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Submission ID: 3; Submission Group: Submitter: Promising Technologies that can Help Advance MS Rehabilitation; Josephine Lyngh Steenberg Patient Involvement in developing a Self-tracking tool for People with Multiple Sclerosis

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Background: Self-tracking may help patients with chronic diseases manage their disease and achieve healthier lifestyles. Studies recommend that digital tools in MS should be developed in close collaboration with people with MS (PwMS) to accommodate individual needs. In this study, we developed a prototype self-tracking app for MS, involving PwMS in all development phases.

Methods: Two preliminary workshops with a total of 10 participants were conducted to explore how PwMS envision using a self-tracking tool and which elements such a tool should optimally contain. A list covering the measures that were defined in the workshops was drafted. 10 individual interviews with PwMS were conducted in which the content and design of the app were further discussed. The list of measures was adjusted based on the interviews and subsequently discussed with three MS healthcare professionals. Finally, 5 cognitive interviews with PwMS were conducted to ensure that all items and response categories contained in the app were understandable and meaningful. The tool was tested among PwMS in a subsequent study phase.

Results: The final app prototype consisted of a self-evaluation module containing measures of physical activity levels, sleep levels, dietary intake, mental health, sensitivity to temperature, menstruation, and the overall experience of the day. The app further consisted of a visualization module, and a library module containing explanatory texts. The visualization module showed graphs of registered data over time. The app was customizable meaning the users could select the measures they wanted to track. Measures shown in the visualization module could also be selected and de-selected as preferred, and the time period over which the graphs were shown was adjustable as well.

Conclusion: With this study, we developed a new digital tool for self-tracking in MS, based on the needs and preferences of PwMS and developed in collaboration with patient representatives.

Submission ID: 4; Submission Group: MS Rehabilitation within and across the ICF Domains; Submitter: Marie Kupjetz

Exercise-related kynurenine pathway modulation depends on baseline inflammatory status in multiple sclerosis

Running title: Inflammation and KP training response in MS

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Background: Multiple sclerosis (MS) pathophysiology involves neuroinflammatory and neurodegenerative processes. MS-related inflammation is associated with dysregulation of the immunomodulatory and neuroactive kynurenine pathway (KP). KP dysregulation is characterized by chronic overactivity, indicated by elevated kynurenine-to-tryptophan ratio (KTR), and predominance of neurotoxic (e.g., quinolinic acid, QA) over neuroprotective kynurenines (e.g., kynurenic acid, KA). As benefits of endurance training are partly attributed to anti-inflammatory effects, this study aimed to investigate whether training responses on systemic inflammation and KP dysregulation in persons with MS (pwMS) depend on baseline inflammatory status, as indicated by the neutrophil-to-lymphocyte ratio (NLR).

Methods: This secondary analysis of a randomized controlled trial (NCT04356248) included 104 pwMS that performed three-week endurance training regimens on bicycle ergometers thrice weekly. Participants were dichotomized to a high-inflammatory (HIG) and low-inflammatory status group (LIG) according to hemogram-derived baseline NLR (cut-off value 3.0). Targeted metabolomics (LC-MS/MS) was performed to determine serum levels of kynurenines. Training response differences between HIG and LIG on NLR, levels of kynurenines, and respective ratios were analysed using ANCOVA.

Results: Significant time*group interactions were identified for NLR ($p < .001$), kynurenine level (KYN, $p = .014$), KTR ($p = .017$), kynurenic acid-to-kynurenine ratio (KA/KYN, $p = .014$), and quinolinic acid-to-kynurenic acid ratio (QA/KA, $p = .003$). Results indicate greater training responses, reflected by decreased NLR, KYN, KTR and QA/KA, and increased KA/KYN, in HIG ($n = 30$, 66.7% female, 48.77 (10.30) years, Expanded Disability Status Scale (EDSS) score = 4.65 (1.23)) compared to LIG ($n = 74$, 67.6% female, 49.93 (9.73) years, EDSS score = 4.61 (1.36)) participants.

Conclusion: Effects of endurance training on systemic inflammation and KP dysregulation are more pronounced among pwMS with greater systemic inflammation. This is indicated by greater improvement of systemic inflammation itself (i.e., NLR), decreased KP overactivity (i.e., KTR, KYN), and a shift in circulating levels of neurotoxic towards neuroprotective kynurenines (i.e., QA/KA, KA/KYN).

Funding: The randomized controlled trial (NCT04356248) was funded by the Swiss Multiple Sclerosis Society (SMSG-2020-1). For this secondary analysis, no funding was obtained.

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Submission ID: 5; Submission Group: Application of Current Technologies in MS Rehabilitation; Submitter: YONCA ZENGİNLER YAZGAN

Examining The Effectiveness Of Two Different Web-Based Telerehabilitation Programs In People With Multiple Sclerosis

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Background: It has been reported that people with multiple sclerosis (PwMS) have difficulty in reaching the rehabilitation service they need due to personal and environmental problems, and their disease burden is increasing. Today, it is seen that the use of telerehabilitation applications in PwMS has become widespread.

Objective: Examining the effectiveness of two different web-based telerehabilitation programs on functionality, balance, and fatigue in PwMS.

Methods: Fifty PwMS (31 female, 19 male) were included and randomized to telerehabilitation (mean age=40.28±10.07 year, EDSS=3.26±1.26) and control groups (mean age=45.04±10.81 year, EDSS=3.48±1.53). They were evaluated with The 5 Times Sit To Stand Test (5XSST) for functionality, Modified Fall Efficacy Scale for balance and Fatigue Severity Scale for fatigue before and after the rehabilitation programmes. In addition, at the end of the program system usability and the change perceived by the patients were also evaluated. After the online evaluation with a physiotherapist through the system, individualized treatment programs that applied 3 days a week for 8 weeks were assigned to the participants via the www.telenorehab.com website. While the programs of the PwMS in the telerehabilitation group were created with exercise videos, exercise brochures were used in the control group.

Results: All parameters evaluated showed statistically significant improvement in both groups after treatment ($p < 0.05$). There were no differences between the groups in functionality, balance, and fatigue ($p > 0.05$). System usability and the change perceived by the patients were (82%; 80%) and (2.52±1.22; 2.12±1.30) for telerehabilitation and control groups, respectively.

Conclusion: Programs implemented by exercise videos or exercise brochures via the web-based telerehabilitation system have

the potential to improve balance, increases functionality, and reduces fatigue severity in PwMS. We think web-based telerehabilitation programs can be used as alternative methods in PwMS who have difficulties participating in physiotherapy and rehabilitation programs due to personal and environmental reasons.

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Disclosure: All authors have nothing to disclose.

Submission ID: 6; Submission Group: MS Rehabilitation within and across the ICF Domains; Submitter: Pelin Vural

Comparison of Respiratory Functions, Respiratory Muscle Strength and Fatigue Level of Patients with Pediatric-Onset Multiple Sclerosis and Healthy Peers
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Background: Patients with pediatric-onset multiple sclerosis (PwPOMS) have lower physical capacity and higher fatigue severity compared to their healthy peers. Although respiratory function is closely related to these parameters, it has not been evaluated in PwPOMS.

Objective: The aim of this study is to compare respiratory functions, respiratory muscle strength and fatigue level of PwPOMS and healthy peers.

Methods: 18 patients diagnosed with POMS (mean age:17.67±1.6 years, 15 girls and 3 boys, mean EDSS:1.36±0.83) and 13 healthy peers (mean age:16.69±1.31 years, 7 girls and 6 boys) were included in the study. “Minispir Light Spirometer” and “MD Diagnostics RP Check” were used to assess respiratory functions ($FEV1_{pred}$, $\%FVC_{pred}$, $\%FEV1/FVC_{pred}$, $\%PEF_{pred}$) and respiratory muscle strength. “Pediatric Quality of Life Inventory (PedsQL)-Multidimensional Fatigue Scale” was used for fatigue assessment. Total scores and subgroups scores (general fatigue, sleep, cognitive) for PedsQL-Child and PedsQL-Parent were calculated.

Results: $\%FEV1_{pred}$ ($p=0.046$), $\%FEV1/FVC_{pred}$ ($p=0.039$), PEF_{pred} ($p=0.010$), $\%PEF_{pred}$ ($p=0.012$) and MIP ($p=0.010$) were significantly decreased in PwPOMS compared to healthy peers. In addition, PedsQL-Child cognitive fatigue score ($p=0.020$), PedsQL-Parent total ($p=0.024$) and PedsQL-Parent sleep scores ($p=0.005$) were significantly impaired in PwPOMS.

Conclusion: The results of our study showed that PwPOMS, even with lower EDSS levels, may experience decreased respiratory muscle function and inspiratory muscle strength and also fatigue compared to their healthy peers. Future studies should investigate

the effects of adding respiratory therapy to the rehabilitation programs in PwPOMS.

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Disclosure: Authors have nothing to disclose.

Submission ID: 7; Submission Group: MS Rehabilitation within and across the ICF Domains; Submitter: Peter Feys Functional effects of peripheral cooling in MS patients with upper limb intention tremor

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Background & Objective: Upper limb intention tremor in MS affects a patient's ability to perform activities of daily life and is difficult to treat. The study investigates the effect of upper limb cooling on tremor severity and functional performance in MS patients with intention tremor.

Methods: In experiment 1, 17 subjects performed three different conditions: two cooling conditions of the forearm lasting 15 minutes (cold pack and cryomanchet) and one control condition. In experiment 2, 22 patients underwent whole arm cooling for 15 minutes using multiple cold packs. In both experiments, patients were tested 4 times (pre, post 0', post 25' and post 50' cooling on the following: handgrip force, unilateral tasks of the TEMPA, Fahn's tremor rating scale (FTRS), Nine Hole Peg Test (NHPT), Visual Analogue Scale (VAS), and the Patient's Global Impression of Change. The skin temperature of the shoulder, elbow, and wrist were also measured.

Results: Cooling the forearm with a cold pack or a cryomanchet significantly reduced the FTRS, the performance on the NHPT, and three quarters of items of the TEMPA. Cooling the whole arm reduced the FTRS and the time needed to execute half of the items of the TEMPA. Most patients rated their performance after cooling as much better. All these effects occurred immediately after cooling and lasted up to 25 minutes. Forearm cooling with a cryomanchet and whole arm cooling had a greater effect on part A of the FTRS than cooling of the forearm only. Other effects were similar across cooling modalities.

Conclusion: Cooling the upper limb led to a clinically noticeable effect on tremor severity and the functional performance, pronounced during the first half-hour after cooling.

Submission ID: 8; Submission Group: Multidisciplinary Rehabilitation in MS; Submitter: Rosario Giacalone Stand up paddle boarding: a promising adapted physical activity for people with Multiple Sclerosis

Running Title: SUP adapted activity in persons with MS
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Abstract

Introduction: Stand Up Paddle boarding (SUP) is a recreational and sporting activity that consists in paddling with a single paddle while standing on a large and wide board. SUP can bring different benefits, such as cardiovascular, musculoskeletal and psychological improvements. This activity has a low impact and a low risk of injuries. Since Multiple Sclerosis (MS) can affect the motor system, with weakness, spasticity, balance disturbances, sensibility impairments and fatigue, we investigated the feasibility of this adapted activity in pwMS.

Methods: We enrolled 3 pwMS (2F/1M) with EDSS range 2-5 (mean 3.5 ± 1.5). Inclusion criteria: age between 18 and 75, EDSS lower than 6. Exclusion criteria: acute phase of the disease and water fear/discomfort. We performed the following tests at T0 (before SUP lessons) and at T1 (at the end of SUP experience): SPPB, TUG, stabilometric test. Moreover, we recorded the Heart Rate Variability (HRV) at T0, T1 and during the SUP lessons, reporting the Borg scale at the same time. We planned 3 group lessons (1 per week) with 45 minutes duration.

Results: Tests SPPB and Tandem Walk did not show any changes, instead TUG had an improvement of 0.26 ± 0.14 sec. Stabilometry showed a reduction of the oscillations after the lessons. HRV parameters did not change significantly if compared to the basal recordings and before the activity. Meanwhile, patients perceived an increased Borg score after every lesson.

Conclusion: This pilot study has been useful verifying the feasibility of the SUP adapted activity in pwMS. Results showed that balance and walking skills can be improved by the SUP activity. HRV parameters showed that this is a low impact activity and the efforts is well tolerated by pwMS. Further studies are needed to demonstrate the benefits of SUP and to investigate the possible risks of this practice on pwMS with higher disability.

Submission ID: 9; Submission Group: Multidisciplinary Rehabilitation in MS; Submitter: Andrea Polidori Sit to stand test can be an interesting tool for disability and ability to ambulate in patients with Multiple Sclerosis Running title: 30SCST and FTSST, two valid scales for MS assessment

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Introduction: Multiple Sclerosis (MS) is a demyelinating and chronic disease, which can lead to moderate-severe disability. Variable symptoms can be present in the disease. There are different scales which score the ability of ambulation and the quality of walking, but only few papers took into consideration the Five-Times Sit to Stand (FTSST) or the Thirty-Seconds Chair Stand Test (30SCST), which are good indicators in other neurological diseases.

Objectives: 30SCST consists in recording the number of stands a person can complete in thirty seconds as fast as possible; FTSST measures the time of five stands.

Aims: The aim of our research is to check the validity, the reliability and the responsiveness of those two tests in Multiple Sclerosis, since we believe that they are very feasible tools in MS walking assessment.

Methods: pwMS with EDSS ≤ 6.5 , followed as outpatients at the AISM rehabilitation center of Genoa, were enrolled in the study. We performed a correlation of the two scales with the AI and the EDSS scale, considered a gold standard scale for people with MS (pwMS); a test-retest was administered by another operator and a comparison between the first evaluation and the last one after ten/twelve sessions of physiotherapy.

Results: We collected the preliminary data of 30pwMS (12 M/18 F, EDSS range 1.5-6.5). In our results, EDSS correlates significantly with 30SCST ($p < 0.0001$) and FTSST ($p < 0.0078$) and AI also correlates significantly with both (30SCST $p < 0.0001$; FTSST $p < 0.0001$). The test-retest analysis shows a very high correlation between the two evaluations (r Pearson 0.9408) and Cronbach's alpha is 0.989. Furthermore, both 30SCST and FTSST shows a great responsiveness to a physiotherapy treatment (30SCST $p < 0.0003$, FTSST $p < 0.0001$).

Conclusion: Data suggest that 30SCST and FTSST seem to be valid and reliable tools. Moreover, they are probably responsive to change. In conclusion, these two tests are simple, reliable, safe and easy to administer.

Submission ID: 10; Submission Group: MS Rehabilitation within and across the ICF Domains; Submitter: Prada Valeria

Sveva calls questionnaire: a novel questionnaire for the assessment of the compliance with "at home" physical activity
Running title: Sveva calls for compliance with the physiotherapy

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Introduction: Multiple Sclerosis (MS) is a chronic demyelinating disease, which can lead to moderate-severe disability. Variable symptoms as fatigue, balance disorders, loss of coordination, strength and sensation are present. An ongoing rehabilitation can bring improvements during post-acute phases and is useful for maintenance, although it can be expensive for the public health system or for the patients. For this reason, "at home" protocols can improve the quality of life of the patients, but we do not have any tool to evaluate the compliance with the "at home" treatments. Sveva calls (SC) is a fast phone-call questionnaire with a range from 0 (no exercises) to 9 (fully compliant) based on the compliance with the pharmacological therapy questionnaires already present in literature.

Methods: pwMS with EDSS ≤ 6.5 were enrolled in the study. At the enrollment, every patient performed 6MWT, TUG and a stabilometric test. A written protocol is assigned to the patients based on the severity of the disease with the recommendation of a 3 days-per-week training. Every 2 weeks they are asked to answer to 9 questions by phone regarding the exercises.

Results: 16 pwMS (EDSS 4.4 ± 1.6 , 3M/13F) have been enrolled. No correlation between the EDSS, TUG, 6MWT and the score of SC. The stabilometric test does not correlate with the SC. The mean score of the questionnaire is 5.6 ± 2.9 (range 0-9) after 2 weeks and mostly it does not change after 4 weeks.

Conclusions: Even though the study is still ongoing and no patients have concluded the follow up of the study yet, we can state that there is no correlation between the severity of the disease and the compliance with the physiotherapy. Moreover, more people stated to be very happy to answer to a professional once every two weeks. We need more studies to understand if this questionnaire has a prognostic function also.

Submission ID: 11; Submission Group: MS Rehabilitation within and across the ICF Domains; Submitter: Cintia Ramari Ferreira

Walking but not cognitive fatigability measurement is reliable in moderate to severe multiple sclerosis patients
Running Title: Reliability of objective fatigability in MS

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Background: Fatigue is a disabling symptom of MS and a multi-dimensional concept. Objectively, fatigue is measured by the capacity to sustain a motor or cognitive task, termed fatigability. Subjectively, one can ask the patient about perceived fatigue. Although walking fatigability affects more impaired patients, reliability of walking and cognitive fatigability, and the association with perceived fatigue are lacking.

Aims: to investigate the reliability of walking and cognitive fatigability in moderate to severe MS patients, and its correlation with perceived fatigue.

Methods: Forty-five persons with MS (age: 54.7 ± 9.3 y; EDSS: 3-6.5) and 21 healthy controls (HC) (age: 51.1 ± 6.0 y) were included. The distance walk index (DWI) was calculated comparing the distance at the last and first minute of the 6-minute walk test (6MWT). Cognitive fatigability index (CFI) was calculated comparing the last and first third of the Symbol Digit Modality Test (SDMT), and the Paced Auditory Serial Addition Test (PASAT). The Modified Fatigue Impact Scale (MFIS) measured perceived fatigue. Participants were tested on two sessions to determine day-to-day reliability (Intraclass Correlation Coefficients-ICC and Bland-Altman method-BA).

Results: For cognitive function, SDMT and PASAT revealed good reliability [ICC range=0.76 to 0.86/ BA range=-6.5 to -3.8] for both groups. Cognitive fatigability showed poor reliability in MS

and HC [ICC range=0.10 to 0.17/ BA range=-4.8 to 2.4]. The 6MWT revealed excellent reliability in both groups. Walking fatigability showed moderate reliability for MS patients, only, [ICC=0.64/ BA=2.6]. MFIS was significant higher in MS patients, with 70% of the MS patients reporting values higher than 38. No correlations were found among MFIS, DWI and CFI.

Conclusions: Clinical measure of walking fatigability is reliable for moderate to severe MS patients. Given the poor reliability of cognitive fatigability, new methods are needed for this population. No correlations among perceived fatigue and fatigability emphasize the different constructs of fatigue in MS.

Submission ID: 12; Submission Group: MS Rehabilitation within and across the ICF Domains; Submitter: Francesco Romanò

MRI correlates of manual dexterity asymmetry in people with multiple sclerosis

Running title: Brain and hand dexterity asymmetries in MS

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Introduction: Motor, sensory and cerebellar symptoms are often lateralized in people with multiple sclerosis (pwMS). In this study, we explored associations between manual dexterity asymmetry and structural damage in pwMS and their relation to disability.

Methods: Three hundred thirty-four pwMS and 124 healthy controls (HC) underwent 3T MRI acquisition of 3D-T1-weighted and dual-echo sequences, used to extract left and right normalized brain volumes (cortical and deep gray matter and cerebellum) and lesion loads (cerebral and cerebellar). Hand dexterity was evaluated with the nine-hole peg test (NHPT). Asymmetry indexes (AIs) for volumetric and hand dexterity measures were calculated by subtracting left and right z-transformed values, computed based on the HC group. Nonparametric correlations between NHPT AI and AIs of structural measures were performed in HC and in pwMS stratified by disability, measured with the Expanded Disability Status Scale (EDSS) (mild=0-3.5; moderate=4.0-5.5; severe>=6.0).

Results: PwMS of all disability categories had worse NHPT scores than HC with both hands ($p<0.001$). No side-specific lateralization of dexterity impairment or structural damage emerged in the examination of AIs in pwMS. Larger degrees of asymmetry (i.e. more dispersed distributions of AI measures) were observed in patients with moderate/severe disability, whereas mildly disabled pwMS had values ranging closer to those of HC. No correlations between structural and NHPT AIs were found in HC and mildly disabled pwMS. In moderately disabled pwMS NHPT AI correlated with cortical ($\rho=0.31$, $p=0.02$) and deep gray matter volume ($\rho=0.40$, $p=0.001$) AIs, while in pwMS with severe disability it was associated with cerebellar lesion load AI ($\rho=0.37$, $p=0.003$).

Conclusion: Structural asymmetries are associated to asymmetry in NHPT and both increase with disability in pwMS. Different structural substrates at different levels of disability underlie asymmetry in manual dexterity impairment.

Submission ID: 13; Submission Group: Promising Technologies that can Help Advance MS Rehabilitation; Submitter: Francesco Romanò

Structural and functional correlates of disability and gait in multiple sclerosis: focus on the globus pallidus

Running title: The globus pallidus in multiple sclerosis

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Introduction: The globus pallidus (GP) is divided into an internal (GPi) and an external (GPe) component. In this work, we explored in people with multiple sclerosis (pwMS) the added role of studying structural and functional GPi/GPe damage, rather than as a whole, in relationship with clinical measures of disability and gait impairment.

Methods: Sixty pwMS and 30 matched healthy controls (HC) underwent 3T MRI including 3D-T1-weighted, dual-echo and resting state (RS) functional MRI. Timed 25-foot walk (T25FW) and Expanded Disability Status Scale (EDSS) were administered. Two operators segmented left and right GP into GPi and GPe starting from FSL FIRST masks. Whole-GP, GPi and GPe normalized volumes and T1/T2 ratio were extracted, and seed-based RS functional connectivity (FC) was analyzed.

Results: PwMS had a higher T25FW than HC ($p<0.001$). The GP and its components were not atrophied in pwMS. Compared to HC, pwMS had higher T1/T2 ratio in all GP regions, which correlated with higher EDSS scores. Whole-GP RS FC analysis showed that pwMS had decreased connectivity between the left GP and right insula and between the right GP and frontal cortices. They also showed increased connectivity between the right GP and thalamus. When looking at RS FC of individual pallidal components, pwMS exhibited decreased connectivity between bilateral GPe and frontal cortices, as well as decreased intra-pallidal and increased thalamo-pallidal GPi connectivity. Lower RS FC between the GPe and frontal areas correlated with worse walking abilities and higher disability.

Conclusion: Structural involvement of the GP in pwMS was similar across the two segmented portions. However, the GPi and GPe showed component-specific RS FC alterations, which correlated with walking impairment and global disability.

Submission ID: 14; Submission Group: Multidisciplinary Rehabilitation in MS; Submitter: Margherita Monti Bragadin

Sleep quality and related clinical features in Multiple Sclerosis

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Sleep disturbances are common in people with Multiple Sclerosis (PwMS) with a prevalence greater than 50%, and they may be due to demyelinating lesions in specific area of the central nervous system or be secondary to other disabling MS symptoms.

This study aimed to examine the relationship between quality of sleep and clinical MS features.

158 PwMS (99 females and 59 males; age 55.5 ± 9.7 ; EDSS: 5.0 ± 1.7 ; disease duration: 21.5 ± 10.0) were enrolled. Demographic and clinical information were collected. Sleep disturbances and quality were investigated by the Pittsburgh Sleep Quality Index (PSQI). The PSQI is a standardized and self-administered questionnaire. A total score > 5 is considered an indicator of poor sleep quality. The assessment also included FIM, MFIS, HADS, OAB-q and LSI. Simple regression statistical analyses were performed to assess the associations between each predictor and sleep quality, and multivariate regression models were performed to select potential predictors of sleep quality in PwMS.

The mean total PSQI was 8.3 ± 3.7 ; 129 PwMS (81.7%) reported a total PSQI score > 5 . Moderate or severe difficulty was identified in habitual sleep efficiency (84.2%), sleep duration (44.9%), sleep latency (29.1%), and sleep disturbance (24.7%). Multivariate analyses revealed that poor sleep quality was correlated with older age, EDSS, secondary progressive (SP) form, higher OAB, and lower MFIS, HADS and LSI. In the final regression model, older age (OR = 1.08, $p = 0.006$), SP course (OR = 5.06, $p = 0.031$), DMD therapy (OR = 2.83, $p = 0.049$), higher MFIS (OR = 1.03, $p = 0.047$), and higher HADS anxiety subscale score (OR = 1.36, $p = 0.001$) were significantly correlated with poor sleep quality.

These data confirm that sleep disturbances are common in PwMS, correlated with fatigue and reduced quality of life. The PSQI proves to be a reliable, valid and quickly administered questionnaire to assess sleep quality in PwMS, also in clinical settings so as to target more appropriate multidisciplinary treatment choices.

Submission ID: 15; Submission Group: Application of Current Technologies in MS Rehabilitation; Submitter: Martina Scalia

Acute responses of spinal excitability to neuromuscular electrical stimulation in patients with Multiple Sclerosis
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Neuromuscular electrical stimulation (NMES) has revealed beneficial effects on muscle endurance, strength, balance, fatigue reduction and walking speed in people with Multiple Sclerosis (PwMS). However, the neurophysiological mechanisms underlying these functional improvements are still unclear. The aim of this study was to assess acute responses in spinal excitability, as measured by Hoffman (H) reflex, in PwMS, after three experimental conditions involving the ankle plantarflexors muscles of the most compromised leg: 1) passive NMES (pNMES), 2) NMES superimposed to isometric voluntary contraction (NMES+) and 3) isometric voluntary contraction (ISO) alone. Twelve PwMS

(EDSS: 2.0 – 5.0) were asked to perform 15 reps of 6 s at 20% of maximal voluntary isometric force (MVIF), with 6 s of recovery in between, for each experimental condition (pNMES, NMES+, ISO). Before and after each condition, soleus H-reflexes were elicited by percutaneous electrical stimulation of the posterior tibial nerve and H-reflex amplitudes were recorded by surface EMG. There were no significant changes in reflex responses following both NMES+ ($p = 0.109$) and ISO ($p = 0.404$), while H-reflex amplitude significantly decreased after pNMES ($p = 0.016$). The depression of the H-reflex after passive NMES may reflect a reduced spinal excitability in MS patients, which could be associated with a decreased force generation capacity. This mechanism could be explained by an increase in presynaptic inhibition via neuronal patterns that reduce input from type Ia afferences to the alpha-motoneurons. On the other hand, the absence of any change in spinal excitability following the NMES+ and ISO conditions suggests that adding NMES to voluntary exercise or carrying out voluntary exercise alone may be preferable than passively applying NMES in the design of exercises interventions to improve neuromuscular function in PwMS.

Submission ID: 16; Submission Group: MS Rehabilitation within and across the ICF Domains; Submitter: Alon Kalron

RIMS 2023 Genoa

Disease-related factors associated with employment and absenteeism in people with multiple sclerosis: Preliminary results from an Israeli cohort

Running title: Employment status amongst pwMS in Israel

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Abstract

Introduction: Paid employment is known to play a key role in a person's overall quality of life, and is a salient life issue for people with multiple sclerosis (pwMS). A better understanding of the disease-related factors affecting the employment status of working-age pwMS are critical when developing an appropriate intervention program.

Aim: The primary objective of the ongoing study was twofold: (1) to examine the extent of unemployment amongst working age pwMS living in Israel; (2) to detect disease-related factors negatively affecting the rate of employment and absenteeism in a community-based sample of pwMS.

Methods: Study design was cross-sectional. The primary outcome measure was the score on the 23-item MS Work Difficulties Questionnaire (MSWDQ-short form). In addition, participants reported his/her employment status which included the average number of working hours per week. MS disease-related factors included level of disability, perceived impact of MS on mobility, cognitive information processing speed, fear of falling, history of falls, perceived fatigue, anxiety, depression, bowel and bladder function.

Results: Preliminary results were based on the responses of 68 pwMS. Thirty-four (50.0%) were fully employed, 18 (26.5%) partially employed and 15 (22.1%) unemployed. A higher level of disability (based on the EDSS score) was found in the unemployed compared with the employed pwMS (fully and/or partially). Furthermore, unemployed pwMS reported more difficulties with

mobility, higher perceived fatigue, greater fear of falling, and a higher level of depression compared with fully employed pwMS. Information processing speed, years of education and anxiety did not differ between employed and unemployed pwMS. No differences were found in disease-related factors between fully to partially employed pwMS.

Discussion: Unemployment is a significant dilemma amongst working-age pwMS living in Israel. Major disease-related factors associated with unemployment include level of disability, increased perceived fatigue, depression and mobility difficulties.

Submission ID: 17; Submission Group: Promising Technologies that can Help Advance MS Rehabilitation; Submitter: Vincent de Groot

Blended versus face-to-face CBT for MS-related fatigue: results of a non-inferiority multicenter randomized clinical trial

Running title: Blended CBT for MS-related fatigue

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Introduction: Cognitive behavioural therapy (CBT) leads to a significant reduction of MS-related fatigue. However, implementation of face-to-face CBT is hindered by limited treatment capacity and strainful traveling for patients to the treatment location. Based on the effective CBT protocol that was used in the TREFAMS-CBT study, a blended CBT called MS Fit was developed in which online treatment modules are supported with guidance by a therapist.

Objective: To evaluate if blended CBT is non-inferior to face-to-face CBT in reducing fatigue severity in severely fatigued patients with MS.

Method: A non-inferiority multicentre randomized clinical trial (RCT), in which 166 patients with MS were allocated to either face-to-face or blended CBT. Primary outcome was fatigue severity assessed with the Checklist Individual Strength fatigue subscale directly post-treatment, at week 20. Mixed model analysis was used to determine between-group differences post-treatment. The upper limit of the 95% CI was compared to a pre-specified non-inferiority margin of 5.32.

Results: Blended CBT (N=82) was non-inferior to face-to-face CBT (N=84) (B=1.70, 95% CI -1.51 to 4.90). The proportions of patients achieving clinically significant improvement was 66.6% in the blended and 63.8% in the face-to-face condition. Blended CBT significantly reduced therapist time (B=-187.1 min, 95% CI

141.0 to 233.3 min). Post-hoc analysis showed that patients improved more (B=-5.35, 95% CI -9.22 to -1.48) when receiving their preferred treatment.

Discussion: Blended CBT is an efficient alternative to face-to-face CBT. Offering the preferred CBT format may optimize treatment outcome.

Acknowledgements: The study was funded by the Dutch MS Research Foundation (16–937 MS).

Submission ID: 18; Submission Group: MS Rehabilitation within and across the ICF Domains; Submitter: Hans Bogaardt

Is benign MS really benign? Cognition, depression and fatigue in benign MS

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Abstract

Multiple Sclerosis (MS) is a chronic disease that affects the central nervous system and causes disability. The severity of disability in people with MS (PwMS) is typically measured with the Expanded Disability Status Scale (EDSS), with a variant known as “benign MS” defined as an EDSS score of 3 or lower and disease duration of 10 years or less. However, the EDSS does not adequately represent the full range of disability experienced by PwMS, including cognitive impairment, communication

dysfunction, fatigue, depression, and anxiety. Although people with benign MS (PwBMS) might not have visible impairments, like problems with gait, they might experience other problems. This study aimed to evaluate the extent of cognitive impairment (CI), fatigue, and depression among 141 PwMS defined as having 'benign' MS (BMS). The study used a computerized test battery to assess cognition and the Fatigue Severity Scale (FSS) and Beck Depression Inventory (BDI) to measure fatigue and depression, respectively. Results showed that 38% of PwBMS had cognitive impairment, with the highest rate in the information processing domain and the lowest in verbal function. Both fatigue and depression were common among PwBMS, with rates of 78% and 55%, respectively. These rates are equal between PwBMS and persons with non-benign MS ($p=0.787$ and $p=0.316$ resp.).

Our findings suggest that cognitive impairment, fatigue, and depression are common among PwMS defined as having "benign MS". The high rate of CI, depression and fatigue in PwBMS found in this study raises the question how PwBMS are coping in everyday life, and how the rate of 38% of cognitive impairments in this group would reflect on their employability, their social life and their partners. Further research is needed into how people with 'benign' MS have currently access to health services and how their needs are supported.

Submission ID: 19; Submission Group: MS Rehabilitation within and across the ICF Domains; Submitter: Matteo Albergoni

The positive effects of aerobic capacity on fatigue are mediated by thalamic nuclei in people with multiple sclerosis
Running title: Thalamus mediates VO₂max effects on fatigue

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Background: Fatigue is a common symptom in people with multiple sclerosis (pwMS) affecting mental and physical domains. Aerobic capacity (AC), disability and cognitive impairments contribute to fatigue perception. The thalamus, with its nuclei related to motor and cognitive processes, has been consistently involved in fatigue pathogenesis. The aim of the study was to identify associations between thalamic nuclei volumes and fatigue and to explore whether the effect of AC on this symptom is mediated by the thalamus in pwMS.

Methods: In this cross-sectional study, Modified Fatigue Impact Scale (MFIS), Expanded Disability Status Scale (EDSS), Symbol Digit Modalities Test (SDMT), maximal oxygen uptake (VO₂max) and brain MRI data of thalamic volumes were collected from 74 pwMS. A group of 47 sex- and age-matched healthy controls (HC) was included for MRI comparison, with a subgroup of 10 presenting VO₂max values.

