Cover Page

Study Title: Protective Stepping & MS (PRO-STEP)

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Protocol

This study used a within-subject, multiple-baseline design. First, baseline demographics and cognition (Symbol Digit Modality Test; SDMT) were collected. Then participants' reactive stepping was assessed across 4 timepoints: baseline 1 and baseline 2 (B1, B2), both 2 weeks apart and before the intervention, then immediately after the intervention (see details below; Post 1), and again 2 months after the intervention (post 2).

Reactive stepping was elicited via balance "perturbations", i.e., quick movements of the support surface. Participants stood on a Bertec split-belt instrumented treadmill (Bertec Corporation, Columbus, Ohio). The treadmill began in a static position, and then moved quickly underfoot with the following ramped protocol: 300ms constant acceleration, 500ms no acceleration (constant speed), and a 300ms deceleration to stop. At the start of B1, 2-3 perturbations were first delivered at varying accelerations to determine a speed that resulted in a quick reactive step but not a fall. The acceleration identified through this process was then held constant throughout all perturbations and all sessions.

Each Assessment (B1, B2, P1, P2), consisted of 8 warm up perturbations (2 each in the forward, backward, leftward, and rightward directions), followed by 3 forward and 3 backward perturbations (used to assess performance at each timepoint). Direction and timing of these 6 perturbations was not known to the participant. Participants were instructed to: "Stand still, do not anticipate the perturbation, and do your best to recover balance after the perturbation".

Between B2 and P1, participants completed 6 sessions of perturbation training across approximately 2 weeks. During these sessions, participants underwent approximately 32 perturbations in the forward, backward, leftward, and rightward directions per session, resulting in a total of approximately 192 perturbations. As with assessments, timing and direction of perturbations were not known by the participant. The acceleration of perturbations was adjusted through training to apply progressive overload. Specifically, across each four-perturbation block, the number of times the harness was used (>10% weight applied to the harness) was captured. If a fall was observed in one of four trials, acceleration was held constant. If zero falls occurred, we increased acceleration by 0.2m/s2. If a fall occurred in ≥2 trials, we reduced acceleration by 0.2m/s2.

Outcomes

Responses to perturbations were assessed via a 14-camera motion capture system at 100hz. Markers were placed bilaterally on the feet, shank, and thigh, as well as on the sacrum and T-12 vertebrae.

Stepping responses were then extracted. Specifically, our primary outcomes were the step kinematics that occurred during a backward loss of balance (ie., falling backward). Primary outcomes included: 1) anterior-posterior (AP) margin of stability (MOS, assessed as the distance between the approximate center of mass and base of support at the moment of first foot contact after the perturbation), 2) reactive step latency (time from perturbation onset to first step onset), and 3) reactive step length (the AP distance traveled by the foot during the first reactive step).

Statistics

R (version 4.4.0) was used for statistical analysis. We performed linear mixed effects (LME) models on the outcome measures noted above (MOS, step latency, step length). We then executed pre-planned contrasts to assess the effect of training on performance. Disease severity (measured as the European Disease Age and disease severity (measured via the European database for multiple sclerosis (EDMUS)) and age were included as covariates in the models. As noted above, the primary variable of interest was MOS during backward stepping, with step length and latency as secondary outcomes.