(1) Aerobic Exercise Improves Fitness and Cognition in Relapsing-Remitting Multiple Sclerosis

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**Background and Purpose:** Aerobic exercise increases hippocampal size and improves memory in older adults. While cross-sectional studies in people with multiple sclerosis (MS) show correlations of fitness with brain substructure volumes, prospective studies have not evaluated cognition. We hypothesized that an aerobic exercise intervention would improve fitness, cognition, and fatigue in relapsing-remitting MS (RRMS). **Methods:** Eleven participants with
RRMS and no walking limitations underwent supervised treadmill or stationary bicycle exercise for 30 minutes, 4 times weekly, for 8 weeks. Seven participants with RRMS matched for age and baseline VO$_{2\text{max}}$ followed a self-guided stretching program of equal frequency and duration, and eight matched non-MS participants followed a self-guided aerobic exercise program as a second control group. Pre- and post-intervention, participants underwent cardiovascular fitness testing, and completed fast and slow walking tests, the Modified Fatigue Impact Scale (MFIS), and the Symbol Digit Modalities Test (SDMT; cognitive processing speed). **Results:** Ten RRMS aerobic exercisers (age 44.7 ± 9.4 years; disease duration 14.6 ± 6.5 years, median Expanded Disability Status Scale [EDSS] score 3.5), seven RRMS stretchers (age 48.7 ± 8.4 years; disease duration 20.2 ± 10.4 years; median EDSS 3), and seven non-MS aerobic exercisers (age 36 ± 7.5 years) completed the protocol. One MS aerobic exerciser terminated early for recurrent exercise-induced syncope. While VO$_{2\text{max}}$ increased significantly in both MS and non-MS aerobic exercisers (12.7%, $P = .0007$, and 19%, $P = .03$, respectively), MS aerobic exercisers also showed significant improvements in maximum work (+29.1%, $P = .0007$) and total exercise time (+20.5%, $P = .002$). MS aerobic exercisers demonstrated improvements in SDMT (+7 points, $P = .037$) and the MFIS cognitive component (−3.8 points, 26%, $P = .03$). No significant changes in VO$_{2\text{max}}$, cognition, or cognitive fatigue were observed following the stretching intervention. **Discussion:** Aerobic exercise improved cardiovascular fitness, cognition, and cognitive fatigue in a brief but intense intervention. Aerobic exercise should be considered first-line therapy for cognitive symptoms in RRMS.

(2) Not Just an Orthotic Device: Use of Torso-Weighting Can Improve Motor Ability Tested with Weights Off in Pilot Test of People with Multiple Sclerosis
Background and Purpose: Strategic placement of light weights using balance-based torso-weighting has improved gait parameters, standing stability, and fall rate in single-session testing with weights on, establishing an orthotic effect in multiple sclerosis (MS). In this pilot test, we had participants wear torso-weights for 2 to 4 hours a day for a multiweek period. We assessed possible therapeutic effects of torso-weights by performing all testing with weights off.

Methods: Five participants with MS were tested at baseline and after periods during which they wore no weights, actual weights, or sham weights. The order of the actual weight and sham weight conditions was randomized. Testing included walking on an instrumented gait mat, the 6-Minute Walk Test, and the Sensory Organization Test. Torso-weighting involved applying weights (totaling 0.25–2 pounds) to a vest-like garment to improve reactive control following manual perturbations and resisted rotations at the shoulders and pelvis. Participants and assessors were blinded. Changes in performance during the three weighting conditions were compared using repeated-measures analysis of variance; effect size was considered large if over 0.4.

Results: After the 2-week period wearing actual weights, average increases were 7.4 points or 14% for the Sensory Organization Test, 47.4 m or 16.6% for the 6-Minute Walk Test, and 12.5 cm/s or 15% for gait velocity. Average performance for each variable decreased or showed negligible improvement after periods of no weight (13.4% decrease to 3.5% increase) or sham weight (5.8% decrease to 1.8% increase). The effect sizes were large (0.7 to 0.9).

Discussion: Strategic torso-weighting does not just act as an orthotic device, supporting function when
donned. Improvement noted with weights doffed implies that motor learning may occur during a period of regular use. Further research is warranted. The large effect size indicates that this study would have .80 power with a sample size of eight people.

