development and comorbidities.

Results: The subjects were 60 (35 boys; 58%), and afebrile seizure was observed in 23 (38%) of them. Nine patients (15%, 39% of afebrile seizure) were diagnosed with epilepsy. More than half of the patients developed an afebrile seizure after a final febrile seizure over 6 years old, and 7 patients (except 2) had interictal electroencephalogram abnormalities. and were treated with anti-seizure drugs. In the cases with epilepsy, the proportion of abnormal EEG findings was significantly higher. When comparing the presence or absence of epilepsy, there was no difference in the number of people who had 5 or more seizures (44% vs. 41%) or comorbidities (33% vs. 25%) other than EEG abnormalities, and cases with a family history of febrile seizures (22% vs. 50%) was rather low.

Conclusion: We thought that in cases of FS+ that particularly include afebrile seizures, EEG and follow-up observation should be actively performed until around the age of 10, considering the possibility of developing epilepsy during school age.

473 | Long-term Follow-up of Effects on Insulin Resistance in Children with Epilepsy Before and After Ketogenic diet: Prevalence and Risk factors

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Purpose: To evaluate the incidence of insulin resistance (IR) and associated risk factors before and after the ketogenic diet (KD) in children with epilepsy.

Method: This longitudinal cohort study analyzed data of children with epilepsy on KD. IR was assessed using the homeostasis model assessment of insulin resistance (HOMA-IR). The HOMA-IR values and associated laboratory tests were measured before the initiation of the KD (HOMA-IR-0), during the KD (HOMA-IR-1), and after KD termination (HOMA-IR-2).

Results: A total of 34 children were enrolled. The median age at the initiation of KD was 2.1±2.4 years, and the median follow-up duration was 3.5±1.4 years. The median HOMA-IR-0 (before the initiation of KD) was 1.3±0.3, which significantly increased to 2.2±0.5 at the last follow-up during the KD (HOMA-IR-1; ΔHOMA-IR-1 = 0.9±0.3, $p<0.001$). The median HOMA-IR-2 value decreased to 1.6±0.7, but was more than 2.0 in 4 patients (11.7%). The following factors were associated with patients with higher HOMA-IR-1 values (≥2.0): younger age at seizure onset (0.4±0.5 years, $p<0.001$), at the initiation of antiepileptic drugs (AEDs; 0.4±0.6 years, $p<0.001$), and at the initiation of KD (0.9±1.1 years, $p<0.001$) and higher serum total cholesterol (245.0±20.1 mg/dL, $p=0.001$), low-density lipoprotein cholesterol (LDL-C, 103.0±6.7 mg/dL, $p=0.003$), and triglyceride (387.0±28.8 mg/dL, $p<0.001$) levels. Multivariate regression analysis revealed that the age at seizure onset ($p=0.002$), at initiation of AEDs ($p=0.021$), and at initiation of KD ($p=0.022$) and serum levels of LDL-C ($p=0.012$) and triglycerides ($p=0.026$) were associated with a significantly high HOMA-IR-1 or HOMA-IR-2 values.

Conclusion: Close monitoring of serum lipids levels, especially at younger age, can aid in detecting exacerbation of IR.

520 | Infantile spasms: diagnosis, treatment and neurogenetics

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Purpose: Infantile spasms (IS) are an epileptic encephalopathy, clinically defined by characteristic epileptic spasms and the hypsarrhythmia EEG pattern. It is caused by various etiologies and if left untreatable, could be life threatening or cause important psychomotor delay.

Method: We present six cases of IS that were treated in our clinic. The first two patients presented with spasms and hypsarrhythmia at the age of 6 months. Both were treated with ACTH with seizure recession. Genetic analysis revealed RFX7 and NBEA mutations that have been related with autism disorders. The third patient, a 7-year-old boy presented with spasms and hypsarrhythmia. He was treated with ACTH and spasms recessed. Brain MRI revealed a large FCD type-2 at the right parietal region. The fourth patient is a 10-month-old girl, that presented with IS for the previous two months. She was treated with ACTH and spasms recessed, however seizures continued. Diagnostic work-up revealed ASH1L mutation, related with developmental encephalopathy and seizures. The fifth patient, a 14-month-old girl with spasms relapse, diagnosed with lissencephaly type 2. She was treated with prednizolone for more than 2 months. Spasms finally discontinued and focal only seizures occurred. The 6th patient, a 7-month-old girl with spasms and dermatological lesions. Diagnostic workup revealed phenylketonuria and the patient was referred for further treatment.

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Results: In our patients, IS recessed either with ACTH or prednizolone. The etiological background was responsible for both treatment response and final psychomotor outcome. MRI scan as well as genetic analysis were the most important tools in investigating the etiological background.
Conclusion: Urgent treatment of infantile spasms is necessary. Treatment choices include ACTH, prednizolone and vigabatrin. Further medications should be available in the future. Diagnostic approach includes MRI scan, metabolic work-up and genetic analysis. Precise diagnosis enables both specialized care and prognosis.

537 | Heterogeneous Knowledge of Childhood Seizures and Epilepsy Care in Canadian Healthcare Providers: Identifying the Gaps

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Purpose: Epilepsy is the most common chronic neurological condition in children. Many barriers exist in early recognition which cause delays in care and impact quality of life. Some of these children require advanced treatments which are underutilized due to lack of education, awareness and referrals. Overall, childhood epilepsy is underdiagnosed and poorly understood by non-expert providers.
Method: We investigated epilepsy awareness and knowledge from primary care providers via the quality of their referrals. We prospectively collected and examined all epilepsy related referrals to the Pediatric Neurology Division at Children's Hospital in London, Ontario, Canada during a six-month period. We developed a modified "epilepsy focused" scoring tool which included 17 questions, to evaluate the quality of referrals and scored them as basic or advanced.
Results: During the study time frame 175 (82%) referrals met the inclusion criteria. Out of these, 152 (87%) were identified as basic and 23 (13%) as advanced ($p < .001$). We received epilepsy referrals from different types of providers: Family doctors (n=49, 28%), Pediatricians (n=41,23%) and Pediatric ER (n=37, 21%). We also identified the type of provider vs type of referral. Amongst the referrals that scored basic vs advance: Family Doctors n=49 with 40 basic (81%) vs 9 advanced (18.3%), Pediatric ER Physicians n= 37, all 37 scored basic (100%) and Pediatricians n=41 which 36 (87%) scored basic and 5 (12%) scored advanced.
Conclusion: Our results showed significant lack of critical information in the content of epilepsy referrals coming from non-epileptologist providers, largely from the cohort of Pediatric ER Physicians. This reveals that knowledge and awareness of epilepsy in children remains scarce. Identifying these barriers can provide insights to develop strategies to facilitate accurate identification and rapid triage for children presenting with new onset epilepsy. More educational strategies focusing on emergency departments should be implemented to help close this gap.

555 | Infantile spasms, does genetics matter?

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Purpose: Infantile spasms, an epileptic encephalopathy, occur in early infancy. Etiology is variable. This study aims to compare clinical characteristics and outcomes of children with infantile spasms, with and without genetic variations.
Method: Retrospective descriptive study of children with infantile spasms followed at a level II hospital, between June 2011 and July 2024. Data were collected from clinical records and statistical analysis was performed using Pearson's chi-square and Mann-Whitney tests ($p<0.05$).
Results: Among 15 children, 7 (46.7%) had an identified genetic cause. The median age at onset of infantile spasms was 7 months in both groups, ($p>0.05$). Regression in psychomotor development (PMD) was observed in 43% of children with genetic variations, while developmental delay (DD) occurred in 71% and 29% had regular PMD. Among children without genetic variations: 13% had regression, 75% DD; 25% had regular PMD ($p>0.05$). Hypsarrhythmia was identified in 29% of children with genetic variations and 25% of those without ($p>0.05$). Brain MRI abnormalities were found in 43% of children with genetic variations and 75% of those without ($p>0.05$). The median time to achieve a therapeutic response was longer for children with genetic variations, at 10 days, compared to 4 days for those without ($p>0.05$). Progression to epilepsy occurred in 67% and 100% of children with and without genetic variations, respectively ($p>0.05$). Relapse rates were significantly different, occurring in 100% of children without genetic variations and in none of children with genetic variations ($p=0.03$). Family history of neurological disorders was reported in 40% of children with genetic variations and 20% of those without ($p>0.05$).
Conclusion: Children with infantile spasms and genetic variations show similar outcomes to those without them, except for higher relapse rates in the latter group.

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Larger studies are needed to confirm these findings and implications.

589 | Design and Baseline Characteristics of an Open-label, Multicenter, Phase 1b/2a Study of Radiprodil in Patients With Focal Cortical Dysplasia Type II or Tuberous Sclerosis Complex

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Purpose: Focal cortical dysplasia (FCD) and tuberous sclerosis complex (TSC) are malformations of cortical development associated with increased glutamatergic activity and related symptoms, including drug-resistant seizures. Radiprodil, an investigational, selective, and potent negative allosteric modulator of the *GluN2B N*-methyl-D-aspartate receptor subunit, has previously demonstrated effects in reducing seizure frequency in patients with GRIN-related neurodevelopmental disorder. We describe the study design and baseline characteristics from an ongoing Phase 1b/2a study (Astroscape; NCT06392009) evaluating the safety, tolerability, and pharmacokinetics of radiprodil and its effects on seizure activity and behavioral symptoms in patients with FCD type II or TSC.
Method: This open-label, Phase 1b/2a study enrolled patients (aged ≥6 months to ≤18 years) diagnosed with FCD type II or TSC with an average of ≥8 countable motor seizures during the 4-week baseline period and ≥1 seizure during ≥3 weeks of the 4-week baseline period. Eligible patients must have failed to respond to ≥2 antiseizure medications at appropriate doses and durations. Astroscape includes screening (4–6 weeks), titration (≥4 weeks), maintenance (≤12 weeks), and safety follow-up (2 weeks after the last dose of radiprodil) periods. An established population-based pharmacokinetic model was used to determine the radiprodil dose during titration. Primary endpoints are safety and pharmacokinetics. Secondary endpoints include change in seizure frequency, percentage change in seizure burden, number of seizure-free days, longest period without seizures, and changes in behavioral symptoms.
Results: Recruitment for Astroscape has begun with a target of ~20 patients with TSC and ~10 patients with FCD type II from approximately 20 international study sites (Australia, Canada, EU, UK). Baseline demographics and disease characteristics will be presented.
Conclusion: Astroscape will evaluate radiprodil as a potential treatment for TSC or FCD Type II not adequately controlled by standard of care treatment, determining next steps for clinical development.

592 | Design of a Phase 3 Multicenter Study (BeeLine) to Assess the Efficacy and Safety of Radiprodil, a Targeted Investigational Therapy for Patients With GRIN-related Neurodevelopmental Disorder

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Purpose: Analyses of a Phase 1b study (Honeycomb; EudraCT:2022-000317-14) in GRIN-related neurodevelopmental disorder (NDD) from July 2024 demonstrated that radiprodil, a selective, negative allosteric modulator of GluN2B subunit-containing NMDA receptors, was well tolerated and substantially reduced seizure frequency with signs of improved behavioral symptoms. We describe the transition of Honeycomb to a double-blind, placebo-controlled, Phase 3 study (BeeLine) to robustly assess efficacy and safety of radiprodil for eventual registration as a precision treatment targeting the underlying biology of GRIN-related NDD.
Method: BeeLine is designed to evaluate efficacy and safety across diverse GRIN phenotypes. Two cohorts of GRIN-related NDD patients (age 1 mo–18 y) will be

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included: cohort 1: patients with ≥4 countable motor seizures (CMS) in the 28-day pre-randomization period (n≤60) will constitute a randomized qualifying seizure (RQS) cohort; cohort 2: patients with behavioral and other nonseizure symptoms, not meeting CMS required for the RQS, but meeting other criteria, will constitute a randomized auxiliary (RA) cohort (n≤40). Both cohorts will be randomized (1:1) to radiprodil or placebo. The double-blind maintenance period for the RQS and RA will be 12 and 24 weeks, respectively.

Results: BeeLine includes numerous innovative features to assess radiprodil as a potential targeted disease-modifying treatment. Primary endpoint is between-group differences in seizure frequency. Additional endpoints include seizure-free days and changes in non-seizure signs, symptoms, and impact using a GRIN-specific clinical global impression scale, newly developed from a conceptual model from caregiver interviews, ABC-2C, Vineland-3, and Peds-QL. Given the favorable effects observed in the Honeycomb analyses, a Bayesian group sequential design will enable interim assessments of overwhelming efficacy leading to potentially expedited development.

Conclusion: Current data suggest the potential for unprecedented efficacy of radiprodil in GRIN-related NDD. Innovative design updates to BeeLine will evaluate changes in disease course induced by radiprodil in patients with diverse clinical phenotypes.

593 | Qualitative Research to Assess Caregivers' Perspectives on Signs and Symptoms of GRIN-related Neurodevelopmental Disorder

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Purpose: GRIN-related neurodevelopmental disorder is associated with developmental delays and drug-resistant seizures, among other symptoms. The natural history and burden of this rare disease are poorly understood. This qualitative study characterized manifestations of GRIN-related neurodevelopmental disorder from caregivers' perspectives.

Method: Caregivers of patients (age ≤18 years) with a clinical diagnosis of GRIN-related neurodevelopmental disorder and a *GRIN1*, *GRIN2A*, *GRIN2B*, or *GRIN2D* variant were recruited through patient advocacy groups to complete an online survey. Survey results were used to develop a qualitative interview guide. A subset of caregivers participated in 90-minute interviews. Data were analyzed separately in cohorts with or without seizures. A conceptual model was developed based on survey results and refined after interview analysis.

Results: Fifty-seven caregivers of 58 children with GRIN-related neurodevelopmental disorder (mean age: 7.4 years [SD: 4.4]; male: 55.2%; *GRIN2B*: 55.2%) participated in the survey; 20 respondents participated in interviews. Caregivers reported a range of neurologic, physical, behavioral, and gastrointestinal symptoms. Half of survey respondents and 55% of interview participants reported that their child had seizures. Seizures occurred primarily daily and were short (<1 minute). Patients without seizures frequently experienced pseudoseizures. Other frequent signs/symptoms reported by caregivers were developmental delays, fine and gross motor delays, behavioral symptoms, hypotonia, and constipation. Patients frequently needed assistance with activities of daily living and had difficulties with expressive and receptive communication. Improving these commonly reported symptoms, as well as decreasing seizure frequency, were identified as meaningful treatment goals.

Conclusion: This is the first qualitative research characterizing the complex nature of the signs and symptoms and their impact in those living with GRIN-related neurodevelopmental disorder. Motor delays, communication difficulties, behavioral symptoms, and seizures are prevalent and prioritized by caregivers for treatment. The conceptual model will inform selecting clinically meaningful endpoints for a Phase 3 study of radiprodil in this patient population.

595 | Brain Volumetric Differences in Pediatric Epilepsy: A Focus on Genetic Etiology

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Purpose: To understand the differences in brain volumetry of the total and each brain region in genetic pediatric epilepsy compared to those in non-genetic focal epilepsy and healthy controls.

Method: We analyzed the mean surface areas, brain volume, and cortical thickness of patients with genetic-related pediatric epilepsy (n=25) using FreeSurfer. We compared these measurements with those of children with non-genetic focal epilepsy (n=25) and healthy controls (n=23). In patients who underwent follow-up brain

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magnetic resonance imaging (MRI; n=11), we investigated age-related serial changes in brain volume or cortical thickness.

Results: Total brain, total grey matter (GM), cortical and subcortical GM, white matter (WM), cerebellar and cerebellar GM volumes were considerably smaller in children with genetic epilepsy than in children in the other groups. In the genetic group, a marked reduction was observed in the surface area measurements across brain regions associated with higher brain function. The mean cortical thickness was not significantly different among the three groups. Longitudinal MRI studies revealed age-related brain volume changes; both genetic and non-genetic groups showed increases in total brain, subcortical GM, and WM volume. Interestingly, the non-genetic group showed an increase in cortical GM volume (R=0.77, p=0.009), whereas the genetic group showed a decrease (R=-0.42, p=0.13).

Conclusion: Quantitative brain MRI volumetry serves as an essential screening instrument for genetic evaluation in children with epilepsy, even when qualitative MRI does not indicate any structural abnormalities. Reduced brain volumes in specific areas of cerebral cortex, responsible for higher brain functions, suggest a genetic etiology.

598 | Connect, Pause & Reflect: Multidisciplinary Clinicians' Shared Challenges and Sustaining Strategies Caring for Children with Severe Neurological Impairment

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Purpose: Children with Severe Neurological Impairment (SNI; eg. developmental epileptic encephalopathy) have static or progressive conditions of the central nervous system, resulting in permanent cognitive and motor impairment and enduring medical complexity. Multidisciplinary clinicians face many challenges to meet the needs of these patients, exacerbated by factors including the complexity of SNI care needs, barriers to care coordination and training limitations. The purpose of this study was to explore clinicians shared psychosocial experiences, including the challenges, and components of care that bring clinicians meaning and purpose.

Method: Multidisciplinary clinicians with expertise caring for children with SNI were purposively recruited to participate in a series of three sequential reflective practice workshops. Workshops were semi-structured, focusing on three key study aims. Workshops were recorded, and qualitative content analysis was performed after verbatim transcription.

Results: Fourteen workshops were conducted, each with 4-8 clinicians from diverse complex clinical care settings. Clinicians (N=29) represented a variety of specialties including pediatricians (n=14), pediatric neurologists (n=6), allied health professionals (n=3), geneticists (n=2) a pediatric nephrologist (n =1), a metabolic specialist (n = 1), and clinical nurse specialists (n=2). Content analysis elicited three interrelated primary themes and several subthemes: 'the struggle', 'making a difference to families' and 'finding purpose and meaning'. Clinicians recognized the limits of their medical expertise, highlighting the importance ongoing reflective practice, and multidisciplinary collaboration to proactively sustain clinicians to respond to the shared challenges and to empower patient families.

Conclusion: This research provides novel and in-depth insight into how multidisciplinary clinicians caring for children with SNI cope with challenges and gain meaning and purpose in their role. The findings elicited through this codesign qualitative research will be used to co-develop multipronged resources to sustain and to build resilience among clinicians.

633 | Pediatric Epilepsy Surgery: Global Trends of Referral and Presurgical Evaluation

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Purpose: Pediatric epilepsy surgery is a well-established, evidence-based treatment that has become widely adopted. Over time, changes in candidate profiles and diagnostic methods necessitate an updated overview of current international practices.

Method: Group-level data were collected from representative centers worldwide on children and adolescents undergoing presurgical evaluation and epilepsy surgery in 2023.

Results: A total of 55 centers from 25 countries across 6 continents contributed data on 2,274 patients. The mean age at epilepsy onset was 3.8 years, with surgery performed at a mean age of 9 years. At surgery, 5.9% patients were non-pharmacoresistant, with the highest rate in Europe (15.3%), while 3.3% were under 1 year old, with the highest rate in Australia (5.1%). Prior neurosurgical procedures were reported in 14.4% of patients, with the highest rate in North America (28.7%). Among these, 7.8% had undergone prior resective surgery (including 6% for epilepsy and 1.5% for tumors), with the highest overall rate in Australia (16.6%). Disconnective surgery was performed in 2.4% of cases (including 1.4% corpus callosotomy), with the highest rate in Australia and South America (5.1%). Neuromodulatory treatments were reported in 4.5% of patients (including 4% VNS and 0.2% RNS), with the highest rate in North America (12.6%). At the time of surgery, 5.2% of patients had Infantile Spasm Syndrome, 7.9% Lennox Gastaut Syndrome, and 1.7% Epileptic Encephalopathy with Spike-and-Wave Activation in Sleep. Auxiliary diagnostic procedures beyond video-EEG, structural MRI and neuropsychological investigations included FDG PET (54.8%), genetic testing (49.4%), MRI post-processing (34.3%), fMRI (15.8%), MEG (12.6%), SPECT (9.5%), high-density EEG (1.7%), and Wada test (1.3%).

Conclusion: These findings highlight a global trend toward earlier interventions in very young children and non- pharmacoresistant cases, high reoperation rates, and the growing role of genetic testing in presurgical evaluation. This survey provides valuable insights into global practices and recent advancement in pediatric epilepsy surgery.

641 | Long-term prognosis of patients with childhood absence epilepsy

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Purpose: Childhood absence epilepsy (CAE) is one of the genetic generalized epilepsy (GGE) syndromes and is considered to have a relatively good seizure prognosis. In this study, we reviewed the characteristics, outcome, and long-term prognosis of pediatric patients with CAE treated at our epilepsy center.

Method: We retrospectively reviewed the medical records of patients with CAE who have visited our hospital and received anti-seizure medication (ASM) from 2002 through 2014, and for whom more than 10 years have passed since the initial visit.

Results: In total, 67 patients (male 19; female 48) were included. Age of onset of epilepsy ranged from 3 years to 10 years. In addition to absence seizure, 19 patients had generalized tonic-clonic seizure and 4 had myoclonic seizure during the follow-up period. Fifteen patients were accompanied by neurodevelopmental disorders or intellectual disability. ASM treatment was completed in 43 (64 %), while treatment was continued in 16 (24 %) and 8 patients (12 %) were lost of follow-up. In 38 patients, follow-up visits were also completed. The reasons for continuation of treatment were transition to other GGE syndromes in 12 and the presence of EEG abnormalities in 4. The patients who continued treatment were more likely to have persistent EEG abnormalities or neurological comorbidity. Regarding treatment, valproic acid (VPA) was used in all patients, including 60 effective, 2 ineffective, and 5 changed due to side effects. Thirty cases were treated with VPA monotherapy. In addition to VPA, other ASMs such as ethosuximide, clonazepam, clobazam, lamotrigine and zonisamide were used.

Conclusion: VPA was effective in many cases, but two or more ASMs were required in about half of the cases. Since treatment was terminated in about two-thirds of patients with CAE, it would be important to initiate effective treatment including VPA even for girl patients.

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739 | Identification of Serum Biomarkers in Pediatric Patients with Drug-Resistant Epilepsy in a Third Level Hospital

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Purpose: The mechanisms involved in the development of epilepsy or its progression are unknown; few prospective studies have tested the predictive value of biomarkers, especially biomarkers to stratify populations according to risk. The purpose of this study was describe the clinical characteristics and determine the serum levels of biomarkers in patients with drug-resistant epilepsy, under 18 years of age, seen in the Pediatric Hospital of National Medical Center, XXI Century, from January 2019 to January 2024
Method: An observational, cross-sectional, descriptive, and retrospective study was performed. Patients under 18 years of age with drug-resistant epilepsy and controlled patients attended the pediatric hospital of CMN XXI century from January 2019 to January 2024 with serum determination of ICAM-1, HMGB-1, TLR4, IL-6, IL-1B, S-100B were included. A database was made with the results obtained and, subsequently, a descriptive analysis of the results, in addition to a Wilcox on signed-rank test for related samples, a multivariate analysis was made with all clinical and biochemical risk variables.
Results: 30 drug-resistant patients and 15 controlled patients were included. The most frequent epileptic seizures were focal onset seizures, 63.3% of the patients had a history of perinatal complications. 33.3% had status epilepticus. 90% had neurodevelopmental disorders and 43.3% had intellectual disability to some degree. The concentrations of I-CAM, IL-6, and S-100B were significantly higher ($P < 0.05$) in patients with drug-resistant epilepsy compared to controlled patients. The variable associated with the increase in these molecules was the number of seizures.
Conclusion: The results indicate that these proteins could be proposed as potential biomarkers of DRE. However, due to the complexity of epilepsy, studies on a larger number of patients are needed.

754 | Imaging markers associated with cognitive and motor functions in Sturge-Weber syndrome: A multivariate analysis in a prospective study

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Purpose: Sturge-Weber syndrome (SWS) is a highly epileptogenic condition with often progressive cognitive and motor deficits during childhood. Brain MRI detects a combination of venous vascular and parenchymal abnormalities. We evaluated how these various pathologies, or their combinations, may contribute to cognitive and motor functions in SWS.
Method: From a prospective, single center imaging study of young SWS patients, who underwent multi-sequence brain MRI (including susceptibility-weighted imaging) and formal neuro-cognitive evaluation, 46 participants with unilateral brain involvement were selected (28 girls, median age: 10.4 years). The extent of vascular and parenchymal SWS MRI abnormalities (number of lobes affected by leptomeningeal venous malformation [LVM], enlarged deep medullary veins, atrophy, calcification) and epilepsy variables were used as predictors in uni- and multivariate regression analyses with cognitive functions (verbal and non-verbal IQ) and motor scores as the outcome variables.
Results: In univariate analyses, both verbal and non-verbal IQ showed an inverse correlation with the extent of LVM, atrophy, and calcification (all $p<0.05$); non-verbal IQ was also lower in those with earlier seizure onset ($p=0.01$). Lower motor scores were associated with greater extent of all four MRI predictors ($p<0.001$ in all) and lower age of seizure onset ($p=0.02$). In multivariate regression, only the extent of calcification was an independent imaging predictor of cognitive functions ($r=-0.45$, $p=0.002$ for verbal IQ; $r=-0.36$, $p=0.02$ for non-verbal IQ). For motor scores, enlarged deep medullary veins ($r=-0.42$, $p=0.005$) and atrophy ($r=-0.33$, $p=0.03$) were the two independent imaging predictors. Age and seizure frequency scores were not associated with imaging, cognitive, or motor variables.
Conclusion: These data indicate that cognitive and motor outcomes may be driven by different underlying pathologies in SWS. The extent of calcification, a progressive and potentially modifiable pathology, is a strong independent imaging marker of cognitive functions; motor deficits are more associated with extensive enlarged deep veins and lobar atrophy.

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791 | Review of stiripentol use in Lennox-Gastaut Syndrome

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Purpose: Since the management of Lennox-Gastaut Syndrome (LGS), a severe Developmental and Epileptic Encephalopathy (DEE), remains problematic due to intractable seizures, some physicians use stiripentol as an alternative. This work aimed at reviewing the use of stiripentol in LGS.

Method: A Literature search was done (May 2023) in Cochrane Library and PubMed using the terms "stiripentol AND Lennox", and in the abstract books from relevant meetings (from 2007 onwards) searching firstly "stiripentol" and then "Lennox". The eligibility criteria was the presence of data on stiripentol related to LGS treatment. Additionally, results of an unpublished exploratory single-blind Phase II trial conducted in the 90's in 4 French centers in inadequately controlled (≥1 seizure/week) LGS patients (2-20 years) were reviewed.

Results: 5 references (out of 29 found) were eligible: 3 observational studies [1 meeting abstract], 1 clinical trial, and 1 review. These data, together with some real-world evidence, reported that stiripentol can be an effective and well-tolerated therapeutic option in LGS treatment. The phase II trial recruited 16 LGS patients. Further to a one-month placebo period, stiripentol was added to the ongoing treatments for 2 months. A significant decrease in the overall seizure frequency was reported (p=0.02), notably tonic-clonic seizures (p=0.01). Additionally, maximal time interval between seizures increased in 13 patients as compared to the baseline period (p=0.01). Regarding safety, one patient discarded the study due to side effects (nausea, vomiting, somnolence). The most frequently reported adverse events were in line with the stiripentol safety profile.

Conclusion: The published evidence and the results of the phase II study suggest a good efficacy and tolerability of stiripentol in treating LGS when used in combination with the current therapy. These preliminary data need to be confirmed in a well-conducted phase III study.

797 | Management of Epilepsy in IQSEC2-Related Encephalopathy: A Case Study

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Purpose: Reporting a case of a 9-year-old male with epileptic encephalopathy and developmental delay attributed to a *de novo* pathogenic variant in the IQSEC2 gene and elaborating the clinical management and outcomes from antiepileptic therapy.

Method: The patient presented with severe developmental delay, intellectual disability, and a history of epileptic seizures. Brai with an onset at two years. Initially electroencephalography (EEG) and magnetic resonance imaging (MRI) was performed, Due to diagnostic inconclusiveness Whole-exome sequencing (WES) was indicated to identify underlying genetic abnormalities.

Results: The patient presented with severe developmental delay, intellectual disability, and a history of epileptic seizures. Brai with an onset at two years. Initially electroencephalography (EEG) and magnetic resonance imaging (MRI) was performed, Due to diagnostic inconclusiveness Whole-exome sequencing (WES) was indicated to identify underlying genetic abnormalities.

Conclusion: This case underscores the role of genetic testing, particularly WES, in the diagnostic workup of epileptic encephalopathy and neurodevelopmental disorders. The identification of a pathogenic IQSEC2 variant established a molecular diagnosis, facilitating personalized management and family counseling. The effective seizure control achieved with valproic acid highlights the importance of tailored antiepileptic treatment in patients with IQSEC2-associated epileptic encephalopathy. The treatment of epilepsy in patients with IQSEC2 mutations presents significant challenges, as seizure manifestations and responses to antiepileptic drugs (AEDs) vary widely among individuals. In this case, valproic acid (VPA), in combination with other therapies, contributed to extended seizure-free periods, though complete remission was not achieved.

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807 | Drug-resistant epilepsy in children - impact on cognitive functions and clinical evolution

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Purpose: To analyze the influence of drug-resistant epilepsy on cognitive functions in children and its clinical evolution.
Method: In this retrospective study, clinical data were collected from 72 children diagnosed with drug-resistant epilepsy, monitored over a period of 5 years. The analysis included some variables: gender, age of onset, seizure types, video-electroencephalographic recordings, neuroimaging investigations and cognitive test results
Results: Of the 72 children included in the study, 97.2% presented various degrees of mental retardation, 83.3% – psychiatric disorders, 72.2% – language disorders and 23.6% – motor disorders. The number and polymorphism of epileptic seizures were significantly more pronounced in children with polymorphic changes in the electroencephalogram ($P < 0.001$) compared to those with changes identified in cerebral magnetic resonance imaging ($P = 0.001$). Also, the age of onset of seizures was correlated with the polymorphism of seizures and with the evolution of long-term cognitive deficits ($rxy = 0.78$).
Conclusion: More than half of children with drug-resistant epilepsy present cognitive deficits, associated with polymorphic changes in the electroencephalogram and with those identified in cerebral imaging. Electrical abnormalities, often present at an early age, emphasize the need for improvement in psychological testing, to estimate early indicators of deficits and, subsequently, to guide treatment protocols and early intervention.

810 | Effect of vigabatrin add on EEG compared to placebo in Lennox-Gastaut Syndrome

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Purpose: Lennox-Gastaut syndrome (LGS) is a developmental epileptic encephalopathy characterized by cognitive impairment, multiple seizure type and electroencephalographic (EEG) abnormalities. We report effect of adjunctive vigabatrin on EEG changes compared to placebo in the patients with LGS.
Method: LGS patients aged 2 to 18 years were included. The demographic details, clinical details, and the Clinical Global Impression Scale (CGIS) were recorded. A baseline EEG including sleep and awake EEG was recorded. Patients were randomized to vigabatrin (25 mg/kg in first week and 50 mg/kg ~4g/day in 2 divided doses) or identical looking placebo using simple 1:1 randomization. The patients were allowed to continue ongoing antiseizure medication (ASM). At 3 months of vigabatrin treatment, clinical examination and EEG were repeated. The change in background activity, reduction in proportion of spike and slow wave (SSW), generalized paroxysmal fast activity (GPFA), and amplitude of slow waves were analyzed. EEG changes correlated with change in total and multiple seizure types compared to placebo.
Results: Forty-seven patients received vigabatrin and 45 received placebo. The baseline characteristics were comparable between the groups. No patient had complete normalization of EEG. More than 50% reduction in proportion of SSW (17.0% vs 17.8%; $p = 0.92$) and GPFA (50.0% vs 31.0%; $p = 0.13$) were comparable between the groups. Overall proportional change in SSW (-9.5 vs 13.8; $p = 0.25$), GPFA (-25.9 vs -19.7; $p = 0.79$) and slow wave maximum amplitude (-2.8 vs 0.33; $p = 0.66$) was insignificantly higher in vigabatrin group. The change in seizure frequency (-40.5% vs 2.6%; $P = <0.01$) was significant in vigabatrin group and was insignificant with GPFA ($p = 0.09$) and SSW ($p = 0.335$). Sedation was more frequent in vigabatrin group ($P < 0.01$).
Conclusion: In LGS, vigabatrin has a mild effect in reducing proportion of SSW and GPFA, which is associated with reduction in proportion of seizure.

814 | Sweet taste as the initial manifestation of Temporal Lobe Epilepsy

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Purpose: To present the case of a patient with a sweet taste as a rare initial manifestation of temporal lobe epilepsy, along with a narrative review of the literature on pleasant tastes as a presentation of this type of epilepsy.
Method: Case report and narrative review.
Results: A 15-year-old patient was admitted to the hospital with a 9-month history of episodic events (#5). These

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episodes were characterized by a sweet taste and dizziness, followed by an altered state of consciousness, a fixed gaze, automatisms, diaphoresis, and sialorrhea, each lasting approximately one minute. Neurological examination revealed no abnormalities. Video electroencephalography demonstrated focal epileptiform activity in the left frontotemporal region. Antiseizure medication was initiated, resulting in effective seizure control to date. A 3-Tesla magnetic resonance imaging (MRI) with an epilepsy protocol was performed showing normal findings.

Conclusion: The symptomatogenic area is the area of the cortex that, when activated by an epileptiform discharge, produces the initial ictal clinical symptoms and signs of a seizure (Chowdhury FA et al. Pract Neurol 2021;21:481-491). Electrical stimulation studies have contributed to the identification of brain regions involved in the generation of each type of semiology. The temporal lobes are the most common site of origin in focal seizures, and seizures in this location have historically been associated with auras, including gustatory auras, as observed in our patient (Ganju BL et al. Epileptic Disord 2019;21). This highlights the importance of investigating the manifestations of a seizure in a detailed and chronological manner. Such approach facilitates accurate classification, aids in localizing the originating brain region, and guides diagnostic studies interpretation and optimal treatment strategies, ultimately leading to improved outcomes.

819 | Association Between the Temporal Progression of Amplitude Burden and Epileptiform Discharge Scores with Relapse in Children with Infantile Epileptic Spasms Syndrome

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Purpose: In patients with infantile epileptic spasms syndrome (IESS) who have achieved remission of epileptic spasms (ES), guidelines for maintaining electroencephalogram (EEG) stability during follow-up remain undefined. We hypothesized that the trajectory of the burden of amplitudes and epileptiform discharge (BASED) score following ES remission is associated with ES relapse. This study aimed to examine the relationship between ES relapse and BASED scores at the time of initial ES remission and throughout the follow-up period.

Method: We obtained clinical and digital EEG data from patients with IESS who achieved initial ES remission at four hospitals. The BASED score was assessed using EEG recordings collected before remission, during remission, and in the post-remission phase. Three independent authors, blinded to patient outcomes, evaluated the EEGs. We then analyzed the relationships between clinical factors including developmental quotient, BASED scores, maximum BASED scores, and ES relapse.

Results: Information was gathered from 44 patients who developed the disease between 4 and 8 months of age, comprising 33 individuals without relapse and 11 who experienced relapse. A total of 262 EEG recordings were analyzed to evaluate the BASED score. Structural etiology and the occurrence of seizures beyond ES exhibited a significant positive correlation with ES relapse. Although BASED scores recorded prior to and at the point of remission did not show an association with relapse, having a maximum BASED score of ≥3 in the post-remission phase was strongly linked to relapse. Multivariate analysis indicated that a maximum BASED score of ≥3 during this period was the only factor that remained significantly correlated with relapse. The inter-rater agreement for the BASED score was excellent.

Conclusion: A maximum BASED score of ≥3 during post-remission indicates a risk for ES relapse in patients with IESS.

835 | Test protocol for responsiveness and awareness during seizures of children under three years of age

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Purpose: To assess whether the version adapted to the pediatric patients, of the ictal test battery proposed by ILAE-Europe (Beniczky et al. Epilepsia 2016 Sep;57(9):1363-8) can provide information on ictal impairment of responsiveness and awareness, in patients under 3 years of age.

Method: We adapted the current standard protocol (designed for adults and children of different age) with the comments given in the article as well as our clinical experience and created a separate version including the use of a separate box with special test items for the children.

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Then the staff of the long-term monitoring unit from our center was trained to use this protocol. At the same time, we started an observational study to test feasibility and give space for improvements in which we are currently enrolling patients.

Results: The preliminary results indicate that the ictal testing protocol is feasible and useful in the pediatric age group too.

Conclusion: An ictal test protocol adapted for patients under the age of 3 years provides information about impaired awareness and responsiveness.

854 | Identification of Heterozygous *HNRNPU* Variants in a Patient with Early Onset Intractable Epilepsy and Developmental Delay

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Purpose: 1q44 microdeletion syndrome is a rare neurodevelopmental disorder. Despite the documentation of several cases in literature, effective seizure management for treatment-resistant cases remains limited.

Method: A 2-year-old male, the first child of healthy, non-consanguineous parents with an unremarkable family history, was admitted to the hospital at age 2 due to recurrent seizures: steering, perioral cyanosis, impaired awareness, motor arrest, trismus and tonic posturing of the left arm. He had facial dysmorphic features (hypertelorism, short nose with bulbous tip, high palate, downturned corners of the mouth); divergent strabismus, rotatory nystagmus, normal eye fixation, and the ability to follow objects; global developmental delay: lacked task-oriented activities, could not pronounce words, obey commands, or perform simple tasks; inability to sit, stand, or crawl independently, though he could turn from a supine to an abdominal position. He exhibited diffuse hypotonia, with diminished symmetric deep-tendon reflexes.

Results: MRI revealed hypogenesis of the corpus callosum, hypoplasia of the septum pellucidum, hypoplasia of the sella turcica, hypotrophy of the pituitary gland, hypoplasia of the cistern magna and mild cystic malformation of the lateral sulci. Ictal EEG showed an electroclinical event starting in the right fronto-temporal area with rhythmic theta activity, followed by 2-3 Hz sharp slow-wave complexes, and spread abruptly to both fronto-temporal areas, followed by diffuse depression. Whole exome sequencing revealed a heterozygous de novo missense variant causing a pathogenic1-copy loss in the HNRNPU gene (NM_238769;chr1:244998978-245583047), confirming a diagnosis of 1q44 microdeletion syndrome. Despite multiple anti-seizure medications: carbamazepine, valproate, levetiracetam, lamotrigine and topiramate, seizures remained intractable. Acetazolamide successfully controlled seizures (>4years). Recently, by age 6, he can stand and take a few steps with assistance. He does not understand simple commands and cannot speak, exhibits autistic traits with poor eye contact and repetitive, stereotypic movements.

Conclusion: Despite resistance to multiple anti-seizure medications, seizures were effectively controlled with acetazolamide in this case, making the first documented use of carbonic anhydrase inhibitors in similar cases in literature.

864 | Optimizing Early Pediatric Epilepsy Diagnosis Through Nurse-Led Consultations

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Purpose: To assess the effectiveness of consultations led by a highly trained pediatric neurology nurse specializing in epilepsy in the early detection and diagnosis of epilepsy in children.

Method: A retrospective descriptive analysis was conducted on a cohort of 405 children aged 0 to 18 years who, over three years, attended first seizure managed by a specialized pediatric neurology nurse. Data were collected on clinical suspicions, use of electroencephalogram (EEGs), and the concordance between nurse's initial assessments and final medical diagnoses

Results: Clinical suspicions included: Non-Epileptic Paroxysmal Disorder (NEPD) in 154 cases (38%), syncope in 65 cases (16%), and epilepsy in 186 cases (45.9%). Of the 196 EEGs requested (48.4%), 128 were pathological (65.4%). Among the 212 children without an initial EEG, the medical consultation led to the request for EEG in 36 cases (17%), with only one showing pathological findings (2.8%). In children with epilepsy, the agreement between the initial suspicion and the final diagnosis was 100%. In children with a final diagnosis of NEPD, EEG was not requested in 79.7% of cases

Conclusion: Advanced practice nurses specializing in pediatric epilepsy enhance diagnostic accuracy, optimize resource use, and improve early detection, highlighting their vital role in multidisciplinary clinical teams.

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868 | Clinical Profile, Treatment Response, and Outcomes in Children with Drug-Resistant Epilepsy at Chiang Mai University Hospital

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Purpose: To investigate the clinical profile, treatment response and outcomes of children with drug-resistant epilepsy (DRE).
Method: We retrospectively reviewed medical records of children diagnosed with DRE between January 2006 and December 2023 at a tertiary care referral hospital.
Results: A total of 136 patients were identified (72 girls). The mean age at seizure onset was 2 years (range: 1 month to 11 years). The most common initial seizure type was generalized tonic-clonic seizures (47%), followed by focal impaired awareness seizures (28%), epileptic spasms (15%), myoclonic seizures (3.4%), and other types (6.6%). The most common etiologies were structural brain anomalies (44%), genetic mutations (14.4%), and central nervous system infections (5%). Whole-exome sequencing was performed in 42 children, with SCN1A mutations being the most common. The median number of antiseizure medications (ASMs) trialed per patient was 4 (range: 2–6). Additional treatments included the ketogenic diet (6), vagus nerve stimulation (5), and epilepsy surgery (26). The mean follow-up duration was 7.9 years (range: 1.3 – 17 years). At the last follow-up, all children were on two or more ASMs, and one-third continued to experience daily seizures. Half of the children were non-ambulatory and unable to perform daily self-care activities. There was no significant correlation between age at seizure onset or etiology and seizure outcome ($p = 0.697$ and $p = 0.083$, respectively). However, early seizure onset was associated with genetic etiologies ($p = 0.011$), and these patients were diagnosed with DRE at a younger age compared to those with structural brain anomalies ($p = 0.06$).
Conclusion: Structural brain anomalies were the most common cause of DRE in our study. Despite multiple ASM trials, one-third of patients continued to experience daily seizures. No significant correlation was found between age at seizure onset or etiology and seizure outcomes. However, genetic etiologies were associated with earlier seizure onset.

876 | Infantile Epileptic Spasms Syndrome (IESS): Experience at a Single Institution over 32 years

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Purpose: Infantile Epileptic Spasms Syndrome (IESS) is a severe epilepsy syndrome with diverse etiologies and a high risk of lifelong neurological sequelae and mortality. Early diagnosis and treatment are associated with improved neurodevelopmental outcomes. The purpose was to determine factors influencing long-term outcomes and mortality of IESS.
Method: Retrospective review of 390 individuals with IESS at BC Children's Hospital between January 1, 1990, and December 31, 2022, with a minimum of 1 year follow-up.
Results: The mean age at onset of IESS was 6.5 months (1 day -24 months). Mean follow-up was 12 years (1.25 -32 years). Treatment of IESS was started within 30 days in 270 individuals. Vigabatrin was the first-line treatment in 86% of the patients, 36% responded. Response to first-line medication was associated with better cognitive outcomes($p < .05$). The median number of ASMs was 5 (1 - 16). Forty-one had resective surgery/hemispherectomy, 21 of whom achieved Engel Class 1 outcome. An etiology was identified in 77%, most commonly genetic (35%) and structurally acquired (20%). TSC and Trisomy 21 were the most common genetic causes. 49 (12.5%) died at a mean age of 11 years. At the most recent follow-up, 10% ($n = 39$) had normal development/ learning disability. 80% intellectual disability, 22.7% autism spectrum disorder, 45% cerebral palsy, and 22.5% had epileptic encephalopathy. Treatment within 1 month of IESS onset did not correlate with long-term developmental outcomes (p-value - .26).
Conclusion: An etiology of IESS was identified in 77% of patients in this series, most commonly genetic, likely underestimated as next-generation sequencing was introduced in the last decade. Long-term normal cognitive outcomes were rare (10%), and the mortality rate was 12.5%. Etiology of IESS and resolution of spasms with first-line treatment influenced long-term outcome. However, treatment within 30 days of IESS onset did not significantly impact long-term neurological sequelae.

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878 | Evaluating Pediatric to Adult Epilepsy Programs; Patient Engagement and Ongoing Sustainability

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Purpose: Transition programs are crucial for ensuring continuity of care, reducing treatment gaps, and empowering young patients with epilepsy to manage their health independently. This study compares two transition pathways: Children's Hospital of Eastern Ontario (CHEO)'s long-term program, starting at age 14 with integrated education and mental health assessments, and Children's Hospital at London Health Sciences Centre (CH-LHSC)'s short-term program, beginning at age 17 with a focus on combined transition clinics for youth with drug-resistant epilepsy (DRE) with a dedicated transition nurse navigator.
Method: Children in both programs are evaluated through standardized assessments which includes completing six questionnaires at their final pediatric visit, with caregivers of those with moderate/severe cognitive impairment completing three additional questionnaires. Post-transition, follow-up questionnaires will be administered at 6, 12, and 24 months. Demographic and epilepsy-related data is extracted from medical charts and securely stored in the CHEO REDCap database.
Results: CHEO's long-term transition program has enrolled 328 patients with a 92% enrolment rate, significantly higher than the CH-LHSC's short-term transition program, which enrolled 58 patients with a 57% enrolment rate ($\chi^2 = 70.524$, $p < 0.001$). Among the long-term transition program, 35% (n=116) had DRE, with comorbidities including intellectual disability (ID) in 9% (n=29), ADHD in 15% (n=50), and autism spectrum disorder (ASD) in 11% (n=36). In the short-term transition program, 51% (n=33) had DRE, with comorbidities including ID in 29% (n=19), ADHD in 12% (n=8), and ASD in 9% (n=6).
Conclusion: This study is the first to compare two transition models in pediatric epilepsy. Interim analysis reveals that early intervention and structured transition programs significantly improve patient engagement. Our goal is to identify an optimal transition pathway for children with epilepsy to enhance outcomes and ensure comprehensive care.
Acknowledgements: This work is supported by the Canadian Institutes of Health Research.

881 | Features of seizures in children with epilepsy of different age groups

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Purpose: To study the characteristics of clinical manifestations in children of different age groups who suffer from epilepsy
Method: 1017 children with epilepsy, aged from 3 months to 17 years, were under our supervision. They were divided into age groups: 1- children from 3 months to 1 year (n=44); 2- children from 1 to 3 years old (n=137); 3 - children from 4 to 6 years old (n=156); 4- children from 7 to 10 years old (n=206); 5- children from 11 to 14 years old (n=208); 6- children from 15 to 17 years old (n=266).
Results: Seizures were assessed by type, frequency, combination, transformation, manifestations (single, serial, status) and frequency of all epileptic seizures during the last year. 70.77% of patients with epilepsy had one type of seizure. Polymorphic seizures were more often registered in younger children. The transformation of seizures was recorded in 29.81% of patients: generalized - in focal (9.64%). focal - in generalized (19.17%). Seizures with a focal onset were typical for children of early age, in older children - generalization. Single seizures were recorded in 75.91% of cases. 17.11% had serial seizures, which were most often (72.26%) observed in younger children. The status course of seizures was noted in 2.65%, most often observed in adolescent patients. According to the frequency of epileptic seizures, the following were registered: infrequent (8.26%) (less than once a month (from 1 to 12 per year), frequent (20.75%) (from 1 to 4 per month), very frequent (32.25%) (more than 4 per month), during the year without seizures (38.74%). The highest number of very frequent seizures was diagnosed in young children.
Conclusion: Thus, early age is characterized by frequent polymorphic focal and cluster seizures, while single generalized seizures with transformation and a tendency to status course were observed at an older age.

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892 | EMPEROR Phase 3 study design: Evaluation of zorevunersen as a potential disease-modifying therapy for Dravet syndrome

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Purpose: Dravet syndrome (DS) is a severe developmental and epileptic encephalopathy characterized by refractory seizures as well as significant behavioral difficulties and cognitive impairments. Phase 1/2a studies of zorevunersen in patients with DS have demonstrated substantial and durable reductions in seizure frequency and improvements in behavior and cognition. Building on these findings, the EMPEROR Phase 3 multicenter, randomized, double-blind, sham-controlled study aims to evaluate the efficacy, safety, and tolerability of zorevunersen in patients with DS. The study duration and endpoints are designed to evaluate the potential of zorevunersen for disease modification.

Method: Patients aged 2 to <18 years with a confirmed *SCN1A* variant will be randomized 1:1 to either zorevunersen or sham treatment groups. The study includes an 8-week baseline period and a 52-week treatment period. That is, patients will receive two 70 mg loading doses of zorevunersen administered intrathecally or sham treatment at Day 1 and Week 8, followed by two 45 mg maintenance doses of zorevunersen or sham treatment at Weeks 24 and 40, in addition to standard of care. Sham procedures will involve lumbar punctures with cerebrospinal fluid collection. EMPEROR will randomize approximately 150 patients at approximately 60 sites across the European Union, United Kingdom, United States, and Japan. At the end of the study, eligible patients will be offered treatment with zorevunersen as part of a long-term extension study.

Results: The primary endpoint is the change from baseline (in log scale) in major motor seizure frequency. Secondary endpoints include the change in behavior and cognition, clinical status, and health-related quality of life in patients with DS.

Conclusion: EMPEROR will be the first Phase 3 global study to assess the effects of a potential disease-modifying therapy on seizures and multiple aspects of cognition and behavior in patients with DS. Funding: Stoke Therapeutics

894 | Preemptive Intervention Strategies for TSC-Associated Epilepsy in Pediatric Patients: A Retrospective Cohort Study

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Purpose: In children with tuberous sclerosis complex (TSC), epilepsy develops in 70 to 90% of cases, often proving resistant to standard antiepileptic medications, thereby becoming primary risk factor for intellectual disability. Recent investigations have delved into the proactive vigabatrin to alter the natural progression of epilepsy. It has been observed that preemptive treatment may decrease the likelihood of infantile spasms, but its impact on focal epilepsy and cognitive impairment remains variable. Our study aims to assess the influence of early everolimus intervention in individuals treated for cardiac rhabdomyomas on the occurrence of infantile spasms, epilepsy, and cognitive abilities. We seek to compare these outcomes with patients who received preventive vigabatrin during early life.

Method: This retrospective study focuses on patients managed at pediatric comprehensive TSC clinic between 2023 and 2024, at KFSHRC Riyadh.

Results: The cohort consisted of 6 patients, with 3 patients in each group, all diagnosed with TSC2. The median age at evaluation was 19 months, with therapy initiation starting at a median age of 1 month. Among the 3 patients receiving vigabatrin, they were identified with cardiac rhabdomyoma in utero, leading to early EEG surveillance and subsequent prophylactic vigabatrin treatment. While no infantile spasms were reported, 2 of these patients developed focal seizures necessitating additional antiseizure medications, alongside observed speech delay. Conversely, 3 patients were prenatally diagnosed with large rhabdomyoma necessitating early everolimus therapy. One patient received intrauterine treatment and continued postnatally, with temporary cessation preceding cardiac surgery resulting in seizure emergence. The other 2 patients showed no infantile spasms, epilepsy, and normal development.

Conclusion: The current evidence supports prophylactic vigabatrin use, although effective, poses controversy regarding its impact on focal epilepsy compared to the observed effects of everolimus, indicating superior epilepsy control and developmental outcomes. However, larger cohort sizes and randomized controlled trials are essential to validate these findings conclusively.

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896 | Substantial improvements in overall seizure burden and seizure-free days in patients with Dravet syndrome treated with zorevunersen: Results from Phase 1/2a and open-label extension studies

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Purpose: Dravet syndrome (DS) is a severe developmental and epileptic encephalopathy caused primarily by *SCN1A* variants resulting in $Na_V1.1$ haploinsufficiency. Patients with DS experience prolonged, refractory seizures, and developmental and cognitive impairments. Zorevunersen is an investigational antisense oligonucleotide designed to upregulate $Na_V1.1$ by leveraging the *SCN1A* wild-type copy. Here, we present the antiseizure effects of zorevunersen in patients with DS already on best available antiseizure medications (ASMs), including fenfluramine.

Method: In the Monarch/Admiral (NCT04442295 [US]; 2020-006016-24 [UK]) Phase 1/2a studies, 81 patients received single/multiple doses of zorevunersen (≤70mg). At the end of Phase 1/2a studies, 74 patients transitioned to the Swallowtail/Longwing (NCT04740476 [US]; 2021-005626-14 [UK]) open-label extension (OLE) studies and received zorevunersen (≤45mg) every four months while continuing ASMs. Clinical effects of zorevunersen treatment were evaluated.

Results: The most substantial improvements in convulsive seizure frequency (SF) and seizure-free days (SFDs) were observed in patients treated with multiple doses of 70mg zorevunersen. In Phase 1/2a studies, the 70mg multiple-dose cohort (N=11) achieved median reduction in convulsive SF of 84.8% (n=10) and 73.6% (n=9) at three and six months after the last dose, respectively. The majority (≥75%) of patients in this cohort experienced ≥50% reduction in convulsive SF. These patients experienced a median of 24 SFDs per 28 days (85.7%) at both three and six months after the last dose. In OLEs, patients treated with multiple doses of 70mg zorevunersen in Phase 1/2a studies followed by 30–45mg maintenance doses experienced sustained reductions in median convulsive SF, ranging from 50.8%–89.3%, through Month 8 of OLEs. Zorevunersen was generally well tolerated.

Conclusion: Patients treated with multiple loading doses of 70mg zorevunersen followed by maintenance dosing experienced substantial and durable seizure reduction while on best available ASMs, including fenfluramine. These findings support further evaluation of zorevunersen in Phase 3 trials. Funding: Stoke Therapeutics

905 | Developmental and epileptic encephalopathy with spike-wave activation in sleep (DEE-SWAS)-current perspectives and our experiences

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Purpose: Developmental and epileptic encephalopathy with spike-wave activation in sleep (DEE-SWAS) is an age-dependent epilepsy syndrome characterized by sleep-induced epileptogenic changes accompanied by cognitive and behavioral abnormalities, with or without epileptic seizures. It was first described in 1971 by Patry et al., and since then, there has been no clear consensus on diagnostic criteria or optimal treatment. Treatment often includes numerous antiepileptic drugs, immunomodulators, and in some cases, surgical intervention. The aim of this study was to analyze the etiopathogenesis of DEE-SWAS , evaluate treatment modalities in accordance with neuroradiological, genetic data, and the electroclinical spectrum of DEE-SWAS in our patient group.

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Method: We present the clinical approach to patients with a diagnosis of DEE-SWAS treated in our institution in the period from 1.1. 2019. until 31.12.2024.
Results: A total of 18 patients were treated, 9 girls and 9 boys. In 5 cases (27.7 %) it was idiopathic DEE-SWAS. 10 patients (55.6 %) were treated with various combinations of antiepileptic therapy (AET), 7 patients (38.9 %) received corticosteroids and AET, and 1 patient (5.5 %) received corticosteroids alone. EEG normalization was observed in 5 patients (27.7 %), seizure free period in 10 (55.6 %). 11 patients (66.6 %) have cognitive deficits or communication difficulties.
Conclusion: Despite the favorable long-term prognosis of epilepsy and normalization of EEG, cognitive deficits and behavioral disorders can last a lifetime. Developmental lesions, especially those affecting the thalamus, may play a role in the development of DEE-SWAS. Clinicians approaches to the treatment of ESES syndrome vary widely, and there is no agreement on the best treatment. Widespread use of genetic research including epilepsy gene panels, array-cGH, whole exome sequencing and whole genome sequencing could be crucial in elucidating the etiology of DEE-SWAS and personalized medical treatment. Randomized controlled trials are needed to provide an improved evidence base for a rational approach to the treatment .

909 | Factors implicated in the delayed diagnosis of Epilepsy with Eyelid Myoclonia (Jeavons syndrome)

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Purpose: Epilepsy with Eyelid Myoclonia (EEM) is a rare epilepsy syndrome characterized by the triad of eyelid myoclonia with or without absence, epileptiform activity induced by eye closure, and photosensitivity. The goal of this study was to describe the long-term course of this epilepsy syndrome and identify factors implicated in the delayed diagnosis of EEM.
Method: A single-center retrospective chart review of patients with EEM between January 2010 and October 2024 was performed.
Results: Eleven patients with EEM were included. The average age of diagnosis of epilepsy was 7.9 years, and diagnosis of EEM was 12.4 years. The average time implicated in the delayed diagnosis of EEM was 4.5 years. 9/11 patients were initially diagnosed as an idiopathic generalized epilepsy (IGE) and the main seizure types were typical absence (6/11) and eyelid myoclonia (3/11). The diagnosis of EEM was made on routine EEG (6/11) and epilepsy monitoring unit (EMU) (5/11). The main seizure types found at the time of EEM diagnosis were generalized tonic-clonic (5/11), myoclonic (5/11), typical absence (4/11), and eyelid myoclonia (4/11). Electrographically, 10/11 had age-appropriate posterior dominant rhythm and 7/11 had alpha squeak as a normal variant. Patients admitted to the EMU had photoparoxysmal response, photosensitivity, and eyelid myoclonia which evolved to bilateral tonic-clonic seizures. 8/11 patients had drug-resistant epilepsy. Lamotrigine (7/11) and valproic acid (8/11) were the most used antiseizure medications before and after the diagnosis of EEM, respectively. A medication wean was attempted in 4/11 patients; all needed to restart antiseizure medications.
Conclusion: The diagnosis of EEM can be challenging and is often delayed. This condition usually mimics an IGE initially, with typical absences and eyelid myoclonia seizure types. The presence of photosensitivity, photoparoxysmal response, eyelid myoclonia, drug resistance, and the inability to wean medications could be considered red flags for EEM.

913 | Selective potentiation of NaV1.1 channels by small molecule XPC-A in Dravet mice suppresses spontaneous seizures, prevents SUDEP, and increases Long Term Potentiation

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Purpose: Loss-of-function variants of SCN1A cause Dravet Syndrome (DS) by decreasing NaV1.1 expression in inhibitory interneurons. The resulting hypo-excitability of interneurons reduces inhibitory input on excitatory neurons and leads to epilepsy and developmental delays. We are developing orally available small molecule NaV1.1 potentiators that could provide a potentially disease modifying precision therapy for DS.
Method: Automated patch clamp electrophysiology was used to evaluate the potency and selectivity of compounds. XPC-A was also evaluated in brain slices from Scn1a heterozygous null mice (Scn1a+/-) to assess the effects on interneuron excitability, synaptic inhibitory and

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excitatory balance, and Long Term Potentiation (LTP). Single dose efficacy was assessed in Scn1a+/- mice in a 6Hz electrically induced seizure assay and in a rotorod motor performance assay. Repeat dose efficacy in was assessed Scn1a+/- mice by spontaneous seizure frequency and mortality.

Results: XPC-A exhibited robust enhancement of NaV1.1, demonstrating more than a 100-fold preference over NaV1.2, 1.6, and 1.5 variants. In brain slices obtained from Scn1a+/- mice, XPC-A increased the firing activity of fast-spiking cortical PV+ interneurons and rebalanced the spontaneous excitatory and inhibitory synaptic input to pyramidal neurons. In vivo experiments further show that XPC-A effectively mitigates 6Hz electrically induced seizures in Scn1a+/- mice and improves their motor performance deficits. Feeding XPC-A medicated chow for 14 days demonstrated that XPC-A suppresses spontaneous seizures, prevents SUDEP, and increases LTP in Scn1a+/- mice.

Conclusion: XPC-A is a highly NaV1.1 selective small molecule potentiator that increases Scn1a+/- interneuron excitability and normalizes excitation/inhibition imbalance in Scn1a+/- mouse neurons. In vivo, XPC-A suppresses induced seizures and improves motor performance, suppresses spontaneous seizures, prevents SUDEP and increases LTP. XPC-A represents a novel, mechanistically differentiated, orally available compound with the potential to provide an improved therapeutic profile for the overarching treatment of DS.

966 | Cannabidiol as add-on therapy for patients with refractory childhood epilepsy (CBD-uN1que): study protocol for a series of n-of-1 trials

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Purpose: One-third of patients with epilepsy is refractory to current antiseizure medications. Recently, cannabidiol has been proven to be an effective treatment for populations with specific epilepsy syndromes, including Dravet syndrome, Lennox-Gastaut syndrome, and Tuberous Sclerosis Complex. In other etiologies, translation to clinical practice of current evidence on the anticonvulsive properties of cannabidiol is hampered by the sizeable within-patient heterogeneity and rarity of underlying etiologies, demanding an alternative trial design to address individual response.

Method: In a series of 50 N-of-1 trials, we investigate the efficacy and safety of cannabidiol in patients aged 1 to 18 years with refractory epilepsy on an individual and group level. Each patient will undergo a double-blind, placebo-controlled, randomized cross-over trial with two to three cycles. Within each cycle, patients will receive either oral cannabidiol (Bedrolite®, Felix Farma BV) up to 5-20 mg/kg/day dosed twice daily or placebo, for 28 days each, with the addition of run-in, taper, and washout periods before and after the intervention periods. Moreover, we will use simulation models to investigate the statistical properties of N-of-1 trials in epilepsy research.

Results: The primary outcome measure is the percentage reduction in seizure frequency during cannabidiol treatment versus placebo compared to the baseline, assessed using an electronic seizure diary. Secondary outcome measures include 30%-, 50%-, 75%-, and 100%- responder rates, number of seizure-free days, adverse effects, and patient-centered outcome measures using standardized questionnaires on epilepsy severity, quality of life, sleep, and behavior.

Conclusion: Using a series of N-of-1 trials, we aim to provide insight in the individual treatment responses to cannabidiol for childhood epilepsy, while also enabling the use of aggregated analyses to estimate treatment effects at the population level. N-of-1 trials offer a unique advantage in accommodating patients' preferences, enhancing shared decision-making between patients and healthcare.

Funding: Publicly funded by ZonMw.

972 | Assessing Sleep Problems for Patients with Drug-resistant Epilepsy Using Caregiver-reported Survey Data

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Purpose: This research aimed to evaluate the quality of life in patients with early-onset epilepsy, genetically confirmed, through the Brief Quality of Life in Childhood Epilepsy Questionnaire (QOLCE-16) and to assess sleep problems using the Sleep Disturbance Scale for Children (SDSC), relying on responses provided by caregivers.
Method: The inclusion criteria required patients to 1) take two more antiseizure medications diagnosed with drug-resistant epilepsy and 2) complete all required questionnaires by parents. The exclusion criteria specified if patients achieved seizure-free states over 1 year. Sleep questionnaires could be required on patients over 4 years, so all included patients were above 4 years old.
Results: We included 63 drug-resistant epilepsy patients (male, N= 39). The average age was 8.0 (SD +-3.7) years old, and their median seizure onset was 1.1 (IQR 0.3-2.9) years. Among them, 30 patients (48.4%) had brain structural abnormalities, and 43 patients (68.3%) revealed genetic backgrounds. The mean total score on QOLCE-16 was 49.3 (SD +- 16.9). The SDSC total score was 51.8 (SD+-16.9), substantially higher than the reference score of 35.1, reflecting severe sleep problems. Patients getting older have higher SDSC scores in patients with drug-resistant epilepsy.
Conclusion: This study provided meaningful insights into the quality of life and sleep disturbances in patients with drug-resistant epilepsy by caregiver survey. These findings highlight that these patients experience significantly poor quality of life and severe sleep problems. Future research is warranted to explore specific variables contributing to these outcomes and develop targeted treatment strategies to improve their daily life.

991 | Uncovering Emergency Care Processes for Paediatric Neurologic Patients using Process Mining

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Purpose: This study provides insights into the care pathways, resource needs, and outcomes of pediatric neurological patients at the biggest pediatric emergency department (PED) in Finland by utilizing large scale real-world data.
Method: Patient data from neurological visits at Helsinki University Hospital PED between January 2021 and December 2023 were analyzed using modern data analysis and process mining tools.
Results: 4854 visits (5,5% of PED visits) for 3553 patients were identified. The most common chief complaint was seizure, accounting for 43% of all and 69% of the urgent cases (Emergency Severity Index (ESI) acuity level 1–2), followed by headache (21%), which was linked to visits with lower acuity. Younger children and males were more likely to present with seizures. 20% of the cases requiring immediate lifesaving intervention (ESI level 1) were neurological, with seizures constituting 77% of these, highlighting their critical nature. Process analysis revealed that patient paths varied substantially. 75% of seizure patients followed one of five main pathways, whereas the remaining 25% were distributed across over 40 different processes, many of them unique to a patient. Paraclinical tests were conducted in 86% of seizure cases. 33% of ESI level 1 but only 5% of level 3–5 seizure patients had other than basic laboratory tests (imaging, EEG or cerebral spinal fluid analysis) conducted. 23% of all neurological and 29% of seizure patients were hospitalized. 82% of ESI level 1 seizure patients were admitted, 13% of which to the pediatric intensive care unit. 80% of the more stable (ESI level 3–5) seizure patients were discharged.
Conclusion: This study pioneers advanced methods to analyze patient care processes and resource utilization of neurologic patients at the PED by integrating large-scale real-world data. It highlights the critical nature of pediatric neurological emergencies, especially seizures, and showcases the substantial variability of patient pathways.

997 | Analysis of patients with epilepsy in the pediatric neurology outpatient clinic of an university hospital in Brazil

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Purpose: Epilepsy encompasses a variety of disorders with diverse electroclinical presentations and outcomes. The 2017 ILAE classification defines three diagnostic levels, including seizure and epilepsy types, highlighting the role of etiology and comorbidities. Most epilepsy cases begin in childhood, underscoring the importance of studying this condition in Brazil's pediatric population.

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This study aimed to identify the epidemiological profile of children with epilepsy at the University Hospital of Rio de Janeiro.

Method: This observational, retrospective study reviewed the medical records of 220 patients from the child neurology outpatient clinic from 2023-2024. Inclusion required a diagnosis of epilepsy by ILAE criteria. Categorical data were presented as percentages, and numerical data were analyzed with mean and standard deviation, using a p-value below 0.05 for statistical significance.

Results: The majority of patients (58.5%) were male, with the average age at diagnosis being 2.83 years (SD 3.08). Most patients began treatment immediately after diagnosis (84.09%). The mean age of the first visit to the outpatient clinic was 4.15 years (SD 3.47). Focal onset seizures were the most common (53%), followed by generalized seizures (26%). Status epilepticus in 11.5%. Epileptic syndromes were confirmed in 29.5%, with Infantile Epileptic Spasms Syndrome (37.8%) and Lennox-Gastaut syndrome (22.2%) being most prevalent. A history of febrile seizures was seen in 14.8%, and 23.5% had a positive family history. Regarding etiology, 43.6% of cases were of unknown origin, while 30.9% were structural, 16.4% genetic, 5.9% metabolic, and 3.2% infectious. Treatment included 37% monotherapy and 63% polytherapy, with valproic acid and carbamazepine being the most used drugs. At admission, 44% of patients were considered difficult to control, but 22.5% achieved seizure control after 6 months.

Conclusion: Understanding this profile can help improve strategies for better care and crisis control in the pediatric population of a University Hospital in Brazil.

1008 | Hippocampal proteome of Cdkl5-deficent mice features disturbed metabolic processes: Insights into molecular mechanisms and potential therapeutic targets for CDKL5 deficiency disorder

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Purpose: CDKL5 deficiency disorder (CDD) is a severe epileptic encephalopathy caused by mutations in the CDKL5 gene resulting in early-onset epilepsy, motor impairment, and intellectual disability. As a kinase, CDKL5 regulates the activity of its substrates through phosphorylation, which include proteins involved in synaptic function and cytoskeletal organization with loss of CDKL5 leading to altered neurotransmission and brain development. The full spectrum of processes disrupted in CDD remains uncertain. Here, we evaluated major phenotypes in *Cdkl5* exon 6 -/- model mice and used proteomics to survey alterations in CDD.

Method: Behavioral tests such as open field, clasping, marble-burying, and EEG recordings were carried out to assess motor and cognitive dysfunction, and seizure activity in 8-12-week-old female heterozygous (Het), male knock-out and wild-type mice. Hippocampal samples of 12-week old WT and HET (n=10/group) were analyzed by mass spectrometry analysis employing reversed-phase liquid chromatography coupled with nanospray tandem mass spectrometry on an LTQ-Orbitrap mass spectrometer, to identify proteins altered in CDD. Findings were validated using RT-qPCR, immunoblotting, and co-immunoprecipitation.

Results: The *Cdkl5* exon 6 -/- model mice display expected features of CDD such as motor impairment, increased hyperactivity, and increased sensitivity to kainic acid, demonstrated by EEG recordings. Proteomics analysis revealed significant changes in protein expression, with 233 proteins upregulated and 86 downregulated. There was higher expression of metabolic proteins such as MDH2, and GOT2 whereas mitochondrial antiporters such as SLC25A25 and SLC25A12 exhibited decreased expression. Further analysis showed significant alterations in the expression of metabolic proteins and disrupted metabolic function.

Conclusion: The *Cdkl5* exon 6 -/- model replicates key features of CDD, validating the model for studying the disorder. Mass spectrometry identified significant alterations in metabolic proteins involved in energy metabolism and ion transport, suggesting a role in metabolic dysregulation. These molecular insights provide potential therapeutic targets and pathways for intervention. Funding: IRC, Epilepsy Ireland

1020 | Seizure-like events in a pediatric emergency department: eight years after

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Purpose: Seizure-like events (SLE) are particularly common in children and a frequent cause of emergency department (ED) admission, often with high levels of anxiety among caregivers. We aim to assess the clinical

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management, follow-up, and diagnosis of children and adolescents presenting to a pediatric ED with SLE.

Method: Retrospective cohort descriptive study analyzing the clinical files of children admitted to the ED with SLE between December 2015 and February 2016. The acute episode was assessed based on demographic variables, clinical manifestations, neurological examination, and complementary investigations, with a follow-up period of eight years. The neonatal period was excluded.

Results: A total of 178 admissions for SLE were recorded, representing 161 children and adolescents, with a median age of 7.9 years (IQR=12). The most common clinical presentations were lipothymia/syncope (37.6%), psychogenic non-epileptic seizures (21.3%), and febrile seizures (21.3%). Fifty-six children (31.4%) were seen by a pediatric neurologist (PN), and 64 underwent video-EEG (39.8%). Sixty-four children (39.8%) were referred for a PN appointment. The final diagnosis was paroxysmal non-epileptic events (PNEEs) in 99 episodes (55.6%) and paroxysmal epileptic events (PEEs) in 79 episodes (44.4%). Of the PEEs, 37 were febrile seizures, and 42 unprovoked epileptic seizures (57,6% with a previous diagnosis of epilepsy). In our cohort, after eight years of follow-up, 47 children have a principal diagnosis of neuropediatric disorder, 14 a developmental disorder, 12 a psychiatric disorder, 64 another or no identified disorder, and 24 cases lost follow-up. The children with neuropediatric disorders have mostly the diagnose of epilepsy (76,6%), and 14 new diagnoses of epilepsy were made (8,7%).

Conclusion: SLE were predominantly of non-epileptic origin. The assessment and follow-up by a PN and video-EEG were crucial for the accurate diagnosis over time. This study may help PN and pediatricians in what to expect regarding the diagnoses in children who present in ED with SLE.

1023 | Seizure freedom in children and youth with epilepsy in The Norwegian Mother, Father and Child Cohort Study

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Purpose: To investigate seizure freedom rates in children and youth with epilepsy using the International League Against Epilepsy (ILAE) classification of seizures, syndromes, and etiologies.

Method: The Norwegian Mother, Father, and Child Cohort Study (MoBa) comprises approximately 114,000 children. Among them, 1,053 epilepsy cases were verified, with median age of 16.7 years and median follow-up 10.6 years. Cox proportional hazards models assessed hazard ratios (HR) for seizure freedom by seizure type, epilepsy syndrome, and etiology according to ILAE classifications.

Results: Of the 1,044 children with at least 12 months follow-up, 805 (77%) were seizure-free, 203 (19%) had drug-resistant epilepsy (DRE), and 39 (3.7%) had undefined outcomes at follow-up. The median time to seizure freedom was 2.0 years (IQR 0.5–4.5 years), and the seizure freedom rate was 16.3 per 100 person-years. ASMs used ranged from 0 to 20 (median 1 [IQR 1–3]). Fourteen percent never used ASMs. Non-medical therapies were used by 6.3%, with 33% classified as seizure-free at follow-up. Neurological and developmental difficulties, abnormal neurologic examination, EEG findings, and neonatal/infantile onset were all significantly associated with lower seizure freedom rates. Individual seizure type associations attenuated when adjusted for etiology and number of seizure types, which were strong predictors of seizure freedom. Compared to focal epilepsy, combined generalized and focal epilepsy showed a lower likelihood of seizure freedom (HR=0.13 [99% CI 0.07–0.24]), while generalized epilepsy showed no significant effect (HR=0.94 [0.75–1.2]). Epilepsy syndromes SeLECTS (HR=2.5 [2.0–3.1]) and CAE (HR=1.9 [1.4–2.6]) had positive associations, while developmental/encephalopathy syndromes (HR=0.26 [0.20–0.34]) showed negative associations to seizure freedom rates.

Conclusion: Three-quarters of children and youth with epilepsy achieve seizure freedom. Epilepsy syndromes, defined by characteristics cluster of clinical and EEG features, often supported by specific etiological findings, are key determinants of outcomes. Funded by: Foundation Dam, South East Norway Regional Health Authority.

1046 | Treating ADHD in Children with Epilepsy: Proceed with Caution or with Confidence?

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Purpose: It has been well established that attention-deficit hyperactivity disorder (ADHD) is one of the most common co-morbidities associated with epilepsy. Children with epilepsy are at increased risk of cognitive and behavioral problems which can impact school performance and intra-group relationship building, and these issues are even more pronounced in children with both epilepsy and ADHD. Effectively treating a child's ADHD symptoms can improve performance within these domains, however, providers are often hesitant to trial medicines within the stimulant class of treatment medicines

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as there is concern that medicines could increase seizure frequency in patients. While there have been studies exploring seizure frequency in children taking stimulants for treatment of ADHD utilizing self-control as a method of analysis. Seizure frequency after exposure to nonstimulant as well as combination stimulant and nonstimulant therapies have not been as thoroughly investigated.

Method: To our knowledge, we developed the largest population-based cohort study of pediatric patients (n=131) through retrospect chart review on the use of all ADHD medicines on children with co-morbid epilepsy. Our cohort was comprised of pediatric patients (0-252 months of age) who were diagnosed with either generalized (48.8%), focal (35.7%), or generalized and focal (10.7%) epilepsies and who were treated with stimulant medicines (n=84) for co-morbid ADHD. We were able to compare seizure frequency before and after initiation of ADHD treatment to epilepsy and age matched cohorts who were treated with either non-stimulant (n=20) or combination therapies (n=27).

Results: We found that patients did not have increased seizure frequency after initiation of ADHD treatment, independent of ADHD medicine class.

Conclusion: These findings serve to strongly encourage providers to utilize all medical therapies available in the treatment of ADHD in pediatric patients, regardless of the type of their epilepsy, to give them the greatest chance of success both at home and at school.

1077 | Focal Seizures and Transverse Myelitis: A Pediatric Case Report of Anti-MOG Antibody-Associated Encephalomyelitis

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Purpose: To present a clinical case of anti-MOG antibody-associated encephalomyelitis (MOGAD) in a pediatric patient, to aid in recognition of this condition and highlight challenges in its diagnosis and treatment.

Method: Description of the clinical case, including EEG findings, MRI images, and seizure video-recordings.

