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Effects of a home-based step training programme on balance, stepping, cognition and functional performance in people with multiple sclerosis – a randomized controlled trial

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Phu Hoang, Daniel Schoene, Simon Gandevia, Stuart Smith and Stephen R Lord

Abstract

Background: Stepping impairments increase fall risk in people with MS. No studies have evaluated step training for reducing fall risk in this population.

Objectives: To determine if step training can improve physical and neuropsychological measures associated with falls in MS.

Methods: 50 PwMS with moderate disability participated in a randomized controlled trial in which intervention group participants ($n=28$) performed step training for 12 weeks while controls ($n=22$) continued usual physical activity. The primary outcomes were choice stepping reaction time (CSRT) and Stroop stepping test (SST) time. Secondary outcomes included balance test (postural sway, CSRT components), gait speed and cognitive tests, nine-hole peg test (9-HPT) and MS functional composite (MSFC) score.

Results: 44 participants completed the study and no adverse events were reported. Compared with the control group, the intervention group performed significantly better at retest in CSRT and SST times, and tests of sway with eyes open, 9-HPT, single and dual task gait speed and MSFC score. There was a non-significant trend for fewer falls in the intervention group.

Conclusions: The findings indicate that the step training programme is feasible, safe and effective in improving stepping, standing balance, coordination and functional performance in people with MS.

Keywords: Rehabilitation, multiple sclerosis

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Introduction

Multiple sclerosis (MS) is a chronic progressive disease of the central nervous system (CNS) that leads to widespread demyelination with symptom onset commonly reported between the ages of 20–50 years. The demyelination process is often located in areas of the CNS that are involved in the control of balance[1] and in consequence, people with MS frequently fall. An individual data meta-analysis from studies of falls in people with MS from Australia, Sweden, the United Kingdom and the United States ($n=537$) found that 56% fell at least once and 37% fell on two or more occasions in a 3-month prospective period.[2] Further, of those who fall, more than 50% suffer fall-related injuries that require medical care.[3] As a consequence of this increased risk, many people with MS report a fear of falling that can restrict daily activities[4] and adversely impact quality of life.

Impaired balance control is the most important risk factor for falling in people with MS[5–7] and is characterized by increased sway in quiet stance, delayed responses to postural perturbations, and a reduced ability to move toward stability limits.[8] Several complementary balance measures including increased postural sway, forward stability limitations, slow choice stepping reaction time (CSRT) and reduced walking speed, along with impaired executive functioning and

Correspondence to:
Phu Hoang
Neuroscience Research Australia, Margarete Ainsworth Building, Barker Street Randwick Sydney NSW 2031, Australia
p.hoang@neura.edu.au

Daniel Schoene
Simon Gandevia
Stephen R Lord
Neuroscience Research Australia, Sydney, Australia

Stuart Smith
Centre for Research and Education in Active Living, University of Tasmania, Hobart, Australia

reduced fine motor control, have been identified as important physical and neuropsychological fall risk factors in people with MS.[6,9]

In related research into fall prevention in older people, a systematic review of exercise interventions found that in order to be effective, balance exercises that reduce the base of support, minimize upper limb support and include weight shifting are required,[10] and it is likely that these components are also necessary for effective fall prevention in people with MS. Step training is an exercise form that meets the criteria for high intensity balance training and provides additional benefits in terms of improving stepping initiation and movement times[11] and the ability to withstand external perturbations.[12] Interactive videogames (exergames) have the advantage of providing step training in a home setting. Moreover, these games may increase motivation and adherence by offering greater levels of enjoyment and the provision of immediate performance feedback.

We have developed an exergame step training system that combines player movements to visually displayed stimuli and that can be undertaken unsupervised at home.[11] Initial research has indicated that this system has excellent convergent validity and test–retest reliability and is effective in improving stepping ability and balance in older people.[11,13] The aims of this study were to determine whether a 12-week step training programme (compared to no step training) can improve balance, stepping, cognition and functional performance in people with MS.

Materials and methods

Study design

The study comprised a two-arm, parallel, single-blinded randomized controlled trial and was registered with the Australian and New Zealand Clinical Trials Registry prior to the first participant being randomized (ACTRN12612001139864).

Participants and ethical approval

Fifty people with MS were recruited from either an MS clinic and or an outpatient rehabilitation gym for people with MS between March 2013 and February 2014. Inclusion criteria were a clinical diagnosis of MS as defined by the modified McDonald criteria,[14] an expanded disability status scale (EDSS) score of 2–6, age 18–65 years, no apparent cognitive impairment (i.e. ability to provide written informed consent and understand and follow instructions), and no exacerbation of MS in the past three months. Exclusion criteria were presence of conditions that preclude stepping exercise, such as severe spasticity that prevented a person taking a full step (from one panel on the mat to another), excessive fatigue or exercise intolerance (judged by the physiotherapist who performed the baseline testing).