(3) Carryover of Gait and Balance–Related Improvements in Patient with Secondary Progressive Multiple Sclerosis During Gait Training with Exoskeleton

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**Background:** Research on exoskeleton use focuses primarily on individuals with spinal cord injury and stroke. Fewer reports exist on the value of these devices for individuals with multiple sclerosis (MS), especially individuals with gait abnormalities from progressive disease.

**Purpose:** Determine if exoskeleton-driven gait training improves gait parameters during overground walking. Determine if observed gains will persist without continuous training. **Case Description:** A 51-year-old female veteran with secondary progressive MS (SPMS) with an Expanded Disability Status Scale (EDSS) score of 5.5 was observed initially during exoskeleton staff training sessions and was subsequently followed as staff sessions continued (approximately 5 months). A training regimen was instituted with weekly sessions for 6 weeks, followed by 2- to 6-week intervals without training, then biweekly sessions, respectively. Outcome measures included the 6-Minute Walk Test, Timed 25-Foot Walk, Dynamic Gait Index, and 5× Sit to Stand. Weekly Timed 25-Foot Walk measurements with Borg Rate of Perceived Exertion rating were also performed at the end of each session. **Outcomes:** Improvements of at least 30% in both the 6-Minute Walk Test and Timed 25-Foot Walk were noted plus improvements in
Dynamic Gait Index score by 3 points and 3.5% in the 5× Sit to Stand. Improved gait quality per observational gait analysis was also seen, as the veteran was able to safely ambulate over indoor level surfaces without the single-point cane previously required. **Conclusions:** Exoskeleton-based gait training is a useful form of moderate-intensity activity to drive gait improvements in an individual with SPMS.

(4) Can Exercise Combined with Cranial Nerve Noninvasive Neuromodulation (CN-NINM) Improve Mobility in Nonambulatory People with Multiple Sclerosis? A Case Series

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**Background and Purpose:** We have developed a novel intervention to improve balance and gait using cranial nerve noninvasive neuromodulation (CN-NINM) in conjunction with targeted physical therapy (PT). In our previous randomized controlled trial, the intervention improved balance and gait in people with mild to moderate multiple sclerosis (MS). The current study was undertaken to determine if CN-NINM can improve balance, gait, and function in subjects with advanced MS symptoms. **Methods:** Six subjects (Expanded Disability Status Scale [EDSS] score 6.5–7.5) participated. Subjects trained for 2 weeks in the laboratory, and continued a home program that included standing/sitting balance training, gait/pre-gait activity, breathing and awareness training, and movement exercise for 6 months (total 2 hours per day). Subjects returned to the lab every fifth week for retraining and testing. Outcome measures included the Repeatable Battery for Assessment of Neuropsychological Status, Trunk Impairment Scale, 29-item Multiple Sclerosis Impact Scale (MSIS-29), Modified Fatigue Impact Scale (MFIS), MS
Walking Scale, Impact of Visual Impairment Scale, Box & Blocks, Medical Outcomes Study Pain Effects Scale, Bladder and Bowel Control Scales, Walking Distance and Speed, Static Standing Balance Test, Gross Motor Function Measure, and Modified Rivermead Mobility Index.

**Results:** Average home program compliance was more than 80%, with no adverse events attributable to study participation. Three of the four subjects with EDSS 6.5–7.0 improved their walking speed and/or distance, MFIS, and MSIS-29 scores. Subjects with EDSS 7.5 showed limited functional gains, but tolerated the protocol without adverse event. The demanding CN-NINM regimen also resulted in significant real-life improvements (re-adopting a walker for community mobility; overcoming home obstacles to increase community access).

**Discussion:** All subjects tolerated CN-NINM well. Those with greater functional ability at the beginning of the study (EDSS 6.5–7.0) made the most significant functional gains. For people at this level, the intervention shows promise to prolong functional ambulation and independence with daily activities.

