(1) Backward Walking and Dual-Task Assessment Improve Identification of Gait Impairments and Fall Risk in Persons with Multiple Sclerosis

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Background and Purpose: Persons with multiple sclerosis (PwMS) experience motor and cognitive deficits, resulting in dual-task walking impairment. Backward walking better differentiates PwMS from healthy controls (HCs) than forward walking, and this effect is heightened under dual-task conditions. Previous studies have not incorporated matched controls. This study compared spatiotemporal measures of forward and backward walking in single and dual-task conditions in PwMS and age and sex-matched HCs. Methods: In a single session, spatiotemporal gait measures for forward and backward walking in single and dual-task conditions, and clinical measures of mobility, cognition, balance and retrospective falls at 6 months were also collected. A 2x2x2 mixed model ANOVA compared differences in the spatiotemporal measures of forward and backward walking in single and dual-task conditions between PwMS and HCs. Spearman correlations examined relationships between spatiotemporal gait measures to cognitive function, retrospective falls, and balance. Results: Eighteen PwMS and 14 matched HCs participated. Backward walking velocity revealed significant differences between groups for single-task (p=0.015) and dual-task (p=0.014) conditions. PwMS demonstrated significant differences between single and dual-task forward and backward walking velocities (p=0.023; p=0.004). This difference was only apparent in the backward walking condition for HCs (p=0.004). In PwMS, there were significant differences in double support time between single and dual-task conditions in both backward (p<0.001) and forward (p=0.001) directions. No differences were observed in HCs (p=0.581; p=0.295). Falls were significantly associated with backward dual-task stride length (r=-0.490; p=0.046) and velocity (r=-0.483; p=0.050). Discussion: Differences in MS and age and sex-matched HCs are more pronounced during backward walking compared to forward walking under single and
dual-task conditions. Future larger scale studies are needed to validate the clinical utility of backward walking and dual-task assessments and mitigate the limitations of the current forward walking dual-task assessments.

(2) Bipedal Coordination in Seated Position in Multiple Sclerosis: Reduced Amplitude Over 6 Minutes and Higher Coordination Variability in Walking Fatigability Group

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Background and Purpose: Walking fatigability is prevalent in MS and can be measured by a percentage distance decline during a six-minute walking test. This study aimed to look at possible differences in coordination during a seated bipedal coordination task in pwMS with walking fatigability (WF), non-walking fatigability (NWF) and Healthy Controls (HC). Methods: Thirty-five PwMS and 13 age-gender matched HC participated. Bipedal coordination was assessed by a seated six-minutes coordination task (6MCT) with the instruction to perform antiphase left-right lower leg movements as fast as possible. Outcomes were Phase Coordination Index (PCI) and spatiotemporal measures (workload=amplitude x frequency). Main interest was change over every minute. Mean values and coordination fatigability index were also calculated. Mixed model analysis and multi-way ANOVAs were performed (SAS JMP). Results: Mixed models revealed a significant effect of time for the PCI, situated in the variability of generating bipedal antiphase movements. A significant group*time interaction effect was found for workload, which was illuminated by movement amplitude. Fatigability index of the WF group differed significantly from HC (movement amplitude, workload) and from NWF group (workload). Discussion: The higher variability in bipedal coordination and decrease in movement amplitude over time during the seated 6MCT in the WF group could be an indicator to investigate central drive in fatigability patients.

(3) Relation of Cognitive Function and Fatigability with Walking Capacity and Fatigability in Persons with Multiple Sclerosis


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Background and Purpose: Fatigability, defined as a task-related performance decline, has a motor and cognitive domain but relations are not well understood. The purpose of this study was to investigate associations between cognitive function-fatigability with walking capacity-fatigability in persons with Multiple Sclerosis (pwMS). Methods: Six-Minute Walking Test (6MWT) determined walking capacity and walking fatigability (Distance Walked index=DWI). Paced Auditory Serial Addition Test (PASAT) and Symbol Digit Modalities Test (SDMT) in oral or written form, measured cognitive function and cognitive fatigability. Correlation (pearson (r) or spearman (r_s)) and regression analyses (R²) were performed. Results: Eighty-nine pwMS with median EDSS 3.0 (range 0-6) were included, and performed the 6MWT and PASAT, as well as the SDMT either in oral (n=49) or written (n=40) form. Analyses showed significant relations between the 6MWT and PASAT (r_s=0.33), PASAT Dyad (r_s=0.27), SDMT oral (r=0.40, R²=0.16) and SDMT written (r=0.54; R²=0.29). No significant associations were found between walking fatigability and cognitive function or cognitive fatigability. Discussion: Cognitive function has small to moderate significant associations with walking capacity, but walking and cognitive fatigability may be distinct symptoms in MS.

(4) A Clinical Reasoning Framework for Fatigue in Neurologic Disease

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Background and Purpose: To present definitions for elements related to fatigue, and describe a clinical reasoning model for rehabilitation clinicians to address fatigue in people with neurologic pathologies like multiple sclerosis. Description: Fatigue often impacts gait and balance; however, it is poorly understood by many clinicians which limits their ability to examine and evaluate its impact and determine appropriate intervention plans. Fatigue is multidimensional, having components that are subjective and objective, primary and secondary, and central and peripheral. Each has a unique presentation requiring specific tests, measures, and intervention strategies. The classification of fatigue is complicated by a lack of consistent definitions. Clear definitions, and a well-defined clinical reasoning framework with which clinicians can identify, evaluate, and treat fatigue, may improve management of fatigue and its impact on gait and balance. Summary of Use: We propose an 8-step process with consideration of specific definitions related to fatigue. 1: Consider Patient Situation, specifically the diagnosis and the complaints of fatigue; 2. Collect Information, through chart review, history and examination, investigating indicators of fatigue, and its varied causes; 3. Process Information, by interpreting information to develop hypotheses regarding patient presentation, and likely outcomes; 4. Identify Problems by developing a problem list specifying areas requiring intervention; 5. Establish Goals where the clinician determines appropriate outcome measures by which hypotheses will be tested; 6. Take Action by deploying specific treatments, management
strategies, and referrals to other team members; 7. Evaluate Outcomes to determine the effectiveness of the intervention strategy, and; 8. Evaluate the Process through reflection on effectiveness of the episode of care, and adding gleaned information to the clinician’s armamentarium. **Discussion**: The use of consistent definitions related to fatigue, and the application of a well-described clinical reasoning framework for care, should improve clinicians’ ability to positively impact fatigue in people with neurologic pathologies.