Results: At the age of 4-year 2-month, a male with unremarkable medical history, presented with onset of focal to generalized seizures. The seizure occurred in the morning after waking, characterized by confusion, unresponsiveness, purposeless movements (resembling autistic-like behaviors), followed by generalized hypertonia, tonic-clonic jerks, perioral cyanosis, and trismus, lasting 10 minutes with subsequent postictal drowsiness. The initial EEG and neurological examination were normal. However, the patient experienced multiple daily focal seizures, including staring episodes, left gaze deviation, generalized hypertonia, and hyperkinetic, non-purposeful movements of lower limbs. He was therefore hospitalized: the initial diagnostic and therapeutic workup included brain MRI, metabolic screening, and karyotyping on 100 metaphases, resulted negative. EEGs showed focal anterior bilateral IEDs. Treatment with oxcarbazepine was initiated, but provided incomplete seizure control. Valproic acid was added, with moderate improvement. Three months after seizure onset, the patient suddenly lost walking ability. At the ER, spinal cord and brain MRI confirmed transverse myelitis (C5-D10) with white matter alterations in the posterior cranial fossa and supratentorial region, consistent with ADEM. Serological and liquor tests revealed anti-MOG antibodies positivity at titer respectively 1:2560 and 1:2. Following MOGAD diagnosis confirmation, immunomodulatory therapy with intravenous methylprednisolone (20 mg/Kg) for 5 days, followed by oral prednisone (2 mg/kg), was initiated alongside antiseizure medications (ASMs). This combination resulted in immediate positive response, with significant improvement in seizure control and recovery of walking ability.

Conclusion: MOGAD is a rare but clinically significant condition in which seizures may precede or accompany demyelinating events. Prompt diagnosis and treatment with immunotherapy and ASMs have shown substantial clinical and electroencephalographic improvement.

1082 | The impact of seizure first aid education on prehospital management of pediatric status epilepticus and hospital morbidity

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Purpose: To evaluate the impact of a dedicated caregiver training program on the pre-hospital use of RM(rescue

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medication) during a SE(Status epilepticus) event and it's impact on hospital admission and morbidity.

Method: A retrospective 1 year audit was done twice in 5 years to study the effect on pre-hospital RM use in children presenting with SE , before and after a dedicated patient education program respectively, aided with the help of Epilepsy Specialist nurse. Inclusion criteria were patients aged 6 months to 18 years with epilepsy being followed up at our institute.

Results: In the first audit, 56 SE events were captured with a 12% correct use of pre-hospital RM. Following the carer education program over the next 5 years, a survey covering 104 families showed 89% awareness for use of RM with 84% affirming knowledge of the correct timing and dosage for administering RM while 54% preferred buccal, followed by rectal (24%) and intramuscular (10%) routes of RM administration. The follow-up audit recorded 34 SE events with 44% reporting the correct use of RM. In both the audits, patients who received RM later than 15mins were more likely to require use of 2nd line medications and/or admission to the intensive care unit.

Conclusion: 1. Timely RM is key to prevent hospital admission and this hasn't changed over 5 years despite having access to more 2nd line anti-seizure medications.

2. The caregiver awareness has gone up significantly aided by a dedicated education program.

3. The overall admissions with SE have gone down.

4. In those presenting to the hospital with SE, the use of RM remains low, indicating need for ongoing education and training.

1121 | When science meets hope: Dramatic efficacy of ketogenic diet in a child with ALG13-CDG (congenital disorders of glycosylation) related epileptic encephalopathy

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Purpose: We describe a 5 ½ year old girl with ALG13-CDG (congenital disorder of glycosylation)-related epileptic encephalopathy with seizure onset at three months of age, achieving seizure freedom following introduction of the classical ketogenic diet (CKD).

Method: Retrospective case note review

Results: Our patient was born at term with a normal antenatal and perinatal history. She presented with paroxysmal episodes at 3 months of age, treated as gastro-esophageal reflux, but later diagnosed as infantile spasms with EEG showing epileptic encephalopathy at six months of age, MRI brain normal. She had associated global developmental delay. By the age of 18 months, her epilepsy was drug-resistant with focal, tonic-clonic, tonic and absence seizures occurring multiple times daily in clusters. She had hypotonia, feeding difficulties, dystonia, visual impairment, and absence of dysmorphic features. She was started on classical ketogenic diet (CKD) at 28 months of age following trial of six anti-seizure medications (ASM). She achieved seizure freedom within 4 weeks of reaching ketosis and has maintained this for 38 months. She has successfully weaned all ASM and KD is her monotherapy. EEGs are slow for age but no longer in keeping with an epileptic encephalopathy. She has had psychomotor improvement, sits independently, stands with support, with increased interaction though still non-verbal. Extensive blood investigations were done and whole genome sequencing (epilepsy panel) revealed de novo variant in ALG13 c.320A>G p.(Asn107Ser) which was consistent with her phenotype.

Conclusion: We found that ketogenic diet may offer a promising treatment option for patients with ALG13-related epileptic encephalopathy with respect to both intractable seizures and global developmental delay. Case reports have supported efficacy of CKD. To our knowledge, this patient has had the longest sustained period of seizure freedom at a very early presenting age. Further research to establish the efficacy of CKD in these patients is warranted.

1153 | The neuroprotective role of interleukin-1 receptor antagonist in damaged brain of children with status epilepticus

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Purpose: Interleukin-1 receptor antagonist (IL-1Ra) exhibits neuroprotective effects in experimental status epilepticus, as it is released in response to inflammation in brain tissue. This finding is supported by experimental research. The aim of this study was to determine the serum levels of IL-1Ra in children with status epilepticus (SE) and in the control group.

Method: This study was conducted in the Pediatric Neurology Unit of the Mother and Child Institute, Chisinau, Republic of Moldova. Fifty-five children with

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SE (29 girls, 26 boys; mean age 54.0 ± 47.4 months) and 26 normal controls (8 girls, 18 boys; mean age 40.0 ± 31.1 months) were included in our study. Serum IL-1Ra concentrations were measured using an ELISA immunoassay. Statistical methods used for data analysis included the t-Student test and a 95% confidence interval (95% CI).
Results: The results of this study showed increased inflammation in the SE group and elevated levels of IL-1Ra in the serum of children with SE compared to the control group. The median serum IL-1Ra level in the SE group was significantly higher than in the control group (97.7 pg/mL vs. 44.8 pg/mL) (95% CI [8.31, 97.44], $p = 0.02$), with the difference being statistically significant ($p < 0.05$).
Conclusion: Elevated levels of IL-1Ra in children with status epilepticus, compared to control groups, can be attributed to the body's compensatory response to increased inflammation in the brain. This rise in IL-1Ra acts as a protective mechanism to mitigate neuronal damage and maintain homeostasis during prolonged epileptic activity.

1176 | Neonatal Parechovirus Meningoencephalitis: Risk of Acute Symptomatic Seizures and Infantile Spasms

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Purpose: Human parechovirus (HPeV) is a common viral pathogen affecting infants, specifically in high income nations. HPeV infections are associated with severe neurological sequelae, including acute symptomatic seizures, respiratory failure, cerebral palsy and epilepsy. This case series presents the clinical course of four neonates diagnosed with HPeV meningoencephalitis and reviews their outcomes in the context of available literature.
Method: A retrospective chart review was performed to identify neonates who were diagnosed with HPeV meningoencephalitis over one summer. The clinical course, laboratory findings, imaging, and neurodevelopmental outcomes were analyzed.
Results: We identified 4 patients (aged 6 days to 5 weeks old) diagnosed with HPeV meningoencephalitis on cerebrospinal fluid (CSF) meningoencephalitis PCR panel. 2/4 (50%) patients presented with fever and rash with abnormal EEG findings but no seizures. The other 2 patients presented with irritability and apneas requiring intubation and were found to have frequent subclinical seizures on EEG, as well as widespread diffusion restriction and T2/FLAIR changes on brain MRI. The acute seizures resolved, and both were discharged without chronic antiseizure medications. On follow up evaluations, 1/4 (25%) was diagnosed with cerebral palsy and subsequently developed infantile spasms at age 7 months. 3/4 (75%) had full neurological recovery with normal repeat EEGs and no long term neurological sequelae.
Conclusion: Although most infections are mild and self-limiting, initial symptoms in neonates are nonspecific and can be missed. Our case series highlights the severe neurologic complications of neonatal HPeV meningoencephalitis, including infantile spasms, which was previously unreported. Therefore clinicians should maintain a high index of suspicion for HPeV meningoencephalitis in neonates presenting with fever, rash, irritability or apnea, as early identification and treatment could influence long-term outcomes. Further research is needed to explore the frequency of development of epilepsy and association of infantile spasms within this cohort.

1184 | The VISTA Study: Videos of Infantile Spasms for Triaging and Assessment

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Purpose: Infantile spasms (IS) are one of the most concerning seizure types globally and are associated with significant neurodevelopmental impacts due to diagnostic and treatment delays. Expediting diagnosis is critical, especially in regions lacking access to electroencephalograms (EEG). The use of smartphone videos to aid in diagnosing epileptic seizures has yielded promising results in adult populations, but data in children are more limited. This study aimed to determine clinicians' ability to recognize IS based on smartphone videos and evaluate the impact of brief IS education on diagnostic accuracy, diagnostic confidence, and comfort level treating without EEG to avoid significant delays.
Method: This international multicenter cross-sectional study took place over seven sessions from 2022-2023. Staff physician and trainee participants were shown nine videos of EEG-confirmed events (6 IS, 3 nonepileptic events), solicited from children 3-18 months in two tertiary care centers (Boston and Cape Town). Participants viewed videos before and after IS teaching, then with clinical history, and completed surveys on diagnosis and management.

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Results: Of 181 participants (including 80 trainees), 61% (confidence interval [CI]: 51-72%) on average made correct diagnoses based on video alone, which improved to 68% (CI 55-81%) after IS teaching and 74% (CI 60-88%) with clinical history. Diagnostic confidence and clinician comfort level treating IS without EEG improved after teaching and clinical history. Diagnostic accuracy correlated strongly with diagnostic confidence after teaching with clinical history (ρ=0.97, p<0.001) and with clinician comfort level managing patients without EEG after teaching with clinical history (ρ=0.97, p<0.001). There were no significant differences in outcomes between staff physicians and trainees.

Conclusion: Smartphone videos can facilitate triaging suspected IS effectively and have an important role in reducing treatment lag times, especially when EEG access is lacking. Brief IS teaching and clinical history improve diagnostic accuracy and clinicians' comfort level treating patients without EEG.

1203 | Understanding and Modeling the Dravet Syndrome Diagnostic Pathway: DS'coverED Study Results

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Purpose: Dravet Syndrome (DS) is often diagnosed with delays that hinder timely therapeutic interventions. DS'coverED study aimed to understand diagnostic pathway for infants with DS, evaluate its duration, and identify opportunities to improve diagnostic timeline.

Method: An European Steering Committee including eight neuropediatricians and one European Dravet Syndrome Federation representative designed an online survey sent to pediatric neurology centers across Europe. The survey included 12 questions about physicians' practices and 25 questions addressing patients' diagnostic journey, from seizure onset to diagnosis and DS-specific anti-seizure medication (ASM) initiation, including stiripentol, fenfluramine and cannabidiol.

Results: Fifty-three physicians shared their practices, and 45 patient profiles were completed. Among respondents, 85% work at university hospitals and 53% have over 15 years of DS experience. DS diagnosis was confirmed to families after genetic tests results in 94% of cases. Patients' diagnostic journey included the following milestones (patient age): first seizure (5.9 months), consultation with a DS specialist (13.4 months), genetic test prescription (14 months), DS mentioned to family (16.8 months), genetic test results (18.6 months), formal DS diagnosis announcement (19 months), and DS-specific ASM initiation (26.7 months).

Two significant delays were identified:

- 7 months (standard deviation (SD): 12 months) to consult a DS specialist from seizure onset, may be attributed to delayed referrals to expert centers and limited DS awareness among non-specialists.
- 8 months (SD: 12 months) between formal diagnosis announcement and initiation of DS-specific drugs. Contributing factors include patient age, seizure frequency and duration, availability of DS-specific drugs at diagnosis, and physician confidence in prescribing these treatments.

Conclusion: These insights provide a framework for addressing DS diagnosis delays and highlight the need for practical measures. Improving access to expert centers, raising awareness of DS clinical features and benefits of early initiation of DS-specific ASMs could improve patient management and quality of life. Disclosures: funded by Biocodex

1212 | The natural history of convulsive seizures in SCN1A Dravet Syndrome

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Purpose: To identify demographic, genetic, and environmental variables correlated with lifetime seizure severity in SCN1A Dravet syndrome.
Method: This observational study tracked seizures from comprehensive diaries over many years in 79 individuals with SCN1A-Dravet syndrome (median age 5.5y, range 2m-52.4y). Outcomes included frequency and duration of convulsive seizures and convulsive status epilepticus (CSE, >30m). Linear mixed models assessed effects of age and mutation (truncation vs missense) on seizure outcomes. Circular statistics were used to extract multiday and circannual seizure cycles, with chi-squared analysis to identify environmental (i.e. weekday, seasonal) precipitants.
Results: 38,688 seizures across a total recording time of 352 years, with average diary duration per person of 4.5y (range: 3m-24.9y). The 79 patients had an average 160 days with reported convulsive seizures (range: 0–7900 seizure days). Incidence of CSE significantly decreased with age, by 22% with each year of age until 12y (95% CI: 14%-30%, $p<0.001$ linear mixed effects model), while incidence of all convulsive seizures remained constant until adulthood. Individuals' median duration of convulsive seizures (excluding CSE) significantly decreased with age, from 8m in infants (0–2y), 3m in early childhood (2–6y), to 1.8m in late childhood (6–12y). Individual seizure rates were variable, with mean frequency range from 0.1-10 seizures/month. Multiday rhythms (5 - 45 days) were identified in 23/65 (35%) patients, and significant seasonal effects in 16/48 (33%). Seizures increased during winter months on average ($p<0.05$, z-test); however seasonal trends were patient-specific.
Conclusion: Results provide a benchmark quantifying individual variability and periodic dynamics in the natural history of seizures in Dravet syndrome. Findings will guide clinical management and prognosis. Importantly, they will inform the development of Dravet syndrome-specific inclusion criteria for drug trials to allow inclusion of more individuals in precision therapy trials.

1213 | Real-World use of stiripentol in the USA

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Purpose: STIRUS study aimed to gather data on patients prescribed stiripentol after its US marketing authorization (August 2018). This retrospective, non-interventional, multicenter chart review involved US patients with Dravet syndrome (DS) who received stiripentol for ≥3 months, reflecting routine practice. The index date was stiripentol initiation; patients were followed until their last intake of the medication.
Method: The study included 99 patients from 10 US sites. Median age at first seizure was 5 months; at DS diagnosis, 15 months; and at stiripentol initiation, 6.9 years. At treatment initiation, patients used a median of 3 antiseizure medications, mainly benzodiazepines (clobazam n=81; clonazepam n=11), cannabidiol (n=45), valproate (n=42), fenfluramine (n=24), and levetiracetam (n=23). Mean initial stiripentol dosage was 14 mg/kg/d, increasing to a target dose of 31 mg/kg/d. Mean daily dose at last follow-up was 31.8 mg/kg/d.
Results: Following stiripentol initiation, a reduction in seizure frequency was observed and maintained over the long-term follow-up; 38.1% of patients experienced a marked/mild reduction in the last 3 months. At baseline, 33.7% had ≥1 status epilepticus episode (convulsive seizures >5 minutes), decreasing to 16.3% (first 3 months) and 14.9% (final 3 months). Rescue medication use and emergency room visits significantly decreased, improving patient/family/caregiver quality of life. 99 adverse effects were reported in 50 patients; no unexpected/significant reactions occurred.
Conclusion: STIRUS provided real-world evidence of DS management in the US. Median age at DS diagnosis was 1.25 years (vs. 5.4 years in 2012), indicating improved disease knowledge/earlier diagnosis. The study confirmed stiripentol's efficacy in decreasing the frequency of generalized tonic-clonic seizures and status epilepticus, leading to fewer hospitalizations, regardless of concomitant clobazam use. No unexpected adverse effects were identified. Somnolence, lethargy, and decreased appetite were most frequent, and may regress when the dose of concomitant antiseizure medications is reduced. This work was supported by Biocodex

1215 | Results of DIAVEY, the European post-marketing safety study on stiripentol use

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Purpose: Following stiripentol marketing authorization in the European Union (EU), the European Medicines Agency required a post-marketing surveillance study to gather real-world safety data, and focusing on neutropenia,

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hepatotoxicity, failure to thrive, behavioral issues, and psychomotor development.

Method: DIAVEY was a prospective, is non-interventional, EU-wide study. Patients with Dravet syndrome (DS) and other epilepsies newly prescribed stiripentol were enrolled between January 2007 and May 2012, with annual evaluations and a minimum one-year participation.

Results: 227 patients from 57 centers across 11 countries were included: 152 with DS and 75 with other epilepsies. Mean age at enrolment was 7.2 years (6.4 in DS, 8.6 in non-Dravet), with 16 DS patients under one year-old and 46 between one and three. At stiripentol initiation, concomitant antiseizure medications in DS patients included valproate (79%), clobazam (71%), and topiramate (24%), while non-Dravet patients received clobazam (56%), valproate (36%), and carbamazepine (25%). Mean ± standard deviation (SD) stiripentol dosage at inclusion was 38.9 ±16.8 mg/kg/day in DS and 33.5 ±17.6 mg/kg/day in non-Dravet. Mean ± SD treatment duration was 22.4 ±13.8 months in DS and 15.9 ±13.7 months in non-Dravet. Stiripentol was discontinued by 83 patients (36.6%), mainly due to lack of efficacy or adverse drug reactions (ADRs). 130 patients (57%) experienced 387 ADRs, including increased γ-glutamyl transferase (17%), increased aspartate aminotransferase (14%), decreased appetite (13%), somnolence (9%), fatigue (8%), and neutropenia (7%). Thrombocytopenia was reported in 7 patients and added to the Summary of Product Characteristics (SmPC). Stiripentol didn't negatively impact growth. A reduction in seizure frequency was observed in most patients, though not a primary objective.

Conclusion: DIAVEY didn't identify new ADRs; only thrombocytopenia was added to the SmPC. Discontinuation was more frequent in non-Dravet patients and those with lower dosages, generally due to lack of efficacy and/or ADRs. This work was supported by Biocodex

1230 | BDNF Rescue of Absence Seizures and Associated Comorbidities: Uncovering Shared Mechanisms

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Purpose: Absence Seizures (ASs) are genetic generalized non-convulsive seizures characterized by sudden, brief lapses in consciousness and spike-and-wave discharges on EEG. Recent studies in Childhood Absence Epilepsy (CAE) cohorts, where ASs are the only seizure type, revealed that 30% of children with ASs are pharmacoresistant, and 60% have neuropsychiatric comorbidities. These comorbidities may precede epilepsy diagnosis and persist even after full pharmacological seizure control. In humans, drugs that increase GABA levels elicit ASs in healthy individuals and exacerbate them in Absence Epilepsy (AE) patients. Magnetic resonance spectroscopy showed elevated GABA levels in a child with unilateral spike-and-wave discharges. In animal models, extrasynaptic GABA-A receptors (GABAARs) tonic inhibition is increased in the thalamus. This evidence suggests that increased, not reduced, GABAAR inhibition contributes to ASs. A reduction in GAT1-mediated GABA uptake, leading to GABA spillover into the extrasynaptic space, has been indirectly linked to this increased tonic inhibition.

Method: We have directly measured GAT1 function in two ASs animal models (the Genetic Absence Epilepsy Rat from Strasbourg (GAERS) and the Stargazer (STG) mice) performing GABA uptake in key brain regions for ASs and comorbidities and assessed recognition and memory deficits in both models. GAT1 expression and cellular location were analyzed. Brain-Derived Neurotrophic Factor (BDNF), which enhances GAT1 activity in normal animals, was tested for its effects on ASs and memory impairments in freely moving GAERS rats.

Results: Our findings reveal reduced GAT1-mediated GABA uptake in all analyzed brain regions of both models, while GAT3-mediated uptake showed no changes. BDNF rescued deficient GAT1-mediated uptake ex vivo, alleviating ASs and memory deficits.

Conclusion: This highlights for the first time the existence of a common molecular and cellular pathway that controls both ASs and their comorbid memory deficits.

1247 | Functional seizures in children: clinical characteristics and comorbidities. Experience of 2 third level centers

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Purpose: To determine the characteristics of Functional seizures (FS) in children and their associated comorbidities.
Method: A retrospective, observational study which included 23 children. Clinical records with video-electroencephalographic recordings and focal seizures were reviewed from 2022 to 2024.
Results: 23 pediatric patients were included, 65.20% (15p.) were female, with a median age of 15 years and 34.8% (8p.) were male, with a median age of 11 years. 52% (12p.) had associated epilepsy, 39% (9) focal epilepsy and 13% (3p.) generalized epilepsy. 78.2% (18 p.) received anti-seizure medication, 44.4% (8 p.) of them did not have epilepsy. Seventy percent (16 patients) of the patients were admitted to the hospital due to the events, and one was admitted to the intensive care unit. Regarding the type of events, 87% (20p) were motor (mostly head and limb movement), 47.8% (11p) autonomic, 13% (3p) visual and 8.7% (2p) sensitive. Regarding comorbidities, oppositional defiant disorder was the most frequent disorder, 21.7% (5p), followed by eating disorder 17.4% (4p) and anxiety disorder in 13% (3p). The latency to diagnosis was 1 year (0.2 - 4 years)
Conclusion: Despite the psychogenic factors that may facilitate the onset of FS, the mechanisms underlying the events are unclear. In our study, boys with FS were younger than girls and presented longer events. Proper and early diagnosis of FS in children can significantly reduce unnecessary hospitalizations and prevent inappropriate treatments.

1271 | The Role of Genetic Awareness in Shortening the Diagnostic Timeline for Dravet Syndrome

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Purpose: Dravet syndrome (DS) is a severe neurodevelopmental and epileptic encephalopathy primarily associated with pathogenic variants in the SCN1A gene. Timely diagnosis is essential for effective management and improved patient outcomes. This study investigates the factors that impact the duration before an accurate diagnosis of DS is made.
Method: In this cross-sectional study, an online survey was conducted among caregivers of individuals with DS, facilitated by the Brazilian Dravet Association. Data regarding demographics, age at epilepsy onset, diagnostic timelines, and treatment were collected and analyzed. Statistical correlations were employed to identify predictors of diagnostic delays.
Results: The study cohort consisted of 140 patients with DS (46.4% female; mean age: 9.1 years), with a median age of epilepsy onset at 5.4 months. Prolonged seizures lasting more than 30 minutes were reported in 43.9% of patients at onset, and 86.4% required hospitalization. SCN1A pathogenic variants were detected in 96.4% of the patients. The mean diagnostic delay was found to be four years; however, younger patients experienced significantly shorter delays ($p<0.001$). An earlier diagnosis was associated with the use of rescue medications ($p=0.003$) and fewer prior misdiagnoses ($p=0.008$), but not with SE ($p=0.253$), private or public health care ($p=0.419$) and hospitalization($p=0.645$). Genetic testing, including exome sequencing and targeted gene panels, enabled accurate diagnosis in 85.7% of cases.
Conclusion: Enhancements in physician awareness and access to genetic testing were linked to shorter diagnostic intervals in younger patients, reflecting progress within healthcare systems. This study highlights the favorable advancements in the diagnosis of DS, with younger patients benefiting from earlier identification. These findings emphasize the need for continued investment in education, diagnostic resources, and patient-centered approaches to further reduce diagnostic delays and optimize outcomes for individuals with DS.

1277 | Clinical and Therapeutic Profile of Adolescents with Epilepsy: A Retrospective Analysis

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Purpose: Epilepsy is a complex and challenging neurological condition with significant impact on the quality of life, mainly in adolescence. This study aimed to describe the demographic, clinical, and therapeutic characteristics of a population of adolescents with epilepsy, and attempts to identify factors linked to disease control, comorbidities and, functional impact.

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Method: Retrospective observational study of adolescents (12-18 years) with epilepsy followed in Neuropediatric Consultation between 2022 and 2024 (3 years). Data from medical records were analyzed in Microsoft Excel®.

Results: A total of 94 adolescents were included, with a median age of 15 years and 52,1% were male. The median age at seizure onset was 9 years (minimum 6 days, maximum 17 years). According to the International League Against Epilepsy classification, the predominant type of epilepsy was generalized (46,8%), followed by focal (43,6%) and only 5,3% was classified as unknown. Epileptic syndromes occurred in 35,1%, the most common being self-limited epilepsy with centrotemporal spikes (42,4%). The first electroencephalogram was normal in 18,1% and neuroimaging showed structural alterations in 28,7%. Epilepsy was controlled in 70,2% of the population and 45,7% was on monotherapy. Levetiracetam (37,2%) and sodium valproate (29,8%) were the main drugs. Refractory epilepsy was identified in 5,3% of the population at some point in the disease. 17% of the patients required Emergency Department (ER) visits in 2024, linked to uncontrolled seizures ($p = 0{,}046$). In this population, 47,9% had intellectual development disorders, the majority (64,4%) being mild to moderate, with 26,6% experiencing grade retention. Regarding other comorbidities, 10,9% also had genetic disorders, 22,3% neurological illnesses, and 24,5% psychiatric illnesses.

Conclusion: In this study generalized epilepsy predominated, with most patients having seizure control with monotherapy. Inadequate control was associated with more ER visits, underscoring the need for alternative care structures. The high prevalence of neuropsychiatric comorbidities highlights the importance of integrated multidisciplinary management.

1294 | *SEMA6B* -related progressive myoclonic epilepsy with response to the use of zonisamide: a case report

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Purpose: Progressive myoclonic epilepsy (PME) associated with mutations in the *SEMA6B* gene is an extremely rare condition with limited documented cases and no standardized treatment guidelines. We aim to present the clinical course and therapeutic response to zonisamide in a patient with *SEMA6B*-related PME.

Method: A 16-year-old male patient with PME carrying a heterozygous de novo c.2149C>T (p.Gln717*) mutation in the *SEMA6B* gene was evaluated.

Results: The patient was born to non-consanguineous parents, with no family history of neurological disorders or epilepsy. His birth and neonatal periods were uneventful. After head control was achieved at 3 months, his developmental milestones were delayed, and independent walking was never attained. Previously capable of producing single words, the patient is now limited to vocalizations and gestures without communicative intent. Recently, the patient developed a swallowing dysfunction. Seizure onset occurred at age 2 with absence episodes, initially treated with ethosuximide and valproate. At age 6, generalized tonic-clonic seizures and movement-induced brief, recurrent myoclonus became evident. Electroencephalography (EEG) revealed multifocal epileptiform discharges predominantly in the frontal and temporal regions, while repeated cranial MRIs remained unremarkable. Despite the use of various medications over the years, including valproate, levetiracetam, clonazepam, and cannabidiol, seizure control was not achieved, myoclonus worsened progressively, and this significantly impacted the quality of life. Zonisamide was added to the patient's treatment, and a reduction in myoclonus was observed. The patient showed improved tolerance to daily activities, and clinical stability was achieved during follow-up.

Conclusion: This case highlights the potential efficacy of zonisamide in reducing myoclonic episodes in *SEMA6B*-associated PME. Despite the rarity of the condition, our findings suggest that zonisamide may serve as a valuable therapeutic option, particularly for the management of myoclonus.

1318 | Optimizing Management of Convulsive Status Epilepticus in Pediatric Intensive Care: A Retrospective Study

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Purpose: Convulsive status epilepticus is a common cause of pediatric intensive care unit admissions, representing a medical emergency with risks of irreversible neurological damage and death. Mortality rates are higher in developing countries, including ours. A clear

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management algorithm could improve outcomes. This study aimed to analyze the epidemiological, clinical, etiological, and evolutionary profiles of children admitted for convulsive status epilepticus. It also sought to identify mortality predictors, compare our findings with existing literature, and develop a decision-making algorithm for patient management.

Method: A retrospective study was conducted over four years (2020–2023) at Hedi Chaker University Hospital's pediatric intensive care unit in Sfax. Data on epidemiology, patient characteristics, seizure details, and management strategies were collected.

Results: Forty children, making up 5.25% of admissions, were included. 52% were boys, and most were under 2 years old. 37.5% of cases were from the Sfax region. Convulsive status epilepticus was the initial presentation in 80% of cases. Five children had psychomotor delays and epilepsy; 33% had consanguineous parents, and 25% had a family history of seizures. Seizures and altered neurological states were the most common admission reasons. Tonic-clonic seizures were the most frequent (37.5%), with durations of 30 minutes to 1 hour in 37.5% of cases. Paraclinical exams revealed symptomatic causes in 45% of cases. Eighteen children were intubated and sedated with midazolam, and diazepam was the most common first-line anticonvulsant. The mortality rate was 22.5%. Risk factors for mortality included seizures lasting over 1-hour, hemodynamic instability, mechanical ventilation, and third-line treatments.

Conclusion: An established management algorithm, from the prehospital phase to intensive care, could significantly improve the prognosis of convulsive status epilepticus.

1341 | Incontinentia Pigmenti and neurological involvement: A focus on epilepsy

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Purpose: Incontinentia pigmenti (IP) is a syndromic ectodermal dysplasia caused by mutations in the IKBKG gene, specifically deletions of exons 4-10. Neurological involvement occurs in 30% of cases and epilepsy is reported in 42% of these patients.

Method: We conducted a retrospective study in the Department of Pediatric Neurology at Hedi Chaker University Hospital, including patients followed for IP with neurological involvement from 2013 to 2024. Clinical and paraclinical characteristics, as well as those related to epilepsy, were studied to identify potential evolutionary patterns.

Results: Four patients were included with a sex ratio of F/M 4:0. A family history of IP was found in only one patient, whose mother presented dermatological and dental manifestations without neurological symptoms. Dermatological involvement was present in all patients from the neonatal period, characterized by linear and whorled lesions with a brownish pigmentation following Blaschko lines. Developmental delay was observed in all patients, with a predominance on the motor aspect. Patient1 and 2 had epileptic spasms at the age of 15th day of life and 6 months. The electroencephalogram(EEG) revealed hypsarrhythmia and the diagnosis of infantile epileptic spasm syndrome was established. The third patient had focal motor seizures at the age of 2 years old, and the EEG showed left frontotemporal spike and spike-wave discharges. Brain imaging showed multiple ischemic lesions in patient 1, while imaging of the other patients was normal. For the treatment, epileptic spasms was controlled with Vigabatrin and Sodium valproate. The third patient was treated with Levetiracetam. The disease course consistently showed good seizure control but led to motor and cognitive sequelae. Only one patient, with the familial form, passed away at the age of 1 year.

Conclusion: Since skin lesions appear from the neonatal period, early neurological monitoring is crucial to prevent severe forms and cognitive decline secondary to epileptic encephalopathy, such us West syndrome

1371 | Thalamic volumetrics in pediatric focal epilepsy demonstrate more significant abnormalities in patients undergoing SEEG compared to those undergoing resective surgery

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Purpose: The thalamus is a key node in epileptogenic networks and is an emerging target for neuromodulation. In this study, we aim to assess volumetric changes in the thalamus and its nuclei in children at our center undergoing resective epilepsy surgery and SEEG evaluation for presumed focal epilepsy.

Method: We assembled a cohort of 64 health controls, 67 patients undergoing resective epilepsy surgery and 136 patients undergoing SEEG at our institution. Volumes of the whole thalamus and thalamic nuclei were calculated following segmentation of volumetric T1 sequences

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acquired on the same scanner using the THOMAS atlas. We calculated age- and sex-corrected Z-scores for each nucleus using the data from healthy controls and compared volumes of 8 pairs of nuclei between the groups using 2-sample t-tests, correcting for multiple comparisons using the Benjamini-Hochberg method. We assessed effect size using Cohen's D and present them for each side (left first).

Results: We found graded responses with more significant abnormalities in the SEEG cohort compared to the resective surgery cohort; there were significant differences in 7 nuclei in the SEEG cohort and only 3 nuclei in the resective surgery cohort. There were significantly reduced volumes of the anterior nucleus bilaterally (Cohen's D 0.52/0.46 between controls and resective surgery, 1.0/1.1 between controls and SEEG and 0.61/0.69 between resective surgery and SEEG cohorts). Whilst the SEEG patients had significantly reduced volumes of the centromedian nucleus (Cohen's d 0.46/0.23), resective surgery patients had larger volumes than controls (Cohen's d 0.33/0.46). There were no differences in pulvinar volumes. Data-driven groupings were explored using UMAP for dimension reduction.

Conclusion: There are more significant abnormalities in thalamic nuclear volumes in patients undergoing SEEG compared to those undergoing resective surgery. Thalamic volumetrics may be an important marker of network dysfunction. This requires correlation with outcomes from resective surgery and neuromodulation.

1400 | Corticosteroids therapy in children and young adults with Developmental and Epileptic Encephalopathies (DEEs) and Drug Resistant Epilepsies (DREs): a multicenter retrospective study

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Purpose: To evaluates efficacy and tolerability of corticosteroid therapy (CST) in patients with Developmental and Epileptic Encephalopathies (DEEs) and Drug-Resistant Epilepsies (DREs). The primary aim is to assess overall CST efficacy on seizure frequency, EEG, and neuropsychological profile. We also compare different CST protocols and identified predictors of clinical response.

Method: In our retrospective multicenter study, we enrolled pediatric patients with DEE/EE with spike-wave activation in sleep (DEE/EE SWAS), Lennox Gastaut syndrome (LGS) or other DEEs/DREs, treated at 6 Epilepsy Centers in Northern Italy from 2010 to 2024. Epilepsy history and etiology were reviewed. Data on seizure frequency, EEG, psychomotor development, cognitive level, comorbidities, CST efficacy and tolerability were collected at baseline, at 6, 12 months, and during long-term follow-up.

Results: A total of 122 patients were included, and four main CST protocols were identified: pulse intravenous (IV) methylprednisolone, continuous oral hydrocortisone or prednisone, pulse IV methylprednisolone followed by an oral prednisone taper, and intramuscular adrenocorticotropic hormone (ACTH). Overall, 80% of patients demonstrated general clinical improvement, with seizure reduction >50% observed in 41.8% of cases. Improvements in EEG findings and cognitive function were noted in 34% and 39% of patients. CST was generally tolerable, with only 4.9% of patients discontinued CST due to adverse effects. Pulse CST showed improved efficacy and tolerability compared to others. Positive predictors of clinical response included a diagnosis of DDE/EE-SWAS, structural etiology, normal development prior to CST initiation, a lower number of antiseizure medications and the presence of focal interictal epileptiform discharges on EEG.

Conclusion: CST was effective for patients with DEEs and DREs, resulting in improvements in seizure control, EEG and cognitive outcomes. This study offers guidance for suitable CST candidates and protocols. However, it highlights the need for standardized guidelines to unify treatment protocols and for further research to identify reliable biomarkers for predicting therapeutic responses.

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1485 | A qualitative study on precision medicine in epilepsy: the clinician's view

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Purpose: Precision medicine (PM) is increasingly recognized as a pivotal approach in the management of rare genetic epilepsies. However, its availability and integration into routine clinical practice remain limited. This study aims to identify the barriers and facilitators influencing the implementation of PM for individuals with epilepsy (PWE).
Method: Semi-structured interviews were conducted with clinicians specializing in epilepsy care across diverse global regions. Participants were purposively selected based on geographical distribution and World Bank income classification. Data were analyzed using framework analysis to identify key thematic domains.
Results: Interviews were conducted with sixteen clinicians from six continents. Five principal themes emerged: (1) Role of the individual clinician: while clinicians acknowledge the significance of PM for the future of epilepsy care, its implementation is largely dependent on individual expertise; (2) Clinician-PWE-caregiver interaction: transparent communication regarding both the benefits and limitations of PM is essential for successful implementation; (3) knowledge gaps: a lack of proficiency in the interpretation of genetic test results and insufficient robust evidence supporting certain PM strategies hinder widespread adoption; (4) collaborative efforts: strengthening both local and international collaborations, including partnerships with patient advocacy groups, is crucial to advancing PM integration; (5) Standardization of epilepsy care pathways: the development and implementation of structured referral pathways and clinical guidelines are necessary to facilitate broader access to PM.
Conclusion: Clinicians perceive PM as a transformative advancement in epilepsy care and anticipate its integration into standard practice in the near future. However, targeted investments in clinician training, particularly in genetic test interpretation, are imperative irrespective of socio-economic context. The establishment of local expert teams dedicated to PM could provide essential support to less-experienced clinicians. Furthermore, the development of integrated care pathways and standardized guidelines for genetic testing and PM will be critical to enhancing its implementation on a wider scale.

1501 | Navigating Treatment Challenges in pediatric GAD65-Antibody-Mediated Encephalitis

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Purpose: GAD65 autoantibodies are associated to autoimmune diseases, including several neurological disorders. Among them: GAD65 autoimmune encephalitis, a neuroinflammatory disorder characterized by a broad spectrum of symptoms including cognitive impairment, behavioral changes and autoimmune-associated drug-resistant epilepsy (DRE).
Method: We present a complex case of a 15-year-old previously healthy boy who was admitted to our hospital after experiencing generalized and focal onset motor seizures that were refractory to treatment with valproic acid, clobazam, and lamotrigine.
Results: CSF analysis showed pleocytosis, elevated protein levels, and type 2 oligoclonal bands. Immunofluorescence analysis by tissue-based assay revealed a neuropil signal and by cell-based assay we detected high titer GAD65 antibodies in CSF and serum. The patient's EEG showed focal epileptic discharges and brain MRI demonstrated a voluminous and signal-altered right hippocampus. We diagnosed a GAD65 antibody-mediated encephalitis with DRE and episodes of confusion and amnesia. Immunotherapy with intravenous methylprednisolone and immunoglobulin resulted in transient resolution of seizures and EEG abnormalities. Within weeks, seizures recurred, along with a worsening of psychological symptoms. Due to persistent GAD65 antibodies and changes in the morphological structure of the controlateral amygdala and hippocampus we intensified treatment with further methylprednisolone pulses, immunoadsorption, various antiepileptic drugs (cenobamate, perampanel, cannabidiol and

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oxcarbazepine), and finally, with the second-line therapy with rituximab.

Conclusion: This case 1) illustrates the role of antineuronal autoantibodies in the etiology of drug-resistant epilepsies, 2) emphasizes the importance of prompt and aggressive immunotherapy in GAD65-mediated neurological disorders, 3) highlights the limited knowledge regarding symptom progression over time and the response to immunotherapy in patients with GAD65 antibody-mediated encephalitis, and 4) emphasizes the need to establish a pediatric patient cohort to assess the long-term outcomes and establish a standardized treatment pathway.

1506 | Electro-clinical and neuroimaging influence on postsurgical cognitive outcome 12 months after epilepsy surgery in children with drug-resistant epilepsy and hypothalamic hamartoma

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Purpose: To describe the cognitive profile of children with hypothalamic hamartoma (HH) before and after epilepsy surgery, related to electro-clinical and neuroimaging aspects.

Method: Eighteen children (age range 2-19 years) with drug-resistant epilepsy and HH, who underwent epilepsy surgery (laser thermal ablation), were included in the study. One surgery was performed in eleven patients, two interventions in six, and four surgeries in one. Engel I-II were considered good seizure control. A cognitive assessment was done before and 12 months after the last surgery. Cognitive outcomes were classified as favorable (improved/stable) or unfavorable (stagnant/deteriorated). MRI and EEG were evaluated before and after surgery.

Results: Fourteen patients had favorable cognitive outcomes after surgery. Among them, 71.4% achieved good seizure control (p=0.46). Patients with a favorable cognitive outcome had an epilepsy onset at 41.3 ±56 months, while those with unfavorable outcomes had an onset at 2.7 ±4.2 months (p=0.037). No statistically significant association was found between long epilepsy duration and unfavorable cognitive outcomes. Seven of the fourteen patients with favorable cognitive outcomes showed an improvement (normalization of background rhythm and/or disappearance of epileptiform activity) in the postsurgical EEG compared to the presurgical EEG According to HH Delalande classification, 80% (4/5) of patients with Delalande I/II had favorable cognitive outcome, compared to 76.9% (10/13) with Delalande III/IV (p=0.88). Regarding post-surgical MRI, 87.5% (7/8) with a complete disconnection of the HH had a favorable cognitive outcome (p=0.37).

Conclusion: The impact of electro-clinical and neuroimaging aspects on the postsurgical cognitive outcome was heterogenous. In our study, the only statistically significant finding was that the seizures onset before the first year of life was related to an unfavorable cognitive outcome.

1507 | Hypnic Negative Myoclonia: A Novel Case of Ictal Negative Motor Signs During Sleep

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Purpose: Epileptic negative myoclonus (ENM) is defined as a brief (<0,5 seconds) interruption of muscle tone time-locked with EEG abnormalities. ENM is a rare ictal sign that can be found in a variety of epilepsy syndromes, from self-limited to epileptic encephalopathies. The aim of this study is to highlight a unique hypnic ictal sign in a patient with drug-resistant epilepsy.

Method: We present a case of a 17-year-old female with a history of refractory epilepsy with tonic deviation of the mouth and possible hypnic seizures. We provide findings from medical history, electroencephalography (EEG) monitoring, brain imaging and genetic tests.

Results: Her personal history revealed impaired awareness seizures with clonic movements of the mouth during wakefulness starting at 12 years of age. Several antiseizure medications were tried, resulting in a reduction in seizure frequency but without complete control. Long-term video-EEG monitoring recorded polyspike-and-wave complexes time-locked with a reduction in left Orbicularis oris muscle activity during NREM sleep. A 3T brain MRI was normal, and whole genome sequencing along with metabolic testing yielded negative results.

Conclusion: This case report features a patient with drug-resistant epilepsy and brief ictal negative motor signs during sleep, which we classified as hypnic negative myoclonia. To the best of our knowledge, this is the first reported case of negative myoclonus during sleep. We emphasize the importance of polygraphy recordings in accurately characterizing seizure phenotypes, particularly in cases with atypical ictal manifestations.

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1516 | Empowering Patients in Research: First insights from 323 Participants in the European SYNGAP1 Registry

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Purpose: EURAS, The EUropean network for neurodevelopmental RASopathies, aims to accelerate the development of treatments for Cardio-facio-cutaneous syndrome, Costello syndrome, Noonan syndrome and SYNGAP1-related encephalopathy. The Horizon Europe project was initiated by the German Syngap1 patient organization and its medical advisory board. Through a dedicated SYNGAP1 registry, the project collects comprehensive health data as a basis for preclinical models. This registry is accessible through a multilingual mobile app to maximize global participation.
Method: The content of the registry is developed together with patient representatives and is complemented by standardized scores. Patients or their caregivers complete questionnaires on epilepsy, behavior, genetic background, behavior and development. The data is collected directly from patients. The registry includes 323 participants speaking German (100), French (46), Italian (46), Spanish (53), Dutch (30), Polish (30), and English (18).
Results: An exemplary analysis of the development questionnaire shows that children with SYNGAP1 experience delayed milestones: sitting unsupported is typically achieved at 12 months, walking independently at 28 months, and forming two-word sentences at 47 months. An exemplary analysis of the PEDI-CAT score shows that SYNGAP1 children are on average at the 4th percentile in the "daily activities" domain, at the 12th percentile in the "mobility" domain, at the 4th percentile in the "social/cognitive" domain and at the 9th percentile in the "responsibility" domain compared to their respective age norm. These findings provide a baseline for understanding developmental progression in SYNGAP1 and highlight areas for targeted intervention.
Conclusion: The SYNGAP1 registry demonstrates the feasibility and value of a patient-centered, app-based data collection approach to gather insights into rare disorders. The robust, multilingual participation underscores the utility of the registry as a tool for patient engagement and data generation. This platform can serve as a model for other rare diseases, contributing to a broader understanding and support for families worldwide.

1535 | Unraveling lissencephaly: insights from clinical, neurophysiological and imaging features

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Purpose: Lissencephalies are a rare and heterogeneous group of cortical malformations associated with epilepsy and cognitive delay. They can be defined by different MRI and EEG patterns. This study aims to analyze a cohort of lissencephaly patients of a tertiary center, exploring potential associations between MRI findings, EEG patterns and clinical presentation.
Method: Retrospective analysis of clinical, imagological and electroencephalographic data of a consecutive sample of lissencephaly patients followed at a tertiary center.
Results: Nineteen patients were included, 63.2% (n=12) female, with a median age at diagnosis of 11 months (IQR 3 years). Genetic mutations were confirmed in 68.4% (n=13), most commonly in the DCX gene (38.5%). The average time between imaging and genetic diagnosis was 6.3 ± 5.1 years. Seventeen patients developed epilepsy (89.5%) at a median age of 2 years (IQR 6.2 years), with tonic seizures being the most frequent (n=11, 64.7%). The most common EEG pattern (n=6; 31.6%) was characterized by diffuse high amplitude alpha/beta activity. Patients with this pattern or with normal EEG had a better functional status ($p<0.001$) and more commonly had non-refractory epilepsy ($p=0.03$). Focal or multifocal epileptiform activity was observed in 11 patients (57.9%). The anterior gradient was the most frequent neuroimaging pattern (n=9, 47.4%) and was not associated with epilepsy severity or functional status.
Conclusion: A high prevalence of early-onset epilepsy was observed among our cohort. Despite the generally symmetrical nature of these cortical malformations, focal epileptiform activity was common. In our cohort, the EEG pattern exhibited a significant association with epilepsy severity and functional status. Conversely, neuroimaging findings were independent from clinical or

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electroencephalographic characteristics. This underscores the complexity of the disease and the need for individualized approaches to diagnosis and management.

1551 | Sleep quality in children with epilepsy – a cross-sectional study

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Purpose: There is a complex interplay between seizures and sleep. Inadequate sleep enhances seizures and seizure activity itself causes sleep fragmentation. Children with epilepsy report more sleep disturbances than healthy ones. We aimed to characterize sleep quality in children with non-structural controlled epilepsy using a parent-report questionnaire.

Method: Observational, descriptive, cross-sectional study. Inclusion criteria were children aged two to ten years with non-structural controlled (with monotherapy or any drug therapy) epilepsies and without cognitive delay nor encephalopathy. The Children's Sleep Habits Questionnaire – Portuguese version, was used as an assessment tool during Epilepsy appointments.

Results: This study included 50 children with epilepsy aged three to ten years. 26 had Self-limited epilepsy (18 with Self-limited Epilepsy with Centrotemporal Spikes, 17 with Self-limited Epilepsy with Autonomic Seizures and 1 with Childhood Occipital Visual Epilepsy), 20 Idiopathic Generalized Epilepsy (11 with Epilepsy with Generalized Tonic-Clonic Seizures Alone, 9 with Childhood Absence Epilepsy), 3 Genetic Epilepsy with Febrile seizures + and 1 Frontal epilepsy. 88% (n=44) exhibited a total scale score over the cutoff of the Portuguese population (48). 94% (n=47) reported problems with sleep duration and 62% (n=31) with the sleep onset delay. Daytime sleepiness and night wakings were the subscales where children scored less, with 4% (n=2) and 12% (n=6) respectively had scores above the cutoffs. A total scale score above 56 was more frequent in children with Idiopathic Generalized Epilepsy (45%, n=10) than in Self-limited Epilepsies (34,6%, n=9).

Conclusion: Children with epilepsy have a high incidence of sleep disturbances. Screening sleep disturbances should be an important component in the management of epilepsy patients.

1554 | Ketogenic Diet for refractory childhood epilepsy: 25 year experience of a tertiary center in Portugal

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Purpose: Ketogenic diet (KD) is a high-fat-low-carbohydrate diet which can be used as a treatment for refractory childhood epilepsy (RCE). The aim of this study was to evaluate the effect of KD on seizure control, general alertness and behavior in children with RCE.

Method: Retrospective analysis of clinical records of patients with refractory childhood epilepsy who underwent KD from January 2000 to December 2024, in a tertiary pediatric hospital. Efficacy was evaluated based on seizure frequency, level of alertness, electroencephalogram (EEG) (obtained before the start of KD, after 3 months and after 24 months) and number of antiseizure medications (ASM).

Results: 51 patients were identified (59% male). Main indications for KD were epileptic encephalopathies (EE): West syndrome (10), Lennox-Gastaut syndrome (9), Ohtahara syndrome (8), myoclonic-atonic epilepsy (4), Dravet syndrome (3) and other EE (6); structural focal epilepsies (5), and myoclonic absence epilepsy (3). The mean age of onset of epilepsy was 1,3 years [0-9; SD 1,7], the mean age of KD initiation was 6,1 years [0-16; SD 4,8], the mean delay between diagnosis and KD initiation was 4,7 years [0-15, SD 4,3] and mean duration of KD was 19,4 months [3-50, SD 11,6]. Most patients (87%) showed reduction in the number of seizures, 81% improved alertness and 74% improved behavior. 36% of EEG records showed improvement at 3 months, and 47% at 24 months. Seven patients (13%) achieved seizure control, 6 without ASM. Main reasons for discontinuing KD were difficulties in implementing KD and treatment inefficacy. Adverse effects were mild and reversible. Better outcomes were achieved with normal magnetic resonance imaging (p=0.032) and older age at the diagnosis (p=0.042).

Conclusion: DK allowed a significant reduction of seizures and improvement in alertness and behavior, including total seizure control in 13% of patients, maintained after DK discontinuation.

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1572 | Predictors of neuropsychiatric disease and seizure outcome in tuberous sclerosis

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Purpose: Tuberous sclerosis (TSC) is a neurocutaneous syndrome with diverse manifestations, among which epilepsy stands out as the most burdensome. The aim of our study was to identify predictors of refractory epilepsy in TSC patients. Additionally, we sought to evaluate the association between TSC-associated neuropsychiatric disorders (TAND) and epilepsy phenotypes as well as seizure outcomes.
Method: Ours is a hospital-based observational study that included patients diagnosed with TSC and epilepsy between 2012 and 2023. We recorded the demographic profile, electroclinical profile and magnetic resonance imaging (MRI) characteristics. The TAND checklist was administered by the principal investigator.
Results: Among the 192 TSC patients screened during the study period, 112 met the inclusion and exclusion criteria. The mean age of the cohort was 12.14 ±9.47 years, with a male-to-female ratio of 1.03:1. The mean follow-up duration prior to inclusion was 5.9 ±3.51 years. Our study identified developmental delay as the most significant predictor of drug-resistant epilepsy (DRE), autism, and intellectual disability. Early onset of epilepsy and the presence of combined epilepsy (Focal and generalized epilepsy) were strongly associated with the development of intellectual disability, autism, and DRE. Among MRI parameters, a higher tuber count was linked with more frequent seizures. Furthermore, a higher tuber count and, not the tuber subtype was significantly associated with DRE in an unadjusted bivariate model. Correlation analysis demonstrated a strong relationship between TAND checklist scores (reflecting the overall burden of TAND on families) and seizure scores at various time points.
Conclusion: Developmental delay was identified as the most significant predictor of drug-resistant epilepsy (DRE), autism, and intellectual disability

1574 | Clinical clusters of pediatric patients with status epilepticus: insights from a large single-center case-cohort study in Switzerland

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Purpose: This study assessed the clinical characteristics of pediatric patients admitted with status epilepticus (SE) to Switzerland´s largest tertiary-level pediatric hospital.
Method: We conducted a retrospective case-cohort study analyzing 642 SE admissions from 467 patients. We applied a combination of traditional descriptive statistics and machine learning approaches. A k-clustering algorithm was used to identify distinct clinical subgroups, while LASSO regression tested whether clinical metrics could predict mortality.
Results: Significant age-related differences in SE etiology emerged: infants and younger children more often presented with acute symptomatic causes, whereas older children and adolescents were more likely to have preexisting epilepsy syndromes. Patients receiving out-of-hospital treatment had faster treatment initiation and better first-line therapy response. Shorter latency from SE onset to first-line treatment correlated with higher response rates and a reduced need for intensive care. Cluster analysis identified three distinct patient subgroups based on clinical presentation and management. At admission, two broad categories emerged: (1) younger patients presenting with SE due to an acute etiology and (2) older patients with more heterogeneous etiologies. These groups were further divided into: (i) younger patients with acute SE associated with an infection, including febrile SE ('Febrile seizure' cluster); (ii) younger patients with acute SE and a more severe in-hospital course ('Para-infectious' cluster); and (iii) older patients with an established epilepsy diagnosis ('Known epilepsy' cluster). Additionally, we identified key clinical predictors of mortality in pediatric SE: progressive semiology and a prior epilepsy diagnosis were associated with increased mortality risk, while infection-related SE was linked to lower mortality risk.
Conclusion: This study, reporting the largest pediatric SE cohort in Switzerland, offers valuable insights into the clinical presentation and management of pediatric SE.

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1630 | Serial organization of movements in children with various forms of epilepsy

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Purpose: To analyze the specificity of movements serial organization in children with idiopathic generalized epilepsies (IGE) and focal lobe epilepsy (FLE) aged 7 to 12 years in comparison with typically developing children.
Method: The study included 3 groups. Group 1: 25 children with IGE receiving antiepileptic drug therapy for at least a year (14 boys, 11 girls), Group 2: 22 children with FLE receiving antiseizure medications for at least a year (13 boys, 9 girls), Group 3: 30 typically developing children (25 boys, 15 girls). To assess the regulatory functions, there were conducted 3 Positions Test and Oseretskii Test of Reciprocal Coordination traditionally used in neuropsychology. Revman 5.3 software with relative risk (RR) calculation was used to compare the groups. Differences were considered significant at $p < 0.05$.
Results: No statistically significant differences were found in Groups 1 and 2, however, when comparing Groups 1 and 3, differences were recorded in three parameters of the 3 Positions Test: spatial kinesthetic errors (p=0.01), kinesthetic and postural-tonic errors (p=0.02), tone changes (p=0.01), and in one parameter of the Oseretskii Test of Reciprocal Coordination: tone errors (p=0.01). When comparing groups 2 and 3, the differences are significantly greater than when comparing groups 1 and 3. 3 Positions test: serial organization errors (p=0.01), memory retention (p=0.01), presence of external mediation (p=0.005), spatial kinesthetic errors (p=0.02), kinesthetic and postural-tonic errors (p=0.004), tone changes (p=0.002). Oseretskii Test of Reciprocal Coordination: quality of performance (p=0.03), interhemispheric interaction errors (p=0.008), kinesthetic errors (p=0.01), tone errors (p=0.008).
Conclusion: The development of movements serial organization in children with FLE has a significant delay compared to children developing typically, while the difference in the groups with IGE and typically developing children affects only individual parameters. In the groups with IGE and FLE, statistically significant differences were not found.

1642 | Dravet Syndrome in Colombia: Insights into Current Diagnosis and Treatment Practices

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Purpose: Dravet Syndrome (DS) is a severe form of infantile onset epilepsy. Incidence and prevalence for Colombia remain unknown, but according to national population data provided by DANE for 2022 and international epidemiological data for DS, we estimate between 622 and 3.360 affected individuals. There are currently no national guidelines for DS diagnosis and treatment in our country.
Method: We conducted an observational study, developing a survey aiming to assess and describe current practices among pediatric neurologists and epileptologists.
Results: We obtained 98 responses from pediatric neurologists and epileptologists, representing 58% of all pediatric neurologists affiliated with the Colombian Pediatric Neurology Association (ASCONI). More than 90% of respondents had managed at least one patient with Dravet syndrome. The main challenges identified included delays in genetic testing, insufficient knowledge of pharmacological treatment, overuse of additional studies in already diagnosed patients, and inadequate transition to adult care. Additionally, there was significant interest in novel predictive tools to assist clinicians in interpreting positive molecular results in very young patients.
Conclusion: This detailed characterization of our knowledge gap will help create and tailor educational strategies to improve adherence to international guidelines, optimizing diagnosis, treatment and follow-up for DS patients in Colombia.

1645 | Lennox-Gastaut Syndrome criteria: linking clinical and electroencephalographic features

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Purpose: The International League Against Epilepsy (ILAE) had recently revised Lennox-Gastaut Syndrome (LGS) diagnostic criteria, emphasizing the importance of

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electroencephalographic features, but not specifying the duration of Generalized paroxysmal fast activity (GPFA). Regardless of their duration, GPFA have been correlated with increased epileptic activity, but there was no evidence about their correlation with clinical criteria. We aimed to identify electroclinical differences among patients with LGS clinical criteria referred to our center.

Method: We analyzed electroencephalographic criteria with descriptive statistics and clinical features with regression techniques. We marked GPFA if duration was longer than one second, Generalized Polyspike Train (GPT) if shorter (Conrad EC et al. Using Generalized Polyspike Train to Predict Drug-Resistant Idiopathic Generalized Epilepsy. J Clin Neurophysiol. 2022 1;39(6):459-465).

Results: Among 90 patients identified, 28 had GPFA, 13 had GPT, 23 had Slow-Spike-and-Wave (SSW) complexes but had not GPT and GPFA, 26 had none (Null). GPT+GPFA group differed from SSW+Null because of an higher mean age of onset (1.83 vs 0.98 years, p-value 0.005), more frequently genetic etiology (51% vs 31%, p-value 0.047) and shorter seizure-free intervals (one-year seizure-free 2% vs 18%, p-value 0.015). The GPFA group compared to remaining subjects had less cognitive (86% vs 97%, p-value 0.051) and motor impairment (39% vs 63%, p-value 0.034), but more psychiatric comorbidities (39% vs 18%, p-value 0.028). They had higher seizure burden than GPT group (weekly seizures 82% vs 38%, p-value 0.005). We found a trend towards more spasms in GPFA group than others (54% vs 27%, p-value 0,056).

Conclusion: The GPFA group presents worse epilepsy, but less cognitive and motor impairment compared to those without LGS criteria. The GPFA+GPT group presents more frequently genetic etiology and higher mean age of onset than SSW+Null. These data suggest a correlation between clinical and electroencephalographic criteria, which could be relevant for patients' selection/stratification.

1655 | Epileptic and neurodevelopmental outcome at 24 months after neonatal hypoxic-ischemic encephalopathy

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Purpose: This retrospective, dual-center Italian study assessed the incidence, electroclinical features, and risk factors for post-neonatal epilepsy in neonates with hypoxic-ischemic encephalopathy (HIE) treated with therapeutic hypothermia (TH). Although previous studies have examined risk factors, few have investigated their relevance at different time points.

Method: We included neonates with HIE2 and HIE3 who underwent TH. Neurological examination and General Movements were assessed before and after TH. Conventional EEGs (cEEG) were performed within 6 hours of life and after TH (72 hours to 10 days). Brain MRI was conducted within 30 days. Developmental outcomes were evaluated at 24 months using Griffiths Mental Development Scales. Polygraphic EEG was performed at 3-9-12-24 months and annually thereafter. The median follow-up duration was 48 months. Epilepsy was classified based on ILAE criteria.

Results: We enrolled 159 patients. Patients with epilepsy were 15/159 (9.4%): 9/159 (5.6%) with onset before 24 months (range 1-21 months); among them, 8 patients' onset was before 6 months of age, 4 of them in the first month of life. These 4 patients presented later with Infantile Epileptic Spasm Syndrome (IESS). Seizures' onset was after 24 months in 6/159 individuals (3,7%). At the last follow-up, all 15 patients have focal epilepsy. Global development was normal in 4 patients, and in 11/15 was pathological (10/15 <2DS; 1/15, <1DS). Identified risk factors for post-neonatal epilepsy included: MRI lesions involving the basal ganglia and thalamus ($p < 0.0001$), encephalopathy ($p = 0.0008$), previous neonatal seizures ($p = 0.0014$), severe anomalies on the cEEG recorded after 6 hours of life ($p = 0.0032$) and after hypothermia ($p = 0.0071$).

Conclusion: Our study confirms post-neonatal epilepsy after HIE2/3 is rare and generally well controlled. MRI and early EEG are key predictors. High-risk patients should be screened for IESS in early months and continue long-term neurological follow-up beyond 24 months.

1672 | Video-game induced orofacial reflex myoclonus

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Purpose: Video-game epilepsy is associated with RS evoked during gameplay. Orofacial reflex myoclonus represents a unique manifestation. Recognition and avoidance of the trigger constitutes the most important treatment approach. With video-gaming's growing popularity, it's essential to recognize the potential triggers it may present for vulnerable individuals.

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Method: A 14-year-old male presented with 30 episodes of orofacial myoclonic jerks while playing the video-game FreeFire on his smartphone after overnight-sleep deprivation. The episodes lasted approximately 1 minute and resolved spontaneously. He had no prior seizure history. Family history was unremarkable. Throughout hospitalization, he continued to play, avoiding rest, with recurrence of seizures. Resting EEG was normal. IPS revealed rapid generalized spike-wave complexes with frontal predominance. Assessment while playing revealed bilateral discharges, time-locked with orofacial myoclonus. Brain MRI was normal. Valproate 900 mg/day was prescribed and advised to stop playing. At follow-up, he was seizure-free. EEG showed no epileptiform discharges.

Results: Video-game epilepsy constitutes a form of RS that manifests during gameplay. The predominant seizure types documented are GTCS, myoclonic jerks, focal[3][4]. ORM is frequently triggered by language or reading, associated with RE and JME[2]. Pathophysiologic mechanisms underlying game-playing-seizures have not been well established. Several factors may contribute to this type of seizure, including photosensitivity, pattern sensitivity, praxis, cognitive activities (decision-making, problem-solving), excitement, stress, while fatigue and sleep-deprivation facilitate by lowering seizure threshold[1][5][6]. To our knowledge, there are no other documented cases of video-game induced ORM, this represents the second reported case of a RS linked to smartphone video-gaming[7].

Conclusion: ORM is a distinct manifestation of video-game epilepsy, contributing to the growing evidence that video-game seizures can manifest in various forms. The patient's successful response to valproate and avoiding video-games emphasizes the importance of managing seizure triggers in RS. As video-gaming remains a popular activity, awareness of this potential trigger in susceptible individuals is crucial.

1676 | Mitochondrial Epilepsy: Gene-Specific Epileptic Phenotypes and Functional Associations

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Purpose: Epilepsy is a major feature of mitochondrial diseases exhibiting diverse phenotypes. This study aimed to investigate the relationship between gene function and epileptic phenotype in cases diagnosed with primary mitochondrial disease-related epilepsy.

Method: Twenty-nine cases (24 families) were included(10 females). Variations in 20 genes (18 nuclear, 2 mitochondrial) were identified. These genes were classified into five functional groups:(1) Oxidative phosphorylation(OXPHOS) subunits and assembly factors (*NDUFV1, NDUFA6, MT-ND5, SURF1, ATPAF2;* 24%), (2) mitochondrial DNA replication, transcription, and translation (*POLG, HSD17B10, RARS2, PARS2, MT-TL1;* 24%), (3) mitochondrial homeostasis (*DNML1, MFF, SERAC1;* 17%), (4) cofactor metabolism (*CoQ4, COX10, SLC19A3;* 14%), and (5) substrate metabolism (*PC, SLC25A22,ACO2, ME2;* 21%).

Results: The mean age at seizure onset was 30.62 months, mostly in infancy (44%). The mean follow-up was 56.3 months (5-240). All cases, except two with *ACO2*-variants presenting with motor delay, exhibited seizures. Multiple seizure types were observed in cases (55%). Myoclonic seizures were the most frequently observed throughout the course (14/29,48%), with none in Group 5. Tonic seizures were present in all groups except Group 1. Fourteen cases (48%) were initially diagnosed with developmental and epileptic encephalopathy (DEE); six with infantile-onset. Final frequency of DEE was 65%, mostly in group 2(71%). Convulsive status epilepticus occurred in 12/29(41%) of cases; prominently in Group 1 (5/12). Electroencephalogram recordings showed background abnormalities in 18/29 cases, most notably in Group 1 (100%). Focal epileptiform discharges (22/29), mostly in posterior regions (12/22), were the dominant interictal finding. No relationship was observed between gene function and seizure onset, initial presentation, or seizure types.

Conclusion: High DEE frequency in mitochondrial DNA replication, transcription and translation defects and high epileptogenic activity associated with defects in OXPHOS-subunits and assembly factors necessitates close-follow-up. The absence of myoclonic seizures in substrate metabolism-related defects warrants further investigation. The fact that nuclear DNA genes constituted the majority of the involved genes is a limitation of our research in drawing conclusions that cover all mitochondrial disease-related epilepsy.

1694 | Febrile Seizures Revealing Familial Cavernomatosis and Diagnostic Dilemmas

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Purpose: Cavernous angiomas are angiographically occult vascular malformations that are present in 0.4-0.9% of people, and represent around 5% of all cerebrovascular malformations. They can be single or multiple, and sporadic or familial. The presence of multiple lesions is more frequent in familial cavernomatosis. Patients are usually asymptomatic, and the most common symptoms are seizures and headache.
Method: Here we report a case with febrile seizures and multiple familial cavernoma.
Results: We report a case of a 4-year-old child who was admitted to the emergency department because of a seizure while awake and during daily activities. A few days later, he had a febrile seizure, and during this period. Neurologic examination revealed no focal findings. A 32-channel standard digital EEG showed normal basal activity with no significant changes. MRI scan revealed multiple small cavernous angiomas. Upon detection of multiple cavernomas, the patient underwent genetic testing. A pathogenic variant was detected in the CCM2 gene. Later, the patient's parents were examined, and multiple cavernomas were detected in the cranial MRI of the father. Treatment with depakine (2 ×100 mg/day) had excellent efficacy with no significant adverse effects. During the follow-up of the patient, headache complaints were added, and no new findings were detected in the imaging studies.
Conclusion: It is important to highlight that imaging and genetic testing are generally not recommended for simple febrile seizures. However, in this particular case of a simple febrile seizure, unnecessary imaging led to the detection of an underlying genetic condition. Although a causal relationship between febrile seizures and cavernomas has not been established, the detection of structural lesions like cavernomas raises questions regarding the initiation of antiseizure treatment and long-term follow-up, which remains a gray area in clinical practice.

1718 | Diagnosing Lennox-Gastaut Syndrome - Experience from a UK tertiary complex epilepsy service

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Purpose: Lennox-Gastaut Syndrome (LGS) can be difficult to diagnose due to variable presentations and evolution. We aimed to investigate time-lag from seizure onset to diagnosis, presence and evolution of ILAE-EEG criteria, etiologies, co-morbidities and seizure outcomes.
Method: Retrospective chart reviews of patients with a clinical LGS diagnosis aged <18 years seen at our institution. Patients were identified from the electronic-patient-record system and EEG database over a 15 year-period (2009 -2024).
Results: The cohort comprised 84 patients with etiologies identified in 54%: Genetic 32%, structural 16%, other 6%. Standardized assessments done in 50% (42/84) confirmed intellectual disability in all, which was severe/profound in 47 (56%). Other co-morbidities included ASD in 33%, ADHD in 12%. LGS was diagnosed at median age 10.5 years (IQR 7.2-13.3) with median time-lag from seizure onset of 7.7 years (IQR 5.1-11.6). EEG recordings at LGS diagnosis (prolonged video-EEG in 65%, sleep captured in 85%) showed slow spike-wave (SSW) and generalized paroxysmal fast activity (GPFA) in 51% (37/73), SSW only in 38% (28/73) and GPFA only in 4% (5/73). On subsequent EEGs (available in 39/84) SSW and GPFA persisted in 78% (29/37) and 68% (17/25) respectively. When not present initially, GPFA was seen later in the course in 57% (8/14). At last follow-up (median age 14.7 years [IQR 10.6-17.5]) seizures occurred daily in 70%, weekly in 24% and monthly in 5%. Etiology and age at seizure onset were not significantly associated with seizure or ID outcomes. SSW and GPFA on initial EEGs were significantly associated with daily (83% [30/36]) compared to weekly/monthly seizures (17% [6/36]) (p=0.035) but not with co-morbidities.
Conclusion: Long time-lag from seizure onset to LGS diagnosis suggests late recognition of evolving diagnostic characteristics. ILAE EEG criteria were often not met, predominantly due to the absence of GPFA. Early presence of SSW and GPFA are associated with higher seizure burden at follow up.

1719 | Efficacy of Cannabidiol in Epilepsy Associated with Germline mTOR Pathway Mutations

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Purpose: Cannabidiol (CBD) has a multifactorial antiepileptic mechanism, and one proposed mechanism of action is the inhibition of the mammalian target of rapamycin (mTOR) pathway. To clinically assess this hypothesis, this study aimed to evaluate the efficacy of CBD in patients with germline mTOR mutations by analyzing seizure reduction, quality of life, sleep disturbances, and behavioral changes.

Method: This study included a cohort of patients with pathologically confirmed germline mTOR pathway mutations in peripheral blood and drug-resistant epilepsy. Six patients were enrolled in a prospective study, with assessments at baseline, 3, and 6 months, measuring seizure frequency (seizure diaries), Clinical Global Impression scale (CGI), Quality of Life (EQ 5D-5L), Sleep Disturbance Scale for Children (SDSC), and Child Behavior Checklist (CBCL). Two additional patients were analyzed retrospectively.

Results: Eight patients with detectable germline mTOR pathway mutations (DEPDC5 (5), NPRL3 (1), AKT3 (1), PIK3CA (1)) received CBD. Of these, six had developmental and epileptic encephalopathy, and two had focal epilepsy. The median age was 10 years (range: 3–15). The mean CBD dose was 16.3 mg/kg/day. At 3 months, six patients achieved ≥90% seizure reduction (two were seizure-free), one had a ≥50% reduction, and one showed a 25–50% reduction. The effect persisted at 6 months in all patients. Significant improvements were observed in clinical scales at 3 and 6 months: CGI (-2), SDSC (-12) with sleep normalization in 5/8 patients, EQ-5D-5L (+5), and CBCL (-21). No adverse effects were reported

Conclusion: CBD may be an effective treatment for epilepsy associated with mTOR pathway mutations, significantly improving seizure control, quality of life, sleep, and behavior. These findings support its potential for clinical trials in mTORopathies.

1724 | 'Age does not matter'. Efficacy of cenobamate in the treatment of children with drug-resistant epilepsy

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Purpose: Cenobamate (CNB) is an emerging anti-seizure medication (ASM) indicated for focal-onset seizures in adults. However, its efficacy and safety in pediatric patients with drug-resistant epilepsy (DRE) remain underexplored. This study evaluates the efficacy, retention rate, and safety profile of CNB in pediatric patients with DRE.

Method: Retrospective, multicenter observational study included pediatric patients (0–18 years) with DRE treated with CNB at multiple hospitals in Spain. Demographic and clinical data, seizure types, previous treatments, CNB dosing, and treatment outcomes were analyzed. We also measured Clinical Global Impression (CGI) scores for cognition, behavior, and sleep.

Results: A total of 169 pediatric patients (median age: 10 years, range: 16 months–17 years) with a median use of previous ASMs of 8 (5-11) were included, of whom 55.7% had developmental epileptic encephalopathies (DEE) and 44.3% focal epilepsy. Seizure response rates after CNB were 73.4% at 3 months, 86.8% at 6 months, and 83.9% at 12 months. Seizure freedom was achieved in 11.8%, 21.1%, and 19.6% of patients at the same time points, respectively. CNB retention rates were high at 3 (92.2%), 6 (91.2%), and 12 months (89.2%). Patients with focal epilepsy had a significantly higher probability of achieving seizure response (OR: 5.46, p=0.02) and seizure freedom (OR: 5.32, p<0.01) compared to those with DEE. CNB dosing was higher in older patients but weight-adjusted doses were lower in this group: mean dose of 2,7 mg/kg/day in 12-18 years group *versus* 5 mg/kg/day in 0-6 years group (p<0,01). Adverse events occurred in 44.9% of patients, predominantly somnolence (42.3%), dizziness (22.4%), and cognitive slowing (9.6%) with most cases being mild to moderate. CGI scores improved at 3 months for cognition in 63,8%, for behavior in 31,3% and sleep for 24,1%.

Conclusion: CNB demonstrates promising efficacy in pediatric DRE, particularly in focal epilepsy, with a favorable safety profile.

1737 | Semiological Differences Of Functional Seizures Between Pediatrics and Adults: Video Electroencephalography Analysis

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Purpose: Diagnosing functional seizures can be challenging, and the semiology may vary between pediatric and

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adult age groups. Identifying those variabilities may be of diagnostic value. This study aimed to compare the semiological characteristics of functional seizures in both the pediatric and adult populations.

Method: All video ictal electroencephalogram (EEG) recordings at Cairo University Epilepsy Unit (CUEU) from 2021 to 2023 were retrospectively reviewed for adults or pediatrics with functional seizures. Detailed semiological characteristics of the ictal events were analyzed independently by at least two epileptologists. Each event was listed under the classification system as either major motor, minor motor, dialeptic, non-epileptic aura, or mixed type

Results: A total of 54 children and 65 adults video ictal EEG studies were evaluated. Minor motor type was the most common clinical semiology among adults and pediatric groups. Yet, it was more prevalent in pediatrics than adults (61.1% vs. 40.0%, *P*-value 0.022). In comparison, the major motor events was significantly higher in adults than in pediatrics (38.5% vs. 16.7%, *P*-value 0.009). No statistically significant differences were found between pediatrics and adults regarding pelvic thrusting (3.7% vs. 9.2%), back arching (7.4% vs. 4.6%), clenched fists (9.3% vs. 15.4%), ictal pain (13.0% vs. 18.5%), ictal fear (5.6% vs. 3.1%), or ictal crying (7.4% vs. 4.6%), respectively.

Conclusion: The semiology of functional seizures varies between pediatric and adult age groups; minor motor events predominate in pediatric patients, while the major motor type is more common in adults

1747 | The autonomic nervous system imbalance in infant epileptic spasms syndrome

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Purpose: Seizures often involve and affect the autonomic nervous system (ANS) leading to various clinical consequences including cardiovascular dysregulation, respiratory irregularities, and gastrointestinal disturbances (Devinsky O. Epilepsy Currents 2004; (2): 43-46). In this study, we aim to investigate ANS disturbances by assessing heart rate variability (HRV) in patients with Infantile Epileptic Spasm Syndrome (IESS).

Method: It was a case-controlled study including IESS patients and healthy controls (HC). A written informed consent was obtained from the parents or legal guardians of all included individuals. IESS patients were either newly diagnosed without treatment or recruited after the beginning of a monotherapy treatment within one week. All participants underwent a twenty minute electrocardiogram recording. An analysis of HRV was performed for both the frequency and time domains and were compared between IESS patients and HC. Thus, The HRV parameters were statistically analyzed using student t-test.

Results: 16 IESS patients (mean-age 8,87 ±6,02 months) and 16 HC (mean-age 9,56± 5,42 months) were included. They were matched by sex and age. IESS patients had significantly higher Root Mean Square of Successive Differences (RMSSD) (p=0,022), Standard Deviation of NN intervals (SDNN) (p=0,005), percentage of consecutive NN intervals that differ by more than 50 ms (pNN50) (p= 0,037) and high frequency (HF) (p= 0,027) compared to HC. However, no significant difference was observed for the very low frequency (VLF) and the low frequency (LF). Importantly, the ratio LF/HF was significantly decreased in IESS patients compared to HC (p=0,021).

Conclusion: Our findings suggested an impairment in the ANS balance indicated by an enhancement of the vagal tone and a higher parasympathetic dominance in IESS patients compared to the HC.

1756 | Evaluation of Ketogenic Diet Compliance and Quality of Life in Pediatric Patients with Pharmacoresistant Epilepsy and Their Caregivers

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Purpose: Pharmacoresistant epilepsy in pediatric patients often requires alternative treatments, such as the ketogenic diet (KD). While KD has proven efficacy, compliance and its impact on the quality of life (QoL) for both patients and their caregivers remain critical areas of evaluation. This study aims to assess the compliance of pediatric patients with pharmacoresistant epilepsy to the ketogenic diet and evaluate the quality of life of both these patients and their caregivers in a tertiary care epilepsy center.

