

**Poster Abstracts from the 11th International Symposium on Gait and Balance in Multiple Sclerosis**  
**Skipping the Middle – A Focus on Mild and Severe Mobility Disability**

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**1) Greater Cognitive Capacity Protects Against Decline in Dual Task Walking Among People with MS with Mild or No Walking Impairment**

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**Background and Purpose:** Multiple sclerosis (MS) is a progressive neurodegenerative disease of the central nervous system that results in motor and cognitive impairment. Physical fitness and cognitive reserve may be neuroprotective in MS, but few studies have examined their role in symptom progression over time. This study investigated whether baseline aerobic fitness, walking, or cognitive function could predict performance in dual task walking 1-2 years later in people with no or mild walking impairment. **Methods:** Participants (n = 50) performed single-task walking, dual-task walking, completed the Montreal Cognitive Assessment (MoCA), and a fitness (VO<sub>2</sub>max) test at two time points (T1 and T2), approximately one year apart. Walking speed, MoCA scores and VO<sub>2</sub>max at baseline (T1) were examined as predictors of decline or maintenance of dual task walking ability over time. **Results:** Cognition, but not fitness or single-task walking, was a significant predictor of change in dual task-walking. For every point increase in MoCA at baseline, participants were 32% less likely to decline in dual task walking speed at T2. **Discussion:** Our results provide evidence that better cognitive function, rather than motor function, may protect against decline in dual task walking ability over 1-2 years.

**2) Heat Sensitivity and its Impact on Living with Multiple Sclerosis: Psychological Influence or Autonomic Dysfunction as Potential Predictors?**

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**Background and Purpose:** There are a variety of physical and psychological symptoms of multiple sclerosis (MS), which may not be reflected in EDSS but severely impact the quality of life. Therefore, it is imperative to find ways to characterize subjective symptoms of MS, such as heat sensitivity (HS), and to determine how they relate to objective measurements of disability. Unfortunately, HS is not fully understood but remains a bothersome symptom of MS. Hence, we explored the relationships between HS and subjective (i.e., fatigue, anxiety, depression, physical and psychological impacts of disease) and objective (i.e., fitness,

autonomic dysfunction, corticospinal excitability) features of MS, to determine the strongest predictors of HS. **Method:** Fifty-nine people with MS were recruited from a local neurology clinic and categorized as experiencing either HS or no HS impact on their daily life, based on responses to a visual analog scale. Participants provided demographic, disease, and lifestyle information. Subjective features of MS were measured using the Hospital Anxiety and Depression Scale, Multiple Sclerosis Impact Scale (MSIS-29), and fatigue impact on daily life. Objective data were examined using a graded maximal exercise test and transcranial magnetic stimulation. Predictors of HS were examined using logistic regression and receiver operator characteristic curves. **Results:** People with HS had significantly greater levels of disease severity, depression, fatigue, and physical and psychological disease impacts (MSIS-29). There were no significant groupwise differences in objective features of MS. HS was moderately correlated with scores from the MSIS-29 Physical subscale, including questions related to hand function. Analysis of predictors showed that difficulty using hands in everyday tasks tended to have the best ability to predict HS ( $\chi^2(4)=+32.121, p=.00002$ ). **Discussion:** Following a comprehensive assessment of subjective and objective features of MS, the greatest predictors of HS impact on daily life were questions related to subjective hand function.

### 3) A Multi-modal Virtual Reality Treadmill Intervention for Enhancing Cognitive Function and Mobility in People with MS: RCT Results

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**Background and Purpose:** Cognitive and mobility impairments are common in people with MS (pwMS) and can interfere with everyday function. We evaluated the benefits of a cognitive-motor virtual-reality training program on cognitive function, mobility, and related MS symptoms, compared to conventional treadmill training (TT) alone. **Methods:** A single-blinded,

two-arm, multi-center (4 sites) RCT with a six-week intervention period randomized pwMS into a TT alone group or TT with virtual-reality group (TT+VR). Both groups received 18 sessions of training (3/week) while walking on a treadmill (gait speed progressed). The TT+VR group received cognitive challenges and feedback in the VR. Inclusion criteria included relapsing remitting MS and EDSS 2 to 6. Primary outcomes were information processing speed (scores on Symbol Digit Modalities Test, SDMT) and dual-task gait speed, measured before training and one week after training. **Results:** 108 subjects completed the intervention (52: TT; 56: TT+VR). At baseline, subjects were 48.9±9.9 years old and 72.2% were female, median EDSS score of 4; age, sex, EDSS scores, SDMT, and gait speed (usual and dual tasking) were similar in both groups ( $p>0.7$ ). After 6 weeks of training, SDMT improved among all subjects ( $p=0.004$ ); a time\*group interaction effect ( $p=0.027$ ) indicated that the TT+VR group improved more than the TT group. Gait speed improved ( $p<0.001$ ) in both groups during dual-task walking, as did other gait parameters (e.g., step regularity and cadence). 25-foot-walking-time improved in both groups, with an advantage to the TT+VR group ( $p=0.032$ ). Subjects in both groups improved in some components of quality of life (MSQOL-54) ( $p=0.025$ ). Interestingly, the TT+VR group also reported fewer depressive symptoms (PHQ) following the intervention ( $p=0.004$ ). **Discussion:** TT with and without VR both improve mobility. Treadmill training that provides feedback and cognitive challenges via VR is apparently advantageous for cognitive processing speed and certain aspects of quality-of-life.