**Blood Flow Restriction Training for Mobility, Fatigue, and Strength in Multiple Sclerosis: A Case Report**

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**Background and Purpose:** Blood flow restriction (BFR) training, where an inflatable cuff partially occludes blood flow around the proximal portion of a limb, coupled with low-intensity resistance training (LIRT) has resulted in gains comparable to traditional progressive resistive exercise in healthy populations. The use of BFR with LIRT may enable people with MS to improve strength without a respective increase in fatigue. This case report describes the use of a BFR/LIRT program for a person with MS. **Case Description:** The patient was a 54-year-old woman with a 13-year history of PPMS. Her baseline PDDS score was 2/8 and her EDSS score was 2.5/10. Medical history was otherwise unremarkable. She underwent a BFR/LIRT program for both lower extremities (LE) twice weekly for 12 weeks. Outcomes included 14 LE strength tests, MSWS-12, FSS, and Patient-Specific Functional Scale (PSFS) goals of: 1. Running for exercise and pleasure for 45 minutes; 2. Be 100% confident in negotiating a flight of stairs; and 3. Confidently and safely drive without restriction. **Outcomes:** The intervention was well tolerated without adverse events. After six weeks, there were improvements that exceeded the minimal detectable change (MDC) for all PSFS goals. There was an improvement in the MSWS-12, however, it did not exceed the MDC. Improvements in strength exceeded the MDC in 2/14 tests. After 12 weeks, the PSFS goals persisted. There were improvements exceeding the MDC for 8/14 strength tests. The remaining 6 strength tests improved but did not exceed the MDCs. MSWS-12 improvements persisted, and the FSS improved, but neither exceeded MDC. **Conclusion:** The use of a BFR/LIRT program resulted in measurable improvements for this patient. BFR/LIRT may be an option for strength training in people with MS, however, additional research is needed to determine its safety and effectiveness across the population of people with MS.
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Background and Purpose: Gait deficit is a hallmark of multiple sclerosis (MS) and the walking capacity can be improved with rehabilitation. Technological advances in biomechanics offer opportunities to assess the effects of rehabilitation objectively. Here we employed wearable sensors to measure electromyography (EMG) and body acceleration during walking and to evaluate the changes of walking pattern pre- and post-rehabilitation. Methods: Forty patients with MS (PwMS, 20 males; mean age: 51±9.8 years; mean EDSS: 5.51±1) were enrolled. All subjects performed 10-meter-walking-test (10MWT) before and after 4 weeks of intensive personalized physical rehabilitation. Clinical symptoms were assessed with self-reported questionnaires. An accelerator attached to the waist and 8 electrodes (BTS Bioengineering, Italy) attached to bilateral thighs (Rectus and Biceps Femoris, RF-BF) and legs (Tibialis anterior and gastrocnemius, TA-GM) for measuring body acceleration and EMG recording. Time, cadence(pace/minutes), step length and Coactivation index (Col) between antagonistic pairs pre- and post-rehabilitation were calculated for both more and less affected side (MA/LA) for statistics. Results: The time(p<.001) and cadence(p=.01) were significantly improved after rehabilitation. Col of RF-BF reduced in both LA sides post-treatment (p = .03). The combined effect size of our measure outcomes (0.55, Cohen d) is greater than what reported in the literature for the traditional fixed program (0.32). Discussion: Our results showed that the improvement of walking capacity after rehabilitation in PwMS may be related to reduced coactivation of the distal muscle. Combining objective assessment allows us to better evaluate and design the personalized rehabilitation program.

(7) Evaluating Effects of Global Proprioceptive Resonance on Gait in Multiple Sclerosis with Kinetic and Electromyography

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Background and Purpose: Global proprioceptive resonance (GPR) mechanically induces multifocal vibration at specific frequency among various cutaneous mechanoreceptors. Preliminary results suggest that GPR can modulate neuromuscular and neuroendocrine systems, therefore it may improve muscle strength and facilitate Lactose metabolism. Therefore, GPR could be beneficial for patients with multiple sclerosis (PwMS) since muscle
weakness is an important factor of their gait impairment. Here we evaluated the acute effects of a single GPR session on gait pattern in patients with MS using wearable sensors to quantitatively measure surface electromyography (sEMG) and body acceleration during walking. **Methods:** Ten patients with MS (PwMS, 8 males; mean age: 48±9.1 years; mean EDSS: 5.9±0.74), in a randomized order, underwent 15 minutes GPR and sham session (Keope GPR, ANDROMEDA, Italy) with a week interval. Nine Hole Peg Test (9HPT) and 6-meter-walking-test (SMWT) were performed pre- and immediately after the sessions. During SMWT, surface EMG and body acceleration were recorded with a wearable accelerator and surface electrodes (BTS Bioengineering, Italy). The SMWT were performed with spontaneous (Vp) and maximum velocity (Vmax). Time of 9HPT, velocity, cadence, step length and Coactivation index (CoI) of MWT of pre- and post-GPR were calculated for further statistics. **Results:** Compared with sham stimulus, significant improvement was found in 9HPT(p=.02) of the dominant hand after the active GPR session. For SMWT, increased velocity (p = .05) and cadence (p =.03) after active stimulus was found under Vp condition only, but not in the Vmax condition. No significant difference was found in other parameters. **Discussion:** Our preliminary results suggest that a single active GPR session can improve the motor performance in both upper and lower limbs. Our results suggest that GPR could boost muscle recovery and can be beneficial to be incorporated into rehabilitation protocols to ameliorate the fatigue level for PwMS.