Method: We conducted a study that evaluated 8 pediatric patients diagnosed with pharmacoresistant epilepsy and their caregivers using three validated scales: KetoCheck – to assess compliance with the ketogenic diet, QOLCE-55 – to measure the quality of life of pediatric patients, BSFC-s – the Short Version of the Burden Scale for Family Caregivers, to evaluate caregiver burden.

Results: In our group only one patient demonstrated poor compliance with the ketogenic diet, and only one had a poor quality of life based on caregiver assessments. However, self-reported caregiver burden, as measured by the BSFC-S, remained significant regardless of the patient's quality of life or adherence to the ketogenic diet.

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Conclusion: This study suggests that the ketogenic diet may benefit patients with drug-resistant epilepsy and does not appear to negatively impact their quality of life. However, it also highlights the substantial burden on caregivers, which remains significant regardless of patient compliance or quality of life. Targeted interventions to support caregivers could enhance overall outcomes for families managing pharmacoresistant epilepsy.

1771 | Real-life Experience with Fenfluramine and Purified Cannabidiol Treatment for Refractory Epilepsy: A Single-center Retrospective Pilot Data

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Purpose: To verify the efficacy and safety of fenfluramine (FFA) and purified cannabidiol (CBD) in real clinical practice in pediatric LGS, DS and TSC patients > 2 years of age.
Method: A retrospective single-center evaluation of the add-on FFA and CBD therapy. Pediatric patients of Brno Epilepsy Center with LGS, DS and/or TSC were enrolled (y 2022-2024) and evaluated in 3- and 6-month follow-up. Patients with > 75% seizure reduction were designated as R1, patients with > 50% seizure reduction as R2 and patients with > 25% seizure reduction as R3. Patients with < 25% seizure reduction or with an obvious worsening of seizures were classified as non-responders (NR). Adverse effects were evaluated.
Results: FFA was used by 11 children (7 x DS and 4 x LGS). At 3-month-FU 3 patients were classified as R1, 3 patients as R2 and 1 patient as R3. 4 patients were NR. At 6-month FU 2 patients were classified as R1, 2 as R2, 4 as R3 and 3 as NR. 6 patients had no adverse effects, others experienced loss of appetite, mild fatigue, emotional lability, and two experienced worsening of seizures. CBD was used by 13 children (4 x DS, 6 x LGS, 2 TSC and 1 SYNGAP1-EE off-label). At 3-month FU 6 patients were classified as R1, 3 as R2 and 1 as R3, 4 were NR. At 6-month FU (7 of 13 patients) 2 patients were classified as R1, 2 as R2, 1 as R3 and 2 were NRs. 7 patients had no adverse effects, others experienced loss of appetite, petechiae, behavioral changes, diarrhea, hepatopathy and two experienced worsening of seizures.
Conclusion: Our initial experience confirms the data from premarketing RCTs, incl. a non-negligible percentage of patients with > 25% seizure reduction, which is promising in such severe and almost always ultra refractory epilepsies.

1775 | "Don't Stimulate, I'm Sleeping!" Sleep-Disordered Breathing in Children with Vagus Nerve Stimulation

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Purpose: Vagus nerve stimulation (VNS) is the most commonly used neurostimulation technique in children with drug resistant epilepsy (DRE). Sleep-disordered breathing (SDB), including sleep apnea-hypopnea syndrome (SAHS), is an important but underexplored complication of VNS. This study aims to evaluate the prevalence of SDB in children with VNS, investigate its pathophysiology, and assess the efficacy of various management strategies.
Method: A retrospective study was conducted on children with DRE receiving VNS therapy. Polysomnography (PSG) was performed to assess clinical suspicion of SAHS, while drug-induced sleep endoscopy (DISE) was conducted in selected cases. The effectiveness of different treatment approaches was evaluated
Results: Fourteen children with a median age of 14 years (range: 8–17) were included. All patients developed snoring after VNS implantation. PSG revealed that 11 out of 14 (78%) had SAHS, classified as severe in 4, moderate in 6, and mild in 1. The mean apnea-hypopnea index (AHI) was 9.6. A characteristic PSG pattern was observed, correlating apnea events with the ON phase of VNS. DISE was performed in 3/10 patients, showing vocal cord adduction during VNS activation, which resolved after reducing the output current. Snoring resolved in all three patients (100%). Among other treatments, 2/10 patients underwent tonsillectomy, with resolution in 1/2 (50%), while 2/10 received CPAP without improvement. Reducing VNS output current resolved snoring in 2/3 (67%) cases without negatively impacting seizure control.
Conclusion: SAHS is a frequent complication in children undergoing VNS therapy. Early recognition and targeted intervention are essential. Adjusting VNS parameters, particularly the output current, is an effective strategy for managing VNS-related SDB, with DISE helping to determine the minimal effective output. In cases where seizure control is compromised, additional treatments such as CPAP, surgery, or DISE-guided adjustments may be required. Proactive management of SAHS in these patients is crucial to optimizing their care.

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1780 | Pediatric Tuberous Sclerosis Complex: Epilepsy Phenotypes and Genetic Correlations in a Tertiary Center Cohort

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Purpose: Tuberous sclerosis complex (TSC) is a rare genetic disorder with high neurological morbidity, particularly epilepsy, which is frequently refractory. This study aims to characterize epileptic phenotypes, genetic background, neurodevelopmental impact, and therapeutic outcomes in pediatric patients with TSC followed in a tertiary neuropediatric clinic in Northern Portugal.
Method: A retrospective observational study was conducted on pediatric patients with genetically or clinically confirmed TSC. Data were extracted from medical records, including genetic mutations, seizure semiology, neurodevelopmental status, treatment strategies, and TSC diagnostic criteria.
Results: A total of 29 pediatric patients (13 females, 16 males) were included, with a mean age of 12 years and a mean age at diagnosis of 58 months (prenatal-8 years). Genetic testing identified TSC1 mutations in 7 patients (24.1%) and TSC2 mutations in 17 (58.6%), 1 negative, 3 pending results, and 1 untested. Epilepsy was present in 86.2%, with 28% meeting criteria for drug-resistant epilepsy, of whom 71,4% had TSC2 mutations. West syndrome was observed in 6 patients (24%), while the most prevalent seizure types beyond spasms included focal motor and non-motor seizures. The mean number of antiseizure medications per patient was 2. One patient underwent resective surgery, and 1 is under evaluation for possible epilepsy surgery. Other treatments included vagus nerve stimulation (1), ketogenic diet (1), and Everolimus (7). Seventeen patients (58.6%) exhibited cognitive and/or psychomotor developmental delay, and three met criteria for autism spectrum disorder (PEA). All PEA cases had TSC2 variants.
Conclusion: This study reinforces the association between TSC2 mutations and severe epilepsy phenotypes, including early-onset epileptic encephalopathies such as West syndrome, as well as neurodevelopmental impairment and PEA. Despite multiple therapeutic approaches, epilepsy remains refractory in a substantial subset, underscoring the need for early referral to a specialized center. Further research is warranted to refine individualized treatment paradigms and improve long-term neurological outcomes in pediatric TSC.

1803 | Long-term follow-up of patients with Dravet syndrome by a multidisciplinary team

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Purpose: General Objective: To characterize patients with Dravet Syndrome diagnosed and followed up in our hospital. Specific Objectives: Describe electroclinical phenotype: type of epilepsy, type of seizures, electroencephalogram and comorbidities. Describe genotype. Describe response to treatment.
Method: Prospective, descriptive study of pediatric patients with genetically confirmed DS who are under control and follow-up at our hospital by a multidisciplinary team from January 2018 to the present. We declare no conflicts of interest.
Results: Electroclinical Phenotype: Our sample consists of 5 patients with a mean age of 7 year (minimum 2 years-maximum 14 years).Female sex predominates by 60%. The mean age of seizure onset is 4.5 months. All initially presented with self-limited focal seizures, 60% afebrile and 40% febrile (low fever). They evolved with episodes of febrile status epilepticus and refractory epilepsy. The initial electroencephalogram was normal, later showing focal frontal interictal epileptiform activity, interspersed with normal EEG. Only in the oldest patient was there an electrical base with scarce development of sleep graphoelements. All had normal brain MRI. All presented normal initial psychomotor development, evolving with global psychomotor developmental delay during the first year. Cognitive abilities were altered in all,20% had global psychomotor developmental delay, and 80% intellectual disability. All presented altered gait. In the oldest patient, parkinsonian signs were noted. Genotype: All presented pathogenic variants in the SCN1A gene. Response to Treatment: 60% of cases, triple-drug antiseizure pharmacological therapy was predominant. 40% were on non-pharmacological treatment with ketogenic therapy(modified Atkins diet);one case had been seizure-free for 3 years.
Conclusion: Dravet Syndrome is a developmental and epileptic encephalopathy starting in the first year with prolonged seizures, refractory epilepsy, and neurological comorbidities. Our study analyzed five patients, confirming pathogenic SCN1A variants. Initially normal

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development later led to cognitive and motor disabilities. While antiseizure drugs are common, ketogenic therapy showed benefits. Early diagnosis, personalized treatment, and multidisciplinary management are crucial for improving patient outcomes.

1810 | Alternating hemiplegia of childhood mimicking epilepsy

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Purpose: The aim of the study is to analyze the course of the disease and genetic mutations in patients with AHC.
Method: The authors conducted a retrospective analysis of 7 patients (2 male, 5 female) diagnosed with AHC and hospitalized at Pediatric Neurology Department, Medical University of Silesia in Katowice. Data on family history, gestation and delivery period, psychomotor development, laboratory and diagnostic studies (brain MRI, EEG, genetic studies) were collected.
Results: All of the patients received the diagnosis of AHC within the age range of 2 to 12 years. The onset of the disease occurred between 6 weeks and 15 months. Hypotonia was observed in six children within the neonatal period. Psychomotor development was delayed in six of the children, with one exhibiting normal development. Six different genetic variants were identified in and categorized in ClinVar as pathogenic or likely pathogenic.
Conclusion: The process of AHC diagnosing can be difficult due to the vast variety of symptoms, usually nonspecific, and similarity to other diseases, especially epilepsy

1834 | Algorithms and Red Flags for Early Diagnosis of Epileptic Encephalopathy Based on the 2022 Epilepsy Syndrome Classification: Enhancing Early Selection and Improving Care in Kazakhstan

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Purpose: Epileptic encephalopathies (EEs) are severe neurological disorders characterized by early-onset epilepsy, developmental regression, and poor prognosis. Early diagnosis is crucial for optimizing outcomes. The 2022 ILAE classification refines epilepsy syndrome criteria, enabling faster identification of EEs. In Kazakhstan, regulatory frameworks on orphan diseases influence diagnostic access, necessitating structured early detection approaches. Objective: To develop an algorithm integrating red flags and ILAE 2022 criteria for improving early EE diagnosis and access to care in Kazakhstan.
Method: A retrospective analysis of 450 pediatric epilepsy cases from tertiary centers (2018–2024) identified key red flags: neonatal-onset seizures, EEG burst-suppression, regression of milestones, and drug-resistant seizures. An algorithm incorporating structured EEG evaluation, metabolic and genetic testing was applied to assess diagnostic efficiency. The impact of Kazakhstan's orphan disease registry on genetic testing accessibility was also evaluated.
Results: Among EE cases (30% of the cohort), 68% met early classification criteria using the algorithm, reducing diagnostic time by an average of 6.4 months. Burst-suppression patterns, focal slowing with epileptiform evolution, and neonatal seizures were key predictors. Genetic screening, integrated via the orphan disease registry, identified pathogenic variants in 57% of cases, enhancing precision diagnosis and possible targeted therapy access.
Based on these findings, we recommend incorporating structured EEG screening in neonatal and pediatric neurology protocols, expanding access to whole-exome sequencing through the orphan disease program, and establishing an early intervention network for high-risk infants. Multidisciplinary case reviews should be mandated for complex cases to facilitate faster decision-making and targeted treatment selection. Standardized training for neurologists on ILAE 2022 criteria should also be prioritized.
Conclusion: Algorithm-based early detection, aligned with ILAE 2022 criteria and Kazakhstan's orphan disease policies, significantly improves EE diagnosis and care. National guidelines emphasizing structured EEG criteria, genetic screening, and multidisciplinary management are needed to optimize patient outcomes.

1700 | Stepwise surgical approach to multiple epileptogenic lesions

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Purpose: Hypothalamic hamartomas (HHs) are rare, non-neoplastic congenital malformations that can occur

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in isolation or in combination with other epileptogenic lesions. This study presents a case of a patient with an HH coexisting with additional potentially epileptogenic focal lesions, who underwent radiofrequency thermocoagulation (RFTC) of the HH with a favorable outcome.

Method: A case report including clinical, EEG, and neuroimaging data.

Results: An 11-year-old female patient was brought to a pediatric neurology clinic with a history of seizures since the age of six. There were no perinatal complications or developmental delays before seizure onset; however, in recent years, her cognition and behavior had worsened. Initially, she experienced gelastic seizures with leftward eye deviation, left hemifacial jerking, and oroalimentary automatisms while maintaining consciousness. Four years later, her seizure pattern changed to generalized asymmetric tonic seizures, followed by clusters of spasms without laughter. She reported unpleasant sensations in her eyes before seizures and diplopia afterward. Carbamazepine was initially prescribed but later became ineffective, prompting the addition of Levetiracetam. Interictal EEG showed clusters of high-amplitude spike-wave complexes and sharp waves over the right frontocentral, parietal, and temporal regions. Ictal EEG revealed rhythmic alpha activity primarily in the right temporal region, which evolved into delta activity as the seizure propagated. Brain MRI identified a right parasagittal HH, small periventricular nodular heterotopias in the frontal and occipital horns of the right lateral ventricle, and focal cortical dysplasia in the right frontoparietal region. RFTC of the HH was chosen as the first surgical treatment based on the initial seizure semiology, confirming its epileptogenicity. After one and a half years of follow-up, the patient remains seizure-free while being on the same medication.

Conclusion: This case illustrates that a stepwise surgical approach can be an optimal strategy for managing multiple epileptogenic lesions.

Psychiatry

316 | Sex disparities in veterans with psychogenic non-epileptic seizures. Do women pay a higher toll?

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Purpose: Women with psychogenic non-epileptic seizures (PNES) may be more vulnerable to psychiatric comorbidities. Previous studies have demonstrated the high prevalence of psychiatric comorbidities in patients with PNES[12, 13, 14], but few have compared gender differences among veterans. This study investigates the potential sex disparities among veterans with PNES treated at Veterans Affairs Medical Centers (VAMCs). The understanding of psychiatric comorbidities associated with PNES could aid in earlier diagnosis and wholistic treatment interventions.

Method: This study included a retrospective cohort design utilizing epilepsy monitoring unit (EMU) admissions records for fiscal years 2012-2022 (N=4,980 unique patients). These records were merged with VA electronic health record (EHR) data and restricted to only Veterans with an EMU-confirmed diagnosis of PNES (N =672). Psychiatric diagnoses and polypharmacy were compared. Secondary analyses included health care utilization in emergency room (ER) visits and Mental Health (MH) care

Results: Women veterans with PNES (WVPNES) had a higher psychiatric burden than men, evidenced by higher frequencies of nearly all psychiatric diagnoses, including depression (71% vs. 48%), posttraumatic stress disorder (65% vs. 55%), anxiety disorder (56% vs. 45%), personality disorders (13% vs. 5%), suicidal ideation or attempt (16% vs. 11%). Psychotropic medication use was also higher among WVPNES than in men: benzodiazepines (19% vs. 13%), antidepressants (65% vs. 59%). Women also had higher health care utilization with more emergency room visits, MH visits and longer duration of symptoms before appropriate diagnosis of PNES was made.

Conclusion: WVPNES represent a unique group with specific comprehensive mental health needs. Recognizing these differences may allow tailoring treatment with evidence-based neurobehavioral therapy through the VA Mind Brain Program. Multidisciplinary care integrating Primary care, Mental health, Neurology, and Gynecology may allow earlier PNES diagnosis, optimal psychiatric care, and improve quality of life, suicidality, and mental health in this population.

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343 | Is felt stigma associated with suicidal risk in patients with epilepsy?

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Purpose: Felt stigma produced by mental or physical disorders may represent a significant risk factor for suicide. However, prior studies have paid limited attention to the relationship between felt stigma and suicidal risk in patients with epilepsy.
Method: This cross-sectional study recruited adults with epilepsy in a tertiary hospital. The Neurological Disorders Depression Inventory for Epilepsy scale (NDDIE-E), Generalized Anxiety Disorders-7 (GAD-7), Stigma scale for Epilepsy (SSE), and the suicidality subscale of the Mini International Neuropsychiatric Interview Plus 5.0.0 were used. Presence of suicide risk and felt stigma was defined as a suicidality score ≥1 and SSE score ≥1, respectively. A stepwise logistic regression was conducted.
Results: Of the 152 adults with epilepsy, 31 (20.4 %) had a risk of suicide. Low (suicidality score, 1-5) and moderate to severe (suicidality score of ≥6) risks of suicide were noted in 19 (12.5%) and 12 (7.9%), respectively. Sixty-seven subjects (44.1%) had felt stigma. Mild (SSE, 1-3) and moderate to severe (SSE ≥4) felt stigma were 49 (32.2%) and 18 (11.8%), respectively. In univariate analyses, suicide risk was significantly associated with NDDIE-E ≥14, GAD-7 ≥7, SSE ≥1, and seizure frequency ≥1 per month, and generalized or focal-to-bilateral tonic-clonic seizure in the last year. The stepwise logistic regression showed that NDDIE-E ≥14 (odds ratio 6.252, 95 % confidence interval 2.142–18.248, p=0.001) and SSE 1-3 points (odds ratio 5.356, 95% confidence interval 1.547-18.537, p=0.008) were significantly associated with the risk of suicide. The remaining factors lost their statistical significance in multivariate analysis.
Conclusion: A risk of suicide is significantly higher in patients with felt stigma than in those without felt stigma independent of depressive symptoms.

694 | Clinical presentation of new-onset psychogenic non-epileptic seizures after epilepsy surgery

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Purpose: Psychogenic non-epileptic seizures (PNES) significantly impact treatment and quality of life. This study aimed to investigate the clinical characteristics of patients with PNES following epilepsy surgery (psPNES) to facilitate accurate diagnosis and treatment.
Method: We retrospectively analyzed 99 patients (48 women, aged 13–66) who underwent epilepsy surgery at Tohoku University Hospital between April 2018 and March 2024. All patients had undergone resective craniotomy and were aged 13 or older. PNES was diagnosed according to the International League Against Epilepsy's criteria for probable PNES or higher. Data were obtained from medical records and self-reported questionnaires. The clinical factors included age, sex, age at seizure onset, full-scale intelligence quotient, general memory index score, and seizure outcomes. Postoperative seizure outcomes were evaluated using the Engel classification system. Psychosocial factors included depression, seizure worry, employment type, and marital status. Data were analyzed using the t-test and χ^2 test.
Results: Among the 99 patients, 21 (21%, 13 women) were diagnosed with psPNES, of whom 20 (95%) had Engel class I outcomes. The characteristics of psPNES presentation were the presence of seizure-free period and emergence of seizures different from habitual seizures. Compared to patients without psPNES, those with psPNES exhibited higher levels of preoperative depressive symptoms [$t(31) = 3.3$, $p < 0.01$] and were more likely to be already married [$\chi^2(2) = 8.4$, $p < 0.05$]. No correlation was observed between psPNES and preoperative IQ. Antiseizure medications were increased in 12 patients (57%) before psPNES diagnosis, and 15 patients (71%) utilized emergency medical resources, such as ambulance services or out-of-hour consultations. Symptom improvement was observed in 14 patients (67%) after patient education and environmental adjustments.
Conclusion: Delayed diagnosis of psPNES may lead to unnecessary treatment and the overuse of medical resources. Preoperative psychosocial evaluation is critical for identifying psPNES and optimizing treatment strategies.

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995 | Get a Grip on Anxiety when your child has epilepsy – a pilot study

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Purpose: To test and adapt a 10-week family at-home intervention program for epileptic children with anxiety and possible other comorbid disorders.
Method: Families with children aged 6-15 were recruited when they were in contact with the Danish Epilepsy Center Filadelfia and included if the child exhibited self- or parent-reported symptoms of one or more anxiety disorders on the Anxiety Disorders Interview Schedule (ADIS-IV). The Revised Children's Anxiety and Depression Scale (RCADS) was used to measure the level of anxiety symptoms at baseline and follow-up two weeks and three months after the program. Developmental-sensitive assessment tools were used to measure the child's level of post-traumatic stress disorder (PTSD) symptomatology at baseline. A starting and midway workshop educated the parents about anxiety and how to deliver the program to their child through a standardized parent manual and child workbook based on cognitive behavioral therapy (CBT). For 10 weeks, the families worked through different weekly program steps at home.
Results: The program was completed by seventeen families. One out of three children showed symptoms of PTSD or Complex PTSD, and a further 31 % showed sub-clinical symptoms of PTSD. Preliminary results show a reduction in the RCADS score at a 2-week follow-up for two out of three families and maintenance of the effect at a 3-month follow-up. There were no differences in the reduction of scores in children with or without symptoms of PTSD.
Conclusion: Results suggest that the program is effective for epileptic children with anxiety and other comorbid disorders.

1355 | Survey on Expectations and Challenges for Psychiatric epileptologist in Transition of Japanese Patients with Childhood-Onset Epilepsy

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Purpose: The presence of psycho-behavioral problems is considered to be factors that obstacle transitions from childhood to adult medicine. Our hospital is staffed by epileptologists from the departments of neuro-pediatrics, neurology, neurosurgery, and psychiatry, who actively treat transition cases both inside and outside the hospital.
Method: Data on patients referred for epilepsy transitions to psychiatry from April 2020 to September 2024 were extracted from electronic medical records and analyzed retrospectively.
Results: Transition patients accounted for 23% (142/607) of patients with epilepsy. There were 82 males and 60 females, with a mean age at presentation of 25.1 years. Epilepsy diagnoses varied widely, with a mean age of onset of epilepsy of 6.3 years. Of the 142 patients, 108 (76%) had neurodevelopmental disorders (NDD), 61required psychotropic medication (43%). Of the 108 NDD patients, 58 were taking psychotropic medications (54 %). The 108 patients with NDD in transitions were classified into 4 groups according to the 2 axes of "psychiatric symptoms" and "epileptic seizure control", thirty-five (32%) had poorly controlled seizures with psychiatric symptoms (Group A), 38 (35%) had poorly controlled seizures without psychiatric symptoms (Group B), 15 (14%) had good seizure control with psychiatric symptoms (Group C), and good seizure control and no psychiatric symptoms (Group D)" were 20 (19%).
Conclusion: When treating patients with epilepsy who are transitioning from pediatrics in an outpatient clinic specializing in epilepsy and psychiatry, it is necessary to not only treat epilepsy but also to address NDD. Although non-pharmacologic treatment of psycho-behavioral problems in NDD is ideal, many patients must rely on pharmacotherapy. By promoting referrals to general psychiatrists who do not specialize in epilepsy for Group C and to general neurology for Group D, the burden on psychiatric epileptologists may be reduced and they may increase practicing non-pharmacologic treatment of psycho-behavioral problems.

1369 | Reinforcement Learning Deficits in Epilepsy and Their Implications for Anhedonia

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Purpose: Difficulties in reinforcement learning (RL) may contribute to cognitive and affective dysfunction in epilepsy, yet the mechanisms underlying these impairments remain unclear. This study examines how epilepsy patients undergoing intracranial EEG (iEEG) recordings (n = 8) and healthy adults (tested online) learn from rewards and punishments and whether these differences relate to anhedonia, a reward-processing deficit frequently co-occurring with epilepsy. Our epilepsy cohort included four temporal, three frontal, and one parietal lobe epilepsy patient.

Method: We compared eight epilepsy patients who performed a reinforcement learning task while undergoing iEEG recordings to healthy online participants. Anhedonia was assessed using the Snaith-Hamilton Pleasure Scale (SHAPS) in both groups. Four of the epilepsy patients met the SHAPS criteria for anhedonia, while the online group consisted of participants pre-screened to fall within the anhedonic range on SHAPS. Behavioral performance was assessed using Win-Stay and Lose-Shift strategies, and a Bayesian RL model was applied to estimate how participants update their choices based on rewards and punishments. Additionally, we will examine iEEG recordings from the amygdala and hippocampus, focusing on gamma-band activity and evoked responses related to reward prediction errors, to investigate the neural mechanisms underlying RL in epilepsy.

Results: Although preliminary, results show that epilepsy patients exhibit significantly lower Win-Stay rates compared to healthy participants ($p < 0.001$), suggesting a reduced ability to use past rewards to guide future decisions. Lose-Shift rates remain high across groups, indicating potential hypersensitivity to negative feedback or increased decision noise in epilepsy.

Conclusion: These findings suggest potential differences in reinforcement learning strategies in epilepsy compared to healthy individuals, with possible variations depending on epilepsy subtype. Further analyses, including Bayesian RL modeling and iEEG-based investigations of amygdala and hippocampal activity, will help clarify the extent and nature of these differences and their relationship to reward-related mood dysfunction, such as anhedonia.

1425 | Recruitment strategies and initial participation outcomes at the civilian university site of a post-traumatic epilepsy mental health treatment trial: CoCarePTE

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Purpose: Interventions are needed to improve quality of life for people with post-traumatic epilepsy(PTE) and mental health comorbidities. We describe recruitment strategies and initial recruitment outcomes at the civilian site of an ongoing PTE mental health treatment trial.

Method: Collaborative Care in Post-traumatic Epilepsy (CoCarePTE) is a civilian and Veterans Administration-based randomized effectiveness-implementation trial of collaborative care for anxiety and/or depression in post-traumatic epilepsy (NCT05353452). We analyzed initial recruitment outcomes among individuals who consented to study team contact/screening at the civilian site (a quaternary academic center in the Southeastern United States). Potential participants were identified via electronic health record (EHR)-based trial screening/consent embedded in routine care anxiety/depression screeners, provider referrals, self-referrals(study website, clinic brochures/flyers), a patient portal-delivered research invitation, clinician letters, and clinic pre-screening/provider notification. Descriptive statistics were calculated among active screening interactions completed by mid-January 2025, examining reasons for ineligibility and screening outcome across the 4 most common identification methods.

Results: Overall, 304 individuals participated in recruitment, with all strategies resulting in one or more study enrollments. Top reasons for ineligibility were lack of PTE (152/204 with known PTE status, 74.5%) and no prior TBI (96/242, 39.7%). The study team was unable to reach 56 individuals (18.4% of those screened), among whom only 9 were definitely eligible (others unknown final eligibility). Overall, 19 declined participation (all before eligibility finalized) and 11 enrolled. Recruitment outcomes differed by identification method: 73-86% identified by portal invitation, self-referral or EHR screening/consent were ineligible, whereas only 47% of referrals were known to be ineligible. However, the study team was ultimately unable to contact 35% of referrals to finalize eligibility/participation (7-17% for other methods).

Conclusion: Though most individuals screened for this trial had experienced a TBI, few met study criteria for

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PTE. More than half of those determined to be fully eligible enrolled, with all recruitment strategies contributing to enrollment despite variability in eligibility/response to contacts. Funding:DOD W81XWH-22-1-0630

1452 | Personality disorders in patients with idiopathic generalized epilepsy

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Purpose: To estimate the prevalence of personality disorders in persons with idiopathic generalized epilepsy (IGE) and to compare it with the general population
Method: The study was conducted in a super specialty epilepsy care center in a tertiary care hospital in South India. Study population included 57 normal control and 57 cases ((≥18 years of age, confirmed cases of IGE). Exclusion criteria included history of any psychiatric disorder, or family history of any psychiatric illness. Self-administered questionnaire was used for study data collection. IPDE-ICD10 screening questionnaire was applied to investigate personality traits and Bear-Fedio inventory (BFI) was used to study different behavior traits in patients with IGE and controls. To compare the prevalence of personality disorders in cases and controls we applied Chi Square test. For ascertaining the relation between different demographic variables with the presence of personality disorders, Pearsons Chi Square test and Fischer exact test was applied. Mann Whitney U test was used to analyze the significant difference of Bear-Fedio inventory (BFI) scores between cases and controls
Results: Comparing with controls, a higher prevalence of personality disorders was noted among idiopathic generalized epilepsy patients (87.72% in cases versus 36.84% in controls). Personality traits like borderline (p=0.000), anankastic (p=0.000), anxious (p=0.000), histrionic (p=0.000), paranoid (p=0.098), and impulsive (p=0.002) were considerably higher in cases with IGE. This was comparatively higher among females (p=0.034) than males. In BFI also significantly higher scores were found among cases in all behavioral traits except hyper moralism, altered sexual and aggression.
Conclusion: Personality disorders were significantly higher in cases with IGE

1660 | Translation, validation, and reliability testing of the Arabic version of the Epilepsy Self-Stigma Scale (ESSS-A) and Its clinical correlation

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Purpose: This study aimed to translate and validate an Arabic version of the Epilepsy Self-Stigma Scale (ESSS-A) to measure self-stigma in Arabic-speaking adults with epilepsy (PWE).
Method: This cross-validation study comprised 254 patients with epilepsy (PWE) who attended epilepsy outpatient clinics at Mansoura University Hospitals in Egypt between February and July 2024. Inclusion criteria required Arabic-speaking participants aged ≥18 years with epilepsy diagnosed according to International League Against Epilepsy (ILAE) 2017 guidelines. ESSS-A was developed using a forward-backwards translation of the original Japanese ESSS and underwent content validity evaluation by 12 experts. Internal consistency was assessed using Cronbach's alpha. Exploratory (EFA) and confirmatory factor analysis (CFA) were performed to assess construct validity. Correlations between ESSS-A scores and anxiety (Hospital Anxiety and Depression Scale - Anxiety Subscale; HADS-A), depression (Hospital Anxiety and Depression Scale - Depression Subscale; HADS-D), and insomnia (Insomnia Severity Index; ISI) were also examined.
Results: This cross-validation study comprised 254 patients with epilepsy (PWE) who attended epilepsy outpatient clinics at Mansoura University Hospitals in Egypt between February and July 2024. Inclusion criteria required Arabic-speaking participants aged ≥18 years with epilepsy diagnosed according to International League Against Epilepsy (ILAE) 2017 guidelines. ESSS-A was developed using a forward-backwards translation of the original Japanese ESSS and underwent content validity evaluation by 12 experts. Internal consistency was assessed using Cronbach's alpha. Exploratory (EFA) and confirmatory factor analysis (CFA) were performed to assess construct validity. Correlations between ESSS-A

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scores and anxiety (Hospital Anxiety and Depression Scale - Anxiety Subscale; HADS-A), depression (Hospital Anxiety and Depression Scale - Depression Subscale; HADS-D), and insomnia (Insomnia Severity Index; ISI) were also examined.
Conclusion: The ESSS-A is a reliable and valid tool for measuring self-stigma in Arabic-speaking PWE. Its adaptation offers a culturally appropriate tool for assessing stigma and tailoring intervention strategies within Arab populations.

1786 | Insomnia preceding post-ictal psychosis during video-EEG

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Purpose: Postictal psychosis (PIP) is a condition affecting approximately 25% of epileptic patients, often preceded by seizure clusters, with insomnia being a potential early symptom. However, the exact relationship between seizures, insomnia, and psychosis is not well established.
Method: We report three patients with PIP during video-electroencephalogram (vEEG), highlighting the variability in the temporal relationship between insomnia, seizures, and psychosis.
Results: The first case involves a 49-year-old male with left hippocampal sclerosis (HS), who underwent amygdalohippocampectomy 8 years prior. After a cluster of seizures on the fourth night, he experienced a night of total insomnia followed by psychosis the next day, representing a typical PIP progression. The second case is a 49-year-old female with left HS and left temporal pole dysplasia. She had an electrographic seizure on the second day of vEEG, followed by worsening insomnia (5 hours on day 3, 1 hour on day 4), and psychosis on day 5, without further seizures. The third case is a 55-year-old male with left HS who had insomnia from the start of the vEEG, sleeping less than 3 hours per night. He experienced an electroclinical seizure on day 3, with persecutory delusions emerging on day 4. He had a prior episode of PIP during a previous vEEG, though no seizures were recorded at that time, despite him reporting one before admission.
Conclusion: These cases emphasize insomnia as a potential early warning for PIP during vEEG. The varied temporal order in our two later patients raises the question of whether insomnia is simply a precursor to PIP or part of the underlying pathophysiology leading to psychosis in epilepsy.

Social Issues

328 | Epilepsy Camp

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Purpose: To analyze the stay, educational and creative programs during weeklong Camp and evaluate the benefits of camping programs for children with epilepsy.
Method: A retrospective review of data collected from all children attending annual epilepsy camps organized by the Croatian Epilepsy Association and the Zagreb City Office for Health during 8 years was performed. Children included were between 6 and 18 years of age with good control of epilepsy, taking AEDs. Each of the participants filled out three questionnaires 1. General data questionnaire and pre-camp knowledge test; 2. Camp satisfaction questionnaire and post-camp knowledge test; 3. Questionnaire on adaptation to epilepsy in young people. Educational activities are designed to improve children's knowledge of epilepsy, importance of taking medication, academic choices, suggested employment, and regulations regarding driving laws. These issues were discussed in groups or in single sessions, depending on the case. Other activities included supervised swimming, team sports, fun activities and games, arts and crafts and entertainment such as disco or movie night.
Results: The analyses of surveys and tests showed that 25% of children in camp did not know that they had epilepsy. In 90% of children, friends and distant family members are aware of their illness. Comparing the knowledge test before and after the camp, the average percentage of correctly solved tasks on the first test is 65%, and on the second 87%. The answers in the questionnaire on adaptation to life with epilepsy are indicators of strong stigma in children with epilepsy.
Conclusion: All children improved their knowledge about epilepsy, medication and everyday life. The main accomplishment of the camp was for children to gain confidence that they can reach their full potential in life and to feel equal to their peers in every aspect of life.

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372 | A cost analysis of ketogenic diet therapy in epilepsy management

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Purpose: The ketogenic diet is an effective treatment option for people with drug-resistant epilepsy and may be considered first-line therapy in some conditions. Despite its effectiveness, a perceived barrier to diet therapy is cost. The affordability of specialized diets for epilepsy has not been well studied. This study aimed to determine the weekly cost of the ketogenic diet, compared to the national dietary guidelines and a typical Australian diet.
Method: Seven-day meal plans were created to meet the nutritional needs of a reference male and female aged 31-50 years. Meal plans for five diets were created including, the classical ketogenic diet, modified ketogenic diet, specialty modified ketogenic diet including low carbohydrate products, a typical Australian diet based on national census data, and the national dietary guidelines. The weekly cost of each meal plan was obtained from the average of three major online supermarkets. Costs of the diets were compared using one-way ANOVA and unpaired T-Tests.
Results: For females, the weekly cost of the classical ketogenic diet ($70.00AUD) and the typical Australian diet ($75.91AUD) were both significantly lower than the dietary guidelines ($99.23AUD, $p<0.05$). For males, the costs of the three ketogenic diets and the dietary guidelines were similar ($94.82-119.61AUD) and were all significantly higher than the typical Australian diet ($82.96, $p<0.05$). Following national dietary guidelines, modified, or specialty modified ketogenic diets increased the percentage of median weekly income spent on food by 1-4% in females and 2-6% in males when compared to the typical Australian diet.
Conclusion: Our study demonstrates that, for males, dietary therapy for epilepsy is significantly more expensive than the typical Australian diet. People with epilepsy may be at risk of food security when implementing specialized ketogenic diets or national dietary guidelines due to increased costs. Financial assistance to reduce the barriers to diet therapy should be considered.

384 | Physical Activity Levels of Adults with Epilepsy in the United Kingdom

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Purpose: Physical activity has physiological and psychological benefits for people with epilepsy (PWE). Population studies have shown that PWE are less physical activity than the general public (Zhang et al. Epilepsy Behav 2024;151:109850), but evidence of physical activity levels of PWE within the United Kingdom (UK) are lacking.
Method: The Recent Physical Activity Questionnaire (RPAQ) was used to gather four weeks of self-reported leisure and recreational physical activity. The online questionnaire was live for three months (April-July 2022). Inclusion criteria included being at least 18 years of age, having a diagnosis of epilepsy, not having a separate chronic condition that prevents physical activity, and living in the UK. Basic socio-demographic information and epilepsy-related factors were collected to explore associations with physical activity. Analysis was descriptive with no formal hypothesis testing.
Results: Ninety-five participants (54.7% female; 44.2% male; age range: 23-70; mean age: 50 years old) were included in analyses. Seizure type was classified as generalized (37.8%), focal (10.5%), focal and generalized (20%), myoclonic (3.1%), and other (28.4%). Regarding seizure frequency, 29 participants (30.5%) reported experiencing <3 seizures per month, 28 participants (29.5%) reported experiencing 3 or more seizures per month, and 38 (40%) did not respond to this item. Sixty-four participants (67.4%) reported having a seizure in the last year, with 31 participants (32.6%) not having a seizure. The most common physical activities were walking (75.8%); gardening (64.2%); and household activities (66.3%). Exercise-related activities were swimming (9.5%), cycling (12.6%), running (10.5%), aerobics (5.3%), exercising with weights (18.9%), conditioning exercise (13.7%), and floor exercise (18.9%).
Conclusion: This research provides key baseline evidence of physical activity for PWE within the UK. Future analysis will examine differences between participants who are and are not seizure-free. This will inform subsequent research and contribute to the development of physical activity interventions for PWE.

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504 | Navigating Regulatory Challenges for Cannabinoid Use in Refractory Epilepsy: A Case Study from Japan's Unique Legal Framework

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Purpose: Cannabinoid therapies have shown promise in managing refractory epilepsy. However, the December 12, 2024, amendment to Japan's Cannabis Control Act classified cannabinoid products containing over 10 ppm of tetrahydrocannabinol (THC) as narcotics, prohibiting general use. To address this, the Ministry of Health, Labour and Welfare (MHLW) has permitted continued use for eligible patients under strict conditions. This study examines Japan's regulatory and clinical strategies for ensuring legal, safe, and effective cannabinoid use while providing insights for addressing similar challenges globally.
Method: Thirty-one refractory epilepsy patients who demonstrated clinical improvement with cannabinoid products were included. Eligibility required failure of standard treatments and measurable benefit from cannabinoids. Applications were reviewed by the head of the MHLW Government Task Force. Telemedicine consultations were conducted on December 3 and 4, 2024. During these consultations, patients voluntarily transferred ownership of their cannabinoid products to consulting physicians. On December 12, 2024, the products were re-prescribed as part of regulated medical acts, ensuring compliance with the revised law. All patients are expected to participate in the STEP1 Study, a publicly funded clinical trial focusing on cannabinoid use in refractory epilepsy.
Results: All 31 patients met eligibility criteria and had their cannabinoid use approved. Telemedicine enabled voluntary product transfers and re-prescription under legal frameworks. Additionally, patients received information on standard treatments and support groups, enhancing their understanding of care options. This structured approach ensured lawful, safe, and continuous therapy while facilitating further evaluation in the STEP1 Study.
Conclusion: This study highlights Japan's innovative approach to integrating cannabinoid therapies within a highly regulated framework. The proactive involvement of the MHLW and public funding study demonstrates the potential for advancing cannabinoid therapies while ensuring regulatory compliance. Japan's model provides a valuable reference for other countries navigating similar challenges, balancing stringent regulations with patient-centered care.

521 | Costs of epilepsy in Mexico

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Purpose: Epilepsy affects 65 million people worldwide, with an estimated prevalence of 1 to 2 million cases in Mexico. The average cost of treatment in Mexico is around 2,646 USD per patient, with higher expenses associated with hospitalization.
Method: An online survey was distributed through social networks, targeting individuals with epilepsy (PWE) and their caregivers in Mexico. The study analyzed both direct and indirect costs, utilizing presenteeism and absenteeism scales (Stanford-6, WPAIQ-GH) along with the PHQ-9 depression scale. Indirect costs were estimated using the Human Capital Method, focusing on productivity losses.
Results: In 2023, a total of 465 responses were collected, including 240 from PWE and 225 from caregivers. The combined annual direct and indirect median cost was $2020.79 USD (IQR: $2474) per patient, with a median allocation of 1,311.40 USD for medications, a figure that increased with the use of third-generation antiseizure drugs. Both PWE and caregivers faced significant productivity losses due to absenteeism and presenteeism.
Conclusion: The economic impact of epilepsy is considerably higher in drug-resistant cases and when third-generation antiseizure medications are used. Furthermore, epilepsy places a heavy burden on caregivers, diminishing their productivity due to absenteeism and presenteeism.

567 | The impact of living with epilepsy in Rio de Janeiro Metropolitan Region/RJ, Brazil: an approach through oral history interviews

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Purpose: To understand the impact of living with epilepsy through oral history interviews.
Method: Oral history is a method that preserves the voice and memory of the interviewees, giving them agency to talk

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about aspects that have direct effect on their social, physical, and mental health fields [Tsui EK et al. Public Health 2018;154:24-30.]. From August 2022 to September 2024, as part of an Oxford Martin Programme on Global Epilepsy project, University of Oxford, a prospective study through oral history interviews was carried out with adults with epilepsy who have been living in Rio de Janeiro Metropolitan Region/RJ, Brazil, and treated at Federal University of Rio de Janeiro hospitals. Interviewees were encouraged to talk about all aspects of their lives. Audios were recorded and data were analyzed in relation to gender, age, marital status, age of symptom onset, age of diagnosis, prejudice, impact on interpersonal relationships, studies, work, and suffering due to beliefs and myths by others.

Results: 34 participants completed one oral interview, with an average duration of 1 hour (11 women and 23 men; age range 22 to 75 years (median 40 years)). Eighteen (53%) were married, 29 (10%) single, and 6 (18%) divorced. The average number of years living with epilepsy was 21, with a maximum of 60 and a minimum of one. Twenty-seven participants (79%) reported have already suffered prejudice. Many reported adverse impacts on interpersonal relationships (68%); on studies (59%) and on employment (82%). Twenty-five people (74%) suffered owing to beliefs and myths imposed by others. At the end of the oral interviews, all participants reported a sense of relief and encouragement by being enabled to talk about the impact of epilepsy on their lives.

Conclusion: Oral history interviews are an efficient method for assessing the broader impact of epilepsy and interviewees may experience positive benefits.

645 | Barriers and Consequences of Prior Authorization for Neurologic Medications: A Scoping Review

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Purpose: Prior authorization (PA)- a strategy utilized by insurance companies to curb costs and promote high-value care––can pose barriers to accessing medications that treat neurologic conditions. We conducted a scoping review to assess the consequences, barriers, and facilitators of PA for six neurologic conditions: Alzheimer's disease, Parkinson disease, multiple sclerosis, migraine, cerebrovascular disease, and epilepsy.

Method: We adhered to the PRISMA scoping review reporting standards and registered the study protocol on Open Science Framework. We searched MEDLINE and Embase up to November 1, 2024 using Ovid for studies that assessed the role of PA as a primary or secondary outcome for the six included neurologic condition after the implementation of the Affordable Care Act in March, 2010. Abstract screening and full text review were done in duplicate. We charted key information in our extraction including study characteristics, demographics, methods, results, and implications for relevant stakeholders. We aggregated and thematically analyzed the results.

Results: A total of 367 studies were identified using both our search strategy on Ovid and hand searching, 281 records were screened, and 20 studies were included in our review. Eight (40%) studied multiple sclerosis, three (15%) studied epilepsy, three (15%) studied headache, two (10%) studied Alzheimer disease, two studied neurology generally (10%), one (5%) studied Parkinson's disease, and one (5%) studied both epilepsy and multiple sclerosis. The most frequent consequences for patients were delays in care (60%) and increase in disease activity (25%). The most frequent consensus for providers (35%) and administrators (15%) were time burden. The most common facilitators were the use of clinical pharmacists/technicians (20%) and health system specialty pharmacies (15%).

Conclusion: PA leads to access barriers for people with neurological conditions and is associated with burden for all stakeholders involved. Reforms to PA are imperative for equitable access to medications for all patients.

798 | IBE Workshop: Women and Epilepsy in Latin America: exploring the unmet needs of women with epilepsy

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Purpose: To explore the specific challenges faced by women with epilepsy in Latin America, identifying unmet needs and practical solutions at different life stages.
Method: The workshop, delivered during the XIII Latin American Epilepsy Congress (LAEC) 2024, was attended by 26 participants from eight Latin American countries, including women with epilepsy, caregivers, and healthcare professionals. Participants were divided into 4 mixed-stakeholder groups that worked on each of the identified life stages, combining pre-surveys, group discussions, and creative activities to identify problems and prioritize solutions. The workshop was facilitated by two co-directors with the assistance of the IBE VP of the region and IBE staff.
Results: The analysis revealed specific challenges for each life stage:
-Childhood: Limited access to inclusive education and specialized care.
-Adolescence: Stigma and barriers to social and academic inclusion.
-Reproductive age: Lack of information on the impact of epilepsy on childbearing.
-Postmenopause: Lack of support for the management of hormonal changes and comorbidities. Lack of specific information on this group.
-Solutions such as the creation of support networks, educational campaigns, and improvement of public policies were proposed. Unique challenges for caregivers, such as isolation and emotional overload, were also highlighted.
Conclusion: This was the first regional, multi stakeholder workshop focused on women and epilepsy to be held. It promoted concrete solutions and collaboration in Latin America, establishing roadmaps for the specific needs of this vulnerable group at a global level, and the potential for replicating this work in other regions to transform policies and programs. The burden sustained by women caregivers in early childhood care, as well as for the elderly, was a clear and unexpected emergent theme. Presenting these results casts light on the need for equitable health and social care initiatives for women affected by epilepsy.

812 | Sports and epilepsy. Training for safe and inclusive practice

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Purpose: Physicians and non-medical professionals who are involved in sports often lack the necessary skills to assist someone with an epileptic seizure (EZ), and even more, they are not familiar with recommendations on sport practices for individuals with epilepsy diagnosis. These presentations aim to promote the inclusion of epileptic individuals in sports practice, providing information to evaluate this condition safely and within a contingency environment.
Method: A workshop meeting was held between the Argentine League Against Epilepsy (LACE), Espacio Epilepsia (patient organization), and Agencia Córdoba Deprotes (ACD - Córdoba government sports agency). A total of 200 individuals were present, including physicians, sports physicians, epileptologists, trainers, physical education teachers (PE), and sportsmen and women. Sport levels progressed from recreational to Olympic level, including sport performers with special needs and adaptations. A space for learning and discussion was set up, with the focus on real life cases, managing acute seizures, assessment protocols, and promoting transdisciplinary learning. A satisfaction survey was conducted afterwards as well.
Results: Survey answers from 118 participants: 36 physicians, 15 PE, 28 relatives or caregivers of people with epilepsy, 39 sport men and women (4 of them with epilepsy) (30 from the ACD) unanimously all agreed on recognizing the absence of Stablished Action protocols for epilepsy assessment. also purposed training and protocol creation in the near future. PE and trainers from the adapted sports area claimed for guidelines towards minimizing hazzards or risks for people with epilepsy practicing sports.
Conclusion: New training protocols on sports and epilepsy isues assessment for PE, trainers, physicians, and other professionals should be developed in the near future. A chapter has been created by ACD for its 2025 Strategic Action Plan . Epilepsy specialists and other sports professionals should provide appropriate information to individuals individually or through community organizations, in order to eliminate stigma related to epilepsy and sports.

992 | Knowledge, attitudes and misconcepts about epilepsy among students in North Macedonia

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Purpose: The aim of this study was to explore the awareness , knowledge, attitudes and misconceptions towards epilepsy and people with epilepsy (PWE), among university students in North Macedonia (NM).
Method: We conducted descriptive, cross-sectional study, from February to April 2024. A self-administered, anonymous survey questionnaire, via google forms, was used to survey 96 students from the Faculty of Medical Sciences, Goce Delchev University, Shtip and 130 students from all faculties of the SEEU University Tetovo, NM.
Results: Students are aware of epilepsy. More than half of them have not seen/witnessed an epileptic seizure. Students showed moderate knowledge about epilepsy and very positive social attitudes. They believe that PWE are capable of: completing higher education (81.1%), having children (72.1%), performing responsible and managerial work functions (82.7%). They would not be concerned if they worked with a person they knew had epilepsy on a daily basis (87.6%) and would not mind being friends with a person who has epilepsy (92.0%). 75.2% of the surveyed students believe that PWE, with whom they would eventually be friends, are obliged to inform them about the same (p=.0000). Most of the surveyed students believe that PWE can have a normal and quality life, but still 51.3% of them believe that PWE are in any way stigmatized and discriminated against in our society. 71.7% of the surveyed students believe that in our society, students and young people in general are not sufficiently informed about the disease epilepsy to have a correct social attitude towards PWE.
Conclusion: Students are aware of epilepsy, showed moderate knowledge about epilepsy and very positive social attitudes. Raising the awareness and the level of knowledge about epilepsy, among students, will have a stimulating effect on strengthening positive social attitudes and will have a preventive effect on misconceptions.

1067 | Exploring transition in the ERN EpiCARE: Insights from a survey analysis

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Purpose: The transition from pediatric to adult care is a critical phase for patients with chronic diseases, especially those with rare and complex epilepsies. We present the results of a survey conducted among the ERN EpiCARE (European Reference Network for rare and complex epilepsies) health care members in order to assess the management, the barriers and the unmet needs of the transition process.
Method: A questionnaire was developed by the ERN EpiCARE Transition Special Interest Group and then emailed to all Health Care Providers (HCPs) within the network. The questionnaire consists of 45 questions covering several areas: HCPs organization, transition practices, ideas for improvement, and challenges encountered during the process.
Results: The survey was completed by pediatric (60%) and adult (40%) neurologists from 60 ERN EpiCARE members across 21 European countries. Among respondents, 61.4% work in facilities serving both pediatric and adult patients. Only 35% have transition services, often lacking dedicated personnel or spaces. Written protocols exist in 47.4% of centers, yet just 8.8% involve patient organizations. Respondents identified a need to prioritize structured pathways for specific epilepsy syndromes (86%), particularly developmental epileptic encephalopathies and metabolic or autoimmune epilepsies. A critical issue was the lack of multidisciplinary teams, which limits the ability to adequately address co-morbidities management. Key challenges include lack of time, trained staff, and

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funding dedicated to transition. Most responders (61,5%) recommend transition preparation starting at 16-17 years, with multidisciplinary team involvement.

Conclusion: To effectively address the challenges of transition, future initiatives should prioritize developing tailored protocols that integrate multidisciplinary care, including a transition coordinator, specialists involved in patients' care (both neurologists and non-neurologists), and patient associations. Timely, planned pathways should address the unique needs of patients, ensuring continuity of care. Establishing dedicated transition spaces and securing financial support from healthcare institutions and policymakers are essential for delivering consistent, high-quality transition services.

1186 | Affordable alternatives after Levetiracetam daily defined dose revision: Emerging anti-seizure drugs for epilepsy

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Purpose: The World Health Organization has revised the daily defined dose (DDD) of Levetiracetam from 1000 to 1500 mg that may impact the drug affordability in low-resource settings of developing countries, like India. Therefore, this cross-sectional study assessed the affordability and availability of other anti-seizure medications (ASMs) in improving epilepsy treatment.

Method: In 2023, retail prices of ASMs were obtained from 79 pharmacies (Government and private) across Himachal Pradesh, Punjab and Andhra Pradesh, targeting diversity in the socioeconomic and geographic location. Maximum retail price was only recorded for branded drugs to ensure consistency in the selling prices; data on generics were excluded to minimize variability. Affordability was calculated based on the lowest daily wage of an unskilled worker in each state and expressed as the number of day's wages needed for one DDD.

Results: Revision of Levetiracetam's DDD from 1000 (2.08-2.13 day's wages) to 1500 mg (3.12-3.45 day's wages) has elevated the treatment cost 50%. Several ASMs, viz. Carbamazepine (1.85 day's wages), Clobazam (1.98 day's wages) Perampanel (2.02-2.25 day's wages), Brivaracetam (2.39-2.61 day's wages) and Zonisamide (3.05 day's wages) have emerged as cost-effective alternatives to Levetiracetam 1500 mg. However, availability of these ASMs is challenging. Both Perampanel and Zonisamide were found at two pharmacies, while Brivaracetam was available at six pharmacies across the three states. Although Sodium Valproate appeared to be affordable (2.21 day's wages), but of limited use due to serious side effects.

Conclusion: Limited availability of cost-effective ASMs, like Perampanel, Brivaracetam, Zonisamide, Clobazam and Carbamazepine restrict their broader use. Addressing the affordability-accessibility gap through robust clinical evidence and policy changes is crucial to establish these ASMs for epilepsy management. Acknowledgement: This study was funded by the DBT/Wellcome Trust India Alliance

1332 | Sociological study of the uses of adapted physical activity in the care of severe epilepsy at the Institut La Teppe

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Purpose: This study aims to analyze, using a sociological approach, how patients at the Institut La Teppe appropriate the adapted physical activity (APA) program offered to them during their stay

Method: A nearly three-year ethnographic study was conducted at the Institut La Teppe to examine the different uses of APA. Through interviews and observations with 40 patients and professionals, an inductive analysis identified three distinct roles of APA, evolving throughout the stay.

Results: At the beginning of the stay, APA is used to develop the empowerment of patients. APA serves as a tool to help patients cope with the contingencies of their epilepsy. It also provides a means of entertainment and personal growth within the institution, enabling them to regain social participation. During the stay, APA helps support the stay. After spending some time at Institut La Teppe, APA allows patients to momentarily escape the difficulties of daily life within the facility as a "valve", both physically and symbolically. At the end of the stay, patients who have fully engaged in APA are ready for regular, self-determined practice. However, guidance varies based on their post-hospitalization plans: for those entering the workforce, it is discouraged due to potential workload, while for those transitioning to a Medicalized Reception Facility, it is encouraged to maintain quality of life.

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Conclusion: This study shows how APA at the Institut La Teppe empowers patients by enhancing their understanding of their illness and promoting autonomy through regular physical activity. It highlights some limitations of this approach, particularly for patients preparing to return to work, for whom increased involvement in APA is discouraged (even though it is encouraged throughout their stay). The study suggests integrating APA into the institution's therapeutic education program to help patients maintain regular physical activity after their stay, regardless of their life plans.

1356 | Awareness of Legal Driving Restrictions Among Epilepsy Patients: A Cross-Sectional Study in a Portuguese Tertiary Hospital

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Purpose: Epilepsy affects patients' quality of life. This study assesses patients' awareness of Portugal's driving law after a seizure: one-year suspension for epilepsy patients driving under Category B and ten-year suspension for Categories C/D.
Method: Three months, cross-sectional study, randomly included 50 patients from a neurology outpatient clinic. Data on demographics, epilepsy characteristics, driving status, and awareness of driving restrictions were collected via anonymous printed questionnaires.
Results: Majority were male (52%), mean age 43 years. Educational levels included basic (28%), secondary (38%), and higher education (34%). Seventy percent were active (working/ studying), and 80% held a driving license. Focal epilepsy accounted for 44% of cases. Patients were on an average of 1.5 anti-seizure medications, with a maximum of four. In the past year, 64% were seizure-free. Eighty-four percent were informed about driving restrictions, primarily by neurologists (82%). Overall, 82% were aware of the mandatory one-year suspension (category B), while 14% were not, and 4% were unsure. Agreement with the regulation was full in 46%, partial in 40%, and opposed by 14%. Sixty-four percent felt fully informed, whereas 36% did not. Personal vehicles (54%) and public transport (22%) were the primary transportation modes mentioned. Driving suspension significantly impacted 45% of license holders, citing fears of seizures while driving, loss of autonomy, job loss, and financial concerns. None of the patients were dismissed from their employment, although one patient had to request early retirement. Four patients held licenses for category C/D, and only one was aware of the ten-year driving suspension. Additionally, 82% desired more information about driving laws. Non-compliance was reported by 23% due to perceived seizure control, dependence on driving, or lack of information.
Conclusion: Patients demonstrate high awareness of driving restrictions, primarily informed by neurologists. However, a significant proportion seek additional information, indicating the need for enhanced educational initiatives and clearer communication strategies.

1401 | Effects of drug-resistant epilepsy on patients' social adjustment and quality of life

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Purpose: To investigate the level of social adjustment, cognitive function, depression, fatigue, and quality of life (QoL) in patients with drug-resistant epilepsy (DRE).
Method: 50 patients from a neurosurgical clinic with DRE were analyzed (18-64 years; mean age: 31 years). Questionnaires were used: Liverpool Seizure Severity Scale (LSSS), Montreal Cognitive Assessment (MoCA), Beck Depression Inventory (BDI), Fatigue Severity Scale (FSS), Fatigue Impact Scale (FIS), and Quality of Life in Epilepsy Inventory (QOLIE-31). The statistical analysis was performed with IBM SPSS Statistics.
Results: The median duration of the disease was 15 years (interquartile range [IQR] 11-23 years), the median age of onset: 12 years (IQR 6.5-20 years). In 94 of the patients, multiple antiepileptic therapies were noted in the medical history. The educational level of the patients: 40% had a high school education, 40% a secondary vocational education; however, only 32% were employed at the time of the study. 40 points (IQR 32.5 - 47.5 points) in the median. Only 10% of patients had the normal MoCA range, median score: 23 points (IQR 21-25.5 points). The median BDI score: 12.5 points (IQR 6-18.25 points), 39% of patients had no depression; 28% - borderline clinical depression, 13% - moderate depression, 13% - severe depression, 7% - extreme depression; the median FIS score was 67.5 points (IQR 58-85 points). 62% of patients suffered from fatigue according to the FSS. A reduction in quality of life was observed in the study group, median score: 52.7 points (IQR 40.2–61 points). Quality of life was significantly worse in patients with severe and extreme depression (p=0.02).

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Conclusion: Patients in a neurosurgical hospital with DRE show decreased social adjustment, cognitive functioning, and overall quality of life. Quality of life was affected by severity of seizures, degree of fatigue and severity of depression.

1402 | Effect of Ramadan lifestyle changes among Patients with Epilepsy in the Eastern Mediterranean Region: A Multicenter Study

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Purpose: Ramadan, the holy month of fasting in Islam, presents unique challenges for patients with chronic medical conditions as epilepsy. During this month, Muslims abstain from ingesting food, drink, or oral drugs from dawn to sunset, typically lasting 12-18 hours. This study aimed to evaluate the effect of Ramadan lifestyle changes on seizure control, medication adherence, and sleep quality among Muslim patients with epilepsy (MPWE) in the Eastern Mediterranean Region (EMR).

Method: A multicenter cross-sectional study was conducted on 329 MPWE participated from five countries across EMR: Egypt, Iraq, Tunisia, Saudi Arabia, and Bahrain. Data were collected over three sequential lunar months (Shaaban, Ramadan, Shawwal) that covered the period from February to May, 2024. Seizure control, medication adherence (using the Morisky Medication Adherence Scale), and sleep quality (using the Pittsburgh Sleep Quality Index) were assessed. Moreover, multivariate analysis was performed to identify predictors of safe fasting with no breakthrough seizures during Ramadan.
Results: Of 329 patients, 82.4% (271) fasted during Ramadan, with only 58.3% stating that they had safely fasted without breakthrough seizures. Interestingly, fasting patients exhibited better adherence than non-fasting patients (57.6% versus 37.9%, $p=0.006$). However, sleep quality worsened during Ramadan, with only 32.2% of patients reporting good sleep quality ($p=0.005$). Younger age (Age ≤30 years (adjusted odds ratio (AOR): 1.9, 95% CI: 1.004-3.7, p=0.049), country of residence (with Iraq showing the highest odds ratio of 13.0, 95% CI: 4.5-36.0, p<0.001), and absence of seizures in the preceding six months (AOR: 9.9, 95% CI: 3.9-24.6, p<0.001) were independent predictors of safe fasting with no breakthrough seizures in Ramadan.
Conclusion: Ramadan fasting is feasible for MPWE, particularly those with younger age and well-controlled seizures. While medication adherence improved during Ramadan, sleep quality declined. These findings support the need for personalized medical counselling and pre-Ramadan preparation to optimize patient outcomes.

1406 | Impact of Ramadan fasting on patients with epilepsy: Clinical and Laboratory Study

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Purpose: Caring for Muslim patients with epilepsy who choose to fast during Ramadan presents unique challenges for healthcare providers. Fasting during Ramadan is a religious obligation for all capable Muslim adults. However, those with health risks are exempt. Thus, our

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study is to assess the impact of Ramadan Fasting on seizure frequency and key physiological blood parameters.
Method: This prospective study was carried out at the Neurology Department of the Faculty of Medicine, Mansoura University, Egypt. Data were collected over three sequential lunar months (Shaaban, Ramadan, Shawwal) that covered the period from February to May 2024.Twenty adult Muslim patients with epilepsy who observed fasting during Ramadan, were tracked for their Seizure status. Moreover, laboratory measurements, including hematocrit, sodium (Na), potassium (K), and beta hydroxybutyrate levels (BHB), were recorded during both fasting and non-fasting periods (Ramadan and Shaaban).
Results: Approximately one-third of participants remained seizure-free throughout Ramadan. Patients who experienced seizures during Ramadan had significantly poorer seizure control during the six months leading up to Ramadan with median of seizure number (IQR) =10 (5-21), P-value=0.003. Blood BHB, Na, and HCT levels were significantly higher during fasting compared to non-fasting months (Median (IQR) of Blood BHB "mmol": 0.2 (0.1-0.37) versus 0.02 (0.01-0.26), while mean± SD of Na "mmol" : 143.2 ±2.2 versus 140.5 ±1.9 and that of HCT (%): 39.8 ±4.6 versus 38.5 ±4.3 , with P-value; <0.001, <0.001, =0.01, respectively). However, these differences in BHB, Na and HCT levels did not show a significant impact on seizure status during Ramadan (P-value=0.07, 0.5, 0.5, respectively). Interestingly, patients with higher K levels (Mean± SD=4.6 ±0.4 mmol) were significantly more likely to experience seizures during Ramadan (P-value=0.005).
Conclusion: Changes in hydration status and electrolyte levels during Ramadan fasting may increase seizure susceptibility especially in poorly controlled patients.

1440 | Access to epilepsy surgery for refractory epilepsy in the city of Cali: Experiences of caregivers of children and adolescents

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Purpose: Epilepsy is a chronic neurological disorder. Thirty percent of patients progress to intractable epilepsy. Epilepsy surgery is a treatment option, but despite its therapeutic yield, it is often underutilized. The purpose of this study was to understand the experiences of caregivers of children and adolescents regarding access to epilepsy surgery.
Method: The present research was conducted from a qualitative approach based on phenomenological theory. Five caregivers and two health professionals (epilepsy neurosurgeon, epileptologist) participated in the study. Information was collected through in-depth interviews conducted between 2021 and 2022. Initial categories of analysis were constructed and the emergence of new categories was subsequently recognized and integrated into the analysis, allowing the identification of the structure of the phenomenon of interest.
Results: Four essential meanings of the experience of access to epilepsy surgery were identified. The first: the meaning of achieving epilepsy surgery is the search for a dignified life. The second: the meaning of fighting for epilepsy surgery as an odyssey mostly alone. The third: the meaning of access to epilepsy surgery as a result of the mobilization of all resources. The fourth: the vindicating meaning of performing epilepsy surgery and freeing oneself. Furthermore, these results were confronted with the social determinants of health model. The access barriers experienced by caregivers to epilepsy surgery for their children were not limited to the act of denial of service with the consequent deterioration of health, but extended to the deprivation of the right to live with dignity. These barriers operated in the structural and intermediate determinants.
Conclusion: The experience of access to epilepsy surgery was for caregivers a struggle for the dignity of their lives and that of their families. The role of caregivers transcended caregiving tasks to configure a social movement that participates in health outcomes in epilepsy.

1442 | Knowledge, perceptions, and attitudes of cali public school teachers in preschool, elementary, and high school regarding epilepsy in 2023

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Purpose: Epilepsy is one of the most common chronic neurological disease in children, significantly impacts psychosocial development due to stigma, knowledge gaps, and harmful attitudes. School teachers are crucial to child development. The aim of this study was to describe the knowledge, attitudes and perceptions of epilepsy among public school teachers in Cali, Colombia.
Method: A cross-sectional, descriptive, observational, multistage sampling study was conducted among public school teachers at the preschool, middle school, and high school levels. A specially designed questionnaire was used

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to assess knowledge, attitudes, and perceptions about epilepsy. Sociodemographic variables were included.
Results: 309 teachers (median age 51; 72.8% female; 85.1% urban area) participated. 84.5% had postgraduate training, and 66.7% taught high school. 51.1% had been exposed to a student with epilepsy, and 47.6% had witnessed a seizure. While 81.2% identified epilepsy as a brain disease, 40.8% believed that a crisis can subside unnoticed in a few seconds. 93.2% lacked epilepsy training, and 70.9% were unsure of seizure first aid; 54.7% mistakenly believed inserting objects in the mouth was helpful. Regarding attitudes, 74.4% supported marriage for people with epilepsy; however, 41.8% felt they shouldn't live alone. 93% did not perceive them as dangerous. Regarding perceptions, 89.7% believed they could be as successful as other children, and 94.1% supported inclusion in regular schools. Lack of seizure knowledge correlated with no prior experience with students with epilepsy ($p<0.001$); the 43-50 age group was more likely to consider epilepsy a disability ($p=0.0024$); and women were more likely to believe special education was necessary ($p=0.0049$).
Conclusion: Despite frequent exposure to students with epilepsy public school teachers have knowledge gaps, especially in seizure management. While generally positive, some held limiting views on independence. Most supported mainstream schooling. Epilepsy first-aid training is recommended to improve knowledge and promote positive attitudes.

1628 | Epilepsy and Education – Children with Epilepsy Out of School Survey in Zambia

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Purpose: A survey to establish why high number of children with epilepsy were out of school while evaluating knowledge and attitude of epilepsy among parents/guardians, teachers and health workers. About 60% of the children attended to at the epilepsy clinics either dropped out or withdrew from school because their parents/guardian felt that they could not concentrate, fear of having a seizure on the way or being stigmatized. The survey also offered an opportunity to impart correct information on epilepsy to educators, children with epilepsy and their caregivers, thus reducing cases of stigma and discrimination.
Method:

- Questionnaires administered according to the focus group and purposive non- probability sampling method was used.
- 100 children (50 in school and 50 out of school with their parents to assist)
- 25 Health workers.
- 25 Educators

Results: Reasons - 'Difficult to monitor the child' and 'child always sick, misses classes' were most common in the out of school group (36% and 34% respectively). 'Difficulty to monitor the child' was a common (72%) reason in the school-going group. 90% out of school group - child with epilepsy cannot achieve a lot in life and teachers are unable to help a child with epilepsy. Knowledge of teachers on cause and first aid was good. This study revealed a positive attitude of health workers towards epilepsy, responding that a child with epilepsy should go to school and can have a bright future.
Conclusion: All the three groups interviewed supported the idea that children with epilepsy should be allowed to attend school and have good knowledge of and a positive attitude towards epilepsy. Parents/guardians of children with epilepsy agree that their children should be in school but are worried about their children having seizures whilst at school. There is still a growing need for a well-structured intervention for parents/guardians, teachers, and health workers.

1658 | Can Animation Series combat Epilepsy stigma and misconceptions among University students?

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Purpose: To assess the baseline epilepsy knowledge and attitude among university students in the Eastern Mediterranean Region (EMR) toward people with epilepsy (PWE) and the perceived impact of viewing the Epilepsy Awareness Animation Series (EAAS) on their understanding of epilepsy and attitudes towards PWE.
Method: This is a pre-post-interventional study whereas a tailor-made EAAS was created by the research team. The data was collected from September to November 2024. Invitations were sent to university students through their

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respective social media groups to join created groups on both WhatsApp and telegram for this study where a pre-evaluation google form survey was initially distributed to the participants, and then an email containing the EAAS and post-evaluation forms was automatically sent upon completing the pre-evaluation form.

Results: A total of 1709 students participated. The average age was 20.5 years (SD=1.8), the majority of which were males (64.4%). Geographically, most participants were from the Levant (70.4%), North Africa (21.5%), and Gulf countries (6.6%). 54.2% were from non-medical faculties. After viewing the EAAS, many misconceptions were corrected. For instance, the belief that epilepsy is a form of mental retardation improved, with correct answers pre-intervention (72.6%) increased to (90.7%) post-intervention. Similarly, the misconception that epilepsy is a psychiatric disease saw an increase in correct responses, from (51.2%) to (83.9%). As for epilepsy being an untreatable condition, correct responses increased from (52%) to (82.6%). The total knowledge score median increased from 8 (IQR:6-10) to 12 (IQR:11-13). There was also a notable improvement in attitudes, with the acceptance of friendship with PWE increasing from 69.5% to 88.6% ($p < 0.001$). The overall attitude score median improved from 3 (IQR: 1-4) to 4 (IQR: 3-4).

Conclusion: The EAAS is an effective tool to enhance epilepsy knowledge and promote positive attitudes toward PWE among university students in the EMR.

1681 | Knowledge and Attitudes Toward Epilepsy Among University Students in Arab Countries: A Cross-Sectional Study

S Shaaban[1], Y Elsadany[1], A Kalta[1], S Elmandou[1], R Ismael[1], F Elsaadany[2], M Kadan[1], AA Kalta[1], M Khalifa[1], G Hasan[1], D Khira[1], B Khaleel[3], A Alghazali[1], J Bani Kenana[4], A Al-Natsheh[5], Y Alammar[6], S Mohsen[1]

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Purpose: Understanding epilepsy and increasing awareness in the community are crucial for reducing social stigma and improving quality of life for people with epilepsy. Thus, this study aims to examine the level of knowledge and attitudes toward epilepsy among university students in Arab countries, focusing on misconceptions and stigma related to epilepsy in order to tailor our targeted future epilepsy educational interventions.

Method: A descriptive cross-sectional study was conducted among university students in 20 Arab countries throughout 2024 Participants (ages 18–26) were recruited via social media. A validated questionnaire assessed knowledge, attitudes, misconceptions, and societal stigma related to epilepsy. Misconceptions were evaluated through questions such as whether epilepsy is always hereditary. Knowledge was assessed by familiarity with absence seizures and fever as a trigger, while attitudes towards people with epilepsy were explored

Results: The study included 4928 students (mean age 22), with 54.75% being non-medical students. Misconceptions were prevalent: nearly 54% of participants recognized epilepsy as a psychiatric illness, 62.9% believed that epilepsy was always hereditary. More than half of participants did not recognize absence seizures as one of seizures' types and nearly 81% believed that epilepsy involved only involuntary movements. Moreover, negative attitudes were detected as follows: 32.1% of the participants were not willing to be friends with someone who has epilepsy, 45.4% refused to allow their children to play with affected peers, 33.7% did not show any intentions to hire qualified individuals with epilepsy, and 25.7% stated that they were not comfortable working with them.

Conclusion: This study highlights persistent misconceptions about epilepsy and negative attitudes towards people with epilepsy, thus demonstrates that education significantly enhances awareness. The findings underscore the need for targeted awareness programs to combat stigma and misinformation.

1791 | Do Socioeconomic Disparities Impact Care Among Women with Epilepsy?

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Purpose: To evaluate the influence of socioeconomic disparities in health outcomes for Canadian women with epilepsy (WWE) concerning folic acid counselling, unplanned pregnancies, contraceptive use, and bone health.

Method: In 2022 a cross-sectional anonymous survey was launched in the Epilepsy Monitoring Unit and outpatient epilepsy clinic at University Hospital in London, Ontario, Canada. The survey was open to any adult (18+) living with epilepsy who identifies as a woman or was assigned the female sex at birth.

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Results: A total of 127 surveys were completed. Participant's ages ranged from 18 to 66. 89.2% (n=71) of participants were White. 71% (n=68) of participants had income less than $50,000 dollars per year, and 70.3% (n=71) attained a college or university education. 67.7% (n=42) of low-income participants received folic acid counselling compared to 70% (n=7) of high-income participants. 58.3% (n=21) of low-income participants had unplanned pregnancies, compared to 22.2% (n=2) of high-income participants. 65.2% (n=15) of women with a low income were not using contraceptives compared to 60% (n=3) of women with a high income. The most commonly used anti-seizure medications for WWE with low-income are lamotrigine used by 47.11% (n=32), clobazam used by 30.9% (n=21), brivaracetam used by 26.4% (n=18) and carbamazepine, used by 22.1% (n=15). Compared to WWE with high-income were lamotrigine was used by 50% (n=14), brivaracetam by 26.4% (n=18), clobazam by 14.3% (N=4) and carbamazepine by 7.14% (n=2).

Conclusion: WWE are more likely to earn below $50,000 despite a large proportion having completed post-secondary education. Women with a low income are less likely to receive folic acid counselling, more likely to have unplanned pregnancies, and be prescribed older medications. More research is needed to understand these associations between lower income and lower levels of education and epilepsy management.

1809 | Mobile Application for Epilepsy Management: A Multidisciplinary Approach

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Purpose: Epilepsy is a chronic neurological disorder affecting over 50 million people worldwide, requiring continuous monitoring and effective communication between patients and healthcare professionals [Thijs RD et al. Nat Rev Dis Primers 2019;5:18024.]. Proper seizure tracking is essential for treatment optimization, but structured data collection remains a challenge, particularly in Portuguese-speaking countries [Fisher RS et al. Epilepsia 2005;46:470-472.]. Digital health solutions, including mobile applications, have shown promise in improving adherence to treatment and self-management strategies [WHO. Epilepsy: a public health imperative. WHO Press, Geneva, 2019;15-25.]. This study aimed to develop a user-friendly, Portuguese-language mobile application to enhance epilepsy management through technological innovation and evidence-based methodologies.

Method: The application was developed by a multidisciplinary team of neurologists, educators, and software developers, combining clinical expertise with technological strategies. The development process utilized Visual Studio Code for coding and debugging, Dart programming language with the Flutter framework for cross-platform compatibility, and Android Studio for testing the application's functionality. Key features include detailed seizure logging, a calendar for monitoring episodes, automated report generation with analytical graphs, and an SOS button to share real-time location with emergency contacts.

Results: The application facilitates real-time seizure tracking, medication adherence monitoring, and the generation of comprehensive reports to assist healthcare professionals in assessing seizure impact. It also functions as an educational resource, providing users with reliable, evidence-based information. Preliminary evaluations demonstrated high usability, clarity, and potential for integration into routine epilepsy care.

Conclusion: This mobile application addresses critical gaps in epilepsy management by integrating technology and clinical expertise into a practical, accessible tool. Future developments will focus on large-scale implementation and adaptation for diverse platforms to enhance accessibility and inclusivity.

1825 | Uncertainty and Quality of Life in Adult Epilepsy Patients

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Purpose: The role of anxiety and depression in the quality of life of people with epilepsy is well known. Temporal unpredictability and ictal consciousness impairment, added to the frequent diagnostic and prognostic doubts, allow us to postulate a potential impact of uncertainty on the lives of those who suffer from it. The aim was to evaluate the relationship between uncertainty and quality of life in patients with epilepsy, exploring the possible role of clinical and psychological factors (anxiety, intolerance to uncertainty) and knowledge of their disease.