#### 4) Frailty and Falls in People Living with Multiple Sclerosis

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**Background and Purpose:** Frailty is extensively used to study and characterize aging. In older adults, frailty leads to vulnerability to many adverse outcomes such as falls, hospitalizations and mortality. However, little is known about frailty among people living with multiple sclerosis (MS). The clinical implications of this biological syndrome on common adverse outcomes, such as falls, have yet to be examined. Therefore, the purpose of this study was to explore the association between frailty and falls in people living with MS. **Methods:** 118 people with relapsing-remitting MS [age=48.9 years (SD=10); 74.6% female; expanded disability status scale (EDSS) range=2.0-6.0] were studied in this cross-sectional analysis. A frailty index was calculated from health deficits across a range of systems (e.g., physical function, cognition, comorbidities, sexual and psychosocial function) by following validated procedures. The number of falls experienced by participants in the previous 12 months was recorded. **Results:** Overall, the study population had a mean frailty index of  $0.32 \pm 0.14$ . Forty (33.9%), 35 (29.7%), and 43 (36.4%) participants were classified as non-frail, moderately frail, and severely frail, respectively. The frailty index was significantly correlated ( $\rho=0.37$ ,  $p<0.001$ ) with scores on the EDSS. Participants experienced 404 falls and 56.9% reported falling at least once. Compared to the non-frail, those who were severely frail had a higher proportion of falls (40% vs 73.8%,  $p=0.02$ ). In univariable negative binomial regression analysis, the frailty index was associated with a higher number of falls (IRR=3.33, 95% CI [1.85-5.99],  $p<0.001$ ). After adjustment for age, gender and EDSS, frailty remained strongly associated with falls (IRR=2.78, 95% CI [1.51-5.10],  $p=0.001$ ). **Discussion:** The current study identifies a significant relationship between frailty and falls in MS, independent of age, gender, and disease severity. These findings support the notion that frailty is a syndrome related to, but independent of, disability in MS.

## 5) The Role of Cognition in Proprioception in Persons with Multiple Sclerosis

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**Background and Purpose:** Balance impairments are common in persons with multiple sclerosis (MS); while poor proprioception has been linked to balance impairments, the cognitive contributions to proprioception have not been examined in MS. The objective of this study was to determine both relationships among cognition and vibration sensation, a proxy measure of proprioception, and predictors of vibratory sensation among persons with MS and healthy controls. **Methods:** One hundred and twenty-two individuals with MS, aged 20-60, with Expanded Disability Status Scale (EDSS) scores  $\leq 5.5$  and 48 healthy controls completed reaction time testing, the Stroop Test and lower extremity vibratory sensation. **Results:** In MS, average vibration was significantly related to Stroop-word; a model with Stroop-word and demographics explained 38.2% of the variance in vibratory sensation. Among healthy controls, no measures of cognition were significantly related to vibration; a model with age and two-choice-reaction-time explained 12.9% of the variance in vibration. The strongest single predictor of vibration in MS

was simple reaction time ( $\text{adj}R^2=0.044$ ), and in controls was two-choice-reaction-time ( $\text{adj}R^2=0.022$ ). **Discussion:** These results provide greater insight into the role of cognitive function and balance control in persons with MS. Clinicians should consider assessment of reaction time and processing speed as markers of proprioception and balance in persons with MS.

## 6) Augmented Balance Training in Persons with Multiple Sclerosis: A Case Series

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**Background and Purpose:** Multiple sclerosis (MS) impacts balance and walking ability. The use of feedback to augment balance training can enhance functional gains in persons with neurologic disorders, but the extent to which these gains are realized in persons with higher and lower disability is unknown. This case series examined how an intensive video-game based training impacted functional performance in persons with higher and lower disability from MS. **Case Description:** Physically inactive individuals with relapsing-remitting MS were randomized to either the video-game intervention group (n=4; n=2 with Expanded Disability Status Score (EDSS) >3, n=2 with EDSS<3) or a wait-list control (n=4; n=2 with EDSS>3, n=2 with EDSS<3) group 3x/week for 8 weeks. **Outcomes:** Individuals in the intervention group demonstrated greater gains in gait, balance, and dual-task performance than those in the control group. Specifically, individuals with EDSS>3 (i.e., greater disability) demonstrated the largest gains in forward walking velocity (35.2% and 6.7% increase), dual task walking velocity (17.7% and 8.1% increase), and Berg Balance Scale (39.6% and 3.9% increase). Further, individuals with EDSS>3 met or exceeded established MDCs for the Berg Balance Scale and 6 Minute Walk Test following training. **Conclusion:** Persons with MS may experience benefits in walking speed, walking endurance, and balance following augmented balance training. In this case series those with greater disability demonstrated the largest gains. The augmented nature of the training may also require increased cognitive demand, as evidenced by post-training improvements in dual-task walking. Thus, intensive balance training is feasible in persons with MS-related disability and may confer greater benefits than in those with lower disability. The study had high adherence levels and no adverse events occurred.