**The Danger of Walking with Socks: Evidence from Kinematic Analysis in People with Progressive MS and Controls**

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**Background and Purpose:** Multiple sclerosis (MS) is a chronic autoimmune disease characterized by multifocal demyelination and neurodegeneration of the central nervous system. The accumulation of neurodegeneration resulted in disability in patients with MS(PwMS) and severely impacts the quality of life. Technological advances in biomechanics offer objective assessments of gait disabilities. Here we employed wearable sensors to measure and compare the gait pattern between walking in socks and in shoes in patients with progressive MS and healthy controls. **Methods:** Forty patients with MS (PwMS, 20 males; mean age: 51±9.8 years; mean EDSS: 5.51±1) and 15 age- and gender-matched healthy controls were enrolled. All subjects performed 10-meter-walking-test (10MWT) with an accelerometer attached on the waist and 8 electrodes (BTS bioengineering, Italy) attached on bilateral thighs (Rectus and Biceps Femoris, RF-BF) and legs (Tibialis anterior and gastrocnemius, TA-GM) for measuring body acceleration and EMG recording. The tests were performed with shoes and socks. Time, Cadence(pace/minutes), step length and Coactivation index (Col) between antagonistic pairs
were calculated for both more and less affected side (MA/LA) for further statistics. **Results:** PwMS showed longer time, lower cadence, and shorter step length in both conditions than controls (p<.05 for all). Increased coactivation than controls was found in RF-BF in both MA and LA sides, while only in MA of TA-GM. PwMS walked worse (longer time, lower cadence, shorter step length) when wearing socks. Higher CoI of RF-BF of MA side positively correlated with 10MWT time (r=.5, p<.01), EDSS (r=.4, p<.05), and negatively correlated with cadence (r =-.6, p<.001). **Discussion:** The results quantified the altered walking pattern in PwMS, the situation worsen when walking in barefoot. Further, increased coactivation was found in both the proximal (RF-BF) and distal (TA-GM) levels and correlated with higher EDSS and worse spatial-temporal parameters. This objective assessment of gait can benefit in evaluating the efficiency of rehabilitation.

(9) **Effect of Cooling on Gait Fatigability in Persons with Multiple Sclerosis**

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**Background and Purpose:** Gait dysfunction is common in persons with MS (pwMS) and is thought to be the result of gait fatigability (GF), characterized by progressive gait worsening during walking. Although GF in pwMS is multifactorial, thermosensitivity is considered to be a major cause, as increased core temperature occurring during exercise leads to decreased conduction through demyelinated nerves. Interventions to prevent core temperature rise could limit GF in pwMS. Cooling has been used to decrease thermosensitivity in pwMS, but its effect on GF have not been examined. The purpose of this study was to investigate whether a cooling vest would decrease GF in pwMS. We hypothesized that vest-wearing for 30 minutes prior to 6-minute walk tests (6MWT) would result in less GF in pwMS when compared to an uncooled condition. **Methods:** A randomized crossover design is being used. Ambulatory pwMS are randomized into cooled and uncooled conditions. Cooling is accomplished by seated wearing of a commercially available cooling vest for 30 minutes. The uncooled condition is sitting for 30 minutes without the vest. Immediately after 30 minutes, subjects perform a 6MWT. For each condition, GF is measured by 1) 6MWT performance, and 2) comparing the distance walked in minutes 1-3 to minutes 4-6. Data collection began for this study in fall of 2019 and will continue through the end of 2020. **Results:** To date, 19 subjects (EDSS4.4) have completed the study. Distance walked was higher in the cooled (241.3m) versus uncooled condition (227.1m), p = .016. Difference between distance walked in minutes 1-3 and 4-6 was more similar in the cooled (1.01 m) vs the uncooled condition (-5.4. m), p = .037. **Discussion:** Preliminary results suggest that a simple, practical cooling device may decrease GF in pwMS. The use of this device in clinical practice should be further investigated.
Cognitive-Motor Interference in People with Multiple Sclerosis: The Influence of Curvilinear Walking and Fatigue

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Background and Purpose: Dual tasks (DT) may lead to cognitive-motor interference in people with multiple sclerosis (PwMS), increasing the risk of falls. In real-life, curvilinear walking and fatigue could enhance this risk. Here, we investigated the effects of different DT on motor performance and neural activity in PwMS according with the perceived levels of fatigue.

Methods: Twelve PwMS (F=10, age=47±10y, EDSS=2.75±1.34) and twelve healthy controls (HC, F=7, age=40±11y) were asked to walk at spontaneous velocity on a 10m-long linear and on a figure-of-eight path. Then, different cognitive tasks were added to the two single motor tasks in order to provide DT stimulation: identifying sounds from the surrounding environment and backward counting. Kinematic parameters (i.e., step length and variability and centre-of-mass velocity) were computed with an infrared motion capture system. Cortical activity was evaluated using functional near-infrared spectroscopy (fNIRS).

Results: Both groups walked slower and performed shorter steps on the curvilinear path and under DT conditions. PwMS performed shorter steps than HC in all conditions. Instead, step variability was similar between PwMS and HC during linear walk, whilst differed on curvilinear path (PwMS>HC). Perceived fatigue correlated with several kinematic measures in DT but not in single task conditions. fNIRS analysis revealed increased brain activation in the supplementary motor and prefrontal areas in PwMS with respect to HC.

Discussion: Curvilinear walking and fatigue highly increase the risk of falls in PwMS. During DT, subjects might experience simple motor tasks (walking) as complex and novel, as suggested by the activity of the supplementary motor area. In PwMS, this could increase the demand of neural resources and lead to cognitive-motor interference.

Variable Exertion Contributes to Walking Impairments in Multiple Sclerosis

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Background and Purpose: Impaired walking function is a frequent disabling symptom in people with multiple sclerosis (MS). MS mobility is typically measured by completion of the Timed 25-Foot Walk Test (T25-FW). However, total time for walking distance does not capture variation of gait functioning during walking. We characterized the dynamic walking pattern across the 2-
minute walking test (2-MWT) to provide additional dimensions of gait measurement in MS.

