



## Abstracts from the 13th International Symposium on Gait and Balance in Multiple Sclerosis, Spring Journal Club and Data Blitz

### Rehabilitation including walking aid training with real-time feedback can induce motor and neural changes in people with multiple sclerosis

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**Background and Purpose:** Gait and balance impairment is common in multiple sclerosis (MS), often leading to walking aids need. Rehabilitation is the most common and effective approach to tackle the burden of these symptoms, but less attention is given to the correct use of an assistive device for ambulation. Here, we aimed to maximise the effect of a rehabilitation program including walking aid training with a sensorized crutch in people with MS (PwMS).

**Methods:** 24 PwMS (15 females, age=57.8±9.8 years, all EDSS=6) underwent a 20-session rehabilitation program focusing on gait, balance, and proper assistive device use. The experimental group (FB\_group, N=12) used a crutch with real-time feedback based on user support load, whilst the control group (NOFB\_group, N=12) used a standard crutch.

Assessment included Timed 25 Foot Walk (T25FW), Timed Up and Go (TUG) and Modified Fatigue Impact Scale (MFIS). Moreover, functional Near-Infrared Spectroscopy (fNIRS) was used to investigate cortical activity during linear and curvilinear walking tasks.

**Results:** At baseline, no differences were found between groups concerning either clinical or neural evaluations. Following rehabilitation, we observed a reduction in fatigue perception in both groups ( $p=0.038$ ). Moreover, FB\_group performed better than NOFB\_group in T25FW and TUG ( $p=0.028$  and  $p=0.038$ , respectively). Further, after treatment, FB\_group showed increased neural activity in areas involved in cognitive functions (Brodmann Areas-BA 9,10,  $p<0.01$ ), multisensory integration and body representation (BA39,  $p=0.01$ ) during both linear and curvilinear walking. Instead, NOFB\_group showed increased activity in motor planning areas (BA 6,8,  $p<0.05$ ). A significant difference was also found between groups in BA9 after treatment (FB\_group>NOFB\_group,  $p=0.04$ ).

**Discussion:** A 20-session rehabilitation period effectively reduces fatigue among PwMS. Moreover, a real-time feedback crutch seems to have a positive impact on walking ability. This might be due to a feedback-induced increased attention focusing on the assistive device, as suggested by the fNIRS results.

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### Examination of proprioceptive reliance during backward walking in individuals with multiple sclerosis

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**Background:** Slowed somatosensory conduction contributes to heightened postural instability and reduced proprioception among persons with multiple sclerosis (PwMS). Despite these delays, previous studies have noted increased proprioceptive reliance for balance in PwMS. The combination of heightened proprioceptive reliance and slowed signal transduction poses challenges in maintaining balance for MS individuals that may contribute to increased fall risk. Our lab has shown backward walking (BW) is more sensitive to detecting falls than forward walking (FW). During BW, there is increased dependence on proprioception due to the elimination of visual cues. However, no study to date has objectively established a definitive relationship between proprioception and BW. Therefore, the objective of this study is to examine the contributions of proprioception to BW compared to FW.

**Methods:** Thirty-five participants (average age:51.20±11.46, median PDDS:1) have completed the study. Participants completed BW and FW at both comfortable and fast speeds. We have previously established vibration sensation as a proxy measure for proprioception. Vibration thresholds were quantified at the great toe bilaterally using a two-alternative forced-choice procedure.

**Results:** Significant correlations were seen for vibration sensation and FW comfortable ( $r=0.59$ ;  $p<0.01$ ), FW fast ( $r=0.60$ ;  $p<0.01$ ), BW comfortable ( $r=0.67$ ;  $p<0.01$ ), and BW fast ( $r=0.65$ ;  $p<0.01$ ). After controlling for age, sex, and PDDS, vibration sensation significantly predicted performance during all walking tasks, with larger Beta coefficients seen

during BW (comfortable  $\beta=0.75$ ; fast  $\beta=0.74$ ) compared to FW (comfortable  $\beta=0.67$ ; fast  $\beta=0.70$ ).

**Discussion:** Given the marked decline in proprioception among individuals with MS and the evident differences in proprioception between fallers and non-fallers in prior studies, there is significant clinical relevance in conducting fall risk assessments and interventions that evaluate and enhance proprioception. Due to its heightened proprioceptive reliance, BW not only provides a more effective approach to assessing fall risk but may potentially represent a more efficacious exercise intervention modality.