## 7) Intermittent versus Continuous Straight Leg Performance in Multiple Sclerosis: Partial Results of an Ongoing Study

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**Background and Purpose:** Muscle weakness is often a reason for impaired gait and balance in persons with MS (pwMS). However, fatigue often limits the dosage of strength training that persons with MS can perform. Intermittent training (INT), where periods of work are interspersed with periods of rest, have been shown to be effective in increasing distance walked in pwMS when compared to Continuous training (CONT). However, it is not known if INT can be used to increase dosage of strength training programs for pwMS. The purpose of this study is to compare an intermittent to a continuous strength training exercise for pwMS. **Methods:** This is a randomized crossover trial. Subjects with MS will be randomized into an INT or a CONT condition where they will perform straight leg raises (SLR) until too fatigued to continue. In the (CONT) condition subjects will perform SLR's continuously while in the (INT) condition they will perform one SLR every 6 seconds. One-week later subjects will crossover with subjects performing SLR's in the opposite condition. **Results:** To date 6 pwMS (4 female, age 56, EDSS 3.7) have completed the study. A greater number of SLR's were performed in the INT condition ( $X=158.7$ ,  $SD=69.1$ ) than in the CONT condition ( $x=78.3$ ,  $SD=59.1$ ). Subjective fatigue during the 2 conditions, measured using the Visual Analog Scale of Fatigue (VAS-F) increased by 45.4mm in the CONT condition 33.8 in the INT condition. **Discussion:** PwMS performed a greater number of SLR's in the INT condition than in the CONT condition suggesting INT training results in less objective fatigability. This study provides preliminary evidence that pwMS can achieve a greater dosage of resistance work as using INT as opposed to CONT exercise. Data collection for this study will continue until December 2021.

## 8) Mismatch Between Subjective Reports of Physical Activity and the Gold Standard Fitness Test Among People with Stroke, Multiple Sclerosis, and Controls

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**Background and Purpose:** Persons with neurological disorders have low participation in physical activity. Although fitness appraisal assists in exercise prescription, certain technology is limited in community settings. We investigated whether more accessible measures could estimate the gold-standard test of cardiorespiratory fitness in this population.

**Methods:** Thirty-two individuals with stroke, eighteen with multiple sclerosis (MS), and twelve controls were recruited. Impairment was measured using NIHSS, EDSS, and self-selected walking speed. Self-reports of physical activity were quantified as metabolic equivalents of task (METs) and further categorized into METs of activities of daily living (ADL) and exercise. A maximal exercise test determined cardiorespiratory fitness indexed by peak oxygen uptake ( $\dot{V}O_{2peak}$ ). **Results:** Fitness in the stroke and MS groups was 41.1% and 68.4% that of controls. There was no association between total METs and  $\dot{V}O_{2peak}$  in any group, indicating that subjective reports of physical activity were not useful proxies of fitness. In the stroke patients, who had moderate disability and slow walking speed (67.0 cm/s), METs of ADLs and walking

speed were correlated with fitness ( $R=0.45$ ,  $p=0.011$ ,  $R=0.64$ ,  $p<.001$ ). However, in MS patients, who displayed mild disability and faster walking speed (92.6 cm/s), only METs of exercise were related to fitness ( $R=0.64$ ,  $p=0.005$ ). Discussion: When categorized, self-reports of physical activity levels can provide insight in levels of fitness for individuals with neurological disease.

### 9) Gait and Balance Interventions in Multiple Sclerosis: An Evidence-based, Comprehensive Review from the MSBEST Project

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**Background and Purpose:** MSBEST (Multiple Sclerosis Best Evidence-Based Strategies and Treatments for Rehabilitation) is a team of researchers and clinicians across North America who have expertise and special interest in MS rehabilitation. MSBEST is developing online modules aiming to summarize the latest evidence and research gaps, and to inform future best practices. Gait and balance impairments are common in individuals living with MS, leading to falls and co-morbidity. Addressing balance and walking dysfunction is paramount in MS physical rehabilitation. We aim to report the latest evidence for interventions addressing gait and balance in MS as part of the MSBEST collaboration. **Methods:** Online databases (PubMed, MEDLINE, CINAHL, Scopus, EMBASE) were searched for studies meeting the following inclusion criteria: clinical RCT, involved a gait and/or balance intervention, report a primary gait outcome and/or a primary or secondary balance outcome, in English, adult participants ( $\geq 18$  years), and  $\geq 50\%$  of participants with a diagnosis of multiple sclerosis, or MS participant results stratified. After an initial online database search, articles were uploaded to the Covidence review software. Articles underwent title and abstract screening (independently by 2 researchers), prior to undergoing full-text review. Studies are summarized in data extraction tables and assessed for quality (PEDro tool). Level of evidence statements are created using the Modified Sackett Scale with expert interpretation provided from MSBEST collaborators. **Results:** The project is currently at the full article screening stage. Results of the review will be presented at the conference. **Discussion:** MSBEST uniquely combines evidence-based reviews with expert input to aid in the interpretation and application of evidence-based rehabilitation interventions. As the evidence-base for MS rehab continues to grow rapidly, this platform may help accelerate best-practice recommendations and clinical practice guideline development.