**Methods:** MS patients (EDSS: 0-6.5; relapsing remitting and secondary progressive subtypes) were enrolled in the experimental protocol consisting in the execution of 2-MWT along 30-meter pathway at fast speed. Trunk acceleration data were collected by an inertial wearable sensor placed on the lower back. The evolution pattern of gait speed and stride length was assessed by partitioning acceleration data into four consecutive blocks of 30 seconds each, used to characterize dynamic changes across the 2-minute period of sustained walking. **Results:** Eighteen participants (median EDSS: 4; age: 53.2±10.3 years; 72% female) were assessed. The average T25-FW was 10.3±5.4 seconds, indicating mild to moderate impairment. The average 2-minute total distance travelled was 122.8±54.6 meters. Across the time blocks, walking speed significantly increased from the first to the second block (1.02 vs. 1.12 m/s, p=0.003), then declined during the third and fourth blocks (1.12 vs. 1.01 m/s or, p=0.001; 1.12 vs. 0.93 m/s, p=0.001). Similarly, stride length increased from the first to the second block (1.20 vs. 1.27 m, p=0.02), and then decreased during the fourth block (1.27 vs. 1.11 m/s, p=0.001). **Discussion:** Rather than a linear deceleration profile across sustained effort, MS participants first tried to accommodate the request to walk with faster speed that then resulted in a more marked decline. The onset of motor fatigability throughout demanding walking tasks could result from an initial increased exertion and provides potential targets for rehabilitative strategies.

**(12) Fatigue – A Key Predictor of Employment Status in People with Multiple Sclerosis**

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**Background and Purpose:** Fatigue affects 80% of people with MS (PwMS). Fatigue’s impact on PwMS and their unemployment status is often overlooked. The present study aims to fill this critical gap by evaluating the impact of fatigue on employment status. **Methods:** PwMS enrolled in a prospective cross-sectional study at the Mandell MS Center were selected if they were 20-65 years old, with a Modified Fatigue Impact Scale (MFIS-5) score and employment status recorded. A one-day assessment consisted of cognition (Symbol Digit Modality Test–SDMT), upper limb (UL) function (Nine-Hole Peg Test–NHPT; Box and Block Test–BBT; Finger-Nose Test–FNT), ambulation (Timed 25-Foot Walk–T25FW) and patient-reported disability (Patient Determined Disease Steps–PDDS; Multiple Sclerosis Walking Scale–MSWS-12; Multiple Sclerosis Impact Scale–MSIS-29; MFIS-5). Univariate binary logistic regression tested the
predictive role of each variable on employment status; a multivariate regression with conditional stepwise selection was performed on significantly associated variables. **Results:** PwMS (n=206) were selected (n=107 employed, n=99 unemployed). Male gender, older age, longer disease duration, and lower educational level predicted higher rate of unemployment. Unemployment risk factors included impaired cognition (SDMT), UL dysfunction (NHPT, BBT, FNT), ambulation (PDDS, MSWS-12, T25FW), fatigue (MFIS-5) and quality of life (MSIS-29). Multivariate regression analysis revealed age (odds ratio [OR]: 1.09, p<0.001), education (OR: 0.61, p=0.01), UL dysfunction (BBT: OR: 0.93, p=0.002) and MFIS-5 (OR: 1.19, p<0.001) were the most important predictors; together predicting employment status of 79.4% (R²=0.54). When categorizing participants by PDDS, MFIS-5 and age were selected among the main predictors of employment in both people with PDDS ≤2 (ambulatory: n=96) and with PDDS ≥3 (ambulatory dysfunction: n=110). **Discussion:** Fatigue is one of the most important predictors of unemployment in PwMS, regardless of the level of disability. New therapeutic strategies targeting fatigue are urgently needed in PwMS as these may impact employment status.

(13) Is Skeletal Muscle Fatigue a Contributory Risk Factor to Falls Among People with Multiple Sclerosis?

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**Background and Purpose:** Multiple sclerosis (MS) is a progressive neurological condition that results in muscle fatigue and increased walking impairment. Studies have shown gait variability and asymmetry are leading fall risk factors among people with MS, however, the influence of muscle fatigability specifically after physical activity is poorly understood. Hence, this study evaluated the relationship between lower leg muscle fatigue and changes in gait function after a 6-min treadmill walk. **Methods:** Eight persons with MS were enrolled, but six persons who were able to walk and demonstrated some impairment within PDDS 3-5 completed the study. Participants completed the Modified Fatigue Index Scale (MFIS) and the Fall Efficacy Scale and provided demographic information. Muscle fatigability of the medial gastrocnemius and tibialis anterior muscles was measured using an accelerometer during a non-invasive 5mins electrical twitch. Gait parameters were measured using a gait mat. These measurements were taken before and immediately after a self-paced 6-minute treadmill walk (6MTW). **Results:** Participant MFIS mean score was 45.2 ± 22. There was 26% increase in double support time variability, 25% increase in stride length variability, 16% increase in step length asymmetry, and 40% increase in single support time asymmetry after the 6MTW. There was a positive correlation between the fatigability of the GA and TA muscles (r = 0.94, p<0.001). Fatigability of the GA muscle negatively correlated with changes in gait variability (r = -0.80, p < 0.05) and gait asymmetry (r = -0.99, p < 0.01) after the 6MTW. **Discussion:** Six minutes of self-selected pace treadmill walk
resulted in impaired gait, suggesting an increased fall risk in these participants with MS. Gait impairment after the walking was associated with muscle fatigue. Therefore, understanding the role of prior physical activity and muscle fatigue might be one of the important approaches to reducing falls in people with MS.

(14) Torque Responses to In-Place Perturbations in People with Mild Multiple Sclerosis

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**Background and Purpose:** Automatic postural responses are critical to prevent falls after a loss of balance. Although responses have been shown to be delayed in people with multiple sclerosis (PwMS), the degree to which other aspects of these movements are impacted by MS remains unknown. The purpose of this study was to determine if responses to support-surface perturbations differ in PwMS compared to neurotypical adults and if they are related to a functional measure of postural response performance—center of mass (COM) displacement. **Method:** 52 PwMS and 20 neurotypical, age-matched adults (NA) experienced backward support surface perturbations resulting in forward loss of balance and requiring an in-place response. Center of pressure (COP) and torque were calculated from force plates while center of mass (COM) approximations were collected via motion capture. Primary outcomes were maximal torque production at the foot and its timing, rate, and onset. **Results:** PwMS and NA demonstrated no differences in maximal torque production (p=0.79), timing of maximal torque (p=0.29), rate of torque development (p=0.76), or COP onset (p=0.55). There was a significant negative association between the rate of torque development and forward center of mass displacement in both groups (NA: r=-0.64, p=0.002; MS: r=-0.35, p=0.01). Larger maximal torque production was also associated with smaller COM displacement in PwMS (r=-0.33, p=0.02). **Discussion:** No significant differences were observed in torque profiles between people with mild MS and neurotypical adults in response to backward support surface translations resulting in feet in-place responses. The rate of development and maximal torque were however correlated to functional postural response outcomes. These findings suggest that while not worse in PwMS during in place perturbations, force-responses are an important predictor of the effectiveness of reactive postural control responses in this population.