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### Overground walking improvements in a person with secondary progressive multiple sclerosis after Alter-G antigravity treadmill training

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**Background:** Multiple sclerosis (MS) deficits in gait stability and automaticity can limit walking endurance. Treadmill training challenges dynamic stability in a repetitive way while allowing for adjustments in exercise's intensity. Body weight support (BWS) facilitate this training for MS-individuals with reduced walking independency, reliance on walking aids and risk of falling. However, harness-based BWS removes the balance challenge and alter the gait pattern, reducing over-ground transfer of gains. Alter-G applies the BWS adaptively, around the pelvis, prompting balance control and gait pattern adaptations.

**Methods:** A 38-year-old female with secondary progressive MS (EDSS=6.5) underwent a BWS-treadmill intervention (5 weeks, twice-weekly) incorporating Alter-G walking (30min, 2.5km/h, BWS=80%) preceded and followed by mobility and balance exercises. Outcome measures of endurance (6-minutes-walk test - 6MWT), safety (Tinetti scale) and fatigue (Modified fatigue impact scale - MFIS) were assessed before, one-week, and six-weeks after intervention.

**Results:** At one-week post-intervention, improvements were observed in walking endurance (56% increase in 6MWT), along with enhanced walking safety (from 15/28 to 21/28 on Tinetti scale) and reduced perceived impact of fatigue (MFIS score from 41/84 to 24/84). At six-weeks these effects were partially maintained.

**Discussion:** This intervention improved ambulatory function in an individual with severe MS-related disability. Alter-G training likely led to a more stable overground walk: the adapted gait pattern included more symmetrical steps and rhythmic weight transfers, resulting in a smoother forward progression and reducing the effort. The removal of visual control and challenges to trunk stability and lower limb coordination likely enhanced automatic multisensory integration, reducing the need for corrective motor plans while walking. Considering the promising results of this case study, we propose to investigate, in appropriately sized samples and with the presence of a control group, the efficacy of this assisted task-specific training in PwMS, with a particular focus on ambulation endurance.

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### Combining Exercise and Cognitive Training to Postpone Cognitive Decline in People with Multiple Sclerosis: Part of the Don't be late! Study Protocol

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**Background:** Up to 65% of people with multiple sclerosis (PwMS) develop cognitive deficits, which hampers participation in day-to-day life and ultimately reduces quality of life (QoL). Treatment of symptoms at a late stage can lead to cognitive impairment and unemployment, highlighting the need for preventative interventions in PwMS. Presenting a combination of exercise and cognitive training early might postpone cognitive decline.

**Aims:** This study highlights one intervention of the Don't be late! study, which aims to evaluate the (cost-)effectiveness of an innovative preventative intervention, aimed at postponing cognitive decline, compared to enhanced usual care in improving health-related QoL (HRQoL).

**Methods:** Randomised controlled trial including 270 PwMS with mild cognitive impairment, who have paid employment  $\geq 12$  hours per week and are able to participate in physical exercise (Expanded Disability Status Scale < 6.0). Participants are assigned to either a lifestyle intervention combining one-on-one personal fitness, mental coaching, dietary advice, and cognitive training, adjusted to the goals and level of the participant or a control group receiving general information about cognitive impairment in MS and receiving care as usual. Intervention duration is four months, with short-term and long-term follow-up measurements at 10 and 16 months, respectively. The overarching study also includes a work-focused intervention. The primary outcome measure will be HRQoL. Secondary outcomes include cognition, structural and functional brain changes, work related outcomes, physical functioning, psychological functioning, and societal costs. Semi-structured interviews and focus groups with stakeholders will be organised to qualitatively reflect on the process and outcome of the interventions.

**Discussion:** This study seeks to prevent (further) cognitive decline due to MS by introducing tailor-made interventions at an early stage of cog-

nitive symptoms, thereby maintaining or improving HRQoL. Qualitative analyses will be performed to allow successful implementation into clinical practice.

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### Neural cortical activation during upright posture in people with Multiple Sclerosis: a cross-sectional fNIRS study

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**Background and purpose:** Balance impairments are common in people with Multiple Sclerosis (PwMS). However, no studies have examined brain activation while performing balance tasks in PwMS.

The present study aims to investigate hemodynamic response function (HRF) between Healthy Subjects (HS) and PwMS during the execution of balance tasks on a stabilometric platform using functional near-infrared spectroscopy (fNIRS).

**Methods:** We recruited 18 PwMS with mean±standard deviation age of 42.1±10.6 years and Expanded Disability Status Scale (EDSS) of 2.0±1 points, and 18 age- and gender-matched HS aged 37.3±9.7 years. Participants underwent fNIRS recordings while maintaining upright standing on a foam with eyes open (EO) and closed (EC) for 30 seconds. We investigated frontal, occipital, and temporal cortices using the NIRScoutX system to measure oxy- and deoxyhemoglobin levels for 44 measurement channels. We concurrently measured the Area of the centre of pressure. We used a t-test to compare between-group differences on Area (Platform variable), while we ran a linear mixed model (Area, channel, and group) to fit HRF changes between EO and EC conditions.