### 10) The Moderating Roles of Self-Efficacy and Depression in Dual-Task Walking in Multiple Sclerosis: A Test of Self-Awareness Theory

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**Background and Purpose:** Multiple sclerosis (MS) is a debilitating condition that results in a variety of psychological, cognitive, and motoric symptoms. Gait is often impacted by MS and is one of the most concerning deficits of MS. Dual-task walking, is a common activity in which people walk *and* engage in a concurrent, discrete task. Dual-task walking has been assessed in MS, but whether little is known about how it fits into the nexus of MS symptoms. Self-awareness theory (SAT) suggests that DTW may be a function of the interactions among psychological, cognitive, and motor processes. **Method:** Data from seventy-three people with MS were collected in a clinical care setting. Cognitive testing, self-report assessments for depression and falls self-efficacy (FSE) and walk evaluations (dual-task walk [DTW] and single-task walk [STW]) were completed. Multiple linear regression analyses were run to determine whether physical or cognitive outcomes predicted dual task walking outcomes (DTW speed and DTW costs) and whether FSE or depression moderated the relationships between physical and cognitive abilities and DTW performance. **Results:** DTW speed related to diverse physical and cognitive predictors. In support of SAT, FSE moderated the relationship between STW and DTW speeds such that lower FSE attenuated the strength of relationship between them. DTW costs—the change in speed normalized by STW speed—did not relate to cognitive and motor predictors. DTW costs did relate to depressive symptoms, and depressive symptoms moderated the effect of information processing on DTW costs. **Discussion:** The findings indicate that an interplay of physical ability and psychological factors—like depression and FSE—may enhance understanding of walking performance under complex, real-world, DTW contexts.

## 11) Effects of Barefoot Training on Balance Performance in Persons with MS: Partial Results of an Ongoing Study

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**Background and Purpose:** Balance impairment in persons with MS (pwMS) is multifactorial but Lower Extremity (LE) sensory loss is often a prominent finding. Interventions which can reduce LE sensory impairment could result in improved balance. There is anecdotal support for barefoot as opposed to shod training resulting in improved balance due to increased use of LE sensory receptors. The purpose of this study is to compare the effects of barefoot to shod balance practice in pwMS on LE sensation and balance performance. **Methods:** Subjects with MS had lower extremity sensation tested with biothesiometry to measure vibration perception threshold (VPT), and balance was tested using the MiniBESTest. Subjects were then randomized a shod or



barefoot condition. Subjects were provided with an HEP balance training program to be performed according to their group assignment (barefoot or shod). After 2 weeks, of daily training, subjects were retested on biothesiometry and the MBT. **Results:** to date 2 subjects (1 barefoot and 1 shod) have been tested. Mean biothesiometry values were derived from 7 LE locations on each leg. The barefoot subject (EDSS 4.5) improved in VPT following training from 34.6 to 23.3hz and on the MBT from 10 to 19. The shod subject (EDSS 1.5) improved VPT from 7.7 to 5.8 and from 24 to 27 on the MBT. **Discussion:** Barefoot training may present a way to improve sensory function in and balance in pwMS. Data collection for this study will continue until December 2021.

## 12) Adapting One-on-One Rehabilitation Research to Prevent Falls in People with MS to the Virtual Environment: a COVID-19 Silver Lining

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**Background and Purpose:** Research evaluating rehabilitation fall prevention interventions in people with MS is generally done in-person. We planned a randomized controlled trial of a one-on-one standardized physical therapy intervention for walking aid selection, fitting and training, (Assistive Device Selection, Training and Education Program [ADSTEP]), to prevent falls in people with MS. Due to the COVID-19 pandemic we adapted this study to virtual delivery by video-conference. **Methods:** ADSTEP consists of six 40-minute 1:1 sessions with a physical therapist. For ADSTEP-at-Home, all visits, including study enrollment, consent, interventions, and outcome assessments were transitioned to video teleconference in the participants' homes. Here we examine the impacts of this transition, including adaptations, barriers, benefits, adverse events, attendance, and satisfaction. **Results:** Adaptations included screening out those needing hands-on assistance for safety, not using the Timed 25 Foot Walk, and converting the Dynamic Gait Index to self-assessment. Barriers included only enrolling in-state due to licensing regulations, and participants needing video capable devices. Benefits included improved access for rural and distant participants, decreased risk of COVID-19 exposure, and less fatigue and time associated with visits. There have been no treatment-related falls or other severe adverse events. The 17 participants who have completed ADSTEP-at-home thus far completed all six visits, reported no difficulties seeing the PT or following their instructions, and found the platform secure and private. Twelve felt the virtual visits were as good as in-person sessions and 10 reported preferring the virtual visits. The therapists reported similar satisfaction with virtual delivery. **Discussion:** Tele-research for randomized trials of one-on-one gait training interventions in MS is feasible, acceptable, and increases access to rehabilitation research to people in rural areas or far from academic centers. This presentation provides guidance for optimizing future tele-rehab research and telehealth delivery of gait training for fall prevention in MS.