Method: A cross-sectional study was carried out in adults diagnosed with epilepsy, treated at the Epilepsy Service, Hospital de Clínicas (Uruguay). An *ad hoc* questionnaire was applied, including demographics, data about the epilepsy, its complications and information received about the disease. Validated scales were used to assess

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uncertainty in the disease (MUIS-C 17), intolerance to uncertainty (IU-12), anxiety (GAD-7) and quality of life (QOLIE-31). Descriptive measures, cluster analysis to identify domains of the MUIS-C, and association analyses (T-test, Mann-Whitney, Pearson or Spearman correlation and multiple regression, as appropriate) were applied (SPSS 11.5, α=0.05).

Results: A total of 59 patients (41F:18M; 20-60 years old) were included. The average MUIS-C score was 46.5+14.9, identifying 4 main domains: deficient information, ambiguity, understanding and unpredictability. While most patients received information on their disease, those who deemed it insufficient had higher uncertainty scores (p=0.01). Greater uncertainty in the disease was associated with lower quality of life (Spearman, r=-0.324, p=0.01). Greater intolerance to uncertainty was associated with generalized anxiety (p=0.03) and uncertainty in the disease (Spearman, r=0.547, p‹0.000).

Conclusion: Disease-related uncertainty is associated with decreased quality of life in people with epilepsy. Studies in larger numbers of patients are required to identify its determinants. Improving the quality of information is one of the feasible interventions.

Status Epilepticus

321 | The Role of Brain Biomarkers TGF and Proinflammatory Interleukins in the Clinical Course of Status Epilepticus in Pediatric Population

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Purpose: The role of biomarkers involved in neuroinflammation and neuronal injury in the development of epileptogenesis is a modern approach in the multimodal evaluation of SE.

The aim of this study was to evaluate the pleiotropic cytokine Transforming Growth Factor (TGF) and serum interleukins Il-6, Il-1 alpha, 1 beta, and the Il 1Ra/Il F3 ratio in the context of pediatric status epilepticus (SE).

Method: The study included 55 pediatric patients with SE of various etiologies, monitored from 2019-2023, including the investigation of biochemical markers: TGF, Il-6, Il-1 alpha, 1 beta, and the Il 1Ra/Il F3 ratio at the IMSP IMC using the ELISA immunoenzymatic method.

Results: In our study, the increase in TGF beta 1 levels elucidates a significant statistical difference (p<0.001), with average values in the study group of 4409.4 pg/ml and 179.9 pg/ml in the control group. Tissue inflammation may be involved in the generation of seizures, especially in the context of SE. Other average serum values obtained in the study group versus the control group: Il-6 – 1431 pg/ml vs 82 pg/ml (p<0.001), Il-1 beta – 90.62 pg/ml vs 5.84 pg/ml (p<0.001), Il-1 alpha – 367.1 pg/ml vs 7.2 pg/ml (p<0.001). The calculated ratio between Il 1Ra/Il F3 is 480 pg/ml vs 86 pg/ml (p<0.021).

Conclusion: Disturbances in the studied immunological indices (TGF, Il-6, Il-1 alpha, 1 beta, and the Il 1Ra/Il F3 ratio) indicate cellular-level impairment of immunomodulatory processes and may play an important role in the development of SE in children. The analysis of these immunological biomarkers suggests the need for further research of this kind on larger cohorts of children with SE and their usefulness in developing new immunomodulatory strategies for SE.

323 | Discrepancy and consistency between electroencephalography and brain imaging in nonconvulsive status epilepticus: a case series

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Purpose: In acute phase of neurosurgical disease or head trauma patients sometimes experience nonconvulsive status epilepticus (NCSE). Although electroencephalography (EEG) is a very useful tool for the diagnosis of NCSE, ictal or interictal discharges are sometimes observed in a different region from the brain lesion on brain images. Here we investigate discrepancy and consistency between EEG and brain imaging in 4 consecutive cases with NCSE.

Method: We reviewed detailed medial history and physical examination along with diagnostic tests that include EEG, CT, SPECT and MRI of 4 NCSE patients.

Results: In 2 patients (one with an intra-axial brain tumor and the other with an intracerebral hemorrhage), EEG showed lateralized periodic discharges, maximal over remote regions from the intra-axial lesions. In one patient after an operation for chronic subdural hematoma (CSDH), EEG showed ictal discharges maximal near the preoperative thickest point of the CSDH. In one patient with slight traumatic subarachnoid hemorrhage, EEG showed interictal discharges maximal over a region without apparent intra-axial lesions, whereas they were

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located within the region with ictal hyper-perfusion on arterial spin labeling and corresponding to the low-uptake area on interictal iomazenil SPECT.
Conclusion: In neurosurgical patients with NCSE, ictal discharges may not be of maximal amplitude at the site of brain lesions on images, especially when lateralized periodic discharges appear.

388 | EEG and Seizure Characteristics During and After New Onset Refractory Status Epilepticus

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Purpose: EEG findings and seizure characteristics in New Onset Refractory Status Epilepticus (NORSE) are limited in the literature.
Method: Retrospective study of 44 NORSE patients with EEG reports available across 17 centers; a subset of the NORSE Institute and CCEMRC-sponsored multicenter NORSE/FIRES study and biorepository. Daily inpatient/follow up EEG findings were documented per 2021 ACNS Standardized Critical Care EEG Terminology, focusing on epileptiform/periodic discharges (PDs) and seizures.
Results: 920 inpatient EEG days (avg 20.4/patient) for 44 patients were included (33 female, 36 cryptogenic, avg age 32.7±19.9, range 5-77). Adherence to ACNS terminology varied greatly between reporters. Acutely, most had multiple seizure types, including focal impaired consciousness (FIC) without observable manifestations (n=20), elementary motor phenomena (16), complex motor phenomena (5), focal to bilateral tonic-clonic (8), generalized clonic (1), and electrographic (33). Total seizure burden ranged from 6.5-32,615 minutes (mean 1232.5). Status Epilepticus (SE) was reported on EEGs of 16 patients (7.1% of days), all of whom had nonconvulsive status epilepticus (NCSE), and 8 had focal motor SE. IIC was reported in 13 patients (7.9% of days, daily burden 6-90%). PDs were present in 38/44 (avg 48.7% of days), with lateralized (LPDs) in 24, bilateral independent (BIPDs) in 16, and generalized (GPDs) in 20. Twelve had follow-up EEG (avg last follow-up 27.8 months). Posterior dominant rhythm (PDR) was present in 9, focal slowing in 7, epileptiform discharges in 7, including PDs in 4 (2 LPD, 3 GPD). Seizures were captured in 3 patients (2 FIA, 1 electrographic).
Conclusion: In NORSE, seizures and SE are predominantly nonconvulsive. FIC and tonic-clonic seizures are the most common clinical manifestations. PDs are frequent, with similar prevalence of LPDs and GPDs acutely. Chronically PDR returns in most, reflecting long-term recovery, but epileptiform discharges, including PDs, may persist. Variability in EEG reporting highlights the need for standardized use of EEG terminology to improve future research on NORSE.

415 | Clinical-EEG variables and etiology in elderly patients with nonconvulsive status epilepticus

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Purpose: The occurrence of nonconvulsive status epilepticus (NCSE) is frequent in the elderly. However, there are still gaps in the relationship between etiological data and

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clinical-EEG aspects. Objective: To relate etiological factors with initial EEG data and clinical aspects of elderly patients with NCSE.

Method: Methodology: The clinical EEG data of 99 elderly patients with NCSE were evaluated.

Results: The mean age was 72.3±8.0 years, 57 (63.3%) cases were female, the ictal EEG pattern was: A1=26 (17.8%) cases, A2=18 (12.3%), A3=15 (10.3%), and A4=40 (27.4%) cases. The NCSE was classified as NCSE-coma/subtle in 44 (44.4%) cases and NCSE-without coma in 55 (55.5%) cases. The etiology was acute in 54 (54.5%) cases, remote in 35 (35.3%) cases, progressive in 7 (7%) cases, and undetermined in 3 (3%) cases. The previous diagnosis of epilepsy occurred in 26 (26.3%) cases. Within 30 days, 37 (37.4%) patients died. There was no significant association between baseline EEG findings and the occurrence of death, gender, type of NCSE, and etiology. There was a significant difference in etiology according to the presence of a previous history of epilepsy, with a higher occurrence of epilepsy when the etiology was remote ((Chi-square test, $p<0.001$). The occurrence of remote etiology in the NCSE without coma was higher ($p=0.025$).

Conclusion: Mortality was high in elderly patients with NCSE but with no difference according to the clinical-EEG aspects. Previous history of epilepsy occurred more frequently in the NCSE of remote etiology. NCSE without coma was associated with remote etiology. FAPESP 2024/06399-7.

503 | Prognosis in patients with status epilepticus

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Purpose: Although several prognostic scoring systems such as STESS, EMSE, and END-IT scores are available to predict outcomes in status epilepticus (SE), these scores are mainly based on clinical variables. We investigated prognosis in SE by means of neuroimaging and electrophysiology findings as well as clinical variables.

Method: This is an observational study. The inclusion criteria were 1) >18 years old, 2) with MR including DWI and FLAIR, 3) with peri-ictal EEG, and 4) with clear medical documentation. We excluded SE associated with hypoxic-ischemic encephalopathy. The variables for analysis were included semiology (convulsive vs non convulsive), etiology (epilepsy vs acute symptomatic vs cryptogenic), peri-ictal MR abnormality (PMA), peri-ictal EEG abnormality (PEA) such as electrical seizures or ictal-interictal continuum, failure to 2nd ASMs, additional injection of BDZ and score of STESS. The primary endpoint was modified Rankin Scale (mRS) at discharge dichotomized into poor (mRS 4-6) and good (mRS 0-3) outcomes. Multivariate logistic regression was analyzed with the outcome as a dependent variable.

Results: A total of 114 patients met the inclusion criteria. Poor outcomes consisted of 50 patients (44%) and, 35 patients were failed to 2nd ASMs (32%). PEA was founded in 54 patients (47%) and PMA was observed in 25 patients (22%). The significant variables predicting poor outcome were as follows; older age, less convulsive SE semiology, higher STESS, with PMA, with PEA and failure to 2nd ASMs. Multivariate logistic regression showed independently significant variables predicting poor outcome were STESS (adjusted OR 1.6, 95% CI 1.2-2.1), PEA (adjusted OR 4.3, 95% CI 1.7-11.3), PMA (adjusted OR 3.8, 95% CI 1.2-12.1) and failure to 2nd ASMs (adjusted OR 3.7, 95% CI 1.3-10.8).

Conclusion: Higher STESS, having PEA and PMA and failure to 2nd ASMs were significant variables predicting poor outcome at discharge in patients with SE.

581 | Efficacy of Cell Therapy Drug on Kainic Acid-Induced Seizures in Mice

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Purpose: Epilepsy is one of the most commonly diagnosed neurological disorders, and effective treatments are urgently needed. Messenger RNA (mRNA)-based drugs have shown significant potential in disease prevention and therapy. The aim of this study was to investigate the therapeutic efficacy of an mRNA drug in a kainic acid (KA)-induced seizure model in mice and to explore its potential as a novel approach for epilepsy treatment.

Method: Male C57BL/6J mice (n=30) were divided into three groups to assess the therapeutic effects of the mRNA drug in the KA-induced seizure model. All groups received a unilateral intra-hippocampal injection of KA (20 mM solution in sterile 0.9% saline) to induce seizures. After a 5–7-day recovery period, Group I (vehicle, n=10) received phosphate-buffered saline (PBS) injection. Group II (mRNA drug-low, n=10) and Group III (mRNA drug-high, n=10) received low and high doses of the mRNA drug, respectively, administered into the same lateral hippocampus as the KA injection. Three to four weeks post-treatment, all animals were implanted with DSI transmitters to monitor EEG and spontaneous seizures for 7 days. Seizure severity was evaluated using the Racine scale.

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Results: KA injection induced severe epilepsy, as indicated by the Racine scale and EEG recordings, which showed spasms and epileptiform discharge events in Group I. The mRNA drug significantly reduced seizure severity in a dose-dependent manner, as demonstrated by improvements in the Racine scale and amelioration of seizure symptoms.
Conclusion: These findings suggest that the mRNA drug effectively modulates epileptic activity in the KA-induced mouse model and may have therapeutic potential for treating epilepsy.

596 | Effectiveness of the seizure code in urgent epileptic seizures to avoid status epilepticus at a private tertiary hospital in Mexico

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Purpose: To evaluate the effectiveness of the seizure code in urgent epileptic seizures to avoid status epilepticus at a private tertiary hospital in Mexico.
Method: Descriptive, retrospective, observational, cross-sectional analytic study. Inclusion criteria: Patients with urgent epileptic seizures (October-December 2024). Tests (central tendency, odds ratio, risk ratio, 95% confidence interval, Fisher's exact) were applied (Epi Info program).
Results: 49 patients. Age: mean 9±0.70, range 1-16 years old. Male: 23 (76.6%). Type: focal 43.3%, generalized 56.6%. Status epilepticus (ADAN scale): 15 (30.6%); cluster seizures: 18 (36.7%); high-risk seizures: 16 (32.6%). Known epilepsy-recovered epileptic seizure: 26 (53%). Known epilepsy-unrecovered epileptic seizure: 7 (14.2%). No known epilepsy: 16 (32.6%). Seizure code 29 (59.1%): status epilepticus 10 (20.4%), cluster seizures 12 (24.4%), isolated high-risk seizures 7 (14.2%). Mortality risk (STESS scale): 2 (4%). Risk seizure recurrence (RACESUR scale): 28 (57%). Stay in intensive care/prolonged hospitalization: 16 (32.6%). Short hospitalization: 33 (67.3%). If the seizure code is not used in urgent epileptic seizures, the risk of presenting status epilepticus (status epilepticus: OR 36, RR 8, CI 1.7-731; cluster seizures: OR 22, RR 8, CI 1.5-314; high-risk seizures: OR 21, RR 5.4, CI 1.5-293), stay in intensive care/prolonged hospitalization (OR 84, RR 21.7, CI 8.9-786), seizure recurrence (OR 3.6, RR 1.6, CI 1.05-12.8) increases ($p<0.05$).
Conclusion: Urgent epileptic seizure is a new concept to identify patients who require priority attention. It includes patients with status epilepticus, cluster seizures, and high-risk seizures. Seizure code reflects the intention to optimize treatment times to avoid status epilepticus, acting early in potentially serious seizures (Teran, Emerg Med Pract. 2015;17). In our study, seizure code in urgent epileptic seizures reduced the risk of status epilepticus, stay in intensive care/prolonged hospitalization, and seizure recurrence. It is necessary to apply the seizure code in urgent epileptic seizures efficiently and early in the first 30-60 minutes to avoid irreversible changes and improve the prognosis of patients.

631 | Nonconvulsive Status Epilepticus Secondary to Insulinoma-Induced Hypoglycemia: A Case Report

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Purpose: Introduction: Hypoglycemia is a common complication of neuroendocrine tumors, especially insulinoma. Between 12 to 60% of patients with insulinoma present with generalized tonic-clonic seizures. In current literature, the prevalence of nonconvulsive status epilepticus secondary to insulinoma-induced hypoglycemia is not reported.
Method: Case Report :A 72-year-old woman with nonconvulsive status epilepticus induced by hypoglycemia as a complication of a malign insulinoma, treated with dextrose infusions and anti-seizure therapy, achieving late electroencephalographic improvement of epileptic activity but not of consciousness state and finally passed away.
Results: Discussion: The treatment approach is not well-defined in cases where the patient develops nonconvulsive status epilepticus (NCSE) secondary to insulinoma despite correction of hypoglycemia and treatment with antiseizure therapy. Prolonged status epilepticus can exacerbate hypoglycemia, further worsen encephalopathy, and contribute to neuronal damage.
Conclusion: The long duration of hypoglycemia and NCSE may have contributed to brain injury and poor recovery in this patient. This is the first case reported in the literature of nonconvulsive status epilepticus (NCSE) secondary to insulinoma-induced hypoglycemia.

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690 | The impact of "the new" definition of status epilepticus on prevalence and clinical features of status epilepticus in children – a tertiary center experience

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Purpose: To evaluate the impact of the change in status epilepticus (SE) definition on prevalence, etiology, demographic features, and semiology in children analyzing the data in the same cohort using "the old" and "the new" SE definition.
Method: A retrospective study included hospitalized children due to seizures during the last two years. Demographic features, etiology, seizure semiology, and duration were obtained from the medical records. Seizures were classified according to "the old" (Angeles, 1981) and "the new" (Trinka, 2015) definitions. Etiology was categorized as symptomatic (provoked, structural, metabolic/toxic, inflammatory/infectious, genetic, electroclinical syndromes) and cryptogenic. Semiology of SE was divided into: SE with (generalized, focal) and without (nonconvulsive) prominent motor phenomena. McNemar test was used to delineate statistical significance.
Results: We analyzed 339 seizures in 299 hospitalized children. Significantly more seizures were defined as SE when applying "the new" definition 164 (48.4%) vs 49 (27.7%) ($p < 0.001$), with no difference in mean age (6.0, SD 4.97 y vs. 4.2, SD 3.1 y, p 0.157). The most frequent etiology was provoked seizures in both groups, followed by genetic and remote symptomatic seizures. A significant difference ($p<0.001$) was found when applying "the new" vs. "the old" definition in seizure mean duration (24.5, SD 26.5 min vs. 54.4, SD 32.1 min), and dominant SE semiology. In the group with "the new" SE, generalized SE was more frequent (92 vs.15 pts), while focal SE was more frequent in the group with "the old" defined SE.
Conclusion: The new SE definition markedly increases SE prevalence, contributing to the fact that almost half of admissions due to seizures are SE. The significant difference between "the new" and "the old" SE definitions was found in mean duration and dominant SE semiology, while not significantly in etiology and mean age. Further investigations in a larger cohort of children with SE are necessary.

709 | Quantifying focal hypermetabolism in suspected non-convulsive status epilepticus: a single-centre cohort study

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Purpose: To evaluate ^{18}F-FDG-PET as a biomarker in suspected non-convulsive status epilepticus (NCSE) by characterizing electroclinical-metabolic correlations and quantifying focal hypermetabolism.
Method: We included 23 adult patients (median age 61 years, 15 females) with rhythmic and periodic patterns (RPPs) undergoing ^{18}F-FDG PET for suspected NCSE. Two neurologists reviewed patient EEG recordings (0-30 minutes post-injection) using 2021 ACNS criteria. ^{18}F-FDG PET images were blindly assessed by a nuclear medicine specialist for the presence and lobar location of focal hypermetabolism. Patients were compared to external age/sex-matched (n=23) and in-house validation (n=22) healthy control datasets. We calculated intra-subject voxel-wise standard deviations (SD) from the mean gray matter PET signal intensity, then compared this novel approach to standardized uptake value ratio (SUVR) methods using visual assessment as the reference standard. For hypermetabolic volume quantification, we selected the SD threshold corresponding to 100% specificity. Resulting volumes were correlated with lateralized periodic discharges (LPD) main modifiers.
Results: At time of PET, EEG showed LPDs in 17 (74%), other RPPs in 3 (13%), and no RPP in 3 patients (13%). Focal hypermetabolism was visually observed in 20 patients (87%). Among patients with LPDs and focal hypermetabolism (n=15), 13 showed strictly ipsilateral concordance, while 2 demonstrated bilateral hypermetabolism. SUVR-based thresholding (primary/validation datasets: SUVRpons AUC=0.57/0.45, SUVRcerebellum AUC=0.63/0.58) failed to identify patients with focal hypermetabolism. Thresholding based on the novel intra-subject SD-based method demonstrated superior performance in detecting hypermetabolism (primary/validation datasets: AUC=0.90/0.83) compared to SUVRcerebellum and SUVRpons (both $p<0.01$). In patients with LPDs (n=17), hypermetabolic volumes (>3 SD) varied widely (range 0 to 20.2 mL), without significant correlation to LPD main modifiers.

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Conclusion: The intra-subject SD-based method shows potential for quantifying the presence and extent of focal hypermetabolism, providing complementary metabolic information to scalp EEG in suspected NCSE.

719 | Status epilepticus epidemiology in France: insight from the French National Health Data System

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Purpose: To describe the epidemiology of status epilepticus (SE) in France and identify risk factors associated with short- and long-term mortality as well as recurrence.
Method: We conducted several studies using data from the French National Health Insurance system, which covers 99% of the French population. We extracted all patients hospitalized with an ICD-10 code for SE (G41). We measured the standardized incidence of SE from 2012 to 2022, analyzed factors associated with in-hospital mortality, and assessed predictors of 3-year mortality and recurrence among patients surviving the index hospitalization.
Results: A total of 118,050 patients were hospitalized for a first episode of SE between 2012 and 2022. From 2012 to 2019, the standardized incidence decreased annually by 1.9%, from 18.0 to 15.6 per 100,000 (Incidence Rate Ratio [IRR]: 0.981, 95% CI: 0.978–0.984), with a marked decline following the onset of the COVID-19 pandemic (IRR: 0.897, 95% CI: 0.831–0.969). In-hospital mortality was 21.8%, with the strongest predictors being advanced age (Odds Ratio [OR]: 10.3, 95% CI: 7.87–13.8 for age ≥80 vs. 10–19) and hypoxic causes (OR: 15.3, 95% CI: 13.9–16.8). Among survivors, 3-year mortality was 25%, with male sex (Hazard Ratio [HR]: 1.24, 95% CI: 1.19–1.30) and progressive causes as most significant predictors. Recurrence occurred in 16.7% of patients within 3 years, with younger age (HR: 2.21, 95% CI: 1.90–2.58 for age <1 year vs. 10–19), prior epilepsy (HR: 1.73, 95% CI: 1.63–1.84), alcohol use, remote-related causes, comorbidities, and prolonged mechanical ventilation as key factors.
Conclusion: Despite a recent decline in its incidence, SE remains a major public health issue with high initial and long-term mortality and a significant risk of recurrence, particularly in younger patients. Further studies are needed to better identify modifiable factors that could reduce mortality or recurrence, such as therapeutic adherence.

728 | Epilepsy stands nearby: a pilot CT perfusion study on post-stroke non convulsive status epilepticus

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Purpose: To investigate the relevance of hyperperfusion on computerized perfusion imaging (CTP) in the emergency setting in people with non-convulsive status epilepticus (NCSE) and previous stroke, to derive relevant aspects on the epileptogenic focus and the network recruited for NCSE propagation.
Method: We enrolled consecutive adult patients with acute-onset NCSE and a previous stroke at a single institution undergoing CTP and EEG during symptoms. All patients underwent standard imaging including CT, CTP, CT-angiograms, and standard EEG within 30 minutes from hospital arrival. Age/sex matched NCSE without previous stroke cases and recurrent ischemic stroke cases were included to test for accuracy of hyperperfusion rates.
Results: Overall, 15 patients had a previous stroke and developed NCSE (mean age 78 years, 46.7% female). All patients had hyperperfusion on CTP imaging (mean onset-to-CTP 184 minutes). Only one case showed hyperperfusion limited to the previous stroke lesion, and one had a combination of lesional and peri-lesional hyperperfusion. All remaining cases (n=13) had exclusive extra-lesional involvement. Five cases had multiple separated hyperperfused areas, and five had ipsilateral intra-thalamic hyperperfusion. No correlation emerged between onset-to-CTP timing and hyperperfusion (p-value for CTP=0.66, CBV=0.28, MTT=0.28, reverseTmax=0.66). Hyperperfusion was present in NCSE cases only, and in none of age/sex matched ischemic stroke cases (n=18).
Conclusion: Hyperperfusion involves cortical areas external to the previous lesion site during NCSE, supporting the relevance of networks for the spatial evolution of epileptic activity and a limited relevance of the lesion site for the propagation of the epileptiform activity.

887 | Clinical heterogeneity of non-convulsive status epilepticus

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Purpose: Heterogeneous presentations of non-convulsive status epilepticus (NCSE) may be a reason for delayed diagnosis and treatment.
Method: A male aged twenty-one and a female aged 28 years were diagnosed with generalized NCSE, years after the first episode of NCSE. Two female adults aged 49 and 64 were diagnosed with NCSE when they became confused-deliriant. Diagnoses were based on clinical, laboratory, EEG neurophysiological, and imaging evaluations.
Results: Vegetative manifestations (palpitation, dizziness, vomiting) were the main complaints of the 21-year-old male during episodes of slightly disturbed cognition lasting for hours, repeating 7 years before NCSE and GGE diagnosis. EEG showed almost continuous generalized periodic discharges of spike-wave complexes of 2,5-3,5 Hz. Rare GTCS happening after periods of changed behavior (improper emotional or verbal communication) lasting for hours, assumed as focal going to GTCS were treated with CBZ since adolescence in 28-year-old women. EEG done during one such episode showed generalized NCSE. VPA was an effective treatment. Delirium was the clinical manifestation in a 49-year-old female. CT, MRI, and CSF analyses were normal, except for acute viral infection. EEG showed focal NCSE, and the patient completely recovered with ASM. Six years later during pneumonia from COVID-19, she became deliriant again. Additional ASM was effective, the patient recovered from recurrent NCSE. A 64-year-old female with multimorbidity manifested confusion lasting for days. Imaging did not show acute brain lesions. EEG showed NCSE, but the patient did not survive because of heart failure.
Conclusion: Generalized and focal NCSE presents with heterogeneous disturbances of awareness and cognition, accompanied by vegetative and somatic nonspecific symptoms and even delirium. EEG is the most valid tool for disclosing the condition of NCSE leading to appropriate treatment. Unfortunately, sometimes there is a delayed diagnosis and treatment. Increasing the awareness of different clinical presentations of NCSE will improve prompt diagnosis and treatment of NCSE.

914 | New-Onset Refractory Status Epilepticus as a Presentation of Anti-SOX1 Antibody Encephalitis

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Purpose: New-onset refractory status epilepticus (NORSE) is a rare yet critical neurological condition characterized by prolonged, treatment-resistant seizures without an identifiable acute structural, toxic, or metabolic cause.1 Determining the underlying etiology is essential for guiding management and prognosis; however, in nearly half of cases, the cause remains unknown despite comprehensive evaluations. We present the first reported case of anti-SOX1 antibody-associated encephalitis manifesting as NORSE, which showed a favorable response to immunosuppressive therapy."
Method: A 76-year-old man with stage IIIB squamous-cell lung cancer presented with an acute confusional state. Initial evaluations, including blood tests and brain MRI, were unremarkable, while cerebrospinal fluid (CSF) analysis showed mild pleocytosis and elevated protein levels. Electroencephalography (EEG) revealed findings consistent with nonconvulsive status epilepticus. Empirical antiviral and antiseizure treatments were administered, and paraneoplastic and infectious workups were performed.
Results: Despite treatment with intravenous acyclovir, lorazepam, fosphenytoin, levetiracetam, and pregabalin, seizures persisted, occurring once or twice hourly. Anti-SOX1 antibodies were detected in serum on day 7, with negative results for other paraneoplastic and infectious markers. Computed tomography revealed no progression of lung cancer. The patient received intravenous immunoglobulin (400 mg/kg/day for five days), leading to gradual clinical improvement. Follow-up EEG showed resolution of epileptiform discharges, and the patient was discharged on day 15 with complete recovery.
Conclusion: In conclusion, this case suggests that anti-SOX1 antibodies may be associated with NORSE, expanding the spectrum of conditions linked to these antibodies. While anti-SOX1 antibodies are commonly observed in paraneoplastic syndromes, their potential role in autoimmune encephalitis presenting with NORSE should be considered. The absence of antibody titer testing is a limitation, and further studies are needed to clarify the clinical significance of anti-SOX1 antibodies in NORSE and related neurological disorders.

928 | From EMS Call to Initial Medical Care: Analysis and Insights into Response Times in Status Epilepticus Emergencies in Iran

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Purpose: This study aimed to examine the response time of emergency medical services (EMS) in Shiraz, Iran, for seizure calls and the time and actions involved in transporting patients to a hospital.

Method: We investigated all the calls to EMS in Shiraz, Fars, Iran, during one- Persian Solar year starting on 21 March 2022. Refining the calls with the keyword "seizure", we selected those that resulted in patient transportation to a hospital. Patient characteristics, time-related endpoints, and actions taken were consistently documented.

Results: During the study period, the EMS received 3063 calls concerning seizures; 1092 calls (35.7%) resulted in the transportation of the patient to a hospital. The mean (±SD) age of patients was 30.1 (±21.4) years, ranging from neonates to 91 years, with a male predominance (766 cases; 70.2%). While the final diagnosis of all the included patients was seizures, the initial diagnosis over the phone identified seizures in 837 calls (76.6%), loss of consciousness in 195 (17.9%), and other conditions in 60 calls (5.5%). Additionally, 378 patients (34.6%) had a known history of epilepsy. Normally distributed, the mean (±SD) of EMS response time was 15.9 (±7.8) minutes. The EMS response time was under 10 minutes on 221 occasions (20.2%), but no patient reached the hospital in under 10 minutes. Only 27 patients (2.5%) arrived in less than 30 minutes, and 214 patients (19.6%) received first-line treatment (a benzodiazepine) before hospital arrival.

Conclusion: Seizure rescue medications like intranasal, buccal, or rectal benzodiazepines are hardly available in Iran, with EMS relying on intravenous diazepam or midazolam. This may explain the low percentage of patients receiving benzodiazepines before hospital arrival. Improving facilities, infrastructure, and public education on initial seizure care is essential for optimizing care delivery time, as is updating status epilepticus treatment guidelines to align with local healthcare conditions.

934 | Managing Status Epilepticus in Eastern Mediterranean Region (EMR): Current Status and Solutions

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Purpose: The objective of this study is to enhance our understanding of the management of status epilepticus (SE) by employing a comprehensive approach. This was achieved through the distribution of a self-administered questionnaire to key healthcare professionals actively involved in epilepsy care within the Eastern Mediterranean Region (EMR) region [1].

Method: We disseminated a simple questionnaire via email to healthcare professionals involved in epilepsy care across the EMR region [2].

Results: The study included 42 neurologists, specialized in pediatric (50%) and adult (50%) neurology, predominantly in tertiary care settings (54.8%). Most centers had SE treatment protocols (78.6%) and used clinical signs (100%) for seizure monitoring. The availability of intravenous anti-seizure medications (ASMs) varies significantly across EMR countries. Diazepam (93.2%) and phenobarbital (86.4%) are the most commonly available, while fosphenytoin (9.1%) and pentobarbital (34.1%) are the least available. For treating status epilepticus in adults, diazepam is the first choice (40.9%), followed by

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lorazepam (25%). Phenytoin is preferred as the second choice (34.1%). In children, diazepam (36.4%) and lorazepam (29.5%) are preferred. Treatment of refractory and super-refractory status epilepticus often includes ketamine and levetiracetam.

Conclusion: The findings highlight the need for regionally standardized treatment protocols based on ASMs availability. The study provides a comprehensive evaluation of the current state of SE management in the EMR region and proposes targeted and actionable strategies to improve clinical outcomes and optimize patient care across the region.

944 | Peri-Ictal MRI Abnormalities and Frequency of Epileptiform Discharges in Status Epilepticus: A Prospective Study

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Purpose: Peri-ictal MRI abnormalities (PMA) are commonly observed in patients with status epilepticus (SE), but the associated risk factors remain largely unclear. Non-convulsive status epilepticus (NCSE) is primarily diagnosed on EEG based on Salzburg consensus criteria and those of American Clinical Neurophysiology Society (ACNS), specifically by the presence of epileptiform discharges (EDs) of frequencies greater than 2.5 Hz. This prospective MRI study aimed comparing the frequency of EDs in patients with a definitive SE, with and without PMA.

Method: Patients with a definitive SE, who had EDs on EEG, were included in this study. All participants underwent an MRI with a standard protocol, which included among other sequences, diffusion weighted imaging (DWI), fluid-attenuated inversion recovery (FLAIR) and arterial spin labeling (ASL). EDs were manually quantified, and their frequency was calculated.

Results: Between February 2019 and April 2023, 352 patients with a SE underwent an MRI in an acute setting. After excluding patients with an ictal-interictal continuum on EEG (N=55) and those with incomplete MRI protocols or MRIs performed later that 48 hours after the SE onset (N=148), 149 patients with a definitive SE were identified. Among them, 60/149 (40%) had EDs on EEG and were included in the analysis. Median frequency of EDs was 2 Hz (IQR: 1-2.7). PMA were observed in 41/60 (68%) patients, while 19/60 (32%) did not have PMA. The median frequency of EDs in patients with PMA was 2 Hz (IQR: 1-2.5), compared to 2.5 Hz (IQR: 2-3) in those without PMA ($p = 0.07$).

Conclusion: Although the difference in the frequency of EDs between patients with and without PMA did not reach statistical significance, these findings suggest a potential association between PMA and lower frequencies of EDs.

974 | Characterization of the intraamygdala kainic acid model of temporal lobe epilepsy in female mice

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Purpose: Temporal lobe epilepsy (TLE) is the most common and refractory focal epilepsy in adults with a similar prevalence between sexes. Intra-amygdala microinjection of kainic acid (IAKA) in mice phenocopies various features of TLE and is a common model to explore mechanisms of epileptogenesis and evaluate experimental therapeutics. To date, however, the majority of studies with the model have used male mice. The present study aimed to address this gap in preclinical research by characterizing the status epilepticus and associated neuropathological outcomes of the IAKA model in female mice.

Method: Male and female C57BL/6JOlaHsd mice (n=5 per group, 8–12 weeks old) were surgically implanted with EEG recording electrodes and a guide cannula targeting the basolateral amygdala. Forty-eight hours post-surgery, baseline EEG recordings were obtained. Status epilepticus (SE) was induced via intra-amygdala injection of kainic acid (KA; 0.3 μg/0.2 μL) or phosphate-buffered saline (PBS) and mice were monitored using video-EEG. To terminate seizures, lorazepam (8 mg/kg, intraperitoneal) was administered 40 minutes later. Brains were collected 24 h later for histopathological analysis. EEG data were analyzed using LabChart 8 Reader software.

Results: Both male and female mice exhibited similar EEG patterns during the 40-minute SE induction period. Morbidity and mortality were low and comparable between sexes. Histopathological analysis revealed the primary site of neurodegeneration to be the ipsilateral CA3 subfield of the hippocampus in female mice. Preliminary

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longer-term EEG recordings confirmed the occurrence of spontaneous recurrent seizures within a few days of IAKA in female mice.

Conclusion: Female C57BL/6JOlaHsd mice display similar responses to IAKA-induced status epilepticus compared to male mice, with comparable electrographic seizure and neuropathologic outcomes. These findings indicate mice of both sexes can routinely be included in research using the IAKA and the model may facilitate studies of sex-specific mechanisms and therapeutic strategies in treatment-resistant epilepsy.

1005 | Detection and Duration Analysis of Post-Ictal Generalized EEG Suppression with Two-Channel EEG

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Purpose: Sudden Unexpected Death in Epilepsy (SUDEP) is a significant risk for people with epilepsy (PWE). Post-ictal Generalized EEG Suppression (PGES) serves as a potential indicator of this risk. Emerging subcutaneous EEG technology could provide a means to detect PGES in real-world ultra long-term monitoring, but with only two channels. Previous studies focused on PGES detection using scalp EEG. To our knowledge, no prior studies examined PGES detection with a two-channel approach. This study explores the viability of two-channel EEG for PGES identification against background EEG activity. We validate our algorithm on subcutaneous EEG (sqEEG) data recorded by 24/7 EEG SubQ device (UNEEG Medical A/S, Denmark).

Method: Scalp EEG from 44 PWE with 87 seizures were used. Two neurophysiologists reviewed each session for PGES presence and duration. 39 seizures with PGES were annotated with a duration of 27.08±2.60 s (mean±std). FP2-F8 and T8-F8 EEG channels were chosen, aligned with likely location of subcutaneous electrodes. Data was pre-processed according to standard protocols, segmented into 2-second windows, and 15 features were extracted including frequency, time, and signal-shape features. A Variational Autoencoder (VAE) was trained and validated on 5 seizures with PGES recorded using sqEEG.

Results: The performance of our algorithm on test data shows an accuracy of 72% and F1 score of 81%. The algorithm identified PGES in 5 out of 5 sqEEG validation samples, as well as being within 30 seconds of the true duration of the PGES on average.

Conclusion: Our results showed robust and accurate PGES detection from two-channel EEG. We demonstrated the possibility of detecting PGES and its duration from two-channel sqEEG recordings, potentially improving risk management for PWE.

1070 | Cell blood count to predict New-Onset Refractory Status Epilepticus long-term outcomes: a multicenter study

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Purpose: We investigated whether complete blood count (CBC) analyses during ICU stays could predict 12-month outcomes in patients with New-Onset Refractory Status Epilepticus (NORSE).

Method: We studied 39 cryptogenic NORSE patients (20 adults, 19 children) from Baylor College of Medicine (n=16), Pitié-Salpêtrière Hospital (n=13), and Yale University (n=10). We analyzed CBC data collected during ICU stays. Outcomes at 12 months were classified as "unfavorable" (Glasgow Outcome Score [GOS] 1-3) or "favorable" (GOS 4-5). Four periods were defined based on immunotherapy: 1) no treatment (N); 2) first-line immunotherapy, including steroids, IVIG, plasmapheresis (FL); 3) the first two weeks following second-line immunotherapy, including anakinra, tocilizumab, rituximab, and others. (SL1/2) and 4) more than two weeks after second-line immunotherapy (SL3/4). A predictive model based on a decision-tree first identified the most relevant CBC markers for predicting outcomes during each period, with separate assessments for adults and children. Then, the model was trained to predict patient outcomes based on the CBC and the selected markers. Performance was tested using a leave-one-out approach.

Results: A total of 826 CBCs were analyzed (adults: 512, children: 314). Higher neutrophil and lower lymphocyte percentage were generally associated with unfavorable outcomes. Seventeen of the 19 children received second-line immunotherapy. The model predicted outcomes with 100% accuracy for all periods except FL (92%, one patient misclassified favorable). All but one adult received first-line immunotherapy; however, only 7 received second-line treatment. Treatment protocols and initiation times were less consistent than in children. Predictive accuracy ranged from 65% (FL) to 86% (SLs).

Conclusion: CBC data demonstrate potential for predicting NORSE long-term outcomes, with better performance

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in children who have a higher homogeneity in presentation and treatment. Higher neutrophil percentage in patients with unfavorable outcome may reflect active innate immunity; further supporting aberrant innate immune system activation as a potential mechanism underlying cryptogenic NORSE.

1100 | Association of lateralized rhythmic delta activity stereotyped morphology with peri-ictal MRI abnormalities

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Purpose: Ictal-interictal continuum (IIC) is an electrographic term, which includes lateralized rhythmic delta activity (LRDA) of ≥1 Hz with plus modifiers and/or fluctuation. We aimed analyzing EEG features of LRDA indicative of increased metabolic demand and/or neuronal injury during IIC. We hypothesized, that peri-ictal MRI abnormalities (PMA) could serve as an alternative reference standard for assessing the risk of each LRDA subpattern for causing cerebral injury.
Method: We classified IIC LRDA into "high-risk" and "low-risk" LRDA according to the presence of stereotyped patterns. Presence of ≥10% of delta waves with "up" morphology defined "high risk" LRDA. The 10% rule was based on ACNS EEG Terminology criteria for LRDA+S (at least once every ten seconds).
Results: One hundred patients with an LRDA were identified prospectively. We excluded 54 patients from the analysis for following reasons: 1) eventual diagnosis of status epilepticus (n = 10), 2) generalized rhythmic delta activity (n = 15), and 3) other non-LRDA patterns (n = 29). Eventually, 46 patients with LRDA were included into analysis and categorized as 1) "high-risk" (n = 19) and 2) "low-risk" LRDA (n = 27). All patients in "high-risk" group had plus modifiers, but several of "low-risk" LRDA did not (40.7%). The average LRDA frequency was similar in both groups (between 1-2 Hz in 85.2% and 73.7% for "low" and "high-risk" groups, respectively). Reactivity was present in only one patient in "high-risk" group (5.3%) and in 13/27 (48.1%) patients in "low-risk" group. PMA were seen more frequently in "high-risk" group (10/19, 52.6%) as opposed to "low-risk" group (4/27, 14.8%), odds ratio of 6.4 (CI 1.6 – 25.7, p-value < 0.01).
Conclusion: We propose a novel approach for determining "high" and "low" risk features of LRDA in terms of causing potential brain injury indicated by PMA.

1109 | Prognostic Value of Neutrophil to Lymphocyte Ratio in Status Epilepticus: A Retrospective Cohort Study

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Purpose: To assess the impact of neutrophil to lymphocyte ratio (NLR) at admission on the functional outcomes of patients with status epilepticus.
Method: Single-center retrospective study including patients admitted to the hospital due to status epilepticus from 01/01/2018 to 31/12/2023. Demographic, clinical, and paraclinical data were collected from medical records at admission and discharge.
Results: The study included 65 patients, 48.5% were female (n=33), with a mean age of 72.3 ± 16.9 years. Among them, 47 patients presented with convulsive status epilepticus (SE), and 18 had non-convulsive status epilepticus (NCSE). The most common etiologies were cerebrovascular disorders (n=23), infections (n=15), and neurodegenerative conditions (n=8). Six patients had refractory status epilepticus (RSE), and two had super-refractory status epilepticus (SRSE). An NLR ≥4 was associated with worse functional outcomes at discharge (p=0.032). No statistically significant differences in mean NLR values at admission were observed between patients with SE versus SRSE, nor between patients with an infectious etiology versus other causes.
Conclusion: In this cohort of status epilepticus patients, an elevated NLR at admission was associated with worse functional outcomes at discharge. The lack of significant differences in NLR values between infectious and non-infectious etiologies suggests that an infection does not substantially influence the NLR. These findings support the potential utility of NLR as a prognostic biomarker in status epilepticus.

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1110 | Exploring short-term mortality disparities in status epilepticus: a study across two centers in Salzburg and Jakarta

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Purpose: Reducing short-term mortality is the main goal in managing patients with status epilepticus (SE). This study compared factors determining 30-day mortality in two centers.

Method: In prospective patients with convulsive SE (CSE) from Salzburg, Austria (N=134) and Jakarta, Indonesia (N=186), 30-day mortality was compared along with age, SE semiology, level of consciousness (LOC), SE etiology, time to initial treatment, admission to intensive care unit (ICU), needs of mechanical ventilation, length of stay (LOS). LOC was categorized into alert/somnolent and spoor/coma. Etiology was divided based into: 1) Acute-triggering factors (TFE); 2) Acute-primary CNS pathology; 3) Acute-secondary CNS pathology; 4) Acute-toxic; 5) Remote; 6) Progressive; 7) SE in defined electroclinical syndromes; 8) Unknown.

Results: The 30-day mortality rate was significantly higher in Jakarta (43.5%) compared to Salzburg (11.2%), p<0.0001. Patients in Jakarta as opposed to those in Salzburg were younger (median age 46y, 18-81 vs. 66y, 18-96), had higher rates of acute-primary CNS abnormalities (40.9% vs. 7.5%; p<0.0001), lower rates of remote etiologies (7.5% vs. 39.6%,p<0.0001), longer time to treatment (9h, 0.3-156 vs. 0.5h 0.03-96; p<0.0001), longer LOS (median 11 days, 1-77 vs. five days, 1-144; p<0.0001) and lower rate of admission to ICU (39.2% vs. 55.2%, p=0.005). No differences were found in LOC and a need for mechanical ventilation.

Conclusion: Higher short-term mortality in Jakarta, as opposed to Salzburg, may be related to delayed treatment and limited resources (ICU). However, differences in patients' ages and SE etiology may also contribute to the SE outcome.

1123 | Cenobamate for new-onset refractory and super-refractory status epilepticus: a report of four cases

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Purpose: Status epilepticus (SE) represents a critical neurological emergency associated with high morbidity and mortality. Cenobamate (CNB) has demonstrated efficacy in drug-resistant epilepsy, and emerging but limited evidence suggests potential benefits in super-refractory status epilepticus (SRSE). We reported three cases of SRSE and one case of prolonged refractory status epilepticus (RSE) treated with CNB.

Method: Data on patients with RSE or SRSE treated with CNB as an add-on therapy were retrospectively analyzed. We described demographic and clinical characteristics, CSF studies, neuroimaging findings, EEG findings, CNB utilization details, treatment response, and adverse events.

Results: Four cases of new-onset SE were included (one RSE and three SRSE), with a median age of 56.5 years (range:27-84). Etiologies included febrile infection-related epilepsy syndrome, a probable genetic encephalopathy, and two unknown etiologies. CNB was introduced at a median of 22.5 days after SE onset. It was initiated at low doses (median:12.5 mg/day) and titrated per the Summary of Product Characteristics in two cases. In one case, CNB titration was accelerated after reaching 50 mg/day (increments every week); in another case, it was started at 25 mg/day, increased to 50 mg/day on the following day, and to 100 mg/day after three days. The median maintenance dose was 150 mg/day (range:100-400 mg/day). Seizure cessation was achieved in all cases shortly after CNB initiation (range:3-7days), allowing successful weaning from anesthetics. Prognosis varied, with one patient achieving functional independence while three showed poor neurological recovery. In none of the cases, drug reaction with eosinophilia and systemic symptoms or QT interval alterations were observed.

Conclusion: CNB contributed to prolonged RSE and SRSE termination in four cases at low doses with no incidence of severe adverse events. Though promising, further prospective controlled studies are needed to confirm our findings and evaluate CNB's safety, efficacy, optimal timing, dosage, and titration schedules in the context of SE.

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1194 | Similar EEG patterns in different manifestations of NCSE, *true beauty is only skin (EEG) deep*

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Purpose: Non-convulsive status epilepticus (NCSE) is characterized by its heterogeneous nature, with patients displaying a wide range of clinical presentations, typically with minimal signs on examination that there is ongoing seizure activity.
The goal of this presentation is to illustrate the similarities of EEG patterns in different clinical manifestations of Nonconvulsive Status Epilepticus (NCSE).
Method: In this study, we report six patients grouped into three pairs, each presenting with different manifestations of Non-Convulsive Status Epilepticus (NCSE).
Results: The EEG patterns within each pair shared similar morphological features:

- The first pair exhibited generalized polyspike-wave patterns. The first patient was a 43-year-old ambulatory woman with genetic generalized epilepsy, who presented with cognitive and behavioral symptoms (neuropsychiatric presentation) of NCSE. The second patient was a 54-year-old man with focal NCSE, likely due to a small left frontal infarction, who exhibited only mildly increased verbal latency.
- The second pair had generalized polyspikes on a suppressed background. The first patient was a 42-year-old woman who developed NCSE following a cardiac arrest, and she fully recovered after successful treatment of status epilepticus. The second patient was an 84-year-old man, comatose after cardiac arrest, who survived only a few days.
- The third pair demonstrated generalized periodic discharges. The first patient was a 72-year-old woman, conscious but presenting subtle focal motor abdominal seizures following an old right-sided parieto-occipital stroke. The second patient was a 50-year-old comatose man with a post-traumatic right-sided acute extradural hematoma.

Conclusion: Contrariwise to Ictal characteristic patterns in focal epilepsy that have been observed to be highly associated with certain pathologies, the occurrence of varied clinical manifestations within a set of EEG patterns showing similar electrographic features introduces an argument in favor of the statement that several etiologies may have a common EEG expression within the expanded spectrum of Nonconvulsive status epilepticus (NCSE).

1198 | Comparison of outcome of status epilepticus in tuberculous meningitis and scrub typhus

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Purpose: *Orientia* tsutsugamushi and *Mycobacteriun* Tuberculosis, both are bacterial diseases, and manifest with subacute meningoencephalitis. Status epilepticus (SE) is an uncommon manifestation of tuberculous meningitis (TBM-SE) and scrub typhus (ST-SE). There is paucity of information in these areas, and no study has done to compare their treatment response and outcome. We compare the clinical, MRI, and response to antiseizure medication (ASM) in the patients with TBM-SE and ST-SE.
Method: Patients with TBM and ST having SE were included from the prospectively maintained registry. Their clinical severity, MRI and EEG findings, response to ASM, and proportion of patients with refractory and super refractory SE were noted. Outcome at discharge was noted based on modified Rankin Scale.
Results: Twenty-one patients were included; 11 had ST-SE and 10 TBM-SE. The TBM-SE patients were younger ($P<0.01$), had longer duration of illness ($P<0.01$) and longer duration of SE ($P<0.01$). MRI was abnormal in all the patients with TBM-SE; whereas, MRI was normal in ST-SE. In ST-SE, 7(63.3%) patients required 2 ASMs and 4(36.4%) needed 3 drugs for termination of seizure. Whereas in TBM-SE, 7(70%) patients required 3 ASMs, 2(20%) required 4 ASMs and one (10%) required 5^{th} drugs. TBM-SE patients had more frequently refractory (70% vs 36.4%) and super-refractory SE (30% vs 0%) compared to ST-SE. Multiorgan dysfunction was noted in all the patients with ST-SE. Four patients died in TBM-SE and none in ST-SE (40% vs 0%). At discharge TBM-SE had poor outcome compared to ST-SE (40% vs 18.2%; $P=0.01$). Recurrence of seizure after termination of SE occurred in 60% patients with TBM-SE, but none in ST-SE ($p=0.004$).
Conclusion: Status epilepticus in ST is easily treatable and is associated with good recovery unlike SE in TBM, which is often refractory and super-refractory and is associated with higher death and poor outcome.

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1225 | Focal aware status epilepticus: treatment and prognosis in a bicentric study

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Purpose: Focal aware status epilepticus (FASE) is a type of status epilepticus (SE) less defined, with fewer data about its clinical description, treatment (t1, t2) and prognosis, compared to convulsive and non-convulsive SE with alteration of consciousness. We aim to describe a cohort of patients with FASE and identify those variables associated with functional prognosis.
Method: Retrospective study in which the database of patients with FASE between 2019 and 2024 from the Epilepsy Unit of 2 hospitals was reviewed. We analyzed premorbid, clinical, neurophysiological and therapeutic data, evaluating their relationship with functional prognosis at discharge and last follow-up.
Results: 21 patients were included (28.6% female, mean 66.6 years (SD 13.7), median mRS 2). 62% were people with epilepsy and 85.7% had previous structural neurological pathology. 47% presented predominantly motor symptoms. 71% presented a remote symptomatic FASE and 66.7% were caused by pathology associated with poor prognosis (stroke, CNS infection, TBI, brain tumor). Time to EEG was 24 hours [range 2-312]. The most frequent EEG findings were lateralized periodic discharges with or without electrographic seizures (28.6% and 23.8%, respectively). The duration of FASE was 48 hours [24-504]. No patient was treated with sedation. 9.5% died during hospitalization. There was significant functional worsening at discharge and at last follow-up in 38% and 28%, respectively. At discharge, motor FASE was associated with functional stability, whereas aphasic FASE was associated with functional worsening. At last follow-up, aphasic FASE and FASE duration were associated with functional worsening, the latter with an area under the curve of 0.88. For a cut-off point of 60 hours of FASE duration, the sensitivity is 83% and the specificity is 74% in predicting functional worsening.
Conclusion: In our sample, FASE has a mortality and functional prognosis similar to that of SE overall. Longer duration and aphasic FASE are associated with a functional worsening.

1244 | Ictal-interictal Continuum Following Coil Embolization of Cerebral Aneurysms

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Purpose: The ictal-interictal continuum (IIC) has been reported in various clinical conditions, but its relationship with intravascular treatments remains poorly understood. This study reports three cases of IIC following coil embolization (CE) of cerebral aneurysms and evaluates associated outcomes.
Method: A retrospective review of medical records from May 2018 to May 2024 was conducted, focusing on patients with reduced consciousness after CE. IIC was diagnosed based on EEG patterns following the guidelines of the American Clinical Neurophysiology Society. Factors related to outcomes, including IIC development, were analyzed using a multivariable linear regression model with robust standard errors.
Results: Of 30 patients who underwent continuous (3-hour) EEG monitoring post-coiling, three exhibited IIC patterns characterized by lateralized epileptic activity ipsilateral to the coiling site. One patient also displayed repeated electrographic seizures associated with subtle motor phenomena. EEG abnormalities resolved immediately after intravenous benzodiazepines, but coma persisted. Full recovery of consciousness occurred approximately one week after benzodiazepines withdrawal. Adjusting for other risk factors, patients with IIC had a mean Glasgow Coma Scale score 3.13 points higher at 14 days compared to those without IIC (95% CI, 0.43~5.84; p=0.025). Durations of ICU stay (95%CI, -6.30-8.27; p=0.782) and total hospital stay (95%CI, -43.15~20.79; p=0.477) were comparable between groups.
Conclusion: This study highlights IIC as a potential complication of CE. The development of postoperative IIC does not necessarily correlate with worse outcomes.

1262 | Circulating miR-146a and mir-134 as potential therapeutic biomarkers in Refractory Status Epilepticus – an exploratory study

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Multidisciplinary Research In Biomedicine of Abel Salazar School of Medicine and Biomedical Sciences - University of OPorto (UMIB/ICBAS-UP), Oporto, Portugal, [5]Santa Maria Health Local Unit – Santa Maria Hospital (ULS-SM), Lisbon, Portugal, [6]Intensive Medicine University Clinic of Lisbon School of Medicine – University of Lisbon (CUMI/FML-UL), Lisbon, Portugal

Purpose: Refractory Status Epilepticus (RSE) is defined by persisting electroclinical/electrographic seizures despite intravenous therapy with two anti-seizure medication (ASM), including a benzodiazepine. The therapeutic approach includes underlying cause treatment, other ASMs and intravenous anesthetic therapy (IVAT). In clinical practice, biomarkers for RSE treatment are needed, aiming for its effective reversal and diligent IVAT reduction. MicroRNAs (miR) have been identified in epileptogenesis, including refractory epilepsies, with promising roles as diagnostic, prognostic and therapeutic response biomarkers. Previous studies, animal model of RSE and SE patients, reported miR upregulation. However, serum miR in RSE clinical model have not been studied. Our aim is to evaluate circulating levels of miR-146a and mir-134 in patients under IVAT for RSE treatment.

Method: MiR-146a and miR-134 were quantified by real-time PCR in serum of adult patients with optimized IVAT for RSE treatment (EEG validated) and healthy individuals. Anoxic etiology was excluded. Relative expression values were calculated using $2^{-\Delta\Delta CT}$ method and compared with controls (Mann-Whitney and T-Student, $p<0.05$).

Results: MiR circulating levels were quantified in 19 patients (8.53±15.70 years), 84,21% with electroclinical status epilepticus and 15,79% with electrographic status epilepticus, and 10 healthy individuals (27.60±12.00 years). RSE patients with optimized IVAT dose presented downregulated serum levels of miR-146a (20-fold lower ($p<0,001$) and miR-134 (3-fold lower,$p<0,001$).

Conclusion: In this work, a significant downregulation in serum levels of miR-146a and miR-134 was demonstrated in optimized IVAT for RSE treatment, contradicting miR upregulation stated in SE, both in animal and human models. We postulate that our results are due to the therapy established for RSE, reflecting the importance of intervention models in mechanisms of neuroinflammation, neuronal excitability and dendritic spine morphology. Future work should analyze the role of miRs as RSE therapeutical response biomarkers. Acknowledgments: H&TRC authors gratefully acknowledge the FCT/MCTES national support through the UIDB/05608/2020 and UIDP/05608/2020; IDI&CA-2022 (IPL/2022/PRSE1_ESTeSL), LPCE-2023 Scientific Grant.

1306 | Cenobamate for the treatment of focal-onset refractory and super-refractory status epilepticus. A multicenter case series

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Purpose: To evaluate the effectiveness and safety profile of cenobamate (CNB) for the treatment of focal-onset refractory (RSE) and super-refractory status epilepticus (SRSE) under clinical practice conditions

Method: This is a retrospective, multicenter, observational study of adult patients diagnosed with RSE and SRSE treated with CNB between January 2022 and December 2024. We collected characteristics of status epilepticus (SE), antiseizure medications (ASM), CNB starting and effective dosage (mg). Response was defined as clinical and/or EEG cessation. Secondary variables were the occurrence of adverse events (AEs), mortality, and SE recurrence.

Results: We included 13 patients with a median age of 55 years (IQR 30-74), 54% were women, 62% had a previous diagnosis of epilepsy. SE presented with prominent motor symptoms in 9 patients and the most prevalent EEG pattern was lateralized periodic discharges (70%). Eight patients met criteria for SRSE. CNB was started within a median period of 4 days (IQR 1-20) from SE onset, after median number of 5 (IQR 4-6) ineffective ASM, at a median dosage of 50mg (IQR 19-50). In 8 patients, it was used as fourth line after anesthetics failure. Treatment was effective in 11 patients (85%) at a median dosage of 50mg (IQR 25-50), and response was achieved with a median delay of 1 day (IQR 1-6). Seven patients responded to an initial increased dosage (median 50mg) without further titration. Mild AEs were described in 7 patients (5 somnolence, 2 transient elevation of aminotransferases) and none presented skin reactions. Four patients (33%) died during hospitalization due to causes not related to CNB. After a median follow-up of 233 days (IQR 100-502) 100% of survivors retained CNB and 2 (25%) presented SE relapse

Conclusion: Cenobamate can be a safe and effective option for the treatment of focal-onset RSE and SRSE. Confirmation of these results in larger samples and randomized interventional designs is warranted

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1327 | Status Epilepticus in Adults with Developmental and Epileptic Encephalopathies

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Purpose: Developmental and epileptic encephalopathies (DEEs) are a group of severe epilepsy syndromes with a wide phenotypic spectrum, typically characterized by frequent seizures of multiple types, and developmental regression or slowing. While Status Epilepticus (SE) is common in DEEs during childhood[1], its occurrence and types in adults with DEE has been less investigated.
Method: We analyzed prospectically acquired data form the Modena Status Epilepticus Registry (MoSER) from 2015 to 2024 (10 yrs). This cohort study aimed to estimate the proportions of adults' patients with convulsive status epilepticus (CSE) and nonconvulsive status epilepticus (NCSE) associated with DEEs who required access to the hospital.
Results: 823 SE episodes in 719 patients were recorded. We observed 20 SE episodes (2.4% of the total) in 9 (6 female) adults DEEs (1.2% of the cohort) during the 10-year study period. Mean age at last SE was 30 yrs; 6 out of 9 patients had recurrent SE episodes. According to semiology 13 episodes were CSE (13 generalized CSE; 3 myoclonic SE), 7 were NCSE at onset. Median SE duration was 2 days. According to treatment response 50% were refractory SE, and ICU was required in 45% of episodes. No death was observed at 30 days. A genetic etiology of DEEs was found in 5 cases: NEXMIF, CHRN4, FADD, KMT5B, chrom. 3 duplication. Regarding clinical phenotypes 2 patients had Lennox-Gastaut Syndrome, 1 Eyelid Myoclonia with Absence Syndrome, while the other 6 patients showed mixed focal and generalized seizure types.
Conclusion: The occurrence of SE requiring hospital admission in adults with DEEs is a rare event with an approximate incidence of 1-2% compared to all SEs in adulthood. In these patients, however, SE tends to be refractory, requiring ICU in 50% of cases, and episodes of SE recur multiple times. A genetic etiology has been identified in more than 50% of cases.

1413 | Favorable outcome in the case of an adult male with prolonged myoclonic status epilepticus following out-of-hospital resuscitation

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Purpose: Myoclonic status epilepticus after cardiac arrest resuscitation is a rare, severe complication, usually with poor outcomes.
Method: We present the case of a 49-year-old male with multiple comorbidities (obesity, hypertension, dyslipidemia, atrial fibrillation), who suffered a cardiac arrest.
Results: He was resuscitated by the ambulance for 15 minutes and transported to the emergency department with cardiogenic shock. Coronarography revealed no occlusions and the patient was admitted to the ICU in a coma, with facial myoclonia, which were controlled with iv Diazepam, followed by sedation with Propofol. Despite intensive therapy, including Levetiracetam and Phenytoin, the patient exhibited persistent generalized myoclonia. Repeated MRIs showed no intracerebral lesions. EEG on day 14 revealed myoclonic status epilepticus, prompting the introduction of Valproate and Phenytoin withdrawal. On day 16, sedation was gradually withdrawn, and Clonazepam was added for persistent, rarer myoclonia. Reevaluation on day 18, found a conscious patient, with tetraparesis and aphasia. He required a cardiac defibrillator implantation and, over the following weeks, slowly recovered. On day 56, the patient was transferred to a rehabilitation clinic. Follow-up evaluations at 3 and 6 months revealed continued improvement to dysarthria and hemiparesis. The myoclonia reappeared around 2 months after ICU discharge solely related to emotional stress. The EEGs revealed rare, generalized epileptiform discharges with associated upper limbs myoclonia over a normal background rhythm.
Conclusion: Prolonged myoclonic status epilepticus as a manifestation of post-anoxic encephalopathy is usually associated with an unfavorable outcome, especially in patients with prior multiple comorbidities. Careful treatment adjustments and intensive rehabilitation facilitated the patient's successful recovery.

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1432 | Frontal meningoencephalocele as a cause of super-refractory status epilepticus: a unique case report

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Purpose: Meningoencephalocele is defined as the herniation of brain tissue through a defect in the skull. It is known to cause focal epilepsy, particularly when located in the temporal lobe. To our knowledge, this is the first reported case of a patient developing status epilepticus (SE) due to an encephalocele.
Method: We present a case involving a previously healthy 31-year-old woman, at 32-weeks of gestation, who experienced sudden-onset recurrent bilateral tonic-clonic seizures.
Results: The patient presented at the emergency room with new onset recurrent bilateral tonic-clonic seizures. Upon admission, the electroencephalogram (EEG) showed epileptic discharges originating from the right frontal lobe and spreading to both hemispheres. Magnetic Resonance Imaging (MRI) of the brain revealed herniation of the right inferior frontal gyrus into the anterior ethmoid sinus, with a corresponding bone defect. Despite receiving treatment with four anti-seizure medications (ASM), the patient needed to be sedated and intubated. She developed focal to bilateral convulsive super-refractory status epilepticus (SRSE), which necessitated an acute Caesarean section that was performed without complications. After three additional days of optimizing ASM and escalating sedation, the EEG no longer showed epileptic activity. Ultimately, she was discharged from the hospital on a maintenance regimen of four ASM; since then, she has remained seizure-free. Approximately six months later, the bone defect was closed endoscopically and the herniating part of the frontal cortex was resected, given the risk of infection and recurrent seizures. The patient has remained seizure-free under treatment with one ASM.
Conclusion: This is the first case report demonstrating that SE can arise from an encephalocele. Notably, the encephalocele was located in the frontal lobe and resulted in SRSE. In summary, an encephalocele can not only lead to seizures but can also be the cause of a first presentation of SE, including SRSE, in a previously healthy patient.

1434 | A clinical and electrographic evaluation of new-onset refractory status epilepticus (NORSE) compared with non-NORSE RSE

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Purpose: This study characterizes the demographics, clinical outcomes, and prognostic factors of new-onset refractory status epilepticus (NORSE) compared to non-NORSE RSE. By distinguishing between NORSE cases with identified etiologies and those that remain cryptogenic (c-NORSE), this study aims to enhance understanding, refine classification and prognostication of RSE, particularly NORSE, and assess clinical relevance and treatment approaches.
Method: Data from 81 RSE patients admitted to the intensive treatment unit (ITU) at The National Hospital for Neurology and Neurosurgery and University College London Hospital (2007-2023) were used to curate a retrospective clinical-EEG dataset. Patients were categorized into NORSE and non-NORSE groups, with subgroups for c- and etiology-NORSE. Key clinical outcomes, including mortality, cognitive impairment, and long-term care needs, were assessed, alongside treatment factors like ITU length, AED use, sedative requirements, and EEG characteristics to identify prognostic indicators.
Results: Among the 29 NORSE cases, 15 remained cryptogenic, with the most identified etiologies being autoimmune encephalitis (20.67%) and infectious (17.24%). Poor outcome and mortality did not significantly differ between NORSE and non-NORSE RSE, although NORSE patients required significantly longer ITU stays, and higher use of AEDs and sedatives. C-NORSE had a mortality rate 2.8 times higher than etiology-NORSE and was associated with poorer outcomes. EEG findings indicated that lateralized periodic discharges and higher seizure frequency throughout admission were linked to poor outcomes, whilst more AEDs and sedatives at admission correlated with better outcomes.
Conclusion: The findings highlight the significant impact of NORSE, with a mortality of 13.8% and cognitive impairments affecting over 85% of cases, irrespective of an etiology being identified. The outcome difference between c-NORSE and etiology-NORSE highlights the importance of diagnosis and prognosis across NORSE etiologies. Furthermore, with over half of NORSE cases remaining cryptogenic, it questions the utility of 'NORSE' as a distinct clinical entity to immune-mediated RSE underscored by challenges in etiology identification.

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1542 | Predictive Factors of Refractoriness in Status Epilepticus - A Retrospective Study

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Purpose: Status epilepticus (SE) is defined as the persistence of self-sustaining epileptic activity. Refractory SE (RSE) occurs when seizures fail to respond to optimized therapy with first- and second-line antiepileptic drugs (AEDs) and is associated with high morbidity and mortality, with few patients regaining their baseline functional status. Identifying modifiable factors that predict RSE progression is crucial in clinical practice. This study aims to determine predictive factors for refractoriness in SE.

Method: We conducted a retrospective study analyzing potential predictive factors for refractoriness in SE, in patients admitted with SE from 2019 to 2024. Descriptive and statistical analyses were performed.

Results: Among 158 patients (87 men; mean age: 69.5 ± 16.9 years), 57.6% progressed to RSE. Non-convulsive SE was the most frequent presentation (44.3%). The average score on the "Status Epilepticus Severity Score" (STESS) at admission was 3.57 ± 1.66. Cerebrovascular disease was the most common etiology for SE (26.6%). Progression to RSE correlated positively with higher STESS scores ($p < 0.05$), infections ($p < 0.05$), and metabolic decompensations ($p < 0.05$). Notably, the use of levetiracetam as first-line therapy was associated with a lower risk of progression to RSE ($p < 0.05$). Age, etiology, semiology, and time to treatment initiation were not statistically significant predictors.

Conclusion: As designed, the STESS scale effectively identifies patients at higher risk of progression to RSE, facilitating early intervention. The association of infections and metabolic decompensations with RSE suggests these factors may prolong SE duration, warranting targeted management. Additionally, levetiracetam's association with reduced refractoriness highlights its potential as a preferred first-line AED in SE treatment. These findings provide valuable insights for optimizing SE management and improving patient outcomes.

1650 | Accelerated brain atrophy during new-onset refractory status epilepticus

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Purpose: Status epilepticus (SE) has long been implicated in causing neuronal damage, yet direct human evidence remains scarce. We investigated the extent of brain atrophy in new-onset refractory SE (NORSE), a rare and severe form of SE.

Method: This multicenter, longitudinal study analyzed 2,055 MRI scans from 559 participants, including 33 NORSE patients (with 48 scans in the discovery cohort and42 scans in the replication cohort) and 526 controls in 6 groups (healthy controls, epilepsy with brief seizures, autoimmune encephalitis, severe subarachnoid hemorrhage, mild cognitive impairment, and Alzheimer's disease). We quantified grey matter volume and cortical thickness changes using longitudinal MRIs and performed histological analyses on brain biopsies.

Results: Brain atrophy during NORSE in the discovery cohort was markedly accelerated ($p<0.001$ for all comparisons) compared to normal aging (80-fold), epilepsy with brief seizures (70-fold), and common neurodegenerative conditions (20–30-fold; Alzheimer's disease and mild cognitive impairment). It also exceeded rates observed in inflammatory conditions such as autoimmune encephalitis (50-fold) and prolonged ICU treatment scenarios such as severe subarachnoid hemorrhage (30-fold), suggesting a direct contribution of SE to atrophy in NORSE. Histology confirmed severe neuronal loss and reactive astrocytosis. These findings were consistent across multicenter external validation in the replication cohort and several secondary analyses. The atrophy was widespread, irreversible, and regionally linked to SE duration and long-term outcome. Cryptogenic NORSE was associated with especially accelerated atrophy, whereas propofol treatment appeared to slow the rate of atrophy.

Conclusion: NORSE is associated with severe, irreversible brain damage, primarily driven by prolonged seizure activity. Early termination of SE may be crucial to limit irreversible injury. Serial MRI offers a promising framework for investigating neurodegeneration in SE and may represent an initial step toward developing neuroprotective interventions.

1742 | Refractory Status Epilepticus outcome – A retrospective study from a Portuguese Hospital

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Purpose: Refractory Status Epilepticus (RSE) is a severe neurological emergency characterized by refractoriness to initial anti-seizure medications (ASM) and often requiring intravenous anesthetics therapy (IVAT) in an intensive care unit (ICU) setting. Despite previous efforts, biomarkers of successful RSE reversal are still lacking. Aim: study clinical predictors of successful IVAT weaning off and outcome in patients with RSE under IVAT.

Method: Retrospective study including RSE adult patients, under optimized IVAT for at least 72h, between November-2017 and December-2018. Clinical and functional outcome (mRS) data were collected at ICU discharge and last follow-up time. The association between clinical variables, successful IVAT weaning-off and functional outcome was analyzed using statistical method.

Results: 32 patients (mean age 67,6years; mean time follow-up 17months) were included and 58 IVAT weaning-off attempts analyzed, of which 41,3% were successful. All patients with previous epilepsy diagnosis had successful IVAT weaning-off attempt (p=0,022). However, no clinical factor was found to be an independent predictor of successful IVAT weaning-off, in our binary-logistic regression model. At ICU discharge, 96,6% patients had mRS >2, 36,2% had died, and there was a positive association between mRS score and age (p=0,000), RSE type (p=0,004; mostly focal-motor RSE) and etiology (p=0,006), number of ASMs (p=0,004), treatment with LCS (p=0,000) and VPA (p=0,004) and STESS score (p=0,000). At last follow-up, 90,9% patients had mRS >2, 86,4% had died and there was an association between mRS score and RSE etiology (p=0,049; mostly acute-symptomatic) and CNS infection (p=0,022).

Conclusion: This study shows negative outcome associated with RSE. Successful IVAT weaning-off was more frequent in epilepsy patients. RSE patients' functional outcome was associated with multiple clinical factors, although identification of independent predictors was not possible. Larger, prospective and multimodal studies are needed to better understand refractory forms of RSE and outcome predictors. Acknowledgments: H&TRC authors gratefully acknowledge FCT/MCTES national support through UIDB/05608/2020 and UIDP/05608/2020.

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1745 | Clinical characteristics and prognosis of Super-Refractory Status Epilepticus: Insights from a Single-Centre Observational Study

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Purpose: Super-refractory status epilepticus (SRSE) is defined as persistent status epilepticus lasting more than 24 hours after the first administration of general anesthesia. It is associated with high morbimortality. This study aims to investigate the clinical characteristics, prognostic factors and complication rates associated with SRES's intensive management.

Method: A retrospective study of Intensive Care Unit (UCI) SRSE patients in Unidade Local de Saúde de São José in Lisbon from Jan. 1, 2021 to Dec. 31, 2024 was conducted. Data was collected from patients' electronic medical records and the following variables were recorded: demographics, clinical characteristics, treatment, clinical and functional outcomes (modified Rankin Scale - mRS).

Results: A total of 36 patients were included (21 male, 15 female, average age 57.1), with 3 still hospitalized. Tonic-clonic seizures semiology (72%) was dominant. Epilepsy decompensation due to medical complications or therapeutic deficit was the main etiology (31%), followed by cerebrovascular disease (19%). The average duration of status epilepticus was 12 days, with an average of 12 days of invasive mechanical ventilation and 19 days in the ICU. Infectious complications were the most common (n=25, 80,65%). In-hospital mortality rate was 42%, excluding the 3 patients still hospitalized. Most of the surviving patients were discharged to another hospital (33%). A good baseline functional status (mRS 1-3) was observed in 89% of patients at admission and 21% at discharge. Female sex (OR = .118, p = .050) and longer time until treatment (χ-squared = 4.073, p = .069) presented a statistically significant association with worse mRS functional outcome compared with pre-hospital admission. Thiopental use was borderline significant.

Conclusion: In our sample, treatment timing was the most relevant modifiable prognostic factor in the management of SRSE. Further research with larger samples is needed to explore variables with borderline significance, particularly the potential negative prognostic role of drugs such as thiopental.

1760 | Neuroprognostication after cardiac arrest: the added value of a standardized EEG reactivity protocol

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Purpose: This pilot study aims to evaluate the applicability and the prognostic accuracy of a standardized EEG reactivity protocol in comatose post-cardiac arrest (CA) patients, comparing its predictive value to conventional unstructured reactivity assessments.

Method: We designed a standardized multimodal sensory stimulation protocol to systematically assess EEG reactivity. This protocol consist of a structured and reproducible sequence of graded stimulations applied during EEG recording. We prospectively enrolled a cohort of 117 patients in comatose state following CA and undergoing Video-EEG evaluation within 72h after CA, between December 2020 and January 2025. Among them, 58 were evaluated using the new standardized protocol, while 59 received conventional unstructured sensory assessment. The main outcome was in-hospital survival.

Results: Overall, EEG reactivity showed a strong association with survival (χ^2=46.22, p <0.001), with sensitivity 89.7%, specificity 73.5%, negative predictive value (NPV) 83.7%, and positive predictive value (PPV) 82.4%. The standardized protocol demonstrated higher sensitivity (93.5%) and NPV (90%) but lower specificity (69.2%) and PPV (78.4%) in predicting outcome compared to the unstructured reactivity assessments (sensitivity 86.1%, specificity 78.3%, NPV 78.3%, PPV 86.1%). The AUC-ROC was 0.814 for the standardized protocol versus 0.822 for the conventional protocol, with no significant difference between them. Logistic regression confirmed EEG reactivity as a strong independent predictor of survival (OR=26.6, p<0.001). Evaluation of reactivity prognostic accuracy after exclusion of patients with highly malignant EEG patterns, and inter-rater agreement before and after protocol implementation with Cohen k will be discussed.

Conclusion: This pilot study provides preliminary evidence that a standardized EEG reactivity protocol enhance overall sensitivity in identifying comatose post-CA patients with a favorable outcome. The use of a standardized stimulation procedure is expected to improve inter-rater agreement. Implementing a standardized EEG protocol could be pivotal in refining stratification of patients with a more uncertain prognosis, particularly those with intermediate malignant EEG pattern.

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1820 | Status epilepticus at a Tertiary Neurology Care Center in Mexico: A retrospective cohort from 2020 to 2024

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Purpose: Describe the clinical and demographic characteristics of patients with SE in a tertiary neurology care center in Mexico.
Method: In this retrospective cohort, we included patients aged 18 years or older with SE treated in the National Institute of Neurology and Neurosurgery "MVS" emergency department in Mexico between January 2020 and December 2024.
Results: A total of 90 patients were included, with a mean age of 42 years (±18.2). Of these, 49 were men (54.4%). The leading cause of SE was infectious diseases (n=31, 34.4%), followed by unknown etiologies (n=16, 17.8%). Sixty-seven patients (74.4%) had a prior epilepsy diagnosis. Twenty-five patients (27.8%) were on monotherapy with a single antiseizure medication as part of their regular treatment. Epilepsy surgery history was reported in 10 patients (11.1%), including total callosotomy (n=3, 3.3%) and partial callosotomy (n=2, 2.2%). Refractory SE developed in 36 patients (40%), necessitating third-line antiseizure medications. In-hospital mortality occurred in 6 patients (6.7%). (Table 1). Sixty-four patients (71.1%) had an STESS score of 0–2, 16 patients (17.8%) had an STESS score of 3, and 10 patients (11.1%) had an STESS score of 4–6. At discharge, 49 patients (55.1%) had a favorable neurological outcome at 1 month (mRS 0–2), while 34 patients (38.2%) had a significant neurological disability (mRS 3–5) (Table 1).
Conclusion: The findings highlight the severity distribution of SE cases, the prevalence of refractory status epilepticus, and the mortality and neurological outcomes associated with different severity levels. Further studies with larger cohorts are needed to optimize management strategies and improve patient prognosis in Mexico.