Results: In pwMS, fatigue was associated with atrophy of left latero-dorsal nucleus (left-Dor) (r -value = -0.278; $p \leq 0.018$),

with a stronger association with cognitive rather than physical fatigue. More severe disability (r -value = 0.355; $p = 0.004$) and worse cognitive processing speed (r -value = -0.353; $p = 0.003$) were associated with more severe fatigue and diffuse thalamic atrophy. In contrast, higher aerobic capacity was associated with less severe fatigue (r -value = -0.263; $p = 0.027$) and atrophy only of the left-Dor (r -value = -0.288; $p = 0.015$). A mediation model showed that in pwMS there was a significant indirect effect of VO₂max on fatigue through the left-Dor nucleus ($b = -0.305$, CI [-0.678; -0.005]).

Conclusions: AC exerts a positive effect on fatigue in MS, which is mediated by a preserved volume of the left-Dor.

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Submission ID: 20; Submission Group: MS Rehabilitation within and across the ICF Domains; Submitter: Tetsu Morozumi

Influence of cardiorespiratory fitness and MRI measures of neuroinflammation on hippocampal volume in multiple sclerosis patients

Running title: VO₂max influences hippocampal volume in MS

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Introduction. The hippocampus is a clinically relevant region that is characterized by neuroplasticity and neurogenesis also in adulthood. Neuroinflammation and cardiorespiratory fitness (CRF) may influence hippocampal integrity by modulating the processes promoting neurogenesis and neuroprotection that contribute to the preservation of functions. The aim of this study was to investigate whether higher CRF may limit the detrimental effects of neuroinflammation on hippocampal volume in the different multiple sclerosis (MS) clinical phenotypes.

Design/Methods. Brain structural MRI scans and maximum oxygen consumption (VO₂max), a proxy of CRF, were acquired from 81 MS patients (27 relapsing-remitting [RR] and 54 progressive [P]), and 45 age- and sex-matched healthy controls (HC). White matter T2-hyperintense lesion volume (T2-LV) and choroid plexus volume (CPV) were quantified as neuroinflammatory measures. Association of demographic, clinical, neuroinflammatory and CRF measures with normalized brain, gray matter, hippocampal and thalamic volumes in RRMS and PMS patients were assessed using Shapley and best subset selection regression.

Results. RRMS and PMS patients did not differ significantly in age ($p = 0.174$) and sex ($p = 0.623$). Compared to RRMS, PMS patients had higher EDSS score ($p < 0.001$), longer disease duration ($p = 0.003$), and a lower value of VO₂max ($p < 0.001$). For most volumetric outcomes, largest portions of variance were explained by T2-LV (variable importance [VI] = 9.4-39.4) and

CPV (VI=4.5-26.2). $\dot{V}O_{2\max}$ explained the largest portion of variance of normalized hippocampal volume in RRMS patients (VI=16.9) and was retained as a relevant predictor (Std. β =0.374, p =0.023) together with T2-LV (Std. β =-0.330, p =0.016), while explaining a small amount of variance of this outcome in PMS subjects (VI=0.1) and of all the other volumetric outcomes in both groups (VI from 0.3 to 2.2).

Conclusions. By exerting beneficial neurotrophic effects, a higher CRF may have a specific neuroprotective role for the hippocampus, mainly in the early phases of MS.

Submission ID: 21; Submission Group: MS Rehabilitation within and across the ICF Domains; Submitter: Gillian Quinn

The prevalence of vestibular dysfunction in people with Multiple Sclerosis attending the outpatient service in St. James's hospital Dublin

Gillian Quinn

St. James's Hospital, Dublin

Background: Vestibular pathology including vertigo, impairment of gaze stability and balance related dysfunction are common in people with Multiple Sclerosis (MS). Vestibular rehabilitation (VR) is a specialised, non-invasive form of therapy which has been shown to be effective in people with MS for improving balance, quality of life and fatigue. Vestibular issues are not routinely asked about during clinic assessment and vestibular rehabilitation may not always be offered.

Aim: to determine the prevalence of vestibular dysfunction in people attending the MS service in St. James's hospital.

Methods: a cross-sectional study exploring prevalence rates of vestibular dysfunction. A consecutive sample of patients with MS attending the Neurology service in St. James's hospital was invited to participate.

Analysis: descriptive statistics were used for the analysis of demographic data and self-report symptoms of vestibular dysfunction.

Results: The mean age of the cohort was 47 years (N=41) and 83% were female. The mean disease duration was 13 years with a mean EDSS of 3. Relapse-remitting MS was the most common sub type (76%). 41% reported using a mobility aid, the most common aid used was a stick and 49% had experienced a fall in the past year.

All participants bar one, reported experiencing vestibular symptoms in the past; the most common symptoms experienced were imbalance (85%), vertigo (66%) and dizziness (63%). 44% of the cohort reported having been assessed by a doctor or physiotherapist in the past regarding their vestibular system, but only 34% had been previously prescribed any form of VR.

Conclusion: Vestibular dysfunction is very common among people with MS and should be routinely assessed. Depending on clinical presentation, people with MS should be offered a review with a physiotherapist who is specialised in VR. Further research should explore the intensity and type of VR most effective for people with MS.

Submission ID: 22; Submission Group: MS Rehabilitation within and across the ICF Domains; Submitter: Marit Lea Schlagheck

Cardiorespiratory fitness across the adult lifespan in persons with multiple sclerosis

Running title: $\dot{V}O_{2\text{peak}}$ and ageing in multiple sclerosis

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Introduction: Cardiorespiratory fitness (CF) is linked to factors at all levels of the ICF model. As such, it's a key indicator of the general health and well-being of persons with multiple sclerosis (pwMS). In the general population, CF declines with age. Whether the decline is more pronounced in pwMS is currently unknown.

Aim: The aim of this study is to examine potential differences in CF (peak oxygen consumption; $\dot{V}O_{2\text{peak}}$) across the adult lifespan in pwMS vs. healthy controls (HC).

Methods: Data of n=469 pwMS (EDSS 1.0–7.0) who conducted graded cardiopulmonary exercise testing during their rehabilitation at Clinic Valens from 07/2010 to 10/2022 were retrospectively analysed. Participants were divided into age groups (18-29, 30-39, 40-49, 50-59, 60-69, \geq 70). The percentage differences (\sim deficits) in $\dot{V}O_{2\text{peak}}$ between pwMS and published normative data on matched HC (n=21063) were calculated for each age group as well as for males and females, respectively. Two-way ANOVAs were performed to investigate differences in $\dot{V}O_{2\text{peak}}$ between pwMS vs. HC across the age groups.

Results: The average $\dot{V}O_{2\text{peak}}$ ranged from 15.9-27.4 ml/kg/min in pwMS and from 23.8-42.9 ml/kg/min in HC across different age groups. With advanced age (i.e., across age groups), a continuous substantial deterioration of $\dot{V}O_{2\text{peak}}$ was observed in both pwMS (males and females; p <.05) and HC (males and females; p <.05). Within all age groups, pwMS showed reduced $\dot{V}O_{2\text{peak}}$ compared to HC with deficits ranging from 29%- 40% for females (p <.05) and from 35%- 41% for males (p <.05). However, no age group*group interaction was observed in neither males (p =.626) nor females (p =.557).

Conclusion: The present data on CF provide evidence for a parallel deterioration in pwMS and HC with advanced age, with reduced $\dot{V}O_{2\text{peak}}$ already present in young adulthood in pwMS. Understanding the age trajectories of CF in pwMS is crucial for designing optimal rehabilitative and preventive interventions.

Funding No external funding was provided for this study.

Disclosures MLS, JB, MLC and PZ have no competing interest to declare. LGH has received travel grants and/or teaching honorary from Biogen and Sanofi Genzyme, yet unrelated to the present study.

Submission ID: 23; Submission Group: Multidisciplinary Rehabilitation in MS; Submitter: Sarah Chatfield
Is fatigue associated with physical activity and psychological factors in people with progressive multiple sclerosis?

Chatfield S, Connolly L, Freeman J, Salter A, Amato MP, Bricchetto G, Chataway J, Chiaravalloti ND, Cutter G, DeLuca J, Dalgas U, Farrell R, Feys P, Inglese M, Meza C, Moore NB, Motl RW, Rocca MA, Sandroff BM, Feinstein A. On behalf of the CogEx Research Team.

Background: MS-related fatigue is managed by exercise and/or behavioural interventions. Understanding the relationship between fatigue, physical and psychological factors is important to inform practice. Few studies explore this in people with progressive MS (pwPMS).

Objective: Explore relationships between self-reported fatigue, physical activity (PA) measures, and psychological factors in pwPMS recruited to the CogEx trial (Feinstein 2020).

Methods: Baseline assessments of fatigue (Modified Fatigue Impact Scale; MFIS), aerobic capacity (VO_{2peak}), time in moderate-vigorous activity (MVPA; accelerometry), walking performance (6-minute walk test; 6MWT), self-reported walking difficulty (MS Walking Scale; MSWS-12), anxiety and depression (Hospital Anxiety and Depression Scale; HADS), and disease impact (MS Impact Scale-29, MSIS). Participants were categorised as fatigued (MFIS > 38) or not (MFIS < 38).

Statistical Analysis: Differences in fatigue categories were assessed (t-tests, chi square). Pearson's correlation determined associations with MFIS (total) and PA measures. Multivariable linear regression evaluated the association between MFIS (total) and PA measures adjusting for sex, EDSS score, country and depression.

Results: 311 pwPMS (62.3% female, 27.3% primary progressive, 72.7% secondary progressive, mean age 52.5yrs, mean EDSS 6.0 (4.5,6.5). MFIS (total) mean 44.1 (± 17.1), with 67.2% categorised as fatigued. Fatigued participants walked shorter distances (6MWT, $p=0.043$), had higher MSWS-12 scores ($p<0.001$), and lower average % in MVPA ($p=0.026$). Associations were mostly weak between MFIS (total) and PA measures ($r=-0.13$ to -0.16), apart from moderate association with MSWS-12 ($r=0.51$). MFIS (total) was moderately correlated with anxiety ($r=0.56$), depression ($r=0.59$) and disease impact (MSIS-physical $r=0.67$; MSIS-mental $r=0.71$). After adjustment, a one point increase in MSWS-12 was associated with a 0.26 increase in MFIS ($p<0.001$).

Conclusion: Management of fatigue should consider both physical and psychological factors. In contrast to systematic review evidence from mixed MS samples, the association between most PA factors and fatigue in this progressive MS sample appears weak.

Refs: Feinstein A, Amato MP, Bricchetto G, et al. Study protocol: improving cognition in people with progressive multiple sclerosis: a multi-arm, randomized, blinded, sham-controlled trial of cognitive rehabilitation and aerobic exercise (COGEx). *BMC Neurol* 2020; **20**(1): 204

Submission ID: 24; Submission Group: Translation of New Rehab Knowledge into Practice; Submitter: Lauren Taylor

Who benefits most from cognitive rehabilitation for multiple sclerosis: An algorithm based on secondary data analysis

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Abstract

Background: Up to 70% of people with Multiple Sclerosis (MS) experience cognitive problems including difficulties with memory, attention, problem-solving, and language. Cognitive rehabilitation can help manage cognitive difficulties. A recent systematic review found evidence to support the effectiveness of cognitive rehabilitation for people with MS, however, the degree to which patients benefit from this intervention appears to vary.

Objectives: The Cognitive Rehabilitation for Attention and Memory in MS (CRAMMS) trial showed *some* evidence of effectiveness of cognitive rehabilitation in improving cognitive function, with some participants benefiting more than others. However, we do not know who benefits most. We therefore conducted a secondary analysis of the CRAMMS data to understand who benefits most.

Methods: We grouped baseline data from 449 participants into five categories of possible predictors (socio-demographics, clinical variables, cognitive impairment, neuropsychological test performance, and treatment dose). Using regression models, we identified specific factors/characteristics that could predict the likelihood that an individual will benefit from cognitive rehabilitation.

Results: The regression models predicted whether a participant improved or did not improve in objective neuropsychological function following cognitive rehabilitation in up to 86% of participants. Results suggest that younger participants with medium to high education, diagnosed with relapsing remitting and primary progressive MS who have not experienced any recent relapses, with mild to moderate cognitive difficulties, and living with a partner or other family, were more likely to benefit from cognitive rehabilitation than other groups.

Conclusion: We can predict which participants are most likely to demonstrate significant improvements in neuropsychological function following group-based cognitive rehabilitation. Clinically, this allows us to optimise limited neuropsychology resources by offering such cognitive rehabilitation to those most likely to benefit and offer other therapies to others. Routine cognitive screening may help us identify patients who are most likely to benefit.

Submission ID: 25; Submission Group: MS Rehabilitation within and across the ICF Domains; Submitter: Rachel Dennett

Peer Coaching for Adults with Long-term Conditions: PEER CONNECT a Feasibility RCT

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Background: People with low levels of knowledge, skills and confidence to manage their health and well-being (activation) are more likely to have unmet health needs. In the United Kingdom, estimates suggest this may be applicable to 25%–40% of patients with long-term health conditions. Peer coaching may support people to increase their level of activation and could be particularly effective for those with low activation (patient activation measure, levels 1 and 2).

Methods: Single-site, block randomised, controlled feasibility trial of a co-designed volunteer peer health and well-being coaching intervention. Coach training and peer coaching delivered via video-call for people with multiple sclerosis (MS), rheumatic diseases or chronic pain. Feasibility outcomes included recruitment and retention data. Additionally, patient activation, mental health and well-being were measured. Semi-structured interviews exploring service and study feasibility, acceptability and deliverability were conducted with coaches post-training and post-coaching, peers and service staff.

Results: To-date, 27 potential volunteer peer coaches have been screened with 21 recruited (n=14 MS). Seven (n=3 MS) have withdrawn, citing time commitment (n=2); waiting too long for a peer (n=1); not feeling equipped enough to coach (n=1) and personal circumstances (n=3) as reasons. Nineteen potential peers have been screened with seven (n=2 MS) recruited; 11 were ineligible as their activation score was too high. One peer withdrew due to health problems. Twelve interviews with coaches and peers have been completed. Further results will be available by May 2023.

Conclusions: Our findings to-date suggest that coach recruitment is feasible. Contemporaneous co-design led to greater acceptability of the training programme and creation of a ‘coaching community’ improved coach retention. Recruitment of peers has been challenging despite employing different strategies. Future work will explore how peer coaching can be better integrated into patient care pathways and how people with low activation can be more effectively recruited.

Trial registration number ISRCTN12623577.

Submission ID: 26; Submission Group: Multidisciplinary Rehabilitation in MS; Submitter: Nadine Patt

Inpatient energy management education and high-intensity interval training in fatigued persons with MS - a randomized controlled superiority trial with six-month follow-up

Running title: Effects of energy management + HIIT in MS
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Background: Fatigue has a major impact on the health-related quality of life (HRQoL) of persons with multiple sclerosis (pwMS). Energy management and exercise show strong evidence for reducing fatigue.

Objective: To investigate the effects of two combined therapy modalities: inpatient energy management education (IEME) and high-intensity interval training (HIIT) compared with progressive muscle relaxation (PMR) and moderate continuous training (MCT), on HRQoL and fatigue.

Methods: 106 fatigued pwMS, with an Expanded Disability Status Scale (EDSS) score ≤ 6.5 , were recruited at the Valens clinic, Switzerland (NCT04356248) and randomized (1:1) to either an experimental (IEME 2x/week and HIIT 3x/week) or a usual care group (PMR 2x/week and MCT 3x/week). Interventions were delivered during a 3-week inpatient rehabilitation stay. HRQoL was assessed with the Medical Outcome Study 36-item Short Form Health Survey (SF-36) and fatigue with the Fatigue Scale for Motor and Cognitive Functions (FSMC), at entry to the clinic (T₀), at discharge (T₁), 4 (T₂) and 6 (T₃) months after T₀. Data was analysed using a mixed model for repeated measures approach.

Results: There was no significant group*time interaction in HRQoL and fatigue. There was a significant between-group difference in the pairwise comparisons of the group*time interaction in the SF-36 mental health ($p=0.022$, $d=0.459$ [95% CI 0.062–0.856]) at T₂ and in the SF-36 physical functioning ($p=0.012$, $d=0.511$ [95% CI 0.11–0.911]) at T₃, with the IEME + HIIT group having higher scores. Time effects were significant for all outcomes, except SF-36 role emotional.

Conclusion: These results provide new information on a multimodal therapy approach that combines education and endurance exercise. In clinical practice, treatment choices must take into account the promising effects of the IEME + HIIT group, reflected by higher scores in mental health and physical functioning compared to PMR + MCT at 4- and 6-month follow-up, respectively.

Funding: This study was funded by the Swiss Multiple Sclerosis Society (SMSG-2020-1).

Disclosures: Nothing to disclose.

Submission ID: 27; Submission Group: Multidisciplinary Rehabilitation in MS; Submitter: Andrea Giordano

Italian cross-cultural adaptation of the Quality of Communication questionnaire and the 4-item Advance Care Planning Engagement questionnaire

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Abstract

Background: Advance care planning (ACP) is influenced by several factors (e.g., patient's readiness to engage, clinician's skills, and the cultural environment). Availability of reliable and valid self-reported measures of the ACP domains is crucial, including cross-cultural equivalence.

Aim: To culturally adapt into Italian the 19-item Quality of Communication (QOC) and the 4-item ACP Engagement (4-item ACP-E) questionnaires.

Methods: We translated and culturally adapted the two questionnaires and produced a significant other (SO) version of the QOC (QOC-SO). Each questionnaire was field tested via cognitive interviews with users: nine patients (QOC, 4-item ACP-E) and three SOs (QOC-SO) enrolled at three palliative care services.

Results: We made minor changes to 5/19 QOC items, to improve clarity and internal consistency; we changed the response option 'didn't do' into 'not applicable'. Finally, we slightly revised the QOC to adapt it to the paper/electronic format. QOC debriefing revealed that the section on end of life was emotionally challenging for both patients and SOs. We simplified the 4-item ACP-E layout, added a sentence in the introduction, and revised the wording of one item, to improve coherence with the Italian ACP legislation. ACP-E debriefing did not reveal any major issue.

Conclusions: Results were satisfactory in terms of semantic, conceptual and normative equivalence of both questionnaires. Acceptability was satisfactory for the 4-item ACP-E, while findings of the QOC cognitive debriefing informed a major amendment of a pilot trial protocol on ACP in multiple sclerosis (ConCure-SM): use of the interviewer version only, in an adaptive form. Psychometric testing of both questionnaires on a large, independent sample will follow.

Submission ID: 28; Submission Group: Translation of New Rehab Knowledge into Practice; Submitter: Sofie Bergien

Translating MS research into practice – a participatory approach

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Background: Translating research results into practice is often hindered by research designs not reflecting the complexity of people's real-life environment. To overcome this challenge within the field of healthcare, the participatory research (PAR) approach has been introduced. Involving and empowering the people being subjects of the research through PAR has shown great potential in making research more relevant and easier to implement in both clinical practice as well as in people's everyday life. However, little is known about barriers and advantages when conducting PAR among persons with Multiple Sclerosis (PwMS).

Objective: This study aimed to investigate how older PwMS experience being engaged in PAR and hence to map potential barriers and advantages related to such engagement.

Method: Seven PwMS aged 65 to 80 years participated in a focus group. To ensure a safe environment allowing the participants to discuss both good and bad experiences, a researcher external to the original PAR project carried out the interviews. All interviews were performed using an interview guide, recorded, and transcribed. Meaningful units were extracted and categorized using a thematic network analysis.

Results: From the analysis, three main themes emerged relating to how the participants had experienced being engaged in PAR: 1) Doubting the value of own contribution, 2) Being challenged in participating due to MS symptoms, and 3) A room for sharing experiences.

Conclusion: The results of the study pointed out that PwMS experience both barriers and advantages when engaging in PAR. Doubting the value of own contribution and being challenged due to MS symptoms constitute potential barriers. However, if these barriers are addressed, PAR also holds the potential to empower research participants and stimulate the sharing of real-life experiences, which is essential for translating research into adoptable solutions for the people targeted.

Submission ID: 29; Submission Group: Translation of New Rehab Knowledge into Practice; Submitter: Julia Peper
Information and support needs of women with multiple sclerosis on motherhood choice – a qualitative interview study

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Background: Pregnancy is an important issue for women with multiple sclerosis (wwMS), as the disease is often diagnosed in

young women. However, misunderstandings and uncertainties about MS and pregnancy are common.

Our mixed-methods study aims to develop and pilot a decision-support programme for wwMS on motherhood choice. For this purpose, we explored the information and support needs of wwMS regarding motherhood in MS.

Methods: We conducted a qualitative study with semi-structured interviews with wwMS and experts to address the experiences, information needs, and concerns of wwMS, and experts' perceptions of motherhood in MS. We developed two interview guides based on literature searches. WwMS aged 18-45 years, who are dealing with or have dealt with the topic of motherhood, were recruited via flyers and mailing lists. Experts were eligible if they were experienced in pregnancy/motherhood in MS. All interviews were recorded, transcribed and analysed using qualitative thematic analysis.

Results: We conducted three focus groups (n=12) and individual interviews with wwMS (n=3) and experts (n=4). WwMS felt inadequately advised and supported by healthcare professionals about MS and pregnancy and had sometimes received incorrect information. Most wwMS described a need for support from professionals experienced in pregnancy in MS and for trustworthy and accessible information. Experts emphasised that pregnancy in MS is a common and important issue with the need for good preparation and planning. They stated that decision-making regarding motherhood is an individual process that might be complex and challenging for wwMS. Therefore, evidence-based information and professional advice on motherhood in MS are needed. WwMS and experts highlighted the need to consider the issue of pregnancy in the context of decisions about immunotherapy.

Discussion: Our findings highlight the need for evidence-based information and support programmes for wwMS on motherhood in Germany. The results were included in the development of a decision-support programme.

Submission ID: 30; Submission Group: Promising Technologies that can Help Advance MS Rehabilitation; Submitter: Asiye Tuba Ozdogar
Feasibility of exergaming for upper extremity rehabilitation in people with multiple sclerosis
Running Head: Feasibility of exergaming for upper extremity

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Abstract

Introduction: Exergaming has been suggested as a rehabilitation method since it is more motivational for people with multiple sclerosis (MS, pwMS). However, the major disadvantage of this method is the lack of specific scenarios designed for pwMS. This study aims to assess the feasibility of exergaming, which was developed for pwMS.

Methods: This study was performed in the outpatient MS Clinic of Dokuz Eylül University Hospital. Exergaming scenarios were developed in collaboration with medical personnel consisting of physiotherapists and doctors, and computer engineers. A total of 30 participants who had definite MS diagnoses were included. The exergaming scenarios were implemented using the Microsoft Kinect. A physiotherapist applied custom-made exergames for one session. All the participants were assessed immediately after the session. The User Satisfaction Evaluation Questionnaire was used to assess the user's satisfaction with the system and exergaming.

Results: The mean age was 41.5, the mean Expanded Disability Status Scale was 4.5 (range between 0-7), and the mean disease duration was 10.0 years. Twenty patients were relapsing-remitting, and 10 were secondary-progressive. The mean scores of the User Satisfaction Evaluation Questionnaire were 4.33 (SD=0.84) for helpfulness for rehabilitation, 0.97 (SD=1.52) for not disturbing, 4.50 (SD=1.07) for understandability, 4.0 (SD=0.91) for easiness to control easy to use, and 4.33 (SD=0.84) for enjoyability.

Conclusion: These results showed that our custom-made exergaming scenario could be feasible in upper extremity rehabilitation in MS. More research is needed to investigate its effectiveness in the rehabilitation of upper limbs.

Submission ID: 31; Submission Group: Translation of New Rehab Knowledge into Practice; Submitter: Mustafacan Salamci

Ankle anticipatory postural adjustments during gait initiation in multiple sclerosis

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Objective: Anticipatory postural adjustments (APAs) appearing during the postural phase of gait initiation (GI) cause electromyographic activity in the ankle muscles and centre of pressure (COP) displacement as a biomechanical response. The aim of this study was to investigate in electromyographic activity of APAs and COP displacement during GI in multiple sclerosis (MS) patients with and without functional loss.

Material-Method: Aged 20-40 years, 13 relapsing-remitting MS (RRMS) patients without functional loss (Expanded Disability Status Scale (EDSS) 0-1.5) were included in group-I and 17 RRMS patients with functional loss (EDSS 2-3) were included in group-II. Also, 13 healthy individuals were included in group-III. Bilateral electromyographic activity of APAs in tibialis anterior (TA) and gastrocnemius medialis (GM) were collected, filtered, and amplified by a surface electromyography system (Trigno,

Delsys®). Peak COP displacement in posterior direction was recorded by a force plate (Model BP5050, Bertec®).

Results: There were significant differences in magnitude levels of APAs of bilateral TA and GM among the 3 groups ($p < 0.0001$). Between group-I and group-III, there were significant differences in TA of swing ($p = 0.01$) and stance ($p = 0.01$) limb and GM of swing limb ($p < 0.0001$). Besides, group-I had less magnitude levels than group-III. Between group-II and group-III, there were significant differences in all muscles ($p < 0.0001$) and group-II had the lowest magnitude levels. In terms of COP displacement, there were significant differences among all groups ($p < 0.0001$) and group-II had the lowest posterior shift among the 3 groups ($p < 0.0001$).

Discussion: Our findings indicate that RRMS patients with or without functional loss present dysfunction in ankle APAs of GI. Although there is no functional loss, the postural phase of GI which are associated with central nervous system regulation and gait performance are affected in the EDSS 0-1.5 group. From EDSS score 2, the postural phase of GI becomes more affected.

Keywords: Multiple Sclerosis, Gait Initiation, Anticipatory Postural Adjustments, Centre of Pressure

Submission ID: 32; Submission Group: MS Rehabilitation within and across the ICF Domains; Submitter: Blanca De Dios Pérez

Development of a Job Retention Vocational Rehabilitation Intervention for People with Multiple Sclerosis Following the Person-Based Approach

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Abstract

Aim: To describe the process of developing a job retention vocational rehabilitation intervention for people with multiple sclerosis (MS) to support people with MS to remain at work for as long as they wish.

Design: We used the person-based approach to intervention development; an iterative process incorporating the views of stakeholders, resulting in an intervention that is more likely to be acceptable, contextually relevant, and implementable for end-users. The intervention was developed in two phases. Phase 1 combined the results of a systematic review and interview study to develop the guiding principles and intervention logic model for a vocational rehabilitation intervention for people with MS. Phase 2 involved conceptual testing and refining the intervention guiding principles and logic model with stakeholder feedback. The intervention was underpinned by the International Classification of Functioning Disability and Health (ICF).

Participants: We recruited 20 participants for Phase 1 (10 people with MS, four employers, and six healthcare professionals). For Phase 2, we recruited 10 stakeholders (three people with MS and

seven healthcare professionals) who contributed to the intervention refinement process.

Results: The stakeholders described the need for an individually tailored intervention to support people with MS to manage symptoms and workplace relationships. A stepped-care approach and the possibility of receiving support remotely were deemed essential to improve intervention acceptability. The resulting intervention involves an individualised vocational assessment, vocational goal setting, up to 10 hours of support (e.g., reasonable adjustments, employer engagement, legal rights, etc.), and a progress review to discuss future steps. The intervention also provides the person with MS the opportunity to include their employer to receive support managing their employee with MS at work.

Conclusions: Future research should assess the feasibility and acceptability of delivering the intervention to people with MS and their employers.

Submission ID: 33; Submission Group: MS Rehabilitation within and across the ICF Domains; Submitter: Blanca De Dios Pérez

The Impact of COVID-19 on the Employment of People with Multiple Sclerosis:

Multi-methods study

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Abstract

Background: The spread of the coronavirus disease (Covid-19) led to more than half of the working population in the UK being unable to work. This study aimed to understand the employment needs and experiences of people with multiple sclerosis (MS) working in the UK during the Covid-19 pandemic.

Methods: Multiple methods involving an online survey and follow-up semi-structured interviews underpinned by the International Classification of Functioning Disability and Health (ICF). We recruited people with MS who were employed pre-pandemic (March 2020). Data from the survey were analysed using descriptive statistics and interviews were analysed following the framework method.

Results: 101 people completed the online survey, and 15 participated in the follow-up interview. Survey data indicated that not travelling to work and working from home improved self-reported work performance and work-life balance. Almost half of the participants (45%) reported no vocational rehabilitation needs; however, others identified the need for help with managing mood (30%), managing MS symptoms (25%), and

employers' expectations (19%). Five themes were extracted from the interviews reporting on 1) the benefits of working from home; 2) the challenges experienced working during Covid-19; 3) the relevance of line manager support; 4) the impact of returning to 'normality'; and 5) future vocational needs.

Conclusions: Although people with MS experienced feelings of isolation, and fears of catching Covid-19 during the pandemic, there were some unintended benefits for this population. Working from home allowed people with MS to manage their symptoms and workload without having to request additional support from their employers. Participants reported improved performance at work associated with these changes, which suggests that working from home should be offered as a reasonable adjustment wherever possible for people with MS. Future research should explore the support needs of people with MS who are working remotely.

Submission ID: 34; Submission Group: MS Rehabilitation within and across the ICF Domains; Submitter: Leena Maria Heikkola

Do social cognition and psychosocial functioning predict pragmatic language abilities in people with MS?

Running title: Predicting pragmatic abilities in MS

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Abstract

Pragmatic abilities refer to the ability to produce and comprehend language appropriately in different social contexts. Previous research suggests that pragmatic abilities may be linked to several cognitive substrates, such as executive functions and social cognition. There is some evidence that pragmatic abilities in MS are linked to deficits in social cognition, as well as psychosocial functioning in MS. Previous research has also shown some links between cognitive fatigue and general language abilities. However, research on pragmatic abilities and their predictors in MS is scarce. The aim of this study is to investigate whether social cognition or psychosocial functioning predicts pragmatic abilities in MS, and whether persons with MS differ from healthy individuals in their pragmatic abilities.

The participants ($n=14$) were assessed for pragmatic abilities (APACS), social cognition (SET), fatigue (FSS) and depression (CES-D). Due to COVID-19 concerns, 6 participants were tested online via Zoom, and the rest were tested in-person. In addition, 10 healthy individuals were assessed for pragmatic abilities. Multiple regression analyses were used to investigate whether social cognition (ToM, SET) or psychosocial functioning (fatigue, FSS; depression, CES-D) predicted pragmatic analysis in persons with MS. Independent samples t-tests were used to compare the groups' pragmatic abilities.

Over 70% of the persons with MS showed deficits in their pragmatic abilities. Deficits were found both for pragmatic production and pragmatic comprehension, although production was more impaired. Both social cognition (ToM) and psychosocial functioning (fatigue, depression), as well as education, were predictors for different measurements of pragmatic abilities. The MS groups

differed statistically from the group with healthy individuals regarding their pragmatic abilities, especially pragmatic production. The results of this study confirm previous results that persons with MS seem to have pragmatic deficits. The results also indicate that social cognition, psychosocial functioning, and education predict pragmatic abilities in MS. Further research with larger participant groups is warranted.

Submission ID: 35; Submission Group: Translation of New Rehab Knowledge into Practice; Submitter: Roshan das Nair
Developing and delivering a digital cognitive screening and rehabilitation programme for routine clinical use

Running title: Digital cognitive screening & rehabilitation

Roshan das Nair, Gogem Topcu, Jacqueline Mhizha-Murira, Shirley Thomas, Stephen Timmons, Jennifer Martin, & Nikos Evangelou on behalf of the NEuRoMS collective.

Cognitive problems affect 40-60% of people with MS (pwMS), and can have a negative impact on people's personal, social, and professional life. Although there is now some evidence to suggest that cognitive rehabilitation is effective in reducing the effects of these cognitive problems, they are not routinely delivered in MS clinics in the United Kingdom (UK). Reasons for this are myriad, and staffing shortages to deliver such an intervention is a key issue. Another problem is how to systematically identify people with cognitive problems, triage them according to need, and provide them with cognitive rehabilitation.

We developed an online technology (www.neuroms.org) that has screened >2500 pwMS in 3 UK MS clinics, with pwMS completing the cognitive screening on their electronic devices at home before their routine clinical appointments. We have been able to group people as having no, mild-moderate, and severe cognitive problems, and have developed an online cognitive rehabilitation intervention delivered by assistant psychologists for those with mild-moderate cognitive problems. We have chosen to offer the intervention to this group because (i) they are often not represented in cognitive rehabilitation research, (ii) they are most likely to benefit from it, and (iii) the online intervention may suit those who are in work or education (and cannot come into clinics for several sessions).

In this presentation, I will outline how we developed this online cognitive screening and rehabilitation programme, what we have learnt from the delivery of this programme over the last year (challenges and opportunities), and our plans to implement this programme to a wider number of MS clinics in the UK.

This project is funded by the National Institute for Health and Care Research (NIHR; RP-PG-0218-20002). Views expressed are those of the authors and not necessarily those of the NIHR or the Department of Health and Social Care.

Submission ID: 36; Submission Group: Multidisciplinary Rehabilitation in MS; Submitter: Marie Lynning
Prevalence of comorbidities in people with MS and exploration of associated factors

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Background and aim: With an aging MS population, a rise in the occurrence of comorbidities is seen. The prevalence of comorbidities in persons with MS (PwMS) has been studied previously, with heterogenous results depending on methods and criteria used. With this study we aimed to assess the prevalence of common chronic health conditions among PwMS in Denmark and to explore associations between comorbidities and background factors.

Methods: A questionnaire investigating the presence of 27 chronic conditions (other than MS) as well as socio-economic background factors was distributed to a sample of 6,785 persons with MS (PwMS) from the membership base of the Danish MS Society. We collected 3,114 full responses. Multiple logistic regression was carried out for each individual comorbidity with age, gender, and education level as independent variables.