### 13) Adapting Group Rehabilitation Research to Manage MS-Related Spasticity to the Virtual Environment: a COVID-19 Silver Lining

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**Background and Purpose:** Research evaluating exercise for improving gait and balance in MS is usually done in-person. Daily stretching is the current cornerstone of MS-related spasticity treatment, but its efficacy is unknown. We are comparing, in a randomized controlled trial, a group program teaching lower body standardized yet customizable stretching exercises, MS Spasticity: Take Control (STC), with an active control using a National MS Society brochure emphasizing full body Range of Motion exercises (ROM). **Methods:** STC and ROM both have two 2-hour group classes of education and exercise led by trained facilitators without formal exercise training. Participants learn exercises they are instructed to do daily for the next six months. We have transitioned study visits from in-person to tele-research with WebEx due to Covid-19. We describe this transition, including adaptations, barriers, benefits, adverse events, attendance, and evaluation of virtual delivery. **Results:** Adaptations include training with WebEx, smaller groups, omitting walking performance outcomes, and adding an evaluation of the WebEx interventions. Barriers include need for connectivity and video equipped devices, and ability to use them. Benefits include decreased risk of COVID-19 exposure, improved rural and nation-wide access, accelerated recruitment, and less fatigue and time associated with traveling for visits. There have been no falls or severe adverse events. Missed classes have been made up with later cohorts. Thus far, 47 participants have completed the programs remotely and over 80% were satisfied with the training to use WebEx, their ability to see and hear the facilitator, and the security and privacy of WebEx. **Discussion:** Tele-research for randomized trials of group exercise interventions in MS is feasible, acceptable, and increases access to rehabilitation research to people in rural areas or far from academic centers. This presentation provides guidance for optimizing future tele-rehab research and group telehealth delivery of exercise training at home.

### 14) The Feasibility of Internet-based Tai Chi Easy Program on Gait-related Parameters, Quality of Life, and Fatigue in People with Multiple Sclerosis

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**Background and Purpose:** The benefits of exercise for patients with Multiple Sclerosis (MS) is well documented, to include participation in Tai Chi. Our purpose was to explore the feasibility of implementing a safe internet- based Tai Chi intervention and evaluate impact on health and

performance. **Methods:** Four patients with MS participated in this random block-design study, initially assigned to a seated Tai Chi Easy (Exercise) group, or home stretching group. During both 6-week interventions, a total of 18, 60-minute exercise/sessions were performed with a certified instructor using Zoom, or a home-based static stretching program, with a two-week wash out period between interventions. Participants were assessed at the beginning of the study and after each intervention using the Multiple Sclerosis Quality of Life (MSQOL), Multiple Sclerosis Questionnaire for Physiotherapists (MSQPT), 12-Item Multiple Sclerosis Walking Scale (MSWS-12), Modified Fatigue Impact Scale (MFIS), Hamburg Quality of Life Questionnaire in Multiple Sclerosis (HAQUAMS), and Functional Assessment of Multiple Sclerosis. **Results:** Participants reported high levels of satisfaction with using technology and the exercise intervention generally improved posture, breathing, meditation, muscle tension, coordination, flexibility, strength, and fatigue. Neither the exercise or stretching groups demonstrated statistically significant differences in gait-related parameters. However, promising results were noted for the exercise intervention with clinically meaningful change observed in the MSQOL for physical and mental health, the HAQUAMS and reported fatigue level (MFIS). **Discussion:** This small pilot study confirmed that we can successfully evaluate the impact of a virtual exercise program in participants with MS. Additionally, it appears that the dosage of activity is sufficient in the exercise intervention to observe both significant and clinically meaningful change in physical health, mental health, psychosocial, and general function including fatigue, when compared to a home stretching program. The benefits of using a virtual platform increased patient motivation and access to the intervention.

## 15) Modeling Gait in People with Multiple Sclerosis: A Principal Component Analysis Approach

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**Background and Purpose:** People with multiple sclerosis (PwMS) demonstrate gait impairments that are related to falls. However, gait outcomes frequently reported to characterize gait in MS are often redundant and heterogeneous. Therefore, this study aimed to 1) use a principal component analysis (PCA) to establish specific domains of gait in PwMS, 2) identify domains that are distinct between MS-fallers (MS-F) and non-fallers (MS-NF), and 3) relate model-derived gait domains to cognition, quality of life, and fear of falling. **Method:** 122 people with relapsing-remitting MS 45 controls performed 3 timed up-and-go trials wearing inertial sensors. 21 gait parameters were entered into a PCA. Executive function was assessed from the Stroop Color and Word Test. The Short Form-36 assessed quality of life, fear of falling was measured using the Falls Efficacy Scale, and functional mobility was assessed using the Berg Balance Scale. **Results:** The PCA identified 6 orthogonal components accounting for 79% of gait variance: pace (24.81%), rhythm (16.57%), variability (13.02%), asymmetry (9.27%), anterior-posterior dynamic stability (8%), and mediolateral dynamic stability (7.47%). PwMS exhibited a slower pace, larger variability, and increased medial-lateral trunk motion than controls ( $p < 0.05$ ). The pace and asymmetry domains were significantly worse (i.e., slower and