The trial was approved by the Human Research Ethics Committee of the University of New South Wales and conducted according to the principles of the Declaration of Helsinki (2008). Written informed consent was obtained from participants before entering the study.

Randomization

After completion of the baseline assessment, participants were formally entered into the study and randomized to intervention or control groups. Randomization was performed centrally by an investigator not involved in recruitment or assessments (allocation concealment) using a computer-generated random number schedule with block sizes of six.

Step training intervention

Participants allocated in the control group received no intervention and continued their usual physical activity. For participants allocated in the intervention group, an exercise therapist visited participants at home to conduct a risk assessment, set up the step training system and teach participants how to use the system (Figure 1). The exercises involved two interactive exergames. The first used Stepmania open source software (www.stepmania.com) to develop a rhythm video game that required participants to step as accurately as possible, both in terms of direction and timing, while synchronizing their step responses to stimuli presented on the television screen. To enhance compliance, participants could choose music from a list of songs. CSRT training comprised the second game that required quick, accurate steps with both legs. Detailed descriptions of the exergames are presented elsewhere.[11] Participants were instructed to undertake at least two 30-minute training sessions per week for 12 weeks and were provided with written instructions and contact numbers in case they had any queries or problems. They also received a follow-up phone call in the first two weeks to ensure safe use and progression of training and address any issues related to use of the training system.

Outcome measures

Assessments were performed in a gym setting and all participants were assessed under the same conditions

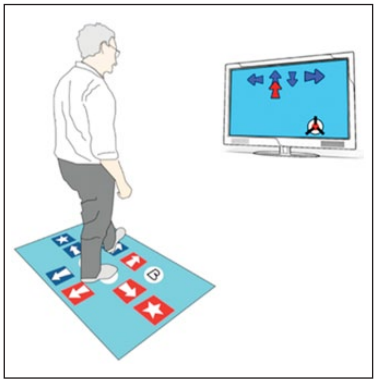

Figure 1. A step training system installed at a participant's home: the stepping mat is wirelessly connected to the television via a console. The exergames combine player movement to visually displayed stimuli (Adapted from Schoene et al., PLoS One, March 2013. DOI: 10.1371/journal.pone.0057734).

at baseline and within seven days of trial completion. Re-assessments were conducted by a physiotherapist blinded to group allocation.

The primary outcome measures were choice stepping reaction time (CSRT) and the Stroop stepping test time. These measures were chosen because they comprised complementary measures of simple and more complex stepping ability comprising selective attention and response inhibition.

Secondary outcome measures included CSRT decision time (time between the appearance of the sign of computer screen and the lift of the foot off the stance panel), and CSRT movement time (time between the lift of the foot off the stance panel and placing the foot on the appropriate panel on the stepping mat), balance, mobility, upper limb function and cognitive performance.

Choice stepping reaction time (CSRT): For CSRT, participants were required to use six panels of the step pad that were depicted on the computer display screen: two central stance panels, two stepping front panels (left and right) and two stepping lateral panels (left and right). In a random sequence, one of the displayed arrows was highlighted on the display screen and participants were instructed to step as quickly as possible onto the corresponding panel of the pad and afterwards return to the central panels (Figure 1).[13] Time was recorded in milliseconds for decision time (DT) measured from stimulus occurrence to movement initiation (lift off) and movement time (MT) measured from movement initiation to step down. Total response time was measured as the sum of DT and MT.

Stroop stepping test (SST): For SST, one arrow pointing in one of four directions (up, down, left, right) was presented in the centre of the computer display screen. Inside the arrow was a written word in a high contrast colour indicating a different direction. Participants were instructed to step on the step pad as fast as possible to the word and by doing so, selectively attended to word stimulus and inhibiting the response indicated by the arrow's shape.[15] The time in seconds to complete a random sequence of 20 trials was recorded.

Secondary outcome measures

Postural sway with eyes open and closed was measured using a swaymeter that measured displacements of the body at the level of the waist.[16] Participants performed the test standing on the floor with the eyes open and closed. Dynamic balance and mobility were assessed using the timed up-and-go (TUG), ten-metre walk and six-minute walk tests. The TUG measures mobility by taking the time in seconds to get up from a chair, walk three metres at comfortable pace, turn, return and sit down again.[17] Gait speed over ten metres was assessed using a 14-metre area to allow for acceleration and deceleration (two metres at both ends). The distance covered by walking at normal speed for six minutes was measured with participants walking on a 15-metre walkway.