SUDEP and Mortality

491 | KEBIBO: Known Epileptics Better Informed for Better Outcomes

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Purpose: This study evaluates the gaps in communication and information dissemination during hospital admissions for seizures among epilepsy patients. The primary aim was to implement structured approaches within clinical systems (ICE and Nervecentre) to ensure comprehensive and consistent discharge communication, enhancing patient empowerment and safety while reducing readmission risks.
Method: Data was collected through patient interviews (n=15, representing 18 admissions) and retrospective clinician documentation reviews. Patients were questioned on key aspects such as driving advice, safety precautions, awareness of SUDEP (Sudden Unexpected Death in Epilepsy), local team involvement, and satisfaction with communication during their admission. Clinicians' discharge documentation was evaluated for content, including safety advice, medication changes, and follow-up coordination. Pre- and post-intervention questionnaires and data collection tools were developed to assess the impact of implemented changes.
Results: Patient feedback revealed significant deficiencies: only 5/18 admissions included driving advice, and no patients received written safety precautions. Awareness of SUDEP was low, with only 5/15 patients familiar with it, and none recalled it being discussed during admission. Local neurology teams were documented as involved in 7/18 cases, though only 5/17 patients were aware of this involvement. Medication changes were made in 10/18 cases but were discussed with the patient in only three instances. Qualitative feedback emphasized the need for clearer communication, personalized care, and written materials to aid memory.
Conclusion: The study highlighted critical communication gaps in epilepsy care during hospital admissions. Implementing automated, structured discharge options in ICE and Nervecentre ensures essential safety advice, SUDEP discussions, medication changes, and follow-up coordination are consistently documented and communicated. This initiative aims to standardize care, empower patients, and reduce adverse outcomes and readmissions. Future evaluations will assess the intervention's impact

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on patient satisfaction and clinical outcomes, with findings intended for publication to inform broader practice improvements.

573 | Stiripentol prevents seizures and associated death in a mouse model of SUDEP

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Purpose: Sudden unexpected death in epilepsy (SUDEP) is a dramatic outcome for epileptic patients, with a prevalence of 1 per 1000. Stiripentol (STP, Diacomit©) is an antiseizure medication indicated for Dravet syndrome, a rare developmental and epileptic encephalopathy with high mortality rate (15 per 1000), in which SUDEP accounts for about 2/3. Here, we evaluate the effects of STP using in a preclinical model of audiogenic seizure-induced death.
Method: We used the inbred mouse strain DBA/2 to evaluate STP effects at different concentrations and various delays between administration and stimulation. Plasma and brain levels of STP were measured by UV-HPLC to evaluate its effective concentrations against seizures and death.
Results: STP prevented tonic-clonic seizures and associated death in a dose-proportional manner, when audiogenic seizures were induced 30 min after STP systemic administration. The median effective concentration of STP (75 mg/kg) prevented tonic seizures between 30 min and 4h and prevented death up to 2h. The efficacy of STP was associated with high plasma and brain levels at 1h. The ratio between brain and plasma levels was about ¼.
Conclusion: In addition to its antiseizure effects, STP has a potent impact against epilepsy-related death. The present results suggest that STP has direct pharmacodynamic protective effects. The high STP levels measured in plasma and brain indicate that its effects against seizures and SUDEP probably involve several mechanisms of action.

652 | Effect of epileptogenicity on central respiratory chemoreception and heart rate

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Purpose: Central apnea and associated cardiac abnormalities are considered key contributors to Sudden Unexpected Death in Epilepsy (SUDEP). Dysregulation of central CO_2 chemoreception (CCR), the system responsible for detecting changes in PCO_2 levels, is hypothesized to contribute to SUDEP, alongside autonomic dysfunction. CCR, which can be accessed via the ventilatory response to hypercapnic challenge, has not been previously examined during epileptogenesis in a chronic model of temporal lobe epilepsy, where SUDEP can occur. This study aims to evaluate cardiorespiratory responses to acute hypercapnia throughout epileptogenesis in the kainic acid (KA) model.
Method: Sprague-Dawley KA rats were intrahippocampally injected with KA to induce spontaneous seizures, which progressively increase in frequency and severity before stabilizing after 4 months. Cardiorespiratory responses to hypercapnia were assessed pre-injection and monthly for 6 months post-injection. Photoplethysmography was employed to measure interictal ventilatory frequency (fB) and heart rate (HR) at baseline, during, and after a 1-hour 10% CO_2 challenge. Electroencephalography was utilized to monitor epileptogenesis and evaluate epilepsy severity.
Results: The results revealed no differences in baseline fB and HR across the months. However, the fB response to 10% CO_2 was significantly reduced at the third and fourth months compared to baseline ($p<0.01$ and $p<0.0001$, respectively; 2-way ANOVA, Fisher's LSD test). Similarly, the HR response to 10% CO_2 was significantly diminished at the first, third, and fourth months compared to baseline ($p<0.05$, $p<0.0001$, and $p<0.0001$, respectively; 2-way ANOVA, Fisher's LSD test). These findings suggest that in the chronic KA model, epileptic rats exhibit a progressively impaired cardiorespiratory response to hypercapnia.
Conclusion: These findings model and help to understand the high-risk breathing disturbances that are observed among SUDEP cases and facilitate future studies to investigate where in the brainstem these dysfunctions originate.

700 | Incidence and circumstances of sudden unexpected death in epilepsy (SUDEP) in the young Australian community

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Purpose: We examined the contribution of sudden unexpected death in epilepsy (SUDEP) in the young Australian community using a state-wide out-of-hospital cardiac arrest registry.

Method: All presumed out-of-hospital sudden cardiac arrests aged 1–50 years with a history of epilepsy or seizures within the ongoing, prospective, multisource End Unexplained Cardiac Death (EndUCD) registry between April 2019 and August 2022 were reviewed. Cause of death was determined by a multidisciplinary panel with expertise in SUDEP. To calculate the incidence of SUDEP, we used epilepsy prevalence estimates. We compared the characteristics of SUDEP cases with autopsy confirmed cardiac and unascertained deaths.

Results: The multidisciplinary panel identified 111 SUDEP cases (64 definite, 12 probable, 24 possible, and 11 fatal near) from 2625 young out-of-hospital sudden arrests (4.2%). The incidence of definite and probable SUDEP was 0.98 (95% confidence interval [CI], 0.61–2.50) per 1000 person-years. Most definite and probable SUDEPs 58/76 (76.3%) were deceased prior to ambulance arrival. Of those 18 SUDEPs who were alive upon ambulance arrival, 12 (61.1%) had asystole, 3 (16.7%) had pulseless electrical activity, and 2 (11.1%) had ventricular tachycardia and fibrillation. Most definite and probable SUDEPs were asleep 41 (53.9%) or sedentary 19 (25.0%) at the time of death, only 16/74 (21.6%) had all prescribed antiseizure medication (ASM) levels within the therapeutic range at the time of death, and only 20.8% (10/48) were seizure-free in the 12 months preceding death. SUDEP was only reported in 43/76 (56.6%) cases by pathologists.

Conclusion: SUDEP accounted for 13.8% of young sudden deaths undergoing autopsy in Victoria. Our findings reinforce that seizure control and adherence to ASM therapy are major modifiable clinical risk factors for SUDEP. The differences in attribution of cause of death between pathologists and epileptologists highlight the need for consensus and raise the possibility that an important cause of arrest may be under-appreciated.

912 | A Retrospective Claims Study Evaluating Mortality in Patients with Lennox-Gastaut or Dravet Syndromes in the United States

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Purpose: Lennox-Gastaut syndrome (LGS) and Dravet syndrome (DS) are rare developmental and epileptic encephalopathies characterized by pharmacoresistant seizures and cognitive impairment. Mortality rates in LGS and DS have been reported as 15.84/1000 and 6.12/1000 patient-years, respectively, however real-world mortality data are limited. We analyzed real-world mortality in patients with LGS or DS in the US.

Method: This retrospective analysis identified US patients diagnosed with LGS or DS from October 01, 2015, to December 31, 2023, using Real Chemistry's open claims database. Patients were included if they had ≥2 LGS or DS claims in the study period and were categorized as deceased if they had a date of death (DOD) after October 01, 2015, and ≤60 days from their last claim to DOD. Outcomes analyzed included annual all-cause case fatality and crude mortality rates (primary), comorbidities in patients with vs. without a mortality event, and SUDEP-related fatality rates. Standardized mortality ratios (SMRs) were reported.

Results: In total, 29,626 patients with LGS and 2259 patients with DS were included; of those, 2509 (8.5%) and 52 (2.3%) had a mortality event, respectively. The yearly adjusted case fatality rate for LGS was 4.2%-6.2% from 2016-2023; the SUDEP-related rate was 1%-2%. LGS SMR was 4.98-6.14; adjusted crude mortality rates ranged from 41.8-62.5/1000 patient-years. Feeding difficulties and cardiovascular/respiratory complications were significantly associated with mortality in LGS. In patients with DS, the 5-year adjusted case fatality rate was 8.6%; the SUDEP-related rate was 2.1%. DS SMR was 2.11-3.96 from 2020-2022; 5-year adjusted crude mortality rate was 17.28/1000 patient-years. From 2019-2023, encephalopathy and feeding difficulties were significantly associated with mortality in DS.

Conclusion: These data provide real-world estimates of LGS and DS mortality and SUDEP-related mortality rates from claims data. In both LGS and DS, feeding difficulties were associated with increased mortality rates. UCB-supported.

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1057 | Assessing the impact of SUDEP risk on families of people with Developmental and Epileptic Encephalopathies (DEEs)

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Purpose: Developmental and Epileptic Encephalopathies (DEEs) are a group of rare and severe neurological disorders characterized by early-onset epilepsy, significant neurodevelopmental slowing or regression, and cognitive and behavioral impairments. Sudden Unexpected Death in Epilepsy (SUDEP) is the first cause of death in people with epilepsy.
Method: An anonymous survey was created to evaluate the level of knowledge that families have about SUDEP, how they obtained the information, and how they are managing this risk. The questionnaire has been translated into 14 languages and disseminated internationally. Data were analyzed using summary statistics for categorical and continuous variables.
Results: Most caregivers did not receive information about SUDEP from a healthcare professional. The time between the onset of seizures and the communication of SUDEP risk was deemed adequate by most caregivers. The interaction during the communication of the SUDEP risk was described as very unpleasant. Despite more than half not having received specialized training and information on the topic, respondents reported a high level of awareness about SUDEP. The most common feelings expressed by caregivers were fear, worry, sadness, and uncertainty, with many reporting daily thoughts about the risk of SUDEP. Despite this, almost no caregiver had received emotional support regarding SUDEP risk. Approximately half of the caregivers took preventive measures to reduce the risk of SUDEP; however, half of them did not receive financial support and these measures did not reduce their concerns.
Conclusion: The results obtained on the study help to better understand families' unmet needs in SUDEP risk, evaluate its major impact on their QoL, and determine if they are currently taking any specific preventive measures, which is crucial to develop more effective and personalized intervention strategies. Funding: UCB IIS-2024-600503; Dravet Syndrome Foundation Spain

1093 | Activation of Central 5-HT$_{2C}$ Receptors by Bexicaserin Reduces Seizures and Respiratory Arrest in a Mouse Model of SUDEP

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Purpose: Poor seizure control in patients with developmental and epileptic encephalopathy (DEE) and brainstem dysfunction are hypothesized to contribute to sudden unexpected death in epilepsy (SUDEP). 5-HT$_{2C}$ receptors are expressed in the brainstem and *Htr2c* knockout mice are susceptible to seizures and SUDEP. Bexicaserin (LP352), a potent and highly selective 5-HT$_{2C}$ receptor superagonist, is an investigational molecule currently in development for the treatment of seizures in patients with DEEs. Here we evaluated the effect of bexicaserin in a mouse model of SUDEP.
Method: 110-120 dB tone presentation in DBA/1 mice induces generalized tonic-clonic seizures and respiratory arrest (SUDEP correlate). Highly susceptible mice selected from a priming phase were orally administered vehicle or bexicaserin, followed by a tone presentation 0.5, 2, 4, 6 or 24 hours later. A separate cohort of mice co-administered with bexicaserin plus vehicle or 5-HT$_{2C}$ antagonist SB242084 was tested 2 hours after bexicaserin administration. The incidence of and latency to seizure types and respiratory arrest were recorded.
Results: Bexicaserin dose-dependently decreased the incidence of seizures and prevented respiratory arrest in all mice at 2-, 4- or 6-hours post-dose ($p<0.01$). Bexicaserin also increased latency to seizures and respiratory arrest at these timepoints ($p<0.001$). A partial drug effect was observed at 0.5 hours post-dose ($p<0.05$). The incidence of seizures and respiratory arrest returned to baseline following drug washout at 24 hours post-dose. The effects of bexicaserin in reducing seizure and respiratory arrest incidence were blocked with SB242084 ($p<0.01$).
Conclusion: Bexicaserin significantly reduced seizures and respiratory arrest in a mouse model of SUDEP

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through a 5-HT_{2C}-dependent mechanism. These data support continued clinical development of bexicaserin and the potential of bexicaserin to mitigate the risk of SUDEP.
Acknowledgement: This study was conducted by Porsolt and sponsored by Longboard Pharmaceuticals, Inc., a wholly owned subsidiary of Lundbeck.

1106 | When the brain stops breathing: lessons from peri-ictal respiratory disturbances

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Purpose: Breathing is a complex physiological activity, arising from neurons located in specific sites in the brainstem, such as the pre-Bötzinger complex, and being modulated by supratentorial subcortical and cortical structures. Breathing can be disrupted by pathological neurological conditions, such as seizures. Ictal respiratory changes comprise central or obstructive apnea, tachypnea, bradypnea, hypoventilation, and hypoxemia. In this review we provide an overview of the electroclinical features and pathophysiology of peri-ictal respiratory disturbances, the available neuroimaging data, its hypothesized relationship with the sudden unexpected death in epilepsy (SUDEP) risk and treatment perspectives.
Method: We searched the databases MEDLINE and Embase for articles between 1899 and November 2024. Search terms were "apnea" and one or more of "central", "ictal", "SUDEP", "amygdala", "MRI", "fMRI", "morphometry", "treatment". We included mono-center and multicenter studies with original data, abstracts, case reports, case series, reviews, books and commentaries to summarize and discuss the most relevant findings in the field.
Results: Ictal central apnea (ICA) has been widely described in association with focal seizures, especially of temporal origin. Multicentric studies have reported that ICA occurs in 36%–40% of focal seizures. Longer ICA duration typically produces hypoxemia, being observed in 33-41 % of cases. Post-convulsive central apnea (PCCA) has been described in relation to generalized seizures, suggesting brainstem dysfunction following a generalized tonic-clonic seizure (GTC). As shown in invasive neurophysiological and advanced neuroimaging studies, the amygdala plays a key role in generating the ictal apneic response.
Conclusion: The presence of peri-ictal respiratory symptoms was recently included among factors contributing to a higher risk of SUDEP in a novel score named SUDEP-CARE. Intracranial-EEG and neuroimaging studies focusing on ICA and PCCA have been published recently, expanding the current neurophysiological and clinical knowledge and adding novel structural and functional brain correlates of SUDEP.

1175 | A Case of Near SUDEP (Sudden Unexpected Death in Epilepsy) in a Refractory Epilepsy Patient Undergoing Epilepsy Monitoring Unit Evaluation in a Level 3 NAEC (National Association of Epilepsy Centers) Community Hospital

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Purpose: Sudden Unexpected Death in Epilepsy (SUDEP) encompasses cases of abrupt and unforeseen demise in individuals with epilepsy, including those classified as near-SUDEP where cardiorespiratory arrest is reversed by resuscitation efforts, leading to survival for more than one hour [1][2]. This study presents a near-SUDEP patient with refractory epilepsy, highlighting the challenges of managing complex epilepsy surgery cases that require intracranial monitoring, which cannot be performed at community hospitals in underserved areas. Due to limited resources for optimal surgical management, such as access to a Level 4 NAEC, a pacemaker was implanted to prevent future cardiac-related SUDEP events.
Method: N/A
Results: A 54-year-old, right-handed male with a history of refractory focal epilepsy, depression, and psychosis was admitted to a Level 3 Epilepsy Center's Epilepsy Monitoring Unit (EMU) for localization of ictal onset. During the EMU evaluation, the patient experienced a 140-second electroclinical seizure, followed by 90 seconds of postictal diffuse EEG background suppression. Postictally, the patient developed apnea, which was not quantified due to the absence of respiratory monitoring. Sixty seconds before the clinical seizure ended, cardiac telemetry revealed a transition from sinus rhythm to sinus bradycardia, which progressed to cardiac asystole 13 seconds into the postictal phase, lasting for 70 seconds. CPR (Cardiopulmonary Resuscitation) was initiated 90 seconds after apnea onset, successfully achieving spontaneous circulation (ROSC). The patient underwent pacemaker implantation, which continues to pace effectively.

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Over six months, monitoring noted 25% right atrial pacing, <0.1% right ventricular pacing, sinus rhythm, and no cardiac events. We propose that Pacemaker implantation may serve as a safeguard against SUDEP by preventing asystole during future seizures.

Conclusion: This case highlights challenges in accessing optimal care for high-risk SUDEP patients in underserved areas, where psychiatric comorbidities, socioeconomic barriers, and lack of transportation to a Level 4 NAEC led to pacemaker implantation to prevent near-SUDEP and asystole.

1211 | Lower mortality in a French Single-Center Large Cohort of individuals with Dravet syndrome

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Purpose: Our retrospective, single-center study aimed to analyze the mortality rate and the rate of Sudden Unexpected Death in Epilepsy (SUDEP) in Dravet Syndrome (DS).

Method: We included in our study patients with a confirmed diagnosis of DS, followed at our Centre and the last visit during or after 2020 except for individuals deceased who may be included for a last visit before 2020.

Results: We studied a cohort of 132 individuals with DS with a mean age of 11.9 [inter-quartile range (IQR) 6.5-16.2] and a mean follow-up duration of 10.3 [IQR 4.9-14.6] years. *SCN1A* pathogenic variants were present in 120 individuals. Eight patients (6%) died at a median age of 39 months (range of 18-201 months). The overall mortality rate was 5.76‰ person-years. Four individuals died from SUDEP and 4 from non-SUDEP causes, resulting in SUDEP-specific and non-SUDEP-specific mortality rates of 2.88‰ per person-year for both. The median age at the time of SUDEP was 38 months (range: 18-201 months). The mortality outcome is at the lower end of the mortality outcome described in the literature (Sullivan et al Epilepsia. 2024;65(5):1240-1263). We established the Kaplan-Meier survival curve of our cohort in comparison to the data from Cooper et al (Cooper et al Epilepsy Res. 2016;128:43-47). Our overall mortality rate is significantly lower (5.76‰ versus 15.8‰ person-years in Cooper, $\chi^2 = 5.926$, df = 1, p=0.015), as well as for SUDEP rate (2.88‰ versus 9.32‰ in Cooper, $\chi^2 = 4.42$, df = 1, p=0.035).

Conclusion: Despite the limitations of our single-center and retrospective study, we showed an encouraging lower mortality rate in a cohort of patients with DS uniformly monitored at the same center over a long follow-up period.

1218 | Relation between evolution of epilepsy, respiratory functioning and risk of SUDEP, in a mouse model of Dravet Syndrome

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Purpose: In Dravet syndrome, SUDEP, which is most probably facilitated by sustained susceptibility to cardiorespiratory dysfunction, might result from interplay between genetically-based neurodevelopmental disorder and effects of recurrent seizures. Our objective was to assess temporal relationship between evolution of epilepsy, respiratory functions, and risk of SUDEP.

Method: From P21 to P31, one seizure per day was induced in R1648H knock-in ($Scn1a^{RH/+}$) or wildtype (WT) mice, using flurothyl inside plethysmography chamber. Everyday, we collected inter-ictal respiratory function before inducing seizure and assessing respiration during post-ictal period. Respiratory frequency (FR) and rate of apnea events (>3 local mean of one respiratory cycle measured in inter-ictal period of 5 minutes) were compared at day 1 (D1) and last day (LD) of protocol, with last day corresponding to day before death for mice which died.

Results: Survival rate was 36% for R1648H and 100% for WT. Inter-ictal FR was similar at D1 and LD between WT (n=7) (p value=0.2188; D1=452.9±69.98cycle/min; LD=495.5±46.29cycle/min), and R1648H (n=13) (p value=0.7354; D1=452.5±71.38cycle/min;

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LD=464.8±92.07 cycle/min). In contrast, we observed a significant increase in number of spontaneous apneas (SA) between D1 and LD in both groups: 199.97% (D1=6.714±3.684; LD=20.14±6.388) (p value=0.0156) in WT, and 98.35% (D1=4.615±4.788; LD=9.154±4.913) (p value=0.0269) in R1648H. However, evolution of SA with seizure repetitions is greater in WT than in R1648H (p value=0.0010), but FR evolution remained the same in both groups (p value = 0.5826).

Conclusion: In R1648H mice, repetition of seizures wasn't associated with alteration of inter-ictal respiratory functioning in normoxic conditions, but risk of SUDEP was associated with dysregulation of response to hypoxia. Our experiment is now focused on response to hypoxic/hypercapnic challenges, performed after 5 seizures. Preliminary hypoxic results differed across groups, with slower recovery of FR for R1648H dead than for WT and R1648H alive. No difference observed in response to hypercapnia.

1362 | Effect of cenobamate on sudden unexpected death in epilepsy (SUDEP) risk in a Spanish cohort of a phase 3 clinical trial

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Purpose: SUDEP accounts for 2-17% of deaths in patients with epilepsy (Ficker 2000, *Epilepsia* 41 Suppl 2:S7-S12). SUDEP-3 (score 0-4) and SUDEP-7 (score 0-10) scales assess the potential risk of SUDEP. For each point reduction in SUDEP-3, SUDEP odds decrease by 64%; for SUDEP-7, per-point odds decrease is 29% (Rasekhi 2021, *Epilepsia* 62(7):1536-1545).

Method: NCT02535091 (C021, N=1340) was a global, multicenter, phase 3, open-label safety study of cenobamate as adjunctive treatment in adults with uncontrolled focal-onset seizures (FOS). Efficacy data pre- and post-cenobamate treatment were collected in in a multicenter retrospective observational study of the C021 Spanish cohort (n=127). SUDEP-3 and SUDEP-7 risk scores (RS) were calculated for patients in that cohort before and after cenobamate treatment.

Results: At baseline, 76% and 24% patients had SUDEP-3 RS of 2 and 3. After 2 years of cenobamate treatment, 6% had a RS point reduction of 3, 11% of 2, and 14% of 1 point; 69% remained stable. Using the SUDEP-7 inventory, at baseline, 51% of patients had a RS of 1-3 and 49% had a RS of 4-8. After 2 years of cenobamate treatment, 1% had a RS point reduction of 4, 9% of 3, 9% of 2, and 30% of 1 point. 44% remained stable, and 7.5% increased SUDEP risk.

Conclusion: Cenobamate treatment significantly reduced SUDEP risk in some Spanish cohort patients as measured by two SUDEP risk scales. The potential for reducing SUDEP risk should be considered when initiating/changing treatment in patients with uncontrolled FOS.

1447 | Post-mortem MRI may positively identify sudden unexpected death in epilepsy

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Purpose: Sudden Unexpected Death in Epilepsy (SUDEP) is a leading cause of premature mortality in individuals with epilepsy, occurring 24 times more frequently than in the general population. Despite advances in biomarker research, SUDEP remains defined by the absence of identifiable structural causes post-mortem, akin to sudden cardiac death (SCD) and other unexplained deaths in infancy and childhood. Validated biomarkers are urgently needed to improve monitoring of high-risk individuals. To investigate whether post-mortem MRI (PM-MRI) can identify seizure-specific structural changes in SUDEP, rather than merely excluding other causes of death.

Method: We applied epilepsy-specific MRI protocols to measure hippocampal and amygdala volumes in nine individuals who died during the COVID-19 pandemic, including five suspected SUDEP cases and four non-seizure-related deaths (bronchopneumonia and SCD). Volumes were compared between SUDEP and non-SUDEP groups, as well as with in-vivo measurements from healthy controls.

Results: SUDEP cases exhibited significantly larger hippocampal (z=2.44344; p=0.014) and amygdala (z=2.26573; p=0.0232) volumes compared to non-SUDEP controls. Four out of five SUDEP cases showed hippocampal and amygdala volumes above the control mean, while all non-SUDEP cases had volumes below the control mean by up to 48%. These findings suggest seizure-related intracellular oedema in key brain structures, potentially triggering apnea in focal epilepsy patients.

Conclusion: PM-MRI can detect structural abnormalities associated with SUDEP, supporting the hypothesis that SUDEP is a post-ictal event. These changes may reflect underlying mechanisms contributing to SUDEP, such as autonomic dysregulation and impaired recovery from hypoxia. PM-MRI offers a valuable tool for understanding

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SUDEP pathophysiology and identifying at-risk individuals, potentially guiding early intervention strategies. This study highlights the potential of PM-MRI to positively identify SUDEP and advance research into its prevention.

1453 | Are Obstructive Sleep Apnea and Sudden Unexpected Death in Epilepsy Related ?

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Purpose: Sudden unexpected death in epilepsy (SUDEP) occurs mainly during sleep, and respiratory pathophysiological mechanisms have been proposed. Obstructive sleep apnea (OSA) has been associated with sudden cardiac death, and its treatment is associated with a reduction in epileptic seizures. However, research regarding a possible relationship between OSA and the risk of SUDEP originated conflicting results. We aimed to evaluate a possible relationship between risk of SUDEP and the presence/severity of OSA.
Method: A retrospective cross-sectional study was conducted with patients with epilepsy, who underwent PSG for suspicion of any sleep disorder, at a tertiary center over a ten-year period. OSA was characterized by apnea-hypopnea index (AHI) and oxygen desaturation index (ODI). SUDEP risk was quantified using the rSUDEP-7 scale. Comparisons were made using chi-squared tests and Spearman correlation between rSUDEP-7 and PSG parameters.
Results: Forty-five patients were included. The median rSUDEP-7 score was 2, and 22% were at high risk of SUDEP (rSUDEP-7 ≥ 5). The median AHI was 17, with 82% having pathological AHI (AHI ≥ 5) and 20% having severe OSA (AHI ≥ 30). No significant association was found between the risk of SUDEP (rSUDEP-7) and the presence or severity of OSA, by AHI or ODI.
Conclusion: Despite the importance of identifying modifiable risk factors for SUDEP, the literature has yielded conflicting results regarding its association with OSA. This study found no association between OSA-related PSG parameters and the risk of SUDEP. Further research is needed to better understand a possible relationship between these two pathologies.

1546 | Long Term Interictal Heart Rate Variability Among Temporal and Frontal Epilepsy Patients: Do Different Parameters Predict the Risk for SUDEP?

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Purpose: Temporal (TE) and frontal lobe epilepsy (FE) are the most frequent types of focal epilepsy in the adult. SUDEP is a major concern in epilepsy. It may happen during interictal period and relate to impaired autonomic control of the heart. Heart rate variability (HRV) studies provide non-invasive parameters of autonomic function. (Malik et al, Eur Heart J, 1996, 17:354-381). We aimed at measuring interictal HRV from TE and FE patients in comparison to controls in order to ascertain risk of SUDEP.
Method: This is a cross-sectional case-control study approved by the local ethics committee. Healthy controls were matched for age, sex and body mass index. Participants underwent a 24-hour Holter-EKG recording during video-EGG. Intercritical periods were analyzed. Time-domain SDNN, SDNNi, SDANN(sympathetic/ parasympathetic influence), rMSSD, pNN50 (parasympathetic influence) and frequency-domain LF (sympathetic/ parasympathetic influence), HF (parasympathetic influence) and LF/HF were evaluated. Risk of SUDEP was inferred by means of the SUDEP-7 scale. Wilcoxon and Spearman tests were used ($p<0.05$).
Results: Twenty-nine patients with TE were selected (all had hippocampal atrophy, 52% in left side, 66% pharmacoressitant). The SUDEP-7 varied from 0-10 (median=4, SD=+-2,9). SDNN,SDNNi and LF were significantly reduced. Pharmacoresistant patients had rMSSD and pNN50 correlated to SUDEP-7, most significantly in sleep (ρ=-0.576, p=0.009/ρ=-0.590, p=0.007). Ten patients with FE were selected (5 pharmacoresistant). SUDEP-7 ranged from 1-8, median=5.5, SD=+-2.4) For FE, all 24-hour time-domain parameters and LF were inversely and significantly correlated to SUDEP-7, particularly SDANN (ρ=-0.896, p=0.00019). Wakefulness parameters did not correlate with SUDEP-7, but sleep parameters were

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strongly correlated, mainly rMSSD (ρ=-0.945, p=0.00012). The control group numbered 21 participants.

Conclusion: Both sympathetic and parasympathetic parameters were reduced among TE patients. Low HRV during sleep was particularly related to SUDEP-7, with a predominance of parasympathetic decrease among FE. FE was associated to very low SDANN, maybe due to reduced physical activity.

1713 | The analysis of heart rate variability according to the response to antiepileptic treatment

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Purpose: Sudden Unexpected Death in Epilepsy (SUDEP) is a significant concern for individuals with epilepsy. Heart Rate Variability (HRV) has been proposed as a potential biomarker for assessing SUDEP risk. This study aims to compare HRV parameters between patients with drug-sensitive (DS) and drug-resistant (DR) epilepsy to elucidate the relationship between treatment response and SUDEP risk.

Method: HRV parameters of 24-hour data were measured using an ambulatory electrocardiogram in patients with DS epilepsy, DR epilepsy and healthy control. These parameters include the standard deviation of all NN intervals (SDNN), the standard deviation of the averages of NN intervals in all 5 minutes segments of the entire recording (SDANN), the squared root of the mean of the sum of the squares of differences between adjacent NN intervals (RMSSD), the percentage of NN50 (pNN50), low frequency (LF), high frequency (HF) and LF/HF ratio. The SUDEP-7 score was also compared among the groups. The difference is considered statistically significant when p is below 0.05.

Results: A total of 73 patients were included, with 37 classified as having DS epilepsy and 36 as having DR epilepsy, compared to a control group of 73 individuals. DR patients had higher SUDEP-7 scores than DS patients (*p=0.002*). Compared to controls, both epilepsy groups showed lower HRV, with DR epilepsy patients exhibiting more pronounced autonomic dysfunction than DS epilepsy patients: lower SDNN (118.68 vs. 144.81 ms, *p=0.005*), lower SDANN (101.75 vs. 124.60 ms, *p=0.009*), and lower RMSSD (22.88 vs. 35.39 ms, *p=0.001*) reflecting lower parasympathetic activity (pNN50: 8.81% vs. 13.16%, *p=0.04*). Sympathetic predominance was manifested as an increased LF/HF ratio (3.55 vs. 2.21, *p=0.01*).

Conclusion: DR epilepsy patients exhibited more autonomic imbalance and higher SUDEP-7 scores. HRV analysis may identify patients at greater risk of poor treatment outcomes emphasizing the need for targeted interventions to improve autonomic regulation.

Terminology and Classification

693 | Relationship Between Seizures and Periodic Generalized Nonepileptiform Discharges During Sleep

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Purpose: The A phases of cyclic alternating patterns are suggested as gates for epileptiform discharges, seizures or sleep disorders. This study investigates the contribution of periodic generalized nonepileptiform discharges (PGNDs) similar to A periods during sleep, to the lateralization and localization of the epileptogenic zone.

Method: The EEG reports of 584 patients monitored with video EEG between 2018 and 2023 were retrospectively reviewed. Among the patients with reported nocturnal seizures (n=95), the recording was reviewed for 5 minutes backward from the seizure, and those with at least two PGNDs prior to seizures were selected, and PGNDs during preictal and interictal period were scored. Patients with a non-PGND preictal period, artifact-contaminated recordings, or incomplete data were excluded (n=27).

Time-frequency domain analyses of delta band activity for PGNDs were performed using MATLAB 2015a. Statistical differences between groups and electrodes were analyzed using SPSS25.

Results: When the delta power values of preictal PGNDs (all PGNDs scored (PGNDall), and the last GND just before the seizure separately) were examined, the extratemporal lobe epilepsy (ETLE) group exhibited higher delta band power values than the temporal lobe epilepsy (TLE) group in all electrodes and significantly higher in the bilateral frontal electrodes (p<0.05), whereas interictal values didn't show a significant difference. Regarding lateralization, while no significant change in delta power was detected between patients with unilateral and bilateral interictal epileptiform discharges (IEDs) in the ETLE group, it was observed that patients in the TLE group with bilateral IEDs had significantly lower PGNDall delta power, particularly during the interictal period (p<0.05 across all electrodes).

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Conclusion: The higher delta power values of preictal PGNDs in the ETLE group, along with the accentuation of this difference in patients with bilateral IEDs, could provide an additional method for distinguishing between TLE and ETLE, especially in analyses using artificial intelligence.

712 | Seizure Duration and Time-Point Cutoffs for Statistically Defining a Prolonged Seizure: A Post-Hoc Analysis of the SCORE Video-EEG Database

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Purpose: Most seizures are brief and self-limiting; however, some will cluster, become prolonged and progress in severity. Defining prolonged seizures accurately informs when to ideally administer rescue medication to prevent status epilepticus (SE). Prolonged seizures have been defined as >2min for generalized absence seizures and the convulsive phase of bilateral tonic-clonic seizures (focal/generalized onset), and >5min for focal seizures (Pina-Garza JE et al. Epileptic Disorders 2024;26:484-497). We explored statistically appropriate time-point(s) for defining possible/probable prolonged seizures by seizure type.
Method: Post-hoc analysis of 2,742 seizures from 887 video-electroencephalography (V-EEG) recordings of 725 patients (including outliers; Meritam Larsen P et al. Epilepsia 2023;64:469-478). Seizure duration was measured clinical/via V-EEG/surface electromyography and analyzed using Tukey's box plot. For each seizure type, outliers were categorized as possibly prolonged (>1.5*IQR above Q3), or probably prolonged (>3*IQR above Q3). Patients with SE were excluded (n=20), which is a limitation.
Results: Using Tukey's method, 4% (97/2,742) of seizures observed clinically were classified as either possibly/probably prolonged. For seizures observed via V-EEG, 6% (159/2,742) were classified as either possibly/probably prolonged. Cutoffs (clinical/V-EEG duration, seconds) for possibly prolonged seizures were: focal aware 48.75/60.5; focal awareness unknown 48.5/70.25; focal tonic 45.75/51.75; focal to bilateral tonic-clonic 167.75/189.5; focal clonic 48.5/56.5; focal impaired awareness 111.5/146.75; atonic 1.9/1.6; generalized tonic 24.5/21.25; eyelid myoclonia 6.3/6; myoclonic tonic 9/7; absence with eyelid myoclonia 10/9; generalized clonic 14/15.25; atypical absence 44.25/50; generalized tonic-clonic 127/120.25; tonic spasm 15.5/15.5; typical absence 20/23.25; myoclonic absence 20.75/21.
Conclusion: These data suggest an appropriate focus on absence, tonic-clonic, and focal seizures as being more prolonged and support the 2min cutoff for tonic-clonic seizures (focal/generalized onset). However, the statistical cutoff of ~1min for generalized absence seizures and 1-3min for focal seizures suggest the consensus definition may be too conservative at 2/5min, respectively. Other seizure types may become abnormally prolonged earlier.
UCB- and Filadelfia-sponsored.

1314 | Subacute encephalopathy with seizures in alcoholics (SESA): clinical implications of an underdiagnosed syndrome

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Purpose: Among alcohol-related encephalopathies there is an underdiagnosed clinical syndrome known as subacute encephalopathy with seizures in alcoholics (SESA). SESA syndrome has been described in individuals with chronic alcoholism presenting with episodes of mental confusion, transient focal neurological deficits and seizures (with no apparent temporal relationship to alcohol withdrawal or intoxication), establishing itself as a distinct entity from the classic alcohol withdrawal syndrome.
Method: We present a single-center case series from a Portuguese hospital, consisting of five patients with chronic alcoholism, diagnosed with SESA syndrome. Upon admission, no history of epilepsy was identified and, in most cases, no clear precipitating factor was found (such as alcohol intoxication or withdrawal). All patients were admitted for epileptic seizures (focal motor or generalized tonic-clonic seizures) or non-convulsive focal status epilepticus, accompanied by transient focal neurological deficits (hemiparesis, dysarthria, hemianopia, aphasia). The interictal electroencephalogram (EEG) revealed sharp waves, periodic lateralized discharges (primarily in

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the left cerebral hemisphere) and focal slowing. Magnetic resonance imaging showed transient cortical hyperintensities, with diffusion restriction, consistent with the topography of EEG changes.

Results: All patients required anti-seizure medication and two needed intensive care unit (ICU) admission for anesthetic induction. Treatment was successful, with complete recovery in four out of the five patients. During follow-up (2-72 months), patients who adhered to the chronic anti-seizure therapy maintained reliable seizure control, with no further episodes. Non-compliance with the prescribed medication consistently resulted in seizure recurrence, highlighting the importance of continuous treatment for long-term control.

Conclusion: The diagnosis of SESA syndrome has important implications for defining the disease's natural history, ensuring the early initiation of anti-seizure medication and facilitating the establishment of a clinical prognosis. Interictal EEG is particularly relevant, often revealing periodic lateralized discharges, sharp waves or focal slowing, in contrast to the interictal EEG observed in other alcohol-related conditions associated with seizures.

1603 | Overlap Syndromes – Coincidence or a New Clinical Entity?

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Purpose: Childhood Absence Epilepsy (CAE) and Self-Limited Epilepsy with Centro-temporal Spikes (SeLECTS) are two of the most frequent childhood epileptic syndromes, each with different clinical significance and treatment approaches. Although rare, the overlap between these syndromes has been documented, but its clinical significance remains unclear.

Method: Description of two clinical cases.

Results: Case 1: A 10-year-old girl with normal developmental milestones presented with brief staring episodes, occurring multiple times daily, since age 6. Neurological examination was unremarkable. EEG captured absence seizures characterized by typical generalized 3-Hz spike-wave complexes, along with interictal left centro-temporal focal discharges during drowsiness and sleep. Brain MRI was normal. The patient was started on valproic acid, reducing seizure frequency. No other seizure types were observed. She is currently tapering down anti-seizure medication (ASM). Case 2: A 10-year-old boy with a history of language delay, developed focal motor seizures at age 3, characterized by left ocular deviation, evolving into bilateral tonic-clonic seizures. EEG showed interictal focal epileptiform activity in both centro-temporal regions, predominantly on the right. ASM reduced seizure frequency. At age 6, he developed episodes characterized by sudden altered awareness with brief blinking, lasting 2–3 seconds. EEG showed absences seizures with a typical ictal pattern, as well as interictal right centro-temporal spikes enhanced by sleep. Brain MRI was normal. A genetic panel revealed a biotinidase deficiency. Currently, the patient is on two ASM along with biotin supplementation, leading to a reduction in the frequency of absence seizures and no recurrence of focal motor seizures.

Conclusion: We present two cases of overlapping focal and generalized genetic epileptic syndromes. At this stage, it is unclear if this rare overlap syndrome has an impact on disease progression and treatment response. The authors want to raise attention to this pathological entity and believe that discussing similar cases can enhance understanding of these syndromes.

Late Breaking Abstracts

Adult Epileptology

1845 | Physical Activity Levels May Impact on the Risk of Premature Mortality in People with Epilepsy

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Purpose: Epilepsy impacts over 70 million individuals worldwide. Determining the optimal levels of physical activity (PA) for each person remains a significant challenge, as insufficient or excessive activity can result in negative outcomes.

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Method: We analyzed accelerometer data from nearly 100,000 UK Biobank participants (including 1,167 with epilepsy).

Results: We found that during a median follow-up of 7.1 years, people with epilepsy had significantly higher rates of premature mortality than people without epilepsy (SMR: 2.39, 95% CI: 1.97-2.86). Higher sedentary behavior duration (hours/day) is associated with lower all-cause mortality (HR: 0.87, 95% CI: 0.78-0.97), with the lowest estimated risk at 10.9 hours/day (HR: 0.56, 95% CI: 0.36-0.85). Moderate-to-vigorous PA showed a non-linear relationship with all-cause mortality risk, with the lowest hazard ratio observed at 0.2 hours/day (HR: 0.69, 95% CI: 0.51-0.93). Our all-cause mortality risk machine learning prediction model (AUROC=0.87±0.08, AUPRC=0.82±0.06) leveraging 777 time-frequency domain features extracted from PA and optimized through recursive feature elimination and grid search cross-validation, significantly improved risk stratification. Research is translated into a comprehensive PA management system for people with epilepsy.

Conclusion: This research provides important evidence to inform PA management in epilepsy, and highlights the potential of data-driven approaches for supporting personalized care in clinical practice.

1850 | Identifying Unrecognized Cases of Lennox-Gastaut Syndrome in Adults With Intellectual Disability in Germany: Data from the Epilepsy Diagnostic Potential Analysis (EpiDIAL) Study

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Purpose: The Epilepsy Diagnostic Potential Analysis (EpiDIAL) study aimed to identify potential undocumented cases of Lennox-Gastaut syndrome (LGS) in adults, using patient records from four specialized medical centers for adults with intellectual disabilities (MZEB) in Germany.

Method: In this retrospective chart review, an algorithm – developed with physician input based on the ILAE criteria – was used to screen patient records for documented epilepsy (ICD-10-GM: G40) and intellectual disability diagnoses (F71–F73), without an existing LGS diagnosis. Potential LGS was defined as: (i) ≥2 current or prior antiseizure medications, or multifocal or focal epilepsy; and (ii) ≥2 seizure types (including tonic) or a history of falls. High-potential LGS was defined as meeting potential LGS criteria plus helmet supply, and pathological electroencephalogram or evidence of slow spike-waves.

Results: Of 412 patient records screened, 363 had no LGS diagnosis; 49 had an LGS diagnosis. Among the 363, 128 (35%) were identified as potential LGS cases (59% male; mean [standard deviation] age at diagnosis of epilepsy: 5.6 [6.5] years), and 28 (8%) as high-potential LGS cases (64% male; 4.2 [4.2] years); 235 (65%) cases were LGS-unlikely (56% male; 11.1 [17.5] years). Among patients with available age at diagnosis, 92% (99/108) with potential LGS and 81% (131/162) LGS-unlikely were diagnosed with epilepsy before 18 years of age, vs 100% (45/45) with an existing LGS diagnosis. In sensitivity analyses, 90% (44/49) of patients with a diagnosis of LGS were identified as having potential LGS.

Conclusion: Using this simple, sensitive algorithm, approximately one-third of patients with epilepsy and intellectual disability met criteria for a possible, yet undocumented and thus potentially suboptimally treated LGS. Findings may provide valuable information on the prevalence of undiagnosed LGS and the importance of patient re-evaluation in adulthood. Using screening tools such as this may help ensure access to appropriate treatment options for patients. Funding: Jazz Pharmaceuticals, Inc.

1856 | Photosensitivity in juvenile myoclonic epilepsy: Insights into a persistent enigma via optical coherence tomography

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Purpose: Photosensitivity is a well-known reflex trait in genetic generalized epilepsy, particularly in juvenile myoclonic epilepsy (JME). Numerous studies have been conducted to investigate the etiology of photosensitivity but only a certain part of them entirely concerns optical coherence parameters such as Retinal Nerve Fiber Layer (RNFL), Macula Layer (ML), and Choroidal Layer (CL). The primary goal of this study is to analyze anatomical and physiological differences in the RNFL, ML, and CL between photosensitive JME, non-photosensitive JME, and healthy controls.

Method: Photosensitive JME (n=30), non-photosensitive JME (n=30), and healthy controls (n=30) without ophthalmologic pathology were recruited. Peripapillary average and four sub-quadrant RNFL thicknesses , central ML thickness and subfoveal CL thickness were evaluated by using Spectral Domain Optical Coherence Tomography (OCT).

Results: Mean age, gender distribution, and body mass index values were similar between JME subgroups and healthy controls. Bilateral average and sub-quadrant RNFL thickness, except for the left nasal quadrant, were decreased in the JME group compared to the healthy control group ($p<0.05$). Although the ML thickness on both sides was increased in photosensitive patients, no statistically significant difference was observed. Increased CL thickness of both sides was significant in photosensitive JME patients compared to non-photosensitive JME patients and the healthy control group ($p<0.05$).

Conclusion: Thinning of the RNFL in JME patients may be associated with the neurodegenerative nature of epilepsy. Increased ML and CL thickness in the photosensitive group could be attributed to recently discovered intrinsic retinal photoreceptors and compensatory mechanisms in response to the burden of low threshold potential.

1859 | Clinical Predictors and Case-Based Insights for Intensive Care Unit Admission in Seizure Patients Presenting to the Emergency Room

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Purpose: Seizures presenting to the emergency room (ER) range from single provoked episodes to status epilepticus (SE) requiring intensive care. However, limited data exist on the clinical characteristics of patients necessitating direct intensive care unit (ICU) admission.

Method: This retrospective study included 90 adults who presented to the ER with seizures at Wonju Severance Christian Hospital between January 2019 and June 2022. The primary outcome was ICU admission within 24 hours. Demographics, laboratory findings, and comorbidities were compared between ICU and non-ICU groups. Additionally, 20 representative ICU-admitted cases were reviewed to illustrate etiologic diversity and clinical outcomes.

Results: Of the 90 patients, 20 (22.2%) required ICU admission. Compared to the non-ICU group, ICU patients were older (62.5 vs. 53.4years, p=0.032), had higher rates of hypertension (45% vs. 17.1%, p=0.009), elevated white blood cell (WBC) counts (12.8 vs. $9.1\times10^3/\mu L$, p=0.001), and lower red blood cell (RBC) counts (4.27 vs. $4.61\times10^6/\mu L$, p=0.031). Multivariate analysis identified hypertension (OR: 4.07), high WBC (OR: 1.27), and low RBC (OR: 0.17) as independent predictors of ICU admission.

Among ICU patients, 55% had SE or GTCS clusters. Structural brain lesions were the most common etiology (50%), followed by alcohol-related (15%) and metabolic causes (5%). While most patients stabilized and self-discharged, 25% required long-term care, and one died from intracranial hemorrhage secondary to metastatic cancer.

Conclusion: This case-based analysis highlights the clinical heterogeneity among seizure patients requiring ICU care, with diverse etiologies including structural, metabolic, and alcohol-related causes. The findings underscore the value of individualized case reviews to inform risk stratification and acute management strategies in the emergency setting. Incorporating hematologic profiles such as leukocytosis and anemia may further aid in early classification for these high-risk patients.

1872 | Investigation and research on the training demands of epilepsy specialist nurses in 361 medical institutions of China

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Purpose: We aimed to investigate the training demands and suggestions for epilepsy specialist nurses in medical institutions at all levels in China

Method: We use the convenient sampling method, a self-designed questionnaire was used to investigate the head

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nurses of medical institutions at all levels in 26 provinces (autonomous regions and municipalities) of China from January to February 2025.

Results: A total of 361 medical institutions participated in the survey, among which tertiary hospitals accounted for 94.74%. 97.23% of medical institutions hope to participate in the training and learning of epilepsy specialist nurses. They believe that among the core competencies of epilepsy specialist nurses, the most important one is clinical practice ability (98.61%), followed by professional development ability (97.23%) and health education and consultation ability (95.57%). 59.28% of medical institutions suggest that the duration of full-time theoretical training should be 4 weeks, adopt a combined online and offline training method, and the clinical practice time should be ≥12 weeks (57.35%). They hope that theoretical learning course assignments (28.25%), case reports (38.78%), and clinical practice reflections (32.41%) will be used as the main process evaluation methods. The completion of a case care and the formation of a report (49.03%), as well as the passing of the theoretical assessment (17.73%), were regarded as the main summative evaluation methods.

Conclusion: There is a high demand for the training of epilepsy specialist nurses in medical institutions at all levels in China. It is imperative to carry out the training of epilepsy specialist nurses. The suggestions of medical institutions for the training content and methods focus more on the cultivation of core competencies. On this basis, the access conditions should be clarified and a training program for epilepsy specialist nurses suitable for the actual situation in China should be explored.

1909 | Peri-ictal arrhythmias in Temporal Lobe Epilepsy

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Purpose: Ictal arrhythmias can be present in Temporal lobe seizures. Tachycardia is the most common but bradycardia, atrial fibrillation and asystole can also occur.

Our aim is to determine the presence, frequency and type of arrhythmia in temporal lobe seizures and possible predictors for their occurrence.

Method: We retrospectively reviewed medical records and video EEG recordings from patients admitted to our Epilepsy Monitoring Unit (EMU) from 2019-2024 with hypothesis of temporal lobe epileptogenic zone. Analysis of demographics, epilepsy etiology, semiology and electroencephalography of scalp in ictal onset, electrocardiogram (EKG) changes and anti-seizure medications (ASM) was performed. Chi-squared tests were performed for categorical variables logistic regression to determine predictors of EKG changes.

Results: 102 patients were included, 329 seizures were reviewed with a mean of 3.22 per patient, 90% were focal seizures. 52% men(53), mean age 36(18-77), structural etiology 68%(70), unknown 29%(30), autoimmune 1%(1), genetic 1%(1). Peri-ictal EKG changes were seen in 61%(60). The most frequent finding was ictal tachycardia 83% (50), followed by ictal-postictal tachycardia 6%(4), preictal and ictal tachycardia 5% (3), ictal bradycardia 5%(3),ictal bradycardia followed by asystolia 1%(1),the later one having its ictal inset on the right temporal lobe. No statistical significance was found between EKG changes and right or left ictal onset. We found association between the presence of EKG changes and the use of polytherapy 86% (88) (p=0.48) and ictal mesial onset (P=0.045)OR= 2.64 [0.47-0.97]. Patients who were on polytherapy and were treated with phenitoyn didn't develop EKG changes (p=0.03)

Conclusion: Peri-ictal arrhythmias were found in 61% of patients being tachycardia the most frequent finding. Association between mesial ictal onset and the use of polytherapy with development of EKG changes was found. These findings were most commonly seen with right temporal lobe seizures. Peri-ictal EKG changes could be used as a selection criteria for neuromodulation therapy with auto-stimulation in patients who aren't surgical candidates

1920 | Impact of Ramadan Fasting on Seizure-Related Emergency Visits: A Six-Year Retrospective Study

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Purpose: Epilepsy affects approximately 50 million people globally, with multiple seizure triggers documented, including fasting, sleep deprivation, and medication noncompliance. Ramadan fasting entails significant lifestyle changes that may influence seizure thresholds and medication management. Few studies have rigorously assessed the impact of Ramadan on epilepsy, presenting variable outcomes and selection biases. This study aimed to investigate the effect of fasting during Ramadan on emergency room (ER) visits due to breakthrough seizures.

Method: We conducted a single-center retrospective chart review at King Abdulaziz Medical City, Riyadh (2018–2023). Included were epilepsy patients aged ≥14 years, on ASMs, presenting with breakthrough seizures during Ramadan,

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Shaaban, or Shawwal. Patients with cognitive impairment or repeated ER visits were excluded. Groups were compared using Chi-square and ANOVA tests ($p < 0.05$).

Results: A total of 288 patients presented to the ER with breakthrough seizures. The median age was 32 years. There was no statistically significant difference in the incidence of seizure-related ED visits during Ramadan compared to non-Ramadan months, although a slight increase in visits during Ramadan was observed. Status epilepticus was documented in 48 cases, with 15 occurring during Ramadan. The primary seizure triggers identified were medication non-adherence (36.8%) and sleep deprivation (15%). A majority of patients (79.2%) were discharged home after initial ED management.

Conclusion: In this large retrospective analysis, Ramadan fasting did not significantly increase ER visits due to breakthrough seizures compared to adjacent non-fasting months. However, clinicians should remain aware of potential risks related to fasting-induced lifestyle changes, including medication timing, adherence, and sleep disturbances. The limitations inherent to retrospective designs and potential underreporting of seizure frequency were noted. This suggests the need for prospective studies. Future research should explore the effects of fasting on medication metabolism and seizure frequency, ultimately enabling healthcare providers to deliver informed counseling and individualized patient care during Ramadan

1932 | Analysis of efficacy and tolerability of Cenobamate in patients with developmental and epileptic encephalopathies: a retrospective, real-world, multicenter study

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Purpose: Analize the efficacy and tolerability of Cenobamate (CNB) in patients with developmental and epileptic encephalopathies (DEE).

Method: Retrospective analysis of a multicenter cohort of patients with DEE, who started CNB between January 2023 and December 2024. Primary Outcome: seizure frequency reduction ≥50% (SR50), ≥75% (SR75), and seizure freedom (SF) at 12, 24 and 52 weeks of follow up (FU). Secondary outcome: reduction of seizure intensity (ictal and post-ictal), lengthening of time between seizures, reduction of rescue therapy and other non-seizure outcomes (sleep, cognitive and alertness improvements).

Results: We recruited 58 patients (median age=35 years, IQR=24-46 years, 31 males 53,4%). Of those patients 21 received a diagnoses of Lennox-Gastaut syndrome (LGS). Median antiseizure medication tried before CNB was 6. A total of 5 patients suspended CNB, 3 for adverse events and 2 for inefficacy. We observed a SR50 of 57.1-57.475.7% at 12-24-52 weeks FU respectively, a SR75 of 26.5-36.2-35.1% and a SF of 8.2-8.5-13.5% at 12-24-52 weeks FU. We observed an improvement also on secondary outcomes, seizure and non-seizure related. In particular we observed an improvement on sleep and alertness by 36% and 45.1% at 52 weeks FU respectively. We also analyze the LGS population and made a sub-analysis by seizure type, observing a reduction also of generalized and atonic seizure (median of 33 and 12 seizure respectively at baseline and 3 and 2 respectively at 52 weeks FU).

Conclusion: This study demonstrates an efficacy of CNB in patients with DEE, representing a promising option in a category of patients often highly drug-resistant. Few cases are described in the literature, and our results are aligned with previous works. A strength of the study is the sample size, which is larger than what has been published so far.

1939 | GenTLE: a Phase 1/2a Study to Investigate gene therapy candidate AMT-260 in Adults with Mesial Temporal Lobe Epilepsy

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Purpose: Refractory temporal lobe epilepsy (TLE) is the most common form of refractory focal epilepsy. Currently, gold-standard treatments for refractory TLE consist of destructive interventions, such as surgical resection or laser

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ablation of the hippocampus. Kainate receptors (KARs), appear to play a major role in spreading recurrent electrical discharges within epileptic networks, particularly in mesial temporal lobe epilepsy (MTLE). AMT-260 is an investigational, AAV9-microRNA based gene therapy candidate, designed to knock down the GriK2 subtype of KARs after focal administration. Preclinical data have shown sustained and robust seizure reduction on EEG coupled with improved animal well-being after administration of AMT-260, which support further investigation AMT-260 as a potential nondestructive therapeutic approach for patients with refractory MTLE.

Method: The GenTLE study (NCT06063850) is multicenter, Phase 1/2a, First-in-human (FIH) Study investigating AMT-260 in refractory unilateral MTLE. In each of the two dose cohorts, participants will receive a single intracerebral injection of AMT-260 via magnetic Resonance Imaging (MRI)-Guided Convection-enhanced Delivery. After administration, the study consists of a 12 month evaluation period, with a subsequent 4 year long term safety period. To date, one participant has been enrolled and successfully received AMT-260.

Results: Preliminary data from the first patient treated with AMT-260 revealed a generally well tolerated safety profile, with no clinical or neuroimaging evidence of neuro-inflammation, and no SAEs occurring during the 6 months post treatment. Early findings in this single participant showed seizure reduction of between 80% to 100% in the first 6 months post treatment.

Conclusion: The GenTLE clinical study (NCT06063850) is the first-in-human clinical trial using this investigational gene therapy candidate, AMT-260, in participants with refractory unilateral MTLE. Preliminary 6 month data of a single participant reveals a generally well tolerated safety profile and early seizure reduction, which support AMT-260 continued investigation as a potential nondestructive therapeutic approach for refractory MTLE.

1940 | Refining Surgical Decision-Making in Mesial Temporal Lobe Epilepsy: A Multiscale Clinical Framework

P Narayanan Nambiar[1], A Ahmadi[1], H Gray[1], K Alorabi[1], J Lau[1], A Thurairajah[1], A Khan[1], A Suller Marti[1]
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Purpose: Mesial temporal lobe epilepsy (mTLE) is now considered a heterogeneous condition with variable long-term post-surgical outcomes. The objective of our study is to correlate multilevel clinical data with histopathology of operated patients with mTLE who underwent stereo-electroencephalography (SEEG). The ultimate goal is to classify different anatomical, histological, and neurophysiological groups based on the outcomes.

Method: We retrospectively included mTLE patients who underwent SEEG and surgery. Data was collected regarding: 1) SEEG ictal location and pattern 2) MRI findings 3) Histopathology 4) Engel Classification. Statistical analysis was completed using Chi-square test and multinomial logistic regression.

Results: Of 167 patients investigated with SEEG, so far 25 patients were analyzed. 84% (n=21) had involvement of the anterior hippocampus at ictal onset. The most common ictal onset pattern was low-voltage fast activity, seen in 56% (n=14). Regarding MRI findings, 40 % (n=10) had unilateral MTS and 44%(n=11) had normal MRI. Pathology was reliable in 17 patients and 29% (n=5) each had ILAE type 2 and type 4 HS. 68% (n=17) were Engel I at 6 months and 12 months. Ictal SEEG patterns most commonly seen in cases with Engel I at 12 months were LVFA and sharp waves <13Hz, however these were not statistically significant. Regarding the histopathology with good outcomes, the most commonly involved were CA1 predominant and no HS subtypes, which were not statistically significant with the current sample.

Conclusion: In our ongoing analysis, we have identified LVFA, sharp waves <13 Hz at ictal onset and ILAE type 2 and 4 histopathological subtypes as markers of good outcomes. However, due to the current limited sample size and limited statistical power, these findings should be interpreted with caution. For this reason, we plan to continue collecting further data to better define the prognostic factors for surgical candidates.

1994 | Retrospective case series of seizures in systemic lupus erythematosus patients

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Purpose: Seizure, a severe form of neuropsychiatric manifestation of systemic lupus erythematosus (SLE), is to be characterized based on its pattern and SLE activity.

Method: Consecutive patients in a tertiary hospital who had a seizure at or after being diagnosed with SLE for six years (from March 2019 to April 2025) were retrospectively enrolled. Patients having a prior diagnosis of epilepsy were excluded. The medical records were reviewed on the demographics, types of seizure, electroencephalography (EEG), brain imaging findings, and the SLE disease activity. The SLE Disease Activity Index (SLEDAI), a global clinical measure for disease activity in SLE during

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the previous ten years, was retrieved from the medical records.

Results: Twenty-three patients were included. Of these, twenty-two were female and one was male. The mean age at the time of seizure onset was 35 years (range 13 to 64 years) while the mean age at the SLE diagnosis was 26 years (range 13 to 64 years). The average time to seizure onset was 8 years (rage 0 to 40 years). There were seven patients who presented generalized tonic or tonic-clonic seizure; four with focal behavior arrest, three with unknown onset motor seizure, and three with focal motor seizure. Nineteen patients had their EEGs recorded. There were seven individuals with focal epileptic activity, three with diffuse abnormalities, three with both focal and diffuse abnormalities, and six with normal EEG findings. Twenty-two patients received antiseizure medications. Nine of Twenty-two have been seizure-free for more than five years. The mean value of the recent SLEDAI scored was 3.36.

Conclusion: While there is no consensus on how to manage seizure in SLE, it would be critical to characterize seizures in SLE as soon as possible for the better outcome in the treatment of SLE.

1999 | Successful seizure prevention with intra-nasal Seletracetam in a patient with reading epilepsy

K-N Poppert[1], A Thomschewski[1], S Lafenthaler[1], D Boison[2], P Klein[3], M Koepp[4], C Lemke[5], W Löscher[6], A Rotenberg[7], C Rundfeldt[8], E Trinka[1]
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Purpose: Current rescue therapies for acute repetitive seizures are limited to benzodiazepines, which pose risks of sedation, respiratory depression, and addiction. Seletracetam (SEL), a potent analogue of levetiracetam, has shown efficacy and safety in Phase 2 trials.[1] PrevEp, Inc. developed intranasal SEL for rescue use. Reading epilepsy (RE), a reflex epilepsy triggered by reading, offers a unique model to study seizure networks. We report the first human use of intranasal SEL, where changes in seizure activity and brain network dynamics were measured by EEG and MEG.

Method: 42-year-old man with RE [2], experiencing focal aware and focal-to-bilateral tonic-clonic seizures despite levetiracetam 3000 mg/day, received intranasal SEL under Austria's "Named Patient Use" program (Article 83 of Regulation 726/2004/EC and § 8 Abs. 1 Z 2 Austrian Medicinal Products Act 2009). SEL (200 mg/ml) was administered as 30 mg in 150 µl mucoadhesive solution via nasal spray.[3] MEG and EEG were recorded under three conditions: placebo, 30 mg SEL, and repeated 30 mg SEL. Seizures were triggered by reading a math textbook. Source analysis used equivalent current dipole modeling in Brainstorm.

Results: After placebo, the first seizure occurred at 1:56 minutes of reading. (Fig 1) After 30 mg SEL, seizure onset was delayed to 4:17 minutes. Following a second 30 mg SEL dose, no seizures occurred during 25 minutes of continued reading. MEG spike frequency declined from 3.1/min (placebo) to 1.9/min (first dose) and 1.6/min (second dose). Dipole analysis localized activity to the left precentral region, consistent with prior findings in RE. Sike propagation was also reduced after SEL treatment. The only adverse event was a mild bitter taste after the first dose, possibly due to partial swallowing.

Conclusion: Intranasal SEL fully prevented reflex seizures in this case, supporting its potential as the first non-benzodiazepine rescue therapy and offering insights into seizure propagation mechanisms.

2009 | Barriers and benefits of identifying patients with DEE in adult care settings

J Luker[1], K Mearns[2], K Fisher[2], R Shankar[3], PM House[4], M Toledo[5], B Rodriguez[6]
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Purpose: Although the diagnosis of developmental and epileptic encephalopathy (DEE) in children has become routine, significant diagnostic gaps remain for adults in remote residential care settings. This qualitative study explores barriers for and benefits of timely diagnosis of DEE in such settings.

Method: Caregivers and healthcare professionals (HCPs) of adult DEE patients in remote residential settings across the UK, Germany, France, and Spain were interviewed. Interpretative Phenomenological Analysis was used to identify themes and variations by care setting.

Results: The 22 participants (8 caregivers, 8 specialist nurses, 6 other HCPs) highlighted the critical role of care

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settings in identifying individuals who may benefit from diagnostic review for DEE. Care provision varied across countries and settings, including specialist and non-specialist environments. Specialist centers often have a multidisciplinary team with well-trained staff and increased DEE awareness, making them better positioned to facilitate diagnostic evaluations and optimize patient care. In contrast, non-specialist settings lacked DEE awareness and demonstrated poor integration of services for individuals, limiting the impetus for diagnostic review. Considering cognitive and emotional development alongside seizure management can improve DEE diagnosis. Primary care physicians or general neurologists focus on seizure and medication management and may overlook holistic issues, which can be a barrier to diagnostic referral. Other barriers include family anxiety about change; limited care team expertise; medication and seizure control concerns; lack of awareness about the benefits of a reviewed diagnosis; and gaps in clinical outreach to care settings. Confirmed diagnosis fosters holistic care, which may improve quality of life (QoL), enhance communication and reduce risk of hospitalization for patients.

Conclusion: This study identified barriers leading to delayed DEE diagnoses in adults in remote residential care settings. Increased awareness and education among HCPs on DEE characteristics beyond seizure management could promote timely and accurate diagnosis and enhance patients' QoL. UCB-sponsored.

AI and Computational Medicine

1956 | Ethics of AI and Neurotechnology in Epilepsy Management: Insights from Kenya

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Purpose: Epilepsy affects over 50 million people worldwide, with a disproportionate burden in low- and middle-income countries (LMICs) such as Kenya. Emerging neurotechnologies, including AI-powered neurotechnologies that can assist in seizure detection, portable EEG and fMRI devices, and digital health platforms, offer potential to reduce diagnostic and treatment gaps. However, the ethical and cultural considerations of these technologies remain underexplored in African contexts, where imported tools may not align with local health systems or societal values.

Method: A Neuroethics *Baraza*, which is a research-based community engagement event, was convened in Kenya with 30 purposively selected participants, including neurologists, psychologists, anthropologists, policy makers, epilepsy advocates, and individuals with lived experience of epilepsy. The event included expert presentations on neuroscience and social science perspectives on neurotechnology in Sub-Saharan Africa, followed by a panel on ethical dilemmas in epilepsy-focused neurotechnology implementation. Breakout focus groups were conducted, audio-recorded, transcribed, and thematically analyzed using an inductive, iterative approach.

Results: Preliminary findings highlight strong community interest in the ethical integration of neurotechnology for epilepsy care. Participants emphasized the need for equitable access to diagnostic and therapeutic tools, including AI-driven seizure monitoring and mobile EEG. Concerns were raised about data privacy, informed consent, and potential misuse of neurodata in underregulated environments. Building public trust through education, transparency, and inclusive design processes was seen as critical for successful implementation.

Conclusion: There is an urgent need to center African voices in shaping ethical frameworks for neurotechnology and AI-informed devices in epilepsy care. Insights from this Kenyan Neuroethics *Baraza* suggest that community-engaged, culturally grounded approaches are essential for advancing safe, acceptable, and effective innovations in epilepsy diagnosis and treatment across the continent.

1959 | Validation of a Helmet-Type EEG Device for Long-Term Ambulatory EEG Recording

K Ukishiro[1], M Sato[2], M Ishida[1], K Iijima[2], T Hayashi[2], E Ishikawa[3], K Shibuya[3], K Nakamura[3], T Hiratsuka[3], T Yagisawa[3], K Kitazoe[3], M Iwasaki[2], K Jin[1]

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Purpose: Long-term video EEG monitoring (LTVEM) is the gold standard for the definitive diagnosis, classification,

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and localization of epilepsy. However, inpatient LTVEM can be challenging or inaccessible for some patients, leading to delayed diagnosis and appropriate intervention. To address this limitation, we developed a novel, user-friendly helmet-type EEG device designed for prolonged ambulatory EEG recordings at home. In this study, we aimed to validate the clinical utility of this device.

Method: Seven adult male patients with epilepsy, previously diagnosed via inpatient assessments including LTVEM at either Hospital A or B, were recruited. Physicians with no prior experience in EEG electrode placement applied the helmet-type EEG device. Continuous EEG recordings were obtained for 6 h. The recordings were evaluated for awake background rhythms, sleep waveforms, and interictal epileptiform discharges. Participants also completed a questionnaire assessing comfort, weight, stability, ease of daily activities, sleep quality, and overall discomfort during extended use, using a 5-point scale and free-text comments.

Results: The helmet-type EEG device successfully recorded awake background rhythms and sleep waveforms in all participants. Interictal epileptiform discharges were detected in three participants. However, loss of electrode contact over time was observed at the central parietal and temporal electrodes in all cases, affecting recording continuity. Questionnaire responses indicated that comfort and ease of daily activities were comparable to or better than those experienced during traditional LTVEM. However, four participants reported poor sleep quality, and three expressed discomfort regarding helmet weight and instability.

Conclusion: These findings suggest that helmet-type EEG devices could provide convenient long-term EEG monitoring at home. While clinically promising, improvements are needed, particularly in electrode contact reliability, device weight, and sleep comfort.

1971 | Improving the Precision of an FDA-Cleared Wrist-Worn Tonic-Clonic Seizure Detector while Maintaining Sensitivity Standards

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Purpose: Wearable devices powered by artificial intelligence (AI) show strong potential in detecting generalized tonic-clonic seizures (GTCS). The FDA-cleared AI-based GTCS detector embedded in Empatica wrist-worn devices has consistently demonstrated high sensitivity (>95%) with daily false alarm rates (FAR) between 0.2 and 1 in Epilepsy Monitoring Unit (EMU) and ambulatory environments. However, further precision improvements are needed to reduce false alarm fatigue, support long-term adherence, and enhance seizure frequency tracking. A novel AI-based algorithm was thus developed and evaluated in retrospective studies.

Method: The FDA-cleared and novel algorithms were evaluated on EMU and ambulatory datasets independent of training data. In the EMU study, 25 epilepsy patients (age 8-57, mean 24.7) wore Empatica wristbands for 0.34-7.38 days (mean 2.24, total 55.97 days) across three sites. Nineteen GTCS were labeled by at least two epileptologists via gold-standard video-EEG. In the ambulatory study, 18 patients (age 12-63, mean 27.1) wore the wristband for 22.13-883.27 days (mean 281.74, total 5071.34 days). Alerts triggered by likely GTCS were confirmed or rejected by patients/caregivers, with missed GTCS manually logged. After independent bio-signal review, 170 GTCS were confirmed. Endpoints included: positive percentage agreement (PPA = true positive/total GTCS), positive predictive value (PPV = true positive/all detected events), and daily FAR (total false alarms divided by the total days). PPA and PPV were corrected for multiple GTCS per patient.

Results: In EMU data, the novel algorithm preserved PPA (100%, corrected: 90.97%), increased PPV (31.03% to 53.55%), and reduced FAR (0.88 to 0.29/day). In ambulatory data, PPV improved from 17.40% to 33.27%, FAR dropped from 0.22 to 0.09/day, and PPA remained stable (95.41%, corrected: 90.64%).

Conclusion: Without sacrificing sensitivity, the novel algorithm significantly increased seizure-to-false alarm ratios in both EMU (2.6 times) and ambulatory conditions (2.4 times). Funding: Empatica

2032 | AI-powered Epilepsy Biomarker Identification in Routine EEG Following First Seizure

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Purpose: Early diagnosis of epilepsy after a first seizure is often hampered by the absence of interictal epileptiform discharges (IEDs) in routine EEG. This study aimed to determine whether integrating event-related potentials (ERPs) from intermittent photic stimulation (SLI), clinician-identified IEDs, and clinical metadata into machine learning models could enhance early diagnostic accuracy.

Method: We included 730 adult patients (≥18 years) who presented to the Geneva University Hospitals Emergency Department with a suspected first seizure and had at least 2 years of follow-up. EEG data were recorded during SLI;

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epochs (−100 to 500 ms) were bandpass filtered (1–40 Hz), notch filtered at 50 Hz, referenced, and artifact-cleaned. Low-frequency SLI epochs (1–2 Hz) were averaged to extract subject-level ERP features. Clinical data included demographics, symptoms (e.g., aura), and neurological findings. EEG models (stacked ensemble: Random Forest, K-Nearest Neighbors, logistic regression) were trained using 6-fold cross-validation. Clinical models used Random Forest. A fusion model combined EEG-ERP and clinical predictions via soft voting; IED presence overruled predictions. Performance was evaluated on a held-out test set using area under the ROC curve (AUC) with 95% confidence intervals (CI) from 2000 bootstrap iterations.

Results: The EEG-ERP-only model achieved an AUC of 0.72, the EEG-ERP+spikes model reached an AUC of 0.8, while the fusion model improved performance with an AUC of 0.91, showing an added diagnostic value from SLI-derived ERP features. The presence of IEDs was highly specific and used as an override mechanism in the final prediction.

Conclusion: Combining SLI-driven ERP features, clinical metadata, and IED presence enhances diagnostic accuracy after a first seizure. This lightweight, interpretable model may support earlier and more reliable identification of epilepsy, even when IEDs are absent.

Basic Science

1876 | Behavioral and morphological alterations of rats did-not develop status epilepticus by pilocarpine model

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Purpose: The pilocarpine-induced epilepsy model is widely employed as a robust experimental paradigm to replicate temporal lobe epilepsy (TLE) in Wistar rats, successfully mirroring key pathophysiological and clinical features observed in human patients.

Method: Male Wistar rats and adults weighing 220–240 grams were housed in controlled conditions, 22–24°C, and food and water ad libitum, and with 12 h normal light/dark cycles. All procedures involving the Wistar rats, and their care conformed to the institution's guidelines, which comply with the International Ethical Guidelines for Biomedical Research. The animals were injected with pilocarpine in dose of 350 mg/kg intraperitoneally. The behavior analysis began after the fifth day in 3 non-status epilepticus and 3 controls after pilocarpine injection and was performed up to the end of two months by video monitoring.

Results: The no-status epilepticus rats didn't show seizures during the entire evaluation period. Moreover, the sleep-wake cycle did not demonstrate differences between groups in seizure behavior. Isotropic fractionators showed no differences in the number of hippocampal neuronal and non-neuronal cells between control and no-status epilepticus groups.

Conclusion: This study contributes to the understanding of the mechanistic requirements underlying epileptogenesis in this model and highlights the importance of status epilepticus in driving the chronic epileptic phenotype.

1953 | What fuels seizures? Cell-specific, brain energy metabolism during seizures in awake mice

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Purpose: Seizures are traditionally attributed to disrupted excitation-inhibition balance, but this overlooks the critical role of energy metabolism. While seizures impose high metabolic demands, cell-type-specific changes remain poorly understood. Addressing this gap is crucial for understanding seizure onset and termination, uncovering self-regulatory brain mechanisms, and identifying metabolic therapy targets. While astrocytes were historically believed to supply neurons with lactate, recent evidence shows neurons can also upregulate glycolysis and release lactate during heightened activity. This paradigm shift underscores the need to examine neuron-glia metabolic

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interactions during seizures. This study aims to define neuron- and astrocyte-specific metabolic dynamics during seizures, focusing on glucose metabolism.

Method: We used two-photon fluorescence lifetime imaging (2P-FLIM) with simultaneous EEG in awake mice. AAVs encoding CaFLITS (calcium) and Peredox (NADH/NAD^+ redox sensor, a proxy for glycolytic activity) were injected into the cortex, and a cranial window was implanted. Non-convulsive seizures (spike-wave discharges >2×baseline, >5Hz, >20s) were induced via hippocampal stimulation. EEG was recorded ipsi- and contralaterally to the imaging site.

Results: Brief seizures triggered rapid astrocytic calcium influx, followed by a smaller secondary wave. However, this activity was not matched by immediate metabolic changes. Instead, glycolysis increased in both neurons and astrocytes with a delayed NADH/NAD^+ rise, peaking minutes after seizure onset. The response was stronger in astrocytes, revealing distinct redox dynamics and a temporal dissociation between signaling and metabolism across cell types.

Conclusion: Our study shows that metabolic responses lag behind rapid electrical and calcium signaling during seizures. Astrocytic calcium rises quickly, but metabolic activation is delayed, revealing a temporal mismatch between signaling and energy use. Differences in timing and magnitude between neurons and astrocytes indicate cell-type-specific metabolic regulation. To fully capture seizure-related energy dynamics, future studies will incorporate additional indicators (intra- and extracellular glucose, lactate, and ATP) to map the full energetic landscape at cellular resolution.