asymmetrical) in MS-F than MS-NF ( $p < 0.001$  and  $p = 0.03$ , respectively). Fear of falling, cognitive performance, and functional mobility were associated with slower a slower gait ( $p < 0.05$ ). **Discussion:** This study identified a six-component, MS-specific gait model, demonstrating that PwMS, particularly fallers, exhibit deficits in pace and asymmetry. Slower pace was associated with reduced functional mobility and increased fear of falling. Establishing a more streamlined gait model in PwMS may reduce redundancy in gait outcome reporting. Identifying specific domains related to falls and fear of falling may assist in the early prediction of fall-risk in MS and support targeted fall-prevention interventions.

## 16) Using Myelin Water Imaging to Link Underlying Pathology to Clinical Function in Multiple Sclerosis: A Scoping Review

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**Background and Purpose:** Given the heterogeneity of multiple sclerosis (MS) symptoms and pathology, identifying links between MS-related pathology (i.e., myelin damage) and associated clinical symptoms is critical for developing targeted therapeutics. Conventional MRI, commonly used for MS diagnosis and disease monitoring, lacks specificity with functional performance. Myelin water imaging (MWI) demonstrates increased specificity to myelin and is viewed as the gold standard for imaging myelin content *in vivo*. However, MWI studies in MS are sparse and it remains unclear whether MWI measures in MS demonstrate strong correspondence with physical and cognitive performance. Therefore, the purpose of this study was to conduct a scoping review of the literature to determine relationships among MWI, as a measure of myelin content, and physical, cognitive, and overall disability in persons with MS. **Methods:** Seven databases were searched from their inception to March 1, 2021. Studies of adults with MS that included both brain MWI and either a measure of physical function, a measure of cognitive function, or a measure of disease severity were included. Fourteen studies (11 observational, 3 intervention) met the inclusion criteria. **Results:** Data extraction is ongoing; however, preliminary screening shows that the most commonly investigated MWI metric is the myelin water fraction (MWF). Additional MWI metrics include myelin heterogeneity index (MHI) and geometric  $T_{2IEW}$ . MWI metrics significantly differentiate those with MS from healthy controls, strongly correspond to MS-related disability. Only 5 studies examined structure-function relationships in brain areas related to walking and cognitive function. **Discussion:** Our preliminary findings suggest that MWI is sensitive to myelin and predicts disability in MS better than conventional imaging metrics. There is emerging evidence that MWI metrics demonstrate relationships with functional performance, though future studies examining explicit regions of interest related to motor and cognitive function are critically needed.

## 17) Predicting Exercise Potential with Tract-specific MR Imaging and Clinical Measures

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**Background and Purpose:** Strength training is known to promote neural adaptations which can lead to favorable functional outcomes in persons with multiple sclerosis (PwMS). The purpose of this work was to examine the role of MRI in predicting recovery to progressive resistance training. **Methods:** Twenty-eight persons with relapsing-remitting MS (age: 49.3(11.1); 10M, 18F; EDSS: 3.8 (1.6)) and 26 healthy age and sex-matched controls (age: 50.2 (11.9); 9M, 17F) participated. Participants completed a pre-and post-intervention assessment that included clinical measures of walking, cognition, strength, sensory function, quality of life, and a 3T MRI. All participants completed 3x/week for 8 weeks of progressive resistance training. A random forest procedure using baseline predictors was used for prediction of exercise responsiveness. The predictive accuracy was measured using the normalized mean squared error (MSE) within a leave-one-out cross-validation procedure. **Results:** To examine exercise responsiveness, we calculated the change from pre-to post-intervention on both walking velocity and summed hip strength. Within each model, we considered the baseline walking velocity or summed strength, respectively, as well as baseline demographics, falls, cognitive performance, quality of life, vibration sensation, corticospinal tract (CST) fractional anisotropy (FA), mean diffusivity (MD) and magnetization transfer ratio (MTR). Change in walking velocity was best predicted by baseline walking velocity, demographics, disease severity, cognition, vibration, CST FA, CST MD, and CST MTR (MSE: 0.0543; normalized MSE: 0.2311). Change in strength is best predicted by summed strength at baseline, demographics, disease severity, falls, cognition, quality of life, vibration, CST FA, CST MD, and CST MTR (MSE: 1647.19; normalized MSE: 0.1328). **Discussion:** A combination of motor, cognitive, and MRI measures predicts responsiveness in PwMS. Given the heterogeneous nature of MS, accounting for individual pathologic differences with tract-specific imaging and precise measurement of impairments may provide the needed information to determine who is likely to benefit from exercise.