(5) **Pilot Study to Examine the Safety and Feasibility of Positive Pressure Treadmill Training in People with Multiple Sclerosis**

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**Background and Purpose:** Seventy-five percent of people with multiple sclerosis (MS) demonstrate walking dysfunction and cite this as the most devastating consequence of MS. Positive pressure treadmill training (PPTT) is a novel form of body-weight–supported treadmill training that is showing promising results in other neurologic populations, but people with MS
experience unique symptoms and may respond differently. The purpose of this pilot study is to evaluate the safety and feasibility of PPTT in people with MS with moderate to severe walking disability. **Methods:** Two participants with MS (Expanded Disability Status Scale score 6.5) completed training for approximately 25 minutes, twice a week for 8 weeks, on the Alter-G positive pressure treadmill (Alter-G Inc., Fremont, CA). Vital signs and ratings of pain, spasticity, and fatigue were monitored throughout each session. Fatigue was assessed pre and post intervention using the Modified Fatigue Impact Scale (MFIS). **Results:** There were variable responses in blood pressure and heart rate that were maintained within safe parameters. Pain did not increase within session or pre to post intervention. Fatigue did increase within session, but MFIS scores decreased post intervention. Spasticity increased minimally within session and pre to post intervention in one participant. There were no adverse events. **Discussion:** Similar fluctuations in vital signs have been reported in healthy participants, suggesting that PPTT training is also safe for people with MS. We expected training to increase fatigue within session, but the finding that fatigue decreased post intervention is promising. The increase in spasticity may be attributed to factors that have been shown to increase symptoms of MS such as fatigue and stress, but further investigation is warranted to examine this increase in spasticity. PPTT appears to be a safe and feasible intervention for people with moderate MS. Findings from these two cases will be used to inform this ongoing pilot study.

(6) **Neurorehabilitation of Multiple Sclerosis Symptoms Using Cranial Nerve Noninvasive Neuromodulation (CN-NINM): Controlled Study**

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**Purpose:** Cranial nerve noninvasive neuromodulation (CN-NINM) combines electrical stimulation of the tongue with special sensory-motor conditioning exercises to effect rehabilitation of motor, cognitive, and emotional symptoms resulting from neurologic disorders. The goal of this research was to investigate how neurostimulation can facilitate physiotherapy in rehabilitation of multiple sclerosis (MS) symptoms. **Methods:** At the laboratory, CN-NINM therapy was administered twice daily, 5 days per week for 2 weeks, to 20 adult human subjects with MS, 10/10 in active (stimulation)/control groups (no stimulation). Daily sessions comprised instructing the subject, physical conditioning, and sets of targeted exercises with tongue stimulation. At home, subjects continue exercises during 3 months with regular checking in the laboratory. **Results:** Functional recovery was evaluated using several physical and cognitive quantitative metrics; in all cases, we observed a statistically significant improvement in performance. The gait improvement in the active group was significantly better than in the control group after 4 weeks of training. Subjects reported improvement in the majority of their MS symptoms: spasticity, tremor (leg, hand, and head tremor), posture, balance, gait, speech, sleep, facial expression, eye movements, oscillopsia, fatigue, headache, thermal regulation, bladder control, and constipation. Improvements included not only physical and physiological aspects, but also cognitive (short-term memory, spatial memory, attention, comprehension) and emotional aspects of disease (depression). Not all measurements were statistically different between groups. We hypothesize that the beneficial effects observed in this study result from lasting and cumulative neuroplastic changes (functional, synaptic, and neuronal) in the brainstem and cerebellum on the cellular, neural network, and systemic levels. **Conclusions:** Our study establishes proof of effectiveness of an advanced noninvasive neuromodulation therapy for
balance, posture, movement disorders, and other physiological and cognitive signs and symptoms associated with MS.