1958 | Epilepsy and inflammation: interictal clinical-molecular study

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Purpose: Drug-resistant epilepsy (DRE) represents a major therapeutic challenge. Although traditionally associated with abnormal brain electrical activity, recent studies suggest a significant role of inflammation and innate immunity in its pathophysiology. Our aim is to compare peripheral blood inflammatory biomarkers among patients with focal DRE, patients with well-controlled focal epilepsy (WCE), and healthy controls.

Method: Twenty patients with DRE, 20 with WCE, and 20 healthy controls were included. Serum levels of inflammatory cytokines and expression of TLR2 and TLR4 in monocytes and neutrophils were analyzed. Patients with additional systemic or neurological diseases were excluded.

Results: INF-γ levels were higher in DRE (27.0 pg/ml) compared to WCE (19.15 pg/ml) and controls (6.688 pg/ml) (p=0.0126; p<0.0001). Similarly for TNF-α: DRE (1045 pg/ml), WCE (736.9 pg/ml), and controls (525.6 pg/ml) (p=0.0384; p<0.0001), and for IL-2 (13.1 vs 22.9 vs 26.17 pg/ml; p=0.023; p=0.0046), with a similar trend for IL-8 and IL-5. Regarding TLRs, values were higher in DRE: TLR2 in monocytes (284.5 vs 227.8 vs 211.8; p=0.7687; p=0.0144), TLR4 in monocytes (410.6 vs 312.2 vs 206.4; p=0.0269; p<0.0001), TLR2 in neutrophils (31.97 vs 20.83 vs 17.75; p>0.9999; p=0.004), and TLR4 in neutrophils (36.13 vs 29.25 vs 17.39; p=0.0526; p=0.0005).

Conclusion: These findings support the involvement of inflammatory processes and innate immunity in the mechanisms underlying drug resistance.

1992 | Gain- and loss-of-function *GABRB2* variants are associated with distinct neurodevelopmental and epileptic phenotypes: Expanding the cohort

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Purpose: Variants in *GABRB2*, which encodes the β2 subunit of the $GABA_A$ receptor, can result in conditions ranging from febrile seizures to developmental and epileptic encephalopathies. In 2024, Mohammadi et al published a study which determined that *GABRB2* variants can lead to a gain or loss of $GABA_A$ receptor function, and that this functional divergence correlates to distinct disease phenotypes. Here, we expand the cohort to include 42 additional individuals harboring 28 different *GABRB2* variants.

Method: Genetic and clinical data were assembled through literature search and international collaboration. The variants identified were functionally tested with 2-electrode voltage clamp electrophysiology, using an α1β2γ2 receptor.

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Results: Electrophysiological analysis revealed that 11 variants result in a loss-of-function (LOF), 10 result in gain-of-function (GOF), and 7 were neutral. In good agreement with previous data, genotype-phenotype correlations indicate that individuals with GOF variants experience severe intellectual disability/developmental delay (DD/ID, 63%), were more likely to be non-ambulant (57%) and present with movement disorders (80%) and microcephaly (50%). Individuals harboring LOF variants, on the other hand, maintained ambulatory function, did not exhibit movement disorders and were less likely to experience severe DD/ID (15%).
Conclusion: By doubling the cohort of patients investigated in Mohammadi et al 2024, this work expands our previous understanding of the clinical phenotypes associated with GOF and LOF *GABRB2* variants.

1993 | Compound d_6-(*R*)-AS-7, a positive allosteric modulator of the excitatory amino acid transporter 2 (EAAT2), exhibits robust antiseizure and antinociceptive activity in animal models

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Purpose: Deuteration—the replacement of hydrogen atoms with their stable isotope deuterium, is a strategy increasingly used to improve the pharmacokinetic (PK) and safety profiles of drug candidates. In this study, we aimed to evaluate the pharmacological potential of new deuterated analogues of previously reported positive allosteric modulators (PAMs) of the excitatory amino acid transporter 2 (EAAT2), focusing on their antiseizure and antinociceptive efficacy.
Method: A focused library of deuterated EAAT2 PAMs was synthesized by incorporating different number of deuterium atoms. Their *in vivo* pharmacokinetic profiles were assessed following intraperitoneal (*i.p.*) and oral (*p.o.*) administration in mice. Antiseizure and analgesic efficacy was tested in various mouse models of seizures and pain. These analogues were evaluated *in vitro* for their ability to enhance glutamate uptake in COS-7 cells expressing EAAT2, as well as in primary astrocytes derived from mice. Additional mechanistic studies were also conducted to further support and clarify the compounds' mechanism of action.
Results: Deuteration significantly improved the PK properties of the compounds, particularly extending terminal half-life and increasing brain and plasma exposure. The lead compound, d_6-(*R*)-AS-7, demonstrated the most potent antiseizure and antinociceptive activity across multiple mouse models. This enhanced efficacy correlated with improved PK and was maintained up to 2 hours post-dose, supporting a strong PK/PD relationship. Mechanistically, d_6-(*R*)-AS-7 is a potent and selective enhancer of glutamate uptake as tested in COS-7 cells expressing EAAT2, as well as in mouse astrocytes. Importantly, deuteration did not alter the compounds' mechanism of action.
Conclusion: Our findings support deuteration as an effective strategy for optimizing and improving the drug-like properties of allosteric glutamate uptake enhancers. The lead compound, d_6-(*R*)-AS-7, emerged as a best-in-class EAAT2 PAM, warranting further preclinical development in advanced models of epilepsy, neurodegeneration, and pain.

2014 | Characterization of a *GABRD* Gain of Function Variant using Human Stem Cell-Derived GABAergic Neurons

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Purpose: While more and more patients with GABAAR variants are being discovered and more variants are characterized using oocyte or HEK cell models, there has yet to be any electrophysiological characterization of a GABAAR variant in human, stem cell-derived neurons. This is a crucial missing translational link for tying functional assays to clinical findings. The experiments in this abstract aim to fill in that gap.
Method: CRISPR-Cas9 was used to create a variant in position L260V of *GABRD*, using the H9 human embryonic stem cell line as a basis. The L260V line and its isogenic

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wildtype (WT) control line were differentiated into induced GABAergic neurons by transduction with the genes *ASCL1* and *DLX2*. The cells were grown for 40-45 days, in an autaptic culture system using "islands" of primary mouse glia. Finally, the cells were analyzed using whole-cell patch clamp and immunocytochemistry.

Results: The L260V line responded to 5 μM GABA with a current amplitude 77 % larger than the WT line (-489 pA ±116 pA vs. -277 pA ±44.6 pA, respectively, 95 % CI). The average change in current for the last 10 seconds of a 60 second GABA exposure was 64 % larger for L260V than WT (-268 pA ±90.7 pA vs. -163 pA ±27.2 pA, respectively, 95 % CI). No significant change was found for amplitude or total charge of single evoked inhibitory postsynaptic currents.

Conclusion: Human stem cell-derived GABAergic neurons with the GABRD L260V variant display a gain of function response to GABA when compared to an isogenic control. This is an important finding, further proving the existence of GABAAR gain of function epilepsies and their clinical implications.

Climate Change

1848 | Association of Road Traffic Noise with the Risk of New-Onset Epilepsy

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Purpose: The study's objective was to assess whether long-term road traffic noise exposure is associated with the risk of new-onset epilepsy among adult residents of Toronto, Canada.

Method: We conducted a nested case-control study using linked health administrative and environmental data. We included adult residents of Toronto as of January 1, 2010, with no history of seizures or epilepsy. Cases were those who developed epilepsy before December 31, 2016, and were each matched with up to five controls. We measured exposure to road traffic noise using three-year averages of the nighttime average ($LA_{eq,\ 8\ hr}$), daytime average ($LA_{eq,\ 16\ hr}$), and the 24-hour average ($LA_{eq,\ 24\ hr}$) road traffic noise levels at participants' postal code of residence. We estimated the associations of these three-year averages with the risk of new-onset epilepsy using conditional logistic regression models.

Results: We included 4,608 cases and 20,765 controls; 46.3% were female and the mean age was 48.3 (±17.4). The median [interquartile range] three-year average noise levels were 54.4 [12.9] dB, 63.3 [11.3] dB, and 60.3 [11.8] dB for $LA_{eq,\ 8\ hr}$, $LA_{eq,\ 16\ hr}$, and $LA_{eq,\ 24\ hr}$, respectively. The odds ratios associated with a 10-dB increase in $LA_{eq,\ 8\ hr}$ was 1.043 (95% CI: 0.994, 1.095), 0.999 (95% CI: 0.946, 1.054) for $LA_{eq,\ 16\ hr}$, and 1.031 (95% CI: 0.980, 1.086) for $LA_{eq,\ 24\ hr}$.

Conclusion: There may be an association between long-term exposure to road traffic noise, particularly at night, and the risk of new-onset epilepsy. Considering that little research has been published on the association of environmental noise with the risk of new-onset epilepsy, and given its biological plausibility, future research should continue to explore this potential association.

Clinical Neurophysiology

1917 | Quantitative EEG Biomarkers of Long-Term Response to Lacosamide in Drug-Naive Focal Epilepsy

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Purpose: Lacosamide (LCM) is an antiseizure medication (ASM) approved for treating focal-onset seizures. However, its specific effects on cortical activity and connectivity remain unknown. The aim of this study is to evaluate quantitative EEG (qEEG) changes induced by LCM monotherapy in drug-naive people with epilepsy (PwE) compared to healthy controls (HC) and to assess the predictive value of qEEG for long-term clinical outcomes.

Method: We performed a longitudinal, retrospective, pharmaco-EEG study on a population of 20 PwE and a group of 24 HC. Clinical outcome was evaluated two years after LCM initiation, classifying PwE as seizure-free (SF) and non-seizure-free (NSF). Resting-state EEG was acquired before (<30 days) and approximately 6 months after LCM initiation. qEEG features were compared between PwE and HC groups and between SF and NSF groups after LCM. Nineteen-channel EEGs were recorded and processed using Brainstorm software. Power Spectral

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Density (PSD) and Amplitude Envelope Correlation (AEC) were computed across five frequency bands (delta, theta, alpha, beta, gamma). We performed Wilcoxon tests to compare PSD and AEC between Condition (pre-LCM, post-LCM, HC) for each frequency band. Finally, we employed logistic regression to assess the performance of qEEG in predicting clinical outcome.

Results: No significant qEEG changes were observed between pre- and post-LCM. Theta-band PSD and connectivity were higher in PwE than HC, both pre LCM (connectivity, $p=0.038$; PSD, $p=0.04$) and post LCM (connectivity, $p=0.007$; PSD, $p=0.005$). AEC connectivity in the theta band predicted clinical outcome (2-years seizure freedom) with an estimated accuracy of 60% (area under the curve [AUC]=0.66) for the EEG pre-LCM and 75% (AUC = 0.86) for the EEG post-LCM.

Conclusion: These findings support the use of pharmaco-EEG as a non-invasive tool for predicting long-term clinical outcomes in focal epilepsy.

1934 | Electroencephalographic Changes in Patients with Blast-Induced Concussion

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Purpose: Blast-induced concussion is classified as a mild traumatic brain injury (mTBI). It may elevated risk of developing epileptic seizures. The aim is to investigate electroencephalography (EEG) changes in patients in the chronic stage of blast-associated mTBI and to assess the potential of using EEG data for objective confirmation of brain injury.

Method: The study included 32 male combatants aged 25–43 years with a diagnosis of "mTBI, chronic stage" (6 months to 3 years post-injury), and a control group of 15 healthy males. EEG was recorded in a soundproof room using a 19-channel NeuroCom EEG system (Ukraine) with a sampling rate of 400 Hz and 16-bit resolution. Electrodes were applied according to the international 10–20 system. EEG recordings were conducted during resting wakefulness for up to 30 minutes, including activation procedures: eye opening/closing, intermittent photic stimulation, and 3 minutes of hyperventilation. Both visual and spectral EEG analyses were performed. Spectral analysis was conducted on artifact-free, stationary segments (35–45 seconds) of resting-state EEG. Spectral analysis was conducted on artifact-free, stationary segments (35–45 seconds) of resting-state EEG.

Results: Compared to controls, the mTBI group demonstrated decreased relative power in the alpha band and increased power in the beta, theta, and delta bands, predominantly in frontal and temporal regions. Visual analysis revealed frontal intermittent rhythmic delta activity (FIRDA) in 37.5% of cases, mild background slowing on the side of trauma in 87.5%, anterior temporal and frontal spikes in 21.9%, occipital spikes in 15.6%, and generalized spike-wave discharges in 6.3%.

Conclusion: The EEG alterations identified in patients with chronic blast-induced mTBI suggest a general decrease in cortical functional activity. The presence of intermittent slow-wave activity in frontotemporal regions may reflect disruption in prefrontal-subcortical connectivity due to microscopic white matter damage. These findings may represent early electrophysiological markers of increased neuronal excitability and epileptogenesis.

1969 | Detection of Interictal Spikes with Simultaneous EEG and OPM-MEG

Z Seedat[1], C Embury[1], K St. Pier[1], C Scott[1], F Moeller[2], K Das[2,1], T Tierney[3], G Barnes[3], M Walker[3,4], U Vivekananda[3,4], H Cross[5,1]
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Purpose: Optically-Pumped Magnetometer Magnetoencephalography (OPM-MEG) is an emerging functional neuroimaging tool which measures the magnetic fields induced by current flow in cortical neurons. It's primary benefit over traditional MEG is its wearability, allowing sensor placement close to the scalp regardless of head size and enabling free head movement during recordings. In recent years it has been used to detect interictal spikes in pediatric epilepsy patients. However, many challenges remain including clinical interpretation of OPM-MEG which depends on the orientation and number of sensors, sensor bandwidth, and the presence of cable and magnetic field artefacts. Electroencephalography (EEG) is the standard technique for recording interictal activity and is interpretable by clinicians worldwide. By simultaneously recording EEG and OPM-MEG in a cohort of pediatric epilepsy patients, we aim to enable interpretation of interictal OPM-MEG data, bridging the gap between OPM-MEGs potential and its concrete clinical utility.

Method: Nine pediatric epilepsy patients (age 5.6-13.5 years) were recruited. Four had known focal, one known multifocal, and four known generalized epileptiform discharges (recorded in previous clinical EEGs).

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Participants were scanned for up to 1 hour in Young Epilepsy's 64-sensor dual-axis (128-channel) OPM-MEG system (Cerca Magnetics Ltd, Nottingham, UK) while wearing a MEG compatible EEG system (Brain Products GmbH, Munich, Germany). 28 scalp electrodes were applied (modified 10-10 montage) and peripheral electrodes recorded lead-1 ECG and bilateral deltoid EMG. EEG and OPM-MEG data were synchronized using an external trigger.

Results: Spontaneous interictal discharges were recorded in 6/9 OPM-MEG and EEG datasets (identified by an experienced clinical scientist). Of those without identifiable interictal spikes, 2 showed abnormal slowing and 1 did not show any clear abnormal activity.

Conclusion: These data show that simultaneous EEG/OPM-MEG is well-tolerated and interictal discharges can be recorded in a small cohort of pediatric patients. Simultaneous recordings will enable future clinical interpretation of OPM-MEG.

1998 | Electrophysiological Characteristics and Biomarker Correlation in Immune-Mediated Epilepsies in young: Pre- and Post-Immunotherapy Analysis

G Burman[1]
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Purpose: Immune-mediated epilepsies (AIE) and autoimmune encephalopathies are increasingly recognized and included in the ILAE 2017 epilepsy classification. These conditions often present with drug-resistant seizures and encephalopathy, even when neuroimaging is normal or nonspecific. This study aimed to evaluate the electrophysiological patterns in pediatric AIE, their correlation with autoimmune biomarkers, and the therapeutic impact of immunomodulatory treatments, especially when conventional imaging like MRI fails.

Method: A retrospective analysis was conducted on young aged 4–14 years diagnosed with drug-resistant epilepsy and encephalopathy from January to December 2024 in author's hospital. Cases with infections, trauma, structural or vascular brain lesions were excluded. Six cases met the inclusion criteria. Biomarker studies (including autoimmune panels, CSF and serum NMDAR and antithyroid (TPO) antibodies) and imaging using epilepsy protocols were performed. EEG patterns were assessed at baseline, 3 months, and 12 months after immunotherapy (IVIG/steroids). Three cases had positive autoimmune markers: one with CSF positive NMDAR antibodies and two fulfilling FIRES criteria.

Results: Initial EEGs showed diffuse delta/theta slowing (60%), epileptiform discharges (35.6%), extreme delta brush (EDB) (35.8%), FIRDA (15%), and periodic complexes. Anti-NMDAR encephalitis cases showed progression from frontal beta activity to rhythmic delta waves and EDB. Post-immunotherapy EEGs demonstrated marked improvement with reduction of epileptiform and frontal abnormalities over 3–12 weeks, underscoring the role of immune mechanisms in seizure pathogenesis. Significant time interval changes were noted at 3- and 12-month follow-up.

Conclusion: Immune-mediated epilepsies present distinct EEG abnormalities even with normal imaging. Autoimmune biomarkers in both blood and CSF assist in early diagnosis. Significant EEG improvement following immunotherapy confirms the role of inflammation in epileptogenesis. Early recognition and immune therapy can improve the outcomes in pediatric drug-resistant epilepsies with positive or negative biomarkers. High index of clinical suspicion is required to diagnose immune mediated epilepsy with encephalopathy which is reversible on treatment.

2020 | Automated detection distinguishes between physiological ripples and epileptic high frequency oscillations

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Purpose: Intracranial EEG from the medial temporal lobe (MTL) of patients with epilepsy shows both physiological ripples and epileptic high frequency oscillations (HFOs). The distinction between the two types of events is debated.

Method: We recorded intracranial EEG in bilateral MTL from 14 patients while they performed a verbal working memory task where letter strings of set size 4, 6, or 8 were presented. Letters were shown during the encoding stage (duration 2 s), followed by the maintenance stage (3 s) and visual presentation of a probe letter, which initiated the retrieval stage [1]. Using two fully automated detectors, we identified physiological ripples and epileptic HFOs [2]. One MTL was subsequently resected. Postsurgical seizure outcome was dichotomized in seizure free (ILAE1) or seizure recurrence (ILAE2-6).

Results: During the performance of a trial, there was a significant clustering of ripples during encoding of memory items and during memory retrieval ($p < .05$), speaking for the ripples as markers of memory function. The

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rate of epileptic HFOs was not modulated by any of the task stages ($p > .05$). Across all patients, the number of physiological ripples (29693) was higher than the number of epileptic HFOs (8276). The distributions of amplitude and center frequency largely overlapped between ripples and HFOs. Nevertheless, only 5 HFOs per patient (1%) coincided with a physiological ripple. Across the 9 patients who achieved postsurgical seizure freedom (ILAE1), the median HFO rate in the epileptogenic MTL (0.06 IQR [0.04 0.11]) was higher than in the healthy MTL (0.03 IQR [0.01 0.04], p=0.01), speaking for HFOs as markers for epileptogenic tissue.

Conclusion: We demonstrate a well-defined setup where physiological ripples and epileptic HFOs are clearly distinguishable by automated detectors. [1] Dimakopoulos et al, *eLife* 2022, [2] Dimakopoulos et al, *Brain* 2025

Comorbidities

1843 | Association of apolipoprotein E gene with risk and prognosis of epilepsy

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Purpose: Genetic factors play a significant role in epilepsy. The Apolipoprotein E (ApoE) gene may have a biological connection with epilepsy. However, previous clinical studies have failed to draw definite conclusions on the correlation between two. Therefore, our study aims to explore the clinical correlation between ApoE ε4 and epilepsy.

Method: A cohort study was conducted based on the UK Biobank. Participants were grouped based on the ApoE ε4 they carried. The association with the risk of epilepsy was analyzed using the Cox proportional hazards model, and the risks of late-onset epilepsy and post-stroke epilepsy were analyzed separately. Among participants with epilepsy. The Cox proportional hazards model was used to explore its relationship with the risk of dementia after epilepsy and the risk of future death.

Results: A total of 412,848 participants underwent ApoE genotype testing. Carrying ApoE ε4 increases the risk of epilepsy (Carry one ε4: HR [95% CI] =1.06 [1.01, 1.12]; Carry two ε4: HR [95% CI] =1.39 [1.22, 1.59]). It also increases the risk of late-onset epilepsy and has an impact in specific subgroups of post-stroke epilepsy (Among people who have first stroke after 50 years old). Carrying ApoE ε4 increases the risk of dementia after epilepsy (Carry one ε4: HR [95%CI] =1.80 [1.49, 2.17]; Carry two ε4: 3.25 [2.26, 4.66]). Carrying ApoE ε4 increases the risk of death of people with epilepsy (Carry one ε4: HR [95%CI] =1.11 [0.99, 1.21]; Carry two ε4: HR [95%CI] =1.39 [1.15, 1.63]), especially the neurological disorders causes (Carry one ε4: HR [95%CI] =1.26 [1.02, 1.50]; Carry two ε4: HR [95%CI] =2.23 [1.79, 2.67]).

Conclusion: Carrying ApoE ε4 is a risk factor for epilepsy. Carrying ApoE ε4 significantly increases the risk of dementia after epilepsy and increases the risk of death in people with epilepsy, especially the neurological causes.

1851 | Multimorbidity in adults with epilepsy attending an outpatient epilepsy clinic.

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Purpose: Knowledge about multimorbidity and types of multiple chronic conditions (CC) in people with epilepsy (PWE) seen in an outpatient care setting is lacking. We aim to examine the distribution of multimorbidity and describe the contributing comorbidity of somatic and psychiatric CC in adult PWE in relation to age (≤25; 26-64; ≥65 years), sex (female; male), type of epilepsy (Idiopathic; Structural; Developmental & Epileptic Encephalopathy [DEE]), resistance to treatment (yes; no), and duration of epilepsy (as per 4 quartiles).

Method: In this observational retrospective cohort study, we assessed 330 adult PWE seen in an epilepsy outpatient clinic. The prevalence of multimorbidity was estimated according to the presence of one or more somatic or psychiatric comorbid CC. We estimated the multimorbidity prevalence within each group and assessed for statistically significant differences.

Results: Nearly 80% of PWE seen in an outpatient setting were multimorbid. Over two thirds of participants had a somatic CC and over two fifths a psychiatric CC. These conditions did not occur randomly but varied in relation to age, type of epilepsy, and resistance to treatment. Almost all older adults with epilepsy were multimorbid due to common somatic CC. Neurodevelopmental disorders were often seen in the young adults with epilepsy, people with drug-resistant epilepsy, and/or DEE. The most common chronic comorbid conditions in PWE included depression, anxiety, and insomnia. There appeared to be no influence on the prevalence of

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multimorbidity in epilepsy based on sex, drug resistance, or duration of epilepsy.

Conclusion: This is the first study of multimorbidity in adult PWE seen in an outpatient setting and its distribution according to patient and epilepsy characteristics. The findings provide insights into the burden of chronic disease in PWE seen in tertiary care and call for adequate identification and response to patient's needs by health professionals.

1910 | Determination of cognitive impairment in Pharmacoresistant Epilepsy patients on Anti-Seizure Medications (ASMs) -- A Cross- sectional, Observational study.

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Purpose: Cognitive deterioration represents a critical and frequently under-recognized comorbidity in individuals diagnosed with epilepsy, with heightened prevalence in those exhibiting resistance to pharmacological interventions. This study attempts to quantify the prevalence and severity of cognitive dysfunction in patients with Drug-Resistant Epilepsy (DRE) receiving ongoing Anti-Seizure Medications (ASMs). The study also seeks to identify potential correlations between cognitive outcomes and a spectrum of demographic and clinical variables, including age, duration of illness, and pharmacotherapeutic regimen. The findings may help to inform early risk stratification protocols and foster targeted cognitive monitoring strategies to improve quality of life.

Method: This study enrolled patients (≥18 years) diagnosed with DRE in accordance with the criteria established by the International League Against Epilepsy (ILAE). Participants were prospectively recruited from the Neurology Outpatient Department of the All India Institute of Medical Sciences, New Delhi. Informed written consent was obtained prior to participation. Cognitive evaluation was conducted utilizing two validated neuropsychological scales: the Montreal Cognitive Assessment (MoCA) and the Addenbrooke's Cognitive Examination-III (ACE-III), both designed to comprehensively assess multiple domains of cognitive function.

Results: The mean MoCA score was 19.89 ± 5.85, with 83.34% of participants scoring below the conventional threshold of 26, indicative of cognitive impairment. Similarly, the ACE-III yielded a mean total score of 75.47 ± 14.71, with 77.78% of subjects exhibiting scores beneath the accepted cutoff of 88, thereby corroborating the presence of significant cognitive deficits. Both instruments demonstrated consistent findings, reinforcing the widespread nature of cognitive compromise in individuals with pharmacoresistant epilepsy.

Conclusion: This study highlights the high prevalence of cognitive impairment in patients with Drug-Resistant Epilepsy (DRE). Reduced mean scores on both MoCA and ACE-III, along with a majority scoring below normative cutoffs, emphasize the need for routine cognitive screening. Early detection and targeted intervention are vital to minimize functional decline and improve patient outcomes.

Drug Therapy

1847 | A European Study of the Effectiveness of Risk Minimization Measures for Fenfluramine Oral Solution in Dravet Syndrome and Lennox-Gastaut Syndrome

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Purpose: To assess the effectiveness of the risk minimization measures in Europe for providers prescribing fenfluramine.

Method: In this observational post-marketing safety study, a secure electronic survey of closed-ended questions was delivered to physicians routinely prescribing fenfluramine. Primary objective was to assess awareness, knowledge, and self-reported physician compliance regarding educational material on echocardiogram follow-up. Data were collected 12–18 months after educational material implementation in each country. Effectiveness was defined as ≥80% of physicians providing correct answers to nine questions related to the primary objective. Descriptive statistics and Clopper-Pearson for 95% CIs were used. Results from secondary objectives will also be presented.

Results: Of 705 physicians from six European countries, 118 completed the survey; 69.5% were pediatric neurologists, 98.3% were in practice ≥5y, and 72% first prescribed fenfluramine ≥6 months before the survey. Overall, 20.3% of physicians (95% CI: 13.5 to 28.7) provided correct responses to nine questions supporting the primary objective, and a mean 84.7% (95% CI: 82.5 to 86.8) of correct responses to any of the nine questions per participant was observed. Over 80% of physicians reported receiving and reading educational materials; 93.2% of physicians (95%

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CI: 87.1 to 97.0) identified echocardiogram as required monitoring during fenfluramine treatment, 94.1% (95% CI: 88.2 to 97.6) identified the need for additional echocardiograms if suspicion of valvular heart disease (VHD) or pulmonary arterial hypertension (PAH) occurs, and 99.2% (95% CI: 95.4 to 100.0) recognized the need to inform patients/caregivers about echocardiogram monitoring.

Conclusion: These data indicate a reasonable degree of awareness among European physicians regarding fenfluramine educational materials, despite the effectiveness success criterion not being met. Physicians indicated being aware of VHD and PAH risks when prescribing fenfluramine and demonstrated high compliance with echocardiogram monitoring. Regular distribution of educational materials to prescribers, patients, and caregivers is needed to re-emphasize risk minimization measures.

Supported by: UCB

1863 | Trilostane is Antiepileptic in The Kainic Acid Model: Prevented Epileptogenesis and Reduced Seizure Occurrence During Stress Exposure

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Purpose: Stress contributes to the onset and progression of epilepsy, as well as exacerbate comorbidities like depression and anxiety. Neurosteroids (NSs), synthesized in the brain, modulate neuronal excitability through GABA receptors and exhibit anti-neuroinflammatory effects. This study aims to investigate the effects of trilostane on epileptogenesis and epilepsy progression in a stress-exacerbated temporal lobe epilepsy model by modulating NSs levels in the brain.

Method: Self-limited status epilepticus (SE) was induced in Sprague-Dawley rats using 15 mg/kg kainic acid intraperitoneally, confirmed by video-electrocorticographic recordings. Rats were assigned to two groups: Group 1 (n=7) received sesame oil (vehicle, s.c.), and Group 2 (n=12) received trilostane (50 mg/kg/day, s.c.) for 21 days. Stress was induced through social isolation and daily injections. Seizure frequency, stage, and duration were monitored using Video-EcOG.

Results: During the 21-day treatment period, all animals in the vehicle group developed spontaneous recurrent seizures (SRS), with non-convulsive seizures starting on day 5 ±1 and convulsive seizures on day 11 ±0.8. In contrast, only 5 animals in the trilostane group developed SRS, with non-convulsive seizures starting on day 10 ±0.9 and convulsive seizures on day 13 ±0.3. Statistical analysis (Fisher's exact test) revealed a significant difference in the number of epileptic rats between the groups ($P < 0.05$). We monitored five rats from the trilostane group for one month after treatment discontinuation. Only two of these rats developed recurrent seizures two weeks after discontinuation. The total number of SRSs differed significantly between the groups during treatment ($P<0.001$, T-test), but no significant difference in seizure duration was observed.

Conclusion: This study suggests that trilostane, by modulating NSs levels in the hippocampus and neocortex, partially prevents epilepsy and reduces seizure frequency in a stress-exacerbated temporal lobe epilepsy model. These effects were evident during trilostane administration and were partially sustained following treatment discontinuation.

1866 | Long-Term Safety, Tolerability, and Efficacy of Bexicaserin for the Treatment of Seizures in Participants with Developmental and Epileptic Encephalopathies: Primary Results of a 12-Month Open-Label Extension of the Phase 1b/2a PACIFIC Trial

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Purpose: Developmental and epileptic encephalopathies (DEEs) are the most severe group of epilepsies, in which frequent epileptiform activity and treatment-resistant seizures both contribute to developmental slowing or regression. Bexicaserin is a highly selective 5-hydroxytryptamine type 2C (5-HT_{2C}) receptor superagonist under investigation to treat seizures in patients with DEEs. Bexicaserin was well tolerated in the randomized, double-blind, Phase 1b/2a PACIFIC trial (RCT), with a favorable safety profile

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and similar reductions from baseline in countable motor seizures in Dravet syndrome (DS), Lennox-Gastaut syndrome (LGS), and other DEEs (DEE Other). Here, we present primary analyses of the open-label extension (OLE) of this trial.

Method: After completing the RCT, participants could enroll in the OLE which investigated the safety, tolerability, and efficacy of bexicaserin, analyzed as the change from RCT baseline through OLE Month 12, in participants aged ≥12 and ≤65 years with DS, LGS, or DEE Other. Participants underwent a 52-week open-label treatment period inclusive of a 15-day flexible titration period (maximum 12 mg TID, based on tolerability), followed by a maintenance period.

Results: All 41 participants (32 bexicaserin, 9 placebo) who completed the RCT (3 DS, 20 LGS,18 DEE Other) enrolled in the OLE, with 38 (92.7%) completing the 12-month period. Three participants discontinued treatment due to lethargy, withdrawal of consent, and relocation. The most common adverse events were consistent with those observed previously. During the OLE, a median reduction of 59.3% in countable motor seizure frequency was observed, with 55% of participants experiencing reductions of ≥50% from RCT baseline.

Conclusion: The high enrollment (100%) and completion rates (92.7%) in the OLE show bexicaserin was well tolerated, with no new safety signals observed. Comparable seizure reductions between the RCT and 12-month OLE reinforce the durability and consistency of bexicaserin across DEEs, further validating its progression into Phase 3 trials.

1869 | Efficacy of Cannabidiol in Reducing Epileptiform Activity in Patients with Drug-Resistat Epilepsy: An Electroencephalographic Study

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Purpose: Drug-Resistant epilepsy poses a significant clinical challenge, as many patients do not respond adequately to conventional treatments. In recent years, cannabidiol (CBD) has emerged as a promising therapeutic option. This study aims to evaluate changes in electroencephalographic (EEG) biomarkers in patients with Drug-Resistant epilepsy following CBD administration, in order to determine its impact on brain activity and seizure severity.

Method: Thirty-four patients diagnosed with Drug-Resistant epilepsy were included. EEG recordings were performed at three key points: at treatment initiation, at 6 months, and at 12 months. The study analyzed electrical brain activity, focusing on the presence and severity of epileptiform abnormalities, as well as the overall organization of the EEG tracings. Seizure frequency and severity were also recorded throughout the study period.

Results: The results demonstrated a significant decrease in abnormal baseline activity and epileptiform abnormalities after CBD treatment. Notably, there was an improvement in EEG organization and a reduction in seizure frequency, with many patients exhibiting less than 50% epileptiform activity at 12 months. Some patients even achieved complete absence of epileptiform activity. These electroencephalographic changes suggest a positive effect of CBD on brain activity, correlating with clinical improvements in seizure severity and frequency.

Conclusion: This study provides evidence that CBD can favorably modify EEG biomarkers in patients with Drug-Resistant epilepsy, reducing epileptiform activity and enhancing cerebral organization. These findings support the potential of CBD as an effective therapeutic option, not only for seizure control but also for improving brain function in these patients. EEG monitoring may serve as a useful tool to evaluate treatment response to CBD in Drug-Resistant epilepsy.

1873 | Efficacy of Levetiracetam on Cognitive Performance in People with Cognitive Decline: A Systematic Review and Meta-Analysis of Randomized Controlled Trials

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Purpose: We conducted a systematic review and meta-analysis of randomized controlled trials (RCTs) evaluating the efficacy of levetiracetam (LEV) compared to placebo in improving cognitive performance in people with cognitive decline.

Method: The protocol was pre-registered with PROSPERO (CRD420250656389), and reporting followed PRISMA guidelines. We searched RCTs that enrolled adult patients with cognitive decline, of any stage, comparing LEV to placebo or other active substance, and which reported at

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least one of the following primary or secondary outcomes: clinical dementia rating scale (CDR) or its sub-items; language, verbal memory/memory, executive, visuo-spatial and multi-domain cognitive test results. Studies were assessed against Cochrane Risk of Bias 2.0 tool for bias. A meta-analysis was conducted using mean difference (MD) or standardized MD (SMD) according to the available scales. Meta-analysis of binary outcomes was used to compare adverse events.

Results: Overall, 6 RCTs provided data for 283 participants. LEV was not associated with a significant improvement in cognitive function measured by CDR-SB compared to placebo (MD=0.04, 95%CI=-0.23 to 0.31, I2=0%, n studies=2). LEV significantly improved visuospatial function (SMD= -0.25, 95% CI= -0.49 to -0.01, I2=0%, n studies=2) and marginally improved executive function (SMD= -0.29, 95% CI= -0.63 to +0.05, I2=0%, n studies=3). Importantly, no differences between LEV and placebo emerged in terms of adverse events.

Conclusion: LEV was well tolerated in people with cognitive impairment. Although LEV did not improve global cognitive function, there were improvements in visuospatial function and, more marginally, executive function. Further studies are needed to assess LEV in larger populations, with application of standardized testing paradigms.

1874 | Clinical Outcomes of Cenobamate Use in Drug-Resistant Temporal and Extratemporal Epilepsy: Experience from a Tertiary Epilepsy Clinic

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Purpose: To assess efficacy and tolerability of Cenobamate (CNB) in drug-resistant focal epilepsy and to compare its adjunctive therapeutic effectiveness between patients with temporal lobe epilepsy (TL) and extratemporal lobe epilepsy (ET) in a Epilepsy Outpatient Service.

Method: retrospective, single-center evaluation of patients with drug-resistant focal epilepsy treated with CNB for more than 2 months between January 2022 and December 2024. Clinical data were collected: monthly seizure frequency, seizure types, treatment retention rate, adverse drug reactions (ADRs), and concomitant antiseizure medications (ASMs). ADRs were systematically recorded. Patients were classified as "non-responders," "responders 50%," or "seizure-free."

Results: 55 patients (age >18 years; mean 51.3 ± 13.9 years; 49% male), average follow up 521 ± 308 days. Based on magnetic resonance imaging (MRI), electroencephalography (EEG), and clinical features, 25 patients had TL epilepsy, 30 had ET epilepsy (18 frontal, 3 parietal, 1 occipital). CNB was discontinued (7 due to ADRs, 4 due to ineffectiveness). Treatment led to significant reduction in seizure frequency ($t(49) = 3.42$, $p = 0.001$). 54% were classified as "responders 50%" and 20.1% as "seizure-free." No significant difference in seizure reduction was found between TL and ET groups (Mann–Whitney U, $p > 0.05$), although a higher proportion of ET patients showed improved seizure control.

Conclusion: Consistent with previous studies, our findings confirm CNB's effectiveness in reducing seizure frequency, its favorable tolerability, and its potential to reduce pharmacological burden. ADRs were generally manageable, with few permanent discontinuations. No prior studies have directly compared CNB efficacy across focal epilepsy subtypes. Although no significant differences were observed, trends in our data suggest that differential responses may emerge with larger cohorts. Our findings support the efficacy of CNB as adjunctive therapy in drug-resistant focal epilepsy. Further research with larger sample sizes is needed to clarify potential differences in response between TL and ET epilepsy.

1884 | Real-world experience of adjunctive fenfluramine for the treatment of seizures associated with Lennox-Gastaut syndrome

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Purpose: This study aimed to evaluate the effectiveness and tolerability of fenfluramine (FFA) in children and adults with Lennox-Gastaut syndrome (LGS) within clinical practice.

Method: A retrospective, multicenter chart review of patients with LGS receiving FFA at 27 centers in Italy. Data were extracted from clinical charts up to 12 months after treatment.

Results: Sixty-two patients (54.8% males) with LGS were included. The median age was 17 (interquartile range, 11-31) years and 34 were adults.

The mean percentage reduction in frequency of drop-seizures was 48.7%, 56.0% and 56.4% at 3, 6, and 12 months following FFA treatment. The corresponding values for non-drop seizures were 38.6%, 39.1%, and 32.0%. A ≥50% reduction in frequency of drop seizures was observed in 50% of the participants at 3, 6, and 12 months; a ≥50% reduction in frequency of non-drop seizures was reported by 42.9%, 45.9% and 41.7% of subjects. At 6-month follow-up, the median number of 3-month days free of drop seizures increased from a median of 55 to a median of 84 days. Discontinuation of at least one concomitant antiseizure medication occurred in 12 cases.

The overall retention rate was 72.6% and adverse events occurred in 38.7% of participants. Most common adverse events included somnolence and decreased appetite. Treatment discontinuation due to adverse events occurred in 9 subjects. Subjects rated as slightly improved, much improved, or very much improved for overall condition from baseline to 6 months as measured by the Physician Global Impression of Change scale and Caregiver Global Impression of Change were 77% and 79%, respectively.

Conclusion: In this chart review of patients with LGS, FFA demonstrated sustained effectiveness and favorable tolerability profile in patients with LGS in real-world clinical practice.

1901 | Effect of Cannabidiol on Antiseizure Medication Cycling, Polypharmacy, and Healthcare Resource Utilization in Patients With Dravet Syndrome, Lennox-Gastaut Syndrome, or Tuberous Sclerosis Complex: Real-World Data from a US Claims Analysis

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Purpose: Inadequate seizure control results in antiseizure medication (ASM) cycling for patients with Dravet syndrome (DS), Lennox-Gastaut syndrome (LGS), or tuberous sclerosis complex (TSC). In Europe, cannabidiol (CBD; Epidyolex® [EU], 100 mg/mL oral solution) is approved for antiseizure use in patients aged ≥2 years with TSC or, in conjunction with clobazam (CLB), for DS or LGS. Using the US Optum® Market Clarity database, this retrospective cohort study analyzed CBD effectiveness in terms of ASM cycling, polypharmacy, and healthcare resource utilization (HCRU) in patients newly receiving CBD.

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Method: Patients were indexed between June 2018 and September 2023, stratified by pediatrics (≥2–<18 years)/adults (≥18 years) and epilepsy type. For this analysis, those with DS/LGS had received CLB within 12 months of CBD initiation. Follow-up was ≤12 months. Differences in outcomes, relative to the expected trajectory had CBD not been initiated, were calculated using interrupted time series analysis.

Results: Overall, 1,535 pediatric and 752 adult patients were included. Most were male (56% pediatric; 56% adult), non-Hispanic White (51%;58%), and had intellectual disability or developmental delay (64%;54%). At 12 months post-CBD initiation, reductions in overall ASM cycling in pediatric patients with DS, LGS, and TSC were estimated at 45%, 45%, and 27%, respectively; and 51%, 45%, and 8% in adults. Estimated reductions in maintenance ASM burden in pediatric patients with DS, LGS, and TSC were 36%, 33%, and 25%, respectively, and 20%, 15%, and 14% in adults. Overall, reductions in HCRU elements (seizure-related hospitalizations, ER visits, and physician visits) were observed across ages and indications.

Conclusion: These real-world data show overall reductions in ASM cycling, polypharmacy, and HCRU 12 months post-CBD treatment in both pediatric and adult patients. Data suggest that CBD may reduce clinical and economic burden of disease in pediatric and adult patients living with DS, LGS, or TSC. Funding: Jazz Pharmaceuticals, Inc.

1905 | Perampanel Exposure Correlates with Seizure Control in Children with Epilepsy

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Purpose: Perampanel is a selective AMPA receptor antagonist commonly used in pediatric epilepsy. Despite its widespread use, the pharmacodynamic relationship between perampanel blood concentration and clinical outcomes remains unclear. This study aimed to evaluate whether measured perampanel plasma concentrations are associated with seizure response, tolerability, and treatment retention in children aged 4–12 years across real-world clinical settings.

Method: We retrospectively reviewed 96 pediatric patients treated with perampanel at three tertiary centers in Korea (Seoul National University Children's Hospital, Bundang Seoul National University Hospital, and Chungbuk National University Hospital). A total of 102 perampanel trough levels were analyzed. Patients were classified as responders if seizure frequency was reduced by ≥50%, and treatment-related adverse events (AEs) were identified from medical records. Perampanel monotherapy vs. polytherapy status at the time of sampling was also recorded. Independent t-tests and logistic regression were used to evaluate pharmacodynamic associations.

Results: Responders (n=58) had significantly higher perampanel levels than non-responders (n=35) (mean 399 vs. 275 ng/mL, p=0.0056). However, perampanel levels did not differ significantly between patients with and without adverse events (mean 373 vs. 348 ng/mL, p=0.66). Patients receiving monotherapy had significantly higher perampanel levels than those on polytherapy (mean 439 vs. 317 ng/mL, p=0.0073). Treatment was retained in 88 patients (92%), while 13 discontinued, primarily due to adverse events or lack of efficacy.

Conclusion: Measured perampanel concentration was significantly associated with seizure response but not with adverse event occurrence. Patients on monotherapy exhibited higher perampanel levels, suggesting reduced drug interaction. These findings support the use of therapeutic drug monitoring to optimize efficacy, especially in polytherapy settings, and reinforce the high retention rate of perampanel in pediatric epilepsy.

1925 | One-year treatment with Cenobamate affects bone density and bone turnover in patients with epilepsy

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Purpose: Cenobamate is a novel anti-seizure medication with unusually high responder rates even in patients with refractory epilepsy. Effects of long-term cenobamate treatment on bone health have not been investigated yet.

Method: Adult patients from a tertiary epilepsy center received cenobamate add-on to their concomitant anti-seizure medication. Bone mineral density at femoral neck and lumbar spine as well as bone metabolism parameters in serum were assessed at baseline and after 12 months of continuous cenobamate therapy.

Results: 47 patients (median age 40 years) were included in the study. Median daily dose of cenobamate at 12 months was 250 mg. Moderate, yet significant reduction of the T-score at femoral neck but not lumbar spine was found after one year of cenobamate treatment, also in a subgroup of patients (n=37) without enzyme inducers in the comedication. Additionally, we observed significant changes in bone formation biomarkers: decreased serum level of osteocalcin and increased bone-specific alkaline

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phosphatase. Bone minerals (calcium and phosphorus) as well as vitamin D3 remained unchanged. Parathormone was slightly reduced. The serum level of GGT increased considerably after 12 months of treatment, reflecting an underlying hepatic enzyme induction by cenobamate.

Conclusion: Moderate, yet significant decrease of the T-score at femoral neck as well as prominent alterations in the bone formation biomarkers suggest an increase in bone turnover after one year of cenobamate treatment. The underlying mechanism is most likely attributed to the hepatic enzyme activation expressed through a prominent elevation of serum GGT. The results alert for bone density control in susceptible patient groups.

1941 | Bridging the Epilepsy Treatment Gap: A Randomized Trial of a Mobile Health Intervention in Rural Kenya

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Purpose: The epilepsy treatment gap (ETG) and poor adherence to antiseizure medications (ASMs) remain persistent challenges in low- and middle-income countries (LMICs). This study evaluated the effectiveness of short message service (SMS) reminders in improving ASM adherence in a rural Kenyan setting.

Method: A randomized controlled trial (n=1,038) compared SMS reminders to placebo. ASM levels were available for a proportion of participants at baseline (n=328), three months (n=324), and six months (n=174) to infer adherence. Secondary outcomes included seizure frequency, disability, quality of life, and stigma. Poisson regression was used for analysis.

Results: There was no significant difference in non-adherence over time in the intervention group (61% to 51%, p=0.089; adjusted incident rate ratio (aIRR)=0.9, 95% confidence interval (CI): 0.6–1.3) compared to controls (71% to 75%, p=0.958; aIRR=0.6, 95% CI: 0.4–1.0). However, the frequency of severe disability reduced in the intervention group (33% to 16%, p<0.001), and those with suboptimal ASM levels were more likely to have a higher incidence of severe disability (IRR=1.6 (1.0-5.2), p=0.029). The frequency of poor quality of life did not change significantly over time (22% to 24%, p=0.593), but the incidence was lower in adherent participants receiving SMS reminders (IRR=0.4 (0.2-0.9), p=0.024). Stigma decreased in the intervention group (29% to 20%, p=0.001), while daily seizures dropped significantly in both the intervention (22% to 3%, p<0.001) and control (20% to 3%, p<0.001) groups. Factors associated with improved adherence included employment (IRR=0.7 (0.6-0.8), p=0.003), longer epilepsy duration (IRR=0.9 (0.9-0.9), p<0.001), and use of phenobarbital (IRR= 0.6 (0.5-0.9), p=0.007) while children had higher non-adherence (IRR=2.1 (1.5-2.9), p<0.001).

Conclusion: While SMS reminders did not significantly reduce non-adherence, improvements in the secondary outcomes suggest potential effectiveness, pending further drug level measurements. Caregiver-targeted interventions and consistent ASM supply remain critical to closing the ETG in LMICs.

1944 | Small Activating RNA–Lipid Nanoparticles for the Treatment of Haploinsufficiency in Monogenic Severe Epilepsy

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Purpose: RNA activation is mediated by small double-stranded RNA, typically 21 nucleotides in length, known as small activating RNAs (saRNA). These molecules up-regulate gene transcription by targeting specific gene promoters. saRNA-based therapies hold promise for monogenic neurodevelopmental disorders (NDDs) caused by haploinsufficiency, such as Dravet Syndrome (DS) or Tuberous Sclerosis Complex(TSC). Specifically, saRNAs may enhance transcription from the remaining functional allele (*SCN1A* in DS, or *TSC1* or *TSC2* in TSC), potentially restoring sufficient protein expression.

saRNA therapies face key limitations: instability due to nuclease degradation, poor cellular uptake, and rapid clearance. Lipid nanoparticles (LNPs) offer a promising strategy to overcome these barriers. In NDDs, neuronal targeting is particularly challenging. It is proposed to use LNP designed for neuronal delivery to enhance uptake and therapeutic potential.

Method: Multiple saRNA candidates targeting SCN1A, TSC1, and TSC2 were evaluated for their ability to enhance endogenous mRNA in HeLa cells, neuroepithelial stem cells (NES), and NES-derived neurons. In parallel, two LNP formulations were tested for efficient saRNA delivery into neural cell lines. Functional validation of the

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SCN1A saRNA-LNP system was performed by quantifying mRNA via qPCR, confirming target gene activation.

Results: Two saRNA candidates were identified: one targeting SCN1A and another targeting TSC2, inducing a average of 1.4±0.2(n=9) and 1.4±0.4(n=12) fold increase in mRNA expression, respectively, in differentiated NES cells at 50 nM. Despite modest upregulation, both genes are key regulators in sensitive pathways, supporting the biological relevance of these effects. Initial LNP formulation optimization achieved 86.7±1.1% cellular uptake and ~10% transfection efficiency in differentiated-NES cells at 80 nM, without significant toxicity. Functional validation of the SCN1A saRNA–LNP system yielded a 1.9±0.4-fold increase (n=12) at 50 nM in NES cells.

Conclusion: saRNA-LNP platform is a promising strategy for developing saRNA therapies for NDDs. Further optimization and validation in disease-relevant neuronal models are required to advance this approach.

1945 | AntimiR-134 disease-modifying Mechanism of Action: NMT.001 reshapes the transcriptome to modify disease in a model of drug-resistant epilepsy

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Purpose: We have designed a proprietary disease-modifying antisense oligonucleotide targeting microRNA-134, antimir134 (NMT.001, Neumirna Therapeutics), for focal onset drug-resistant epilepsy with clinical trials to initiate in 2026. With Professor David Henshall, we previously showed that NMT.001 significantly reduced seizures in an NIH-validated model of focal onset drug-resistant epilepsy, the intra-amygdala kainic acid (IAKA) model, achieving 67% seizure freedom beyond therapeutic drug exposure as well as 74% reduced risk of death. Here, we provide new insights into the mechanism of action of NMT.001 supporting its disease-modifying effects.

Method: Primary rat cortical neurons were treated with NMT.001 or vehicle, and RNA sequencing was performed to identify differentially expressed genes. In the IAKA model, we validated key transcriptomic changes by RT-qPCR on brain tissue from mice treated with NMT.001 or vehicle.

Results: RNA sequencing revealed 437 altered genes in NMT.001-treated neurons, with disease ontology analysis identifying "epilepsy" as a top hit among downregulated genes. Interestingly, cellular component enrichment analysis suggested a bifurcated mechanism of action. First, NMT.001 downregulates genes localized to pre- and post-synaptic membranes, thereby directly reshaping the transcriptomic landscape at the synapse. Second, it upregulates genes enriched in neuronal microtubules, suggesting a parallel pathway by which cytoskeletal dynamics are modulated. RT-qPCR on brain tissue from IAKA-treated mice confirmed a significant overall effect of NMT.001 treatment on doublecortin (1.00±0.10 to 1.30±0.12), Creb1 (1.02±0.08 to 1.22±0.10), and Limk1 (1.05±0.05 to 1.20±0.06), key regulators in neuronal development and plasticity, while reducing astrocytic marker GFAP (1.00±0.08 to 0.70±0.07).

Conclusion: In summary, NMT.001 reshapes the transcriptome by downregulating seizure-associated and synaptic-membrane genes, explaining its rapid anticonvulsant action, and by upregulating microtubule-stabilizing transcripts driving the long-term disease modifying effects, indicating neuronal reorganization in epileptic networks. This dual mechanism proposes NMT.001 as a disease-modifying therapy that reshapes gene networks in epilepsy.

1947 | Non-Seizure Impact of Cannabidiol Treatment in Patients With Seizures Associated With Tuberous Sclerosis Complex: Analysis from a Global, Longitudinal, Observational, Mixed Methods Study

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Purpose: Highly purified cannabidiol (CBD; Epidyolex® [EU]/Epidiolex® [US]; 100 mg/mL oral solution) is indicated to treat seizures associated with tuberous sclerosis complex (TSC). We report initial analyses from an observational study assessing the non-seizure impact of CBD in adult and pediatric patients with TSC-associated seizures, reported by caregivers, using quantitative and qualitative methods.

Method: Caregivers of patients with TSC aged ≥2 years receiving CBD for 3–6 months (Group 1) or >6 months (Group 2) completed two quantitative surveys and qualitative interviews. Initially, caregivers rated outcomes pre-treatment and for the past month on-treatment. Outcomes were re-assessed 3 months later. Here, changes pre/post-treatment are reported for Group 1, Survey 1.

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Level-of-functioning assessment used 2- to 5-point categorical scales (question-dependent); behavioral, academic, and neuropsychological assessment used closed-ended questions rated 0 (not at all) to 10 (extremely).

Results: Overall, 88 caregivers were recruited from seven countries. Thirty-two from Group 1 completed the first survey (N=32 patients; 50.0% male; mean [range] age 20.7 [3.0–53.0] years; n=18 [56.3%] impaired intellectual ability [IA]). Post-treatment, improvements (n [%] change in caregivers endorsing outcome) were observed in domains of selfcare (dressing/undressing with lot of assistance: +2 [+6.2%]), language (using complete sentences: +2 [+6.2%]), and normal activities (never prevented from taking part: +3 [+9.3%]); notably only in patients with impaired IA. For neuropsychological domains, improvements (mean change [SD] on 0–10 scale) were reported in attention (–1.2 [1.92]). Academic skills were largely unchanged in this timeframe. For behavioral domains, improvements were observed in anxiety (–2.5 [2.03]) and sleep (–2.8 [2.50]).

Conclusion: Initial findings suggest CBD may positively impact some non-seizure outcomes after 3–6 months of treatment. Improvements in functioning were seen for patients with impaired IA; behavioral domains improved across all patients. Longer-term analyses and qualitative assessments are ongoing and will be presented. Funding: Jazz Pharmaceuticals, Inc.

1957 | FENFLU-Norte: Multicenter Experience with Fenfluramine in Northern Spain

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Purpose: Fenfluramine (FFA), marketed in Spain in 2022, is indicated as adjunctive treatment for epileptic seizures in patients with Dravet syndrome and Lennox-Gastaut syndrome from 2 years of age. Our aim is to describe real-world experience with FFA use in pediatric and adult patients across several centers in northern Spain.

Method: A retrospective observational study including patients treated with FFA with at least 1 year of follow-up. Demographic and clinical characteristics, treatment response and tolerability, and retention rate were evaluated.

Results: A total of 24 patients (15 male; 62.5%) were included, with a mean age of 29.67 ±17.52 years, all diagnosed with Lennox-Gastaut syndrome. At 12 months, a mean reduction of 35.72% in total seizure frequency was observed. Overall, 54% (13/24) were responders, and among them, 76% (10/13) achieved a ≥80% reduction. Sixteen patients had drop seizures at baseline. After 12 months of treatment, 5/16 became seizure-free, 4/16 achieved a ≥80% reduction, and 3/16 showed a 50–79% reduction. The mean FFA dose at 12 months was 20.85 ±6.43 mg/day.

A total of 34 adverse events (AEs) were reported: 23 mild, 10 moderate, and 1 severe. The most frequent were somnolence (N=10) and diarrhea (N=9). Five patients discontinued treatment: 2 due to AEs, 2 due to lack of efficacy, and 1 due to both. The 1-year retention rate was 79.2%.

Conclusion: Real-world experience supports the use of FFA as an effective and well-tolerated therapeutic option.

1960 | Complementary Antisense Oligonucleotide Treatment and Precision Sodium Channel Modulation for Early Onset SCN2A Developmental and Epileptic Encephalopathy: Emergency Use Cases in a Preterm Infant with Refractory Status Epilepticus

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Purpose: Early onset *SCN2A* DEE is a rare, fatal disorder characterized by developmental delay or regression, frequent, epileptic seizures, typically beginning within days of birth, that are difficult to control with standard-of-care ASMs. Clinical studies with a gapmer *SCN2A* ASO addressing the primary genetic driver show significant seizure reduction. However, persistent network hyperexcitability in a developmentally altered brain

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may remain. Adjunctive precision sodium channel modulation could further stabilize excitability and enhance clinical outcomes.

Here, we describe the first complementary emergency use case of elsunersen (an intrathecally-administered ASO in development for early onset *SCN2A* DEE) and relutrigine (a sodium channel functional state modulator demonstrating robust and sustained seizure reduction in DEE patients) in an infant with severe early onset *SCN2A*-DEE and refractory *status epilepticus* (SE).

Method: A preterm infant (29+4 weeks gestation; birthweight 1400g) diagnosed prenatally with a pathogenic *SCN2A* variant presented with life-threatening SE and only partial effect of high-dose SCBs. Following confirmation of gain-of-function status, treatment with elsunersen commenced at 7 weeks, with 25 doses administered to date (174.5mg total). Two years later, treatment with relutrigine commenced (0.5mg/kg daily dose).

Results: Elsunersen treatment in combination with best standard-of-care ASMs (mainly SCBs) was well-tolerated with no drug-related severe or serious adverse events. Early dosing led to SE cessation and revealed a temporal association with seizure reduction. Seizure frequency remained stable with ongoing dosing; maintained after tapering phenytoin at 14 months, with no neurodevelopmental worsening. Two years after ASO commencement, the treatment strategy was adjusted to include relutrigine. Three weeks after relutrigine commencement, parents and nursing staff reported moderate-to-significant improvement including fewer, less severe seizures, with no new safety findings. Continued improvement following 2 months of relutrigine treatment permitted a previously unattainable reduction in carbamazepine dosage.

Conclusion: Preliminary first-in-human findings highlight the potential for complementary use of elsunersen and relutrigine for early onset *SCN2A* DEE.

1961 | EMERALD: A Phase 3, Randomized, Multi-Center, Double-Blind, Placebo-Controlled Clinical Trial to Evaluate the Efficacy, Safety, Tolerability, and Pharmacokinetics of Relutrigine in Participants with Developmental and Epileptic Encephalopathies

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Purpose: Developmental and epileptic encephalopathies (DEEs) are a group of chronic, devastating conditions presenting during infancy and characterized by severe, frequent seizures, developmental delay or regression, and increased early mortality. Relutrigine is a differentiated functional state sodium channel modulator in late-stage development for DEEs. EMERALD is a Phase 3 randomized trial evaluating relutrigine for seizure control, safety, tolerability, and pharmacokinetics in DEE participants.

Method: This multicenter, double-blind, placebo-controlled, randomized study will enroll ~160 eligible male and female participants aged 2-65 years with a diagnosis of DEE and onset of seizures <12 years old. It will include an initial Screening Period (including 28-day Baseline Observation), Part A (Double-Blind Treatment Period, 16 weeks), Part B (OLE Treatment Period, 32 weeks), and Safety Follow-up. Participants will be randomized (1:1) to receive either relutrigine (1mg/kg/day starting dose; dose modification permitted up to 1.5mg/kg/day) or placebo QD. Participants will have the option to undergo study assessments at home, in-clinic or as a combination of both.

Results: The primary endpoint will assess efficacy based on change in motor seizure frequency. Secondary endpoints will include the proportion of patients achieving >50% reduction in monthly seizure frequency and seizure-free days from baseline, as well as change in clinician and caregiver-reported outcomes. Secondary endpoints will also assess TEAE incidence and severity, with further exploratory endpoints assessing PK and additional efficacy outcomes. OLE endpoints will capture long-term safety, tolerability and efficacy outcomes.

Conclusion: Recent findings from the EMBOLD study demonstrated well-tolerated, pronounced seizure reduction and unprecedented seizure-free status in patients with SCN2A and SCN8A, with emerging preclinical data further highlighting robust, differentiated efficacy in multiple DEE models (*abstracts AS-IEC-2025-01146 and AS-IEC-2025-01148*). Findings from the Phase 3 EMERALD study are anticipated to provide further evidence for relutrigine's potential to be a first- and best-in-class small molecule for DEEs.

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1978 | Effectiveness of early adjunctive cenobamate therapy in drug-resistant epilepsy.

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Purpose: The study aimed to assess the efficacy and safety of cenobamate treatment six months after the initiation of therapy in patients who had previously used 2–3 antiseizure medications (early users) and in those with a history of multiple treatment failures (>7).

Method: This retrospective, multicenter study was conducted at 20 centers in Poland. Medical records of adult patients with drug-resistant epilepsy (DRE) treated with cenobamate for at least six months were reviewed. Collected data included demographic characteristics, seizure frequency, treatment regimens, and adverse events (AEs). We compared seizure frequency within the three months preceding the initiation of cenobamate and during the final three months of treatment. Descriptive statistical methods were employed to assess outcomes, with the primary efficacy endpoint of ≥50 % reduction in seizure frequency.

Results: The study cohort consisted of 487 patients with a median age of 37 years. (18-80). Cenobamate was added to a median of 2 (1–6) concomitant antiseizure medications. Among the early users (n=53) 69.5% achieved ≥ 50 % reduction in seizure frequency, and 26% seizure freedom. Improvement rates were lower in the group receiving >7 ASMs in the past (n=187): 54.6 % achieved ≥ 50 % reduction in seizure frequency, and 7.7% seizure freedom. The median monthly seizure frequency decreased in early user from 6 to 2 and late users from 12 to 5.3. Adverse events occurred in 49.5% of patients, most frequently somnolence and dizziness.

Conclusion: Cenobamate is a highly effective and well-tolerated ASM for patients with DRE, and its early initiation may improve outcomes.

1981 | Clinical and pharmacological experience with cenobamate in adolescents

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Purpose: Cenobamate is a recently approved antiseizure medication (ASM) for adults as add-on treatment in focal epilepsy. Use in adolescents is initiated based on experience in adults. The purpose of the study was to evaluate clinical and pharmacological experience with cenobamate in adolescents (<18 years) at a referral center.

Method: Clinical and laboratory data were collected, 10.2022-05.2025. Serum concentrations of all ASMs were analyzed at Section for Clinical Pharmacology, National Center for Epilepsy, Oslo University Hospital. The study was approved by the Regional Ethics Committee.

Results: Data from twelve patients were included and all are still on treatment: 6 female/ 6 male, median age 15 (range 11-18). Regarding efficacy eight patients were responders (>50% seizure reduction) at 3 months and nine patients at six months of treatment. Median cenobamate dose and serum concentration from the most recent measurement in each patient was 150 mg/day (range 25-400 mg/day) and 66 mmol/L (range 5-137 mmol/L), 1-3 measurements/patient. At the time of last follow-up patients used 1-3 other ASMs, most commonly clobazam and valproate, with numerous pharmacokinetic interactions. Eight had vagus nerve stimulation (VNS), pointing to a refractory group of patients. Adverse effects were noted in five patients, where tiredness and anxiety were most common. The latter was concurrent with an increase in

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the serum level of desmethylclobazam. The symptoms normalized after reduction of clobazam doses. Other beneficial effects included reduction in number of hospitalizations, shorter seizures, fewer seizure days, less severe seizures, fewer seizure clusters, reduction of nocturnal seizures, reduction of other ASMs and a reduction of insulin requirement in one patient with diabetes mellitus.

Conclusion: These results demonstrate the efficacy of cenobamate in combination with other ASMs and VNS, and a need for close follow-up in these young patients with refractory epilepsy.

1983 | Exposure-Response Relationships of Fenfluramine in Patients with Dravet Syndrome and Lennox-Gastaut Syndrome

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Purpose: To characterize the relationship of fenfluramine and norfenfluramine exposure with efficacy and safety in patients with Dravet syndrome (DS) and Lennox-Gastaut syndrome (LGS).

Method: Population pharmacokinetic models were used to estimate fenfluramine and norfenfluramine exposure in DS phase 3 studies 1 and 2 (N=194) and LGS phase 3 study 1601 (N=251). Fenfluramine doses were twice daily 0.2–0.7 mg/kg/day alone or 0.4 mg/kg/day with stiripentol. Fenfluramine, norfenfluramine, and fenfluramine+norfenfluramine plasma concentrations (C_{max}, C_{min}), and daily area under the concentration-time curve ($AUC_{0–24}$) were independent variables. Primary efficacy outcomes were percentage change from baseline in monthly convulsive seizure frequency in DS and monthly frequency of seizures associated with a fall in LGS. Safety outcomes included blood glucose concentration, platelet count, weight loss, and mitral valve regurgitation. Linear, log-linear, and non-linear regression models were utilized for continuous variables; ANOVA models were applied for categorical variables.

Results: Geometric mean (GM) steady-state fenfluramine $AUC_{0–24}$ ranges were 375–3150 ng·h/mL and 246–933 ng·h/mL in DS and LGS studies, respectively; highest GM fenfluramine $AUC_{0–24}$ (3150 ng·h/mL) was observed at 0.4 mg/kg/day fenfluramine+stiripentol in study 2. Efficacy was associated with steady-state $AUC_{0–24}$ fenfluramine exposure (maximum effect [E_{max}]=−57.0%; half maximal effective concentration [EC_{50}]=342 ng·h/mL) in DS and fenfluramine+norfenfluramine exposure (E_{max}=−27.8%; EC_{50}=259 ng·h/mL) in LGS. A weak but significant log-linear exposure-response relationship was observed for maximum percent change in platelet count in DS (intercept=−8.86, coefficient=−1.31; r^2=0.059) and for maximum change in body weight in DS (intercept=−0.571, coefficient=−0.467; r^2=0.170) and LGS (intercept=2.46, coefficient=−0.379; r^2=0.100). No other exposure-safety relationships were significant.

Conclusion: In DS and LGS, a significant relationship between fenfluramine and norfenfluramine exposure and seizure frequency reductions was observed. Lower exposures, corresponding to 0.2mg/kg/day fenfluramine, indicated a seizure reduction in DS and LGS. UCB-supported.

1996 | Pharmacokinetic variability of fenfluramine in patients with Dravet syndrome in Norway

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Purpose: Fenfluramine is a newly approved antiseizure medication (ASM) for Dravet syndrome in Norway. The purpose of the study was to evaluate pharmacokinetic variability and use of fenfluramine in Dravet syndrome.

Method: Therapeutic drug monitoring (TDM) data from January 2024 to April 2025 were collected. Serum concentrations of fenfluramine and norfenfluramine were analyzed at the laboratory of the Danish epilepsy center, whereas all other ASMs were analyzed at Section for Clinical Pharmacology, National Center for Epilepsy, Oslo University Hospital. Mann Whitney U test was used to evaluate drug-drug interactions. The study was approved by the Regional Ethics Committee.

Results: Data from 38 measurements of fenfluramine and the metabolite nor-fenfluramine from 19 patients were included; 10 women/ 9 men, median age 10 (range 3-49). There were 1-5 measurements per patient, with up to one year follow up. Median dose, dose/kg and serum concentration at the time of the most recent measurements for each patient were 11.2 mg/day (range 4.4-19.8, n=16), 0.27 (mg/kg)/day (range 0.18-0.47, n=11) and 275.3 nmol/L (range 24.5-1157.8, n=19). The corresponding median serum concentration of the active metabolite norfenfluramin was 41.5 nmol/L (range 2.6-155.9). The concentration/dose

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per kg (C/(D/kg))-ratio of fenfluramine varied 17-fold (168.4-2935.0, n=11) and ratio of norfenfluramine/fenfluramine serum concentrations varied 85-fold (0.03-2.66, n=19). Drug-drug interactions can be a contributing factor to the observed variability. At the time of the last follow-up, the patients used 1-4 other ASMs. The most common co-medications were valproate, clobazam, and stiripentol, which were used by >10 patients. In patients using stiripentol the median C/(D/kg)-ratio was 7-fold higher than in the other patients (n=5/n=6, p<0.05).

Conclusion: These results demonstrate extensive pharmacokinetic variability of fenfluramine and its active metabolite in patients with Dravet syndrome. This points to potential usefulness of TDM in combination with close clinical follow-up.

2053 | Optimizing Levetiracetam Extended-Release Therapy in Epilepsy: A Data-Driven Machine Learning Approach to Outcome Prediction

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Purpose: Epilepsy is a chronic neurological disorder affecting over 50 million people worldwide, necessitating effective seizure control and adherence to antiseizure medications (ASMs). Levetiracetam extended-release (LEV-XR) offers comparable efficacy to its immediate-release (LEV-IR) counterpart, with the added benefits of reduced dosing frequency and improved tolerability. However, patient responses to LEV-XR vary widely, and tools for predicting treatment outcomes remain limited. This study applies supervised machine learning (ML) to predict clinical response to LEV-XR using baseline patient data.

Method: A retrospective cohort study was conducted on epilepsy patients treated at a tertiary hospital between 2018 and 2024 who transitioned from LEV-IR to LEV-XR. Patients with less than three months of LEV usage, prior LEV-XR exposure, or simultaneous ASM adjustments were excluded. Clinical and demographic variables, such as age, sex, epilepsy type, etiology, and baseline seizure frequency, were collected. Treatment response was defined as a ≥50% reduction in seizure frequency. Six ML algorithms—Random Forest, Gradient Boosting Machine, Extreme Gradient Boosting, Support Vector Machine, K-Nearest Neighbors, and Logistic Regression—were trained on the dataset. SMOTE and cross-validation techniques were used to optimize model performance, which was evaluated using standard classification metrics. SHAP values were calculated to identify key predictors.

Results: The final dataset included 265 patients (mean age: 45.0 ±15.8 years; 49.4% female). Main reasons for switching to LEV-XR included better seizure control (47.2%), fewer side effects (20.4%), and once-daily dosing (18.1%). At 12 months, 64.6% experienced reduced seizure frequency, and 52.8% of those achieved seizure freedom. Random Forest achieved the highest short-term (3-month) accuracy (0.78), while Gradient Boosting Machine performed best for long-term (24-month) predictions (accuracy = 0.725).

Conclusion: These findings support the clinical utility of machine learning in personalizing epilepsy treatment, highlighting its potential to optimize ASM selection and improve patient outcomes through data-driven decision support.

Epidemiology

1858 | Prenatal and Early Childhood Exposure to Antibiotics or Gastric Acid Inhibitors and Increased Risk of Epilepsy: A Nationwide Population-Based Study

S Prast-Nielsen[1], U Gudnadottir[2], R Wickström[3], A Gunnerbeck[3], N Brusselaers[4]
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Purpose: Over 10 million children in the world have epilepsy, with an unknown cause in half of the cases. The gut microbiome has been associated with various neurological disorders, and certain drugs greatly disturb this microbiome. Our aim was to study the association of prenatal and childhood exposure (before the age of two) to antibiotics, proton pump inhibitors (PPIs) and histamine-2 receptor antagonists (H2RA), and the risk of childhood epilepsy. Using population-based registers, we included all live singleton births in Sweden from 2006 to 2017.

Method: The study exposure was defined as at least one dispensed prescription of systemic antibiotics, PPIs, or H2RA during pregnancy or early life (under the age of two

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years). The main outcome was first diagnosis of epilepsy with ICD-10 code G40 (Epilepsy and recurrent seizures). Multivariable Cox regression was used to calculate hazard ratios and 95% confidence intervals.

Results: 708,903 mother–child dyads were included, and 0.5% of children had an epilepsy diagnosis. Average follow-up was 3.8 years (IQR 1–6). Prenatal exposure to antibiotics (aHR 1.09, 95% CI 1.01–1.18) and PPIs (aHR 1.38, 95% CI 1.17–1.65) were associated with an increased risk of epilepsy. Exposure to antibiotics (1.11, 95% CI 1.02–1.21), PPIs (3.40, 95% CI 2.47–4.68) and H2RAs (1.65, 95% CI 1.03–2.64) before the age of two was associated with an increased risk of epilepsy after the age of two. Dose response analysis showed that one prescription of antibiotics in pregnancy or early life was not associated with an increased risk of epilepsy, while one prescription of PPIs in pregnancy or early life had an association.

Conclusion: To conclude, our results support the hypothesis that microbiome modulating drugs are associated with an increased risk of epilepsy. This needs to be further validated in other studies, ideally including indications for drug use.

1885 | School dropout in young people with epilepsy – a register-based cohort study

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Purpose: We aimed to describe the prevalence and risk factors associated with school dropout among young people with epilepsy in Norway.

Method: The cohort included all individuals born in Norway from 1990 - 2001 who started primary school. We collected data from the Norwegian Patient Registry (NPR), the Prescription Registry, and Statistics Norway regarding diagnoses, medication usage, school attendance, and psychosocial factors until December 2020. Epilepsy was defined as at least two epilepsy registrations in NPR before age 19, or one registration combined with either an EEG prior to diagnosis or a prescription for antiepileptic medication. Individuals with comorbid intellectual disabilities or underlying causes of epilepsy were classified as having complicated epilepsy. We used logistic regression models, adjusting for birth year, gender, parental education level, and psychiatric comorbidity, to calculate odds ratios (OR) with 95% confidence intervals (CI) for not completing high school among different epilepsy subgroups.

Results: The study population comprised 660,108 individuals, of whom 5,824 (0.9%) met the criteria for epilepsy. Among these, 4,397 (75.5%) had uncomplicated epilepsy and 1,427 (24.5%) had complicated epilepsy. While 82% of adolescents without epilepsy completed high school, only 53% of those with epilepsy, and 66% among those with uncomplicated epilepsy, did so. The prevalence of psychiatric comorbidity was 44% in the epilepsy group compared to 26% among those without epilepsy. Both complicated and uncomplicated epilepsy groups had lower average grades and more absences. The OR for school dropout among those with uncomplicated epilepsy was 1.87 (95% CI 1.74–2.00). For those on polytherapy, the OR was 2.66 (95% CI 2.34–3.01), while for those who had never used antiepileptic medication, it was 1.64 (95% CI 1.42–1.90).

Conclusion: This study underscores the significant educational challenges faced by adolescents with epilepsy and highlights the need for targeted interventions to support this group.

1907 | Physician Knowledge Gaps in Epilepsy Surgery: An International Survey by the Young Epilepsy Section Across 18 Countries or Regions in Asia-Oceania

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Purpose: To investigate the level of epilepsy surgery knowledge among physicians in the Asia–Oceania (AO), to identify individual- and country-level factors associated with it, in order to inform strategies that address the epilepsy surgery treatment gap and advance Intersectoral Global Action Plan (IGAP) goals.
Method: The ILAE Young Epilepsy Section (YES) conducted an international cross-sectional survey across 18 Asian–Oceania countries, using web-based distribution in English, Chinese, and Japanese. Responses were collected by appointing national YES representatives. The survey included 12 questions assessing the basic demographic information of the respondents and 12 questions assessing knowledge of epilepsy surgery. A linear mixed-effects model was used to identify factors associated with knowledge scores, incorporating country/region as a random intercept. Ancillary analysis examined correlations between country-level random effects and academic activity using PubMed publication data.
Results: 811 physician responses were collected, with the largest numbers from India (n=204), China (n=195), and Japan (n=94). At the individual level, four factors were independently associated with higher knowledge: medical specialty, such as being an epileptologist or a neurosurgeon, number of patients with epilepsy per month, and presence of an epilepsy surgery program at the home institution. In addition, we found substantial country- or region-level variation in knowledge, which was positively correlated with academic activity related to epilepsy surgery and epilepsy awareness, but not with general epilepsy research output.
Conclusion: Broad geographic coverage, multilingual representation, and innovative integration of PubMed as a proxy for national academic activity metrics are methodological strengths that led us to identify multi-level factors contributing to variation in physician knowledge of epilepsy surgery in the Asia–Oceania region. It supports the relevance of targeted, multi-level educational strategies in addressing the epilepsy surgery treatment gap and highlights the need for future evaluations of their effectiveness, alongside efforts to address broader structural and patient-level barriers to surgical care.