(15) Functional Intermuscular Reduction in Spasticity in MS (MS-FIRST)

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Background and Purpose: Multiple Sclerosis (MS) is a debilitating progressive condition affecting young adults. Altered gait is a signature impairment impacting walking efficiency in 85% of the 2.3 million people who live with MS, and leading to fatigue affecting 83.1%. The aim of this study was to determine if a combination of intermuscular electrical stimulation, followed by external functional electrical stimulation combined with treadmill training would decrease spasticity, improve gait, decrease fatigue, and improve functional mobility in individuals with MS. Methods: Using a repeated measure, pre-post experimental design, we implemented a combination protocol consisting of intermuscular and functional electrical stimulation with supported treadmill training in 12 individuals with MS. We measured spasticity and strength using the number of toe taps and heel raises each participant could complete. Outcome measures included the Berg Balance Test (BBT), the six-minute walk test (6MWT), the 25-foot walk test (25FWT), and the Fatigue Impact Scale (MFIS). We used General Estimating Equations to assess changes in the outcome measures over time. Results: Preliminary results indicated a statistically significant mean increase of 38.9 meters (p<0.0001) during the 6MWT, a mean decrease of 0.9 seconds (p=0.0027) in the 25FWT, and an increase in the mean number of toe taps (4.7 taps; p= 0.0009). The mean increase in BBT scores (0.6 points; p=0.65), the mean increase in the number of heel raises (5.0 p=0.003), and the mean decrease in FIS (2.9 points; p=0.6076), were not statistically significant. Discussion: Preliminary results of this novel protocol suggest it may be a viable treatment to decrease spasticity, increase strength, and improve walking in individuals with MS. Although changes in balance and fatigue were not significant, the positive trend may suggest a latent response in balance and fatigue from the changes in spasticity and strength measured in this study.

(16) Patient Perspectives on Falls in Persons with Multiple Sclerosis: A Pilot Study

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Background and Purpose: Falls and their consequences are known to be a major contributor to decreased health and well-being in older adults. Several studies suggest that fall rates are higher among individuals with disabling conditions such as Multiple Sclerosis (MS). Despite these data, it is unclear how individuals with disability define falls or think about their consequences. We sought to gain the perspective of community-dwelling adults living with MS on falls. Methods: Focus groups or one-on-one interviews were conducted with 20 people with MS (men=8 [34.7%], mean age 63.2 years (SD 5.3, range 55-75)). Average time since diagnosis was 20.6 years (SD 9.6, range 9-44). Results: All participants agreed that the definition of a fall required ending up on the floor. However, the starting point differed depending on mobility ability and device use. Using the most common research definition, individuals reported an increase in their number of falls compared to their personal definition. Most participants
viewed fear of falling different from concern about falling. Participants wanted to learn how to fall and would not join a program with the word “fall” in the title. **Discussion:** Results suggest that falls in those with MS may not be captured accurately. This suggests that healthcare providers need to use specific definitions for falls, fear and concern about falling to gather accurate information. Finally, patient-centered programming needs to be developed that include both how to fall and consider how to engage people with MS, including the name and potential facilitators and barriers to participation.

**Developing a Fall Risk Algorithm for Independent Fall Risk Screening in People with Multiple Sclerosis**

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**Background and Purpose:** Approximately half of people with Multiple Sclerosis (pwMS) fall in a six-month period. However, assessing overall fall risk is limited to research or clinical settings. Smartphone technology offers potential to increase access to fall risk assessment using an affordable, ubiquitous, and portable device. The purpose of this study was to develop an algorithm to measure overall fall risk in pwMS that can be implemented through a smartphone application (app). **Methods:** Twenty-seven pwMS (age = 53.4 ± 13.4 years; gender = 22 females; MS duration = 15.7 ± 11.1 years) participated. Participants completed five standing balance tasks while holding a smartphone against their chest: 1) eyes open, 2) eyes closed, 3) semi-tandem, 4) tandem, and 5) single leg. Participants then completed demographics and questionnaires related to MS symptoms, such as the Modified Impact Fatigue Scale (MIFS), Multiple Sclerosis Walking Scale (MSWS-12), and Activities Balance Confidence Scale (ABC). Bivariate analyses were performed to determine differences between fallers and non-fallers. Outcomes with p ≤ 0.1 were inputted into a binary logistic regression model. Interpretation based on the Wald statistic and beta value determined the final algorithm. **Results:** From the bivariate analysis, fallers had a significantly greater postural instability as measured through the smartphone accelerometer (p = 0.03), worse perceived walking ability (p = 0.02), worse balance confidence (p = 0.002), and used an assisted device (p = 0.05). There were no significant differences for number of medications, fatigue, or age. The final model from regression analysis included the ABC-6, MSWS-12, postural control, and number of balance tasks completed. **Discussion:** This is the first algorithm to include multiple fall risk factors that can be independently assessed using a smartphone app. The next step is to develop an app incorporating this algorithm, ultimately increasing access for pwMS to independently assess their fall risk.
(18) Self-Report Measures of Fatigue in Multiple Sclerosis: Systematic Review of Psychometrics and Usability with Evaluation of Evidence