(7) Effects of a Group Spasticity Management Program Versus Usual Care in People with Multiple Sclerosis: A Randomized Controlled Pilot Trial
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Background: Spasticity affects over 80% of people with multiple sclerosis (MS), impacting activity, participation, and quality of life. An international guideline for spasticity management was published in 2003. A comprehensive spasticity management program, including a DVD with education based on this guideline and a lower-extremity stretching DVD, were developed. The efficacy of this comprehensive spasticity management program, MS Spasticity: Take Control (STC), has not been assessed. Purpose: To determine whether participation in group delivery of the STC program is associated with greater changes in spasticity compared to usual care (UC) in people with MS. Methods: Ambulatory MS subjects with self-reported spasticity interfering with daily activities were randomized to STC, with two 2-hour group sessions and home practice, or UC, with home practice using the National Multiple Sclerosis Society’s stretching brochure without instruction or group support. Subjects completed the self-reported MS Spasticity Scale-88 (MSSS) and examiner-assessed Modified Ashworth Scale (MAS) at baseline and following 4 weeks of either intervention. Results: Forty subjects were randomized and 38 completed both baseline and outcome measurements. Baseline MSSS and MAS scores did not differ between the
two groups. Mean MSSS total scores improved more in the STC group than in the UC group between baseline and follow-up (STC −27.8, UC −3.7; P < .03) and on the MSSS Pain and Discomfort subscale (STC −3.9, UC +0.3; P < .02) and MSSS Muscle Spasms subscale (STC −5.0, UC −0.8; P < .03). Change in MAS did not differ between groups (P > .05). **Discussion:** Participation in a small group spasticity education and stretching program improved subjective spasticity more than usual care in subjects with MS. This suggests benefit of a comprehensive spasticity management program to help manage MS-related lower-extremity spasticity. Results of this pilot study need replicating in a fully powered trial.

(8) **Effects of Methylphenidate on Mobility, Cognition, and Fatigue in Multiple Sclerosis: A Pilot Study**

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**Background:** Methylphenidate, an amphetamine-like stimulant, is often prescribed off-label for fatigue in people with multiple sclerosis (MS). Methylphenidate has been shown to improve balance and walking and reduce fall risk in various populations. There are no published studies evaluating the impact of methylphenidate on mobility, cognition, or fatigue in people with MS.

**Goals:** To determine the impact of methylphenidate on mobility, cognition, and fatigue in people with MS. **Methods:** Twenty-four people with MS with impaired walking or imbalance enrolled in this 6-week double-blind placebo-controlled pilot trial were randomized to receive active oral methylphenidate or matched placebo, starting at 10 mg twice a day, and increasing by 10 mg twice a day every 2 weeks to a maximum of 60 mg/day, exiting for intolerance of any dose.
Mobility (Timed 25-Foot Walk [T25FW], Timed Up and Go [TUG]), cognition (Symbol Digit Modalities Test [SDMT]), and fatigue (Modified Fatigue Impact Scale [MFIS]) were assessed at baseline and every 2 weeks. Tolerability and changes in measures between groups were compared. **Results:** Eight of 12 subjects in the methylphenidate arm and 6 of 12 in the placebo arm completed all visits. In the methylphenidate arm, two subjects exited after the 20-mg twice-daily dose (one due to escalating blood pressure, the other due to nightmares), and two exited during the 30-mg twice-daily dose (one due to insomnia and another due to tachycardia). In the placebo arm, two exited after the 10-mg twice-daily dose (one due to hypertension, one due to a fall), and four exited during the 20-mg twice-daily dose (two due to hypertension, one had a family emergency, and one felt lightheaded). At baseline the groups were well matched on all outcomes. Mean scores on placebo improved on all measures by visit 4 compared with on methylphenidate: T25FW: placebo 8.4 seconds at baseline, 6.7 at visit 4; active 8.8 seconds to 8.7 seconds. TUG: placebo 12.9 seconds to 10.3 seconds; active 13.2 seconds to 12.3 seconds. SDMT: placebo 52.4 to 61.3; active 47.0 to 46.8. MFIS: placebo 42.8 to 30.5; active 41.4 to 33.7. **Conclusions:** Although limited by small sample size, this study suggests that methylphenidate up to 30 mg twice a day is well tolerated but likely does not improve mobility, cognition, or fatigue in people with MS, and is likely less effective than placebo.