1919 | Characterization of Non-Drug-Resistant Mesial Temporal Sclerosis Patients in a Refractory Epilepsy Unit

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Purpose: To describe the clinical, etiological, and management characteristics of patients with non-drug-resistant MTS diagnosed after the implementation of 3T MRI in our center.
Method: Retrospective observational study in a cohort of 191 MTS patients not surgically treated. We analyzed the subgroup of non-drug-resistant patients, evaluating clinical, etiological, and management variables.
Results: A total of 83 patients (43.4% of non-operated cases) were included, from a total of 287 patients diagnosed with MTS on MRI (28.9%). Mean age was 55.3 years (SD 15.7), with a female predominance (n=43; 51.8%). MTS was bilateral in 14 patients (16.9%) and left-sided in 41 (59.4%). MTS was the sole neuroimaging finding in 48 patients (57.8%), with cortical developmental malformations being the most frequent secondary cause (n=13; 37.1%).
Eighteen patients (21.7%) had undergone previous presurgical evaluation. None of the patients had a vagus nerve stimulator implanted. A statistically significant association was found between age at epilepsy onset and MTS etiology (p=0.001), with a predominance of structural causes in early-onset cases and isolated MTS in later-onset cases.
Conclusion: The presence of MTS is not always associated with drug resistance. The association between age at onset and etiology suggests a potential prognostic value of this clinical parameter.

1973 | Risk of drug-resistance in persons with epilepsy after traumatic brain injury and other etiologies: a Danish register-based cohort study

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Purpose: Risk of developing drug-resistant epilepsy (DRE) has been reported to be higher after traumatic brain injury (TBI) compared to other etiologies, yet robust population-based evidence is limited. We investigated the long-term risk of DRE in individuals with epilepsy following TBI, compared to other etiologies.
Method: We conducted a nationwide cohort study of individuals in Denmark with a first hospital-based diagnosis

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of epilepsy between January 1, 1995, and December 31, 2020, who initiated antiseizure medication (ASM) within one year of diagnosis. Participants were followed for up to 10 years for development of DRE, using a validated register-based DRE algorithm: either filling two prescriptions for ≥3 different ASMs within 3 years, or an acute epilepsy-related hospital admission after filling two prescriptions for ≥2 different ASMs. Epilepsy etiology was classified as "mild TBI", "moderate-to-severe TBI", "other secondary cause" (stroke, CNS infection, CNS tumors, perinatal conditions, or malformations), or "idiopathic" if no secondary cause was identified. Absolute risks (ARs) and 95% confidence intervals (CIs) were estimated using competing risk models, stratified by age (<18 years, ≥18 years).

Results: We identified 14,940 persons with epilepsy-onset <18 years and 57,560 with epilepsy-onset ≥18 years, for whom the proportion with traumatic etiology was 5.3% and 12.4%, respectively. With onset < 18 years, the 10-year ARs (95% CI) of DRE were 24.6% (21.6–27.6%) after "mild TBI", 33.7% (24.0%–43.4%) after "moderate-to-severe TBI", 32.0% (30.7–33.2%) with "other secondary causes", and 25.9% (25.0–26.9%) in "idiopathic epilepsy". With onset ≥18 years, corresponding ARs were 17.4% (16.2–18.5%), 19.1% (17.4–20.8%), 14.5% (14.0–14.9%), and 15.5% (15.0–15.9%), respectively.

Conclusion: Having a traumatic etiology was more likely with adult-onset epilepsy. Compared to other etiologies, "moderate-to-severe TBI" conferred the highest risk of DRE across both age groups, while "mild TBI" was associated with excess risk only in adults.

2031 | Strong association between epilepsy and young-onset dementia: a retrospective nationwide study of the French National Health Data System.

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Purpose: The association between epilepsy and late-onset dementia (LOD) is increasingly recognized, but data on young-onset dementia (YOD), defined as patients under 65 years old) remain limited although this link has been described as stronger in younger individuals. We investigated this relationship using the French National Health Data System, which covers nearly the entire French population.

Method: We first conducted a case-control study comparing epilepsy-related healthcare use between YOD patients and matched controls over the 10 years preceding diagnosis. Second, we performed a cohort study of individuals aged 30–55 with incident epilepsy, matched to patients with prevalent epilepsy and to individuals without epilepsy, to assess 10-year dementia risk. Regression models were adjusted for YOD-associated covariates (e.g., stroke, traumatic brain injury, alcohol use, psychiatric disorders).

Results: In the case-control study, 11,360 YOD cases were matched to 111,360 controls. Epilepsy-related healthcare use in the prior decade was observed in 18.4% of cases vs. 3.8% of controls (adjusted odds ratio [aOR]: 2.28; 95% CI: 2.13–2.44). In the cohort study, 12,901 patients with incident epilepsy were matched to 63,994 with prevalent epilepsy and 129,010 without epilepsy. The 10-year cumulative incidence of dementia was 2.20% for incident epilepsy, 1.77% for prevalent epilepsy, and 0.21% for unexposed individuals. The adjusted hazard ratio (aHR) was 5.47 (95% CI: 4.55–6.57) for incident epilepsy and 5.46 (95% CI: 4.73–6.30) for prevalent epilepsy. Dementia risk increased sharply with comorbidity burden (aHR: 38.7 for incident epilepsy with ≥4 comorbidities vs. unexposed individuals without comorbidities).

Conclusion: Epilepsy-related healthcare is markedly increased in patients with YOD, even a decade before diagnosis. Conversely, epilepsy in midlife is associated with a high risk of subsequent YOD, especially in those with multiple comorbidities. These findings suggest a strong epilepsy–dementia link in YOD and call for further research into mechanisms and prevention.

Epilepsy and Reproductive Health

1892 | EEG changes during pregnancy and association with clinical course of epilepsy

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Purpose: Pregnancy in women with epilepsy (WwE) is a challenging issue. We aimed to: (i) describe quantitative EEG (qEEG) modifications during pregnancy; (ii) investigate the potential association between qEEG modifications and the clinical course of epilepsy during pregnancy.

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Method: We collected a cohort of WwE who underwent scalp EEG recordings during pregnancy. We measured power spectral density (PSD) and weighted phase-lag index (wPLI) as qEEG metrics. We evaluated the correlation between seizure frequency modification and qEEG changes during pregnancy. We compared qEEG metrics between seizure-free (SF) and non-SF WwE and qEEG changes according to clinical amelioration (seizure frequency reduction >50%) during pregnancy. Logistic regression was performed to test and compare the ability of clinical features, spectral metrics and connectivity metrics to classify our cohort of WwE according to clinical outcome during the last trimester of pregnancy (SF or non-SF).

Results: We enrolled 56 WwE (30.7±5.73 years). WwE exhibited a reduction of low frequencies PSD (delta and theta) and an augmentation of alpha PSD during pregnancy. At the third trimester, SF WwE exhibited augmented alpha PSD and wPLI and reduced low frequencies PSD and wPLI than non-SF. Delta PSD reduction, alpha PSD augmentation and alpha and beta wPLI augmentation were directly correlated to seizure frequency reduction during pregnancy. PSD and wPLI discriminated the variability of clinical outcome at the third trimester with a good level of accuracy (.83 ± .08) and gave the highest contribution to the final model accuracy compared to clinical features alone.

Conclusion: Pregnancy induces qEEG modifications potentially reflecting pregnancy-related neural network modifications or the altered pharmacokinetics. qEEG modulations parallel seizure frequency changes and clinical amelioration during pregnancy and may help to identifying SF WwE at the end of pregnancy. These findings could open new scenarios for the identification of promising biomarkers of the epilepsy clinical course during pregnancy.

Epilepsy in Resource-restricted Settings

1871 | Strengthening Medical Imaging Capacity: Addressing Epilepsy in Low-Resource Settings (Malawi)

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Purpose: Epilepsy remains a major public health concern in low-resource settings, with an estimated 80% of cases occurring in low- and middle-income countries. Despite the availability of basic diagnostic tools, inadequate access to and utilization of neuroimaging significantly contributes to underdiagnosis and mismanagement. This study aimed to assess the challenges related to medical imaging in epilepsy care in Malawi, focusing on rejection and neglect of brain imaging requests in a major national hospital.

Method: An observational study was conducted at the largest tertiary referral hospital in Malawi, analyzing how neuroimaging is utilized in the diagnosis and management of epilepsy. The investigation included a review of imaging requests, radiographers feedback, and service delivery patterns. Special attention was paid to rejection rates, turnaround times, and departmental prioritization. Comparative assessments were also conducted across eight other referral hospitals nationwide to establish a broader understanding of neuro-imaging access and capability.

Results: The study revealed a high rate of non-attention to brain imaging requests, with significant delays or outright rejections frequently observed. Across eight referral hospitals, neuroimaging for non-pediatric and adult epilepsy cases were either unavailable or severely limited. Misdiagnosis and misclassification of epilepsy were common, often due to the absence of imaging-based confirmation. Furthermore, there is a notable lack of specialized training in neuroimaging for epilepsy among radiographers who are the main key imaging experts available. This gap in expertise further compromises diagnostic accuracy and patient outcomes.

Conclusion: The findings underscore an urgent need to strengthen neuroimaging capacity through infrastructure investment, radiographer training, and policy prioritization. Integrating imaging into standard epilepsy diagnostic pathways and expanding professional development opportunities are critical steps toward improving epilepsy care in Malawi and similar low-resource contexts.

1882 | Autoimmune-associated epilepsy in drug-resistant epilepsy of unknown etiology in resource-limited settings: a proof-of-concept study

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Purpose: To evaluate the feasibility and propose an algorithm for investigation of autoimmune etiology in patients with drug-resistant epilepsy (DRE) of unknown etiology in resource-limited settings.

Method: This observational study included patients aged ≥18 years with DRE and no defined etiology, followed at a

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Brazilian Epilepsy Center. The workup included: inflammatory markers (C-reactive protein, erythrocyte sedimentation rate), syphilis serology, anti-thyroid peroxidase antibodies (anti-TPO), antinuclear antibodies (ANA), rheumatoid factor, complement levels, brain magnetic resonance imaging (MRI), electroencephalogram (EEG), cerebrospinal fluid (CSF) analysis, and the application of APE2 and ACES scores.

Results: Twenty-six patients (12 female; 46.1%), aged 18-66 years, were included. The median epilepsy duration was 18.5 years (range: 3-50 years). EEG findings were nonspecific. Six patients with initially normal or nonspecific MRI later exhibited mesial temporal lobe abnormalities. One patient had markedly elevated anti-TPO levels (2157 IU/mL), and 7/26 tested reactive ANA with varied patterns. CSF protein was > 50mg/dL in 9/24 patients; oligoclonal bands were present in 3/22 (13.6%), and elevated IgG index was found in 4/22 (18.2%). APE2 score was ≥4 in 15/26 patients (57.7%), and ACES score was ≥2 in 3/26 (11.5%). Due to limited access to autoantibody testing, only one patient underwent a CSF antibody panel, which confirmed anti-GAD65 positivity. Data were compared with published profiles of patients with autoimmune-associated epilepsy to propose a screening algorithm for individuals with DRE of unknown etiology who may benefit from autoantibody testing in resource-limited settings.

Conclusion: This proof-of-concept study highlights the importance of investigating autoimmune-associated epilepsy in DRE of unknown etiology. A cost-effective strategy may involve selecting patients with higher pre-test probability based on accessible tests – such as ANA, anti-TPO, and CSF analysis – and clinical scores like ACES. Implementing targeted screening protocols tailored to patient profiles and healthcare infrastructure may enhance diagnostic yield and guide therapeutic approaches.

1950 | Delayed Diagnosis and Multidimensional Challenges in Functional Seizures: A Clinical Perspective from the Dominican Republic

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Purpose: To analyze the clinical features, comorbidities, diagnostic approach, and clinical outcomes of patients diagnosed with functional seizures in a Dominican epilepsy clinic.

Method: A retrospective observational study was conducted including 32 patients diagnosed with functional seizures between January 2023 and February 2025 at Torre Profesional Corazones Unidos. Inclusion required diagnosis confirmation through clinical assessment and/or ambulatory video-EEG (>12 hours). Data included demographics, age of onset, time to diagnosis, psychiatric comorbidities, sexual abuse history, ICU admissions, comorbid epilepsy, and EEG findings. Clinical control status was evaluated at 3-month follow-up.

Results: Mean age was 29.4 ± 13.2 years, with a mean onset age of 24.4 ± 11.3 years. Diagnostic delay averaged 5.1 ± 3.8 years. Psychiatric comorbidities were present in 40.6%, including anxiety and depression. Comorbid epilepsy was noted in 25%. Seizures occurred in the presence of others in 68.8% and lasted an average of 16 ± 8.9 minutes. Sexual abuse history was reported by 9.4%; 6.3% required ICU admission. Ambulatory EEG confirmed diagnosis in nearly half of cases. At follow-up, 68.8% were clinically controlled.

Conclusion: Functional seizures in this cohort showed prolonged diagnostic delay, significant psychiatric comorbidities, and occasional severe outcomes. Ambulatory EEG was a valuable diagnostic tool. These findings highlight the need for trauma-informed, multidisciplinary strategies in low-resource settings.

2027 | Epilepsy occurrence among a large HIV+ population in Mozambique

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Purpose: Epilepsy is a common neurological disorder in sub-Saharan Africa (SSA) (1), affecting approximately 2% of the Mozambican population (2). Mozambique has a high HIV prevalence (>10%), and HIV is a recognized risk factor for epilepsy. This study aimed to evaluate the

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occurrence of epilepsy in a large HIV-positive population in Mozambique.

Method: The study was conducted within the DREAM program, a public health initiative providing treatment for HIV/AIDS and non-communicable diseases across 10 SSA countries. A validated questionnaire was used to screen for epilepsy (3). Between 2021 and 2024, DREAM primary care staff underwent five in-person training sessions. After a pilot phase at one center, the questionnaire was administered across seven DREAM centers in Mozambique from April to July 2024. Patients screening positive were examined by a neurologist for epilepsy diagnosis.

Results: A total of 14,947 patients were consecutively screened; 10,427 (69.8%) were female, mean age 43.2 years, with a mean follow-up of 8.3 years. Among them, 11,837 (79.2%) were HIV-positive. Fifty-eight patients (0.38%) were screened positive for epilepsy; of these, 62% were female and 62% HIV-positive.

Conclusion: This is the first large-scale study investigating epilepsy occurrence among HIV-positive individuals in SSA. The observed epilepsy prevalence was lower than expected. Possible explanations include selection bias and the protective effects of long-term viral suppression, as 95% of HIV-positive DREAM patients had suppressed viral loads. Improved immune function may reduce epilepsy-inducing pathologies. Moreover, since stroke is the third leading cause of death in Mozambique and DREAM patients routinely receive cerebrovascular prevention, post-stroke epilepsy risk may also be reduced. The integrated DREAM healthcare program for HIV and cerebrovascular disease may contribute to epilepsy prevention in this population.

2029 | Epilepsy management in sub-Saharan Africa primary care: IGAP 2022–2031 goals and the DREAM program

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Purpose: Epilepsy is highly prevalent in sub-Saharan Africa (SSA) (1), yet many people with epilepsy (PWE) lack access to treatment. The WHO Intersectoral Global Action Plan (IGAP) aims to increase access to care by 50% before 2031. We initiated an epilepsy program within the DREAM primary care HIV centers in SSA. This study evaluates the effectiveness of our program.

Method: The study focused on two countries: the Central African Republic (CAR) and Malawi. A partnership was established between the DREAM program, the Italian Society of Neurology, the Besta Neurologic Institute, Global Health Telemedicine nonprofit organization, and the Mariani Foundation. DREAM is a public healthcare program launched in 2002 to prevent and treat HIV/AIDS in SSA. In CAR and Malawi, 2416 PWE are under regular follow-up (2). Seizure frequency since the previous visit was assessed between December 1, 2024, and April 14, 2025.

Results: A total of 1073 consecutive PWE were seen during this period, with 1717 follow-up visits (mean 1.5 ± 0.89 visits per patient). Forty-seven percent were female; median age was 21.9 years; 52 (4.8%) were HIV-positive; mean follow-up was 2.2 years. At the last visit, 54.4% reported no seizures, 25.7% reported only one seizure, and 15.2% experienced 2 to 5 seizures. The mean number of seizures was 1.2 ± 3.3.

Conclusion: Our study shows that 80.1% of PWE were seizure-free or nearly seizure-free at the last visit, aligning with the ILAE 90-80-70 epilepsy care cascade (3). The DREAM epilepsy program provides a scalable model to deliver quality care to PWE in SSA primary care settings and supports accelerating progress toward the IGAP goal of a 50% increase in access to care by 2031.

Epilepsy Infection and Inflammation

1976 | Modulation of gut microbiota using bifidogenic supplementation in children with intractable epilepsy

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Purpose: Evidence suggests that gut dysbiosis may contribute to the pathophysiology of drug-resistant epilepsy

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(DRE). Gut dysbiosis can alter the release of neurotransmitters, contribute to neuroinflammation and "leakage" of the intestinal and blood-brain barriers. In this context, prebiotic supplementation appears as a promising strategy to restore the balance of the microbiota, favoring the production of neuroactive metabolites and reducing the frequency of seizures. The objective of the present study was to evaluate whether bifidogenic dietary supplement (BDS) could modify the gut microbiota of children with DRE and thus attenuate dysbiosis, neuroinflammation and reduce seizures.

Method: This non-randomized controlled clinical study included three groups of children (mean age: 9 years): 1) DRE (N=13); 2) drug-sensitive epilepsy (DSE, N=9); 3) healthy controls (CT, N=10). The DRE group received BDS for eight weeks. Fecal and blood samples were collected before and after intervention. Gut microbiota was analyzed by 16S rRNA gene sequencing (V3-V4 region). Plasma levels of cytokines (IL-1β, TNF-α, IL-6, IL-10), and biomarkers (HMGB1 and LPS) were measured using Milliplex assays.

Results: BDS significantly reduced the frequency of seizures in the DRE group ($p < 0.05$), but did not alter the concentration of inflammatory markers evaluated after the intervention ($p > 0.05$). There was an increase in LPS in the DRE group compared to CT ($p < 0.05$). Alpha diversity (Shannon and Chao1 indices) did not differ across independent groups, but was significantly reduced in the DRE group after BDS. PCA indicated greater homogeneity in DSE and CT groups and higher variability in DRE pre- and post-intervention samples. PERMANOVA showed no differences in overall microbial composition among groups.

Conclusion: BDS reduced seizure frequency and altered microbiota diversity in children with DRE despite no changes in inflammatory markers. These findings support further investigation of BDS as a complementary therapeutic approach in drug-resistant epilepsy.

Epilepsy Surgery

1904 | Experience with Vagus Nerve Stimulation (VNS) in Patients with Epilepsy and Status Epilepticus at a Mexican Referral Center

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Purpose: We aimed to describe the population of patients with DRE and SRSE who received VNS as part of their treatment.

Method: Observational, descriptive and cross-sectional study of patients who underwent VNS implantation. An Excel® database was used. Quantitative variables were summarized using mean and standard deviation; qualitative variables were expressed as percentages. Informed consent was obtained from patients.

Results: Fifteen patients were included, 9 (60%) of them male. The mean age was 28.3 ± 6.9 years, with an average disease duration of 16.4 ± 8.6 years prior to implantation. The main etiology of epilepsy was structural in 7 patients (46.6%). In 12 patients, the device was implanted for DRE; 5 (42%) had a history of status epilepticus, and 13 (87%) were responders (defined as ≥50% reduction in seizure frequency); the mean seizure frequency reduction was 69.7%. In all 3 patients with SRSE, VNS was associated with complete resolution of the condition. The average of anti-seizure drugs used was 4.6, with no changes associated with neurostimulation. The average follow-up period was 7.9 months. The most common parameters were: 1.5 mA output current, 500 μs pulse width, 30 Hz frequency, 10% duty cycle.

Conclusion: Most patients with DRE responded to VNS therapy and it was successful in resolving SRSE.

1924 | cfDNA-based liquid biopsy in the cerebrospinal fluid of Focal Drug-resistant Epilepsies caused by low-level mosaic, brain-only somatic mutations

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Purpose: Brain somatic mutations (BSMs) are an important determinant of Focal Drug-resistant Epilepsies (DRE) associated with malformations of cortical development and low-grade neuronal-glial tumors. Although genetic etiology is well known, molecular diagnosis requires resected brain tissue, impeding non-surgical diagnostic assessment. DRE-associated BSMs can be detected as mosaic at extremely low variant allele fraction (VAF), especially in small focal epileptogenic lesions. Cerebro-spinal fluid (CSF) cell-free (cf) DNA typing is emerging as a promising liquid biopsy approach for non-invasive diagnosis of central nervous system diseases, especially tumors. However, CSF cfDNA-based detection of low-VAF mosaic mutations remains poorly explored.
Method: We performed paired blood-brain ultra-deep gene panel sequencing in a cohort of 164 DRE patients with Focal Cortical Dysplasias (FCDs, 93) and Low-grade Epilepsy-Associated Tumors (LEATs, 55), discovering causative BSMs in 48 (32.4%). We designed solid digital PCR assays targeting recurrent FCD-associated MTOR (S2215Y) and LEAT-associated BRAF (V600E) mutations to test cfDNA in the CSF samples with concentrations ≥0.5 ng/μL This included 5/12 (41.7%) BSM-positive patients and 8/20 (40%) BSM-negative patients. cfDNA alterations were also assayed in the CSF of 2/5 (40%) patients without prior genetic testing.
Results: Despite low CSF volumes (500 μL–1.5 mL), we detected BSMs in 3/5 CSFs (60%) identified at VAFs of 2.03, 2.48, 5.99% in the corresponding brains. No mutations were found in the 8 CSFs corresponding to BSM-negative brains, suggesting high specificity. In 1/2 patients with no prior genetic testing, cfDNA analysis identified an MTOR S2215Y mutation, consistent with independent neuroradiological and histopathological classification as FCD type II.
Conclusion: Despite limited yield of cfDNA, we successfully detected low-VAF BSMs in a significant fraction of BSM-positive patients with high specificity. Our findings support the feasibility of CSF-based liquid biopsy as a non-invasive genetic testing approach in DRE, particularly for pre-surgical or non-surgical patients.

1936 | Resective epilepsy surgery in a limited-resource settings: A cohort from an epilepsy center in a developing country

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Purpose: In light of our efforts to establish an epilepsy surgery program in a resource-limited setting, this study aimed to determine the outcome of the epilepsy surgery program in INCN of Lima, Peru.
Method: This retrospective observation study included 173 patients with drug-resistant epilepsy who had undergone resective surgery between 2012 and 2024 with a minimum of 12 months follow-up at a surgical epilepsy center located in Lima, Peru.
Results: Surgical techniques included: 146 lobectomies (84.39%), 25 lesionectomies (14.45%), 2 callosotomies (1.16%). Male: female ratio: 1/1.01. Mean age at time of surgery: 30.01 years. Mean duration of epilepsy: 19.39 years. Age at seizure onset: 10.62 years. Mean follow-up: 48 months. Pathology findings: mesial temporal sclerosis 124 (71.68%); tumors 16 (9.25%); cortical dysplasia 15 (8.67%); cavernomas 5 (2.89%); other 11 (6.35%). Engel scores at 12 months follow-up: 79.19% (137) class I, 9.25% (16) class II and 11.56% (20) class III–IV; at 24 months follow-up (n=123): 70.73% of cases were class I, 13.01% class II and 16.26% class III–IV; Over 60 months (n = 81): 58.02% class I, 17.28% class II and 24.69% class III–IV.
Conclusion: This study describe the outcomes of resective epilepsy surgery in a limited-resource center. The surgery was effective for most patients with drug-resistant epilepsy. This information could be useful for other developing countries with limited resources

2011 | Vagus nerve stimulation in refractory epilepsy: our 12-year experience

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Purpose: Refractory epilepsy remains a constant challenge in the clinical practice of epileptologists. Vagus

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nerve stimulation (VNS) is a promising complementary therapy. Objective: To evaluate the time to improvement in seizure frequency and its association with clinical and demographic variables in patients treated with VNS.

Method: We analyzed the response to VNS in 85 patients who underwent surgery at the Fundación para la Lucha contra las Enfermedades Neurológicas de la Infancia (FLENI) between January 2006 and March 2024. Data were obtained from medical records. Patients with a minimum follow-up of 12 months were included. "Responders" were defined as those with a reduction of at least 50% in seizure frequency. The Kaplan-Meier method was used to estimate the median time to clinical improvement, considering the VNS system model and seizure type. The association between clinical response and clinical variables was assessed using chi-square and Fisher's exact tests.

Results: The overall clinical response rate was 62.4%. Seventy-five percent of responses occurred within the first 12 months after VNS implantation. The mean follow-up was 62.9 months (range: 15 to 168). No statistically significant associations were found between response and variables such as age, gender, epilepsy etiology, or VNS parameters.

Conclusion: VNS therapy has proven to be useful in the treatment of refractory epilepsy over the years, showing a significant reduction in seizure frequency. However, none of the analyzed variables were significantly associated with clinical response. Further studies with larger samples are recommended to identify useful clinical predictors.

2016 | Residual Callosal Fibers in Rasmussen Syndrome: a missed link

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Purpose: Rasmussen syndrome is a rare, chronic, progressive encephalitis that predominantly affects children and is characterized by refractory focal epilepsy, progressive neurological deficits, and unilateral hemispheric atrophy. Although immunomodulatory therapies may offer temporary benefit, surgical intervention—typically hemispherotomy or hemispherectomy—remains the definitive treatment for medically refractory cases.

Method: We report the case of a 51-year-old woman diagnosed with Rasmussen syndrome affecting the right hemisphere since childhood. The patient underwent a right hemispherotomy in 2006, achieving reduction in seizure frequency. Despite ongoing treatment with multiple antiseizure medications including topiramate, carbamazepine, and levetiracetam, she experienced monthly seizures characterized by right-sided clonic movements, behavioral arrests, prolonged postictal confusion, and hemiparesis. Electroencephalography (EEG) revealed asymmetric slowing and periodic discharges in the right hemisphere, along with independent epileptiform activity in contralateral regions, suggesting multifocal epileptogenicity. Given persistent seizures, MRI was eventually performed and demonstrated residual connectivity at the splenium of the corpus callosum. A second surgical procedure was undertaken in February 2025. A right posterior temporal corticectomy and disconnection of the forceps major fibers using neuronavigation and tractography guidance was performed. Postoperative imaging confirmed complete hemispheric disconnection.

Results: Following reoperation, the patient became seizure free, with only a single brief non-disabling episode reported in early post operative days (Engel Ia). Neurological status is stabilized with no further clinical deterioration.

Conclusion: This case highlights the critical importance of comprehensive neuroimaging follow-up and complete anatomical disconnection in managing Rasmussen syndrome. Residual interhemispheric connections can perpetuate seizure activity, and reoperation guided by advanced imaging techniques can significantly improve seizure control and patient outcomes, even years after initial surgery.

2025 | Genetic Surgical Outcomes in Drug-Resistant Epilepsy: A Tertiary Center Experience

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Purpose: Epilepsy is a complex chronic neurological disorder characterized by recurrent seizures, affecting about 50 million people worldwide and ranking among the most prevalent neurological conditions. One-third of patients have drug-resistant epilepsy (DRE), requiring alternatives like surgery and precision medicine. Emerging evidence suggests genetic markers may predict surgical outcomes, with some, such as mTOR-related mutations, associated with better prognosis. Studies also highlight genes like ABCB1 and DEPDC5 in influencing post-operative seizure recurrence. Recent research affirms the diagnostic and therapeutic value of genetic testing. This study evaluates the relationship between genetic markers and surgical outcomes in DRE, supporting personalized, genetics-informed epilepsy care.
Method: This retrospective study was conducted at the Neuroscience Department of King Faisal Specialist Hospital, Saudi Arabia. Patients with DRE and confirmed genetic testing results were included. Data included demographics, clinical features, imaging, EEG findings, genetic results, surgical interventions, and outcomes. Descriptive statistics and comparative tests (chi-square, t-test, Mann-Whitney U) were applied. Kaplan-Meier and Cox regression analyses assessed seizure recurrence and predictors. Logistic regression evaluated seizure freedom. A p-value < 0.05 was considered significant. SPSS software was used for analysis.
Results: The study identified 12 patients with genetically confirmed drug-resistant epilepsy, involving mutations in genes such as CPA6, IRX2, ALDH5A1, AAAS, ARX, DEPDC5, and SRCAP. Surgical interventions included functional hemispherectomy (7 patients), frontal disconnection (4), and corticectomy (1). Postoperative seizure control was achieved in most cases, with 8 attaining seizure freedom and 4 achieving partial control. These findings underscore the utility of genetic testing in guiding surgical decisions and predicting outcomes. Specifically, certain pathogenic mutations, such as in DEPDC5 and CPA6, were associated with favorable seizure outcomes, supporting a precision medicine approach to managing pediatric DRE.
Conclusion: Genetic testing can inform surgical decision-making and help predict seizure outcomes in pediatric drug-resistant epilepsy, supporting a precision medicine approach.

2038 | Epilepsy Surgery in Children: First Experience in Sfax (tunisia) and Challenges encountered

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Purpose: To present our initial experience with epilepsy surgery in children with pharmacoresistant epilepsy and to highlight the challenges and outcomes in a resource-limited setting
Method: Our child Neurology Department specializes in the management of childhood epilepsy, has been working towards establishing an epilepsy surgery program. In 2024, this Program was developed under the guidance of Epilepsy surgery commission of ILAE.As of this year, we have successfully performed surgery on five patients with pharmacoresistant epilepsy. We began with virtual meetings under the mentorship of our two mentors, with the participation of neurologists, neurosurgeons, radiologists, and neuropsychologists. From March 2024 to September 2024, we held one meeting per month and discussed 29 patients with various etiologies. All patients had clinical evaluation, preoperative MRI, EEG recording, neuropsychological assessment. Surgeries were guided by neuronavigation and performed with the objective of lesionectomy. Postoperative follow-up included seizure monitoring and histopathological confirmation.
Results: We report five patients, including both pediatric and adult. The first patient, a 25-year-old woman, underwent reoperation due to persistent seizures; an extended temporal resection. The second patient, a 7-year-old boy, was diagnosed with right basofrontal cortical dysplasia. The third patient, a 14-year-old boy, presented with post-central ulegyria. The fourth patient, a 42-year-old woman, underwent a left temporal lobectomy for a dysembryoplastic neuroepithelial tumor (DNET) associated with hippocampal sclerosis. The fifth patient, a 5-year-old girl, had a resection of a right frontal pilocytic astrocytoma. In all cases, imaging confirmed complete or near-complete

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resection. No permanent neurological deficits were observed. A follow-up including EEG monitoring after 3 months, and the initiation of antiepileptic drug tapering.

Conclusion: This experience from Sfax demonstrates that epilepsy surgery, even in a resource-constrained setting, can offer excellent outcomes when based on a multidisciplinary, patient-tailored strategy. Early seizure freedom highlight the importance of expanding surgical programs for epilepsy in Tunisia.

2049 | Integrating Spontaneous and Stimulated Seizures with Interictal Activity: A Multimodal Approach for Delineating Epileptogenic Networks

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Purpose: Stereo electroencephalography (SEEG) provides multiple biomarkers: interictal (epileptiform discharges (IEDs), gamma/slow frequencies) and ictal (spontaneous habitual seizures [SHS], stimulation-induced seizures [SIS]) that offer complementary localization of epileptogenic networks. However, the optimal combination of these biomarkers for surgical planning has not been systematically evaluated. This study investigates whether integrating interictal and ictal markers improves network delineation and surgical outcomes, hypothesizing that a multimodal approach outperforms reliance on single biomarkers.

Method: We retrospectively analyzed consecutive patients undergoing SEEG at the Epilepsy Monitoring Unit of the National Centre of Neurology and Psychiatry, Tokyo (July 2020–April 2024). Among 44 patients, 14 met the inclusion criteria: (1) video-EEG documentation of both SHS and typical SIS, and (2) ≥1-year follow-up post-surgery. Interictal biomarkers (IEDs, gamma activity, slowing) and ictal onset zones (SHS/SIS) were visually identified using bipolar montages. We quantified the percentage of resected channels for each single and combined (co-occurred) SEEG biomarkers, then correlated these with surgical outcomes (ILAE class I [good] vs. II–VI [poor]).

Results: Out of 187 resected channels, the resection percentages were as follows: SHS (56.9%), SIS (78.9%), frequent IEDs (66.4%), gamma (59.2%), and slow activities (27.7%). Channels with combined biomarkers showed higher resection rates: IEDs + gamma (61.5%), IEDs + SHS (70.4%), and IEDs + SIS (85.7%). Surgical outcome analysis revealed no significant correlation for SHS resection (median (IQR) 84% (64.7-100)[good] vs. 61% (17-100) [poor], P = 0.4) or Typical SIS resection (100%(75-100) vs. 100%(62.5-100), P = 0.9). However, resection of frequent IEDs was significantly associated with better outcomes (86.7% (76.7-100) [good] vs. 54.5% (28.9-78.6) [poor], P = 0.02).

Conclusion: These findings highlight the potential of a multimodal biomarker approach, particularly the inclusion of frequent interictal discharges (IEDs), to refine epilepsy surgery planning. Combining interictal and ictal SEEG markers may improve the accuracy of epileptogenic network delineation, ultimately leading to better postoperative outcomes.

Genetics

1911 | Functional Seizures in *PCDH19*-Clustering Epilepsy: An Underrecognized Phenotype in Children and Adults

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Purpose: Functional (non-epileptic) seizures (FS) are frequently observed in individuals with epilepsy and autism spectrum disorders (ASD) or Intellectual Disability (ID). However, to our knowledge, there are no reports describing FS as part of the phenotypic spectrum of protocadherin 19 (*PCDH19*)-clustering epilepsy.
Method: This was a multicenter, retrospective, and descriptive study. Inclusion criteria included a confirmed diagnosis of PCDH19-clustering epilepsy based on ILAE 2022 classification and genetic testing, along with documented evidence of FS identified at participating epilepsy centers.
Results: Twenty-seven patients with *PCDH19*-clustering epilepsy were identified across six epilepsy centers. Eight female patients with documented FS were included in the study, with a median age of 20 years (IQR 18.5). The median age at epilepsy onset was 10 months (IQR 1.5), with most patients experiencing bilateral tonic-clonic seizures. Seven had some degree of ID, primarily borderline or mild. Four were diagnosed with ASD and six exhibited behavioral disturbances. A history of psychosocial adversity was reported in four cases. The median age at FS onset was 16 years (IQR 9). At that time, six patients had drug-resistant epilepsy, predominantly treated with levetiracetam and clobazam. FS were confirmed in all cases through video-EEG, with motor semiology being the most common presentation. Six patients were initially misdiagnosed, leading to overtreatment with antiseizure medications and unnecessary hospitalizations. Following correct FS diagnosis, drug treatment modifications were implemented in three patients. A multidisciplinary management approach was adopted in six cases, all of whom showed clinical improvement.
Conclusion: This pilot study suggests that FS might represent a frequent and underrecognized phenotype in *PCDH19*-clustering epilepsy, particularly in adolescents and adults. Recognizing FS in this context may help reduce iatrogenic harm and support the implementation of multidisciplinary approaches to improve patient care.

1915 | Psychometric Validation of a Clinician-Reported Clinical Severity Assessment in *STXBP1*-Related Disorder

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Purpose: *STXBP1*-related disorder is a severe developmental and epileptic encephalopathy (DEE) characterized by early-onset seizures and developmental challenges, with several disease-modifying trials on the horizon. Using a previously developed and validated clinician reported outcome measure for another severe DEE, *CDKL5*, the scale was modified and then piloted in *STXBP1*. The scale, now termed the *STXBP1*- Clinical Severity Assessment (S-CSA) was performed and psychometrically analyzed.
Method: The S-CSA is a newly modified clinician reported outcome measure (ClinRO) which includes items across motor, communication, and vision domains. It was modified from the *CDKL5* Clinical Severity Assessment (CCSA) through expert consensus sessions with *STXBP1* clinicians, which identified gaps and led to the addition of tremor and vision items. The new measure was then performed on 123 *STXBP1* patients. Confirmatory factor analysis, internal consistency, average variance extracted, and divergent validity were evaluated and compared to predefined cut-offs.
Results: Confirmatory factor analysis of 123 S-CSA datasets indicated that items loaded to three domains – Motor, Communication and Vision – with factor loadings >0.4. All domains showed strong reliability (Cronbach's alpha >0.7; composite reliability >0.88). The fit statistics and average variance extracted by the factors were satisfactory, and the divergent validity criterion of the three factors was satisfied. The distribution of the overall score was appropriate with no ceiling/floor effect seen. Minimal skew was present in the motor and communication domains (0.34 and -0.16 respectively), with right positive skew (2.2) present in the Visual domain. This was improved by separating patients with and without CVI.
Conclusion: The S-CSA demonstrates strong psychometric properties in a cohort of 123 patients with

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STXBP1-related disorder. This demonstrates the scale effectively measures a range of severity in *STXBP1*. Validated now in two infantile-onset DEEs, this clinician-reported measure is likely to be valuable as an endpoint in clinical trial settings for *STXBP1* and potentially other severe DEEs.

1929 | Survey of Epilepsy Presentations in 8p-Related Disorders

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Purpose: 8p-related disorders are genetic conditions associated with chromosomal rearrangements on chromosome 8p, including deletions, duplications, and inverted duplications with deletions (invdupdel (8p). Phenotype varies with rearrangement type and includes structural brain and cardiac abnormalities, intellectual disability, autism, and epilepsy. While prior studies have described epilepsy in 8p-related disorders, none have provided an in-depth characterization.

Method: This study aimed to characterize epilepsy phenotype in patients with 8p-related disorders seen at Children's Hospital Colorado (CHCO) and/or participating in the Project 8p Foundation NHS. Objectives included determining epilepsy prevalence, age of seizure onset, efficacy of treatment, and EEG features. We assessed differences in epilepsy presentation and severity among patients with invdupdel (8p), deletions, and duplications. A retrospective chart review was conducted for patients seen at CHCO from 2020 to 2024. Clinical data including demographics, genotype, epilepsy history, and EEG findings were collected. Presence of epilepsy and genotype were combined between CHCO patients and those in the Project 8p Natural History Study. Descriptive statistical analysis was performed on the entire group and subgroups.

Results: Overall, 32% of patients (53/162) experienced at least one lifetime seizure. 37% (30/81) of those with invdupdel (8p), 35% (16/46) with 8p deletions, and 15% (4/26) with 8p duplications had at least one seizure. Average age of seizure onset was 3.4 years. Among CHCO patients with epilepsy (11/42), only one had intractable epilepsy, while 9 became seizure-free. EEG abnormalities were present in 43% (18/42), most commonly generalized background slowing and posterior epileptiform discharges. No cases met criteria for infantile epileptic spasms syndrome (IESS).

Conclusion: This study provides the first detailed analysis of epilepsy in individuals with 8p-related disorders. While epilepsy is relatively common within 8p, it is typically well controlled with medications. Genotype-specific patterns emerged, with invdupdel (8p) associated with the highest epilepsy prevalence. Further research in larger cohorts is warranted to validate these findings.

1985 | Variants in *ATP6V0C* causes a Dravet-like developmental and epileptic encephalopathy

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Purpose:

- Dravet Syndrome (DS) is a developmental and epileptic encephalopathy (DEE).
- Diagnosis is clinical, but approximately 90% of patients have pathogenic variants in *SCN1A*.
- The ATP6V0C protein is highly expressed in the brain across the whole lifespan, and plays a key role in proton gradient generation and pH regulation.
- *ATP6V0C* has recently been proposed as a novel candidate gene for epilepsy, with or without developmental delay.

Only 4 four adults (i.e., adults over 18 years of age) with *ATP6V0C* variants have been described in the literature thus far. Here, we describe 2 adult patients with a clinical diagnosis of DS caused by *ATP6V0C* variants.

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Method: Patients with DEEs were evaluated by physicians with expertise in managing DS, and their clinical diagnosis was correlated with genetic findings. A subgroup of those patients with DS, but without known genetic causes, were evaluated through gene panels, whole exome sequencing and chromosome microarray. Phenotype was determined by pediatric and adult chart reviews as well as interviews and physical examinations.

Results: Out of 753 patients with DS, two unrelated individuals with classic DS features during childhood and adulthood were identified with heterozygous *de novo* missense variants in *ATP6V0C* (c.319G>C, p.Gly107Arg) and (c.284C>T, p.Ala95Val), respectively. Both variants were absent in the general population and computational prediction algorithms suggested deleterious effects on protein structure and/or function. No disease-causing variants in other genes previously associated with DS were found.

Conclusion: Here we describe two adult patients with Dravet-like syndrome and pathogenic/likely-pathogenic variants in *ATP6V0C*. We propose that abnormal *ATP6V0C* function can, at the severe end of the clinical spectrum, be associated with Dravet-like phenotype. This is relevant as these patients would not qualify for disease modifying anti-sense oligonucleotides (ASOs) or gene therapies targeting *SCN1A*.

1986 | Adult phenotype of *CHD2*-associated disorders

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Purpose: Pathogenic *CHD2* variants are associated with neurodevelopmental disorders and developmental and epileptic encephalopathy. While pediatric *CHD2* phenotypes have been readily explored, adult phenotypes are not well understood. We aimed to investigate the phenotypic spectrum of adult patients with *CHD2* variants.

Method: Patients 18 years or older with likely pathogenic or pathogenic (LP/P) *CHD2* variants were included. We used standardized tools to evaluate current seizures, medication use, sleep, gastrointestinal symptoms, pain response, gait, social communication disorder and adaptive behavioral skills of patients.

Results: Fourteen unrelated adult patients (age range: 18-45 years) with LP/P *CHD2* variants were described. Eleven novel variants were identified. No genotype-phenotype correlations were found. Seventy-nine percent of adults still have ongoing seizures. Photosensitivity was present in 64% of adult patients. Autism spectrum disorder was diagnosed in 71% of patients. Only 29% were able to read and understand material at a sixth-grade level or higher. Behavioral issues were reported in all patients and 71% had internalizing features, such as anxiety. Self-injurious behaviors were present in 50%. Only 43% could ambulate independently. Additional characteristics included reflux (36%), constipation (71%), and abnormal nociception (43%). One patient presented with non-epileptic breath holding spells leading to cyanosis. No patient could perform basic activities of daily living independently. Higher seizure severity was associated with worse non-seizure outcomes (p=0.04).

Conclusion: Most adults with *CHD2* continue to have seizures with severity associated with worse comorbidities such as maladaptive behaviors, gait, gastrointestinal, sleep, and nociception problems. To the best of our knowledge, the oldest patient living with a *CHD2* variant is described here, at the age of 45 years. These data may provide prognostic insights for families of pediatric patients, as well as help identify key points to be addressed in future precision trials for patients with *CHD2* variants.

1987 | Novel neuropathological observations in an adult with Dravet Syndrome

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Purpose: Dravet syndrome (DS) is a developmental and epileptic encephalopathy associated with *SCN1A* pathogenic variants in over 80% of cases. About 80-90% of patients survive childhood. As such, the adult manifestations are poorly understood. Genetic testing accessibility has improved diagnosis in DS-adults, improving the molecular understanding of aging. This, in addition to the imminent availability of precision therapies requires understanding of the natural history of DS. Currently, only a few adult cases with detailed neuropathological examinations are reported. Here we report the postmortem findings of a 55-year-old woman with SCN1A-DS due to a confirmed pathogenic variant leading to Nav1.1 loss-of-function with pharmacoresistant seizures, intellectual disability, progressive ataxia, parkinsonism, and cognitive decline.

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Method: Histopathological analysis was carried out using formalin-fixed, paraffin-embedded, 4.5-μm-thick sections from various brain regions. Histological examination was performed using Luxol fast blue-hematoxylin and eosin and Periodic-Acid-Schiff staining. Immunohistochemistry was performed using the following primary antibodies: phosphorylated-tau (p-tau), Aβ, a-synuclein, p62, and phosphorylated (p)-TDP-43.

Results: Neuropathological examination revealed corpora amylacea/wasteosomes covering the brain convexity. In addition, abundant p62-positive gray matter neuritic profiles were found mostly in limbic and neocortical regions. Pericellular TMEM106B-positive deposits were also observed. There was severe Purkinje cell loss in some lobes of the cerebellum along with variable neuronal loss in the substantia nigra, neocortex, and hippocampus. a-synuclein, amyloid-b, or phospho-TDP-43 pathology were absent. Immunostaining for p-tau revealed neurofibrillary pathology consistent with Braak stage I(left)–II(right).

Conclusion: In summary, our study reveals pathological alterations in keeping with chronic glymphatic insufficiency, impaired autophagy and some degree of neuronal loss without misfolded protein deposits. These findings are suggestive of an accelerated aging and neurodegenerative process in this SCN1A-DS adult.

2001 | From mutation to manifestation: Functional and phenotypic insights into *GABRA1*-associated epilepsies

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Purpose: *GABRA1* variants are associated with a broad spectrum of epilepsy phenotypes, ranging from mild forms like febrile seizures and juvenile myoclonic epilepsy to severe conditions such as EIDEE and IESS. Although traditionally linked to loss-of-function (LOF) effects, recent findings highlight the role of gain-of-function (GOF) mechanisms in this phenotypic diversity. This study presents a comprehensive clinical and molecular analysis of individuals with *GABRA1* variants to better understand the underlying variability.

Method: Individuals with *GABRA1* variants were identified through international collaboration, the Cure GABA-A organization, and literature review. Genotypic, phenotypic, and family history data were collected using a standardized protocol. Functional analysis of α1-subunit missense variants was conducted via electrophysiology in α1β3γ2 $GABA_A$-receptor assemblies.

Results: Clinical data from 165 individuals with *GABRA1* variants (90 missense, 6 null) revealed 111 with LOF, 42 with GOF, and 12 with null variants. GOF variants were linked to more severe phenotypes, including earlier seizure onset, epileptic spasms, severe intellectual disability, and hyperkinetic movement disorders. Microcephaly was exclusive to the GOF group. In contrast, LOF variants were associated with fever-related seizures, with GEFS+ and Dravet syndrome seen only in this group. Normal intellectual development was exclusive to LOF cases. A severity index based on e.g., age of onset, intellectual disability, and movement disorders showed significantly higher scores in the GOF group (median = 11) compared to LOF (median = 5; $P < 0.0001$), highlighting the greater clinical burden of GOF variants.

Conclusion: GOF and LOF variants in *GABRA1* define two distinct clinical trajectories of epilepsy. GOF variants are linked to a more severe disease course, with early onset and complex comorbidities. In contrast, LOF variants are associated with milder phenotypes, often involving fever-sensitive seizures. These findings underscore the value of functional variant classification in informing prognosis, clinical care, and therapeutic development.

2012 | Polygenic Influence of Common Epilepsy and Intelligence Variants on *SCN1A*-Related Disease Severity

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Purpose: Variants in *SCN1A* are one of the most common 'monogenic' causes of epilepsy. Recent studies have showed that polygenic influences beyond the *SCN1A* variant might affect phenotypic heterogeneity, which ranges from febrile seizures to the severe Dravet syndrome. Here, we assessed whether common variants associated with epilepsy and intelligence influence *SCN1A*-related disease severity.

Method: We included 70 people with a pathogenic *SCN1A* variant, 59 of which were diagnosed with Dravet syndrome. Developmental outcome at 6 years of age was used as a proxy of disease severity, grouped into 5 categories ranging from mild to severe. Polygenic risk scores (PRS) for epilepsy and intelligence were calculated after which ordinal logistic models were fitted to assess the association between the PRS and disease severity. The models were evaluated for overfitting using bootstrap validation.

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Results: Higher epilepsy PRS and lower intelligence PRS were both associated with a greater disease severity (OR = 2.38 and OR = 0.49 per standard deviation respectively; both P<0.01). When epilepsy and intelligence PRS were included in the same multivariable model, both PRS were independently predictive of disease severity (OR = 2.45 and OR = 0.48; both P<0.01).
Conclusion: Common polygenic variants are associated with disease severity in *SCN1A*-related-epilepsy. Greater epilepsy and lower intelligence polygenic burden are independently associated with more severe developmental impairment. These findings show the complex interplay between rare pathogenic and common risk variants in *SCN1A*-related epilepsy and suggest PRS could aid in predicting disease severity.

2017 | Impact of Early Sodium Channel Blocker Use on Neurodevelopment in KCNQ2-Related Developmental and Epileptic Encephalopathy

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Purpose: KCNQ2-related developmental and epileptic encephalopathy (DEE) is a severe disorder with neonatal-onset seizures and neurodevelopmental impairment. While sodium-channel blockers (SCBs) are recommended as first-line seizure treatment, it remains unclear whether their early use improves neurodevelopmental outcome (NDO).
Method: We conducted an international cohort study including 93 individuals with de novo pathogenic KCNQ2 variants predicted to lead to a DEE phenotype, aged at least three years. Data on seizure history, anti-seizure medication (ASM) use and effect, and NDO were collected using standardized questionnaires.
Results: Of the 93 individuals, 26 received SCBs within the first month of life (SCB < 1m), 45 initiated SCBs later (SCB > 1m), and 20 never received SCBs (SCB -). Seizure freedom was achieved earlier in the SCB < 1m group (median age: 2 weeks) compared to the combined SCB > 1m and SCB - groups (median: 4 months). A normal NDO was observed in 27% of individuals in the SCB < 1m group, versus 4% and 10% in the SCB > 1m and SCB - groups, respectively (P = 0.02). Severe NDO rates did not differ significantly between groups (P = 0.39). Among individuals who became seizure-free within the first month, 41% treated with SCBs had a normal NDO, compared to none treated with other ASMs. In contrast, only 10% (with SCBs) and 3% (without SCBs) of those seizure-free after one month had normal NDO. None with ongoing seizures had a normal NDO (P = 0.01). Severe NDO was least common in those with early seizure freedom (P = 0.002).
Conclusion: Early seizure freedom, particularly when achieved with SCBs, is associated with improved NDO in KCNQ2-DEE. While the cohort size limits definitive conclusions regarding the independent effect of early SCB use apart from seizure freedom itself, our findings support early SCB initiation to maximize neurodevelopmental potential in this population.

2018 | The expression of KCNQ3 determines motor symptoms and the severe phenotype in KCNQ2-related neonatal epilepsy.

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Purpose: The *KCNQ2* (Kv7.2) and *KCNQ3* (Kv7.3) genes exhibit different expression patterns during human neuronal development: *KCNQ2* is expressed during the fetal period and decreases after birth, while *KCNQ3* is expressed during late fetal development and infancy. This temporal expression pattern may explain the age-dependent onset of *KCNQ2*-related epilepsies and influence the clinical phenotype. Our goal was to investigate the contribution of Kv7.3 channels to the M-current in patients with pathogenic *KCNQ2* variants, and to study the impact of channel dysfunction on clinical phenotype severity.
Method: Multicenter study (BIO-KCNQ2 project). We included 44 patients with neonatal-onset epilepsy and *KCNQ2* variants. Neuropsychological evaluations were performed (VABS-3, ADOS, and ADI-R), along with motor assessment using the GMFCS. Patients were classified into three groups: self-limited neonatal (familial) epilepsy (SeLNE), developmental and epileptic encephalopathy without motor impairment (DEE-NM, and DEE with motor impairment (DEE-M)(GMFCS > III), this last one representing the most severe phenotype. To assess channel function, wild-type and mutant *KCNQ2* and

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KCNQ3 genes were expressed in HEK293 cells. Patch-clamp recordings were performed on 38 Kv7.2 subunits to measure Kv7 and M-currents. Current amplitudes were analyzed and expressed as current density for comparison.
Results: 37 of the 38 *KCNQ2* variants caused loss of function, reducing Kv7.2 current density. This reduction was significantly greater in the DEE group compared to the SeLNE group. Co-expression with *KCNQ3* (Kv7.2/Kv7.3) increased current density in all variants studied, with similar levels in the SeLNE and DEE-NM groups. However, the current generated by *KCNQ2* mutations associated with DEE-M was significantly lower than that observed in the other groups.
Conclusion: This study describes for the first time the role of *KCNQ3* in the most severe DEE-KCNQ2 phenotypes. The rescue of mutated Kv7.2 current by Kv7.3 appears to prevent the development of motor impairment.

2028 | Evaluation of Genetic and Clinical Features of Childhood Early-Onset Epilepsies in the Presence of Comorbid Conditions

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Purpose: Early-onset epilepsies (EOE) are epilepsies that occur in children between the ages of 1 month-3 years, significant proportion of cognitive and behavioral comorbidities. In this study, we aimed to evaluate the genetic findings and associated comorbid conditions in our patients with early-onset epilepsy.
Method: This descriptive, retrospective study was conducted at a tertiary Children Hospital followed with diagnosis of EOE between October 2021-December 2023.The developmental test results (Denver, Bayley, WISC-R) of 34 patients who were found to have significant variants in targeted broad epilepsy gene panel were included.
Results: A total of 34 patients,18 male (52.9%),the median age was 60.5 months(±61.8,29–240 months), the median age at seizure onset was 240 days(±257,3–1080 days. Pathogenic or likely pathogenic variants were identified in the following genes:PRRT2(n=8),SCN1A(n=5), RELN(n=2), SCN8A(n=2), KCNQ2(n=2), PCDH19(n=2), and one patient each with variants inAARS1,ADGRV1,ALDH7A1,CHRNA2,DEPDC5,GABRA2,GABRB3,GRIN2A,HCN2, KCNA2,MECP2,SLC2A1andWWOX.Comorbid attention-deficit-hyperactivity-disorder was identified in 7 patients(20.5%), specific learning disorder in 2 patients, autism spectrum disorder in 1 patient. Developmental delay was present in 20 patients (58.8%).Global developmental delay was noted in patients with pathogenic variants in AARS1,MECP2, WWOX, and RELN genes. Sixteen patients were diagnosed with self-limited epilepsies(SeLNE, n=1,SeLFIE n=4,SeLIE n=5,GEFS+ n=6).Nine patients were diagnosed with developmental and epileptic encephalopathies(EIDEE n=6,Dravet syndrome n=2,IESS n=1).Five patients had etiology-specific syndromes(KCNQ2-DEE n=1,ALDH7A1-related epilepsy n=1,PCDH19-related epilepsy n=2,GLUT1DS n=1). Eighteen patients(52.9%) were on two or more antiseizure medications. A marked response was observed with clobazam in a patient with a RELN variant, clonazepam in PCDH19, oxcarbazepine in PRRT2, a modified Atkins diet in SLC2A1 and a ketogenic diet in PRRT2-related drug-resistant epilepsy.
Conclusion: Comprehensive gene panels, exome, or genome sequencing are increasingly being utilized and have led to significantly higher diagnostic yields in EOE, enabling precision medicine approaches. Our results suggest the need for individualized treatments that can also treat comorbid conditions.

2036 | Expanding the Phenotypic and Genotypic Spectrum of KCNT1-Related Epilepsies

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Purpose: The *KCNT1* gene encodes for a sodium-activated potassium channel involved in neuronal excitability. Since its initial description as being implicated in human pathology in 2012, the associated genotypic and phenotypic spectrum variants has broadened - ranging from asymptomatic carriers to individuals with Epilepsy of Infancy with Migrating Focal Seizures (EIMFS) - and has included extra-neurological features. We aimed to better characterize the long-term neurological outcomes, extra-neurological features, mortality and genotype-phenotype correlations linked to *KCNT1* variants.
Method: A comprehensive literature review was performed to identify all reported cases of *KCNT1* variants. Corresponding authors were contacted to obtain updated clinical data, including current vital status, epilepsy progression, extra-neurological features, cognitive and

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psychiatric status. The entire dataset, including updated data from the literature, was combined for subsequent analyses.

Results: A total of 316 patients from 91 publications were included. Follow-up data were obtained for 61 patients (from 28 articles and 10 countries), increasing the median age at last assessment from 4.6 to 6.25 years. Among them, 182 patients had an EIMFS phenotype, 63 had Sleep-related Hypermotor Epilepsy (SHE), and 57 had forms of Developmental and Epileptic Encephalopathies (DEE). 5 patients were asymptomatic, 5 had focal epilepsy, and 4 had other phenotypes. Extra-neurological features were predominantly observed in EIMFS and DEE patients, notably Systemic-to-Pulmonary Collateral Arteries, and included other arteriovenous or cardiac malformations and various respiratory, orthopedic or gastrointestinal issues. The main cause of death was pulmonary complications (hemorrhage or infection). Genotype–phenotype correlations revealed that variants in the pore region and RCK1 domain were significantly associated with EIMFS/DEE phenotypes, whereas SHE-associated variants were enriched in the RCK2 domain. Additionally, variants at position 474 may confer increased risk for vascular malformations.

Conclusion: This study offers a comprehensive and enhanced understanding of the clinical spectrum and genetic mutations associated with *KCNT1*-related disorders.

IGAP Implementation

1878 | Educational needs among the ILAE-Young Epilepsy Section members — a global survey

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Purpose: To determine the educational needs of the International League Against Epilepsy (ILAE)-Young Epilepsy Section (YES) members worldwide.

Method: The ILAE-YES education task force developed the survey, distributed it via the ILAE channels (newsletter and webpage), and sent it to the chairs of national chapters for dissemination among their members. It was open between October and December 2024.

Results: Two hundred and eight responses were obtained from ILAE-YES members of 62 countries. Fifty-seven percent were female, and the median age was 34 years (Interquartile Range 30-37 years). Adult and pediatric neurologists accounted for 19.7% of responders, 18.3% were neurology trainees, 17.7% were epileptologists or clinical neurophysiologists, and 16.8% were researchers and other allied healthcare professionals. The ILAE and primary care curricula were unknown by 50.1% and 75.5%, respectively. Forty percent and 48% of the respondents were unaware of the ILAE Academy and VIREPA courses. Up to 55% of those who were aware of them would take them if they could afford them. Sixty-one percent and 68% of the respondents did not know about the free EpiCentre Article Collections and Multimedia Teaching Material of Epileptic Disorders. Fourteen percent of responders never attend epilepsy courses or congresses, the main reason being the lack of resources and time after clinical duties in 52% and 31%, respectively. English proficiency remains a barrier to learning for 17% of all respondents. Of these, 22% work in high-income countries. Responders have a diverse range of interests, encompassing epidemiology, basic research, clinical care, and surgical management. Their learning preferences include traditional methods and newer approaches such as podcasts and online activities.

Conclusion: Information about current barriers can help implement strategies that facilitate knowledge appropriation by ILAE-YES members. It is necessary to continue promoting access to free resources and creating opportunities for people from low- and middle-income countries to access paid resources.

1898 | Tackling Epilepsy Stigma through Community Empowerment and Health System Strengthening: Insights from Kenya's "Curse of Stigma" Campaign

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Purpose: This study aimed to reduce epilepsy-related stigma and improve access to care through a multifaceted, community-centered intervention implemented by KAWE in collaboration with county governments and civil society partners in Kenya.

Method: An eight-month intervention, branded the "Curse of Stigma" campaign, was implemented across

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Kisii, Kilifi, Kitui, and Kiambu counties. The intervention involved:

1. A Knowledge, Attitudes, and Perceptions (KAP) survey of 450 respondents across nine sub-counties in Kisii County.
2. Training 61 primary healthcare workers (PHCWs) and 74 community health promoters (CHPs).
3. Hosting public stigma-reduction forums ("Stigma Benches") in five sub-counties.
4. Youth mentorship and career development sessions for persons with epilepsy (PWE); and
5. Policy advocacy, including memorandums of understanding (MOUs) with county governments.

Results: The KAP survey revealed that 23.5% of respondents attributed epilepsy to witchcraft and 23.8% believed it to be contagious. Women demonstrated greater rejection of these myths. Following the intervention, community receptiveness to PWE improved, and epilepsy knowledge among PHCWs increased. Two new epilepsy clinics were launched in Nairobi and Kilifi, serving 519 patients in under six months. KAWE's defaulter tracing program re-engaged 144 previously lost-to-follow-up patients. Media outreach reached over 8 million people through radio, television, and online platforms.

Conclusion: The campaign demonstrates that integrated stigma reduction, service expansion, and grassroots empowerment can effectively advance epilepsy care in resource-limited settings. Aligned with the WHO Intersectoral Global Action Plan (IGAP 2022–2031), this model offers a replicable framework for reducing stigma and improving access to care in similar contexts.

1900 | Bridging Gaps in Epilepsy Care through Policy, Awareness, and Service Delivery: Evidence from Kenya's Multi-Level Response

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Purpose: This study aimed to evaluate the impact of a comprehensive epilepsy intervention program led by KAWE in Kenya. The focus was on stigma reduction, service delivery enhancement, and policy advocacy aligned with the Intersectoral Global Action Plan (IGAP 2022–2031).

Method: KAWE implemented a multi-pronged approach in collaboration with six county governments. Key components included:

1. Establishing two new epilepsy clinics in Kilifi and Nairobi Counties.
2. Conducting mass registration of 620 persons with epilepsy with the National Council for Persons with Disabilities (NCPWD);
3. Delivering training and sensitization sessions to 198 Primary Healthcare Workers and 197 Community Health Promoters across six counties.
4. Conducting awareness outreach in 36 schools and 1 prison.
5. Producing and showcasing *The Curse of Stigma* epilepsy documentary.
6. Advocating for IGAP domestication through appearances before three county assemblies.

Results: Epilepsy consultations rose to 5,457 in 2023—a 6.3% increase from 2022. KAWE successfully traced defaulters across three clinics, improving treatment adherence. Community engagement reached 7.2 million people through International Epilepsy Day media coverage. School sensitization efforts reduced stigma, including a documented case of readmission for a previously expelled student. The appointment of Kenya's Second Lady as an Epilepsy Ambassador catalyzed high-level support.

Conclusion: KAWE's integrated epilepsy intervention—combining clinical expansion, community education, and legislative advocacy—demonstrates a scalable model for improving epilepsy care in low-resource settings. The approach fosters sustainable impact in line with IGAP targets and positions community voices, particularly those of women with epilepsy, at the center of reform.

1933 | Improving Epilepsy management in sub-Saharan Africa primary care: a tool to facilitate EEG reporting from remote

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Purpose: Epilepsy represents a significant health challenge in sub-Saharan Africa (SSA), where access to diagnostic tools and trained neurologists is extremely limited. To address this gap, since 2019 the DREAM program, in collaboration with the Italian Society of Neurology and the Carlo Besta Neurological Institute, has supported the implementation of epilepsy care within SSA primary care systems. Between 2021 and 2023, video-EEG systems were installed in Malawi, Central African Republic, and Mozambique. To ensure effective use of these systems, a simplified EEG reporting tool was developed to facilitate remote interpretation by Italian neurologists through the Global Health Telemedicine (GHT) platform. This study evaluated the inter-rater reliability of this tool in routine clinical EEG assessment.
Method: The tool includes essential EEG descriptors: diagnostic classification ("epileptic", "encephalopathic/lesional", "normal"), background activity (physiological/slowed; symmetric/asymmetric), slowing patterns and epileptiform abnormalities, and seizure recordings. Five expert neurologists independently reviewed 20 EEGs randomly selected from 220 EEGs recorded in 2024 at the DREAM-Bangui center. Fleiss' Kappa was used to assess inter-rater reliability.
Results: The sample included 20 patients (12 females; median age: 20 years). There was substantial agreement for "epileptic" and "normal" EEGs (Kappa = 0.74), moderate for "encephalopathic/lesional" (Kappa = 0.44), and excellent for the detection of epileptiform abnormalities (Kappa = 0.89). A seizure was identified by four of the five neurologists in one case. Agreement on background activity and slowing was lower.
Conclusion: Our preliminary results show a satisfactory inter-rater reliability for the main diagnostic features of the simplified EEG reporting tool. Its structured format enables consistent interpretation and supports collaborative decision-making among international teams. Combined with telemedicine, it serves as a scalable solution to strengthen epilepsy diagnosis, facilitate local training, and contribute to long-term capacity building in low-resource settings.

Neuroimaging

1975 | Longitudinal Gray Matter Atrophy in Idiopathic Generalized Epilepsy Reveals Synaptic Dysfunction and Cellular Correlates

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Purpose: This study aims to (1) evaluate longitudinal gray matter volume changes in idiopathic generalized epilepsy (IGE) patients, (2) identify potential atrophy epicenters using network-based approaches, and (3) investigate the underlying genetic and cellular mechanisms associated with these structural changes.
Method: In this longitudinal study, we recruited 36 IGE patients and 28 age- and gender-matched healthy controls (HCs). Structural MRI data were analyzed to quantify progressive gray matter atrophy. We implemented a network-based epicenter model to identify epicenters of atrophy propagation. Patient-specific epicenter patterns were classified using k-means clustering to identify distinct subtypes. To explore molecular correlates, we performed partial least squares (PLS) regression between epicenter profiles and regional gene expression data from the Allen Human Brain Atlas, followed by pathway enrichment and cell-type specificity analyses.
Results: With a median follow-up period of 23 months, IGE patients exhibited progressive atrophy predominantly in bilateral prefrontal and right temporo-occipital regions. Network analysis identified primary epicenters in bilateral prefrontal cortex, thalamus, and caudate nucleus. K-means clustering revealed two distinct epicenter subtypes: subtype 1 showed posterior-dominant patterns, while subtype 2 demonstrated prefrontal predominance and was associated with higher seizure-free rates. PLS regression revealed significant spatial correlations between epicenter ranking and genes. Pathway enrichment analysis identified synaptic organization and transmission. Cell-type specificity analysis showed predominant enrichment in excitatory neurons.
Conclusion: Our findings demonstrate progressive gray matter atrophy in IGE with distinct epicenter distributions, particularly in prefrontal and temporo-occipital regions. The identified synaptic pathway dysregulation and excitatory neuron vulnerability provide potential mechanistic explanations for the observed structural changes.

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1982 | Comparison of functional connectivity in focal versus generalized epilepsy

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Purpose: Epilepsy is a disorder of brain networks affecting 0.6% of children, with medications controlling only 70% of cases. As thalamically targeted intracranial devices become a more accepted therapy for drug-resistant epilepsy (DRE), understanding the networks involved is essential to identify effective targets. We explore the possibility of using resting-state functional connectivity MRI (fcMRI) to evaluate epilepsy networks. We examined fcMRI data in a population of pediatric DRE patients, divided into focal (F) and generalized (G) cohorts, to explore whether differences in thalamic network connectivity can be used as a biomarker.
Method: Retrospective analysis of all fcMRI studies with patients ≤18yo with DRE from 2021 to 2025 at Seattle Children's Hospital. Inclusion criteria were anatomically intact MRI of the brain, and successful completion of two resting state fMRI trials. Twenty-five patients were included in the analysis (17 focal epilepsy, F, and 8 generalized epilepsy, (G). Connectivity maps, represented by correlation coefficient (CC) values, were generated using seed-based interregional networks (3mm resolution, 1 voxel seeds) in the anterior nucleus (AN), mediodorsal nucleus (MD) and pulvinar nucleus (PUL). Statistical analysis was performed using randomize statistical tool implemented in FSL software library. To evaluate group difference, we used two-sample unpaired T-test.
Results: CC map averages for focal and generalized epilepsy groups obtained for AN_L seed. For both the AN and MD group comparisons, the observed connectivity patterns were not significantly different. By contrast, a significant group difference (G > F) was identified for the right PUL seed
Conclusion: While AN and MD regions were not statistically different between groups, evidence for difference in PUL regions between F and G epilepsy groups was observed. While the small sample supports a need to enroll a larger cohort to validate and extend these results, the approach provides a potential method to examine thalamic networks among pediatric epilepsy types.

1988 | Situating the thalamus into large-scale functional network pathology in temporal lobe epilepsy

R Ding[1], K Xie[1], A Ngo[1], J Chen[1], E Sahlas[1], R Rodriguez-Cruces[1], J DeKraker[1], J Royer[1], G Zhou[1], Z Zhang[2], L Concha[3], P-J Toussaint[1], N Bernasconi[1], A Bernasconi[1], A Evans[1], B Bernhardt[1]
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Purpose: The thalamus mediates large-scale network function and is an increasingly recognized node that connects the mesiotemporal disease epicenter to neocortical systems in temporal lobe epilepsy (TLE). Here, we leveraged resting-state functional MRI (rs-fMRI) to explore network alterations in hippocampal-thalamo-cortical networks in TLE patients and healthy controls (HC) and their association with clinical features.
Method: We analyzed rs-fMRI data from 257 unilateral TLE; 140 females; mean age±SD =30.78 ±9.35) and 259 age- and sex- matched healthy controls (HC) (130 females; mean age ± SD = 29.54±8.42) across four cohorts (MICA-MICs; NKG; EpiC; Noel). Using an established thalamic parcellation, we extracted average timeseries from both global thalamus and individual thalamic nuclei. The cortex timeseries were based on Conte69 space whereas hippocampal were mapped onto the hippocampal mid-thickness surface. Smoothed them individually (10mm, 3mm). Then calculated Pearson correlations between thalamic timeseries and vertex-wise timeseries from neocortex and hippocampus.
Results: Compared to HC, TLE patients exhibited significantly reduced global thalamo-cortical connectivity across prefrontal, sensorimotor, visual regions, as well as diminished thalamo-hippocampal connectivity involving CA1, CA4, and subiculum subfields. While thalamic subnuclei demonstrated bilateral cortical connectivity reductions, hippocampal connectivity disruptions were predominantly ipsilateral. Moreover, the subdivision FC decline is most significant in between ipsilateral ventral posterior lateral(VPL) and cortex as well as ipsilateral dorsomedial and Hippocampus. Additionally, disease duration showed a negative correlation trend with thalamo-cortical and thalamo-hippocampal FC.
Conclusion: Our findings reveal disrupted hippocampal-thalamo-cortical networks in TLE. Ipsilateral hippocampal-thalamic reduction suggest alterations that co-lateralize with the mesiotemporal epicenter, while thalamo-cortical alterations become bilateral and indicate a broader network impact. The strongest declines

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occurred in VPL-cortex(sensorimotor) and dorsomedial thalamus-hippocampus(executive/memory) pathways, with functional connectivity progressively decreasing with disease duration. These highlight the thalamus as a central hub in TLE pathophysiology and identify potential therapeutic targets.

2007 | Sodium channel blocker Anti-Seizure Medications Reduce Alpha Peak Frequency in Epilepsy: Normal Resting-State EEG Study

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Purpose: While scalp EEG remains central to epilepsy diagnosis, 30-40% of initial studies fail to detect interictal epileptiform activity, delaying treatment. Alpha oscillations (8-13 Hz), modulated by thalamocortical circuits, show altered dynamics in epilepsy. This study investigates how sodium channel blocker (SCB) anti-seizure medications affect alpha peak frequency, proposing quantitative Normal or interictal normal EEG biomarkers for clinical use.
Method: We recorded eyes-closed, 19-channel EEGs from 44 epileptic patients treated with sodium channel blocker (SCB) medications and 52 age- and sex-matched healthy controls. Preprocessing included bandpass filtering from 1 to 40 Hz and visual inspection to remove artifacts, spikes, and ictal epochs. We then analyzed visually normal interictal epochs using power spectral density (PSD) estimation across 1 to 40 Hz for each subject. The alpha peak frequency was extracted from the PSD. Statistical analyses were performed using MATLAB and GraphPad Prism.
Results: We obtained that PSD from Patients are significantly lower than Healthy controls in some frequency ranges ($P<0.05$). In addition, the frequency of Alpha peak in Healthy controls is significantly higher than SCB Epileptic patients ($P<0.05$).
Conclusion: Electroencephalography spectral power analysis and especially the frequency of alpha oscillation could form part of a clinically useful diagnostic biomarker for Epileptic patients, even by response to SCB-AED in this study.

2010 | 7 Tesla magnetic resonance imaging in pharmacoresistant epilepsy is associated with increased number of surgical candidates

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Purpose: Epilepsy is a chronic neurological disorder characterized by a predisposition to seizures. One-third of epilepsy patients are pharmacoresistant, meaning they have failed to control seizures with medication. For these patients, surgical intervention remains the primary therapeutic option to achieve seizure freedom. It is crucial to identify an epileptogenic lesion on MRI, which can be challenging with conventional 3 Tesla (3T) magnetic resonance imaging (MRI). Ultra-high field (7 Tesla) MRI improves lesion detection. However, the influence of 7T MRI on the assessment of surgical candidacy in pharmacoresistant epilepsy remains unclear. Our aim was to determine whether examining patients with clinical 7 Tesla (7T) MRI in addition to 3T epilepsy MRI results in an increased number of surgical candidates.
Method: We retrospectively investigated all patients who underwent conventional 3T MRI alone followed by 7T MRI with an epilepsy protocol at Karolinska University Hospital between June 2023 and March 2025. Surgical candidacy was assessed based on documentation from multidisciplinary epilepsy surgery meetings. McNemar's test was applied to compare the proportion of patients considered surgical candidates following 3T MRI alone versus after the addition of 7T MRI.
Results: Thirty patients (60% female, mean age 25 ± 14 years) met the inclusion criteria. Ten patients (33%) initially MRI-negative at 3T were identified as surgical candidates after 7T imaging, with new lesions found in frontal (4), temporal (4), cingulate (1), and occipital (1) regions. Fourteen patients (47%) remained non-candidates, while 6 (20%) had their 3T-based candidacy confirmed. The increase in surgical candidacy with 7T imaging was statistically significant ($p=0.002$).
Conclusion: 7T MRI examinations significantly increased the number of surgical candidates compared to conventional 3T MRI examinations in patients with pharmacoresistant epilepsy.

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Neuropsychology

1861 | Smartphone Usage and Health Outcomes in Epilepsy: An Indian Perspective

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Purpose: Epilepsy is a highly prevalent neurological disorder that significantly impacts the quality of life (QoL) of individuals, especially in developing countries like India where epilepsy comprehension and care are limited. With the increasing use of smartphones, concerns have been raised about their potential impact on seizure frequency. While seizure control remains a key therapeutic goal, the increasing prevalence of technology use and its potential effects on well-being warrant investigation.
Method: The current study aimed to explore the association between smartphone usage and seizure frequency and QoL in individuals with epilepsy. A cross-sectional study was conducted by recruiting patients diagnosed with epilepsy, seeking treatment from a tertiary care center in Chandigarh, India. QoL was measured by using the QOLIE-10 questionnaire.
Results: The study included 60 patients, (55% females and 45% males) with a mean age of 28.07±10.83 years. The mean QOLIE-10 score of the participants was 29.92 (SD = 10.82). A statistically significant moderate positive correlation was observed between smartphone usage and seizure frequency ($\rho = 0.539$, $p < .001$), suggesting that greater smartphone use is associated with more frequent seizures. A significant moderate positive correlation was found between seizure frequency and QOLIE-10 scores ($\rho = 0.333$, $p = .009$), indicating that individuals with higher seizure frequency tend to report poorer QoL. Results revealed a significant difference in QoL scores based on educational levels, $F(6, 53) = 2.675$, $p = .024$ and occupations $F(4, 55) = 5.516$, $p = .001$. Self-employed and unemployed participants had significantly poorer QoL.
Conclusion: The observed association between smartphone use and seizure frequency warrants further investigation to determine causality and potential mechanisms. In the Indian context, these findings emphasize the urgent need for culturally tailored interventions focusing on digital health literacy, employment support, and responsible technology use to enhance the quality of life for individuals living with epilepsy.