Results: Prevalence of any comorbidity (out of the 27 specified conditions) was 75.8%. Most common comorbidities were hypertension (25.1%), hyperlipidemia (18.4%), allergy (18.2%), back/spine disorders (17.9%), and osteoarthritis (17.9%). Regression analyses showed that most comorbidities were associated with age. Whereas most somatic diseases were associated with higher age, an inverse relationship with age was seen for mental disorders as well as for allergy and migraine. Several conditions, such as osteoporosis, migraine and irritable bowel syndrome, were associated with female gender, while diabetes, cardiovascular disease, and tinnitus were associated with male gender. A number of conditions which are commonly linked to lifestyle, such as diabetes and chronic lung disease, were associated with lower level of education.

Conclusion: Comorbidity is highly prevalent in PwMS. Results indicate that increasing age predicts many comorbidities, but that it also may play a protective role in some comorbidities. Moreover, the results are in line with existing knowledge regarding how gender and education level associate with certain diseases or disease patterns in the general population.

Submission ID: 37; Submission Group: Multidisciplinary Rehabilitation in MS; Submitter: Marie Lynning Resilience as a predictor of treatment burden in persons with multiple sclerosis and comorbidities

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Background and aim: Multimorbidity is a topic of increasing interest in the research area of Multiple Sclerosis (MS), and many persons with MS (PwMS) and comorbidity struggle with a high burden of treatment (BoT). Research points to patients' lack of resources as an important predictor of a high treatment burden. However, the association between BoT and resilience in PwMS requires further investigation. This study aimed to investigate whether resilience predicts BoT in PwMS and comorbidity.

Method: An online survey was sent to 1721 PwMS who had in a previous survey stated that they had one or more chronic comorbidities. In total, 1163 persons (68 %) responded. Burden of treatment was measured via the Multimorbidity Treatment Burden Questionnaire (MTBQ). Resilience was measured via the Connor-Davidson Resilience Scale (CD-RISC-10). Backwards stepwise logistic regression analyses were applied to predict the impact of

resilience on burden of treatment. Control variables applied in the model were self-rated health, number of chronic conditions, number of contacts to the healthcare system, number of medical treatments used, perceived emotional support from relatives, age, education level, and employment status.

Results: 27% of respondents had high treatment burden according to the MTBQ. Average resilience score on a scale from 0 to 40 was 25.5. When controlled for possible confounders, resilience (OR=0,94 $p < 0,001$) was significantly associated with a high burden of treatment. Thus, each one unit increase in resilience score is associated with a 6% decrease in the odds of having a high treatment burden. All control variables except number of conditions and employment status were significantly associated with BoT in the regression model.

Conclusion: The results indicate that resilience is an important personal trait to reduce the treatment burden for PwMS and comorbidity. Nevertheless, resilience is not the only variable associated with high BoT.

Submission ID: 38; Submission Group: Multidisciplinary Rehabilitation in MS; Submitter: Marie Lynning Profiling of people with multiple sclerosis via cluster analysis

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Background and aim: Interventions for people with MS (PwMS) may target sub-groups based on criteria such as age, MS subtype or disability level. With this study we wished to explore whether and how PwMS can be profiled in a meaningful way, based on a range of MS-specific and socio-demographic characteristics.

Methods: Cluster analysis was conducted using background data from a large cross-sectional multimorbidity survey among 3,114 PwMS. Seven socio-demographic variables were included in the analysis along with MS subtype, MS duration, DMT status, and 17 symptom level variables. Multiple Correspondence Analysis (MCA) was carried out initially to reduce dimensions, followed by a k-means analysis to define clusters.

Results: Five clusters/groups were identified. First and second groups consisted of relatively young people; the first was the least affected by MS out of all the groups in terms of symptom severity, employment status, etc. The second younger group had the highest levels of fatigue, cognitive impairment, depression and anxiety out of all groups, and had considerably lower employment status and lower level of education compared to the first group. Third group was average on most measures and mildly to averagely affected by MS in terms of symptom levels. Fourth and fifth groups were older but differed in terms of symptom levels and disability level. Group four was less affected by symptoms compared to group five, who had highest average levels of many symptoms, including walking impairment, fine motor and sensory problems, spasticity, bladder and bowel dysfunction and sexual dysfunction.

Conclusion: We identified five distinct clusters among PwMS based on a range of socio-demographic and MS-specific information. The results indicate that cluster analysis may be a useful tool to identify sub-groups among PwMS as it can allow for more complex relationships between background factors to be considered.

Submission ID: 39; Submission Group: MS Rehabilitation within and across the ICF Domains; Submitter: Cecilie Thruue
Patients with early phase relapsing remitting multiple sclerosis show substantial deficits across physical functional, cognitive- and patient reported outcomes compared to age- and gender matched healthy controls
Running title: Deficits in early multiple sclerosis

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Introduction: Not much is known about the consequences of multiple sclerosis (MS) in the very early phases of the disease course - especially not across physical functional, cognitive, and patient-reported outcomes. Therefore, the aim of the present study was to compare physical- and cognitive function and patient-reported outcomes asking about health-related quality of life (HRQoL) and physical activity in patients very early in the disease course with MS and matched healthy controls.

Methods: This cross-sectional study included 84 patients very early in the disease course of MS (≤ 2 years from diagnosis) and 84 age- (± 5 years) and gender matched healthy controls. All participants underwent a comprehensive test battery including physical functional, cognitive, and patient reported outcomes.

Results: Differences between groups was observed across all domains. The most pronounced deficits in early MS patients, compared to controls, were related to physical functional outcomes. Relative deficits in walking capacity were in the range 13-33% (Timed 25-Foot Walk Test, Six Spot Step Test, Six Minute Walk Test), 10% for upper limb function (Nine Hole Peg Test), 24% for aerobic fitness level, 13% for Baecke Sport Index, and 26% for physical activity level. Smaller however significant reductions were present for memory with deficits in the range 5-12% (Selective Reminding Test). No significant reductions were found regarding attention and processing speed (Symbol Digit Modality Test and Paced Auditory Serial Addition Test). HRQoL was found to be reduced $\sim 10\%$ (SF36 health survey).

Discussion and conclusion: Patients very early in the disease course with MS show substantial deficits in the physical functional domain, moderate deficits in the cognitive domain of memory, and a reduced HRQoL. Early detection of impairments seems crucial to optimize both pharmacological and non-pharmacological MS treatment strategies and highlights the importance of early initiatives aimed at preserving and/or building up reserve capacity, if possible.

Submission ID: 40; Submission Group: Application of Current Technologies in MS Rehabilitation; Submitter: Giacinto Barresi

ENACT-VR: A Virtual Reality Setting for Investigating Eye-Hand Coordination in Multiple Sclerosis

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Abstract

The ability to manipulate various objects is crucial for engaging many aspects of everyday life. Among the processes underlying such an ability, eye-hand coordination is clearly compulsory for smoothly controlling hand movements based on visuospatial cognition. Overall, the eye directs the attention to stimuli (or stimuli attract our mental focus) and is used to help the brain understand where the body is in space, enabling dexterous hand motions oriented towards a goal. However, impaired eye-hand coordination means you struggle with even the simplest activities of daily living (ADLs). Considering how conditions like Multiple Sclerosis (MS) can have detrimental effects on our eye-hand coordination, this paper proposes a technological solution for investigating such a process, providing clinicians and researchers with further diagnostic and prognostic data (possibly leading to the selection and the design of effective and efficient rehabilitation procedures). Specifically, the relationship between symptoms like cerebellar tremor – in this case, in terms of upper limbs intention tremor – and the eye-hand coordination can be studied during repetitive motor tasks requiring pick-and-place actions. The same tasks can also be performed for enabling rehabilitative procedures for the recovery of both motor and cognitive capabilities in people with MS. According to these goals, one of the activities of the ENACT Project (funded by Fondazione Italiana Sclerosi Multipla and Istituto Italiano di Tecnologia) is dedicated to the user-centered design and development of a virtual reality setting for investigating the eye-hand coordination in MS. The ENACT-VR setting provides the clinicians with a fully customizable interactive environment for engaging the patients in repetitive motor tasks based on exergames that can also be enriched by biofeedback features (for increasing the user engagement through dual tasks) according to medical requests on user data collection or user training. Feasibility and pilot studies on this environment will be presented.

Keywords: multiple sclerosis, cerebellar tremor, upper limb, virtual reality, eye-hand coordination, exergame

Submission ID: 41; Submission Group: Promising Technologies that can Help Advance MS Rehabilitation; Submitter: Costanza Iester

Resting-state functional connectivity through fNIRS in healthy subjects and people with multiple sclerosis

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Resting-state functional connectivity (RSFC) has been mainly investigated with functional Magnetic Resonance Imaging

(fMRI). It is known in the literature that RSFC is altered in certain neurodegenerative diseases, such as multiple sclerosis (MS). Functional near-infrared spectroscopy (fNIRS) may be an alternative tool for the analysis of RSFC. In this study, we aimed to identify RSFC by fNIRS in both healthy control and people with MS (PwMS). Currently, 11 control subjects and 8 PwMS were recruited. The experiment consisted of 15 minutes resting-state during an fNIRS recording. The change in oxy-hemoglobin concentration was recorded through 44 measurement channels. For each subject, channel signals belonging to the same Brodmann area were averaged, obtaining 18 regions of interest. Then, the correlation matrix was calculated for each subject. The results showed that in the control group there is a strong inter-hemispheric correlation specific to homologous areas, with clusters in prefrontal, sensorimotor, and associative areas. On the contrary, PwMS generally lost or reduced some correlations compared to the control group. In particular, PwMS had connections between motor areas and parietal areas significantly inferior to the control group. Moreover, the homologous areas of the two hemispheres had a lower connection in PwMS. However, some correlations, mainly involving frontal areas, were significantly higher in PwMS than in the healthy one. This behaviour suggests compensatory activities following possible myelin damage. Impaired RSFC can lead to inadequate performance of daily life tasks. Thus, by exploiting the advantages of fNIRS, such as portability, noiselessness, and robustness to motion, it might be possible to acquire RSFC concurrently with motor and/or cognitive tasks to investigate its relationship with the respective behavioral data.

Submission ID: 42; Submission Group: Application of Current Technologies in MS Rehabilitation; Submitter: Gaizka Loyola

Blended rehabilitation programs are as effective as face-to-face only programs

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Background: As health authorities regulations during the Covid-19 pandemic were changing, rehabilitation delivery was adapted from a pre-pandemic fully face-to-face delivery to virtual blended programs. Our objective was to compare the effectiveness of the different delivery methods of physiotherapy used before and during that period.

Methods: Delivery was organized in three different categories: 1) pre-pandemic (FF3): face-to-face physiotherapy program 3 times per week; 2) intra-pandemic (V2F1): virtual 2 days / face-to-face 1 day; 3) post-pandemic (V1F2): virtual 1 days / face-to-face 2 days (2022)). All included patients had EDSS 6.5 or above and rehabilitation lasted 4 months. Pre- and post-intervention values of the following tests were obtained: Tinetti Test (TT), 10 meters

walking test (10MWT), and Berg Balance Scale (BBS). Intergroup a non-inferiority approach was used with a minimal clinically significant difference was established for each test: 1) 20% for 10MWT, 2) 3 points for BBS, and 3) 1 point for TT. Between-groups we use an ANOVA to determine if there are differences between the means obtained in the three groups.

Results: One hundred fifty-six people were included (FF3 (n=55), V2F1 (n=58), V1F2 (n=43)). Mean (standard deviation) age in years was: V1F2 53.0 (10), V2F1 50.0 (8.5), FF3 53.8 (11.2). Median EDSS was V1F2 4.0 (IQR 3.0), V2F1 5.0 (IQR 2.0), and FF3 4.0 (SD 1.45). All intragroup analyzes were statistically significant, showing improvements at end of each intervention: BBS 46.5%/55.2%/43.6%; 10MWT 39.5%/46.6%/30.9% and TT 44.2%/41.4%/36.4%. No significant difference between-groups were observed for any of the outcomes (ANOVA): BBS p=0.25, 10MWT p=0.11 and TT p=0.49.

Conclusions: No differences in effectiveness were observed between the three delivery modality programs. Blended programs could be an option in specific settings when face-to-face delivery is not available / advisable. Further studies with improved designs are warranted to confirm these findings.

Submission ID: 44; Submission Group: Multidisciplinary Rehabilitation in MS; Submitter: Lucia Ventura
Comparing the effects of common exercise-based interventions for subjective and objective fatigue in people with multiple sclerosis: a randomized controlled pilot trial

Running Title: Exercise for fatigue, mobility and QoL in MS

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Abstract

Fatigue is one of the most disabling symptoms of people with multiple sclerosis (PwMS), affecting the activities of daily living, motor function, and social life. While scientific evidence supports exercise therapy as a safe and effective tool to counteract fatigue impact on PwMS, firm indication is lacking on which exercise programs are most effective to manage fatigue in this population. Therefore, we aimed at evaluating subjective fatigue in PwMS and identifying which protocol is capable to positively impact on patient's function.

Design was set as a parallel, 4-armed randomized pilot trial. Twenty-nine PwMS with fatigue as their main complaint were assessed for fatigue impact via Modified Fatigue Impact Scale (MFIS) and Scoring Forms for Multiple Sclerosis Quality of Life (MSQoL-54), mobility, strength, cardio-fitness, and mood before and after completing one of the following 8-week (2-session/week) interventions: aerobic reconditioning, strength training, aerobic plus strength training (combined) and global rehabilitation.

Repeated-measures ANOVA with corrected pairwise comparisons was employed to test for changes in the clinical/functional outcomes.

No adverse events and/or relapses were reported during any of the interventions. Within-subjects comparisons showed significant changes for: MFIS_total following aerobic (-17.25 pts, $p=0.001$) and combined (-15.5 pts, $p=0.004$), MFIS_physical following aerobic (-9.5 pts, $p=0.003$) and combined (-9.75 pts, $p=0.003$), MSQoL_physical_health following aerobic (+12.93 pts, $p=0.006$) and combined (+13.32 pts, $p=0.005$), MSQoL_physical_function (+2.55 pts, $p=0.007$) and MSQoL_energy_fatigue (+1.32 pts, $p=0.028$) were found increased only after combined. Significant changes in mood were also observed after aerobic (-4.5 pts, $p=0.012$) and combined (-6.5 pts, $p=0.001$). Only global rehabilitation was associated to increased comfortable (+0.20 m/s, $p=0.006$) and fast (+0.34 m/s, $p=0.001$) walking speed.

These preliminary data introduce superiority for aerobic and combined aerobic-strength training over the other interventions on MS-related fatigue and fatigue-related quality of life.

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Submission ID: 46; Submission Group: Translation of New Rehab Knowledge into Practice; Submitter: Michela Ponzio

Work-related difficulties in persons with multiple sclerosis
Short title: Work and disability

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Background: Literature shows that work maintenance is central in order to guarantee social participation of persons with disability. Identifying potential sources of difficulties is key to design interventions aimed at facilitating their work maintenance and career development.

Aim: To describe the work-related difficulties and their determinants in workers with multiple sclerosis (w-MS)

Methods: 234 w-MS working in Italy participated in a cross-sectional study carried out in 2021-2022. Participants completed a self-assessment online questionnaire that collects socio-demographic,

clinical and work-related data alongside several validated scales: fatigue (Visual Analog Scale); mood disorders (Hospital Anxiety and Depression Scale); social support (Multidimensional Scale of Perceived Social Support) and quality of life (EQ-5D). Work-related difficulties were assessed using the Multiple Sclerosis Questionnaire for Job, analyzing three main aspects: physical, mental health-related and workplace-related difficulties through linear regression models.

Results: The multivariate regression models showed a negative impact of clinical variables, such as high disability ($\beta=3.72$, $p<0.001$) and fatigue level ($\beta=1.99$, $p<0.001$), on physical health-related difficulties, while a positive effect was noted for good quality of life ($\beta=-4.01$, $p<0.001$). For mental health-related difficulties we found a negative strong impact produced by mood disorders (anxiety, $\beta=11.29$, $p<0.001$ and depression, $\beta=12.21$, $p<0.001$, respectively) and high fatigue level ($\beta=1.23$, $p=0.004$), while an improvement was observed in presence of good quality of life ($\beta=-2.71$, $p=0.001$). Finally, high fatigue level ($\beta=2.43$, $p<0.001$) and presence of clinically significant depression ($\beta=14.36$, $p<0.001$) emerged as potential determinants of work-related difficulties.

Conclusion: As MS affects the central nervous system, it has a high probability of negatively impacting cognition, ambulation, coordination, strength, and fatigue, with potential negative effects on performance of essential job functions, motivation to continue employment, and quality of life. The evidence produced could be useful to plan multidisciplinary interventions targeting single areas where the most severe problems are experienced.

Submission ID: 47; Submission Group: Multidisciplinary Rehabilitation in MS; Submitter: Jonathan Hostyn
Impact of psychiatric conditions on burden of care in an MS Center

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Abstract

Background: Reportedly, burden of care for inpatients at the Melsbroek MS-Center can be high while the patients' physical needs are limited whereas their needs at the psychosocial level demand a lot of attention. The occurrence of psychiatric conditions in this population have not been systematically studied. If these conditions prove to impact burden of care importantly, the monitoring of psychiatric conditions should be part of hospitalization policy.

Objective: to test a simple, brief screening procedure to detect the occurrence of psychiatric conditions and their consequences to intensity of care in an MS-hospital setting.

Methods: At four different moments separated by 10-week intervals, the hospital population was screened for psychiatric conditions that are most prevalent in neurological hospitals according to literature. In each patient, psychologists clinically judged the presence of different mental health or brain-related conditions (maximum of two) and rated their impact on intensity of care on a 4-point scale. To facilitate judgements, only broad DSM-5 main categories of psychiatric conditions were used and burden of care

was judged only quantitatively, that is, impact scores were defined as the amount of additional clinical attention the patient needed because of psychiatric conditions.

Results: 57% of an average of 82,5 hospitalized patients suffered at least one psychiatric condition with impact on intensity of care. Personality disorders were most common, followed by cognitive disorders without behavioral problems. By far, cognitive disorders had the highest impact on intensity of care.

Conclusion: A brief screening of our MS-hospital population for psychiatric conditions with clinically significant impact on intensity of care showed that these conditions are common and, therefore, should be part of hospitalization policy. Based on both frequency and impact score, cognitive and personality disorders proved to have the highest impact on burden of care. Methodological aspects of this exploratory study are further discussed.

Submission ID: 48; Submission Group: Translation of New Rehab Knowledge into Practice; Submitter: Nele Vanbilsen

Walking to music and metronome ticks at high and low tempi in persons with progressive MS: preliminary findings

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Background: Walking dysfunctions are prevalent in persons with MS (PwMS), even more in progressive subtypes. The use of auditory stimuli is feasible in people with mild MS (PwMS) and may maximize rehabilitation outcomes. We investigated if progressive PwMS are able to synchronize gait to beats in music and metronomes during walking and its effects on perceived cognitive and physical fatigue.

Methods: Participants walked to music and metronomes at preferred walking cadence (0%), -8%, -4%, +4% and +8%), while synchronization (Resultant Vector Length (RVL)), spatiotemporal gait parameters (cadence, speed, double support and stride length) and self-reported outcomes (concentration to synchronise and fatigue) were measured. To examine adaptability and to adjust for possible auditory processing delays, tempi higher or lower than preferred cadence were included.

Results: 10 HC's and 9 progressive PwMS were included (age median=49.4, EDSS (median=4.4), gait speed (median=0.84),

cadence (median=100.25)). All participants synchronised, yet HC's synchronised more consistently ($p = 0.007$). Better synchronization was found for metronomes (RVL=0.83) compared to music (RVL=0.69) ($p=0.003$). Participants were able to adapt speed and cadence ($p < 0.001$) to the various tempi. Less double support was needed for higher (mean=-2.52) compared to lower (mean=1.86) tempi and was higher for metronome (mean=1.81) compared to music (mean=-2.23) ($p=0.002$).

Perceived physical and cognitive fatigue were significantly higher for walking to metronome compared to music. Higher perceived concentration to synchronise was reported for music ($p < 0.001$), and was higher for patients compared to HC's ($p=0.002$).

Conclusion: Progressive PwMS were able to synchronize to both stimuli but better to metronomes, and alter their cadence and speed to the various tempi. Higher double support was needed for lower compared to higher tempi. The results indicate that walking to music and metronomes is feasible in progressive PwMS, however, tempo should be adequately considered for balance (double support) and safety.

Submission ID: 49; Submission Group: Promising Technologies that can Help Advance MS Rehabilitation; Submitter: Laura Bonzano

A multimodal approach to investigate the microstructural integrity and effective connectivity of inter-hemispheric fibers in people with multiple sclerosis

Running title: Structural and functional callosal integrity

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Demyelination causes axonal conduction deficits in people with Multiple Sclerosis (PwMS). The Corpus Callosum (CC) is commonly affected in MS; thus, the study of interhemispheric information transfer through callosal fibers is of great interest. Diffusion Tensor Imaging (DTI) demonstrated reduced CC structural integrity, related to cognitive and sensorimotor deficits on the basis of the CC region involved. Transcranial magnetic stimulation-electroencephalography (TMS-EEG) co-registration allows to measure effective connectivity because the activation evoked in the target area spreads to connected regions, and TMS-evoked potentials (TEPs) can be measured with high temporal resolution.

We developed a new multimodal methodology to investigate callosal microstructural integrity and effective connectivity in PwMS.

Twenty healthy controls (HC, mean age 34 years) and twenty-six PwMS (no clinical relapse in the previous 12 months, minimal-moderate disability, mean age 38.5 years) underwent DTI and TMS-EEG with stimulation of the left and right primary motor cortices (M1).

From DTI, fractional anisotropy (FA), mean diffusivity (MD), axial diffusivity (AD) and radial diffusivity (RD) were calculated in three CC regions: genu, body, and splenium.

A complex TEP response was found in both groups; at early latencies, a positive component peaking over contralateral frontocentral sites was detected (M1-P15).

White matter integrity was lower in PwMS than HC in all CC regions.

Interestingly, M1-P15 latency in PwMS was related to the microstructural integrity of the CC body. RD, which is associated with demyelination, was positively related with M1-P15 latency: the higher the RD, the longer the latency of M1-P15. Conversely, the higher the FA, the shorter the latency of M1-P15.

This innovative multimodal approach could provide a tool to monitor treatment effects with potential translation into clinical practice. Our methodology could help shed light on the consequences of myelin degradation and the neuro-anatomical substrates of sensorimotor impairments in MS, giving important hints for rehabilitation.

Submission ID: 50; Submission Group: Promising Technologies that can Help Advance MS Rehabilitation; Submitter: Massimiliano Pau

Safety and Tolerance of Immersive Virtual Reality in people with Multiple Sclerosis: a posturographic analysis

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Background: In recent years, immersive Virtual Reality (VR) gained popularity as rehabilitative tool for several neurologic conditions, including Multiple Sclerosis (MS). However, there are evidence that exposure to VR can disrupt the sensory system, leading to several negative side effects such as disorientation, nausea, dizziness, loss of balance, etc., commonly defined as “cybersickness”. To date, no information is available about the magnitude of such effects in people with MS (pwMS).

Aims: To assess safety and tolerance of immersive VR through: 1) postural sway analysis to verify the existence of balance impairments consequent to a game session and 2) self-report measures of cybersickness

Methods: Postural sway, quantified by processing center of pressure (COP) time-series acquired during upright stance in presence and absence of visual input, was investigated for 33 pwMS (mean age 43.9, mean EDSS 3.3). Measurements were performed before

and after a game session carried out in seated position using a commercial immersive VR system and at 10 minutes follow-up. Sway parameters included: sway area, COP path length, COP displacements and velocities. Participants were also administered the Simulator Sickness Questionnaire (SSQ) before and after the VR experience.

Results: In presence of visual input, a trend of increase for most sway parameters after the VR session was observed, but such effect was not statistically significant. Interestingly, when visual input was removed, COP Path Length and velocity were found significantly reduced after the VR session. SSQ score significantly increased after the VR experience, however no serious side effects were reported.

Conclusions: Short bouts of immersive VR appear well tolerated by pwMS. The slight increase of postural sway observed under eyes open condition seems not sufficient to increase the risk of falls. A sort of acute positive effect associated with the VR session was present when pwMS were tested with eyes closed.

Submission ID: 51; Submission Group: MS Rehabilitation within and across the ICF Domains; Submitter: Andrea Giordano

Needs of people with primary progressive multiple sclerosis (NIPS) – a scoping review

Running Title: A review on the needs of people with primary progressive MS

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Abstract

Background: About 10-15% of people with multiple sclerosis (MS) have a primary progressive disease course (PPMS). The mean age of onset is approximately ten years later than relapsing-remitting MS, and very limited immunotherapeutic and evaluated management options exist. This mirrors a substantial psychological and physical burden for people with PPMS (pwPPMS). Evidence about the needs of pwPPMS is scarce. The NIPS project

aims to address these needs. As a preparatory step, we performed a literature review to identify the studies reporting on the needs of pwPPMS.

Methods: We performed a scoping review to map the existing literature guided by the Arksey & O'Malley framework. We searched MEDLINE, EMBASE, PsycINFO, and PsyINDEX from inception to 30 September 2022. The search terms included the population of pwPPMS in combination with terms related to their perspectives and experiences on their disease. We included primary research reporting on the needs of pwPPMS. We appraised quality of evidence using different tools according to the different study designs.

Results: From 3721 initial identified records, we included six studies. Of these, 4 (67%) were qualitative studies, and two (33%) were mixed methods conducted in UK and US between 2011 and 2022. Identified needs pertain to information (e.g. medical), self-management (e.g. physical and psychological), health care (e.g. psychosocial support), and financial issues (e.g. insurance coverage), and vary across disease trajectory. For qualitative studies quality ratings ranged from 4/9 to 8/9, and for mixed-methods studies from 3/7 to 5/7.

Conclusion: Despite the importance of this topic, only a few research results have been published targeting the needs of pwPPMS. No interventions to empower and support pwPPMS are available, and more research is needed to address patient information gaps in PPMS and to set-up an intervention development agenda.

Submission ID: 52; Submission Group: Multidisciplinary Rehabilitation in MS; Submitter: Claire Dolan
Exploring the cognitive trends of the MS population attending a single-centre MS Unit in Ireland
 Researcher-C Dolan (Principle) & Dr S Hynes

Introduction: Multiple Sclerosis (MS) impacts the central nervous system. Over 9,000 people in Ireland are impacted by MS. Cognitive impairment (CI) affects up to 70% of People with MS (PWMS) resulting in domain-specific deficits rather than uniform global cognitive decline. Common deficits include changes in speed of information process, attention and memory. Executive functioning deficits can occur in advanced progressive stages. CI in MS can impact quality of life, engagement and employability. Best practice guidelines for cognitive care recommend baseline cognitive screening, reviews and access to specialist cognitive interventions including Occupational Therapy (OT).

The overall aim of this research is to evaluate the impact that the OT service has on the provision of cognitive care for PwMS.

Objectives:

1. To define current service provision in the area of cognitive care.
2. To compare current cognitive care with cognitive care provided prior to inception of OT service.

Method: This study will take a cross-sectional design. Data will be collected from a single neurorehabilitation service in an acute hospital in Ireland. A data collection tool was designed to capture demographic and cognitive data of participants. This tool was piloted on 20 participants and required changes were made.

Following this, a random sample of 140 participants were identified from two time points. Time 1 (n=70): current cognitive care. Time 2 (n=70): prior to the inception of the OT services. Data shall be analysed to identify current service provision, the MS population currently receiving care, and differences, if any, in the care provided across the two time points.

Results: This study is in the initial phase of data collection. Results will be shared with clinical staff in order to support quality improvement and the development of cognitive care pathways. A manuscript will be prepared for publication based on the results of the research.

Submission ID: 54; Submission Group: Application of Current Technologies in MS Rehabilitation; Submitter: Maria Jesus

Instruments to assess gait in individuals with Multiple Sclerosis: A systematic review

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Abstract

Background: Gait impairment are considered a significant cause of disability and are a clinical feature of Multiple Sclerosis. For this reason, their regular assessment is essential for better management and treatment and to evaluate the effectiveness of rehabilitation.

Objective: The aim of this study is to know what instruments are available in the literature to assess gait in patients diagnosed with MS.

Data Sources and Searches: A complete literature search was conducted in MEDLINE, Web of Science, Embase, and Scopus, following Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA). The study protocol was registered at the International Prospective Register of Systematic Reviews (PROSPERO).

Study Selection: The authors selected studies written in English and representing validation of gait assessment tools exclusively for adults with a diagnosis of MS.

Data Extraction and Quality Assessment: Two authors independently extracted the data for reliability, measurement error, validity and assessed methodological quality using the COnsensus-based standards to select health Measurement Instruments (COSMIN).

Data Synthesis and Analysis: All authors performed data synthesis to determine the level of evidence per measurement property per tool.

Results: The search identified 556 studies. After removing duplicates and articles that did not meet the criteria, 38 studies remain. In this studies were identified 25 instruments for measuring gait in people with MS. There are five categories of the most commonly used instruments (performance-based, patient-reported, clinician-reported observer-reported, and biomarker outcome).

Conclusion: There are countless instruments (PerFOMs, PROMs, ClinROMs, ObsROMs, and Biomarker Outcomes) that allow evaluating gait in different ways and contexts. It is necessary to know which measures exist and choose the best ones that suit the environment and the objective. This work concludes that the

T25FW, 6MWT, MSWS-12, and wearable, wireless and inertial sensors appear to provide gait assessments as they have high-reliability evidence.

Keywords: Multiple sclerosis, gait, walking, assessment

Submission ID: 55; Submission Group: MS Rehabilitation within and across the ICF Domains; Submitter: Rita Bertoni
Changes of upper limb function after rehabilitation in Persons with Multiple Sclerosis

Running title: Upper limb rehabilitation in MS

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Introduction: There is increasing interest in rehabilitation of the upper limb (UL) in persons with Multiple Sclerosis (pwMS), but the effectiveness of these interventions is still debated. We inquired on changes in UL-function after arm rehabilitation in a wide sample of PwMS, both across disability levels and MS types.

Material and methods: We collected the Nine hole peg test (NHPT) and the Box and blocks test (BBT) from 215 pwMS, mean (SD) age 54.92 (11.69) years, mean EDSS 6.15 (1.55), mean disease duration 19.37 (10.73) years, who underwent a rehabilitation intervention for improving UL-function.

Pre-post data were analysed with paired t-tests or paired Wilcoxon tests. Effect sizes (ES) were investigated with Cohen's D or Wilcoxon ES test. Analysis was carried out for the dominant and non-dominant side, EDSS level (mild:0-3.5; moderate: 4-5.5; severe: 6-6.5; severe-non-ambulant: 7-8.5) and the type of MS (RR-PP-SP).

Results: In the whole sample, we found differences after treatment ($p < 0.001$) with moderate effects on the NHPT (ES 0.38 (CI: 0.22-0.51) dominant; 0.41 (CI: 0.25-0.56) non-dominant) and the BBT (0.56 (CI: 0.43-0.72) dominant; 0.57 (CI: 0.46-0.69) non-dominant). On the NHPT, the EDSS-mild responded well to rehabilitation (ES: 0.66 (CI: 0.29-0.87) dominant; (0.71 (CI: 0.38-0.88) non-dominant), EDSS-moderate had weak ES, while no differences were found for the dominant side of the severe, and the severe-non-ambulant group. The RR-group had good ES for both sides and the PP-group for the non-dominant side. On the BBT, the EDSS-mild showed a good ES for the dominant side (0.52 (CI: 0.09-0.85) with no difference on the non-dominant side ($p = 0.27$); all disability levels and MS types showed small to moderate effect sizes for both sides.

Conclusions: Rehabilitation for the UL-function in PwMS was more effective at the milder disability levels and for the RR-type. Overall, rehabilitation appeared more effective for gross movements, while for fine hand function there were small or no effects for higher disability and progressive types.

Submission ID: 56; Submission Group: MS Rehabilitation within and across the ICF Domains; Submitter: Uğur Ovacik

Does Perceived Performance Reflect Upper Extremity Capacity in People with Early Multiple Sclerosis?

Objective: The aim of our study was to examine the upper extremity (UE) function, which is often overlooked, in early-stage people with Multiple Sclerosis (pwMS) who are thought to have minimal or no involvement.

Methods: Thirty-two pwMS (EDSS ≤ 2.5 , getting full points from ABILHAND, and those who did not report problems in daily living activities for UE) were included. pwMS were evaluated with 'Nine Hole Peg Test (NHPT)' and 'Minnesota Manual Dexterity Test (MMDT)' for unilateral and bilateral function, 'Hand Held dynamometer' for grip strength (GS) and 'aesthesiometer' for two-point discrimination (TPD) sense. Except for bilateral UE function, all evaluations were repeated twice in both the dominant (dom.) and non-dominant (non-dom.) extremity, and the mean score was recorded. The results of pwMS were compared with thirty-two healthy controls (HC).