**Berg Balance Scale and Timed Up and Go Discriminate Between Fallers and Nonfallers in People with Multiple Sclerosis**

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**Background and Purpose:** The Berg Balance Scale (BBS) and Timed Up and Go (TUG) target dynamic balance. The BBS contains 14 items with a maximum score of 56. In the TUG, the time is measured from when the person stands up from a chair, walks 3 m, rounds a cone, walks back, and sits down again. Different cutoffs have been used for the BBS. With a cutoff at >44, high specificity (90%) but low sensitivity (40%) were found. Using ≤55 as the cutoff yielded high sensitivity (94%) but low specificity (32%). The TUG has not shown discriminant ability. The aim was to examine discriminant validity for the BBS and TUG for fallers versus nonfallers and predictive properties using previously suggested cutoffs. **Methods:** Data from three samples of people with multiple sclerosis (MS) (n = 220) with imbalance were used. Testing was conducted by experienced research physiotherapists. Falls were prospectively self-reported daily. Participants were classified as fallers (≥1 fall during 3 months) or nonfallers. The Mann-Whitney U test and receiver operating characteristic curve were used. **Results:** Discriminant validity was established. The BBS median for fallers was 45 points (n = 108; Q137–Q351) and for nonfallers was 50 points (n = 99; Q140–Q354) (P = .003). The TUG median was 17.5 seconds (n = 108; Q112.8–Q327.4) for fallers and 13.2 seconds (n = 99; Q110.1–Q320.3) for nonfallers (P = .003). BBS: Using >44 points as cutoff correctly identified 51% of the fallers and 37% of the nonfallers. Using ≤55 points correctly identified 96% of the fallers and 15% of the nonfallers. TUG: A cutoff (19.34 seconds) was chosen by maximizing the sum of sensitivity and specificity, resulting in sensitivity at 70% and specificity at 43%. **Discussion:** The BBS showed discriminant validity for fallers versus nonfallers. However, a cutoff yielding both high sensitivity and specificity was not found. A BBS cutoff at ≤55 points is recommended in order to identify as many fallers as possible.
References


(10) Patient-Perceived Bladder Dysfunction Is Associated with Step Count in Multiple Sclerosis

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**Background and Purpose:** Multiple sclerosis (MS), an inflammatory and neurodegenerative disease of the central nervous system, is a leading cause of nontraumatic ambulatory disability in working-age adults. Urinary incontinence (UI) affects over half of individuals with MS. We examined associations between UI and physical activity in people with MS. **Methods:** Eighty-seven ambulatory participants with relapsing or progressive MS (54 women, 62%; 55 relapsing diagnosis, 63%) were recruited into a prospective cohort study and given a Fitbit Flex for remote
step count monitoring. Participants were excluded if they had a clinical relapse within 30 days or major physical comorbidities contributing to gait impairment. In-clinic assessments included the bladder control scale (BLCS), Timed 25-Foot Walk (T25FW), and Kurtzke Expanded Disability Status Scale (EDSS). **Results:** UI symptoms (BLCS >1) were reported by 55 participants (63%); of these, 28 (51%) needed an assistive device (EDSS >5.5). Lower average daily step count over 4 weeks was correlated with greater urinary symptoms (BLCS) in a generalized linear model ($P < .001$) when adjusting for age, sex, and T25FW. In a stepwise regression model, BLCS accounted for 10% of the variance in EDSS. Average daily step count was not significantly lower in people with UI with the greatest disability (EDSS ≥6). **Discussion:** MS patients with greater bladder symptoms had lower average daily step count, suggesting an association between bladder and ambulatory dysfunction; however, EDSS remains the major contributor to average daily step count variability. Neither EDSS nor BLCS differentiates between urinary storage and emptying dysfunction, which may affect activity levels due to social discomfiture and energy needed to plan restroom breaks. Larger prospective studies are needed to determine whether bladder dysfunction contributes to sedentarism independent of other components of disability covered by the EDSS.

(11) Adaptive Locomotor Performance in the Early Stages of Multiple Sclerosis: A Pilot Study