## 18) Phase I/II, Single-center, Single-blind Randomized Clinical Trial of Aerobic Exercise as a Remyelination Therapy in Multiple Sclerosis: Study Design

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**Background and Purpose:** There is an urgent need for remyelinating therapies that improve function in people with multiple sclerosis (pwMS). Aerobic exercise is a promising remyelinating strategy because it: 1) promotes remyelination in animal models both independently and synergistically with medications, and 2) improves mobility in pwMS. Here we present an innovative clinical trial designed to explore if aerobic exercise promotes remyelination in pwMS. **Methods:** This is a randomized, single-blind, parallel clinical trial of a 24-week aerobic stationary cycling intervention. **Results:** Sedentary participants (n=60; aged 18-64 years) with stable MS will undergo a baseline visit to quantify spinal cord demyelination with somatosensory evoked potentials (SSEP), mobility (6-Minute Timed Walk, Timed 25 Foot Walk, Timed Up and Go), patient reported outcome measures, and plasma extracellular vesicle (EV) profiles. The mobility outcome with the strongest association to spinal cord demyelination as determined by SSEP latency will become the primary clinical endpoint for the clinical trial. After baseline testing, 44 pwMS with SSEP latency z-score  $\geq 2$  will advance to the clinical trial. The active group (n=22) will perform aerobic stationary cycling thrice weekly for 24 weeks with graded virtual supervision. The control group (n=22) will participate in a monthly 24-week virtual MS symptom education group. SSEP latency (the primary remyelination endpoint), mobility outcomes, questionnaires, and EV profiles will be measured at 12 and 24 weeks in all clinical trial participants. A subset of 11 active and 11 control participants will undergo a brain MRI with quantitative T<sub>1</sub> Myelin Water Fraction at baseline and 24 weeks (exploratory remyelination endpoint). **Discussion:** The proposed study will explore if aerobic exercise promotes remyelination. It will also inform the feasibility, clinical outcome measures, study design and sample size for a fully powered clinical trial of aerobic exercise to promote remyelination and improve mobility in pwMS.

### 19) Self-Report Measures of Fatigue in MS: Recommendations Following Systematic Review of Psychometrics and Evaluation of Evidence and Usability

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**Background and Purpose:** Fatigue is a common, debilitating impairment in multiple sclerosis (MS). Clinicians rely on individuals' self-report to assess their experience of fatigue and its impact. However, choosing appropriate standardized self-report measures of fatigue in MS can be challenging. The Academy of Neurologic Physical Therapy appointed the MS Outcome Measures Task Force to systematically review fatigue measures and provide recommendations. The purpose of this report is to document the psychometrics and usability of fatigue measures tested in people with MS using a modified COnsensus-based Standards for the selection of health

Measurement INstruments (COSMIN) rating system. **Methods:** PubMed, CINAHL, and Embase databases were searched through January 2020 using search terms related to fatigue and MS. Studies were included if they reported on a self-report fatigue measure in at least 30 people with MS and included information on reliability, content validity, responsiveness, interpretability, or generalizability of the measure. Data were extracted by two independent reviewers; discrepancies remaining after discussion were resolved by a third reviewer. Risk of bias and quality were appraised within the relevant COSMIN sections; usability was assessed based on information retrieved for each measure. **Results:** 45 studies met eligibility criteria, with information on 17 fatigue measures used in people with MS. Data was available for all psychometric properties of interest for five measures: Fatigue Impact Scale (FIS), Fatigue Severity Scale, Modified Fatigue Impact Scale (MFIS), Neurological Fatigue Index for MS, and Unidimensional-FIS. Final recommendations were based on positive and complete information, plus positive usability factors. **Discussion:** Few fatigue measures have evidence across all COSMIN items. Additional research on promising measures is needed. The Task Force recommends the MFIS for both research and clinical practice due to psychometrics, ease-of-use, and inclusion of physical, cognitive, and psychosocial domains of fatigue.

## 20) Perceptions of Newly Diagnosed Persons with Multiple Sclerosis on Exercise and Physical Activity – A Qualitative Study

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**Background and Purpose:** Multiple Sclerosis (MS) is a progressive neurodegenerative disease marked by declines in walking and balance. Individuals with MS commonly receive rehabilitation services throughout their disease course, but rarely after initial diagnosis. The purpose of this qualitative study is to understand the perspectives of persons newly diagnosed with MS on exercise and physical activity. **Methods:** Three focus groups were conducted with persons with MS (n=8) who had been diagnosed within the past 5 years. Participants were asked open-ended questions related to barriers and facilitators of exercise, helpful information about exercise to know at diagnosis, and how they prefer to receive exercise information. All focus groups were recorded, and transcriptions were analyzed using combined deductive and inductive coding and validated through researcher triangulation. Concepts were categorized according to emerging themes and findings were verified by participants. **Results:** The major themes identified included knowledge and literacy, perceptions of exercise, strategies to overcome barriers and engage in exercise and physical activity, and barriers to exercise and physical activity. **Discussion:** Results from this study will directly inform the adaptation of a physical activity coaching program for newly diagnosed individuals with MS.