Results: The scores of the dom. and non-dom. extremity in pwMS were follows as; for NHPT 19.77 ± 2.05 s, for GS 26.8 ± 8.01 kg, for TPD 4.37 ± 0.97 mm; for NHPT 20.88 ± 3.01 s, for GS 25.96 ± 8.64 kg; for TPD 4.21 ± 0.87 mm. The scores of the dom. and non-dom. extremity in HC were follows as; for NHPT 17.06 ± 1.87 s, for GS 28.72 ± 6.50 kg, for TPD 3.87 ± 1.03 mm; for NHPT 18.2 ± 1.97 s, for GS 27.48 ± 7.33 kg, for TPD 3.75 ± 0.98 mm. The MMDT scores of pwMS and HC were 54.65 ± 16.0 s and 44.38 ± 5.43 s, respectively. There was a significant difference between the groups dom. NHPT ($p < 0.001$), non-dom. NHPT ($p < 0.001$), MMDT ($p = 0.001$) and non-dom. TPD ($p = 0.048$) scores.

Conclusions: The results of our study show that although pwMS seem to be sufficient to perform activities of daily living for the UE, their capacities begin to be affected from an early period according to functional evaluation. EDSS and ABILHAND scores may be misleading, as UE involvement does not seem to be reflected in activity yet in early-stage pwMS.

Submission ID: 57; Submission Group: Promising Technologies that can Help Advance MS Rehabilitation; Submitter: Fausto Panizzolo

Experience of a hip passive assistive device in the treatment of MS patients

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Multiple sclerosis (MS) patients display a reduction in independence and quality of life caused by gait alterations associated with the disease. For this reason, it is evident that the rehabilitation processes can play an important role to improve gait in patients affected by MS. In the present study, we aimed to investigate the effect of a passive orthosis assisting hip flexion in the treatment of MS patients. The effects were evaluated in different ways: 1) Two patients underwent 3D gait analysis, walking with and without the orthosis (acute effect); 2) Two groups of patients ($n = 4$ for each group) underwent a rehabilitation protocol of 10 sessions, including 40 mins of physiotherapists' manipulation, 40 mins of exercises and 20 mins of walking. One group conducted the walking part using the orthosis and the second one without (training effect

in hospital); 3) Two patients underwent a 4-week customized remote training program (training effect at home). The training had a duration of ~30 mins and was executed via remote telemonitoring, it involved dynamic exercises and walking wearing the assistive device. Patients evaluated with gait analysis displayed an average increase in speed (+13,4%) and cadence (+7,4%) while walking with the orthosis with respect to not using it. Patients undergoing the traditional rehabilitation protocol improved their baseline walking speed by +3,0% at session 10 with respect to session 1, and those who used the assistive device by 12,3%. Lastly, patients who underwent remote training program showed an increase in distance covered by 15,3% (10 MWT) and of 11,0% in stability (BBS) comparing their performance before starting the training protocol. Although only on few subjects and therefore needed to be confirmed by further studies, these results seem to indicate an interesting potential for the applicability of the used assistive passive device in the MS' treatment.

Submission ID: 58; Submission Group: Application of Current Technologies in MS Rehabilitation; Submitter: gözde deniz ünal

Instrumental measurement of functional gait assessment during single and dual tasks in mildly disabled persons with multiple sclerosis

Zeynep Beylik, Özge Ertekin, Zuhul Abasıyanık, Gözde Deniz Ünal, Turhan Kahraman, Serkan Özakbaş

Objective: We aimed to assess Functional Gait Assessment (FGA) in persons with multiple sclerosis (pwMS) with a mild disability using wearable gait sensors under single and dual-task conditions and to compare gait parameters with healthy controls (HC). Secondly, we investigated the relationship between gait parameters, falls, and perceived dual-task difficulties in pwMS.

Methods: Subjects performed FGA consisting of 10 conditions with three wearable gait sensors (opal APDM) under single and dual-task conditions, and dual-task cost (DTC) was calculated. The test was also scored observationally by the assessor. We measured perceived dual-task difficulties using Dual Task Impact on Daily-Life Activities Questionnaire (DIDA-Q) and documented fall history in the last six months. A 2×2 mixed model ANOVA was used to compare differences in subtests of FGA and single- and dual-task conditions between pwMS and HCs.

Results: 16 pwMS (mean EDSS: 1.09) and 17 age-matched healthy controls (HCs) were recruited. There was no difference between groups in the observational assessment of all FGA subtests under both single and dual-task conditions. However, pwMS showed poorer performance in subtests of walking with eyes closed (speed, double support, stride length, swing phase), walking backward (stride length), crossing an obstacle (duration), and pivot turning (duration) during the instrumental assessment. Significant differences were found between task conditions (single vs dual) for all participants. Non-significant scores were found for the group*condition factor. DTC was significantly different between the two groups only in the steps subtest. A greater number of falls was related to poorer performance in walking backward and walking with head turns ($r=-0.494$ to -0.499). DIDA-Q correlated with most of the subtests of FGA ($r=-0.548$ to -0.901).

Conclusion: This study suggests that instrumental assessment of FGA discriminates pwMS from HCs even in individuals with no to mild disabilities. Walking with head turns might be a target for fall prevention strategies.

Keywords: multiple sclerosis, dual-task, gait, functional gait, falls

Submission ID: 59; Submission Group: Promising Technologies that can Help Advance MS Rehabilitation; Submitter: Edwin-Roger Meza-Murillo

Background: In recent years, the evidence supporting the benefits of robotic rehabilitation in people with multiple sclerosis (MS) has been growing. However, whereas a number of studies have shown data on physical improvement, the impact of robotic rehabilitation on fatigue and quality of life still needs to be evaluated. The aim of this study was to evaluate the longitudinal changes in fatigue and quality of life that occur in patients with MS who carry out a robotic gait training (RAGT).

Methods: In this experimental single-arm (non-randomised) study we included patients with MS with an expanded disability status scale (EDSS) score between 6.0 and 7.0. Patients were prospectively followed up after starting RAGT, which included 12 one-hour training sessions over 4 weeks, three times a week.

Patients were assessed at the beginning and the end of the intervention using the Hospital Anxiety and Depression scale (HADS-A, HADS-D), the MSQol Physical and Mental subscales (MSQol-PH, MSQol-MH), and the Modified Fatigue Impact Scale (MFIS). Paired t-tests were used to assess intragroup differences. The RAGT device used in this study was the Atalante self-balancing walking system from Wandercraft (France).

Results: Fourteen people with MS were included (6 female; mean age [standard deviation, SD]: 53.1 [SD 7.8] years). Thirteen patients had progressive MS. Median EDSS score was 6.5 (range: 6.0-7.0) and mean disease duration was 18.7 (SD 8.9) years.

At the end of the RAGT intervention, patients showed significant improvements in HADS-A (mean change: 0.57 [SD 2.6], $p=0.01$), HADS-D (0.71 [SD 2.5], $p<0.01$), and MSQol PH (-4.0 [SD 11.7], $p<0.01$).

Conclusions: In people with MS and restricted walking ability, a 4-week RAGT intervention is associated with an improvement in several clinical domains, including depression, anxiety and quality of life. This needs to be evaluated in future randomised controlled trials.

Submission ID: 60; Submission Group: Multidisciplinary Rehabilitation in MS; Submitter: Andrea Giordano
Advance Care Planning in Multiple Sclerosis (ConCure-SM): an ongoing multicenter feasibility trial
Running title: Advance Care Planning in Multiple Sclerosis

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Abstract

Background: Multiple sclerosis (MS) is the most common cause of progressive neurological disability in young adults. The use of Advance Care Planning (ACP) for people with progressive MS (pwPMS) remains limited. The ConCure-SM project aims to assess the effectiveness of a structured ACP intervention for pwPMS consisting of a training program on ACP for healthcare professionals (HPs) caring for pwPMS, and a booklet to be used during the ACP conversations.

Methods: A single-arm pilot/feasibility trial with nested qualitative study is being conducted involving pwPMS, their significant others, and HPs from six MS and rehabilitation centers in Italy. The primary study outcome is completion of an advance care plan document in the six months following the intervention. Other outcomes include adverse events (AEs), a range of measures to capture the full process of ACP, quality of patient-clinician communication, and caregiver burden.

Results: Between March 2022 and February 2023, 111 pwPMS were screened, and 43 were excluded. Main reasons for exclusion were: severe cognitive compromise (n=16); distance from the center (n=11); relapsing MS (n=5); communication impairment (n=5); absence of the ‘surprise question’ or of any other ACP-relevant conditions (n=3). Of 68 eligible patients, 51 refused to participate. Seventeen pwPMS were included in the study (mean age 61 years [SD 8.1], 47% women). Of these, 11 pwPMS completed the advance care plan document (primary outcome). One serious AE and eight AEs were reported, all considered unrelated to the intervention. Recruitment will close in March 2023, follow up will end in August 2023.

Discussion: Results of our pilot/feasibility study will be available in autumn. Findings of the pre-recruitment stage, with 75% of the eligible pwPMS refusing participation, support our decision to adopt a multiphase design, and indicate the need of a systemic approach to ACP implementation in the Italian context.

Submission ID: 61; Submission Group: Promising Technologies that can Help Advance MS Rehabilitation; Submitter: Marie Lynning

Self-tracking in multiple sclerosis: App user statistics from a trial

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Background and aim: Self-tracking may help people with MS (PwMS) manage their disease and achieve healthier lifestyles. We developed a prototype app for self-tracking based on needs and wishes of PwMS. The aim of this sub-study was to determine how and how much the app was used during and after the trial period, based on user statistics from the app.

Methods: The self-evaluation module of the prototype app contained 48 measures, including symptom levels (of 23 different symptoms), physical activity levels, sleep levels, and general wellbeing. Some physical activity and sleep levels were measured via an activity tracker (Fitbit Charge 4). All other measures were self-evaluated. Fifty-eight participants with MS tested the app for 42 days. Participants were invited to continue using the app for two additional months. We used data from the app to assess frequency of overall use during and after the trial, and to assess which measures were most frequently tracked.

Results: During the first week the average proportion of participants who used the app (tracking at least one measure daily) was 90%. Use fell steadily to 70% in the final week. Post-trial user data showed a steep decline in use, and only two participants were using the app 25 days after the trial ended. Sleep and physical activity were the most frequently tracked measures, primarily via the Fitbit and secondarily self-reported. The most frequently tracked symptoms were fatigue, sensory disturbances, physical exhaustion, headache, and cognitive problems.

Conclusion: Results showed a high level of use of the prototype app during the trial and a steep decline in use post-trial. Sleep and physical activity were the most popular measures to track. The frequency of tracking of symptoms may give an indication of which symptoms have the largest impact in the daily lives of PwMS.

Submission ID: 62; Submission Group: Promising Technologies that can Help Advance MS Rehabilitation; Submitter: Matteo Moro

Markerless Motion Analysis in People with Multiple Sclerosis
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Abstract

Human motion analysis is a fundamental task in rehabilitation. It helps expert physicians to monitor motion patterns in people with

neurological diseases, *e.g.* multiple sclerosis (MS). Furthermore, it can be used to tailor appropriate rehabilitation treatments.

Due to their high level of precision, infrared marker-based systems (MoCap) are considered the gold standard in modern human motion analysis. However, they have limitations. In fact, they require many markers to be attached precisely to the body of the person resulting in a time consuming, cumbersome and operator-dependent process.

Recent advances on markerless pose estimation algorithms, based on computer vision and deep neural networks, are opening the possibility of adopting efficient methods for extracting motion information starting from common red-green-blue (RGB) video data. This leads to the question of whether markerless approaches can be adopted to accurately characterize human motion. Video-based techniques present many advantages with respect to marker-based systems. In fact, they are less expensive, fully automatic and less invasive, not affecting the naturalness of the motion. Furthermore, they can be used at home.

We implemented a markerless pipeline that takes as input RGB videos (single viewpoint for 2D analysis and multiple viewpoints for 3D analysis) and gives as output kinematic parameters. Here, in particular, we focused on gait analysis. We acquired and studied three different gait tasks (normal gait, tandem gait, toe walk) of 30 MS participants (22 females, 8 males, mean age \pm standard deviation (std): 39 ± 11 years old, mean disease duration \pm std: 8.7 ± 7.5 years, mean Expanded Disability Status Scale score [minimum, maximum]: 2.6 [0, 6]) and 30 healthy subjects with age and sex matched with people with MS.

We found encouraging results proving the ability of video-based methods to highlight differences in the kinematic parameters of people with asymmetric gait.

Keywords: Multiple Sclerosis, Video analysis, Deep Learning, Computer Vision, Gait Analysis

Funding information: This research was funded by Fondazione Italiana Sclerosi Multipla (FISM – 2019/PRsingle050) and by RAISE, NextGeneration EU (PNRR Italy, innovation ecosystems program).

Submission ID: 63; Submission Group: Multidisciplinary Rehabilitation in MS; Submitter: Claudio Marcello Solaro

Does the target NEDA comply with functional measure changes after 2 years in early phase of Multiple Sclerosis?

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Intruduction: Few studies investigated the longitudinal changes of functional measures in people with MS (PwMS) with low

disability. The aim of the study is to evaluate after two years of follow-up (2FU) the evolution of clinical and functional measures stratified for NEDA (no-evident-disease-activity)

Methods: We assessed PwMS at baseline and after 2FU: Six Minute Walking Test (6MWT), Timed up and Go test (TUG), Timed-25 Foot Walking (T-25FW), Fatigue Severity Scale (FSS), Twelve-Multiple Sclerosis Walking Scale (MSWS₁₂), Fullerton Advanced Balance-short (FAB-s), 9-Hole Peg Test (9-HPT), Manual Ability Measure-36 (MAM-36), Brief International Cognitive Assessment for Multiple Sclerosis (BICAMS).

Results: 57 PwMS were enrolled [baseline: 35F, mean age 38.97 (SD=10.76) years, mean disease duration 2.14 (SD=1.84) years, mean EDSS 1.41], 57 relapsing-remitting MS course; 2FU: mean EDSS 1.83]. At 2FU, 30 PwMS were NEDA (NEDA_{group}) while 27 not (noNEDA_{group}). In the NEDA_{group} the number of PwMS worsened: 14 at 6MWT, 9 at TUG, 13 at FSS, 14 at T-25FW, 9 at MSWS-12, 10 at FAB, 21 at 9-HPT, 5 at MAM-36, 12 at SDMT, 11 at CVLT-II, 8 at BVMT-R. In the noNEDA_{group} the number of improved: 9 at 6MWT, 12 at TUG, 14 at FSS, 11 at T-25FW, 10 MSWS-12, 8 at FAB, 12 at 9-HPT, 8 at MAM-36, 10 at SDMT, 14 at CVLT-II, 9 at BVMT-R.

Conclusions: Overall, 29 MS subjects classified as NEDA showed a decrease of function in at least one domain at 2FU. Several subjects showed an improvement underline the importance of an extensive clinical evaluation beyond the EDSS.

Submission ID: 64; Submission Group: Promising Technologies that can Help Advance MS Rehabilitation; Submitter: Amy Webster
RiMS Conference 2023 Abstract

Investigating immersive virtual reality in upper limb rehabilitation in multiple sclerosis: preliminary results from a feasibility, randomised controlled study

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Background: Virtual reality (VR) and Gamification have the potential to become valuable methods for promoting motivational, engaging, and long-term exercise for people with multiple sclerosis (MS). However, there are few studies investigating immersive VR for upper limb rehabilitation/exercise, therefore refined protocols involving VR within MS are lacking and overall inconsistent.

Aims: To investigate the feasibility of an eight-week intervention of co-produced VR games delivered using the Oculus Quest 2 headset for improving the upper limb function of people with MS.

Methods: A randomised controlled feasibility trial was conducted. Participants were randomised to either an intervention group consisting of 30 minutes of VR co-produced games, twice/week, for eight weeks, or to a control group of usual care. Participants were recruited from the NHS and third sector organisations. Feasibility data collected included: recruitment rate; adverse events; adherence and drop-outs. Outcome measures included: nine-hole peg

test; hand grip strength, Action Research Arm test, ABILHAND questionnaire, and Spasticity-related Quality of Life 6-Dimensions instrument. The intervention group completed the USE questionnaire to explore usefulness, satisfaction and ease-of-use of the co-produced games and semi-structured interviews were performed with a sub-set of participants to explore the acceptability and views of the intervention.

Results: To date 16 participants [(VR intervention (n=10), Control group (n=6)] have been enrolled in the study (11 females, 5 males; aged 32–66 years; 9 relapse-remitting, 6 secondary progressive MS, and 1 primary progressive MS). One dropout was recorded in the Control group due to scheduling difficulties. Preliminary adherence to the intervention is an average 90.6% (SD: 11). Participants have reported increased fatigue (n=1) and arm discomfort (n=1) however there have been no other adverse events such as cyber-sickness reported.

Conclusions: This study is ongoing and results will be available on completion (April 2023).

Submission ID: 65; Submission Group: Multidisciplinary Rehabilitation in MS; Submitter: Rachele Di Giovanni
Development of the Heat Sensitivity Impact Questionnaire (HSI-Q): an ongoing validation study

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Introduction: An estimated 60–80% of People with MS (PwMS) have been reported as being sensitive to environmental heat. Clinically, increased body temperature in PwMS can result in experiencing a temporary worsening of clinical signs and neurologic symptoms (Uhthoff's phenomenon). There is a lack of validated tools to assess the patients' perspective on heat sensitivity in this population. Through consensus conference of expert and PwMS and content validity analysis, we developed the Heat Sensitivity Impact Questionnaire (HSI-Q).

The aim of the study is to validate and test the psychometric properties of the HSI-Q in a sample of PwMS.

Methods: HSI-Q (38 items) was administered to a preliminary sample of PwMS. We assessed criterion validity, using a general question ("are you heat-sensitive?"), and construct validity, analysing the correlations (Spearman rank correlation coefficient) between HSI-Q total score and EDSS, Modified Fatigue Impact Scale (MFIS) and Multiple Sclerosis Walking Scale-12 (MSWS-12). We reported the correlation between HSI-Q total score and 2 Minute Walk Test (2MWT), Timed Up and Go (TUG) on a subgroup of PwMS.

Results: 70 PwMS completed the HSI-Q (38F/32M, mean age 51.32(10.62) years, mean disease duration 13.90 (9.90) years, mean EDSS 5.68 (1.70), 30 RRSM, 23 SPSM, 17 PPSM). Scores obtained: HSI-Q tot 3.99 (2.58), general question 5.97 (3.02), MFIS 34.09 (20.49), MSWS-12 33.94 (19.52), 2MWT 83.4 (54.85), TUG 22.54 (17.11).

Total HSI-Q score showed high correlation ($r=0.644$, $p<0.000$) with the general question "are you heat-sensitive?", low correlation with EDSS ($r=0.294$, $p=0.013$), moderate correlations with MFIS ($r=0.497$, $p<0.000$) and MSWS-12 ($r=0.430$, $p<0.000$).

Regarding the subgroup of 50 PwMS, no significant correlations were found between HSI-Q total score and 2MWT and TUG.

Conclusion: The preliminary assessment of HSI-Q validity showed high criterion validity and moderate construct validity. This is an ongoing study and the sample of PwMS will be implemented in the upcoming months.

Submission ID: 66; Submission Group: Multidisciplinary Rehabilitation in MS; Submitter: Davide Cattaneo
Effects of voice rehabilitation on acoustical parameters in People with Multiple Sclerosis

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Background: People with Multiple Sclerosis (PwMS) often suffer from alterations in voice intensity and quality, which can be quantified by means of acoustical parameters. To date, the effects of treatments on voice intensity have been addressed. However, little is known about its impact on voice quality and stability.

Objective: This study was designed to compare voice quality following two forms of treatment.

Methods: In this secondary analysis of a previous randomized controlled trial on voice intensity, PwMS were randomized to the LSVT-LOUD[®], and conventional treatment (ACTIVE) group and received 16 treatments (4 sessions/week) lasting 45 minutes.

A subsample of 15 (ACTIVE) and 10 (LSVT) subjects, having good data quality, were re-analysed for the present investigation. The new outcomes investigating voice quality and stability were the Cepstral Peak Prominence Smoothed (CPPS) and Noise-to-Harmonic Ratio (NHR) in monologue. Mann-Whitney test was used to assess statistically significant between group differences in change scores (Post-Pre values).

Results: At baseline, the mean (\pm standard deviation) sample age was 56.9 ± 9.5 years with an EDSS score of 7.3 ± 1.1 points. PwMS showed abnormal performance when compared to normative data with median acoustic values of 6.99 dB [I quart=6.52; III quart=7.77] for CPPS, 8.63 dB [I quart = 6.62; III quart=10.22] for NHR.

We did not find a significant between-group median difference of change scores (LSVT=0.6 dB [-0.20; 0.58], ACTIVE=0.26 dB [-0.74; 0.61], $p=0.86$) for CPPS and for HNR (LSVT=1.99 dB [-0.57;3.03], ACTIVE=0.82 dB [-0.38; 1.35], $p=0.33$).

Conclusion: PwMS showed alterations in voice quality, and stability. Compared to our previous study, it seems that LSVT improves voice intensity but does not impact on parameters related to voice quality.

Submission ID: 67; Submission Group: Multidisciplinary Rehabilitation in MS; Submitter: Rachele Di Giovanni

Activity and efficacy of radial shock wave therapy in reducing spasticity in people with Multiple Sclerosis

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Introduction: Spasticity is frequent in People with Multiple Sclerosis (PwMS). Stretch reflex can be studied using surface electromyography (sEMG). Radial shock wave therapy (RSWT) has been used to treat spasticity in neurological conditions in few studies.

The study aims to evaluate RSWT efficacy in treating spasticity in PwMS and the effect on spasticity patterns at sEMG.

Methods: Inclusion criteria: MS diagnosis, age > 18, MAS ≥ 1 of plantar flexors.

Assessments: Modified Ashworth Scale (MAS), Medical Research Council (MRC), Numeric Rating Scale (NRS) for spasticity, NRS for pain, sEMG (stretch reflex), Global Perceived Effect (GPE).

The sEMG patterns evaluated before and after the treatment were: activity in dynamic phase (DSR-alone); activity in dynamic and static phase (DSR+SSR); spastic dystonia (SD), activity in dynamic and static phase (SD+DSR+SSR); SD and activity in dynamic phase (SD+DSR); noEMG activity.

Treatment: 4-session, 1-week interval. Each session: 2000 shots, frequency of 4 Hz, pressure of 1.5 Bars.

Results: 23 PwMS: 9F/14M, mean age 52.13 [SD=8.68] years, mean EDSS 5.39 [SD=1.41], mean disease duration 14.17 [SD=1.41] years, 9 RRMS, 9 SPMS and 5 PPMS course. Muscles treated: 17 right and 15 left plantar flexors.

Muscles sEMG patterns before RSWT: 36 DSR-alone, 30 DSR+SSR, 26 SD+DSR+SSR, 4 noEMG.

Scores before RSWT: MAS 1.66 [SD=0.66], MRC 4.44 [SD=0.9], NRSpain 1.16 [SD=2.68], NRSspasticity 4.13 [SD=4.11]. After RSWT: MAS 1.34 [SD=0.66], MRC 4.59 [SD=0.87], NRSpain 0.19 [SD=1.05], NRSspasticity 2.70 [SD=2.97].

After RSWT: 33 DSR-alone, 26 DSR+SSR, 22 SD+DSR+SSR, 15 noEMG.

Activity measured at DSR during stretch reflex before RSWT was 20.35 [SD=13.73] uV, while it was 17.11 [SD=16.40] uV after treatment. MAS ($Z=-3.435$, $p=0.001$), MRC ($Z=-2.014$, $p=0.044$), NRSpain ($Z=-3.112$, $p=0.002$), NRSspasticity ($Z=-2.915$, $p=0.004$) and activity at DSR ($Z=-3.464$, $p=0.001$) resulted statistically different between the two time points.

Mean GPE for subjective perception was 5.04 [SD=1.11]; 16 subjects perceived a benefit ($GPE \geq 5$).

Conclusion: RSWT is a new approach to treat spasticity in PwMS and sEMG could be a useful tool to assess sEMG patterns and treatment effect.

Submission ID: 68; Submission Group: Multidisciplinary Rehabilitation in MS; Submitter: Martha Ghijselings
Respiratory function pre- and post- COVID-19 infection in people with multiple sclerosis

Running title: Post-COVID-19 respiratory function in MS

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Introduction: The COVID-19 pandemic has resulted in increased respiratory infections worldwide. Respiratory infections are major causes of morbidity and mortality in multiple sclerosis (MS). The aim of this retrospective observational cohort study is to explore the impact of COVID-19 on pulmonary function in people with MS (pwMS).

Methods: Clinical data and pulmonary function test (PFT) results of pwMS who developed COVID-19 between March 2020 and August 2022 were collected at the Belgian National MS Center in Melsbroek. We compared PFTs performed as part of clinical follow-up prior to with PFTs after a PCR-confirmed COVID-19 infection. The following PFT parameters were extracted: history of smoking, respiratory comorbidities, BMI (body mass index), VC (vital capacity), FVC (forced vital capacity), FEV₁ (forced expiratory volume in one second), FEV₁/FVC ratio and PEF (peak expiratory flow). Clinical data include the date of COVID-19 diagnosis, age, sex, Expanded Disability Status Scale (EDSS) score, MS duration, clinical subtype at the time of COVID-19 diagnosis and COVID-19 severity.

Results: We have identified 62 people with MS (age 56 ± 12 years, 62% women, median EDSS 6.5) of whom 75.8% had a mild COVID-19 severity and 12.9% required hospitalization. Mean time from pre- and post-PFT to COVID-19 infection was 5 ± 3 and 3 ± 3 months, respectively. There were no significant statistical differences in PFT results pre- and post-COVID-19 infection. For VC and PEF, a clinically relevant deterioration (i.e. more than 10%) was found in 21% and 25.8% of the sample. Duration of MS explained 13.8% of this deterioration in VC and 22.8% of changes in PEF. Other clinical variables did not explain clinically relevant changes.

Conclusion: The majority of pwMS had mild COVID-19, which appeared to have a limited (non-significant) effect on pulmonary function tests within 3 months post-infection. Future research may explore the impact in severe COVID-19-infection and possibilities for rehabilitation.

Submission ID: 69; Submission Group: Multidisciplinary Rehabilitation in MS; Submitter: Erica Grange
Test-retest reliability and minimal detectable change of 9-Hole Peg Test, Box and Block test, Hand Grip Strength test and Manual Ability Measure-36 in moderate-to-severe upper limb impaired PwMS

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Introduction: In literature, no studies reported the test-retest reliability of the Box and Block Test (BBT), Hand Grip Strength (HGS) and Manual Ability Measure-36 (MAM-36) in people with Multiple Sclerosis (PwMS), while few studies reported the test-retest reliability of the Nine Hole Peg Test (9-HPT) in mild UL impaired samples.

The aim of the study is to evaluate test-retest reliability, precision and clinical important change of the 9HPT, BBT, HGS and MAM-36.

Methods: Subjects with MS were assessed through 9HPT, BBT, HGS and MAM-36 at baseline and after 7 days. Test-retest reliability was established by Intraclass Correlation Coefficient (ICC) analysis (ICC exceeding 0.9 indicate excellent reliability), precision was based on Standard Error of Measurement (SEM) and coefficient of variation (CV), and Minimal Detectable Change (MDC) was calculated.

Results: Fifty-seven PwMS were included [age: 51.95 (12.57); disease duration 15.60 (10.22); gender: 33 F and 24 M; disease course: 22 RR, 14 PP, 19 SP, EDSS 5.83(1.37)].

Measure scores as M(SD) at baseline(T0):9HPT_r 39.82(30.90), 9HPT_l 43.80(30.94) seconds; BBT_r 46.49(13.73), BBT_l 45.37(12.80) blocks; HGS_r 22.06(10.16), HGS_l 20.52(9.55) kg, and MAM-36 123.47(18.14). Measure scores as M(SD) after 1-week (T1): 9HPT_r 35.73(22.60), 9HPT_l 41.69(28.95) seconds; BBT_r 48.44(13.47), BBT_l 47.18(12.84) blocks; HGS_r 21.84(9.09), HGS_l 20.08(8.34) kg, and MAM-36 122.02(19.41).

ICC (95%CI), SEM, CV and MDC of the measures: 9HPT_r [ICC (95%CI)=0.937 (0.888-0.964), SEM=7.76 s, CV=8.76, MDC=21.5 s], 9HPT_l [ICC (95%CI)=0.948 (0.912-0.969), SEM=7.06, CV=8.68, MDC=19.56 s]; BBT_r [ICC (95%CI)=0.950 (0.909-0.971), SEM=3.07, CV 7.32, MDC=8.51], BBT_l [ICC (95%CI)=0.952 (0.914-0.973), SEM=2.81, CV=6.67 and MDC=7.78]; HGS_r [ICC (95%CI)=0.965 (0.941-0.980), SEM=1.90, CV=10.88, MDC=5.27], HGS_l [ICC (95%CI)=0.946 (0.908-0.968), SEM=2.22, CV=12.83, MDC=6.15]; and MAM-36 [ICC (95%CI)=0.927 (0.876-0.957), SEM=4.90, CV=4.13, MDC=13.59]

Conclusion: Overall 9HPT, BBT, HGS and MAM-36 showed an excellent test-retest reliability also in a sample of moderate-to-severe UL impaired PwMS.

Submission ID: 70; Submission Group: Multidisciplinary Rehabilitation in MS; Submitter: Catarina Martins

The impact of an integrative exercise program for people with multiple sclerosis on physical function: an exploratory study

The impact of exercise on physical function in people with Multiple Sclerosis

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Abstract

Problem: The growth of multiple sclerosis incidence has a significant influence on public health and economy in Portugal. It is important to found non-pharmacological therapeutic approaches.

Objective: To determine the effects of a 6-month integrative exercise program (IEP) on physical function outcomes in persons with multiple sclerosis (PwMS).

Methods: The sample, composed of 22 PwMS (17 females and 5 males), with ages between 30-66 years, was distributed in two groups, a control group (CG=8) and experimental group (EG=14). The participants, associates of the Sociedade Portuguesa de Esclerose Múltipla (SPEM), meet the following inclusion criteria (non-practitioners of regular exercise, not pregnant, PwMS with a score of 0-8 on The Extended Disability Status Scale (EDSS)). The IEP included 45 sessions (24 weeks) of aerobic exercise, strength, and mind-body techniques, with a frequency of 2 times per week (24 weeks).

Results: Intra-group significant changes were found in the EG on Chair Stand (39.1%, $p<0.001$), Chair Sit and Reach (181%, $p=0.031$), Back Scratch (91.5%, $p=0.031$), 6-Min Walk (19.0%, $p=0.001$), Fullerton Advanced Balance Scale (11.7%, $p=0.002$), Timed Up and Go Test (TUG) (-24.0%, $p=0.033$), Timed Up and Go - Dual Task (TUGDT) (-18.8%, $p=0.034$) and 25 Foot Walk (-20.2%, $p=0.016$). Inter-group analyzes revealed significant differences between groups due to the intervention in the tests Chair Stand (39.1% for EG and 0% for CG; $F(1,15) = 8.302, p=0.011, \eta_p^2=0.356$), Chair Sit and Reach (181% for EG and -55.1% for CG; $F(1, 18) = 5.310, p=0.033, \eta_p^2=0.228$); 6-Min Walk (19.0% for EG and -5.8% for CG; $F(1,15) = 9.358, p=0.008, \eta_p^2=0.384$).

Conclusion: The IEP promoted improvements in several components of physical fitness, including strength, flexibility, and cardiorespiratory fitness. This could help PwMS to be more independent in performing the daily activities and have a better quality of life.

Keywords: Multiple Sclerosis, Physical Function, Integrative Program, Combined Exercise

Submission ID: 71; Submission Group: MS Rehabilitation within and across the ICF Domains; Submitter: Erica Grange

Evaluation of work difficulties in MS subjects and its association with socio-demographic factors and performance measures

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Background: One of the social consequences of MS is the reduction of work activity that occur early in the disease course. The aim of the study is to investigate the frequency of work-related difficulties in workers with MS using the Multiple Sclerosis Questionnaire for Job Difficulties (MSQ-Job) and to evaluate the differences between subjects with job difficulties (wJD) and without job difficulties (woJD)

Methods: The study involved 2 Italian centres. Inclusion criteria: diagnosis of MS, age < 65, employed. Subjects were assessed through MSQ-Job, Work Productivity and Activity Impairment Questionnaire (WPAI), TUG, 2MWT, T25-FW, 9-HPT, HGS, MFIS-21, SDMT, Beck Depression Inventory (BDI-II), MSQoL-29, EDSS.

The sample was stratified based on MSQ-Job cut-off and divided into 2 groups (wJD vs. woJD).

Results: Eighty-one subjects were recruited: 33M, 48F, age 43.41(10.50)yrs, disease duration 9.90(8.10)yrs, education 15.26(4.17)yrs, mean EDSS 3.7(2.4), disease course: 71.6 %RR, 12.3%PP and 16%SP.

Twenty-one % of the sample had reduced working hours and 14.8% had to change work role in the last 6 months.

Clinical scales' score: MSQ-Job 13.74 (11.11), WPAI:MS 24.05 (26.49), SDMT 51.68 (12.07), BDI-II 7.65 (7.33), TUG 10.97 (8.25)s, T25-FW 7.28 (5.30)s, 2MWT 154.68 (65.78)m, MSWS-12 29.19% (26.19), 9HPT_R 32.46 (30.42)s, 9HPT_L 30.58 (20.58)s, HGS_R 26.72 (9.86)Kg, HGS_L 23.97 (11.39)Kg, MFIS-21 21.27 (17.45), MSQoL-29 66.85% (16.28).

Thirty subjects (37%) results at risk of job loss, based on MSQ-Job cut-off. The two groups differ for: sex, WPAI:MS, HGS, MFIS, BDI-II and MSQoL-29.