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Background: Maintaining and improving mobility is a major goal in the rehabilitation of people with multiple sclerosis (MS). Challenges commonly encountered in the natural environment (e.g., obstacle crossing) require adaptations to walking parameters to prevent loss of balance and achieve safe walking. Purpose: 1) To compare performance of people with MS with low disability to age-matched healthy controls (HC) on adaptive locomotor tasks (ALTs) that impose specific challenges, and 2) to examine the ability to integrate sensory systems in order to compensate for suboptimal sensory information while performing ALTs. Methods: People with MS (Patient-Determined Disease Steps ≤ 3) and HC (age- and sex-matched) walked along a 6-m path during four ALTs (obstacle crossing, narrow walking, walking-while-talking, and fast walking) and a control condition (self-selected normal walking). Visual information was intact or suboptimal using custom-made blurring goggles. A motion capture system tracked body segment position and step characteristics. Following the walking tasks, participants completed a sensorimotor assessment that included leg extensor strength, ankle proprioception, visual contrast sensitivity, and standing balance. Results: Preliminary findings demonstrate that people with MS had similar walking speeds compared to HC in general. However, people with MS had larger mediolateral center of mass displacement during the ALTs than HC. During obstacle crossing, people with MS had less trunk velocity compared to HC, despite similar trunk displacement. Suboptimal vision did not affect the performance on ALTs. Discussion: Despite comparable walking speeds, people in early stages of MS have reduced overall postural control during walking compared to HC. This instability occurs during all ALTs. During obstacle crossing, people with MS may have to slow down their trunk movement to safely accomplish the clearance of the obstacle. Both groups were able to integrate appropriate sensory systems to
compensate for suboptimal vision. Our preliminary findings demonstrate that subclinical changes in postural control occur at the early stage of the disease, before mobility-related disability arises.

(12) Unplanned Gait Termination in Multiple Sclerosis Under Normal and Cognitively Distracting Conditions

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**Background and Purpose:** Despite the pervasive nature of gait impairment in multiple sclerosis (MS), there is limited information concerning the control of gait termination in individuals with MS. Recently, impairments in people with MS in preplanned gait termination were reported. The purpose of this investigation was to examine unplanned gait termination in individuals with MS and healthy controls with and without cognitive distractors. **Methods:** Thirty-two individuals with MS and 14 age-matched controls completed a series of unplanned gait termination tasks over a pressure-sensitive walkway under nondistracting and distracting conditions. Individuals with MS had an average age of $56.8 \pm 10.9$ years, and controls had an average age of $57.6 \pm 13.1$ years. Individuals with MS were further broken down into disease severity groups based on self-reported Expanded Disability Status Scale (SR-EDSS). Five individuals were mild (SR-EDSS < 3.5), 14 individuals were moderate (SR-EDSS 3.5–5.5), and 13 were severe (SR-EDSS > 5.5).

**Results:** As expected, the MS group walked more slowly than controls ($97.4 \pm 35.6$ vs. $131.3 \pm 27.4$ cm/s; $P < .01$) and there was a significant reduction in velocity in both groups under the cognitively distracting condition (MS: $85.3 \pm 31.5$ cm/s; control: $108.8 \pm 29.1$ cm/s; $P = .031$).
All participants took longer to stop during the distracting condition (1.77 ± 0.66 second) than during the nondistracting condition (1.41 ± 0.40 second) \((F = 9.0; P < .01)\). After controlling for gait velocity, post hoc analysis revealed that the individuals with MS who required a walking aid took significantly longer to stop compared to the control \((P = .023)\) and mild MS \((P = .047)\) groups. **Discussion:** Cognitively distracting conditions significantly impacted stopping time for a sample of individuals with MS and healthy controls. Longer stop times were observed for individuals with greatest gait impairment compared to healthy controls and individuals with mild MS. Further research investigating unplanned gait termination in individuals with severe MS is warranted.