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Background and Purpose: Fatigue is a common, debilitating impairment in multiple sclerosis (MS). To assess an individual’s experience of fatigue and its impact, clinicians rely on self-report information. However, choosing appropriate standardized self-report measures of fatigue in MS can be challenging. The Academy of Neurologic Physical Therapy assigned the task of systematically reviewing fatigue measures to the MS Outcome Measures Task Force. The purpose of this report is to provide initial results regarding psychometrics and usability of fatigue measures tested in people with MS. We also provide an evaluation of the evidence using a modified COSMIn rating system. Methods: Multiple databases were searched through February 2020 using search terms related to fatigue and MS: PubMed, CINAHL, and Embase. 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 on psychometric properties were extracted by two independent reviewers; discrepancies remaining after discussion were resolved by a third reviewer. Properties were appraised for risk of bias and quality according to the relevant COSMIN sections. Results: Preliminary results indicate that 22 studies met eligibility criteria, with information on 14 fatigue measures used in people with MS. Reliability was reported on 8 measures; responsiveness on 6; content validity on 12; interpretability on 12; and generalizability regarding EDSS and phenotype on 14. Three measures had information across all properties: Fatigue Impact Scale, Neurological Fatigue Index for MS, and Unidimensional Fatigue Impact Scale. Discussion: Few fatigue measures have evidence across all COSMIN items for people with MS. Future studies are needed to fill in missing psychometric data. Clinicians should aim to select measures with psychometric data and content important to their patient.

(19) Function, Not Structure: Neurophysiology May Be More Important Than Neuroanatomy for Controlling Turning Performance in People with Multiple Sclerosis

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**Background and Purpose:** Neurodegenerative effects of multiple sclerosis (MS) are associated with decreased mobility and adaptations affecting neural structure and function. Due to cortical influences on mobility, it’s likely these neural adaptations negatively affect mobility. MS is associated with volumetric alterations affecting cortical grey matter (GM) thickness along with levels of corticospinal inhibition. The purpose of this project was to understand how motor cortex thickness and inhibition contribute to turning performance in people with MS (PwMS) and age-matched neurotypical participants. **Methods:** Participants completed a series of 360° turns at their self-selected fast pace. Turn duration and turn velocity were assessed using wireless inertial sensors. GM thickness of the motor cortices was measured using a T2-weighted FLAIR image. Corticospinal inhibition was measured through single-pulse TMS targeting the leg regions of each motor cortex. To assess inhibition, participants received a stimulation every 7-10 seconds while performing an isometric dorsiflexion contraction. The primary outcome measure for inhibition was quantified as percentage of electromyography (EMG) depression post-stimulus when compared to the pre-stimulus EMG mean. **Results:** Forty-eight participants (23-controls, 25-PwMS) were included in the analysis. PwMS demonstrated significantly reduced turning performance for both measures. GM thickness revealed main effects of group and hemisphere. PwMS demonstrated reduced thickness and both groups had less thickness in the right motor cortex. PwMS also had significantly less cortical inhibition, regardless of hemisphere. PwMS displayed a significant positive correlation between left hemisphere GM thickness and inhibition. Both turning measures were significantly associated with GM thickness and inhibition for PwMS, although cortical inhibition displayed greater significant associations with turning performance compared to GM thickness for PwMS. **Discussion:** These results indicate that cortical inhibition, rather than GM thickness, may be more associated with dynamic lower limb movements, and that PwMS may utilize different neural resources to perform movements associated with fall risk.

(20) Change in Gait, Fatiguability, and Standing Stability with Daily Use of Torso Weighting in Multiple Sclerosis: A Randomized Pilot Study

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**Background and Purpose:** People with multiple sclerosis (MS) and gait and balance limitations demonstrate improved motor ability with balance-based torso-weighting in single sessions. Daily use of torso-weighting in MS may provide additional benefits. This pilot study examined carry-over effects of daily torso-weighting versus sham weighting or no weighting over a multi-
week period. Gait and fatigability were assessed by comparing gait parameters and walking endurance after 2-week to 4-week periods wearing no weights, torso weights, or sham weights. Postural sway was assessed in standing, using center-of-pressure data recorded on a force plate, with weights on and off. **Methods:** Five participants with MS experienced all three conditions, with no weights first, then double-blinded randomization of order for weights and sham weights. The torso-weighting procedure involved systematically locating small weights on a vest-like garment to improve reactive control following manual perturbations. After optimal torso-weighting, a single researcher removed the vest and replaced weights with actual or equivalent-shaped sham weights before participants took the vest home. Measures included standing for 30 seconds with eyes open/closed on a force plate with and without weights (unblinded), and gait measures without weights: gait on an instrumented gait-mat, and the 6-Minute Walk Test (6MWT). Weight versus sham-weight performances were compared using average percent change and repeated measures with alpha set at 0.05. **Results:** Postural sway showed a statistically significant decrease with weights on versus weights off. Cadence and step width improved significantly after wearing weights. Velocity and 6MWT showed improvements of +15% and +16.6%, respectively. Percentage differences following weighted versus sham weighted conditions was 20.5%, reaching MCID for gait velocity. **Discussion:** This pilot study showed that torso-weighting for 2-4 hours daily for multiple weeks improved performance in standing stability, gait parameters, and fatiguability. Further research is warranted to increase sample size and examine possible interaction effects among variables.

(21) Influence of the Environment on Cognitive-Motor Interaction During Walking in People Living with and without Multiple Sclerosis

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**Background and Purpose:** Motor and cognitive impairments are highly prevalent in people with multiple sclerosis (pwMS). The current theoretical frameworks of cognitive-motor interaction (CMI) suggest that the environment can influence motor/cognitive performance during walking. However, the relationship between the walking environment and CMI in pwMS remains to be elucidated. Therefore, we aimed to explore the impact of increasing environmental demands on CMI during walking in people living with and without MS. **Methods:** Twenty pwMS and 20 age-matched healthy adults (HA) participated in this cross-sectional study. Participants (age = 57.6±7.8 years) performed four walks (baseline walking (BW), obstacle walking (OW), narrow walking (NW), and narrow with obstacles (NO)) in single-task and dual-task (serial-7 subtraction test) conditions. The dual-task costs (DTC) of gait and cognition were calculated to quantify CMI. Secondary outcomes included physiological profile assessment (PPA), measures of cognition and falls efficacy scale international (FES-I). **Results:** Mixed-factor ANOVAs revealed no main effect of task (F = 1.71, p = 0.196) and group (F = 0.71, p = 0.406) on DTC of gait, while
there were significant main effects of both task ($F = 23.75, p < 0.001$) and group ($F = 6.53, p = 0.015$) on DTC of cognition. Simple main effects revealed that pwMS had a significantly higher DTC of cognition during BW (+37.6%, $p = 0.013$), NW (+34.2%, $p = 0.014$) and NO (+49%, $p = 0.016$) compared to HA. Additionally, DTC of cognition increased during the more environmentally demanding conditions compared to BW (range: +28.4% to +54.2%, all $p$-values < 0.01) in both pwMS and HA. Only DTCs of cognition were significantly correlated with PPA and FES-I. **Discussion:** The study findings suggest that CMI may be influenced by the individual/environment at levels above those described by the more mechanistic theories of attention.