## 21) Deep learning for MS prediction using Multi-Stride Dynamics in Gait

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**Background and Purpose:** Multiple Sclerosis (MS) is one of the most common chronic neurodegenerative disorders that impairs the central nervous system. While clinical presentations of MS are highly heterogeneous, mobility limitations are one of the most frequent symptoms. The aims of this study were to examine MS related changes in spatiotemporal and kinetic gait features after normalization; and evaluate the effectiveness of Deep learning for MS prediction using Multi-Stride Dynamics in Gait (DeepMS2G).

**Methods:** In this study, gait data during self-paced walking on an instrumented treadmill from 20 persons with MS and 20 age, weight, height, and gender-matched healthy older adults (HOA) were obtained. We explored two normalization strategies, namely standard body size-based normalization and regression-based normalization using scaling factors derived by regressing gait features on multiple subject demographics, to minimize the dependency of derived gait features on the subject demographics; and proposed DeepMS2G, a deep learning-based methodology to classify strides of older persons with MS (PwMS) from healthy controls, so as to generalize across different walking tasks and subjects. **Results:** We observed that regression-based normalization improved the accuracy of identifying pathological gait when compared to standard body size-based normalization. When generalizing from comfortable walking to walking while talking, a Multiscale Residual neural network achieved a perfect subject classification accuracy of 100% and for subject generalization, a Residual network resulted in the best accuracy of 83%, both with regression normalized data. **Discussion:** The integration of gait data and deep learning to predict MS may provide a viable patient-centric approach to aid clinicians in disease monitoring and relapse treatment. This work is the first attempt to demonstrate the potential of deep learning for this domain.

## 22) Balance Impairments in People with Multiple Sclerosis with Minimal Neurological Disability

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**Background and Purpose:** Balance impairments are experienced by 50-80% of people with MS (pwMS), even when there are minimal or no clinical signs of disability. The overall aim was to examine balance performance under a variety of conditions in pwMS with minimal neurological



disability. **Methods:** Centre of pressure (COP) related measures of balance were recorded using a force platform during two conditions (quiet stance with eyes open and closed) before and after a 20-minute treadmill run (9 female/6 male, age: median 41yrs, EDSS: 1-2.5, n=15) at a self-selected speed in pwMS. Eight age-matched healthy participants (8 female/7 male, age: median 41.8yrs) served as controls. Both groups were engaging in regular exercise (continuous running for at least 30min weekly). **Results:** Balance performance with EO pre-exercise was similar in pwMS and the control group except the COP in mediolateral (ML) direction which was worse in pwMS. However, in the EC condition four of the seven COP balance parameters were significantly worse in pwMS. Balance performance in pwMS decreased further after the exercise task with 5 of the 7 COP parameters in the EO condition and all COP parameters in the EC showing statistically significant higher (i.e., worse) values compared to pre-exercise task. **Discussion:** Balance performance in this highly physically active MS group was similar to those in the control group under 'non-challenging' conditions (i.e., EO before exercise). However, in more challenging conditions like EC immediately after exercise, balance impairments become more pronounced potentially due to reliance on proprioception. Future studies should take into account that higher challenging tasks might be more appropriate to show differences in those people that are highly active and minimally affected by MS.

### 23) The Safety of Acute Exercise for Nonambulatory People with Multiple Sclerosis

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**Background and Purpose:** Current exercise and physical activity guidelines for people with multiple sclerosis (MS) who are nonambulatory (i.e., Expanded Disability Status Scale 7.0 – 8.5) are primarily derived from expert opinion, rather than evidence-based recommendations. Nonambulatory people with MS cite the lack of safety evidence as a barrier to their engagement in exercise. The purpose was to characterize the safety of acute aerobic exercise in nonambulatory individuals with multiple sclerosis (MS) using three accessible exercise modalities. **Methods:** Twelve nonambulatory individuals with MS (mean age = 62.6; median EDSS = 7.5; mean disease duration = 22.3) completed three submaximal exercise sessions on an arm-cycle ergometer (ACE), a recumbent stepper (RS), and a functional electrical stimulation (FES) cycle. All exercise sessions were 15 minutes in length. Adverse events (AE) associated with exercise were recorded and described during and after exercise. Symptomatic responses to exercise were characterized using the Brief Pain Inventory (pain) and the Daily Fatigue Impact Scale (fatigue). **Results:** Six AE were reported across 36 exercise sessions (ACE = 4; RS = 2; FES = 0). None of these adverse events were characterized as severe. There were no significant increases in symptoms of pain or fatigue following RS ( $p = 0.14$ ;  $0.45$ ) or FES ( $p = 0.12$ ;  $0.55$ ) exercise. Significant increases in pain ( $p < 0.01$ ) and fatigue ( $p = 0.02$ ) were observed after ACE exercise. **Discussion:** Both RS and FES represent safe exercise options for nonambulatory people with MS. The higher frequency of AEs and elevated symptomatic burden associated with ACE exercise suggest it may not be tolerated as well as the other modalities by people with MS

who are nonambulatory. Results from this study can be used to inform the design of future trials of exercise training for nonambulatory people with MS.