(13) **Dynamic Balance—An Early Marker of Functional Disability**

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**Background:** Balance and mobility limitations are a hallmark of people with multiple sclerosis (MS), independent of disability level. Disability in MS is evaluated by the Expanded Disability Status Scale (EDSS), in which a significant part of the scoring range is based on ambulation status; however, this scale is known to be insensitive to detect subtle symptoms, such as balance impairment. The aim of this study was to determine when the first disabling symptom appears, according to balance evaluation and EDSS classification. **Methods:** We evaluated 91 consecutive MS outpatients (EDSS 0–3.5) and 27 age- and sex-matched controls. Gait and balance problems were evaluated by the Timed 25-Foot Walk (T25FW) and computerized dynamic posturography (CDP), respectively. The Multiple Sclerosis Walking Scale (MSWS)
was also applied. We divided patients into four subgroups according to EDSS score (0; 1–1.5; 2–2.5; 3–3.5). For statistical analyses, the Student t test, Mann-Whitney U test, and Spearman correlations were applied as appropriate. **Results:** We found significant differences between MS and controls when compared with T25FW and CDP. Compared to control groups, the evaluation for each EDSS subgroup showed that balance limitations started earlier, at EDSS 1.0 ($P < .05$), than gait limitations, at EDSS 2.0 ($P < .05$). Balance changes also got worse for each EDSS level ($P < .05$). The MSWS was more strongly correlated with balance assessment (rho: −0.51) than the T25FW (rho: 0.37). **Conclusion:** Even before walking speed is reduced, MS patients have balance impairments. Computerized balance measures may detect impairments that are not evident in the clinical examination. We also found that imbalance becomes more pronounced as MS progresses. The stronger correlation between the MSWS and balance assessment than the T25FW suggests an important impact of imbalance on functional disability. The balance evaluation allows detection of more subtle mobility problems, enabling the early development of rehabilitation programs. Similar to previous studies, we emphasize that, in contrast to stopwatch-timed measures, quantitative balance measures can detect early mobility changes in MS patients.

(14) **Deficits in Automatic Postural Responses Are Related to Cerebellar Involvement in People with Multiple Sclerosis**

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**Introduction:** Balance problems are prevalent in people with multiple sclerosis (MS); however, little is known about the mechanisms behind such deficits. We aimed to investigate ability of
people with MS to predictively scale their postural responses to gradually increasing magnitudes of discrete surface perturbations. Given that the cerebellum is responsible for predictive scaling or feed-forward control of postural responses, we hypothesized that deficits in scaling postural responses to increased perturbation amplitudes will be related to the involvement of the cerebellum in people with MS. **Methods:** Subjects (24 MS, 14 control) stood on a force platform that translated backward in four blocks of predictable increasing amplitudes (3.6, 6.0, 8.4, and 12 cm). Each block consisted of five trials (total of 20 trials). To determine the role of the feed-forward mechanism, automatic postural responses to displacements were estimated as rate change of center of pressure under each foot before the feedback response could change the postural response. Predictive scaling was estimated by computing the slope of regression between early postural responses and gradually increased perturbation amplitudes. The International Cooperative Ataxia Rating Scale (ICARS) was used as a clinical scale to assess the extent of ataxia. Diffusion-weighted images (DTIs) of the brain were also acquired. Radial diffusivity (RD), an indirect neural marker of myelination, of cerebellar peduncles was calculated for each participant. Lower RD is interpreted as being indicative of better white matter tract microstructure. **Results:** To date, we have analyzed the data of 9 MS and 9 control subjects. Control subjects exhibited better scaling of postural responses to the increasing magnitudes of the postural perturbations than people with MS (regression coefficients: control: 0.75 ± 0.38; MS: 0.37 ± 0.65). For people with MS, slope of the rate change of center of pressure with respect to the perturbation magnitude was negatively correlated with the ICARS scores ($r = -0.65$). ICARS scores were also correlated to the RD of the cerebellar peduncles ($r = 0.5$). However, the RD of cerebellar peduncles was not related to the rate change of center of pressure (control: 0.12; MS: 0.3). **Conclusion:** Preliminary data suggest that deficits in predictive scaling of postural
responses in people with MS seem to be related to cerebellar involvement, as evidenced by the relationship of ICARS and postural response scaling.

(15) Evaluating the Functional Capacity of the Vestibulo-ocular Reflex in People with Multiple Sclerosis: Validity and Reliability of Computerized Testing