**(22) Associations Between Habitual Physical Activity, Postural Control, and Gait Speed in People with Multiple Sclerosis**

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**Background and Purpose:** Approximately 80% of people with MS (PwMS) experience impaired balance and mobility. Exercise interventions improve both balance and mobility in PwMS, however, the effects of the volume, type and intensity of habitual physical activity (PA) on balance and mobility is not well understood. The purpose of this study was to examine associations between PA volume, type and intensity with mobility and balance performance in PwMS. **Methods:** Twenty-seven PwMS (48 ± 12 years, 24.9 ± 3.8 kg·m$^2$) with an expanded disability status score of 0-4.0 ($median=3.5$) reported their typical PA routine, including PA volume [(days per week) x (minutes per exercise bout)], type (resistance and/or plyometric (R/P), or aerobic training (AT), and yoga), and intensity (rating of perceived exertion (RPE) 2-20). Balance performance was assessed by the mini Balance Evaluation Systems Test (Mini-BEST) and its four principle domains: anticipatory postural control, reactive postural control, sensory orientation and dynamic gait. Mobility was measured by the gait speed during two, two-minute walk tests at a self-selected and fast pace. Pearson correlations examined associations between PA volume, intensity, and balance, and gait speeds. Independent $t$-tests examined differences in balance and gait speeds between participants who did vs. did not perform each type of PA. **Results:** PwMS reported $M=252+234$ PA minutes per week, $MRPE=13±3$ and participation in R/P (44%), AT (89%), and yoga (30%). RPE was positively associated with total Mini-BEST score ($r = 0.462, p = 0.020$), reactive postural control ($r = 0.472, p = 0.017$) and sensory orientation ($r = 0.542, p = 0.005$). PwMS who reported R/P training had higher dynamic balance scores ($p < 0.01$) than those who did not. **Discussion:** Higher RPE and habitual R/P training were associated with better balance and mobility among PwMS. Future intervention studies should examine the effects of PA intensity and/or R/P training on balance and mobility among PwMS.
(23) Responsiveness of the Patient-Specific Functional Scale to Changes in Walking Endurance: A Proof-of-Concept Analysis

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Background and Purpose: The Patient-Specific Functional Scale (PSFS) requires the respondent to select 3-5 personally challenging functional activities and score each activity on an 11-point scale (0: unable to perform, 10: performs without difficulty). The PSFS is considered reliable for several musculoskeletal condition populations, with meaningful change deemed as a 2-point average improvement. However, there is insufficient knowledge of PSFS utility for people with multiple sclerosis (PwMS). This proof-of-concept analysis aimed to determine PSFS responsiveness following an exercise intervention in PwMS and describe those changes relative to change in walking endurance and self-reported walking function and fatigue. Methods: Walking endurance (6-Minute Walk Test–6MWT) and self-reported outcomes (PSFS, Multiple Sclerosis Walking Scale–MWSW-12, and Modified Fatigue Inventory Scale–MFIS) were collected using a repeated-measures design with assessments before and following an 8-week strength training intervention. For the PSFS, participants were instructed to select three meaningful activities related to walking. Changes in all outcomes from baseline to follow-up were evaluated using paired t-tests (α = 0.05), and each change value was also compared to published values on clinically important change for the 6MWT (21.6 m), PSFS (2.0 points), MSWS-12 (10.4 points), and the MFIS (4 points). Results: Ten PwMS (Expanded Disability Status Score: 3.5–5.5) were included. Following the intervention, participants had significant and clinically important improvement (+ SEM) in the PSFS (2.53 ± 0.37 points, p < 0.001). All other outcomes improved significantly (p < 0.05) and corresponded to clinically important differences: 6MWT (41.56 ± 30.10 m), MSWS-12 (-10.50 ± 3.68 points), and MFIS (-14.25 ± 4.53 points). Discussion: This report provides initial evidence for the responsiveness and clinical importance of a 2-point improvement of the PSFS in PwMS. Further psychometric evaluation of the PSFS is needed to determine its clinical utility for PwMS.

(24) Head and Trunk Instability and Turning Velocity During a Fatiguing Walk Test in Patients with Multiple Sclerosis

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Background and Purpose: People with Multiple Sclerosis (PwMS) are prone to greater instability that may increase in states of fatigue. We examined whether or not people with MS experienced more instability of the head and trunk and reduced turning velocity during a 6-minute walk test compared to controls and how these variables changed overtime (minutes 1-6) between groups. Methods: 28 PwMS (EDSS=3.26±.82) (age=51.74±11.95) and 10 age matched controls (age=53.8±11.82) walked along a 25.3-m hallway for 6 continuous minutes while wearing inertial measurement units on the head and sternum. Turns completed after each length of walking were selected and peak velocities were captured from the sternum gyroscopic data and averaged for each minute interval (minutes 1-6). Root Mean Square (RMS) of the accelerometer data from the head and trunk sensor was calculated to assess head and trunk stability during straight-line walking over each minute interval in anteroposterior (AP), mediolateral (ML), and craniocaudal (CC) directions. Linear mixed models were used to examine between group and group by time effects, controlling for walking speed and random intercepts and slopes for each individual. Results: PwMS demonstrated slower, but non-significant in our model, turning velocities than controls. AP RMS values were significantly lower in PwMS at the head and trunk and PwMS demonstrated a significantly greater increase in AP RMS over time compared to controls. RMS values did not differ between groups in ML or CC directions and these values did not differ over time between groups. Discussion: In this sample, only AP head stability was sensitive to group and time differences. While head stability and turning velocity may reflect aspects of instability, 6 minutes may not be long enough to demonstrate fatigue related changes. Additionally, PwMS may choose a walking state that allows them stability over a fixed time.