Stratifying the sample based on EDSS [EDSS ≤ 3.5 (52%) vs. EDSS ≥ 4 (48%)], 35.8% of subjects with EDSS ≤ 3.5 and 38.5% of subjects with EDSS ≥ 4 reported work-related difficulties (based on MSQ-Job cut-off).

Conclusion: Factors associated to risk of job loss are female gender, low work productivity, low handgrip strength, higher level of fatigue, depressive symptoms and lower quality of life. Clinical factors such as walking, balance, cognitive functions and disability level (EDSS) do not differ among subjects with and without job difficulties.

Submission ID: 72; Submission Group: Translation of New Rehab Knowledge into Practice; Submitter: Franca Tecchio

Fatigue relief in multiple sclerosis

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To support the recovery from fatigue of people with multiple sclerosis (PWMS), we consider that this condition includes imbalances

in brain processing, which can be balanced by targeted neuropsychological interventions, personalized in the dimensions of sensorimotor integration and metabolites that constrain brain plasticity, and enriched by neuromodulation. It means modifying, in our case by sending transcranial currents with non-invasive devices, the excitability of specific neural targets, thus changing the relationship with the connected brain areas, ultimately modifying the behavioral expression of the functions supported by the networks involving the neuromodulation target.

We will present how to personalize thought-training interventions such as Cognitive Behavioural Therapy (CBT) or Eye Movements Desensitization and Reprocessing (EMDR), which involve multiple sensorimotor channels to defuse brain short-circuits, depending on the individual metabolic profiling, releasing the brain's plasticity potential, and with neuromodulation. According to evidence-based medicine (GRADE) criteria, which rank efficacy together with negligible side effects, low-cost and user-friendly procedures, specific treatments with transcranial direct current stimulation (tDCS) are between moderately and highly recommended to relieve MS fatigue.

The present network will setup protocols for a fatigue-related pathway of diagnosis and rehabilitation with the aim to promote at national level homogeneous guidelines and treatment availability. The protocols will include monitoring of fatigue levels, levels of metabolic markers to personalize the interventions. The therapy strategy includes neuro-psychology, movement and neuromodulation interventions, with particular attention to tDCS.

We aim at: 1. algorithmic personalized protocol for fatigued PWMS; 2. construction of a database to monitor fatigue levels, metabolic and immune profile related to brain plasticity, and optional electrophysiological collections 3. monitoring of fatigue levels (mFIS) to update therapeutic protocols on the base of periodic outcome assessment.

Submission ID: 73; Submission Group: Multidisciplinary Rehabilitation in MS; Submitter: Ezgi Özbaş
Investigation of the reliability and validity of the community balance and mobility scale in people with multiple sclerosis

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Background: Balance disorders are among the most common symptoms in people with Multiple Sclerosis (PwMS), even in the early stages of the disease. On account of this, it is crucial to assess the balance in terms of social mobility and several dimensions. We investigated the reliability and validity of the Community Balance and Mobility Scale (CB&M), which we think can be utilized for this purpose.

Method: The study was included 18-65 PwMS (55 women, 10 men), aged 19-55 years. Test-retest, intra-rater, and inter-rater reliability, as well as Cronbach's alpha value for internal consistency, were all assessed in the CB&M reliability analysis. The construct

validity of the scale was investigated with hypothesis tests and the relationship between the results of the Timed Up and Go Test (TUG), Dynamic Gait Index (DGI), and Multiple Sclerosis Quality of Life Scale-54 (MSQoL-54) was evaluated. In addition, the Berg Balance Scale (BBS) was accepted as the gold standard and the criterion validity of CB&M was checked.

Results: In the analyses performed, CB&M was seen excellent internal consistency (Cronbach $\alpha=0.971$). In addition, the scale had excellent test-retest (ICC=0.995), intra-rater (ICC=0.993), and inter-rater (ICC=0.986) reliability. Furthermore hypothesis tests had an excellent correlation between CB&M and TUG, DGI, and EDSS ($r=-0.854$; $r=0.865$, $r=-0.831$, $p<0,001$, respectively). There was a moderate correlation between Physical Health Composite Score ($r=0.482$, $p<0,001$) and low-moderate correlation Mental Health Composite Score ($r=0,315$, $p<0,001$) with CB&M, which are sub-parameters of the MSQoL-54. Criterion validity indicated an excellent correlation between CB&M and BBS ($r=0.907$ $p<0.001$).

Conclusion: Our research has confirmed that the CB&M is a reliable and valid scale for multi-balance analysis in PwMS. We believe that the scale will contribute to the evaluation and treatment because it evaluates balance in a multidimensional way and comprehensively determines the mobility limitations that occur in PwMS' lives.

Keywords: Balance, Gait, Multiple Sclerosis, Reliability, Validity

Submission ID: 74; Submission Group: Multidisciplinary Rehabilitation in MS; Submitter: Merve Unal
Investigation of the relationship between verticality perception and mental rotation in people with multiple sclerosis

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Background: Tasks requiring mental rotation of the human body in space are known to activate regions involved in vestibular information in a large subcortical-cortical neural network, suggesting that the verticality perception, which requires vestibular integration, is involved in the control of mental rotation. Although different studies have shown that verticality perception and mental rotation are affected in people with multiple sclerosis (PwMS), the relationship between them has not been investigated. We believe that our study investigating this relationship will shed new light on the motor representation of MS.

Methods: The study was included 44 (28 women, 16 men) right-handed PwMS, aged 18-54 years. Mental rotation of the participants was evaluated with NOI Group-Recognise™ applications measuring reaction time and percentage of correct responses for right-left of hand, foot and neck. Verticality perception was assessed with the bucket test by looking at one of its sub-parameters, Subjective Visual Verticality (SVV). The mean of verticality deviation values in clockwise and counterclockwise directions were obtained in five trials.

Results: There was no significant correlation between percent correct responses of left hand and mean of SVV clockwise deviations ($r = -.019$ and $p = .199$). A moderate negative correlation was determined between percent correct responses of left foot and mean of SVV clockwise deviations ($r = -.449$ and $p = .002$). A moderate negative correlation was determined between percent correct responses of left neck and mean of SVV clockwise deviations ($r = -.327$ and $p = .03$).

Conclusion: The results of study showed that there may be a moderate relationship between subjective visual verticality and mental rotation in PwMS, despite the lack of a large sample size. Therefore, we think that exercise designs in which mental rotation is also activated in vestibular rehabilitation protocols may contribute to the development of the MS patients.

Keywords: mental rotation, multiple sclerosis, subjective visual verticality, verticality perception

Submission ID: 75; Submission Group: Multidisciplinary Rehabilitation in MS; Submitter: Elisa Gervasoni
A Comprehensive Picture of Functional Disorders in Non-Disabled People with Multiple Sclerosis: A Longitudinal Study

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Background: Functional disorders appear early in the course of the disease and develop gradually over time impacting on social participation and quality of life.

Objective: Investigating the progression of disability, walking, fatigue, manual dexterity, and cognition in a cohort of People with Multiple Sclerosis (PwMS) in the early stage of the disease.

Methods: We performed a longitudinal 2-year study to unravel functional disorders of 82 non-disabled PwMS with Expanded Disability Status Scale (EDSS) < 2.5 points, disease duration < 5-year, and aged (Mean ± Standard Deviation) 39.5 ± 10.6 years. Participants were assessed at baseline and after 2-year with clinical and instrumented evaluations. Data on disability and functional disorders were collected using EDSS, Six-Minute Walk Test (6MWT), Multiple Sclerosis Walking Scale-12 (MSWS-12), Fatigue Severity Scale (FSS), Nine Hole Peg Test (NHPT), Brief International Cognitive Assessment (BICAMS), while instrumented data were extracted from 6MWT using wearable devices.

Results: EDSS changed from 1.5 ± 0.7 points to 1.8 ± 0.9 points with 34% of PwMS showing deterioration beyond the Minimally Important Changes of deterioration (MIC_{det} EDSS = 1-point). Conversely, the 6MWT, FSS, and MSWS-12 did not change (6MWT from 559.35 ± 84.5m to 577 ± 93.5m, FSS from 3.3 ± 1.8

points to 3.1 ± 1.8 points, and MSWS-12 from 31.3 ± 15.3 points to 30.0 ± 14.9 points) with 10% and 11% PwMS showing walking deterioration beyond MIC_{det} (MIC_{det} 6MWT = 55m; MIC_{det} MSWS-12 = 6 points). We observed similar results considering instrumented variables: stride regularity (from 0.86 ± 0.07 [au] to 0.88 ± 0.08 [au]), antero-posterior gait symmetry (from 81.88 ± 6.60 [au] to 83.74 ± 6.06 [au]) and gait instability (from 0.69 ± 0.11 [au] to 0.74 ± 1.12 [au]). No relevant changes were observed for 9HPT and BICAMS.

Conclusion: Even if EDSS deteriorated over time, fatigue, cognition, and upper/lower limb functions were on average spared 2 years after baseline assessment. The large between-subject variability suggests the use of artificial intelligent techniques to predict subjects prone to deterioration.

Submission ID: 76; Submission Group: Application of Current Technologies in MS Rehabilitation; Submitter: Luca Prosperini

Home-based EXergames To improve cognitive functioning in Multiple Sclerosis: the EXTREMUS study

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Abstract

Introduction: Motor and cognitive dysfunctions are common and disabling symptoms in multiple sclerosis (MS) across all disease stage. Exergaming is an emerging tool in neurorehabilitation that incorporates goal-based training and gross motor exercise, thus having the potential for improving both cognitive and automatic components of motor control by exploiting adaptive plasticity.

Objectives: We tested the hypotheses that: (i) home-based exergaming (Wii balance board) has similar efficacy to working memory-based exercises (COGNI-TRAcK) on information processing speed (IPS), and (ii) superior efficacy on motor outcomes, as compared to a placebo-analogue intervention.

Methods: This was a multicenter, randomized, sham-controlled, single-blind, parallel arm study (ClinicalTrials.gov registration: NCT04169750). Patients with impaired Symbol Digit Modalities Test (SDMT), i.e. <5th percentile of normative value, were

randomized in a 1:1:1 ratio to an 8-week home-based training (five 30-min sessions per week) with commercial exergames [EXE] (intervention of interest), or adaptive COGNI-TRAcK [ACT] (reference comparator), or sham COGNI-TRAcK [SCT] (placebo-analogue intervention).

A post-intervention follow-up was done at week 16. The primary endpoint was the change at the SDMT.

Results: Out of 150 screened for eligibility, 92 patients (F=55, M=37) with mean age of 51.2 ± 14.1 years, disease duration of 14.8 ± 9.7 years, and median EDSS of 4.5 were randomized to EXE (n=30), ACT (n=31), SCT (n=31). Baseline characteristics were comparable across the three arms (p-values >0.25). At 8-week visit, SDMT improved with EX and AC versus SC (mean changes: +5.4, +6.0 and +0.6, respectively; $p < 0.05$ for both comparisons). Such improvement was roughly retained even at week 16, but between-arm comparisons were not longer statistically significant.

A clinically meaningful improvement of ≥ 4 SDMT points was more often observed with EXE (52%) and ACT (47%) than SCT (21%) ($p \leq 0.08$).

Conclusions: Our study provides class II evidence for the efficacy of home-based exergames as a single comprehensive approach to address MS-related cognitive and motor issues.

This study was supported by FISM — Fondazione Italiana Sclerosi Multipla — cod. 2017/R/22 and financed or co-financed with the ‘5 per mille’ public funding.

Submission ID: 77; Submission Group: Application of Current Technologies in MS Rehabilitation; Submitter: Johanna Jonsdottir RIMS Genova 2023

Impact of rehabilitation on physical activity behavior in persons with multiple sclerosis

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Background: People with multiple sclerosis (PwMS) are likely to be less physically active than the general population. It is unknown whether doing rehabilitation aimed at improving mobility changes physical activity behavior in pwMS.

Methods: Inpatients (N=27) and outpatients (N=18) (EDSS 3.5-7.0; mean \pm standard deviation age: 55.6 ± 11.6 years) undergoing rehabilitation were recruited. Participants wore a Fitbit Versa tracker for one week at the beginning (T0) and one week at the end (T1) of their rehabilitation period, recording (primary outcomes) daily steps, minutes of light physical activity (LPA), and of moderate-vigorous physical activity (MVPA). Clinical assessment: Godin Leisure-Time Exercise Questionnaire (GLTEQ), 2-Min Walking Test (2MWT) (T0,T1), Fatigue Severity Scale (FSS), Self-Efficacy in Multiple Sclerosis scale (SEMS) (T0,T1,T2). Inpatients did 2-3 rehabilitation sessions a week, while outpatients did 2 sessions per day. Change scores of primary outcomes were analysed between groups with T-tests.

Results: There were no differences in demographic and clinical characteristics between inpatients and outpatients, except in

EDSS level (5.06 vs 5.88, $p < 0.05$). At T0, the number of daily steps was 4441 ± 2469 for inpatients and 4958 ± 2629 for outpatients, well below recommended activity levels for PwMS. No significant changes were observed within-group (inpatients 4149 ± 2440 steps; outpatients 4812 ± 2390 steps T0-T1, $p > 0.05$) or between-groups ($p > 0.5$).

Inpatients performed 7.16 ± 15.0 minutes of moderate-vigorous activities daily and outpatients 17.8 ± 14.1 minutes, with a statistical difference between groups at T0 (p-value=0.027). At T1, no significant changes were observed within-group (inpatients: 9.9 ± 14.3 ; outpatients: 13.7 ± 16.6 minutes, $p > 0.05$) or between-groups (p=0.1).

GLTEQ (inpatients: 15.6 ± 18.0 ; outpatients: 22.14 ± 22.3 points), SEMS (inpatients: 40.9 ± 9.2 ; outpatients: 40.9 ± 10.8 points), 2MWT (inpatients: 86.5 ± 33.0 m; outpatients: 103.5 ± 45.3 m) and FSS (inpatients: 47.6 ± 16.0 ; outpatients: 44.8 ± 12.0) were similar between groups at T0 ($p > 0.05$) with no statistically different changes in either group at T1 ($p > 0.05$).

Conclusion: PwMS are less physically active than the general population and even when following a rehabilitation program they do not increase their physical activity levels. Physical therapists should be encouraged to counsel pwMS on ways to increase daily physical activity as part of rehabilitation delivery.

Considerations for paper

Introduction: Physical activity includes activities in daily life, such as activities done at work, in the home, to get from place to place, recreation activities, and exercise/sport, including also rehabilitation or exercises led by the physiotherapist.

PA can be light (sing a song), moderate (you can do the activity and talk, but not sing), strenuous/high intensity (you can only utter a few words while doing this activity) find ref, comes from the Loisin paper.

Findings of survey (Moumdjian 2022) showed that during the pandemic wearables were the most frequently used technology to support physical activity. Wearables are highly sensitive in detection of gait disturbances and fatigue in PwMS,31,32 and evidence of their use to sustain physical activity behavior is largely growing33; indicating that they can be a valuable addition to walking programs.

For discussion in article: The findings of a survey on physical activity behavior in persons with MS (Moumdjian 2022) indicate that PwMS could potentially favor walking programs aimed at increasing walking distance or intensity. . .combination of education, information provision and behavior change techniques (change wording a bit). Findings of survey (Moumdjian 2022) showed that during the pandemic wearables were the most frequently used technology to support physical activity. “Wearables are highly sensitive in detection of gait disturbances and fatigue in PwMS,31,32 and evidence of their use to sustain physical activity behavior is largely growing33; indicating that they can be a valuable addition to walking programs.”(mostly direct wording from article).

Silveira 2021, Rates, patterns and correlates of fitness tracker use among older adults with MS: “evidence-based behavioral interventions that utilize fitness trackers as a primary component for initiating and maintaining behavior change in conjunction with education and social support via behavioral coaches.”

Check papers: Jessica F. Baird, Katie L.J. Cederberg, E. Morghen Sikes, Stephanie L. Silveira, Brenda Jeng, Jeffer E. Sasaki, Brian M. Sandroff, Robert W. Motl, **Physical Activity and Walking Performance across the Lifespan among Adults with Multiple Sclerosis**, *Multiple Sclerosis and Related Disorders* (2019), doi: <https://doi.org/10.1016/j.msard.2019.07.003>

The relationship between moderate to vigorous physical activity (MVPA) and walking performance (6mwt) is strong among older adults with MS (60-79 yrs) but not among younger people with MS.

Self-efficacy and Physical and Cognitive Function in Older Adults with Multiple Sclerosis. Rachel E. Bollaert, PhD; Robert W. Motl, PhD

Submission ID: 78; Submission Group: Application of Current Technologies in MS Rehabilitation; Submitter: Matteo Bodrero

Objective and subjective evaluation of walking ability with the use of a passive brace for hip flexors in multiple sclerosis

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Background: Multiple Sclerosis (MS) affects the cognitive and motor domains. Muscle weakness often leads to abnormal gait. Several solutions are rising, including the possibility of using passive exoskeletons. The purpose of this study is to evaluate the effect of a passive exoskeleton for walking ability in people with MS (PwMS).

Methods: All subjects undergone a baseline evaluation comprising: the Multiple Sclerosis Walking Scale (MSWS-12), Modified Fatigue Impact Scale (MFIS) and the Symbol Digit Modalities Test (SDMT) for the cognitive status. Subjects were also assessed through the 2 Minutes Walking Test (2MWT), the Timed 25-Foot Walk Test (T25-FW), and a two-stage rating of perceived exertion (RPE) assessment without exoskeleton (T0) and with exoskeleton on (T1).

Results: We recruited 50 PwMS (27 F, 23M, age of 56.60 ± 8.97 years, 16 RR, 22 SP, 11PP, EDSS 5.84 ± 0.79).

There was no significant change between T0 and T1 at the T25-FW (T0: 15.71 ± 10.30 s; T1: 15.73 ± 11.86 s; $p=0.25$). A significant difference has been found in the 2MWT, observing that at T1 the walked distance was reduced (T0: 65.19 ± 23.37 m; T1: 59.40 ± 22.99 ; $p < 0.0001$). RPE behaved in different way from the 1st minute to the 2nd one during the 2MWT. Taking into account the first minute at T0 and T1, the perceived exertion at T1 was higher compared to T0 (T0: 11.52 ± 3.02 ; T1: 12.48 ± 2.75 ; $p=0.011$; Fig. 1C), while comparing the second minute, at T0 and T1, there was no significant difference. 72% of subjects reported a positive or neutral global perceived effect (GPE) of the exoskeleton. No significant correlation has been found between GPE and MSWS-12, MFIS, SDMT and demographic characteristics.

Conclusions: No fatiguing or negative effects have been experienced using the exoskeleton. Although the walking speed decreases, the overall perception of the subjects is positive. Further studies are

needed to evaluate the effect of the exoskeleton on the quality of the gait. After specific training.

Submission ID: 79; Submission Group: Application of Current Technologies in MS Rehabilitation; Submitter: Giacinto Barresi

User-Centered Design and Evaluation of Motor-Cognitive Exergames in Virtual and Mixed Reality for People with Multiple Sclerosis

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Abstract

Compliance of people with Multiple Sclerosis (MS) in the proper performance of motor-cognitive tasks for clinical assessment and rehabilitation can certainly be limited by factors such as the repetitiveness of the exercises. However, interactive environments based on virtual reality (VR, when the computer generates the environment experienced by the user) or mixed reality (MR, when real and digital elements coexist in the same perceived environment) can offer different solutions to engage and motivate patients, especially through game-like features (as in the approaches of serious games and gamification). In particular, an enactive logic of coupling perception and action (allowing the user to explore and control stimulus conditions, e.g., through biofeedback) can motivate people with MS in clinical exergames (games designed to promote exercise execution) without further fatiguing them. Nevertheless, such systems require an appropriate approach of user-centered design and evaluation to understand the unmet clinical needs and the actual capability of the proposed solutions to face them. In this study, we present the process that led from the analysis of the needs of people with MS to the design of two interactive settings (respectively, in VR and MR) and their preliminary evaluation in terms of usability and user experience. These interactive settings present upper limb exergames enriched with biofeedback features to obtain engaging dual-task features according to the perspective of the ENACT Project (funded by Fondazione Italiana Sclerosi Multipla and Istituto Italiano di Tecnologia) in collaboration with the Control and Computer Engineering Department of Politecnico di Torino. The games are currently being tested by people with and without MS to understand if they are subjectively acceptable and objectively beneficial in engaging the users. The results of the preliminary study are presented to highlight the successful synergy between experts from the clinical and technological domains in the context of user-centered design.

Keywords: multiple sclerosis, rehabilitation, virtual reality, mixed reality, dual-task, exergame, biofeedback

Submission ID: 80; Submission Group: Translation of New Rehab Knowledge into Practice; Submitter: Ellen Arntzen

The effect of exercise and physical activity-interventions on step count in individuals with multiple sclerosis: A systematic review and meta-analysis of randomized controlled trials

Running title: Effect of physical activity on step count in MS
Ellen Christin Arntzen, Britt Normann, Razieh Bidhendi-Yarandi, Marianne Sivertsen, Karina Knutsen, Stine Susanne Haakonsen Dahl, Maria Grytvik Hartvedt & Samira Behboudi-Gandevani

Abstract

Aim: This systematic review and meta-analysis aims to identify the effects of physical activity-interventions on step count in people with multiple sclerosis (pwMS).

Material and Methods: A systematic search of databases; PubMed (including Medline), Scopus, CINAHL and Web of Science studies (English) addressing effectiveness of physical activity-interventions on step count in pwMS from the inception to July 1st 2022. The data was extracted into extraction tables. Quality and risk of bias were appraised using The modified consolidated standards of reporting trials and Cochrane Risk of Bias tool. Pooled standardized mean difference (SMD) and 95% CI of step count before versus after treatment were estimated by the random effect model. The random-effects model and the Harbord test were used to explore heterogeneity between studies and assess publication bias. Sensitivity analysis examined reliability and stability of the results.

Results: Five randomized controlled trials (463 pwMS) were included. Participants (361 (77.9%) female/ 102 (22%) male) were randomly assigned to intervention (n=265) or control-group (n=198). The pooled mean (95% CI) age of pwMS in intervention and control-group were 52.4 (51.4, 53.5) and 47.8 (46.6, 49.1) years, respectively. The overall step count for pooled SMD of 0.13 (95% CI: -0.13,0.37) in intervention and 0.04 (95% CI: -0.06-0.26) in control-group, demonstrated no significant differences in SMD before and after physical activity, in both groups. No significant difference was found in the pooled SMD of step-count for intervention compared to controls (pooled SMD=-0.01, 95% CI: -0.20,0.18). Age, BMI, duration of disease and EDSS were not the potential sources of heterogeneity (all $p > 0.05$).

Conclusion: The results demonstrate no evidence to suggest that physical activity-interventions lead to increased number of steps per day in pwMS. Due to lack of studies examining this outcome, current evidence is still inconclusive, and demonstrate the need for studies that address and measure number of steps in pwMS.

Submission ID: 81; Submission Group: Promising Technologies that can Help Advance MS Rehabilitation; Submitter: Lasse Skovgaard
Self-tracking in multiple sclerosis – a mixed methods evaluation of a trial

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Background and aim: Self-care technologies may support patients with multiple sclerosis (MS) in their everyday disease management by enabling self-monitoring of various health indicators such as symptom levels and physical activity levels. The aim of this study was to assess the usefulness for people with MS of tracking self-selected MS- and health-related measures via an app for a period of six weeks.

Methods: An initial design and development phase was followed by a six-week testing phase including 58 test participants. The evaluation phase followed a sequential, exploratory mixed methods design, consisting of 14 interviews with test participants during the testing phase, followed by a survey among all participants after the testing phase to confirm and elaborate on the findings from the interviews. Interview data was analyzed through five-step thematic analysis, and survey data was analyzed descriptively.

Results: The results of the mixed methods study can be summarized in the following findings: 1) Use of the self-tracking tool assisted users in clarifying patterns regarding their symptoms, physical activity, sleep quality, and emotional well-being. 2) Tracking physical activity, and to some extent sleep, had a motivational effect on participants in relation to increasing activity and/or changing habits. 3) Data quality/accuracy was to many participants an important criterion for finding the app relevant. 4) The app may be a relevant tool to support dialogue between patient and health care professionals and/or play a role in peer-to-peer support.

Conclusion: The results of the present study indicate that self-tracking of symptoms, sleep, physical activity and other measures may contribute positively to everyday self-management among PwMS. Professional support in interpreting and acting upon data should be considered.

Submission ID: 82; Submission Group: Multidisciplinary Rehabilitation in MS; Submitter: Lasse Skovgaard
Development and evaluation of rehabilitative group singing among people with MS

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Background and aim: The involvement of music and arts in MS rehabilitation interventions is limited, but focus on possible gains from such involvement has increased over the past years. We aimed at developing and evaluating a rehabilitative group singing concept among people with Multiple Sclerosis (PwMS).

Methods: A trained choir leader, with experience from Parkinson choirs and lung choirs, completed an introductory course to MS at the Danish MS Rehabilitation Hospital. Specific rehabilitative target points and exercises were defined in collaboration with MS specialists. Two courses of 6 sessions and 25/22 participants, respectively, were completed. A few close relatives took part in the sessions. Evaluation of physical, psychological and social outcomes, integration of habits as well as practical circumstances was conducted through an online survey.

Results: Joint unison or polyphonic singing of well-known as well as new songs was combined with exercises supporting and stimulating breathing, fitness, stretching, posture, vocal strength

and range, coordination and dual-task. Special attention was paid to limited physical and cognitive energy among the participants and time for social interaction was secured.

The majority of the participants found sessions of 2 hours, including a 30 minutes social break, and a group size of 20-25 participants, appropriate. Many would have preferred 8-10 sessions in the course. Experienced outcomes with high prevalence were: Positive effect on MS-symptoms, quality of life and body awareness as well as integration of exercises in everyday life. Experienced outcomes with medium prevalence were: Positive effect on speech and singing voice. Further, the participants highly valued the social interaction developing in the group as well as the positive atmosphere and energy created by the joint engagement in a musical activity.

Conclusion: Rehabilitative group singing among people with MS may be a relevant way of combining relevant MS-targeted exercises, social interaction and motivational factors.

Submission ID: 83; Submission Group: Multidisciplinary Rehabilitation in MS; Submitter: Barbara Lewicka
Sexual dysfunction in Polish patients with multiple sclerosis

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Multiple sclerosis (MS) can affect sexual function both directly and indirectly. Sexual dysfunction (SD) in MS patients can be categorized as primary, secondary, and tertiary. The aim of the study was to assess the prevalence of SD at each level in the Polish population of patients with MS, and to identify associated factors related to the presence of these complications.

Methods: A total of 106 patients with MS (77 females) with a mean age of 42.5 ± 11.4 years were included. Multiple Sclerosis Intimacy and Sexuality Questionnaire 19 (MSISQ19), together with socio-demographic and clinical data, were used.

Results: Sexual dysfunction was reported in 43 patients (40.6%), including 23 (21.7%) patients with primary SD, 32 (30.2%) with secondary SD and 14 (13.2%) with tertiary SD. The most prevalent symptoms at each level of SD were orgasmic problems, spasticity and urinary incontinence or worries about sexual satisfaction of partners. The total score of MSISQ-19 and partial SD scores were significantly correlated with MS duration, present EDSS score and EDSS at diagnosis (all $p < 0.0001$). Moreover, SD was significantly associated with education level ($p < 0.05$), and age ($p < 0.001$). There was no significant relationship between anthropometrical status (BMI, FAT mass) and SD in MS patients.

Conclusion: According to this study, sexual dysfunction, especially secondary SD was one of the most prevalent problems among patients with MS. In addition, this study showed a

complex and multifactorial nature of the SD in MS patients. In order to provide appropriate treatment and management of SD, associated factors and their impacts should be considered.

Submission ID: 84; Submission Group: Multidisciplinary Rehabilitation in MS; Submitter: Kübra Turan
Acute Effects of Cognitive Fatigue on Balance in Patient with Multiple Sclerosis

Kübra Turan¹, Yeliz Salcı¹, Ayla Fil Balkan¹, Elçin Özçelik Eroğlu², Songül Aksoy³, Meryem Ashı Tuncer⁴

Purpose: To investigate the acute effect of cognitive fatigue on balance in patients with Multiple Sclerosis (MS) without cognitive impairment.

Method: A total of 50 MS patients, aged 20-50 years, without cognitive impairment, with an Expanded Disability Status Scale (EDSS) score of 0-4 were enrolled in this study. The patients were randomly divided into control and study groups. The study group received cognitive tasks which cause cognitive fatigue during 30-45 minutes while the control group was rested for 30 minutes. The cognitive fatigue was evaluated with Visual Analog Scale (VAS). Clinical balance tests were performed with Functional Reach Test (FRT) and the Single Leg Standing Test (SLST). Clinical Evaluation of Modified Sensory Integration and Balance Test (m(CTSIB)) with Computerized Static Posturography was used for laboratory balance test. All assessments were made twice, just before and after cognitive activities.

Results: It was found that the study group had cognitive fatigue according to VAS ($p < 0.001$). According to the m(CTSIB) results, a statistically significant difference was found between the two groups in the firm-eyes open, firm-eyes closed, foam-eyes open and composite score ($p < 0.001$, $p = 0.007$, $p = 0.005$, $p < 0.001$ respectively). When the outcomes of the clinical evaluation tests, the FRT and SLST, were compared between two groups, there was a statistically significant difference in both legs with eyes open and closed conditions ($p < 0.001$, $p < 0.001$, $p < 0.001$, $p = 0.004$, $p < 0.001$, respectively).

Conclusion: According to results of this study, which studied for the first time the acute impact of cognitive fatigue on balance in MS patients, cognitive fatigue can occur in patients without cognitive impairment and can have a negative impact on balance. Additional research is also required to examine the long-term effects on the other physical performances.

Keywords: Multiple sclerosis, cognitive fatigue, static balance, dynamic balance

Submission ID: 85; Submission Group: Multidisciplinary Rehabilitation in MS; Submitter: Ellen Arntzen
Feasibility and preliminary effects of a new intervention addressing sensory-motor function, physical activity and work in people with MS

Short title: Feasibility of a new intervention

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Background: Impaired sensory-motor function, reduced physical activity and unemployment are common challenges in persons with multiple sclerosis (pwMS), even in the early phases of the disease when disability is low. CoreDISTparticipation is a new, multidisciplinary intervention delivered across healthcare levels systematically addressing these elements. This study aimed to explore feasibility and preliminary effects of CoreDISTparticipation compared to standard care on barriers for employment, balance, walking, health related quality (HRQOL) of life and physical activity.

Methods: An assessor-blinded prospective randomized controlled pilot-study including 29 pwMS (EDSS0-3,5); randomly allocated to intervention-group (CoreDISTparticipation) (n = 15) or standard care (n = 14). CoreDISTparticipation: 1) Outpatient clinic; MS-nurse work-focused session and physiotherapist exploring balance. 2) Municipality; a digital meeting with pwMS, employer, MS-nurse and physiotherapist addressing employment and physical activity, four weeks indoor CoreDIST-balance training and four weeks outdoor CoreDIST-balance and endurance training (60 minutes x2/week). Assessments at baseline, weeks 5, and 10. Primary outcomes: Multiple Sclerosis Work Difficulties Questionnaire-23 (MSWDQ-23NV) and Six minute walk-test. Secondary outcomes: Trunk Impairment Scale-modified Norwegian Version, Mini-Balance Evaluation Systems Test (Mini-BESTest), Multiple Sclerosis Walking Scale-12 (MSWS-12), Multiple sclerosis Impact Scale-29 Norwegian version (MSIS-29NV), ActiGraph wGT3x-BT monitors, AccuGait Optimized force platform. The statistical analyses included repeated-measures mixed models performed in IBM SPSS Version 28.

Results: One person attended no post-intervention assessments and was excluded, leaving 28 participants in the study. Attendance was high; digital meeting (100%), indoor (85%) and outdoor sessions (57,29%). No serious adverse events were reported. The primary outcome MSWDQ-23NV demonstrated within-group differences from baseline to week 11 (mean difference 5.71 points, $P=0.004$; CI: 2.17-9.25). Mini-BESTest and MSIS-29NV demonstrated within-group differences. MSWS-12 showed between-group difference for group*time ($p=0.04$) at week 10. A tendency for improvement was found in the other outcomes.

Conclusion: CoreDISTparticipation is feasible and demonstrated within-group differences on barriers for employment, balance and HRQOL. A large scale study is needed.

Submission ID: 86; Submission Group: Promising Technologies that can Help Advance MS Rehabilitation; Submitter: Camilla Pierella
Personalized neuromotor rehabilitation of people with Multiple Sclerosis: from characterization to exploitation of residual sensorimotor abilities using a body-machine interface
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*equal contribution

70% of people with multiple sclerosis (PwMS) present upper limb dysfunction that can manifest bilaterally, most of them experience

problems with manual dexterity, bimanual coordination and activities of daily living. Rehabilitation is a key element to maximize the functional status of PwMS.

This work aims at facing such needs developing and validating a novel approach to neuromotor rehabilitation of PwMS based on Body-Machine Interfaces (BoMI). BoMIs explicitly takes subjects' impairments into account individualizing the rehabilitative interventions. Indeed, we proposed a hybrid BoMI that recorded movements of left and right upper-body, and electromyographic activity, and mapped them onto a lower dimensional control space used to control a cursor of a computer and design patient-specific exercises. Moreover, because of the complex nature of the body signals used by the BoMI and the way they are combined to carry out the rehabilitative task, we hypothesize that users will also gain more awareness of their body movements.