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Background and Purpose: The functional capacity of the vestibulo-ocular reflex (VOR) is poorly understood in people with multiple sclerosis (MS), yet may be an important contributor to gait and balance deficits. The computerized Gaze Stabilization Test (GST) and Dynamic Visual Acuity Test (DVAT) are novel tests of VOR function that have favorable psychometric properties in other populations. The purpose of this study was to determine the validity and reliability of the GST and DVAT in people with MS. Methods: This study determined discriminant validity of the GST and DVAT between 30 participants with MS and 15 healthy controls, and between participants with MS who had higher versus lower disability. This study also determined same-day and between-session test-retest reliability, and concurrent validity with patient-reported outcomes (PROs) of balance, dizziness, and fatigue. Results: GST (P < .001) and DVAT (P = .001) scores discriminated between participants with MS and controls. GST (P = .035) but not DVAT (P = .313) scores discriminated between participants with MS who had higher versus lower disability. Test-retest reliability interclass correlation coefficients (ICC [2,1]) were fair to good for the GST (0.48–0.74) and DVAT (0.47–0.60). PROs correlated
significantly with GST but not DVAT scores. **Discussion:** This study provides evidence that the functional capacity of the VOR is impaired in people with MS as measured by the GST and DVAT, and supports the use of both tests as outcomes. The GST, however, had slightly higher across-2-weeks reliability, discriminated between higher and lower disability groups, and correlated with PROs. Future trials are needed to determine the responsiveness of the GST and DVAT to vestibular rehabilitation and to provide further support for the utility of the tests as outcomes. Meanwhile, clinicians should consider routine examination of the functional capacity of VOR in their patients with MS.

(16) **Association Between Perceived Fatigue and Fatigability in Multiple Sclerosis: A Systematic Review and Meta-analysis**

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**Background:** Perceived fatigue (ie, subjective interpretation of a limited capacity for mental or physical tasks) and fatigability (ie, decline in performance of a task over time) have sometimes been linked to gait and balance impairments in people with multiple sclerosis (MS). Interventions improving fatigue and/or fatigability may improve function, and a relationship between perceived fatigue and fatigability in MS has been hypothesized and tested; however, study results are inconsistent to date. **Purpose:** To estimate the population association between measures of perceived fatigue and fatigability among people with MS using meta-analytic techniques, and to determine if the correlation differs as a function of selected study features.
Methods: Google Scholar and MEDLINE will be searched for studies published before August 1, 2016, that include measures of both perceived fatigue and fatigability among people with MS. Data will be extracted to calculate effect size $r$ and the corresponding 95% confidence interval. The moderators identified include study features (geographic region, fatigability measure type, perceived fatigue measure type) and participant features (age, gender, MS type). Results: To date four studies have been identified that match the inclusion criteria, and the full literature search will be completed in July 2016. We expect to present a flow chart of the literature search, mean $r$, forest and funnel plots, and moderator analysis results. Discussion: This systematic review and meta-analysis will help determine the literature state in fatigue and fatigability in MS and needs for future research. Given a large number of studies, a mean effect $r$ that is not statistically significant would support measuring perceived fatigue and fatigability separately, while a larger and significant $r$ suggests that perceived fatigue and fatigability are related in MS and could be linked by similar underlying mechanisms. The moderator analysis will determine what factors (if any) influence the correlation size.

(17) Effect of Intermittent Versus Continuous Walking on Kinetic and Kinematic Variables in People with Multiple Sclerosis: Partial Results of an Ongoing Study

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Background and Purpose: Previous research has shown that people with multiple sclerosis (MS) can walk longer distances with less fatigue when the walking is performed intermittently rather than continuously. The specific reasons for this improved performance have not been
examined. The purpose of this study was to determine if kinetic and kinematic factors could explain the difference between these two walking conditions. We hypothesize that intermittent walking will result in different kinematic and kinetic measurements than continuous walking.

**Methods:** Using a randomized crossover design, ambulatory subjects were recruited from MS practices. In the continuous condition, subjects walked for 6 minutes continuously. In the intermittent condition subjects walked for three 2-minute bouts with a seated 2-minute rest between each 2-minute walk. Kinematic and kinetic data were collected using the Protokinetics Zeno walkway. Distance walked was measured at 1-minute intervals for each condition.

**Results:** Six subjects (mean Expanded Disability Status Scale [EDSS] score 4.2) have so far completed the study. In the intermittent condition, the L/R ratio of percent stance time at minute 1 compared to minute 6 was more equal than in the continuous condition ($P = .054$). Subjects walked significantly farther in the intermittent condition than in the continuous condition (1215 feet vs. 1148 feet, $P = .05$). **Discussion and Conclusions:** Analysis of preliminary results indicates that stance time became less symmetrical in the continuous condition than in the intermittent condition as the distance walked increased. This provides a possible kinematic explanation for the difference in distances walked in these two conditions. It is hoped that with increasing the sample size, a more complete explanation for the differences seen between the two walking conditions will emerge.