**Results:** We observed statistically significant between-group differences in Area in EO (p=0.04) and EC condition (p=0.02). Group means (standard error) adjusted for Area and multiple comparisons denotes statistically significant differences in 3 active channels (Broadman Area 21): right temporal (Channel 1, HS:1.41(0.23) uM; PwMS:0.41(0.26) uM) and left temporal (Channel 2, HS:1.47(0.23) uM; PwMS:0.30(0.25) uM; Channel 3, HS:1.76(0.23) uM; PwMS:0.98(0.26) uM). We did not observe differences in the other cortical areas.

**Discussion:** As expected, balance control is impaired in PwMS on foam with EC. The current study adds to the literature that the increase in HRF observed in EC condition in HS is reduced in PwMS. This reduction occurs explicitly symmetrically in the right and left temporal cortices.

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### Low Referral Rates for Pelvic Floor Physical Therapy in MS Patients with Bladder Dysfunction: An Opportunity to Close the Gap

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**Background and Purpose:** Approximately 80% of people with multiple sclerosis (MS) experience bladder dysfunction (BD). BD decreases quality of life, reduces mobility, and increases disease burden. Pelvic floor

physical therapy (PFPT) is an evidence-based, non-invasive, and effective treatment for MS-related BD. Here, we provide a descriptive study, leveraging longitudinally collected patient-reported (PRO) BD severity scores against coinciding electronic health record (EHR) reports, to understand barriers to timely evaluation and treatment of BD.

**Methods:** The FITriMS study is a prospective cohort of ambulatory participants with progressive or relapsing MS, which included PROs of BD at baseline, 6-months, and 1-year. This analysis compared BD PRO (with Bladder Control Scores  $\geq 1$ ) to evaluations performed by a neurologist on the same participants concurrently. Chart review categorized the clinical treatment plan.

**Results:** 74% (65/88) of participants met inclusion criteria. They were mostly female (57%), mean age 53.5 years (11.8), median disease duration 19 years (range 1-54), and moderate disability (median EDSS 5.5, range 0-6.5). At baseline, 88% of participants reported BD on their PRO, but only 30% had some treatment documented in the EHR: 44% referred Urology, 50% prescribed medication, 6% provided behavioral techniques. At 6-months, 90% of participants reported BD on their PRO, 38% EHR documented treatment (43% referred Urology, 29% prescribed medication, 28% behavioral techniques); the distribution was similar at the 1-year. 93% of participants reported BD; 33% had treatment plans in the EHR (36% prescribed medication, 36% referred Urology, and 28% behavioral techniques). 0% had a documented referral for PFPT.

**Discussion:** A gap was found between participant reports of BD on PROs and those referred for treatment. No direct PFPT referrals were documented, despite it being an evidenced-based, effective treatment. Quality improvement and education efforts for timely PFPT referrals can potentially improve patient care and close this gap.

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### Multimodal Exercise Training to Reduce Frailty in People with Multiple Sclerosis: Study Protocol for a Pilot Randomized Controlled Trial

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**Background and Purpose:** Frailty, a syndrome characterized by decreased reserve and resistance to stressors across multiple physiologic systems, is highly prevalent in people living with multiple sclerosis (MS), independent of age or disability level. Frailty in MS is strongly associated with adverse clinical outcomes, such as falls, and may aggravate MS-related symptoms. Consequently, there is a pressing necessity to explore and evaluate strategies to reduce frailty levels in people with MS. The purpose of this pilot randomized controlled trial (RCT) will be to examine the feasibility and preliminary efficacy of a multimodal exercise training program to reduce frailty in people with MS.

**Methods:** A total of 24 participants will be randomly assigned to six weeks of multimodal exercise or to a waitlist control group with a 1:1

allocation. People with MS aged 40-65 years and living with frailty will be eligible. The multimodal exercise program will consist of cognitive-motor rehabilitation (i.e., virtual reality treadmill training) combined with progressive, evidence-based resistance training. At baseline and postintervention, participants will complete the Evaluative Frailty Index for Physical Activity (EFIP), measures of fall risk, and quality of life. Frailty-related biomarkers will also be assessed. In addition, the feasibility of the multimodal exercise program will be systematically and multidimensionally evaluated.

**Results:** Not applicable.

**Discussion:** To date, no RCT has yet been conducted to evaluate whether targeted exercise interventions can minimize frailty in MS. The current study will provide novel data on the feasibility and preliminary efficacy of multimodal exercise training as a strategy for counteracting frailty in pwMS.

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