Subjects went through an intense training of six weeks and we assessed training-induced motor and proprioceptive changes with clinical tests, brain and cervical spinal cord MRI, and we also proposed an innovative proprioceptive test using virtual reality.

Because of their adaptive nature, BoMIs were able to benefit PwMS with different degrees of impairment adapting to their changing conditions. BoMI motor training improved the quality of their movements in terms of smoothness and control, which was confirmed by clinical tests. Interestingly the proprioceptive test highlighted the importance of the interaction between motor and sensory systems, with an improvement in upper limb position sense deficit following a complex motor training like the one with the hybrid BoMI.

This study is a first proof of concept of a novel class of highly adaptive, personalized devices to improve motor recovery and promote functional reorganization of body abilities in multiple sclerosis.

Submission ID: 87; Submission Group: MS Rehabilitation within and across the ICF Domains; Submitter: Felipe Balistieri Santinelli

Self-reported physical activity is correlated with walking capacity and walking fatigability in people with multiple sclerosis

Short title: Prolonged walking and physical activity in MS

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Introduction: It is hypothesised that walking fatigability (WF), a symptom of slowing down observed during the 6-minute walking test (6MWT), could influence the amount or intensity of physical activity performed by people with multiple sclerosis (pwMS).

Objective: To investigate the relationship of the 6MWT and walking fatigability with different domains of physical activity in pwMS with WF (MS-WF), non-WF (MS-NWF) and healthy controls (HC).

Methods: Twenty-two MS-WF (EDSS 4.7±1.1; 15F/7M), 21 NWF-MS (EDSS: 4.9±1.2; 15F/6M) and 21 HC (18F/3M) responded to the international physical activity questionnaire (IPAQ-long version) and performed the 6MWT. IPAQ was calculated in metabolic equivalent of task for moderate, vigorous and total physical activities domains. Total and minute-by-minute distances were recorded in the 6MWT, and the distance walked index from the last minute (DWI₆₋₁) was calculated for WF. Spearman's rank correlation, separately per group, was used to examine the correlation between IPAQ and total distance on 6MWT and DWI₆₋₁.

Results: Moderate and total physical activities were significantly moderately associated with the 6MWT (MSWF: rho=0.598, p<0.003 and rho=0.608, p<0.003, respectively; NWFMS: rho=0.564, p<0.008 and rho=0.628, p<0.002 respectively) and the DWI₆₋₁ (MSWF: rho=0.524, p<0.012 and rho=0.461, p<0.031 respectively; NWFMS: rho=0.441, p<0.045- moderate). No significant association was observed between moderate and total (HC) and vigorous activities (MS-WF, NWF-MS and HC) with the 6MWT and DWI₆₋₁.

Conclusion: Our results indicate that physical activity is similarly associated with walking capacity and WF. The lower levels of physical activity, normally observed among studies in pwMS, could be related to lower walking capacity (i.e., lower performance on 6MWT) and lower capacity to sustain walking performance over prolonged periods (i.e., lower values on DWI₆₋₁). Improving walking capacity and fatigability may consequently improve physical activity in pwMS and other factors associated as fatigue, quality of life and disability levels.

Submission ID: 88; Submission Group: MS Rehabilitation within and across the ICF Domains; Submitter: Felipe Balistieri Santinelli

Expanding the walking fatigability definition in people with multiple sclerosis: An exploratory study

Short title: Expanding walking fatigability concept in MS
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Introduction: Walking fatigability (WF) has been defined as a 10% decline in distance walked at minute-6 compared to minute-1 in the 6-minute walking test (6MWT) in pwMS, named distance WF (DWF). However, previous studies have shown that pwMS can present abnormal gait changes towards the end of the 6MWT, named biomechanical WF (BWF). Therefore, we hypothesize that

pwMS could behave differently during the 6MWT: no presence of DWF/BWF (NWF), only DWF or BWF, or a combination of both DWF/BWF.

Objective: To identify the hypothesized walking behaviours of pwMS during the 6MWT.

Methods: Fifty pwMS (EDSS-4.8±1.2, 33F/17M, 34RR/4PP/8SP) and 21 healthy controls (HC, 18F/3M) performed the 6MWT while wearing six APDM sensors to quantify gait parameters. Distance walked minute-by-minute (i.e., distance walking index-DWI) was used for DWF grouping. Absolute values and variability (coefficient of variation-CV) were calculated minute-by-minute for foot strike angle, toe-off angle, leg circumduction, and step duration for the strongest/weakest leg (SL/WL- defined by maximal voluntary contraction of leg extension). Significant variables found in a two-way ANOVA (group x timepoint- minute-1 x minute-6) were transformed into relative values: (min6-min1/min1)*100. Discriminative analysis (HC: average±2SD) was used to identify abnormal gait changes (i.e., BWF) in pwMS.

Results: pwMS walked less (359±245m) and presented lower DWI (-7.5±8.2%) compared with HC (593±135M; 0.2±10%). Foot strike angle (HC lower limit: SL- -15.43% and SW- -25.92%), foot strike angle-CV (HC upper limit-UL: SL- 62.5%), and step duration-CV (HC upper limit: SL- 38.52%) were used for discriminative validity, confirming different WF manifestations in pwMS: 17 pwMS presented BWF/DWF, 13 BWF, 5 DWF, and 15 NWF.

Discussion: Our preliminary results confirm our hypothesis of different manifestations of WF in pwMS. The definition of WF should be expanded, including anomalies in gait biomechanics. These results provided new insights for rehabilitation programs to address WF in a tailored manner.

Submission ID: 89; Submission Group: MS Rehabilitation within and across the ICF Domains; Submitter: Anne Rahn

Needs of people with primary progressive multiple sclerosis (NIPS) around diagnosis - A qualitative interview study

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Background: People with primary progressive multiple sclerosis (pwPPMS) have a persistent and high disability, often from diagnosis. They are confronted with a constantly worsening disease and limited treatment options, which can lead to feelings of hopelessness. Currently, there is little research on the needs of pwPPMS, which represent a minority of the MS population. Our qualitative study explored the needs of pwPPMS from the perspective of pwPPMS and healthcare professionals (HPs).

Methods: We conducted a multicentre (five European countries) qualitative study consisting of semi-structured interviews with pwPPMS, and interviews and focus groups with HPs experienced in the care of pwPPMS. The interview guide was based on the findings of a scoping review. PwPPMS were eligible if aged 18-65 years, diagnosed for ≤ 10 years, and had an Expanded Disability Status Scale ≤ 6.0 . Interviews and focus groups were recorded, transcribed, and translated into English. We analysed the data using qualitative thematic analysis.

Results: We conducted 16 pwPPMS interviews, seven HP interviews and two focus groups (15 HPs). Most pwPPMS described the diagnostic process as long and challenging, and some experienced inappropriate specialist referrals or received misdiagnoses. They stated that their social and professional lives had changed noticeably. PwPPMS voiced their need to remain as autonomous as possible and to receive more information about their disease, its course, and treatment options. PwPPMS were aware of the limited treatment strategies; they wished for more therapy options and a cure for the disease. Analysis of HP data is underway and will be presented at the conference.

Conclusion: From diagnosis communication, programmes are needed to support and inform pwPPMS and to help them cope with the disease.

Submission ID: 90; Submission Group: Application of Current Technologies in MS Rehabilitation; Submitter: Fabiola Giovanna Mestanza Mattos
Complementary use of Statistical Parametric Mapping and Gait Profile Score to describe walking alterations in multiple sclerosis

Background: Quantitative locomotor alterations of People with Multiple Sclerosis (PwMS) derived from gait analysis are often complex to interpret. A summary index like Gait Profile Score (GPS), composed by nine Gait Variability Scores (GVS), can reduce kinematic data dimensionality, quantifying the deviation from physiological gait. However, GPS fails to describe when during gait cycle alterations occur. Statistical Parametric Mapping (SPM) overcomes this issue and allows to compare kinematics and kinetics over the gait cycle, still not providing a scalar measure of gait deviation. The aim of this cross-sectional study was to compare kinematics and kinetics of PwMS with healthy controls (HC) using both GPS and SPM.

Methods: Eleven PwMS and 11 speed-matched HC underwent an overground gait analysis. GPS and GVS were compared between groups through independent-sample t-tests. Spearman's correlation coefficients (r) between GPS and clinical outcomes were calculated. Sagittal-plane kinematics and power at hip, knee and

ankle were compared through multivariate SPM Hotelling's-T2 and univariate SPM t-tests.

Results: PwMS had higher (worse) GPS than controls (PwMS: $8.74 \pm 2.13^\circ$; HC: $5.01 \pm 1.41^\circ$; $p < 0.001$) mainly due to altered pelvis, knee, and ankle kinematics, as shown by GVS differences. GPS correlated with Expanded Disability Status Scale ($r = 0.65$, 95% C.I. [0.04; 0.91]) and 2-Minute Walking Test ($r = -0.65$, 95% C.I. [-0.90; -0.04]).

Multivariate SPM highlighted three clusters of statistically significant differences at 0-49%, 70-80%, and 93-99% of stride ($p < 0.05$); univariate analysis showed reduced ankle plantar flexion and power generation during stance, and lower knee flexion during pre-swing and swing.

Conclusions: The combined use of the GPS and the SPM in gait analysis indicates GPS as a valid summary multi-joint kinematic index, it discriminates between groups, and correlates with disability level and walking endurance. Multivariate SPM showed that the largest alterations occurred during the stance phase. GVS and univariate SPM revealed larger deviations at the ankle and knee joints on sagittal plane.

Submission ID: 91; Submission Group: MS Rehabilitation within and across the ICF Domains; Submitter: Sinead Hynes

A Cognitive Occupation-Based programme for people with Multiple Sclerosis (COB-MS): acceptability and experiences of a feasibility cluster-randomised controlled trial

Running title: COB-MS acceptability and feasibility

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*Presenting author

Abstract

Introduction: Up to 65% of people with MS experience a decline in cognitive functioning. This invisible symptom of MS can be one of the most distressing. Although it is commonly occupational therapists who assess and treat cognitive dysfunction in MS, there are few, if any, MS-specific occupation-focused cognitive interventions. The COB-MS programme, an occupation-focused cognitive intervention, was developed to address this. It focuses on both the functional and occupational problems specific to cognition and MS. **Objective:** The aim of this research was to determine the acceptability of COB-MS and investigate the barriers and facilitators to using COB-MS.

Methods: This qualitative study was conducted in the context of a cluster feasibility randomised controlled trial of the COB-MS. Participant experiences of the COB-MS intervention were collected from people with MS who took part in the programme (interviews) and occupational therapists who delivered the COB-MS programme (focus group). Content analysis was used to analyse the data to elicit feedback on specific concepts deemed necessary to determine the acceptability of the COB-MS intervention.

Results: Results revealed that, from a participant with MS perspective, the COB-MS program provided a positive experience and quality materials and resources; and was appropriate for a MS cohort, with a majority of respondents reporting application of learnings following the program, coupled with perceived

improvements. From an occupational therapist perspective, the program and its procedure were found to be acceptable with respect to both feasibility and appropriateness. All phases of data analysis yielded recommendations for further enhancement of COB-MS program.

Conclusion: The COB-MS intervention was found to be an acceptable intervention from participants, and feasible to deliver and participate in online. Participants reported varied, impactful experiences of the impact of from taking part in the programme. COB-MS covers ICF categories:

1. Body function
2. Activity and Participation
3. Environmental factors

Submission ID: 92; Submission Group: Multidisciplinary Rehabilitation in MS; Submitter: Lars Hvid
Comprehensive evaluation of self-management skills following multidisciplinary rehabilitation in persons with multiple sclerosis - The Danish MS Hospitals Rehabilitation Study

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Introduction: Health education is often an integral part of rehabilitation programs for persons with multiple sclerosis (pwMS), aiming to promote self-management behavioral changes and skills. One tool that can be used to comprehensively evaluate this is the Health Education Impact Questionnaire (heiQ; 40 questions), measuring 8 different constructs. However, few (if any) randomized controlled trials have evaluated the effects of personalized multidisciplinary rehabilitation (MDR) on heiQ in pwMS. Therefore, our objective was to evaluate the impact of 4 weeks of inpatient MDR on heiQ in pwMS.

Methods: A total of n=405 pwMS were enrolled in the study, and evenly randomized into 4 weeks of MDR or wait-list control. All pwMS filled out the heiQ questionnaire at baseline and after 2 as well as 12 months of follow-up. The heiQ comprise 8 different constructs (1-4 point scale): health-directed activities (HDA), positive and active engagement in life (PAEL), emotional distress (ED), self-monitoring and insight (SMI), constructive attitudes and approaches (CAA), skill and technique acquisition (STA), social integration and support (SIS), health services navigation (HSN).

Results: Substantial improvements (*between-group difference (mean diff [95%CI]) + effect size (ES)*) were observed at 2 months follow-up for HDA (0.32[0.25:0.39], ES=0.51), PAEL (0.08 [0.03:0.13], ES=0.15), SMI (0.15 [0.11:0.20], ES=0.33), and STA (0.17 [0.12:0.23], ES=0.30). These improvements remained (despite minor reductions) for all 4 constructs at 12 months follow-up; HAD (0.25 [0.12:0.39], ES=0.40), PAEL (0.06 [-0.05:0.16], ES=0.11), SMI (0.09 [0.00:0.19], ES=0.19), and STA (0.14 [0.04:0.25], ES=0.24). In contrast, no noticeable changes were observed for ED, CAA, SIS, or HSN.

Conclusion: Four weeks of personalized MDR effectively improved certain self-management skills (health-directed activities (HDA), positive and active engagement in life (PAEL), self-monitoring and insight (SMI), skill and technique acquisition (STA)) in pwMS. These improvements are likely linked to improvements in health-related quality of life in pwMS.

Submission ID: 93; Submission Group: MS Rehabilitation within and across the ICF Domains; Submitter: Turhan Kahraman

Association between work-related difficulties and dual-task ability in people with multiple sclerosis

Running title: Work difficulties and dual-task in MS

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Aim: Work is one of the most impacted areas in the activities and participation component of the International Classification of Functioning, Disability and Health (ICF) in people with multiple sclerosis (pwMS). Numerous factors associated with difficulties at work have been well studied. However, there is a lack of information about the associations between perceived work difficulties and dual-task ability in pwMS. The aim was to examine the association between perceived work difficulties and dual-task ability in pwMS.

Methods: Forty-two working and 42 non-working pwMS were enrolled in the study. The outcome measures included the Dual-task Impact on Daily-life Activities Questionnaire (DIDA-Q), Timed 25-Foot Walk Test (T25FWT), Nine-Hole Peg Test (NHPT), 12-Item Multiple Sclerosis Walking Scale (MSWS-12), and Brief International Cognitive Assessment for MS (BICAMS). The working group also filled out the Multiple Sclerosis Work Difficulties Questionnaire-23 (MSWDQ-23). Dual-task performance was assessed by adding a secondary word-list generation task to the 9HPT and the walking test (overground walking for 30 sec). The percentage change between single and dual-task (dual-task cost) was calculated.

Results: Although the non-working group had the same disability level, they showed poorer scores on single- and dual-task walking performance, dual-task 9HPT performance, and DIDA-Q compared to the working group (p<0.05). However, the two groups had no significant difference in dual-task cost of upper extremity function and walking. An increase in dual-task difficulties in daily life assessed by DIDA-Q was correlated with MSWDQ-23 (r=0.250–0.877), but dual-task cost was not correlated with MSWDQ-23 in the working group.

Conclusion: Dual-task difficulties may have a detrimental effect on work life, as seen by the correlation between perceived dual-task difficulties and perceived work difficulties and poorer scores in non-working pwMS. Assessing dual-task performance and self-reported dual-task difficulties and designing appropriate therapies for dual-task might be considered for interventions to reduce work-related difficulties.

Submission ID: 94; Submission Group: Promising Technologies that can Help Advance MS Rehabilitation; Submitter: Enrico Valli

A whole-body wearable device for motor function monitoring: testing iFeel Technology in PwMS

Short title: iFeel for motor function monitoring in MS

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Introduction: Since characteristics of MS symptoms may rapidly vary, wearables providing precise, reliable, and valid measures can be the main candidate for balance and mobility assessment.

Aim: The aims of this study are to: 1) examine the capabilities of the quantitative measures derived from iFeel technology, a whole-body wearable perception system developed by Artificial and Mechanical Intelligence (AMI) laboratory at Istituto Italiano di Tecnologia, that consists of a network of wearable devices, a pair of shoes equipped with force/torque sensors, an AI-based estimation algorithm, and 2) test usability of iFeel on a sample of PwMS.

Methods: PwMS followed as outpatients at the AISM Rehabilitation Service of Genoa (Italy) will be enrolled if they have an age of 18 years and older, a confirmed diagnosis of MS (both relapsing-remitting and progressive forms), an EDSS \leq 6.5. Walking and balance will be assessed using clinical evaluations as TUG, T25FWT, 6MWT and SOT from the EquiTest with and without iFeel technology. Furthermore, PROs will be administered to investigate individual perception on mobility (MSWS-12), dual-task (DIDA-Q) and fatigue (MFIS). To investigate iFeel potentialities, the following Key Performance Indexes (KPIs) will be calculated from the acquired dataset: Cycle duration (s); Cadence (steps/min), Stride length (m); Speed (m/s); Double contact (% of cycle duration); Max angular velocity (deg/s); Swing with (% of stride length); Path length (% of stride length); Stance phase (% of cycle duration); Swing time (% of cycle duration). Effectiveness, efficiency and satisfaction of iFeel components will be assessed by asking participants to fulfil specific questionnaires and the System Usability Scale (SUS).

Conclusions: The whole-body wearable iFeel could represent a promising tool also in MS offering the possibility to create more objective, less rate-dependent and fine-grained functional outcomes with the potential for more sensitivity to changes over shorter time intervals than traditional exam-based metrics.

Submission ID: 95; Submission Group: Multidisciplinary Rehabilitation in MS; Submitter: Monica Biggio
Does action observation improve motor performance without causing fatigability in progressive MS patients?

Running title: Action observation, learning and fatigability

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Fatigue and fatigability are some of the most common and disabling symptoms in people with multiple sclerosis (PwMS), with higher prevalence in the progressive forms. Finding new rehabilitation strategies to promote motor learning without causing fatigability has become an urgent need. Action Observation (AO) is a cognitive stimulation technique able to activate the sensorimotor system, and to promote motor learning and plasticity. It is often proposed as add-on to the conventional motor rehabilitation, but it is unknown whether it cause fatigability.

To unveil this issue, we enrolled 21 PwMS with progressive diagnosis, to underwent a training protocol with AO including the observation of a video of a hand performing thumb-index opposition movements at 4 increasing frequency calibrated on the subject. Before (PRE), immediately after (POST0), and 60 minutes after the intervention (POST60) the following tests were performed: self-reported assessment of mental and physical fatigue (VAS); pinch force evaluation; kinematic evaluation of fine hand movements; evaluation of primary motor cortex (M1) activity; cognitive evaluation through trial making test (TMT-B-A).

PwMS reported a significantly increased physical and mental fatigability in POST0 and POST60. No significant differences were found in pinch force and in TMT-B-A after AO. On average, AO training did not improve the motor performance. However, a positive correlation appeared between VAS scores and motor performance suggesting that subjects who reported greater fatigability were those who improved their performance. At last, in POST0 a tendency for M1 excitability reduction was observed, as in cases of post exercise depression.

AO is already used in rehabilitation with encouraging results. However, our findings would suggest to carefully evaluate the patients' characteristics in terms of resources that she/he can actually dedicate to the task in order to propose an individualized training based on the residual functions of the individual.

Submission ID: 96; Submission Group: Application of Current Technologies in MS Rehabilitation; Submitter: Claudio Marcello Solaro

To evaluate the activity and the efficacy of traditional swallowing therapy (TST) plus neuromuscular electrostimulation (NMES) vs TST plus sham-NMES in MS patients with dysphagia

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Introduction: Dysphagia is a disabling, life-threatening symptom that can cause death in people with Multiple Sclerosis (PwMS) through aspiration pneumonia.

To date, no randomized clinical trials have shown that rehabilitative strategies are effective. Only one study applied Neuromuscular electrical stimulation (NMES) to swallowing function on PwMS. The aim of this study is to determine whether NMES added benefit to standard swallowing rehabilitation program in PwMS.

Methods: This is a multicentre double blinded, randomized clinical trial with two arms: standard rehabilitative plus Active NMES vs standard rehabilitative with Sham NMES. Inclusion criteria: MS diagnosis, stable disease activity, ASHA score <6 and DYMUS score >2.

We performed an ad-interim analysis in order to assess if the two groups (NMES vs. sham NMES) are balanced for age, gender, disease duration (DD), disease course and EDSS, and if it is possible to assess a preliminary effect of the treatment.

Results: A total of 125 PwMS were screened, 80 were included in the study, of which 8 dropped out. Till now, 75 subjects completed the treatment.

Thirty-three subjects were allocated to the NMES group and 32 in the sham-NMES group.

Demographic and clinical characteristics of the two groups: NMES [age 55.9 (11.3), DD 17.7 (8.9), 7 RRMS, 7 PPMS, 19 SPMS, EDSS 6.8 (1.0)] and Sham-NMES [age 56.0 (11.8), DD 18.9 (9.0), 6 RRMS, 4 PPMS, 22 SPMS, EDSS 7.0 (1.2)]. The two groups do not statistically differ for gender, age, disease duration, disease course and EDSS ($p > 0.05$).

Pre and post-treatment clinical scores: NMES [pre: ASHA=4.67 (0.74), DYMUS=4.15 (2.2), DOSS=4.63 (0.71); post ASHA=5.30 (0.73), DYMUS=2.76 (2.5), DOSS=5.41 (0.89)] and Sham-NMES [pre: ASHA=4.53 (0.87), DYMUS=4.75 (2.1), DOSS=4.76 (0.79); post ASHA=4.94 (0.91), DYMUS=3.56 (2.3), DOSS=5.21 (0.90)].

Conclusion: The two groups are balanced for disease course, age and EDSS. Ad interim analysis highlighted that the use of the device is well tolerated (5 drop-out are unrelated to the treatment).

Submission ID: 97; Submission Group: Multidisciplinary Rehabilitation in MS; Submitter: Helena Llorente Blasco
Impact of a virtual educational workshop from occupational therapy on fatigue

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Background: Fatigue is a very common symptom among people with sclerosis multiple (MS) with significant impact on activities of daily living and on quality of life.

Methods: The objective of the study is to compare the effectiveness between a virtual fatigue management program with a face-to-face one.

From 2019 to 2022, 277 MS adults with fatigue were attended at the CEMCAT facilities and were included in a 6-week fatigue management program, 1 session per week, including 6 participants per group. Of the 277 participants, 166 fulfilled the Modified Fatigue Scale (MFIS) and were scored with the EDSS at the beginning and at the end of the program. Those participants who were included from 2020 to 2022 received these sessions in a virtual format due to the SARS-COV-2 pandemic.

Results: According to the MFIS scores, the percentage of people who improved in virtual format was higher (24%) than in face-to-face format (14%), but with no significant relevance ($p > 0.05$). As a result, there is no statistical differences that virtual fatigue management therapy is more effective than a face-to-face program. However, 25.3% of the entire sample shown a significant change in fatigue impact and 18.67% decreased their perception of fatigue.

Conclusions: No differences in effectiveness were observed between the two formats. Even with results stating that fatigue management groups have an impact in people with MS, more research is needed to find out what factors affect the intervention group. This program must be accompanied by other rehabilitation strategies such as coping with fatigue and physical improvement. Further studies with improved designs are warranted to confirm these findings.

Submission ID: 98; Submission Group: MS Rehabilitation within and across the ICF Domains; Submitter: Ine Nieste
Effects of a 10-month home-based, periodised running exercise program on brain MRI measures in persons with Multiple Sclerosis: a pilot study

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Background: To date, a plethora of evidence shows the beneficial effects of exercise as symptomatic treatment for persons with Multiple Sclerosis (PwMS). Recently, a 6-month exercise program has also been shown to have potential disease-modifying effects by reducing the annualized relapse rate (ARR). However, this could not be demonstrated in terms of brain preservation.

Therefore, the present pilot study investigated the effect of a longer-term exercise program in PwMS and healthy controls (HC) and compared changes with PwMS and HC who did not perform exercise.

Methods: Twenty mildly-disabled PwMS and 20 HC performed a 10-month home-based exercise program. Ten mildly-disabled PwMS and 10 HC received usual care. Primary outcomes were annualized percentage brain volume changes ([PBVC] of the whole brain, white matter, grey matter and lateral ventricles), black hole and T2 lesion load (count and volume) measured by magnetic resonance imaging. Secondary outcomes were exercise adherence (the number of completed exercise sessions compared to the protocol; %), ARR, changes in cognitive function (spatial recall test and symbol digit modalities test) and cardiorespiratory fitness (CRF). A two-way analysis of covariance was used to analyse the difference scores between groups, including exercise (exercise/control), population (MS/HC) and the interaction between exercise and population as factors, and age, gender and baseline value as covariates.

Results: Baseline CRF and cognitive function did not differ between groups. The exercise groups had a similar exercise adherence ($76.2 \pm 29.7\%$, $p=0.563$) and improved their CRF to the same extent ($+4.7\%$ VS. -2.6% in control groups, exercise effect $p=0.04$). There was no significant exercise or interaction effect on PBVC, black hole and T2 lesion load, ARR nor cognitive function.

Conclusion: The present results show that an exercise program of 10 months does not significantly impact brain changes in PwMS nor HC, while CRF significantly improves. Further research with an even longer-term exercise duration is warranted.

Submission ID: 99; Submission Group: Promising Technologies that can Help Advance MS Rehabilitation; Submitter: Jessica Podda

A new mHealth app for monitoring and self-assessment of cognitive impairment in people with Multiple Sclerosis: DIGICOG-MS

A new app for cognitive deficits: DIGICOG-MS

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Introduction and Aim: Recently, mobile health applications (mHealth apps) have proven useful for people with Multiple Sclerosis (PwMS). Thus, easy-to-use digital solutions are now strongly required to assess and monitor cognitive impairment (CI), one of the most disturbing symptoms in MS, experienced by almost 43-70% of PwMS. In this view, we developed DIGICOG-MS (DIGItal assessment of COGNitive impairment in Multiple Sclerosis), a smartphone- and tablet-based mHealth app for self-assessment and monitoring of CI in MS. This pilot study aimed to demonstrate DIGICOG-MS potentialities and measure its usability on a sample of PwMS.

Methods: DIGICOG-MS includes four digital tests that assess the most affected cognitive domains in MS as visuo-spatial

memory (“Remember and place”), verbal memory (“Listen and repeat”), language (“List the words”) and information processing (“Associate numbers to symbols”), taking inspiration from traditional paper-based tests (i.e., SPART, RAVLT, WLG and SDMT). Participants were required to self-evaluated their cognitive functioning using DIGICOG-MS and then to fulfil the System Usability Scale (SUS) and mHealth App Usability Questionnaire (MAUQ).

Results: Fifteen PwMS with a relapsing-remitting course (female: 9), followed as outpatients at the AISM Rehabilitation Service of Genoa, were enrolled. They had a mean age of 55.40 (9.79), an education of 13.07 (3.53) years, a disease duration of 14.33 (8.83) and an EDSS of 3.40 (1.62). PwMS scored 17.80 (5.21) at the visuo-spatial memory task, 46.73 (10.26) at verbal memory task, 21.93 (7.32) on the language task and 20.00 (10.10) at the information processing test. Interestingly, SUS total score was 77.78 (13.94), while MAUQ total score was 112.44 (21.65), suggesting that DIGICOG-MS was well appreciated by PwMS (mean scores for MAUQ subscales ‘Ease of use’, ‘Interface and satisfaction’, and ‘Usefulness’ were 32.78, 43.67 and 36.00, respectively).

Discussion: Although preliminary, results indicated that DIGICOG-MS is highly usable and well accepted by PwMS.

Submission ID: 100; Submission Group: Application of Current Technologies in MS Rehabilitation; Submitter: Andrea Giordano

Applying Multidimensional Computerized Adaptive Testing to the MSQOL-54: A simulation study

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Abstract

Background: The Multiple Sclerosis Quality of Life-54 (MSQOL-54) is one of the most commonly-used MS-specific health-related quality of life (HRQOL) measures. It is a multidimensional, MS-specific HRQOL inventory, which includes the generic SF-36 core items, supplemented with 18 MS-targeted items. Availability of an adaptive short version providing immediate item scoring may improve instrument usability and validity. However, multi-dimensional computerized adaptive testing (MCAT) has not been previously applied to MSQOL-54 items. We thus aimed to apply MCAT to the MSQOL-54 and assess its performance.

Methods: Responses from a large international sample of 3669 MS patients were assessed. We calibrated 52 (of the 54) items using bifactor graded response model (10 group factors and one general HRQOL factor). Then, eight simulations were run with different termination criteria: standard errors (SE) for general factor and group factors set to different values, and change in factor estimates (θ estimates) from one item to the next set at <0.01 . MCAT θ estimates were evaluated in terms of number of administered items, root mean square difference (RMSD), and correlation.

Results: Eight items were removed due to local dependency. The simulation with SE set to 0.32 (general factor), and no SE thresholds (group factors) provided satisfactory performance: the median number of administered items was 24, RMSD was 0.32, and correlation was 0.94.

Conclusions: Compared to the full-length MSQOL-54, the simulated MCAT required fewer items without losing precision for the general HRQOL factor. Further work is needed to add/integrate/revise MSQOL-54 items in order to make the calibration and MCAT performance efficient also on group factors, so that the MCAT version may be used in clinical practice and research.

Submission ID: 101; Submission Group: Translation of New Rehab Knowledge into Practice; Submitter: Arianne Gravesteijn

The relative aerobic load of walking in people with multiple sclerosis

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Background: In people living with multiple sclerosis (pwMS) mobility impairments often affect walking ability resulting in increased energetic demands during walking. Moreover, pwMS often have a reduced peak aerobic capacity. Together this might result in an increased relative aerobic load of daily walking. The relative aerobic load of walking provides insight into the energetic demand of walking and peak aerobic capacity in pwMS.

Purpose: To examine the energetic demands of walking, relative to the peak aerobic capacity in pwMS.

Method: Prospectively collected data on aerobic capacity from a cardiopulmonary exercise test (CPET), and physiological parameters derived from a 6-minute overground walk test at comfortable walking speed, with mobile gas exchange measurements, were analyzed. The relative aerobic load of walking was determined as energy demand of walking relative to two measures of cardiorespiratory fitness (oxygen uptake at peak and first ventilatory threshold (VT1)).

Results: In total 45 pwMS with an average disease duration of 15 years [IQR: 9-20] and disease severity measured by the Expanded Disability Status scale of 4 [IQR: 3-4.5] were included. PwMS walk at an average relative aerobic load of 89% (range: 57%-153%) and 59% (range: 34%-94%) relative to VT1 and peak aerobic capacity, respectively. During comfortable walking 13 participants used more energy than their VT1. Peak aerobic capacity was low and indicative for improvement in 9 participants. In 11 participants energy demand during walking required improvement and in 6 participants both energy demand of walking and aerobic capacity were indicative for improvement.

Conclusion: PwMS walk at a relative aerobic load close to their VT1. The relative aerobic load can guide clinicians to intervene on the factor(s) causing this high relative aerobic load (i.e. reduced peak aerobic capacity or increased energy demands of walking).

Submission ID: 102; Submission Group: Application of Current Technologies in MS Rehabilitation; Submitter: Arianne Gravesteijn

Perceived strain and physiological strain of societal participation: two different constructs during real-time assessment using digital health applications in people with multiple sclerosis

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Introduction: Impaired body functions in people with multiple sclerosis (pwMS) (e.g. muscle strength, cardiorespiratory fitness, balance, fatigue) can increase patient-perceived and physiological strain of societal participation. During exercise, these measures are expected to measure the same construct; whether this is true for societal participation is unknown.

Purpose Examine the relationship between perceived and physiological strain during societal participation in pwMS.

Method: Perceived and physiological strain were measured real-time in 70 pwMS with the Whereabouts smartphone-app and Fitbit, in a community-based setting for 7 consecutive days. Societal participation was divided in 10 participation at location domains and 9 transportation domains. Perceived strain was determined using a 1-10-point scale (1 not strenuous; 10 most strenuous). Physiological strain was operationalized by heart rate reserve (%HRR). Longitudinal relationships between perceived and physiological strain during total societal participation, and for the recreation, leisure and sports domain were examined (mixed model analyses). Type of event (at location or transportation) was added as co-variate, with further adjustments for MS-related fatigue and disease severity.

Results: Median perceived strain, summarized for all societal participation domains, varied between 3 and 6 (range: 1-10), whereas physiological strain varied between 18.5%-33.2%HRR. Perceived strain (outcome) and physiological strain were not associated (β -0.001, 95%CI -0.008; 0.005), with a 7-day longitudinal correlation coefficient of -0.001. Transportation domains were perceived less strenuous (β -0.80, 95%CI -0.92; -0.68). Higher fatigue levels resulted in higher perceived strain (all societal participation domains taken together) (β 0.05, 95%CI 0.02; 0.08).

Conclusion Societal participation results in low-to-moderate perceived and physiological strain. As these measures are unrelated, they should be considered different constructs.