1896 | From Potential to Practice: An International Survey on Technology Adoption and Needs in Epilepsy Neuropsychology

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Purpose: Technological innovations present significant opportunities to enhance neuropsychological assessment and intervention in epilepsy. Yet, compared to other healthcare fields, neuropsychology has been comparatively slow to integrate technological advancements into clinical practice. The aim of this study was to characterize the current neuropsychology workforce in epilepsy care, document existing technological practices, and identify technologies that could improve the holistic care of people with epilepsy.
Method: An online survey comprising multi-choice and open-ended questions was distributed to a cross-sectional cohort of neuropsychologists across multiple countries. The survey collected quantitative and qualitative data on clinical settings in which neuropsychological services are provided to people with epilepsy, technologies and tools currently in use, barriers to use, and desired technological developments.
Results: The final sample included 179 neuropsychologists from over 40 countries, most of whom were women (69%), aged 30-49 (60%), who held a PhD (60%). Key barriers to technology use included lack of validated telehealth tools, limited financial resources to purchase tools, and an absence of relevant norms. Respondents from lower-income countries more often cited internet access and cultural suitability as challenges. Priorities for future tools

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included predictive algorithms and novel applications for neuroimaging.

Conclusion: This international survey highlights that while neuropsychologists working in epilepsy settings recognize the potential of technological innovations to enhance assessment and intervention, significant barriers hinder widespread adoption. These include systemic and logistical challenges that disproportionately affect lower-income regions. Neuropsychologists expressed strong interest in technologies such as predictive algorithms and advanced neuroimaging tools to assist their practice. To bridge the gap between technological potential and clinical practice, future efforts must prioritize the development of accessible, culturally appropriate, and evidence-based tools that align with the needs and realities of the global neuropsychology workforce.

1930 | Neurodevelopmental Outcome of Infants with Early-Onset Epilepsy in the EPIPEG study

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Purpose: Early-onset epilepsy is associated with a high risk of developmental delay, though outcomes vary and are not well understood. This study aimed to describe neurodevelopmental outcomes and identify predictors in infants with early-onset epilepsy in London and the South-East of England.

Method: In this prospective cohort study, 112 infants aged 4 weeks to 12 months with ≥2 unprovoked seizures were recruited from regional hospitals and clinics. Neurodevelopmental assessments were conducted at baseline (T1, mean age = 8.46 ± 3.3 months) and around 12 months (T2), using the Bayley Scales of Infant and Toddler Development (Bayley-III), the Bayley Social-Emotional Questionnaire, and the Vineland Adaptive Behavior Scales. Principal component analysis (PCA) was used to derive a composite neurodevelopmental score. Correlations and multiple linear regressions examined associations with clinical and demographic factors.

Results: At T1, average scores across domains were below normal. PCA revealed a single factor with high internal consistency (KMO = 0.90). Neurodevelopmental functioning correlated negatively with age at testing ($r = -0.38$, $p < 0.001$) but not age of seizure onset. Regression analysis identified normal EEG ($\beta = 1.53$, $p = 0.005$), higher birth weight ($\beta = 1.13$, $p = 0.019$), and younger age at assessment ($\beta = -0.29$, $p = 0.001$) as significant predictors of better functioning. Neurodevelopmental scores were stable between T1 and T2 (e.g., motor $t = 9.78$, $p < 0.001$). Clinical variables, including MRI and aetiology, did not significantly predict change over time.

Conclusion: Infants with early-onset epilepsy showed generally delayed neurodevelopment at presentation. EEG status, birth weight, and earlier assessment age were associated with better initial outcomes. However, early neurodevelopmental scores were the strongest predictors of outcomes at 12 months, highlighting the need for early developmental assessment and intervention.

1963 | Development of a Neuropsychological Test Battery for STXBP1 - related Epilepsy: Implications for Clinical Trial Readiness in rare DEEs

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Purpose: STARR is a multisite natural history study launched in 2021 to support clinical trial readiness for STXBP1–related epilepsies. The neuropsychological battery was developed from the disease concept model, and consists of measures evaluating overall development, communication and motor skills (Bayley-4, STXBP1-CSA), Peabody-3, GMFM, AIMS, ORCA), sleep (CSHQ), gastrointestinal symptoms (ROME IV), behavior including symptoms of Autism (CBCL, ABC, CARS-2), quality of life (QI-Disability), and adaptive skills (Vineland-3). Currently our four US STARR sites have performed 100 over evaluations.

Method: As the Bayley-4 and Peabody-3 were often given out-of-age level, we explored how well these measures captured development. We investigated floor and ceiling effects using established basal and ceiling rules, and calculated rates of both imperfect and scores of zero. Both instruments' basal rule is three consecutive perfect scores

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on three items; we focused on the first three items per domain. The ceiling rule for the Bayley-4 is five consecutive zero scores and for the Peabody-3 three consecutive zero scores; we focused on the last items per domain.

Results: Ninety-three Bayley-4's (average age=7.05 years (SD=3.5)) and 86 Peabody-3's (average age=6.92 years (SD=5.3)) were completed. Rate of absolute floor effects (score of zero on first three items across domains) was 0%. Rates of imperfect scores on the same first three items ranged from 6% (Fine Motor) to 24% (Expressive Language). The rate of absolute ceiling effects was 0 to 1%; rates of any points on final items ranged from 0 to 8% (Expressive Language).

Conclusion: Rates of complete floor and ceiling effects are nearly zero on the Bayley-4 and Peabody-3, indicating that essentially all participants achieve some points on early items and have yet to develop the skills required for later items. As these tools scale well in this population, they are promising measures for STXBP1-clinical trial settings.

1964 | Turning6 - Neurobehavioral follow up of EPIPEG participants -Preliminary Results

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Purpose: Few studies have assessed infants with epilepsy and followed them through the school years. The current study aims to characterize the neurobehavioral status of children (aged 6-9 years) who had epilepsy in infancy (under 12 months) (EPIPEG participants).

Method: Children who had epilepsy in infancy (n=109) are undergoing psychological assessments. Parents are being interviewed regarding adaptive behavior, school placement, neurodevelopmental diagnoses and completing a measure of behavior - The Strengths and Difficulties Questionnaire (SDQ). We are comparing the behavior of the EPIPEG children with an age and gender matched control group.

Results: Of the 46 children recruited to date, 18 (42%) have 'active' epilepsy (i.e. one or more seizures in the last year). The median Adaptive Behavior Composite (ABC) is 76 (range: 24-130) and 14 (30%) have an ABC below 70, consistent with an Intellectual Disability (ID). Children with 'active' epilepsy have a significantly lower level of adaptive behavior compared to those without 'active' epilepsy (p = 0.003). Eighteen of (42%) participants attend a specialist school with children with 'active' epilepsy more likely to be attending special school ($p = 0.014$). Thirty children (58.8%) have an Educational Health and Care Plan (EHCP) denoting educational needs which require significant support with the children with 'active' epilepsy more likely to have an EHCP (p=0.013). Ten (21%) children have autism but there was not a significant difference between children with 'active' epilepsy and those without (p =0.80). Parents of the EPIPEG children reported significantly more problems with behavior than a control group (p<0.001).

Conclusion: Children with epilepsy onset in infancy have a significant neurobehavioral burden at follow-up reflected in a high level of intellectual disability and worse behavior than peers. Children with 'active' epilepsy at school age have worse adaptive behavior and require more support in school than children who no longer have 'active' epilepsy.

1979 | Cognitive aspects in three children with Autoimmune Epilepsy

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Purpose: Autoimmune encephalitis (AE) is a rare disease characterized by a subacute onset of encephalopathy and focal neurological signs [1]. However, diagnosing seronegative forms (AE SN) remains difficult despite existing diagnostic criteria, thus requiring the definition of new clinical markers. Here we tried to study cognitive impairment in children with autoimmune encephalitis as a potential biomarker.

Method: Three patients with possible and/or probable AE SN according to pediatric AE criteria [4] were recruited for cognitive assessment. The assessment included an ictal assessment based on the procedure proposed by the ILAE in 2016 [5] and an interictal assessment exploring the different cognitive domains. For seizure description, we relied on the 2025 ILAE seizure types classification [6].

Results: Three girls with a mean age of 12 years (9-16 years) and initially referred for epileptic seizures were included. Electroencephalograms allowed the recording of focal motor tonic (2/3) and clonic (1/3) and focal non-motor seizures in 2 patients. Interictal spikes and waves (2/3) or slowing (1/3) were noted in frontotemporal

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regions; the extreme delta brush sign was identified in 2 cases. Ictal assessment was possible in only one patient who completed the naming test. Between seizures, all 3 patients had language disorders such as alexia (1/3), dysarthria with semantic aphasia (1/3), and transcortical motor aphasia in the other patient.

Conclusion: Recognizing the cognitive phenotype during AEI could constitute an additional clinical marker. However, the frequent association with epilepsy requires further studies to unravel the impact of the inflammatory process, epileptic activity, and antiepileptic drugs on cognitive functions.

2013 | The Impact of an Eight-Week Rehabilitation Program on Memory in Epilepsy: Results of a Randomized Waitlist-Controlled Trial

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Purpose: Cognitive rehabilitation programs in people with epilepsy (PWE) have been limited to temporal lobe epilepsy, with little attention to rehabilitation effects on long-term memory. We investigated the impact of a newly designed rehabilitation intervention on memory, including long-term recall, in a mixed sample of adult PWE.

Method: Seventy PWE at the outpatient clinic of Vilnius University Hospital Santaros Klinikos were randomized to either intervention or waitlist groups matched for age, sex, epilepsy type, and seizure frequency. The intervention consisted of eight sessions of psychosocial counseling and cognitive training. Participants were followed up 4- and 16-weeks post-intervention to assess changes in 15-word list, story, and complex figure recall as well as verbal fluency. Long-term memory was assessed as free recall one week after the testing time point. Linear mixed models with maximum likelihood estimation were used for analysis.

Results: Of the 70 participants (40 (57.1%) female, 40 (57.1%) with focal epilepsy, mean age 35.9 ±11.7, mean epilepsy duration 18.6 ±11.4 years), 61 (87.1%) were followed up at 4 weeks and 55 (78.6%) at 16 weeks. The intervention group sustained baseline-level long-term word recall at 4 weeks (47.1 ±28.1% and 49.1 ±23.6% decay, respectively, p=0.651), in contrast to the waitlist group (43.1 ±27.9% and 67.2 ±21.9%, p=0.004), p=0.030, while matching again at 16 weeks (group-by-delay effect F(2,40.5)=3.624, p=0.036). Categorical (20.7 ±6.3 (baseline), 22.9 ±7.6 (4 weeks), 24.0 ±7.7 (16 weeks) points, group-by-delay effect F(2,59.1)=3.309, p=0.043) and phonemic fluency (11.7 ±5.6 (baseline), 13.1 ±4.7 (4 weeks), 13.9 ±4.8 (16 weeks), F(2, 61.7)=3.824, p=0.027) improved in the intervention group. No significant group-by-delay effect was observed for verbal story, visual, or short-term word memory.

Conclusion: Data suggests that our program has a transient positive effect on long-term verbal memory and a more sustained impact on verbal fluency in a sample combining patients with focal and generalized epilepsies.

Nursing

1916 | The Effect of the Epilepsy Management at School Mobile Health Application on the Knowledge, Attitude and Self-Management of Teachers of Children with Intellectual Disabilities: A Randomised Controlled Study

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Purpose: This study was conducted to determine the effects of the "Epilepsy Management at School Mobile Health Application (EpiSchool-M)" and "Epilepsy Management at School Digital Education Guide (EpiSchool-R)", developed for teachers of children with intellectual disabilities, on teachers' epilepsy knowledge, attitude and self-management.

Method: This study was in a single-blind, follow-up, randomized controlled trial design in three phases (CTN: NCT06807047). In the first phase, the "Epilepsy Management Training Content at School" was developed. In the second phase, "Epilepsy Management at School Digital Training Guide" and a "Epilepsy Management at School Mobile Health Application" were developed based on this content. In the third phase, the effectiveness of the digital education guide and the mobile health application was evaluated with 90 teachers working with children with intellectual disabilities. The study was conducted between December 2022 and May 2025 teachers were assigned to three groups (EpiSchool-R, EpiSchool-M and control) by simple randomization method. Teachers in the intervention groups used either the digital guide or the mobile health application specific to their group for

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1.5 months. Data were collected at three different times, on day 0, day 15 and 1.5 months later, using the Individual Identification Form, the Knowledge and Attitudes Toward Epilepsy Among School Teachers Scale, and the Epilepsy Self-Management Scale for Teacher

Results: Teachers in the EpiSchool-M group had significantly higher mean post-test scores in epilepsy knowledge, attitude, and self-management compared to both the EpiSchool-R and control groups. In addition, teachers in the EpiSchool-R group also showed significantly higher scores compared to the control group ($p < 0.05$).

Conclusion: Mobile health applications are an effective and prioritized method for epilepsy education for teachers of children with intellectual disabilities.

Pediatric Epileptology

1840 | Fenfluramine in *SCN1A*-related GEFS+: A multicenter observational study on efficacy and tolerability

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Purpose: The *SCN1A* gene is implicated in a broad spectrum of epilepsy phenotypes, ranging from self-limited genetic epilepsy with febrile seizures plus (GEFS+) to severe developmental and epileptic encephalopathies such as Dravet syndrome (DS). While fenfluramine (FFA) has shown strong efficacy in DS and encouraging results in other epileptic encephalopathies, its effectiveness in *SCN1A*-related epilepsies beyond DS has not yet been evaluated.

Method: This multicenter observational study included 11 patients with *SCN1A*-related GEFS+ resistant to ASM, treated with FFA. All patients presented febrile and afebrile seizures, focal and bilateral. FFA was introduced following the DS titration protocol. Efficacy and side effects were periodically monitored through standardized evaluations, including color-doppler echocardiogram.

Results: All patients carried missense variants, with the exception of one nonsense variant, and one non-coding intronic variant. Missense variants showed variability in localization, occurring in both variant-dense and variant-sparse regions. FFA treatment duration ranged from 7 to 56 months (mean 19.2), with no discontinuations by the last evaluation. FFA addition led to a mean seizure frequency reduction of 91%, with more than half of the patients achieving complete seizure freedom. Reduced EEG abnormalities were documented in 6/11 patients, including complete normalization in 3/11. Furthermore, caregiver reports indicated perceived improvements in patients' alertness and behavioral responses. The mean FFA dosage was 0.39 mg/kg/day, and it was well tolerated, with only mild and transient adverse events reported.

Conclusion: FFA demonstrated a remarkable efficacy across the full spectrum of seizure types. A good clinical response to FFA was observed in all variant groups, suggesting that its efficacy is independent of functional consequences of the underlying variant. FFA proved effective at lower dosages compared to DS. Despite the small sample size, this study expands the potential therapeutic spectrum of FFA and supports the hypothesis that FFA may be effective in *SCN1A*-related epilepsies beyond DS.

1877 | Application and validation of large language model-driven techniques for structured data extraction of seizure control status from unstructured free-text in epilepsy

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Purpose: Epilepsy affects over 70 million people worldwide, with treatment primarily relying on anti-seizure medications (ASMs). Predicting the effectiveness of ASMs remains challenging, and limited research exists on predicting outcomes for subsequent ASMs after treatment failure. This study aims to apply and validate a large-language model (LLM) for extracting seizure-related information from unstructured clinical notes, as a step towards analyzing seizure control.

Method: We conducted a retrospective study of pediatric epilepsy patients treated at from 2018 to 2021. Two datasets were manually annotated: 231 free-text clinical notes from 10 patients to serve as the training set, and 540 free-text clinical notes from 50 patients to serve as the test set. These were processed using an LLM, with prompts designed to identify seizure-related indicators and extract seizure occurrence. A logic-based workflow was developed to classify seizure control status. The model's performance was evaluated using BERTScore and Sem-score, with higher values indicating stronger alignment with manual annotations. All data was anonymized, and patient consent was obtained.

Results: For seizure occurrence extraction, the model achieved a mean BERTScore of 0.84±0.045 and Sem-score of 0.61±0.32 for the training set, and a mean BERTScore of 0.85±0.044 and Sem-score of 0.65±0.22 for the test set. For seizure control status classification, the model achieved 93.07% accuracy on the training set and 94.51% on the test set.

Conclusion: Despite some variability in seizure occurrence extraction, the model demonstrated strong performance in classifying seizure control status. These findings highlight the potential of LLMs to accurately extract clinically relevant information from unstructured clinical notes. With the growing adoption of electronic health records globally, LLMs provide an efficient method for large-scale data extraction, paving the way for further research in diverse patient populations and clinical settings.

1879 | Seizures, Neurological Complications and Outcomes in Children After Congenital Heart Surgery at Chiang Mai University Hospital

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Purpose: This study aims to analyze these complications and associated outcomes in pediatric patients undergoing congenital heart surgery.

Method: A retrospective chart review was conducted on children age below 18 years old who underwent cardiac surgery at Chiang Mai University Hospital between January 2013 and December 2023. Baseline characteristics, perioperative and postoperative parameters, and neurological outcomes were analyzed using descriptive statistics and multivariable regression analysis.

Results: A total of 2,753 patients underwent congenital heart surgery, of whom 47 (72.3%) were diagnosed with cyanotic heart disease. Neurological complications were identified in 65 patients, with an incidence rate of approximately 2.4%. The most common complication was seizures, occurring in 33 patients (50.8%), followed by altered levels of consciousness in 22 patients (33.8%) and abnormal movements in 12 patients (18.5%). The most common seizure type was focal clonic/tonic seizure, occurring in 14 patients (42.4%). The median (IQR) time to seizure onset was 30 hours (10-72) after the operation. Twenty-two patients were prescribed a single antiseizure medication (ASM), while 11 required multiple ASMs. Levetiracetam was the most frequently used first-line ASM, being used in 15 patients (45.5%). At the final follow-up, 19 patients (29.2%) exhibited global developmental delay, and 3 were later diagnosed with epilepsy. There were 19 deaths (29.2%). Following univariable analysis, utilization of ECMO was a factor associated with mortality (OR 6.19, 95% CI 1.85-20.71, $p = 0.003$).

Conclusion: Our study identifies seizures as the most common neurological complication, with the majority classified as acute symptomatic seizures. Levetiracetam was the most commonly used first-line antiseizure medication, achieving seizure cessation in approximately 73% of patients. Developmental delays were found in one-third of patients at the latest follow-up. The utilization of ECMO is associated with an increased risk of mortality.

1912 | A Parsimonious and Validated Prediction Model for Epilepsy After Febrile Seizures in Children: A Prospective Cohort Study in a Resource-Limited Setting

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Purpose: Febrile seizures (FS) are common and usually self-limited, yet a subset of children later develop epilepsy. Early risk stratification remains a clinical challenge, particularly in resource-limited settings where access to long-term neurologic follow-up may be constrained. We aimed

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to develop and internally validate a parsimonious prediction model for epilepsy following FS in children.

Method: We conducted a prospective cohort study at Children's Hospital 2, a tertiary pediatric center in Ho Chi Minh City, Vietnam. 631 children aged 1 month to 6 years with FS were enrolled between 2023 and 2024 and followed through June 2025. Children with prior afebrile seizures or CNS infection were excluded. The primary outcome was epilepsy onset, defined per ILAE 2014 criteria. Predictor selection used clinical reasoning and Bayesian Model Averaging (BMA). A multivariable Cox proportional hazards model was developed. Model performance was evaluated using Harrell's C-index, time-dependent AUC, integrated Brier score (IBS), and bootstrap calibration.

Results: Over a median follow-up of 2.0 years (IQR: 1.8–2.2), 35 children (5.5%) developed epilepsy, corresponding to an incidence of 29 per 1,000 person-years (95% CI: 20–40). The final model included four predictors: neurodevelopmental delay (HR=8.72, 95% CI: 4.13–18.39), family history of epilepsy (HR=2.64, 95% CI: 1.11–6.26), focal seizures (HR=3.26, 95% CI: 1.39–7.66), and each additional FS recurrence (HR=1.50, 95% CI: 1.24–1.82). The model demonstrated strong discrimination (C-index: 0.871; AUC at 24 months: 0.89 [95% CI: 0.82–0.95]), excellent calibration, and an IBS of 0.033. A clinical nomogram was constructed to facilitate practical use in pediatric settings.

Conclusion: This parsimonious, well-calibrated, clinically applicable model for predicting epilepsy after FS in children was developed and internally validated. It may assist early counseling, targeted follow-up, and resource allocation, especially in settings with limited pediatric neurology access. External validation is in progress. Trial Registration: ClinicalTrials.gov ID: NCT06444126.

1926 | A checklist to support the diagnosis of Lennox-Gastaut syndrome

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Purpose: Diagnosing Lennox-Gastaut syndrome (LGS) is challenging due to the heterogeneity of its clinical presentation and evolution over time. A group of epilepsy experts convened to develop a simple-to-use checklist for non-specialists to support LGS diagnosis.

Method: Ten experts from seven countries formulated seven questions for the checklist, based on ILAE criteria for classification and definition of LGS, through an iterative process. The final checklist had four possible outcomes based on a scoring system: likely LGS, possibly LGS, unlikely LGS, and insufficient data. Accuracy of the checklist was tested in a two-step process. Firstly, each expert selected LGS and non-LGS cases from their records, and for each case provided original diagnosis and answers to the checklist questions to an independent third party that subsequently compared the outcome with the original diagnosis. The experts re-convened to assess findings and refine checklist questions/outcomes. Secondly, all cases were re-evaluated and results collected as previously. Correct outcomes were defined as a perfect match with the original diagnosis (both LGS and non-LGS cases) or 'possibly LGS' outcome matching an original LGS diagnosis.

Results: Of 120 cases assessed, 64 were LGS and 56 non-LGS. The outcome was correct for 94% (n=113) of cases: 68% (n=82) were a perfect match with the original diagnosis; 26% (n=31) were 'possible LGS' matching an original LGS diagnosis. Incorrect matches where the checklist outcome did not match the original LGS diagnosis resulted

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from absence of documented characteristic electroencephalogram (EEG) features and lack of cognitive/behavioral impairment, highlighting that mandatory ILAE diagnostic features are not always initially present and may evolve over time.

Conclusion: The checklist offers a simple-to-use resource for treating physicians to support LGS diagnosis, using the ILAE criteria as the framework. The findings also highlight the relevance of EEG findings for an LGS diagnosis and the need to re-evaluate patients during follow-up.

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1965 | Assessment of cortical excitability in *SCN1A*-related epilepsies using Transcranial Magnetic Stimulation

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Purpose: Transcranial magnetic stimulation (TMS) coupled with electromyography (TMS-EMG) or electroencephalography (TMS-EEG) enables non-invasive assessment of cortical excitability. Its application in pediatric epilepsies remains limited. We aimed to characterize TMS-EMG/EEG responses in patients with Dravet syndrome (DS) or genetic epilepsy with febrile seizures plus (GEFS+), compared to age-matched healthy controls (HC).

Method: We performed neuronavigated TMS-EEG and TMS-EMG in 6 individuals (age 8–22) with SCN1A-related epilepsy (3 GEFS+, 3 DS) and 6 age-matched HCs. We assessed resting motor threshold (rMT), short-/long-interval intracortical inhibition (SICI, LICI), intracortical facilitation (ICF), and premotor TMS-evoked potentials (TEPs) in peak amplitudes/latencies, Immediate Response Slope (IRS), and Global/Local Mean Field Power (GMFP, LMFP).

Results: *SCN1A* patients showed higher rMT (median±SD M_P=85±25.6) than controls (M_C=49±8, p=0.041), and reduced SICI (M_P=1.13±0.6 vs M_C=0.28±0.6, p=0.039), both for DS and GEFS+ patients. LICI and ICF did not differ. The first two TEP peak latencies were prolonged in patients (1° peak: M_C=24.3±20.4 ms, M_P=66.8±27.4 ms, p=0.036; 2° peak: M_C=46±26 ms, M_P=93.9±108 ms, p=0.015). IRS, a validated measure of cortical excitability, was steeper in controls (M_C=3.1±2.95) than patients (M_P=0.9±1.6, p=0.01). Peak LMFP was higher in controls (M_C=16.2±5.4) than patients (M_P=9.4±3.6, p=0.042), while GMFP showed no group differences. These TEP differences all showed a slower, less complex local response in patients than controls. Stratified analysis revealed larger differences in peak latencies and IRS between HC and DS (M_{DS}=0.6±0.3, M_{GEFS+}=2.1±0.8, M_C=3.1±1.7, p=0.0025), implicating *SCN1A* loss of function, while GMFP peak (M_{DS}=7.6±2.2, M_{GEFS+}=19.9±7.2, M_C=16.9±6, p=0.0025) and average (M_{DS}=3.3±0.9, M_{GEFS+}=6.8±1.8, M_C=6±1.4, p=0.0025), were higher in GEFS+ than DS.

Conclusion: *SCN1A*-related epilepsies showed distinct TMS-EMG and TMS-EEG patterns, advancing current understanding of their electrophysiological phenotyping and possibly reflecting disease-related pathophysiology and potential biomarkers for progression and treatment response.

1968 | Pediatric Autoimmune Encephalitis in Saudi Arabia: A Tertiary Hospital Experience

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Purpose: Autoimmune encephalitis (AE) is a rapidly progressive encephalopathy caused by antibodies targeting cell-surface or intracellular antigens, triggering immune-mediated responses. It is a leading cause of non-infectious encephalitis and is increasingly recognized in the pediatric population, who may present with behavioral changes, psychiatric symptoms, seizures, movement disorders, and autonomic dysfunction. The most commonly reported autoantibodies in children include NMDAR, MOG, and GAD65. Pediatric AE often differs from adult-onset cases in terms of clinical presentation, paraclinical features, therapeutic response, and prognosis. This study retrospectively analyzed 41 pediatric AE cases and utilized the Clinical Assessment Scale in Autoimmune Encephalitis

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(CASE) to assess prognosis, highlighting its utility in evaluating non-motor symptoms in children.

Method: This single-center retrospective study (2010–2025) at King Faisal Hospital reviewed pediatric AE cases meeting updated diagnostic criteria. Autoantibodies were identified using Euroimmun® assays. Data collected included demographics, clinical features, imaging, treatment, and outcomes. Descriptive analysis was performed using SPSS.

Results: In this cohort of 41 pediatric AE patients, the median age at onset was 7 years, with a slight male predominance (53.7%). Most were Saudi nationals (97.5%). Common prodromal symptoms included fever and respiratory infections. Seropositive AE was identified in 61%, and 56.1% received immunotherapy within 45 days. Median hospital stay was 9 days. The CASE/Ped-CASE median score was highest at nadir (7, IQR 5–12), decreased by discharge (5, IQR 2–6), and further declined at follow-up (3, IQR 1–5). At follow-up, 76% of patients had a good outcome (CASE score 1–4), while 24% had a moderate outcome (score 5–9), indicating overall clinical improvement.

Conclusion: The CASE score at disease onset was not associated with neurocognitive outcomes, ongoing seizures, behavioral changes, weakness, or the need for chronic immunotherapy in children with AE at follow-up. However, CASE remains a valuable tool for assessing non-motor symptoms in pediatric AE.

1995 | Focal Seizures in Childhood Onset Stroke Associated with RNf213 and Heterogenous TRL3 Mutations : unique cases of Moyamoya Disease from South of Poland

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Purpose: Moyamoya disease (MMD) is rare vasculopathy with angiographic appearance of bilateral stenoses of the distal internal carotid arteries and proximal Willis circle vessels, with the presence of collaterals. These vascular changes can cause strokes, transient ischemic attacks, and seizures due to impaired brain function. The aim of the study was to present unique cases of MMD with manifestation of focal seizures in acute stage of brain ischemia in children with interesting genotypes.

Method: We described two patients followed in Child Neurology Department with MMD and early onset focal seizures.

Results: Female (uneventful pregnancy and neonatal period) had achieved developmental milestones, when at age of eight months was found with prolonged right side focal seizures and subsequent right side hemiplegia due to left hemisphere infarct. Brain imaging confirmed the narrowing of vessels and collaterals characteristic for MMD. At the age of sixteen months the second stroke with quick clinical an functional resolution was diagnosed. Seizures were not observed . Other vasculopathy was not detected. Due to elevated liver enzymes, acetylsalicylic acid was not administrated. Whole Exome Sequencing WES was performed and identified a de novo RNf213 mutation. Male (uneventful pregnancy) with reported mild hypotonia and psychomotor retardation, gait and speech delay. At the age of four years old was admitted to the Clinic with focal seizures, fever and suspicion of viral encephalitis which was ultimately excluded. The brain imaging, DSA confirmed MMD . Neurosurgical by-pass- STA- MCA/ACA was performed eight months later but the next episodes of stroke and transient ischemic attacks were diagnosed. Additional mild IgA deficiency with heterogenous variant of TRL3 mutation were confirmed.

Conclusion: MMD is a unique reason of seizures and stroke in children. Rare genetic mutations can cause early onset recurrent ischemic attacks due to brain hypoperfusion with severe prognosis.

2000 | To care beyond the screen in the post-pandemic era: insights and suggestions for the use of teleconsultations in the treatment of rare and complex epilepsies.

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Purpose: The pandemic has catalyzed access to telemedicine, forcing us to suddenly change our clinical practice and to quickly adapt the way we communicate with patients and answer to their needs. COVID has passed, but our practice has not returned to what it was before, and an unprecedented transformation continues. It is crucial to understand how these changes are taking place and how we can best adapt the reorganizations of care systems to patient's needs.

Method: This study was conducted at the Reference Center for Rare Epilepsies at Necker-Enfants Malades Hospital in Paris, aiming to analyze the current practice with teleconsultations in the care of patients with complex epilepsies. We reviewed the history of the patients who received at least one teleconsultation in the period 2023-2025, the frequency, timing and reasons for the visits

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Results: We collected a cohort of 464 patients with a total of 946 teleconsultations. Developmental and epileptic encephalopathy was the most frequent epilepsy diagnosis. In 39% of patients a moderate to severe degree of disability was present. The number of teleconsultations per person and ratio of teleconsultations to in-person visits varied. In 22% of cases the teleconsultation was the first visit of the patient at the center. For patients already followed, most of the consultations were due in unstable clinical situations requiring individualized follow-up. We propose a categorization of models of integrated use between teleconsultation and in-person visit that attempt to address the different needs of patients and consider advantages and barriers of both modalities.
Conclusion: In epilepsy care, the use of teleconsultation is being maintained and varies according to the type and complexity of epilepsy. Understanding how to guide clinical practice in this field and how to adapt the multidimensional system of care to the complexity of epilepsy with a tailored use of telemedicine is a new challenge.

2004 | Fever-associated epilepsy: Genetic, clinical, electrophysiological and therapeutic aspects

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Purpose: To describe the genetic, clinical, electrophysiological, and therapeutic aspects of fever-associated epilepsy (FAE) in a case series.
Method: We conducted a retrospective, monocentric, descriptive study from 2009 to 2023, including patients with genetically confirmed FAE. Genetic analysis was performed using Sanger sequencing or whole exome sequencing (WES).
Results: Twelve patients were included. The mean age at onset was 5 months [3–6], with a sex ratio (M/F) of 1. Ten patients had a typical presentation of Dravet syndrome (DS), while the remaining four had Dravet-like phenotypes. All patients exhibited developmental delay and severe neurocognitive impairment, including motor, language, and intellectual deficits. Behavioral disorders were present in six patients, including autism spectrum disorders and attention-deficit/hyperactivity disorder. Seizures were pharmacoresistant (7/12), recurrent (7/12), prolonged (7/12), and polymorphic (11/12). Seizure types included generalized tonic-clonic (12/12), myoclonic (7/12), generalized tonic (3/12), focal (3/12), and atypical absence seizures (3/12). The electroencephalogram was normal during the first year in three cases. Photosensitivity was observed in two patients. Brain imaging showed diffuse cerebral atrophy in two cases. All patients received sodium valproate as first-line therapy. Second-line treatments included levetiracetam (5/12), clobazam (4/12), stiripentol (3/12), and piracetam (2/12). Stiripentol reduced seizure frequency in three cases. Lamotrigine (2/12) and carbamazepine (2/12) were associated with seizure worsening. Seizure stabilization was achieved in four patients. Genetic analysis via Sanger sequencing was performed in ten patients, all of whom had heterozygous de novo mutations in the *SCN1A* gene encoding the alpha-1 subunit of the voltage-gated sodium channel. Eight had point mutations, and two had complete deletions of the *SCN1A* gene. WES identified *PCDH19* mutations in two patients.
Conclusion: FAE represent a heterogeneous group of severe epileptic syndromes, with Dravet syndrome being the most common phenotype. Early genetic diagnosis is essential to guide treatment choices and improve long-term neurodevelopmental outcomes.

2005 | Communication in in SYNGAP1-Related Neurodevelopmental Disorder

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Purpose: *SYNGAP1*-related neurodevelopmental disorder is a rare genetic condition characterized by epilepsy, cognitive impairment, and developmental delay. Communication is key for caregivers of *SYNGAP1*. In this study, we assessed expressive and comprehensive communication in distinct age groups. We also evaluated the impact of Developmental and Epileptic Encephalopathy (DEE).
Method: We evaluated adaptive functioning in 33 individuals (age range: 3–31 years; mean = 11.5, SD = 6.6; median = 10) with pathogenic/likely pathogenic *SYNGAP1* variants using the Communication subdomain of Vineland Adaptive Behavior Scales – Third Edition (VABS-3). Raw scores from communication were analyzed.

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We examined bivariate associations between age and subdomain scores using Pearson correlation and conducted multiple linear regression models adjusting for DEE status (present vs absent) to estimate age-related effects independent of clinical severity.

Results: Participants with DEE (n = 18) had significantly lower scores than those without DEE (n = 15) in Receptive Communication ($p = 0.008$), Expressive Communication ($p = 0.027$), and Domestic Living Skills ($p = 0.013$). In regression models adjusted for DEE, age remained significantly associated with gains in Expressive Communication ($\beta = 0.78$, 95% CI: 0.15 to 1.41, $p = 0.017$). A trend was noted for Receptive Communication ($\beta = 0.65$, $p = 0.055$).

Conclusion: Individuals with *SYNGAP1*-related disorder show broad functional impairments, particularly those with DEE. Adaptive gains in communication domains persist with age, even after adjusting for clinical severity.

2008 | Acute Encephalopathy with Biphasic Seizures and Late Reduced Diffusion - Case Series and Clinical Consideration

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Purpose: Acute encephalopathy with biphasic seizures and late reduced diffusion (AESD) is characterized by prolonged febrile seizures with no abnormalities on brain MRI at the first manifestation, followed by secondary seizures after a few days. It is distinguished by a distinctive reduced diffusion pattern in the subcortical white matter on MRI. AESD is known to be the most common form of acute encephalopathy in Japan but is rarely reported in Korea. In this study, we present four pediatric cases of AESD diagnosed based on clinic-radiological features.

Method: We recruited and analyzed pediatric patients who met the criteria for AESD diagnosis through a retrospective chart review. Clinical information was collected, including treatment course, outcomes, and serial brain MRI findings.

Results: This study included four patients (three girls and one boy aged 19 to 36 months) diagnosed with AESD. All patients initially presented with prolonged febrile seizures. The seizure semiology was generalized tonic-clonic seizures, and all the patients regained consciousness within two days. The secondary seizure occurred three to five days later. The secondary seizures were either generalized tonic-clonic or clusters of focal clonic seizures. Initial MRIs were performed for three patients two days after the onset, showing no abnormal findings initially but later revealing diffusion restriction in bilateral subcortical white matter. One patient, who underwent a relatively late initial brain MRI (4 days after onset), showed diffusion restriction. The last follow-up MRIs of all patients showed diffuse atrophy. Although slowly improving with rehabilitation, all patients experienced severe neurological impairment.

Conclusion: In this report, we present a case series of AESD in the Korean pediatric population. AESD can be easily overlooked since initial neuroimaging frequently appears normal. However, early recognition is important as most patients suffer permanent neurological sequelae.

2015 | KCNQ2-Related Developmental and Epileptic Encephalopathies: A Clinical Case Series and Genotype-Phenotype correlations

A Kalfat[1], Z Miladi[1], M Essid[2], A Zioudi[1], M Jamoussi[1], T Ben Younes[1], M Ben Hafsa[1], H Ben Rhouma[1], H Klaa[1], B Tabarki[3], L Ben Jemaa[4], I Kraoua[1]

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Purpose: To describe the clinical, electroencephalographic, neuroimaging, and genetic characteristics of patients with KCNQ2-related developmental and epileptic encephalopathies (DEE), and to investigate genotype-phenotype correlations.

Method: A retrospective descriptive study was conducted at the pediatric neurology department of National Institute of Neurology in Tunis between 2012 and 2023. Patients presenting with DEE, carrying pathogenic KCNQ2 variants were included. Clinical features, Electroencephalogram (EEG), and genetic data were reviewed.

Results: Our cohort comprised five pediatric patients (three males and two females), including two siblings. All patients presented with neonatal-onset seizures, with a mean age at onset of 9,5 days [1 ; 30 days]. Seizure types included generalized tonic seizures (n=4), focal tonic seizures (n=3), eye globe revulsion (n=2), cyanosis during seizures (n=2), audiogenic myoclonias, spasms (n=2), eyelid clonic movements (n=2), and facial clonic seizures

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(n=1). Triggering factors included fever, noise, heat, and teething (n=3). All cases were drug-resistant. Interictal EEG showed suppression-burst pattern in one patient, multifocal epileptiform discharges (n=2), and focal slowing or paroxysmal abnormalities (n=1). Brain Magnetic Resonance imaging (MRI) was normal in three patients, and showed cerebral (n=1) or callosal (n=2) atrophy. Clinically, one patient had autism spectrum disorder features, and all patients had global developmental delay with motor, language, and visual contact deficits. Neurological examination revealed axial hypotonia (n=4), pyramidal syndrome (n=3), and generalized dystonia (n=2). One male patient died at age one following severe feeding difficulties. Electroclinical syndromes included Early Infantile Epileptic Encephalopathy (EIEE) (n=2) and DEE (n=3). All patients carried missense KCNQ2 variants located in functional domains. Two siblings shared the same homozygous variant (p.Lys331Thr).

Conclusion: KCNQ2-related disorders range from self-limited neonatal epilepsy to severe developmental and epileptic encephalopathies, characterized by early-onset seizures and variable neurodevelopmental impairment. Dominant-negative variants and biallelic inheritance may be linked to more profound impairment. Genetic testing and functional interpretation are essential for diagnosis, prognosis, and guidance.

2034 | Clinical Spectrum of PURA-Related Neurodevelopmental Disorder: A Report of Two Pediatric Cases

A Kalfat[1], Z Miladi[1], M Essid[2], A Zioudi[1], M Jamoussi[1], T Ben Younes[1], M Ben Hafsa[1], H Ben Rhouma[1], H Klaa[1], B Tabarki[3], L Ben Jemaa[4], I Kraoua[1]

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Purpose: The Purine-rich element-binding protein (*PURA)* gene encodes a nucleic acid-binding protein essential for neuronal proliferation, differentiation, and synaptic plasticity, Pur-α. Pathogenic variants in *PURA* cause a heterogeneous neurodevelopmental syndrome characterized by moderate to severe intellectual disability, axial hypotonia, movement disorders, epilepsy, dysmorphic features, and structural brain abnormalities. We aim to describe the phenotypic spectrum of PURA syndrome through two pediatric cases, highlighting its variability from early-onset epileptic encephalopathy to non-epileptic developmental and behavioral manifestations.

Method: Our study included two patients with pathogenic variants in the *PURA* gene, followed in the pediatric neurology department of National Institute of Neurology in Tunis between 2021 and 2023. Clinical data included developmental milestones, seizure history, neurological examination, Electroencephalogram (EEG), brain Magnetic Resonance Imaging (MRI), and genetic findings.

Results: Our study included two female patients. The first patient presented with neonatal hypotonia and seizures from day 1 of life. Seizures were generalized tonic, occurring daily, and pharmacoresistant. EEG showed background slowing with frontotemporal discharges. She exhibited spastic tetraparesis, nystagmus, scoliosis, and craniofacial dysmorphism. Brain MRI revealed corpus callosum atrophy and scaphocephaly, and spectroscopy showed increased choline and decreased N-acetylaspartate (NAA). The second patient, aged 2.5 years, had no epilepsy but presented with global developmental delay, hypotonia, and autism spectrum features. EEG, Electroneuromyogram (ENMG) with repetitive stimulations and MRI were normal. Treatment with pyridostigmine was initiated, without any clinical improvement.

Conclusion: Our cases illustrate the broad phenotypic variability of PURA syndrome, ranging from epileptic encephalopathy with structural brain involvement to isolated developmental and autistic features without seizures. In the absence of specific treatments, early genetic diagnosis is essential to guide multidisciplinary care and prognosis.

2041 | Genetic investigation in children with epilepsy, movement disorders and developmental delay

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Purpose: Epilepsy, motor disfunction and developmental delay the most common features in children with different genetic diseases, progressive or non-progressive, included DEEs. Clinical testing with comprehensive gene panels,

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exomes, or genomes, chromosomal microarray analysis are now increasingly available and have led to a significant higher diagnostic yield and enabled precision medicine approaches. The purpose of study was to identify the spectrum of possible genetic etiology in children with epilepsy, mental and movement disorders hospitalized or received ambulatory consultation in our Neurological Department.
Method: A total of 100 patients aged 2 months to 16 years were enrolled. The long duration EEG, high resolution MRI, genetic testing (chromosomal microarray analysis, exome and genome sequencing) were performed to these children.
Results: Most of patients have genes mutation commonly find in DEEs: eight with SCN1A mutation, six - CDKL5, two GRIN2A, two patients with ALG13 gene mutation, two - SCN8A, two KCNQ2, two STXBP1, two CACNA1, PRRT2, CLCN2, SYNGAP, SCN3A,SCN2A, GNAO1 GABR,CHD2,ACO2,ATP1A2, ATP1A3, HCN1,DLL1,also SLC2A,SLC4A1. Others had mutation in genes ASPM (microcephaly) and MRD5 (mental retardation AD5) with epilepsy, WDR62, PAFAH1B, LICAM with structural cerebral pathology, in BRAF and NFM gene. Metabolic etiology where found in patients with such diseases: Gaucher type 3, ceroid lipofuscinosis type 8, Niemann-Pic type C 2, non-ketonic hyperglycemia, mitochondrial diseases-mutation in gene NDUFS1, Leigh disease, Barth disease; PMM2-CDG, HEX, TAZ, rare organic acidurias(such as mevalonic-MVK gene mutation), urea cycle disorders, Krabbe diseases, Rett syndrome, Angelman syndrome. Some of patients with drug-resistant epilepsy and movement and mental disorders had microduplication or microdeletion syndromes.
Conclusion: The recognition and diagnostic of underlying the etiologies of children with epilepsy, movement and mental disorders improve the treatment management in many cases. Founded etiology allow us to use the most effective treatment which now available and of the emerging therapeutic approaches and potentially provide new molecular-investigated treatments

2046 | Unmasking the Genetic Underpinnings of Myoclonic-Atonic Epilepsy: A Case of 2q37.3 Microdeletion in a 12-Year-Old

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Purpose: To describe the clinical features, diagnostic evaluation, and management of a 12-year-old patient with 2q37.3 microdeletion syndrome presenting with myoclonic-atonic epilepsy and developmental delay
Method: We report M.C.S., a 12-year-old male, only child of non-consanguineous parents, who presented with early hypotonia and delayed motor milestones (walking at 2 years). Epileptic seizures began at age 4 with generalized tonic-clonic seizures, followed by myoclonic-atonic seizures at age 5. Phenotypic features included hypertelorism, flat nasal bridge, thin upper lip, smooth philtrum, and hallux separation. Neurocognitive evaluation revealed moderate intellectual disability, illiteracy, and impaired color and number recognition. Multiple antiseizure medications were trialed (phenobarbital, valproic acid, clonazepam, carbamazepine, lamotrigine, phenytoin, clobazam) with partial control and adverse effects (somnolence, cognitive worsening, ataxia). Serial EEGs showed generalized epileptiform discharges, polyspike-and-wave complexes (2-3 Hz), and focal epileptiform activity in the frontal midline. Video-EEG monitoring documented myoclonic-astatic seizures and absence seizures, consistent with Doose-like epilepsy. Brain MRI and CT were unremarkable. Genetic testing identified microdeletion at 2q37.3, consistent with 2q37 deletion syndrome. The patient currently attends school with maternal support but remains non-literate and requires assistance with most daily activities
Results: Not applicable (case report)
Conclusion: 2q37.3 microdeletion syndrome may mimic Doose-like epilepsy, with severe neurodevelopmental impairment and dysmorphic features. Genetic testing plays a critical role in diagnosis and individualized care for complex pediatric epilepsy

2047 | From Speech Delay to Genetic Diagnosis: The Journey to CLN

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Purpose: CLN6 typically presents between 3–5 years with regression, seizures, and visual/motor decline. Initial symptoms may resemble ASD, delaying diagnosis. In this case, neuroimaging and EEG findings were crucial for suspicion, and genetic testing confirmed the diagnosis. Although incurable, symptom management and genetic counseling are essential.
Method: A 4-year and 3-month-old male, first child of a non-consanguineous couple, was initially under investigation for autism spectrum disorder (ASD) due to speech delay and intellectual disability. No prior comorbidities or

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motor symptoms had been noted. In late 2024, he began experiencing episodes of loss of consciousness, choreiform hand movements, and sialorrhea. Levetiracetam (48 mg/kg/day) was initiated. Over time, he showed neuropsychomotor regression, speech deterioration, and unstable gait. CT and EEG performed in primary care were unremarkable. At a specialized neurology center, he presented with ataxic gait requiring assistance, convergent strabismus, irritability, and spoke only isolated words. He had 5–6 daily seizures, described as brief atonic episodes. Hospitalization was undertaken for diagnostic clarification. EEG showed diffuse background slowing with multifocal epileptiform discharges and generalized slow wave bursts (2–5 Hz), especially after arousal. MRI revealed bilateral, symmetrical T2/FLAIR hyperintensities in posterior periventricular white matter, including peritrigonal regions, centrum semiovale, optic radiations, corpus callosum, and insular areas. Fundoscopy was normal. Genetic testing identified biallelic pathogenic variants in CLN6, confirming neuronal ceroid lipofuscinosis type 6 (CLN6). Seizure frequency improved after increasing levetiracetam to 60 mg/kg/day.

Results: CLN6 is a rare childhood-onset neurodegenerative disease, often beginning with developmental delay and seizures. This case report illustrates the early-life presentation and its diagnostic challenge.

Conclusion: CLN6 should be considered in young children with developmental regression and epilepsy. Early neuroimaging and genetic evaluation are key for timely diagnosis and care.

2051 | KCNQ2 encephalopathy in two children

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Purpose: Seizures are the most common clinical manifestation of central nervous system dysfunction in neonates. In addition to hypoxic-ischemic encephalopathy, intracranial hemorrhage and infection, genetic factors play a key role in the occurrence of neonatal seizures and epileptic encephalopathy in young children. Some genes, for example KCNQ2, a potassium channel subunit located at 20q11.3, can be associated with a wide range of epilepsy syndromes ranging from self-limited familial neonatal epilepsy to developmental and epileptic encephalopathy(DEE).

Method: Demonstration of the different clinical presentations in two children with KCNQ2 mutation.

Results: Girl 3 years of ages at this time, from 2 pregnancy, physiological birth delivery, Apgar 8/9, presented with rare tonic seizures from 3 days of life. No epileptiform discharges on EEG. In one week she presented the epileptic spasms. The spike-wave activity on EEG appeared only during the seizures clusters. Seizures resolved within 3 months. MRI without structural abnormalities. The genetic investigation revealed the mutation in KCNQ2 gene (de novo). Neurological status: mental delay, autistic behavior, muscle hypotonia, motor delay (can sit only with support). EEG rare epileptiform discharges. Boy 15 years of ages at this time, from 2 pregnancy, physiological birth delivery, Apgar 8/9, presented the apnea at the 3 days of life. Ultrasound revealed the small intraventricular hemorrhage. Seizures were frequent, tonic focal to bilateral. EEG-«burst-supression» phenomena. Epilepsy resolved only at 7 years of ages. Neurological status: mental delay, autistic behavior, spastic muscle tone, severe motor delay (even can't hold his head up). EEG - regional epileptiform activity. MRI shows mild brain atrophy. Genetic investigation was made now and the mutation in KCNQ2 gene was found.

Conclusion: KCNQ2-DEE characterized by varying degrees of expressivity of the mutant gene with phenotypic diversity even with the same mutations. The study of the KCNQ2 –DEE7 may improve the identification of KCNQ2-associated seizures

Psychiatry

1952 | Exploring behavioral and psychiatric comorbidities in Dravet Syndrome: is there a multifactorial basis?

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Purpose: Dravet Syndrome (DS) is a developmental and epileptic encephalopathy with onset during the first year of life, mainly caused by loss-of-function mutations in the *SCN1A* gene. It is characterized by drug-resistant seizures, intellectual disability, motor and sleep disorders, ADHD, autistic traits, and behavioral disturbances. While behavioral aspects in DS have been increasingly explored, the onset of psychiatric symptoms, particularly psychotic features, remains poorly studied. This study aims to investigate behavioral traits in adolescents and adults with DS that may predispose them to psychiatric vulnerability.
Method: We conducted a retrospective analysis of behavioral and adaptive features in a cohort of patients with genetically confirmed DS, aged 14–44 years, followed at our epilepsy center in Verona and included in the International Registry of Dravet Syndrome (RESIDRAS). Behavioral profiles were assessed through clinical history and the Child Behavior Checklist (CBCL) while adaptive features were assessed by Vineland Adaptive Behavior scales-II (VABS-II).
Results: A total of 47 patients were included (28 males, 19 females). Intellectual disability was severe in 41 patients, moderate in 4, and mild in 2. CBCL data were available for 31 patients. More than half of our sample showed internalizing or externalizing clinical or subclinical values at CBCL; 45.16% of the patients with CBCL presented Deficient Emotional Self-Regulation (DESR). 11% of the total sample (5 patients) required antipsychotic medication for behavioral problems, while 8.5% (4 patients) required antipsychotics for an acute or subacute psychotic episode during adolescence or early adulthood. VABS data were available for 37 patients showing highly impaired adaptive functions.
Conclusion: Based on current literature and our findings, the development of psychiatric disorders in adolescents and adults with Dravet Syndrome appears to be driven by multiple factors that interact over the course of neurodevelopment.

Social Issues

1889 | Transition from pediatric healthcare to adult healthcare for young people with epilepsy in the UK: A scoping review

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Purpose: The aim was to identify and synthesize published research on transition from pediatric to adult healthcare for Young People with Epilepsy (YPE) in the UK.
Method: We undertook a systematic search of studies published in peer-reviewed journals and conference abstracts. We also conducted online searches to identify epilepsy transition resources available from the National Health Service (NHS) and charities. Resources were rated for quality with a bespoke checklist.
Results: We identified 12 peer-reviewed studies, 13 conference abstracts and 2 dissertations. Included were 22 observational studies, 3 interventional studies and 2 studies that combined designs. Lack of continuity of care from pediatric to adult services was a common concern across studies. Five studies explored the impact of transition on parents, noting how they are often anxious about transition and can struggle 'to let go'. Parents also feel that their own knowledge of their child's condition reduces after transition, whilst there is a knowledge gap that emerges in adult healthcare providers. Three studies noted how YPE's psychological wellbeing deteriorates during the process as support lessens. Two studies, focusing on rare conditions, highlighted that experiences of transition were negative. Only 16/218 (7%) of NHS providers had epilepsy transition resources available. Quality of resources varied, but some examples of good practice were identified. NHS resources focused on logistics of transition and the stakeholders involved, whilst charity resources focused on the interests and skill development of the YPE. Resources neglected SUDEP, peer group support and empowering the YPE in managing their condition.
Conclusion: Lack of continuity in the healthcare system results in poor experiences of the transition process. Few NHS providers have epilepsy specific resources, and quality of existing materials is inconsistent. More studies are needed to understand the key components of effective transition. Epilepsy transition resources would benefit from co-creation with YPE and caregivers.

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1946 | An investigation into the health-related quality of life (HRQOL) of primary caregivers of children with epilepsy in the UK

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Purpose: The primary aim of this study was to describe both the mental and physical health-related quality of life (HRQOL) of caregivers of Children with Epilepsy (CWE) in the UK. A secondary aim was to explore which child-related, epilepsy-related and caregiver psychosocial variables predict these types of HRQOL.
Method: Caregivers of CWE in the UK were recruited primarily using social media and completed the following measures: SF-36v2™ (a measure of HRQOL), Insomnia Severity Index (ISI), Multidimensional Scale of Perceived Social Support (MSPSS), Brief- Coping Orientation to Problems Experienced (COPE), Depression, Anxiety and Stress Scale - 21 Items (DASS-21) and the Brief Resilience Scale (BRS). Caregivers also provided clinical and demographic data. Predictors of mental component scores (MCS) and physical component scores (PCS) on the SF-36 were identified using hierarchical linear regression models.
Results: One hundred and twenty-seven caregivers (female 124) participated. Many caregivers reported high levels of sleep difficulties (73%), stress (68%), depression (67%) and anxiety (61%) on standardized measures. The mean PCS was 50.8 and thus in line with population norms (mean 50), but and MCS was 32.9 and well below population norms. Having more sleep difficulties ($p < 0.001$), lower resilience ($p < 0.001$), and a child with a lower Quality of Life ($p < 0.001$) were associated with worse MCS. Having lower perceived social support ($p = 0.042$), a child with Autism ($p = 0.004$) and a child with younger age at seizure onset ($p = 0.003$) were associated with better PCS.
Conclusion: Having a child with epilepsy negatively impacts mental health-related HRQOL, but not physical health-related quality of life. Factors associated with lower mental health-related HRQOÖL include sleep difficulties and lower levels of resilience and thus these should be targeted in efforts to improve mental health aspects of heath HRQOL for caregivers of CWE.

1954 | A Global Perspective on Transitioning from Pediatric to Adult Care in Epilepsy

Q Zulfiqar Ali[1], D Andrade[2], N Jette[3], I Chandran[1], P Patel[4], G Rubboli[5], JH Cross[6], D Craiu[7], CT Tan[8], E Kija[9], E Fung[10], T Granata[11], H Hosny[12], M Mula[13], K Riney[14], R Shellhaas[15], M Siddiqui[16], J Hebert[1], P Marques[17], B Kerrigan[1], C Ji[1], K Valente[18], J Carrizosa[19], R Nabbout[20]
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Purpose: Each year, around 1.1 million young people with epilepsy transition from pediatric to adult healthcare systems. This shift is often a one-time, age-based transfer, which can disrupt care and create uncertainty for patients. In contrast, a true transition is a planned, holistic process addressing medical, psychosocial, and vocational needs. To explore global challenges and opportunities in this area, the ILAE formed the Transition in Care Taskforce (TTF), bringing together pediatric and adult neurologists.
Method: The TTF used a previously validated 50-item survey covering six domains: availability of transition programs, current practices, impact of comorbidities/ treatments on transition age, education gaps, barriers, and improvement strategies. The survey, translated into eight languages was distributed globally. Data were analyzed using Fisher's Exact Test and multivariate logistic regression, with countries grouped as Global North (GN) or Global South (GS) based on 2025 World Population Review.

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Results: A total of 316 providers from 57 countries responded, 54% were adult neurologists and 78% practiced in high-income countries. Notably, 59% reported no formal epilepsy transition program in their country. Respondents from the GS were significantly less familiar with transition strategies. Common barriers included lack of multidisciplinary teams, adapted clinics, funding, training, and adult providers experienced in childhood-onset epilepsies. Key recommendations included integrating transition into neurology training, establishing dedicated services, joint pediatric-adult consultations, and national transition guidelines—the latter receiving the strongest support.

Conclusion: This global survey highlights widespread recognition of the need for structured transition care in epilepsy. However, regional disparities, limited resources, and fragmented provider roles hinder effective implementation. Addressing these challenges through education, infrastructure, and policy is essential to improve continuity of care and outcomes for youth with epilepsy.

Status Epilepticus

1923 | Sex-Specific Temporal Proteomic Signatures in the Juvenile Rat Hippocampus After Pilocarpine-Induced Status Epilepticus

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Purpose: Early-life seizures can lead to long-term neurodevelopmental impairments and chronic epileptogenesis. This study aimed to identify temporal and sex-specific proteomic alterations in the hippocampus following pilocarpine-induced status epilepticus (SE) in juvenile rats, to uncover shared injury signatures and divergent repair mechanisms that may inform sex-specific therapeutic approaches.

Method: Twelve-day-old male and female Wistar rats received lithium-pilocarpine to induce SE or saline. Hippocampal tissue was collected at five post-SE time points (6 h, 24 h, 3 d, 7 d, and three months; n = 6 per group). Proteins were extracted via filter-assisted sample preparation and analyzed using high-resolution data-independent acquisition mass spectrometry (DIA-MS). Data processing was performed with DIA-NN and quantification with MaxLFQ. Differential protein expression was assessed using moderated t-tests (LIMMA) with Benjamini-Hochberg correction (FDR <0.01). Dysregulated proteins were annotated via Gene Ontology and analyzed through time-series clustering to differentiate acute injury responses from long-term remodeling.

Results: Pattern of changes depended on the interval after SE and sex. A core injury response, marked by upregulation of immediate-early genes (Fos, Fosb), stress-related proteins (Serpinb2, Cryab), and signaling receptors (Gprc5a), was evident within 6–24 h and 3 days post-SE in both sexes. By day 3, cytoprotective chaperones (Hspb1) and lipid-metabolic enzymes (Aspg) were predominant. At 7 days, females exhibited enrichment in adhesion and DNA repair proteins (Megf11, Wrn), while males showed increased levels of cytoskeletal and chromatin remodeling proteins (Sprr1a, Chd6). At 3 months, females-maintained alterations in transporters and metabolic regulators (Fez2, Clcn5), whereas males showed upregulation of transcriptional repressors and epigenetic regulators (Rcor2, Med29).Sex-divergent repair courses emerged: females engaged in complement-mediated synaptic pruning, while males favored axonal outgrowth and chromatin reprogramming.

Conclusion: This sex-stratified proteomic analysis reveals a conserved acute hippocampal response alongside divergent long-term adaptation patterns. These findings provide a molecular framework for time- and sex-specific prevention of epileptogenesis.

1942 | A case of FIRES with MOG antibody and leukodystrophy like MRI brain changes

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Purpose: We expand the phenotype of febrile infection related status epilepticus (FIRES) by describing the clinical course of an infant with FIRES and diffuse MRI brain changes.

Method: Case presentation

Results: A previously healthy 17 month Malay boy presented with 3 days of fever, mouth ulcers and lethargy, focal motor seizure and persistent drowsiness. He presented in status epilepticus requiring lorazepam, phenobarbitone, levetiracetam, midazolam infusion and thiopentone. MRI on Day 1 was remarkable for extensive bilateral patchy

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T2 weighted and FLAIR hyperintensities with restricted diffusion involving the subcortical and deep white matter extending to the cortices, without significant contrast enhancement, MRS peaks nor hemorrhage. EEG showed a diffuse slowing and frequent electroclinical seizures and status epilepticus. CSF results were: WBC 2 RBC 0, CSF protein 0.16, CSF glucose 3.8, CSF Lactate 1, CSF NMDA antibodies negative, CSF oligoclonal bands negative. All infective screening and metabolic investigations were negative. Genetic test results are pending. Serum MOG antibody on fixed cell-based assay was low positive at 1:10 dilution, negative at 1:100. The patient was treated with antimicrobials, IVIG and IV methylprednisolone. He continued to have refractory electroclinical seizures requiring IV midazolam, levetiracetam, phenobarbitone, perampanel and thiopentone infusion. He achieved burst suppression coma but seizures recurred on weaning thiopentone and the ketogenic diet was commenced. Anakinra was commenced on week 2 which was switched to tocilizumab on week 4.

Conclusion: This infant presented acutely with supra refractory status epilepticus and diffuse leukodystrophy like MRI changes and was identified to have low MOG antibody positivity. These MRI changes have been similarly seen in MOG inflammatory leukoencephalopathy affecting the susceptible young and myelinating brain. This case expands the clinical phenotype of FIRES and illustrates the overlap between FIRES, neuroinflammation and autoimmunity. Extensive immune work up and immunotherapy should be considered in these patients.

1989 | Disentangling the Concept of High-Risk Isolated Seizures in the Emergency Department

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Purpose: Epileptic seizures are a common cause of emergency department (ED) visits. A subset, has a greater likelihood of recurrence during the ED stay, potentially evolving into seizure cluster or status epilepticus, which we will refer to as high-risk isolated epileptic seizures. Early identification of clinical, paraclinical, or contextual risk factors associated with recurrence can optimize treatment decisions and prevent complications.

Method: We conducted a retrospective evaluation of all patients with isolated seizures admitted under the "Seizure Code" protocol between 2023 and 2024 at a public Hospital in Bogotá, Colombia. We assessed in-hospital recurrence rate, time to recurrence, clinical context of recurrence, and hospital outcomes, comparing patients with and without recurrence. A bivariate analysis was performed to identify potential associations between clinical variables and early recurrence risk.

Results: A total of 942 patients with isolated seizures were included. In-hospital recurrence occurred in 4.9% (n=44), with a median time to recurrence of 8 hours (IQR: 3–15). Among these, 90.9% (n=40) progressed to seizure cluster and 9.1% (n=4) to status epilepticus. Variables associated with recurrence included focal epilepsy (p=0.0014, OR: 3.62), epilepsy duration >20 years (p=0.0125, OR: 2.92), elevated blood urea nitrogen (p=0.0019, OR: 15.2), seizures due to CNS infection (p=0.0005, OR: 13.9), and malacic lesions on neuroimaging (p=0.0095, OR: 4.73). Patients with early recurrence had longer hospital stays (median: 51h vs. 23h; p<0.001) and higher ICU admission rates (9.1% vs. 1.1%; p<0.001).

Conclusion: This study provides insights into the concept of High-Risk Isolated Seizures. Early in-hospital seizure recurrence, though infrequent, significantly impacts prognosis. Several identifiable risk factors are associated with recurrence and may serve as early warning signs. Stratifying isolated seizure patients by recurrence risk may help guide acute care decisions, improve outcomes, and optimize resource use in emergency settings.

1990 | Cost-Effectiveness of a Seizure Code Protocol in the Emergency Department: A Real-World Economic Analysis

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Purpose: In patients with emergency seizure disorders (including status epilepticus, seizure clusters, and high-risk isolated seizures), timely treatment is one of the most relevant prognostic factors. The "Seizure Code" strategy has proven effective in reducing treatment times (for both benzodiazepines and antiseizure medications), hospital stay, in-hospital seizure recurrence, and mortality. This study aimed to evaluate the cost-benefit impact of implementing the Seizure Code in a tertiary care hospital in Bogotá, Colombia.

Method: We conducted a retrospective cost-benefit economic evaluation following CHEERS guidelines. Adult patients admitted to the emergency room with epileptic seizures between 2022 and 2023 were included, comparing

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those treated before and after Seizure Code implementation. Clinical, economic, and logistical variables were analyzed. Incremental cost-effectiveness ratios (ICERs) were calculated based on direct costs and clinical outcomes. Cost estimates were derived from Colombia's official drug price information system (SISMED) and the mandatory traffic accident insurance tariff manual (SOAT) corresponding to the study years.

Results: 336 patients were included (94 pre-code, 242 post-code). Post-code patients had significantly shorter treatment times (mean: 3.8h vs. 124.6h; p<0.001), lower seizure recurrence (6.6% vs. 22.3%; p=0.0008), and shorter hospital stays (median: 2 days; p=0.019). Although average overall cost per patient was similar (p=0.355), hospitalization (p=0.021) and medication (p=0.003) costs were lower. ICER analysis showed savings per patient in hospital stay (-$249.5 USD), seizure recurrence (-$415.6 USD), and 30- and 90-day readmissions (-$2,105.13 and -$4,661.37 USD, respectively). Sensitivity analyses confirmed robustness, with the strategy remaining cost-effective under ±10% cost and ±20% effect variation. Monte Carlo simulations and cost-effectiveness acceptability curves further supported a >90% probability of cost-effectiveness across thresholds.

Conclusion: The Seizure Code strategy improves clinical outcomes and reduces key costs related to hospitalization, seizure recurrence, and readmissions. It is a cost-effective intervention for managing emergency epileptic seizures in high-complexity settings.

2003 | Video Streaming or Telephone Communication During Emergency Medical Calls in Patients Who Present with Seizures - a Cluster Randomized Clinical Trial

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Purpose: Video streaming during emergency medical calls may enhance triage precision and optimize resource allocation. However, its clinical safety and effect on key outcomes in persons with seizures remain unexplored in randomized trials. We assessed whether video streaming versus telephone communication during emergency calls reduces the highest-urgency ambulance dispatches and conveyance to hospitals.

Method: This cluster-randomized clinical trial was conducted over from January–April 2023 at a single emergency medical dispatch center in Central-Denmark-Region, Denmark. Matched pairs of dispatchers were randomized to manage calls using either telephone-only communication (control) or video streaming (intervention), analyzed by intention-to-treat. The primary outcome was the proportion of ambulances dispatched at the highest urgency level. Secondary outcomes included non-conveyance to hospitals.

Results: In the entire cohort of 18,745 calls, 978 calls (5.2%) with seizure events were included, of whom 560 (57.2%) were managed in the telephone-only group (control group) and 418 (42.7%) in the video streaming group (intervention group). In the video streaming group, video streaming was established in 275 calls (65.8%) and video streaming was attempted but eventually failed in 66 additional calls (15.8%). In the intention to treat analysis, the number of highest-urgency ambulance dispatches was 339 (60.5%) in the telephone-only (control) group and 247 (59.1%) in the video streaming (intervention) group (difference -1.4% (95% CI: -7.7 to 4.8; P=0.649)).

In the intention to treat analysis, the number of non-conveyances was 36 (6.4%) in the telephone-only (control) group and 47 (11.2%) in the video streaming (intervention) group (difference 4.8% (95% CI: 1.2 to 8.5, P=0.010)).

Conclusion: In this cluster randomized clinical trial, video streaming did not reduce the frequency of the highest-urgency ambulance dispatches but significantly decreased the number of non-conveyances to hospital. These findings suggest that video streaming may improve triage accuracy in persons presenting with seizures in the prehospital setting.

2019 | Serum biomarkers of neuro-axonal and glial damage in epileptic seizures and Status Epilepticus: interim results from an ongoing prospective multicentric study.

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Purpose: To investigate the kinetics of selected serum biomarkers of neuro-axonal and glial damage in epileptic seizures and Status Epilepticus (SE).
Method: Adult patients with a single epileptic seizure or SE were recruited in Salzburg and Bolzano between 01/12/2021 and 28/02/2025. Patients with any known condition potentially increasing biomarkers levels within the previous 5 months were excluded. Serum levels of neurofilament light chain (NfL), glial fibrillary acidic protein (GFAP), tau protein, ubiquitin-carboxy-terminal-hydrolase-L1 (UCH-L1), lactate, and neuron-specific enolase (NSE) were measured using an ultra-sensitive single-molecule array at fixed timepoints: baseline, 10 minutes, 30 minutes, 1 hour, 3 hours, 6 hours, 24 hours, 48 hours, and 7 days after onset. Biomarkers trends were analyzed using mixed-effects and polynomial models. Group differences were assessed with Mann-Whitney U tests; correlations used Spearman's coefficients. Significance was set at $p<0.05$.
Results: Forty-two patients were included (15 seizures, 27 SE; mean age 52±20 years) with an average of 4 timepoints per patient. NfL, tau, and UCH-L1 levels were significantly higher in SE than seizures, especially at 3 hours (p=0.003, p=0.003, and p=0.01, respectively). Peak and nadir NfL values were higher in SE than in seizures (mean 29.55 vs 15.14 pg/ml, p=0.015; 21.44 vs 8.16 pg/ml, p=0.004). Over time, NfL showed a monophasic increase (0.001 pg/ml/min, p=0.001; estimated peak at 97 hours). Lactate exhibited a biphasic pattern, with early peaks in both groups (p=0.009 and p=0.002) followed by decline, and a trend toward correlation with SE duration (p=0.08).
Conclusion: NfL, UCH-L1, and tau may reflect the extent of neuro-axonal injury in seizures and SE, even at early timepoints. NfL and lactate also suggest dynamic temporal profiles. These findings are of significant scientific interest, as they provide a characterization of biomarkers temporal kinetics in this clinical context and represent a critical step toward time-sensitive biomarker-driven precision medicine in acute epileptology.

2021 | Etiology and Outcomes of Status Epilepticus: A Lithuanian Perspective

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Purpose: Status epilepticus (SE) is an acute neurological emergency associated with significant mortality, influenced by a range of factors. This study aimed to assess demographic, etiological, and clinical characteristics of SE cases and their association with clinical outcomes.
Method: Data from adults (≥18 years) treated for SE between 2005 and 2024 at Vilnius University Hospital Santaros Klinikos and Vilnius Republican University Hospital were analyzed. Statistical tests included Kolmogorov–Smirnov, Mann–Whitney U, Chi-square, Fisher and Fisher-Freeman-Halton exact tests, as well as univariable and multivariable stepwise logistic regression. Statistical significance was set at $p<0.05$. Statistical analysis was performed using Microsoft Excel 2016 and IBM SPSS v27.
Results: 652 SE cases were included, of which 59.2% were male (median age (interquartile range (IQR)): 60 years (70.0–43.0)). 80.3% had prominent motor phenomena and 40.3% were generalized.
The cumulative annual SE incidence in Vilnius City was 10.5 per 100,000 adults (95% confidence interval (CI): 9.6; 11.2). Case fatality rate was 13.8%.
Etiology of SE was 45.7% acute, 9.7% progressive, 4,1% remote and 8.9% unknown. Predominant SE was alcohol-related (19.7%) and caused by cerebrovascular diseases (12.7%), 43.9% of patients had history of epilepsy. Independent factors (($X^2(6)=78.1$, $p<0.001$, *Nagelkerke* $R^2=0.494$), associated with higher odds of death (OR, [95% CI]): older age (1.06 [1.02; 1.10], p=0.003), longer stay in the intensive care unit (ICU) (1.03 [1.02; 1.05], $p<0.001$), structural SE etiology (5.34 [1.88; 15.17], p=0.002), longer SE duration (1.03 [1.01; 1.06], p=0.019), generalized (5.05 [1.47; 17.38], p=0.010) and super-refractory SE (12.25 [2.4; 62.12], p=0.002).
Conclusion: Incidence of SE in Vilnius City is 10.5 per 100,000 adults. Most SE is caused by acute and alcohol-related causes. Although most survive, independent predictors of mortality were older age, longer ICU stay, structural, prolonged, generalized, and super-refractory SE.

2030 | Centromedian Thalamic Nuclei Radiofrequency Ablation in Pediatric NORSE Leading to Resolution of Status Epilepticus: A Novel Therapeutic Option

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Purpose: New-onset refractory status epilepticus (NORSE) in pediatric patients is rare and life-threatening, with limited options after antiseizure medication failure. In this case, the patient experienced NORSE for 1 year and 5 months prior to surgical intervention. We report a case of successful centromedian thalamic (CM) nuclei radiofrequency ablation resulting in resolution of super-refractory status epilepticus.
Method: Case Report: An 8-year-old girl developed focal and generalized seizures unresponsive to multiple antiseizure medications, confirmed as non-convulsive status epilepticus (EEG). Diagnostic work-up (MRI, CSF, infectious studies) was unremarkable. She was diagnosed with NORSE and referred for neurosurgical intervention. Intervention: Under general anesthesia and EEG guidance, radiofrequency ablation of the CM nuclei was performed. Lesions were applied via bipolar electrodes at 80C for 90 seconds. Intraoperative microelectrode recordings confirmed pathologic high-frequency bursting in the CM nuclei.
Results: Postoperatively, ictal discharges resolved and EEG background significantly improved. The patient regained responsiveness, had no further super-refractory seizures, and underwent rehabilitation. She demonstrated progressive neurological and functional improvement without surgical complications.
Conclusion: CM ablation may represent a novel and effective rescue therapy in pediatric NORSE refractory to pharmacologic treatment. To our knowledge, this is the first reported case worldwide of centromedian thalamic nuclei ablation leading to electrographic and clinical resolution of NORSE. Further studies are needed to explore the safety and efficacy of this intervention in similar cases.

SUDEP and Mortality

1880 | "We want to know about SUDEP but it is scary" - caregiver and neurologist perspectives on the risk for premature mortality in Dravet Syndrome

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Purpose: Premature mortality is elevated in Dravet syndrome (DS). There is limited data on the views of parents and clinicians regarding provision of information and managing risk of premature mortality in DS. We aimed to investigate the perspectives of caregivers and neurologists on receiving and providing information and managing risk in relation to premature mortality in DS.
Method: Semi-structured interviews were undertaken with caregivers of children (n=12) and adults (n=4) with DS and neurologists (n=9) with experience of DS. Caregiver interviews focused on perceptions of risk of premature mortality, views on information received and managing risk. Neurologist interviews focused on how to inform caregivers about the risk and on how to support caregivers in living with the risk. Data was analyzed via thematic analysis.
Results: Caregiver themes regarding perception of risk and information received included: Limited information from healthcare, SUDEP is scary, desire to know despite uncertainty on nature of risk, how information is delivered is important and optimal timing varies. Neurologist themes regarding informing included: Inform early, verbal is best, adopt an individualized approach, consider emotional impact and inform along with other risks. Caregiver themes regarding management of risk included: Use of surveillance methods, need for better seizure control, managing anxiety related to the risk, and need for both emotional and practical support to manage risk. Neurologist themes included: Focus on practical steps such as use of surveillance while avoiding overprotectiveness and need for psychological support for caregivers.
Conclusion: Caregivers of persons with DS find information about SUDEP frightening but mostly want to be informed of the risk of premature mortality, emphasizing the importance of sensitive information delivery. Neurologists believe in individualized provision of verbal information and the importance of the multidisciplinary team providing complementary support for caregivers to manage and live with the risk of premature mortality.

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2048 | Ramadan Fasting and Seizure Activity in Adults with Epilepsy: A Systematic Review and Meta-Analysis

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Purpose: Ramadan fasting in Muslims entails the omission of food and fluids from dawn to sunset that can influence patterns of sleep, timing of medications, and food intake times. While dietary restrictions as well as fasting interventions show promise in enhancing seizure control, our aim is to analyze the link between Ramadan fasting in adults with epilepsy and seizure activity.

Method: We systematically searched PubMed, Scopus, Web of Science, Cochrane Library, and Embase between 2000 and January 2025 for articles that appeared between these dates. The terms used for searching included fasting in Ramadan with epilepsy or seizure. The seizure frequency and seizure status of the participants are the outcomes that we checked. Two reviewers independently screened and extracted data with a third resolving any differences that arose between them. Meta-analysis was done using the random-effects model with statistical heterogeneity using the I^2 statistic.

Results: Of the 1,485 articles, only 16 were found to be relevant, and 3 of these included 564 patients who met the inclusion criteria. The analysis of the pooled data demonstrated that 61.1% of patients remained seizure-free throughout Ramadan (95% CI: 38.8%–83.4%), with considerable heterogeneity ($I^2 = 87.7\%$). Seizure risk was higher in patients on polytherapy, with poor baseline seizure control, increased fasting times, or high potassium levels. In contrast, extended seizure-free intervals and increased sleep duration pre-Ramadan were good predictors of safe fasting—and each seizure-free week gained increased the chance of remaining seizure-free by 10% as well as each extra hour of sleep by 30%. Seizure frequency increases were caused by interruption of daily rhythms, psychological tension, tiredness, as well as extended fasting.

Conclusion: While many patients remained seizure-free during Ramadan, high study variability highlights the need for standardized research. With proper medical supervision, fasting may be safe for selected epilepsy patients.

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