(25) Cognitive Domains and Dual-Task Walking in Persons with Multiple Sclerosis

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Background and Purpose: Healthy adults can handle activities that require walking concurrent with an additional task (dual-task walking [DTW]). However, persons with MS (PwMS) struggle with DTW, with greater DTW costs (DTWC) in PwMS than healthy controls. DTWC are related to measures of fall risk and predictive of future falls in PwMS. Thus, it is worthwhile to identify contributors to DTW difficulties in PwMS. Researchers suggest that specific cognitive domains should be explored for relationships with DTWC. Methods: The present study measured gait velocity in single-task walking (STW) and DTW in 75 PwMS. Age, Expanded Disability Status...
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Scale⁷ to measure disability, and the NeuroTrax™ battery to evaluate cognitive domains were collected. Achieved power calculations were performed for variable effect sizes across sample sizes given the nascentcy of this line of research and the use of a training/test set approach. Stepwise and Least Absolute Shrinkage and Selection Operator (LASSO) regressions were performed to select from six cognitive domains (Memory, Executive Function, Attention, Information Processing, and Visuospatial and Verbal Abilities) in the training set—sampled randomly from 70 participants with full data. For stepwise regressions, $p = .10$ was used for entry/removal. For LASSO, Mallow’s $C_p$ was used. Models were evaluated in the test set. Then, bivariate, partial, and semi-partial correlations were assessed in the full sample. **Results:** No significant differences existed between sets. Despite predictors being identified in training sets, no replicable predictors of change in velocity or DTWC were identified. The relationship between STW velocity and Executive Function replicated, $p = .078$, and the relationships between DTW velocity and Memory, $p = .033$, and Attention, $p = .027$, replicated. **Discussion:** The findings highlight possible, unique cognitive domains that are relevant to STW and DTW in PwMS, and the need to consider the robustness of predictors identified in small samples.

**(26) Fatigue Is Associated with Reduced Mobility, Depressive Symptoms, Fear of Falling, and Reduced Quality of Life Independent of Disease Severity in Multiple Sclerosis**

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**Background and Purpose:** Fatigue is one of the most common and disabling symptoms experienced by people with multiple sclerosis (MS). It has been reported fatigue affects approximately 75% of people with MS and impacts mental health, general health status, employment and quality of life. In a large community living sample, we examined the extent to which fatigue influenced gait speed, endurance, mood, falls efficacy, physical activity levels and quality of life in people with MS. This study was supported by Multiple Sclerosis Limited and the National Health and Medical Research Council (of Australia). **Methods:** People with MS (n=213, 22-78y, 161 female) completed the Modified Fatigue Impact Scale (MFIS) as well as an assessment of knee extension strength, a postural sway test, the 10m walk test, the six minute walk test, the PHQ9 depression scale, the iconFES fear of falling scale, the IPEQ physical activity questionnaire and the WHODAS quality of life scale. Partial correlational analyses were performed comparing MFIS scores with the remaining variables while controlling for MS disease severity as measured with the MS Disease Step Scale. **Results:** The adjusted analysis revealed high MFIS scores were significantly associated with slow 10m walk speed ($r=-0.297$, $p=0.000$), short six minute walk distances ($r=-0.241$, $p=0.003$), higher depressive symptoms scores ($r=0.695$, $p=0.000$), reduced falls efficacy ($r=0.450$, $p=0.000$) and lower quality of life scores ($r=0.710$, $p=0.000$). MFIS scores were not significantly associated with knee extension strength ($r=-0.112$, $p=0.171$), postural sway ($r=0.047$, $p=0.567$) or total hours of physical activity per
week \((r=0.015, \ p=0.855)\) when adjusting for MS Disease Step. **Discussion:** Fatigue was significantly associated with multiple measures of mobility, mood, fear of falling and quality of life independent of disease severity in people with MS. Interventions aimed at addressing fatigue may have multiple benefits for this group.

**(27) Impact of Intensive End-Effector Robotic Rehabilitation on Fatigue and Quality of Life in Progressive Multiple Sclerosis**

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**Background and Purpose:** Rehabilitation has been recommended for the reduction of disability and restoration of function for individuals with Progressive multiple sclerosis (PMS). An end-effector robot-assisted gait trainer (RAGT) addresses the gait training needs while providing an intensive training environment. The purpose of this randomized control pilot study was to establish the safety and feasibility of intensive RAGT while measuring its impact on fatigue and quality of life. **Methods:** Fifteen subjects completed either RAGT \((n=8)\) or standard of care \((n=7)\). Eleven women and four men averaging 52.5 years of age and an EDSS scores from 4.5 to 6.5. Single-blinded, randomized clinical trial using RAGT. Subjects trained 2 times per week for 10 weeks for a total of 20 sessions. Physical therapists individualized training intensity and RAGT characteristics to maximize benefits. Quality of life measures (Modified Fatigue Impact Scale [MFIS] and the Multiple Sclerosis Impact Scale 29 [MSIS-29]) were assessed at baseline and after the final training session. **Results:** There were no reported adverse events. For quality of life, RAGT had significant greater impact on the physical domain of the MFIS than standard of care \((p<.05)\) with an effect size of .86. The standard group showed significant improvement in the cognitive \((p<.05)\) and psychological \((p<.05)\) domains. The MSIS-29 subscales indicated that RAGT had a significant decrease \((p<.05)\) in physical disability (18%) when compared to SOC. The SOC group had a significant decrease of 40% psychological disability. **Discussion:** All participants with progressive MS tolerated the treatment dosage of two times per week for 10 weeks. The training regimen safely produced a moderately intensive, progressive training environment. The outcomes had significantly positive impact on physical fatigue and quality of life for both groups. These early outcomes warrant further investigation of end-effector RAGT as a viable option for managing individuals with progressive MS.