Submission ID: 103; Submission Group: Multidisciplinary Rehabilitation in MS; Submitter: Sofie Bergien
Loneliness among older adults with multiple sclerosis in Denmark

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Background: Due to improvements in medical treatment and rehabilitation, the average life expectancy has increased among people with multiple sclerosis (MS). Today, approximately 25% of people with MS in Denmark are 65 years or older. Prior research suggests that older adults with MS (OAwMS) have a greater risk of social isolation and loneliness due to physical decline. However, the prevalence of loneliness, and factors associated with loneliness among OAwMS, remain unknown.

Aim: This study investigates the prevalence of loneliness as well as factors associated with loneliness among OAwMS in Denmark.

Method: A cross-sectional survey study was conducted among 2574 OAwMS. Loneliness was measured by the UCLA 3-Item Loneliness Scale. Participants who scored 7 or above were grouped as lonely. Sex, age, and cohabitation were included as sociodemographic factors. 1107 OAwMS (43.0%) responded to the survey. Due to missing values, 82 participants were excluded from the analyses. Descriptive statistics, including Chi-square-tests, were used for the analyses.

Results: 11.8% (n=121) of the participants scored 7 or above on the UCLA scale. Cohabitation was the only variable found to be significantly associated with loneliness among the participants (Pearson's Chi-square test=11.8, P-value=0.001). 16.8% (n=56) of the participants who were living alone, reported being lonely compared to 9.4% (n=65) of those living with a partner or family member.

Conclusion: The results indicate that the prevalence of loneliness is high among OAwMS living in Denmark compared to the general Danish population at the same age. The results further indicate that cohabitation may play an essential role in the experience of loneliness. Future studies should explore the role of potential risk factors for loneliness among OAwMS, among this cohabitation, but also aspects such as resilience, physical and cognitive impairments.

Submission ID: 104; Submission Group: MS Rehabilitation within and across the ICF Domains; Submitter: Yaron Watts

Sexual dysfunction and lower urinary tract symptoms in male patients with multiple sclerosis

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Background: Multiple Sclerosis (MS) is a central nervous system autoimmune disease mainly affecting young adults. Sexual dysfunction (SD) and lower urinary tract symptoms (LUTS) frequently occur in MS patients and can significantly impair patients' quality of life.

Objective: To evaluate the prevalence of SD and LUTS in a large cohort of male patients with MS. and analyzed the relationship

Methods: We retrospectively analyzed data from the Sheba MS Center data registry related to SD and LUTS and collected also clinical variables including age, disease duration, neurological disability assessed using the Expanded Disability Status Scale (EDSS), and immunomodulatory treatments. Data was analyzed using Python software.

Results: The cohort included 281 male MS patients, mean \pm SD age 41.9 ± 10.3 years, disease duration 10.9 ± 8.5 years, 166 had relapsing-remitting and 115 had secondary progressive disease course. Any SD was reported in 55.2% of subjects and any LUTS was reported in 71.4%. Patients with longer disease duration (>10 years), or higher disability (EDSS score >4.0) suffered more frequently from SD and LUTS. Immunomodulatory treatment was not associated with differences in the prevalence of SD or LUTS.

Conclusions: SD and LUTS occur in most male MS patients and the incidence increases with disease progression. No significant effect was noted by immunomodulatory treatments.

Submission ID: 105; Submission Group: Promising Technologies that can Help Advance MS Rehabilitation;

Submitter: Famke Vanderhauwaert

Patient experience of transcutaneous electrical stimulation with Exopulse Mollii Suit

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Background: Transcutaneous electrical stimulation has been used for treatment of spasticity in various neurological diseases. The Exopulse Mollii Suit has 58 soft electrodes for transcutaneous electrical stimulation and aims to reduce spasticity and muscle tone by reciprocal inhibition. Beneficial effects are seen in patients with stroke and CP. So far, there are no studies about the effects of the Exopulse Mollii Suit in persons with Multiple Sclerosis

Objectives: To share our first experiences with the Exopulse Mollii Suit in 3 persons with Multiple Sclerosis. To show our next steps to get more experience with the Exopulse Mollii Suit.

Results: 3 persons with Multiple Sclerosis have been wearing the Exopulse Mollii Suit for 1h/day during at least 1 week. They reported a beneficial effect on spasticity and functionality of the upper and lower limbs, and experienced a positive change in different activities of daily living, such as walking, use of keyboard, dressing, etc. Beneficial effects could also be measured on the level of mobility of the large joints and strength

Important note: I hereby declare not to have any commercial goals nor conflict of interest. We just want to share our surprising beneficial first experiences with the Exopulse Mollii Suit in pwMS.

Submission ID: 106; Submission Group: MS

Rehabilitation within and across the ICF Domains;

Submitter: Laurits Taul-Madsen

Optimizing exercise prescription in MS – elucidating the influence of muscle strength and aerobic capacity on lower extremity physical function

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Introduction: To prescribe a personalized and thus more optimal exercise program for persons with multiple sclerosis (pwMS) having limited physical function, it's important to establish the extent of impairments in the two main contributing physiological systems, namely the neuromuscular system (~muscle strength) and the cardiovascular system (~aerobic capacity). Two of the most applied tests of physical function, the five times sit to stand (5STS) and the six-minute walk test (6MWT), have been claimed to rely on lower limb muscle strength and aerobic capacity, respectively. If correct, these tests would offer simple screening tools when planning exercise programs in pwMS.

Objective: To investigate how aerobic capacity and lower limb muscle strength independently influence physical function (5STS and 6MWT).

Methods: Knee extensor muscle strength (MVC; isokinetic dynamometry), aerobic capacity (VO₂; incremental exercise test), 5STS, and 6MWT were evaluated in all participants. Multiple linear regression was used to evaluate associations.

Results: Sixty-eight pwMS (45 ± 8.8 years) completed evaluation of VO₂ (26.7 ± 7.2 [range 14.5;48.5] mlO₂/min/kg), MVC (1.86 ± 0.66 [range 0.33;3.99] Nm/Kg), 5STS (10.2 ± 2.8 [range 4.8;20.9] s), and 6MWT (560 ± 119 [range 97;765] m). With 5STS as dependent variable $R^2=0.20$ ($p<0.01$) was observed with both VO₂ (std β -0.20, $p=0.08$) and MVC (std β -0.32, $p<0.01$) contributing as independent variables, corresponding to VO₂ explaining 38% and MVC, 62%. With 6MWT as dependent variable $R^2=0.44$ ($p<0.01$) was observed with both VO₂ (std β 0.54, $p<0.01$) and MVC (0.20, $p<0.05$) contributing as independent variables, corresponding to VO₂ explaining 73% and MVC 27%.

Conclusion: Whilst muscle strength and aerobic capacity both contribute to explain physical function, 5STS is preferentially linked to muscle strength whereas 6MWT is preferentially linked to aerobic capacity. Screening pwMS in these tests will help optimize exercise prescription by targeting the associated physiological systems.

Submission ID: 107; Submission Group: Application of Current Technologies in MS Rehabilitation; Submitter: Giulia Bommarito

Cognitive neurorehabilitation in multiple sclerosis using an adaptive exergame

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Cognitive impairment affects the daily life of over 50 % of people with multiple sclerosis (pwMS) [1]. Prevention and treatment of cognitive deficits is still challenging, with limited pharmacotherapeutic options. Non-pharmacological interventions, including emerging computerized cognitive rehabilitation tools, show promising results. The cognitive exergame Body-Brain Training (BBT) combines multimodal cognitive exercise and physical training [2] and may offer a better approach to improve cognitive function in pwMS, when compared to control interventions.

We will test this hypothesis by means of an international multi-site randomized controlled trial (RCT). We expect to recruit 192 pwMS with subjective and/or objective cognitive impairment, over four sites (Lausanne, Bern, Genoa and Valens). Participants will be randomized in three arms and will undergo a six-weeks in-laboratory training program: a) BBT including physical and cognitive components b) cognitive BBT version without physical exercise (CTR1) and c) cognitive training with RehaCom, as a proxy for a standard of care (CTR2). Cognitive and physical assessment will be performed i) before, ii) at the end, and iii) six months after training. Importantly, the protocol includes a run-in phase prior to establishing the cognitive baseline.

We expect an improvement in cognitive and physical measures for participants in the BBT group, compared to the two control groups (CTR1 and CTR2), with a sustained effect at 6 months follow-up. We also aim for better outcomes in terms of measures of everyday life cognition and quality of life.

This Phase-III RCT will offer robust evidence for the potential utilization of BBT as an individualized cognitive neurorehabilitation tool to improve cognitive performance, physical condition, and everyday life of pwMS. The interim results of our ongoing pilot study will be presented.

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Submission ID: 108; Submission Group: Multidisciplinary Rehabilitation in MS; Submitter: Stefania Marfisi
Linguistic profile in patients with Multiple Sclerosis: a comparison between adult-onset and paediatric-onset disease
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Introduction: Approximately 45-65% of Multiple Sclerosis (MS) patients show cognitive impairment during the course of the disease. In the language domain, fluency, especially semantics, is compromised. Paediatric-onset MS (POMS) patients present cognitive impairment in 30% of cases and significant linguistic impairment generally appears within 2 years of onset. However, POMS linguistic profile and its specificity when compared to adult-onset MS (AOMS) remain largely unexplored.

Objectives: We characterised the cognitive and linguistic profiles of MS patients, and tested for differences between AOMS and POMS, under the hypothesis that MS patients exhibit linguistic impairments, which is greater in POMS than in AOMS.

Methods: Clinically and MRI stable patients with AOMS and POMS were assessed cognitively (Brief Repeatable Battery for Neuropsychological evaluation, BRB-N) and linguistically (Neuropsychological Examination for Aphasia, ENPA). Demographic and clinical characteristics were also collected.

Results: AOMS (n=22) differed from POMS (n=12) only in the age at the time of assessment (mean±SD AOMS vs. POMS: 44.8±1.9 vs. 26.3±1.8, $p<0.001$). There was no difference in cognitive scores between groups; BRB-N showed that information processing speed was the most affected cognitive domain in both AOMS and POMS. When compared to AOMS, POMS showed a trend towards higher verbal fluency impairment ($p=0.07$) and was more impaired in word repetition (mean±SD score in POMS vs. AOMS: 9.80±0.00 vs. 9.89±0.06, $p<0.0001$); there was no between group difference in repetition of phrases.

Discussion and Conclusions: POMS presents cognitive dysfunction common to AOMS, but also specific linguistic dysfunction with altered word repetition. This can (i) reflect damage to the arcuate fasciculus, a typical lesion site in MS, (ii) result from compromised construction of linguistic resources when MS strikes during neurodevelopment and (iii) affect the development of cognitive reserve. Therefore, specific language assessments and enrichment interventions should be considered in MS, especially in POMS.

Submission ID: 109; Submission Group: Application of Current Technologies in MS Rehabilitation; Submitter: Robert Motl

Randomized Controlled Trial of the Behavioral Intervention for Physical Activity in Multiple Sclerosis Project: Social Cognitive Theory Variables as Mediators

Background: We recently reported in a phase-III, randomized controlled trial (RCT) that a behavioral intervention based on social cognitive theory (SCT) and delivered through the Internet using e-learning approaches increased device-measured minutes/day of moderate-to-vigorous physical activity (MVPA) over a 6-month period among persons with multiple sclerosis (MS).

Objective: This planned tertiary outcome paper examined SCT variables as mediators of the behavioral intervention effect on change in device-measured minutes/day of MVPA.

Method: Persons with MS ($N=318$) were randomized into behavioral intervention ($n=159$) or attention/social contact control ($n=159$) conditions that were administered over a 6-month period by persons who were uninvolved in screening, recruitment, random assignment, and outcome assessments. We collected MVPA and SCT data before and after the 6-month period. The data analysis involved linear mixed modeling on MVPA and SCT outcomes followed by latent change score modeling for examining SCT variables as mediators of the intervention effect on change in MVPA.

Results: There were statistically significant group by time interactions on device-measured minutes/day of MVPA and scores from SCT measures of exercise self-efficacy, barriers self-efficacy, goal setting, and planning. The effect of the intervention on device-measured minutes/day of MVPA was mediated by the SCT variable of exercise self-efficacy based on the statistical significance of the Wald z-score for the indirect effect in the latent change score model.

Conclusions: This study provides evidence for self-efficacy as a SCT mediator of the behavioral intervention effect on device-measured minutes/day of MVPA in persons with MS.

Submission ID: 110; Submission Group: Application of Current Technologies in MS Rehabilitation; Submitter: Mehrnaz Hamedani

The effectiveness of Robot Erigo in advanced multiple sclerosis (EDSS ≥ 7)- preliminary results

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Rehabilitation therapy adapts to the different phases of Multiple sclerosis (MS), however, patients with advanced MS (EDSS ≥ 7) become inactive and few studies show adequate pain control. Erigo is a robot with an integrated leg movement system and body weight loading, which allows progressive verticalization to the

patient. Aims: verify the effectiveness of Erigo in patients with advanced MS, in order to reduce pain, frequency of spasms, spasticity and improve sphincter function. Inclusion-criteria: MS patients with EDSS ≥ 7 ; exclusion-criteria: weight > 135 kg, cardiovascular impairment, uncontrolled hypertension, severe cognitive disorders, bone instability. Outcome measures: Numerical Rating Scale for pain (NRS), Ashworth Modified (MAS), Barthel Index (BI), Motricity Index (MI), Spasm frequency (SFS), Wexner test, Trunk Control Test (TCT) and Range Of Motion (ROM). Patients conduct clinical assessments at the beginning (T1), at the end (T2) and after a 3-month (T3) follow-up. They received a 1h treatment, twice a week, for 20 individual sessions. Seven patients entered into this study, age $M=57.70 \pm 9.6$. Erigo treatment resulted in significant improvements of NRS score from $T1=5.67 \pm 2.94$ to $T2=2.83 \pm 2.32$ ($P=0.016$) and SFS from $T1=2.33 \pm 1$ to $T2=1.17 \pm 0.41$ ($P=0.038$). MI increased score by 8 points for both limbs, although at not significant level. BI improved from $T1=19.17 \pm 11.14$ to $T2=25 \pm 10$ ($P=0.038$); similar results have been demonstrated in Wexner showing a better sensitivity to stimulus and occasional reduction of faecal incontinence. MAS demonstrated a reduction of spasticity in hip and Knee on both limbs, although not at significant level; no statistical differences between the $TCTT1=26.67$ and $TCTT2=26.67$ were observed. The 3-month follow-up (T3) shows: a gradual diminution in improvement, related to NRS, SFS, BI and Wexner; compared with the end of the treatment period (T2). The final results are still higher than the starting point (T1). Our findings suggest progressive verticalization of the patient might be useful to treat secondary pain.

Submission ID: 111; Submission Group: Multidisciplinary Rehabilitation in MS; Submitter: Ambra Bisio

Motor performance of people with progressive multiple sclerosis can benefit from motor imagery training with no increase in fatigability

Running title: Motor imagery, learning and fatigability

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Fatigability refers to use-dependent decline in performance. In people with multiple sclerosis (PwMS), fatigability and fatigue have higher prevalence in those patients with progressive forms. In rehabilitation, an important goal would be to find new interventions maximizing the effectiveness and contemporary reducing the fatigability of the task. Motor imagery (MI) is a cognitive-motor stimulation technique that activates the sensorimotor system, and promotes motor learning and plasticity in healthy subject, without requiring overt movement production. For these reasons, it could be particularly suited for patients suffering from fatigue because MI could limit the fatigability induced by the physical training and boost its effectiveness.

This study tested if MI improved the motor performance without inducing cognitive and/or motor fatigability. To do that, 21 PwMS were recruited and involved in a MI training requiring to mentally simulate a finger-opposition tapping movement synchronized with a metronome beating on frequencies based on PwMS' maximal movement rate. Before (PRE), immediately (POST0) and 60 minutes (POST60) after the training the participants' maximal movement rate, primary motor cortex (M1) excitability, pinch strength, trial-making-test (TMTA and B), and self-reported evaluation of motor and cognitive fatigability (VAS) were performed. On average, motor performance did not improve, but a significant increase in M1 excitability was observed in POST0. TMTB-A scores significantly increased in POST0 and POST60, likely due to a learning process. No significant differences were found in pinch strength, motor and cognitive VAS values after MI training. Significant negative correlations were found at POST0 between changes in PwMS' movement rate and cognitive and motor VAS, indicating that people who improved the motor performance after MI training were those who reported less fatigability after the task. These results suggest that MI succeeded in increasing M1 excitability in PwMS in the progressive form, who can benefit from MI training without developing fatigability.

Submission ID: 112; Submission Group: Application of Current Technologies in MS Rehabilitation; Submitter: Insa Schiffmann

Understanding magnetic resonance imaging (MRI) in multiple sclerosis (MS) (UMIMS): a randomized controlled trial to assess the effect of an evidence-based patient online educational tool about MRI in MS on people with MS

Background: While magnetic resonance imaging (MRI) plays a major role in the lives of people with multiple sclerosis (pwMS), their MRI-specific knowledge is limited. We hypothesized that MRI-specific knowledge can be increased by using an evidence-based online tool called "Understanding MRI in MS" (UMIMS).

Methods: In this randomized controlled trial with n=120 pwMS UMIMS (intervention group) was compared to an active control (website containing publicly available information from European MS self-help organizations). Primary endpoint was change in MRI-specific knowledge assessed via the 22-point MRI-risk knowledge questionnaire. Secondary endpoints were assessed, e.g. emotions towards MRI (emotions towards MRI-questionnaire) and desired autonomy preference before and realized autonomy level after immunotherapy decision (control preference scale (CPS)).

Results: We report blinded results, unblinded data will be provided at the conference. Of n=120 participants 66.7% were female, average age was 32.4 +/- 8.1 years. 90.8 % had relapsing remitting MS, average disease duration was 3 +/- 2.9 years. 82.9% had had ≥1 relapse within 12 months and their next MRI was relevant e.g. for immunotherapy decision. MRI-risk knowledge increased from 53.6% to 63% correct answers. Emotions towards MRI did not change with little fear of MRI scan, modest

fear of MRI results and feeling of control emitted by MRI results (pre and post: 0.6 +/- 0.7; 1.4 +/- 0.9 and 1.8 +/- 0.8 on a scale of 1-4, respectively). However, feeling of competence regarding MRI increased (pre: 1.2 +/- 0.9, post: 1.7 +/- 0.7). 14.5% of pwMS ended up making the immunotherapy decision alone as measured by CPS, when initially, only 0.9% had desired this.

Conclusion: Even though analysis was performed on a whole-group-level, clear trends towards an increase in MRI-risk knowledge, feeling of competence regarding MRI and a more autonomous decision-making style regarding MRI-based decisions were observed. Unblinded data will reveal statistical differences between the groups.

Submission ID: 113; Submission Group: Application of Current Technologies in MS Rehabilitation; Submitter: Faryân Bouzarpour

The effect of a 6 weeks ERIGO® training on spasticity in Multiple Sclerosis: a case study
Running title: Effect of ERIGO® training on spasticity in MS

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Introduction: Multiple Sclerosis is a neurological disease with a lot of different symptoms. People with Multiple Sclerosis (PwMS) experience spasticity up to sixty to eighty percent. The Erigo® combines gradual verticalization with robotic movement therapy for the legs and may reduce spasticity. This case-study aims to explore the benefits or disadvantages of Erigo®-training on spasticity in PwMS.

Methods: We selected one man with secondary progressive MS (56 years, EDSS 8.5). The treatment consisted of 6 weeks of daily Erigo®- training: 30 minutes at 50 steps per minute and an inclination of 80°. Each session, the Modified Ashworth Scale (MAS) and the VAS for pain were administered before and after training. The selected lower limb muscle groups were: hip adductors, hip extensor and hip flexors; plantar foot flexors. Every Friday the Multiple Sclerosis Spasticity Scale (MSSS-88) was completed to assess the perceived impact of spasticity.

Results: A significant decrease of the mean MAS score after the use of the Erigo® was found in several muscle groups: left hip extensor: 1.043 ± 0.928 (p<0.001); left hip adductor: 0.522 ± 0.593 (p=0.001); left plantar flexor: 0.261 ± 0.449 (p=0.014); right hip extensor: 0.261 ± 0.541 (p=0.034); right hip adductor: 0.565 ± 0.59 (p<0.001) and right plantar flexor: 0.565 ± 0.507 (p<0.001). Differences in left hip flexor (0.043 ± 0.209) and right hip flexor (0.087 ± 0.288) were not significant.

The MSSS-88 and the VAS score for pain did not change significantly. The effect of the Erigo®-training was not sustained the day after.

Conclusion: This case-study showed a positive result in immediately reducing the MAS but has no significant difference on the impact of spasticity and on perceived pain. Additional study with a larger sample is required to confirm results.

Submission ID: 114; Submission Group: Multidisciplinary Rehabilitation in MS; Submitter: Niels Peeters
Measurement of occupational balance in people with multiple sclerosis and their caregivers

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Introduction: People with multiple sclerosis (PwMS) experience functional limitations which threaten the performance of meaningful activities and occupations that belong to different life domains: self-care, productivity, and leisure. Consequently, the balance between these domains (i.e. occupational balance (OB)) is threatened. Also the social context of PwMS experiences often a negative impact of MS on their occupational balance (e.g. one may be threatened in productivity as they act as a social caregiver).

Aim: To develop and select appropriate interventions targeting OB of both PwMS and their social context, professionals should have instruments to measure OB in both groups. The aim is to translate and test the feasibility of two OB questionnaires which are based on the same theoretical background: the OB-Care (i.e. for caregivers) and OB-quest (i.e. for PwMS).

Method: In a first work package (WP) both questionnaires will be translated to Dutch and French and backward to English. In a second WP, both questionnaires will be pilot-tested in a small sample of PwMS and their social caregivers in the National MS Center Melsbroek. Hereby, the usability will be explored using the NASA-TLX questionnaire. In a third WP, both questionnaires will be tested for feasibility and usability in a larger sample of PwMS and their social caregivers. Hereby, also the health care professionals will be asked to evaluate the usability.

Results: At time of abstract submission an international research-consortium is established and the protocol is developed. The protocol will be presented at the euRIMS 2023 annual. Final results are expected at the end of 2024, and will be presented at the euRIMS annual conference.

Submission ID: 115; Submission Group: Application of Current Technologies in MS Rehabilitation; Submitter: Filippo Rumi
Assessing the Quality of Life, Epidemiology, and Burden of Disease in Patients with Multiple Sclerosis in Italy: A Survey Study

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Abstract

Multiple sclerosis (MS) is a chronic autoimmune disease that affects the central nervous system, including the brain and spinal

cord. MS is caused by the immune system mistakenly attacking the protective covering (myelin) around nerve fibers, leading to damage and scarring (sclerosis). Considering the epidemiological burden of the condition, a survey was developed together with the patients' association (AISM) to investigate aspects related to the management of the condition, quality of life and aspects concerning the social burden. The survey will be conducted among a large sample of Italian patients with multiple sclerosis to gather information about their experiences and to provide insight into the challenges they face. We expect that the results of the survey will reveal important findings on those aspects of the condition that can be improved. Patients suffering from MS are usually experiencing a range of symptoms which had a significant impact on their daily activities and overall well-being. Furthermore, the survey results will show that the disease has a significant impact on the patient's ability to work. The survey also will provide important epidemiological data, including the incidence and prevalence of multiple sclerosis and the demographic characteristics of patients with the disease. Furthermore, we expect that the results will indicate that the disease has a high burden of disease, with patients reporting a high level of disability and a reduced quality of life compared to the general population. In conclusion, it is our intention to provide results in order to highlight the need for continued efforts to support and improve the lives of patients with MS. In our opinion the results will provide important insights into the experiences of patients with MS and the challenges they face and can inform the development of policies and interventions to support this patient population.

Submission ID: 116; Submission Group: MS Rehabilitation within and across the ICF Domains; Submitter: Zuhail Abasiyanik
Psychometric properties of three self-report questionnaires assessing dual-task difficulties in people with multiple sclerosis: A multicenter study within the RIMS network

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Abstract

Background: There is a need for questionnaires with good measurement properties to illuminate perceived dual-task difficulties in daily life in persons with multiple sclerosis (pwMS). This multicenter study aimed to translate and evaluate the reliability and validity of the Dual-Tasking Questionnaire (DTQ), Dual-Task Screening-List (DTSL), and Dual-Task-Impact on Daily-life Activities Questionnaire (DIDA-Q) in six countries within the Rehabilitation in MS (RIMS) network (Belgium, Chile, Italy, Israel, Spain, and Turkey).

Methods: The three dual-task questionnaires were translated and culturally adapted in all six countries when applicable. Reliability was assessed by Cronbach's α for internal consistency and intraclass correlation coefficients (ICC) for test-retest reliability. Convergent validity was assessed by formulating hypotheses about correlations between dual-task questionnaires and other self-reported questionnaires (perceived walking difficulties, fatigue, and fear of falling) and performance-based measures [cognitive information processing speed, walking speed, manual dexterity, single and dual-task walking (walking with word list generation task)]. Known-groups validity was assessed against different levels of disability (mild disability: EDSS < 4.0, moderate-to-severe disability: EDSS 4.0 to 6.5).

Results: In total, 339 pwMS from six countries [225 female (66.4%), mean age 47.52 ± 11.76 years, EDSS 3.79 ± 1.85 , disease duration 12.36 ± 9.18 years] participated in the study. The DTQ, DTSL, and DIDA-Q demonstrated high to very high test-retest reliability (ICC: 0.91, 0.87, 0.96, respectively) and excellent internal consistency (Cronbach's α : 0.86, 0.83, 0.90, respectively). The three self-report questionnaires showed a strong correlation with each other, moderate-to-strong correlations with other self-reported questionnaires, low-to-moderate correlations with performance-based measurements. >70% of the hypotheses were confirmed overall. Each of the three questionnaires differentiated pwMS according to disability subgroups.

Conclusion: The DTQ, DTSL, and especially DIDA-Q have good-to-excellent psychometric properties in six different countries and cultures. These self-report questionnaires are now cleared for use in research and clinical practice to assess the impact of dual-task difficulties on the daily life of pwMS.

Submission ID: 117; Submission Group: MS Rehabilitation within and across the ICF Domains; Submitter: Alice Bollini Assessing Interhemispheric Transfer Time in Multiple Sclerosis: Implications for Motor Coordination

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Multiple Sclerosis (MS) is a progressive neurological disease that affects the central nervous system, leading to motor, sensory,

and cognitive impairments. The integrity of the corpus callosum, which serves as the main pathway for interhemispheric transfer (IHT), is frequently affected by demyelination in people with MS (PwMS). Therefore, it is essential to assess the IHT time in PwMS to understand the extent of the corpus callosum and its impact on motor functions. In this study, we employed the Poffenberger paradigm, a widely used measure of IHT time. This paradigm assesses the modulation of the interhemispheric integration time as a function of ipsi- and contralateral reaction times (RTs) to lateralized sensory (visual or tactile) stimulation. Our results showed that PwMS had longer IHT time than healthy controls, particularly in the tactile modality. Moreover, we observed a positive correlation between the IHT time and bimanual coordination indices. These results indicate the sensitivity of our paradigm in the behavioral investigation of interhemispheric function in PwMS, showing the crucial role played by the corpus callosum in facilitating the transfer of sensory and motor information between hemispheres and its implication in motor coordination. The results have important implications for MS rehabilitation. First, by assessing the interhemispheric transfer, our tasks can help to identify the extent of corpus callosum damage in PwMS and its impact on motor function. This information could be used to tailor individual rehabilitation interventions to improve motor coordination. Moreover, providing a rapid performance index allows for monitoring the rehabilitation interventions' evolution.

Submission ID: 118; Submission Group: MS Rehabilitation within and across the ICF Domains; Submitter: Alice Bollini Exploring the Impact of Multiple Sclerosis on Multisensory Integration Abilities: how the senses influence higher cognitive functioning

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Multiple Sclerosis (MS) is a debilitating disease that affects various aspects of the nervous system, including motor, sensory, psychological, and cognitive functioning. In this study, we focused on perceptual impairments, particularly multisensory integration (MSI) abilities, which refer to the ability to synthesize information from different senses in a unique percept. The impairments in multisensory processing may have a cascading effect on the information processing hierarchy and impact higher cognitive domains. To test our hypothesis that MS may disrupt the ability to process multisensory stimuli efficiently, we employed the temporal order judgment (TOJ) task in people with MS (PwMS) in different sensory modalities. The TOJ task measures the temporal binding window (TBW), the specific range of temporal offsets where sensory inputs are merged. Our results showed that PwMS had larger TBW than healthy

controls, indicating more difficulties in integrating bimodal stimuli, especially in audiovisual condition. Additionally, we observed a positive correlation between the TOJ outputs and cognitive and functional scales, suggesting a relationship between MSI ability, functional independence, quality of life, and cognitive performance. In conclusion, our study highlights the importance of considering MSI abilities in MS rehabilitation. These results provide evidence for the relationship between MSI ability and various aspects of functioning and suggest that incorporating MSI assessments into the rehabilitation process may improve the patient's overall functioning. The findings open new perspectives for developing screening and rehabilitation interventions aimed at enhancing MSI abilities in PwMS.

Submission ID: 120; Submission Group: MS Rehabilitation within and across the ICF Domains; Submitter: Ela Tarakci

The Effect of Disease Duration on Upper Extremity Muscle Strength and Function in People with Multiple Sclerosis

Ela Tarakci, Uğur Ovacık, Feray Güngör, Gökçe Leblebici, Zeynep Özdemir, Aysun Soysal

Objective: The aim was to examine the relationship between muscle weakness and dysfunction in the upper extremity (UE) and disease duration (DD) of people with Multiple Sclerosis (pwMS) who have similar EDSS levels.

Methods: 59 pwMS with EDSS levels ≤ 3 were divided into two groups according to their DD as early period (DD < 1 year) and mid-to-late period (DD ≥ 1 year). pwMS were evaluated with 'Hand Held dynamometer' for grip strength (GS) and 'pinchmeter' for pinch strength (type, lateral, palmar), 'Nine Hole Peg Test (NHPT)' and 'Minnesota Manual Dexterity Test (MMDT)' for unilateral and bilateral function. Except for bilateral UE function, all evaluations were repeated twice in the dominant extremity, and the mean score was recorded.

Results: Demographic and clinical characteristics of the early (23F, 6M; mean age: 34.93 ± 8.41 ; EDSS: 1.12 ± 0.54) and mid-to-late (20F, 10M; mean age: 30.36 ± 9.99 ; EDSS: 1.15 ± 0.60) groups properties were similar ($p > 0.05$). The scores of early pwMS were follows as; for GS 23.53 ± 8.46 kg, for type strength 3.45 ± 1.07 kg, for lateral strength 4.37 ± 1.31 kg, for palmar strength 5.18 ± 1.67 kg, for NHPT 19.26 ± 1.72 s, for MMDT 52.19 ± 8.90 s. The scores of mid-to-late pwMS were follows as; for GS 27.41 ± 7.67 kg, for type strength 4.12 ± 1.09 kg, for lateral strength 5.29 ± 1.55 kg, for palmar strength 5.77 ± 1.43 kg, for NHPT 20.97 ± 3.54 s, for MMDT 57.57 ± 16.71 s. There was a significant difference between the type strength ($p = 0.025$), lateral strength ($p = 0.021$), unilateral ($p = 0.022$) and bilateral function (0.038) scores of the two groups.

Conclusions: According to the results of our study, it is seen that the functional conditions are not similar in pwMS who have the same EDSS levels but different DD, and that the disease progresses secretly. We suggest that functional tests should be used when interpreting the UE clinical conditions of pwMS, taking into account the DD.

Submission ID: 121; Submission Group: MS Rehabilitation within and across the ICF Domains; Submitter: Jacqueline R Mhizha-Murira
Providing emotional support around the point of multiple sclerosis diagnosis (PrEliMS): A feasibility randomised controlled trial

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Background and aim: Receiving a diagnosis of Multiple Sclerosis (MS) can be a lengthy and challenging process impacting psychosocial adjustment to MS and future engagement with clinical services. Based on our previous research and feedback from people with MS (pwMS), we designed an intervention to provide emotional support for those newly diagnosed. The intervention incorporated elements of acceptance and commitment therapy, emotional support, information provision, and supportive listening. This study aimed to evaluate the feasibility and acceptability of the trial procedures and the emotional support intervention for newly diagnosed pwMS.

Methods: This was a three-arm, mixed methods, randomised controlled trial comparing usual care, versus usual care plus MS Nurse Support, versus usual care plus MS Nurse Support plus Peer Support. Participants were newly diagnosed pwMS, aged > 18 years, and not currently receiving a psychological intervention. Feasibility and acceptability outcomes explored recruitment rate, acceptability of the intervention, completion of outcome measures at 3- and 6-months post-randomisation (perceived stress, mood, self-efficacy, psychological impact, and service use), and signal of efficacy.

Results: Forty pwMS were randomised (13 usual care, 14 usual care plus MS Nurse Support, 13 usual care plus MS Nurse Support plus Peer Support; mean age 39.9 years, SD=12.1years). The return rates for the 3- and 6-month questionnaires were 90% and 95%, respectively. Participant interviews suggested the trial was feasible, and the intervention acceptable, with some amendments to trial procedures and intervention delivery noted. There were no statistically significant differences between groups at follow-up for any measures, and effect-size estimates ($\eta^2_p \leq 0.086$) were small.

Conclusion: Although the small effect sizes suggest that more work exploring the delivery and integrity of the intervention is needed before this is pursued, it is feasible and acceptable to conduct a definitive trial of a combined MS Nurse-specialist and peer support adjustment to diagnosis intervention.

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Submission ID: 122; Submission Group: Application of Current Technologies in MS Rehabilitation; Submitter: Zuhul Abasıyanık

Effects of prolonged walking on dual-task walking performance in persons with multiple sclerosis

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Objective: Motor impairment and fatigue perception may affect walking automaticity. We aimed to investigate the effect of prolonged walking administered by the 6-Minute Walk Test (6MWT) on motor-cognitive dual-task performance in persons with multiple sclerosis (pwMS) with different levels of disability compared to healthy controls (HC).

Methods: A total of 50 pwMS [30 mildly disabled (EDSS<4.0), 20 moderately-severely disabled (EDSS 4.0 to 6.5)] and 29 age- and sex-matched HC were included. Spatiotemporal gait parameters during single (overground walking for 30 sec) and dual-task walking (overground walking for 30 sec with word list generation task) were assessed before and immediately after the 6MWT using three inertial gait sensors. The dual-task cost (DTC) of gait parameters was calculated as change (in percentage) between the dual-task to the single-task conditions. Perceived walking difficulties, fatigue, history of falls, fear of falling, and perceived dual-task difficulties were evaluated via self-report questionnaires.

Results: PwMS with moderate-to-severe disability group had a significant deterioration in cadence, speed, double support, and asymmetry during dual-task walking after the 6MWT. However, there was no change in mildly disabled pwMS, and HC demonstrated better scores in cadence, speed, and gait variability after the 6MWT. As for the DTC, while mildly disabled pwMS (in speed and gait variability) and HC (in double support, cadence, and gait variability) showed improvements, no significant difference was found in moderate to severely disabled pwMS. Cognitive task performance incremented solely in HC following the 6MWT. Change in DTC was correlated to self-reported walking disability, fatigue, and perceived dual-task difficulties ($r=-0.301$ to -0.337) in pwMS.

Conclusion: Prolonged walking affects severely disabled pwMS regardless of the cognitive task. This suggests that they focus more on walking than cognitive task performance. Mildly disabled pwMS and HC could maintain gait automatization and even reduce DTC after 6MWT, suggesting that 6MWT may not be sufficient to induce performance fatigability as measured by dual-task performance in mildly disabled pwMS and may even make gait more dynamic.

Submission ID: 123; Submission Group: Multidisciplinary Rehabilitation in MS; Submitter: Jelka Jansa
Multidisciplinary Rehabilitation in Progressive Multifocal Leukoencephalopathy - A Case Report

Progressive multifocal encephalopathy (PML) is a potentially fatal opportunistic infection of the central nervous system by John Cunningham virus. We report on a multidisciplinary rehabilitation in a 45-year-old female suffering from PML after 20 natalizumab infusions. After natalizumab discontinuation immune reconstitution inflammatory syndrome (IRIS) developed leading to additional deterioration of the neurological disability of the patient. Initial right sided hemiparesis slowly progressed to hemiplegia, later left sided hemiparesis appeared as well as motoric dysphasia so she became bedridden and completely dependent in activities of daily living (ADL).

Physiotherapy treatment focused on deterioration of posture control, sensorimotor skills of the right-sided limbs and gait pattern. Exercises for postural stability and movement control were performed. Occupational therapy (OT) focused on maintaining ADL, underlying fatigue and sensory-motor impairment in right upper limb. After the deterioration of her health condition, physiotherapists implemented gradual verticalization and bed-wheelchair transfer. OT then focused on body positioning and impairments in both upper limbs, along with improving attitude to her current life situation. Clinical psychologist was included to provide psychological support and improve communication. We used basic cognitive behavioural model, relaxation techniques, normalisation, guided imagery for stress relief and regulation of mood. Speech language pathologist treatment was indicated when deviations in the quality and intelligibility of speech and communication appeared. Communication was maintained through closed-ended, dichotomous questions. With the progression of speech apraxia, the Augmentative and Alternative Communication board was introduced. Apraxia of speech persists at the forefront and significantly disables the patient in everyday communication. Multidisciplinary rehabilitation was essential in maintaining patient's functional level, preventing further decline as well as helping the neurologist monitor disease progression of her primary diagnosis as well as IRIS and in this way influence further diagnostic and therapeutic decisions.

Submission ID: 124; Submission Group: Promising Technologies that can Help Advance MS Rehabilitation; Submitter: Ludovico Pedullà

Innovative techniques for monitoring and enhancing the effects of rehabilitation in people with advanced multiple sclerosis

Running title: Innovative techniques for advanced MS rehab

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In advanced multiple sclerosis (MS), an exacerbation of mobility disorders including balance and gait impairment are often experienced. Rehabilitation is the most common and effective approach to tackle the burden of symptoms in this phase of the disease but neural physio-pathologic and recover mechanisms are still under debate in advanced MS.

Here, we aimed to assess and maximise the effect of rehabilitation in people with MS (PwMS) with walking impairment using innovative techniques.

Besides standard clinical tests on balance and gait, the evaluation included a neuroimaging technique, i.e., functional Near-Infrared Spectroscopy (fNIRS) to investigate cortical activity during different walking tasks. The intervention consisted in alternating rehabilitation and waiting-list periods. Participants were randomized into two groups, both using a sensorized cane (FBKEIN) able to monitor gait for prolonged time and to administer biofeedback stimulation (BF) promoting a proper use of the walking aid. However, only the experimental group received BF in the waiting-list phase in order to support the effect of rehabilitation.

Sixteen PwMS (age=56.3±11.0 years, all EDSS=6, disease duration=14.3±10.4 years) have been recruited until now and homogeneously randomized into the two groups. Twelve of them completed the study. Although not significant due to the limited sample, the experimental group showed better results at the clinical tests after the waiting-list period, suggesting that FBKEIN with BF can help maintain the effect of rehabilitation. From preliminary analysis of fNIRS data obtained at baseline, higher cortical activation was observed during curvilinear with respect to linear walking, mostly in prefrontal areas.

Brain activity is affected by the type of walking task in advanced MS. Whilst the effect of rehabilitation on neural recover mechanisms has still to be unveiled, FBKEIN seems to be a suitable tool allowing to monitor everyday-life walking and providing feedback that could help maintain the effect of the rehabilitative treatment.

Submission ID: 125; Submission Group: Multidisciplinary Rehabilitation in MS; Submitter: Edyta Matusik
The Usefulness of Saccades in the Diagnosis of Cognitive Impairment in Multiple Sclerosis Patients

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Cognitive impairment occurs in up to 70% of patients with multiple sclerosis (MS) and has a devastating impact on their lives. Therefore, cognitive function testing should be a regular part of the evaluation of these patients. Neuropsychological tests have many limitations hence new research tools are being sought. There are indications that saccadic movement testing can be used to assess cognitive function. The aim of the study was to evaluate cognitive function and saccadic movements in patients with MS. Moreover, correlations between cognitive deficits found on the

basis of psychological tests and abnormalities of selected parameters of saccadic movements in this group of patients were assessed. Methods: 79 patients with MS and 53 neurologically healthy volunteers, matched for age, gender and education, were included in the study. Cognitive functions were examined using SDMT (Symbol Digit Modalities Test), PASAT (Paced Auditory Serial Addition Test), verbal fluency test, WCST (Wisconsin Card Sorting Test), CVLT-II (California Verbal Learning Test, second version), BVM-T-R (Brief Visuospatial Memory Test, revised version), JOL (Judgement of Line Orientation test). A study of reflex and volitional saccades in the horizontal and vertical planes was performed using the Research XY saccadometer from Ober Consulting. Results: Cognitive impairment on the basis of neuropsychological examination was found in 35 patients with MS (44.78%). Saccadometry showed impaired saccadic movements in the study group. The patients made fewer correct responses in all tests performed compared to the control group. The saccades had significantly longer latencies and the latency values varied more among the patient group. The results of neuropsychological tests correlated with disorders of selected parameters of reflex and volitional saccades. Conclusions: Saccadometry can be used to assess the cognitive functioning of patients with MS by complementing the neuropsychological examination, and thus enable a more accurate and reliable assessment of disease progression and severity.

Submission ID: 126; Submission Group: Application of Current Technologies in MS Rehabilitation; Submitter: Marcos Maldonado

Efficacy of the therapeutic plan based on a systematic evaluation, conventional training and the use of virtual reality in a patient with Multiple Sclerosis before and during the pandemic. Case report

According to recent findings, there is a significant difference in the functional status of MS patients who undergo rehabilitation and those who do not. However, the COVID-19 pandemic presented a new hurdle to even the routine care of people with MS. Altogether, the use of DMTs, access to rehabilitation therapies, as well as laboratory and MRI monitoring have all been drastically affected by this crisis, with many people unable to continue their rehabilitation. The objective of this study, is to identify the main gaps in reaching optimal cost-effectiveness for treatment. We present the case of a man who is 58 years old and a retired engineer. Few months after the onset of MS, he's been attending rehabilitation twice a week since 2018, which was done through tele-rehabilitation with non-immersive virtual reality during 6 months of the pandemic. We describe the process which he has received a dose of Ocrelizumab every 6 months. He's had 3 relapses treated with intravenous methylprednisolone. He paid nearly 75 thousand US dollars to the private system for the first 4 doses, the last 6 doses, were financed by a study in which he is participating. The patient was able to function longer and walk farther. His normal EDSS was 2.5, rising to 3.5 in the periods of less pharmacological support and as high as 6.0 during his worst period. He maintains an average of close to 6 thousand steps per day, (registered by himself through smartwatch) and high scores on MiniBestTest

and Functional Gait Assessment. He currently has an EDSS of 1.0, however, according to his medical team, he will be confined to a wheelchair within 4 years. This case demonstrates the importance of agreements in the rehabilitation teams, the systematic recording of measurements scales, the self-efficacy of the patient, and the opportunity to access medication appropriate for his health condition.

Submission ID: 128; Submission Group: Application of Current Technologies in MS Rehabilitation; Submitter: Andrea Tacchino

Low-cost smartphone-based assessment of postural sway in people with Multiple Sclerosis

Running Title: Smartphone apps for balance assessment

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Balance disorders are common in people with Multiple Sclerosis (PwMS) and a frequent assessment could allow an early detection of significant clinical changes and, consequently, providing more timely and effective rehabilitative interventions. Current instrumental balance tests are based on laboratory-grade force platforms. Such devices are expensive, requires dedicated space and personnel and are not feasible for home-based or ambulatory use.

Smartphones are common low-cost, portable, and easy-to-use electronic devices embedding inertial sensors suitable to allow balance measurements with sufficient accuracy. Future studies should continue exploring psychometric properties and discriminative ability of smartphone apps measuring balance in PwMS.

Here, we compared the performance of a commercial smartphone (equipped with a general-purpose app able to extract the accelerometric signal) placed either in a fixed or freely chosen position vs. force platform to calculate the postural sway in PwMS.

Four experimental conditions (feet: trochanteric/free, TROC/FREE; eyes: open/close, EO/EC) were presented to the participants. Center-Of-Pressure (COP) time series were acquired with ArgoPlus platform on participants while the smartphone, fixed using a belt, simultaneously acquired the accelerometric signal along three perpendicular axes. Data were processed to calculate sway area (95% confidence ellipse) and sway path with both instruments. A correlation analysis was performed on the two groups of parameters.

Fifteen PwMS, recruited at the AISM Rehabilitation Service (Genoa), took part to this study (male/female: 3/14; age: 46.47±9.88 years; disease course: 11 RR and 4 progressive; EDSS: 3.47±1.64). High correlation between the smartphone-based and platform data was detected for all the conditions. Sway area: TROC_EO, $r=0.85$, $p<0.001$; TROC_EC, $r=0.93$, $p<0.001$; FREE_EO, $r=0.86$, $p<0.001$; FREE_EC, $r=0.91$,

$p<0.001$. Sway path: TROC_EO, $r=0.82$, $p<0.001$; TROC_EC, $r=0.94$, $p<0.001$; FREE_EO, $r=0.91$, $p<0.001$; FREE_EC, $r=0.90$, $p<0.001$.

Our findings confirm the reliability of smartphone apps to assess balance in PwMS; high correlation for FREE conditions suggest a reliable use in real-world settings.

Submission ID: 129; Submission Group: Application of Current Technologies in MS Rehabilitation; Submitter: Andrea Giordano

Development and validation of a Subjective self-Assessed on-line Version questionnaire on Quality of Life (SAVE-QoL)

Running title: SAVE-QoL development and validation

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Abstract

Background and Aim: The overall objective of the present project is to construct and assess the psychometric properties of a Quality of Life (QoL) scale (SAVE -QoL) addressing several needs not fully addressed by a single questionnaire in the current literature. Specifically, we aim to validate a self-administered, digital, and easily accessible QoL scale that i) respects subjectivity and multidimensionality of the QoL construct; ii) is sensitive to change over time; iii) is applicable in both clinical (e.g., multiple sclerosis) and healthy populations, and not affected by cultural differences.

Method and Results: Four hundred and twenty-two healthy Individuals (mean age 38.66 years [SD 19.59]) were recruited for the first phase, i.e., individuating a list of categories associated with the QoL. Based on a previous subjective QoL scale (SEI-QoL), participants were asked to describe five aspects that they considered as important in determining their QoL. The final SAVE-QoL categories were: Emotional Health, Environment, Family, Free time, Independence, Material well-being, Nutrition, Partner, Personal fulfilment, Physical Health, Social relationship, and Values and Spirituality.

One hundred and fifty-eight individuals (mean age 28.96 years [sd 12.94]) were recruited for the second phase, i.e., verifying the SAVE-QoL reliability by measuring the test-retest reliability, and the concurrent validity (comparison with the WHOQOL-BREF and the SF-12). A good degree of reliability was found between the SAVE-QoL total scores at T1 and at T2. Both the SAVE-QoL total scores at T1 and at T2 were highly correlated with all the WHOQOL-BREF scales and Mental Composite Scale of the SF-12-12. Completion time was significantly shorter for SAVE-QoL compared to WHOQOL-BREF and SF-12.

Conclusion: SAVE-QoL represents a feasible self-administered, digital, and easily accessible QoL scale. SAVE-QoL use will extend administration to larger healthy and clinical populations, including people with multiple sclerosis.

Submission ID: 130; Submission Group: Promising Technologies that can Help Advance MS Rehabilitation; Submitter: Michelangelo Dini
TMS-Evoked Motor Threshold as a Predictor of Response to Multidisciplinary Neurorehabilitation Plus rTMS in Multiple Sclerosis

Short Title: Motor threshold predicts gait improvement

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Background: Despite evidence suggesting the effectiveness of neurorehabilitation plus non-invasive repetitive Transcranial Magnetic Stimulation (rTMS) in people with MS (pwMS), little is known about response predictors. Identifying pwMS more susceptible of treatment benefit, such as those with greater motor reserve is key to improve clinical care through tailored treatment protocols. One important neurophysiological measure of corticospinal reserve and excitability is motor threshold (MT) to single-pulse TMS. On the other hand, one important clinical measure of walking performance in pwMS is the 6-Minutes Walk Test (6MWT).

Objective: To explore the usefulness of lower limb MT in predicting improvement of walking endurance to intensive multidisciplinary rehabilitation plus rTMS in pwMS

Methods: We analysed clinical and neurophysiological data from 74 consecutive pwMS with mean age 52.5 ± 9.5 years, mean disease duration 16.1 ± 9.3 years, median inpatient stay 41 (32-57) days (1st-3rd quartile), median EDSS 6 (5.5-6.5) who underwent at least 3 weeks of inpatient intensive multidisciplinary neurorehabilitation plus 9-12 sessions of excitatory (20 Hz) motor cortex rTMS. We investigated differences in TMS-evoked visual MT according to improvement at the 6-Minutes Walk Test (6MWT) using independent-samples t-test, considering a minimal clinically important improvement cutoff of 55 metres.

Results: After treatment, 23 (31.1%) pwMS showed a clinically important improvement of 6MWT performance (42.3 ± 42.7 metres, $p < 0.001$). There were no significant clinical or demographic differences between those who improved and those who did not (all $p > 0.05$). The area under the curve (AUC) of MT distribution was significantly lower in pwMS with clinically important improvement ($6.02 \pm 0.83\%$ vs. $6.61 \pm 1.69\%$, $p = 0.048$), indicating that lower MT values were associated with better motor outcomes.

Conclusion: We found an association of corticospinal reserve to the lower limbs, as from single-pulse motor threshold to TMS, with the effectiveness of intensive multidisciplinary rehabilitation plus rTMS on walking endurance, as from the 6MWT. These findings suggest corticospinal reserve as a potential predictor to be considered in the design of tailored neurorehabilitation and neuromodulation interventions in people with MS.

Submission ID: 131; Submission Group: Application of Current Technologies in MS Rehabilitation; Submitter: Su-Chun Huang
Using Retinal Neural Reserve to Predict the Outcome of Multidisciplinary Rehabilitation in People with Progressive Multiple Sclerosis

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Objective: To assess whether retinal neural reserve measured with optical coherence tomography(OCT) can predict the treatment effects of intensive multidisciplinary neurorehabilitation in people with progressive multiple sclerosis(PwPMS).

Background: Multidisciplinary rehabilitation can enhance neural plasticity and thus induce task-specific neural reorganization leading to clinical improvement in PwPMS. However, it is still unclear whether there is a minimum level of neural reserve required for neural plasticity and how to measure it in PwPMS. Retinal neuroaxonal loss at OCT is highly correlated with brain gray and white matter atrophy, providing an opportunity to investigate the relationship between neural reserve and clinical outcome after rehabilitation.

Methods: Fifty-two PwPMS (age 52.5 ± 9.0 y, EDSS 6.0 ± 1.2) underwent >1 month (45 ± 16 days) of intensive multidisciplinary rehabilitation (including twelve sessions of repetitive transcranial magnetic stimulation, rTMS). OCT peripapillary and macular scans were performed at baseline, while morbidity(6-minutes walking test [6MWT], Timed 25-foot walk test [T25FW]) and patient-reported outcome measures (PROMs: BDI-II, MFIS-21, STAI, MSQOL, FIM) were evaluated pre- and post-treatment. Statistics included correlations between baseline OCT measures (peripapillary retinal nerve fiber layer thickness [pRNFL], macula RNFL volume [mRNFL], macula ganglion cell/inner plexiform layer volume [mGCIPL]) and post-treatment improvements and comparisons between subgroups according to OCT-defined neural reserve cutoffs (25th-Percentile of the OCT parameters).

Results: Improvement of 6MWT was positively correlated with higher baseline mRNFL($r = 0.5093$). Further, improvement of BDI-II was correlated with higher pRNFL ($r = -0.3160$), mRNFL ($r = -0.4617$), and mGCIPL ($r = -0.3233$) at baseline. Subjects with the mGCIPL less than the 25th Percentile (1.56mm^3) showed less improvement in 6MWT ($16.1 \pm 22.1 \text{m}$ vs. $41.7 \pm 40.6 \text{m}$), BDI-II (-0.22 ± 3.7 vs. -5.3 ± 8.0), and MFIS-21 (-5.9 ± 17.4 vs. -22.6 ± 19.0). No significant difference was found according to pRNFL and mRNFL cutoffs.

Conclusion: Higher baseline OCT-measured neural reserve predicts better post-treatment functional recovery, as from correlation analysis and from an OCT-defined mGCIPL cutoff further differentiating post-treatment response. Our findings suggest that OCT measures can be part of algorithms aimed at optimizing patient selection for trials targeting neural plasticity.

Submission ID: 132; Submission Group: Application of Current Technologies in MS Rehabilitation; Submitter: Angela Boschetti

Effectiveness and feasibility of a home-based cognitive rehabilitation protocol in people with Multiple Sclerosis (pwMS)

Short Title: Home-based cognitive rehabilitation.

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Aim: Explore the effectiveness and feasibility of a home-based protocol for cognitive rehabilitation.

Background: Given the growing interest in telerehabilitation techniques based on the newest technologies, it remains to be established whether there is solid evidence regarding their effectiveness in alleviating the cognitive deficits in pwMS, and, whether they can be a feasible option in these individuals.

Methods: PwMS, with impaired cognitive performance on at least one test of the Brief International Cognitive Assessment for MS (BICAMS) or Stroop test or Montreal Cognitive Assessment (MoCA), will be recruited from an MS Rehabilitation Centre. All subjects will undergo baseline assessment remotely with these neuropsychological tests and patient-reported outcome measures (PROMs). Then, participants will be randomised (block 1:1, n=10) in Intervention Group and Control Group. The Intervention Group will train at home with the software RehaCom for 12 weeks, while the Control Group will undergo sham computerised activities at home for the same duration. Additional neuropsychological assessment and PROMs (measures of fatigue, depression, and quality of life) will be administered remotely at the end of the telerehabilitation and at a 6 month-follow-up appointment to look at the long-term effects of home-based cognitive rehabilitation.

At this stage the recruitment is ongoing (n=6).

Efficacy of home-based rehabilitation will be evaluated with an analysis of differences between groups in terms of performance at cognitive tests and scores at PROMs, both at single and looking at group x time interaction effects.

Feasibility will be measured by subtracting the total hours of expected training with total hours of actual training.

Based on recent findings, we expect pwMS to benefit from software-based rehabilitation at home. Telerehabilitation could become an adequate tool for continuity of care in MS, offering equal care opportunities to people with mobility limitations or travel restrictions.

Submission ID: 133; Submission Group: MS Rehabilitation within and across the ICF Domains; Submitter: Feray Güngör

How Does Disease Duration Affect the Muscle Strength and Balance in People with Multiple Sclerosis with Similar EDSS Levels?

Feray Güngör, Uğur Ovacık, Gökçe Leblebici, Zeynep Özdemir, Burcu Yüksel, Aysun Soysal, Ela Tarakçı

Background: The topographic model of Multiple Sclerosis (MS) suggests that the subthreshold disease burden is compensated by functional reserve, appears no physical deficits, and clinical symptoms become evident when lesions cross the clinical threshold. Although the Expanded Disability Status Scale (EDSS) is the gold standard for the classification of disability in MS, it is insufficient to detect mild involvement in the very early period.

Aim: To compare muscle strength and postural sway in people with MS (PwMS) who have similar EDSS levels but different disease duration.

Methods: PwMS with an EDSS of ≤ 1.5 were included in the study. PwMS were divided into two groups according to disease duration as ≤ 6 month (newly diagnosed) (n=21) and above two years (n=20). Knee flexor and extensor muscle strengths were assessed with Biodex Multi-Joint System at the angular velocity of 60°/s. The modified Clinical Test of Sensory Integration of Balance (m-CTSIB) was used with four different conditions (open eyes on firm and foam surfaces, closed eyes on firm and foam surfaces). The Balance Error Scoring System (BESSTest) was used to assess postural sway in feet together and tandem stance, on firm and foam surfaces.

Results: The mean disease duration of the second MS group was 3.60 ± 3.37 years. Knee flexor and extensor muscle strengths were significantly different between MS groups in favor of the newly diagnosed MS ($p < 0.001$ for right and left quadriceps, $p < 0.001$ for right hamstring and $p = 0.03$ for left hamstring). There was no significant difference between MS groups in any m-CTSIB and BESSTest conditions ($p > 0.05$).

Conclusions: As disease duration increases, the muscle strength of the lower extremities decreases significantly. EDSS is not sufficient to determine the severity of the disease. The muscle strength of the patients should be followed routinely from the early period with objective methods.

Submission ID: 135; Submission Group: Promising Technologies that can Help Advance MS Rehabilitation; Submitter: Peppino Tropea

Gait Analysis Synthetic Indexes as predictors of Intensive Multidisciplinary Neurorehabilitation Outcomes in Multiple Sclerosis: Methodological Aspects

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Background and aims: The evaluation of gait deviation in individuals with multiple sclerosis (MS) represents an important issue in assessing the effectiveness of multidisciplinary neurorehabilitation treatments. Despite the availability of tools and devices for

the assessment of the kinematic aspects of gait, there are still some difficulties in interpreting the large amount of data they produce. The introduction of gait analysis synthetic indexes (namely Gait Profile Score (GPS) and Gait Variable Score (GVS)) could help in this perspective.

Objective: The present study aimed to characterize the locomotion of individuals affected by MS involved in an intensive multidisciplinary rehabilitation plus rTMS, using GPS and GVSs as synthetic indexes of gait.

Methods: Patients with MS experienced at least 3 weeks of inpatient intensive multidisciplinary neurorehabilitation plus 9-12 sessions of excitatory (20 Hz) motor cortex repetitive Transcranial Magnetic Stimulation (rTMS). Before and after the treatment the kinematic aspect of the gait was recorded. The evaluation was carried out using a 7-cameras optoelectronic system (VICON, Oxford, UK) with a sampling rate of 100 Hz. After familiarization with the environment, the subjects walked barefoot at their own natural pace along a 10-m walkway. Raw data were pre-processed and processed using the Nexus software (VICON, Oxford, UK) to calculate the spatiotemporal and kinematic parameters for each trial performed by the patients. Using a customized script in MATLAB (MathWorks Inc., Natick, MA, US) the kinematic outputs were used to calculate the Gait Variable Scores (GVSs) (one for each kinematic time-series) and the Gait Profile Score (GPS).

Results and Conclusions: 30 patients with MS (11 females, 49.41±9.50 years, EDSS 5.02±1.29) were enrolled and performed the rehabilitation treatment and no adverse event were recorded. The consistence of gait analysis data was good, indeed, at least six gait trials were collected for each subject.

Full data-analysis and interpretation on potential benefits will be presented during RIMS2022.

Submission ID: 136; Submission Group: Translation of New Rehab Knowledge into Practice; Submitter: Valeria Bergamaschi

Is Circle-line paradigm an effective tool to assess callosal connectivity in Multiple Sclerosis?

Short title: Bimanual coupling in multiple sclerosis

Bergamaschi V, Iester C, Biggio M, Bricchetto G, Bove M

The integrity of white matter in people with Multiple sclerosis (PwMS) is disrupted and its relationship with functional performance is not well understood. Previous data demonstrated that PwMS have difficulty with bimanual coordination which may be also caused by impaired information exchange between hemispheres.

Bimanual coupling has been explored through circle-line drawing task, which has never been studied in people with Multiple Sclerosis.

The aim of this study is to assess if PwMS show alteration in circle-line paradigm.

This paradigm requires to draw simultaneous continuous circles with one hand and continuous lines with the other. Despite these sketches are easy when executed unimanually, when performed together they tend to influence each other, resulting in two "elliptical" figures. To evaluate the bimanual coupling effect, we computed the ovalization index (OI) that allowed quantifying

the deviation from a perfect line or a perfect circle in both congruent (i.e. movement with the right hand as with the left hand, namely circle-circle or line-line) and incongruent (i.e. movement with the right hand different from with the left hand, namely circle-line or line-circle) conditions.

Ten outpatients (female 6, RR 5, SP 4, PP 1) of the Italian Multiple Sclerosis Society Rehabilitation Center (subjects were asked to draw lines or circles with both hands, the left with the Apple Pencil on the iPad, the right with a pen on a LCD board) underwent the circle-line paradigm.

Up to now data from patients are similar to those shown in the literature for healthy subjects. Indeed, ovalization in incongruent conditions is higher than in congruent conditions.

Our future perspective are to increase the number of subjects and to correlate performance measure with neuroimaging data.

Submission ID: 137; Submission Group: Multidisciplinary Rehabilitation in MS; Submitter: Valeria Bergamaschi
Diagnostic block on lateral pectoral nerve as a first step towards a better management of upper limb hyperthonia in People with Multiple Sclerosis

Diagnostic block on lateral pectoral nerve in MS

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Background: People with MS (PwMS) suffer from variety of symptoms that have a deep impact on their everyday life. Spasticity and its related impairment of upper limb (UL; such as shoulder pain or bad posture) can also dominate functional deficits and give a relevant contribution to the individual and socio-economic burden of MS, but the management of upper limbs hypertonia in PwMS represents a complex treatment pathway with insufficient evidence supporting one particular treatment. Spasticity, indeed, is not the only cause of muscle hypertonia in PwMS. In such subjects, muscle immobilization (especially at short lengths) leads to muscle contracture, which makes a significant contribution to hypertonia. The anaesthetic diagnostic nerve block (DNB) is known to differentiate spasticity from other disorders of low mobility and can be useful in determining an appropriate treatment pathway. To assess the contribution of spastic muscle overactivity in UL impairment, we used the lateral pectoral nerve (LPN) block as the primary DNB for the adducted shoulder.

Aim: The aim of this study is to assess the usefulness of the lateral pectoral nerve (LPN) block in the UL spasticity management

Methods: This is an observational study assessing the effects of anaesthetic DNB of the LPN in UL spasticity management. Outpatients of the Multiple Sclerosis Italian Society Rehabilitation Center presenting upper limb spasticity undergo medical evaluation, including Modified Ashworth Scale (MAS), range of motion (ROM) measurement and nerve block if needed.

Results: At this moment 5 PwMS with a progressive course (4 secondary, 1 primary; female: 4), mean age of 55, mean disease duration of 19 underwent the anaesthetics DNB and they all showed an improvement of parameters considered.

Discussion: Although preliminary, results indicated that DNB of the lateral pectoral nerve could be an useful approach to the upper limb hypertonia management

Submission ID: 138; Submission Group: Promising Technologies that can Help Advance MS Rehabilitation; Submitter: Marta Tacchini
A novel paradigm for EEG markers of cognitive involvement in MS: Event-related potentials to the Symbol Digit Modalities Test

Short title: Cognitive potentials to SDMT in MS

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Background: Electrophysiological markers as event-related potentials (ERPs) are valuable tools for the early detection and monitoring of cognitive impairment in pwMS, towards prediction of the onset of cognitive impairment and evaluation of the effectiveness of treatment. Symbol-Digit Modalities Test (SDMT) is a paper-based clinical screening tool for cognitive processing speed, which is often impaired in pwMS. With the aids of ERPs, neurophysiological process during SDMT can be quantitatively assessed and served as an early biomarker for cognitive impairment.

Aim: To explore if EEG-based ERPs to SDMT can measure and predict functional changes pre- and post-cognitive rehabilitation.

Methods: We are going to collect data from 90 pwMS and 30 controls. A modified version of the SDMT (mSDMT) and oddball task will be performed during 32-channel EEG recording. ERPs elicited from the two tasks will be investigated and compared. Similar to traditional SDMT, a legend containing a list of symbols matched to a corresponding number and a symbol-digit pair were simultaneously displayed. The participant was asked to judge if the pair was correct. Raw EEG signal was first filtered, then the traces were segmented and averaged based on the trial onset.

Results: One healthy subject has completed the mSDMT task and detailed waveform assessments were performed. After the stimulus onset, a negative peak at 195ms was elicited over parietal and occipital sites, followed by a subsequent negative peak at 290ms over fronto-central electrodes. Further, a positive peak at 382ms was detected over centro-parietal sites.

Perspectives: Here we proposed mSDMT that is similar to traditional SDMT and is EEG-compatible. The results will be compared with the P300, a general ERP index of cognitive functioning, to evaluate the ERPs that are specific to SDMT. The relationship

of these novel ERPs and the performance to traditional SDMT will be studied, to measure their sensitivity and predictive value in detecting changes associated with cognitive rehabilitation.

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Benefits of multidisciplinary intensive neurorehabilitation on cognitive outcomes and Patient Reported Outcomes in people with Multiple Sclerosis

Background: Treatment of Multiple Sclerosis (MS) has become increasingly multidisciplinary and involves not only pharmacological treatments but also a wide range of therapies. Multidisciplinary MS Rehabilitation despite no change at the level of impairment, can improve perception of disability, quality of life and improve functioning in everyday activities.

Aim: To explore the effects of a multidisciplinary approach on cognition in a MS Rehabilitation Unit.

Methods: We conducted a retrospective analysis of real-world clinical data. Eighty-five consecutive subjects with MS were selected. All subjects underwent (at arrival at the Rehabilitation Unit and before discharge) repeated neuropsychological testing (SDMT, CVLT, BVRT, StroopTest) and Patient Reported Outcomes (BDI-II, FSS, MFIS, STAI, MSQoL-29), and during the hospitalization physical and occupational therapy. Fifty subjects (31F/19M; mean age=55.28years, SD:11,60; mean education=13.20years, SD: 4,25; mean EDSS=6.296, SD: 1,27) were found to be cognitively impaired at SDMT (mean score: 34,16, SD: 10.80) and BVMT (mean score: 17,19, SD: 8,93), and, started cognitive rehabilitation. Thirty-five cognitively unimpaired subjects (17F/18M; mean age=52.34years, SD: 9,43; mean education=14.80years, SD: 3,72; mean EDSS=5.561, SD: 1,18) did not undergo rehabilitation. Subjects were compared with a repeated-measures GLM within-subjects (pre-post evaluations) and between-subjects (Impaired-Unimpaired).

Results: All subjects with cognitive impairment undergo cognitive rehabilitation. All the sample improved on SDMT, CVLT, Stroop (all p for time effect<0.05; all p for interaction effect>0.05), PROMS (all p for time effect<0.05; all p for interaction effect>0.05). There was one significant interaction for the BVMT, for which impaired subjects showed greater improvement (p=.040).

Conclusion: Multidisciplinary intensive neurorehabilitation benefits cognition even the absence of a formal cognitive rehabilitation. Regarding the SDMT, these individuals scored in the lower normal range, therefore, we cannot exclude the role of their baseline performance on cognitive improvement. The findings may be limited by the presence of practise-effect even if alternative versions of tests were used.