Cognitive function was assessed using the trail making test (TMT), symbol digit modalities test (SDMT) and divided attention. TMT evaluates scanning, visuomotor tracking and cognitive flexibility and consists of two parts, part A (TMT-A) and part B (TMT-B). The difference in execution time between TMT-B and TMT-A was computed to provide a good estimate of executive function that is less dependent on visuomotor speed.[18] The SDMT is a measure of attention, information processing speed and working memory[19] that has been used in previous studies involving people with MS.[20] Participants were asked to view a key presenting nine numbers paired with unique symbols on a sheet of paper. Below the key was an array of symbols paired with empty spaces, participants' task being to fill the matching number for each symbol with a pen as rapidly as possible. The number of correct answers was recorded. Divided attention was assessed using the TUG under dual task conditions (counting backward by 3s starting at 100).[21]

Three of the above secondary outcome measures: ten-metre walk test, SDMT and the 9-HPT were combined to form multiple sclerosis functional composite (MSFC) scores – a clinical outcome measure that has

been widely used as a measure of impairment and disability in MS and to assess treatment effects.[22,23] The SDMT was selected as the cognitive measure (instead of PASAT) as it is a simpler test to administer,[24] an important test characteristic when part of an extensive test battery. MSFC scores were calculated as the average of z-scores for the three component measures.[25]

A fall was defined as unintentionally coming to the ground, floor or lower level.[26] The number of falls during the six-month period following randomization was recorded using monthly falls calendars and follow-up telephone calls if required.

Statistical and power analyses

All variables were tested for normality and normalised via log transformation when appropriate. Between group differences at follow-up were assessed by analysis of covariance (ANCOVA) adjusting for baseline scores of the outcome measures. Visual inspection of change scores and the calculation of contrasts with corresponding 95% confidence interval between intervention group and control group at different levels of the covariate were used in case of significant covariate-by-group interactions. Effects sizes were estimated with the Cohen's f statistic for one-way ANCOVA regression where values of 0.10, 0.25 and 0.40 indicate small, medium and large effect sizes respectively. Between-group differences for falls during follow-up were analysed using binomial negative regression, a statistical procedure that assumes the recurrent events being counted are occurring independently of each other and randomly in time but not restricted to one event per person. All between-groups comparisons were performed according to intention to treat principles. We determined to set p values at <0.05 and not adjust to Bonferroni despite the multiple comparisons made in this exploratory study because such adjustments may increase type II errors.[27] Analyses were performed with SPSS (version 22 for Windows) and Stata (version 13.1 for Windows).

Based on our recent RCT of step mat exercise training conducted in older people,[11] we conducted a power analysis for the CSRT total time. We used a SD of 120ms, a delta of 100ms, a power of 0.8 and an alpha of 0.05. This indicated that 23 participants were required per group. With a projected 10% loss to follow-up, we increased this figure to 25 per group.

Results

Figure 2 shows the flow of participants through the study between March 2013 and June 2014. Fifty

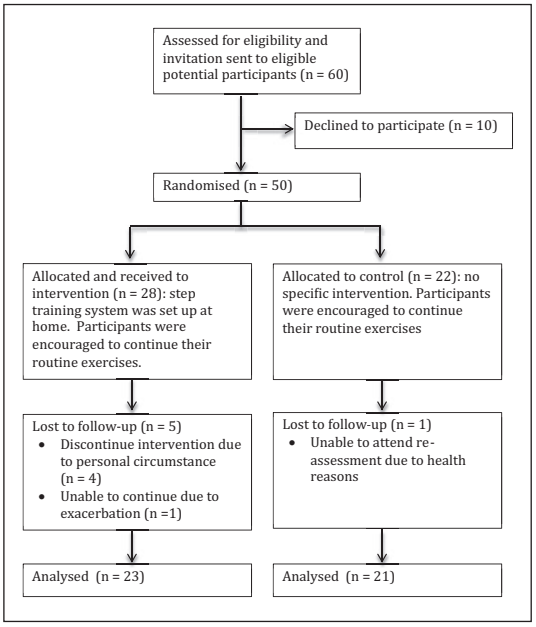

Figure 2. Flow chart of the study.

participants, 38 females and 12 males, were enrolled in the study (28 in the intervention group and 22 in control group). Characteristics of participants are described in Table 1. Five participants (18%) in the intervention group withdrew due to either family matters or a relapse of MS (1). One participant in control group was unable to attend re-assessment due to a health problem (not related to MS). Forty-four participants (88%; 23 in intervention group, 21 in control group) completed the study. Participants in both groups were similar at baseline for the primary and secondary outcome measures (Table 2).

Twenty-three intervention participants used the step training system throughout the 12-week intervention period. The mean duration of practice was 71 min/week (±60 SD). Two participants in intervention group with EDSS 6 required the use of a frame and two others with EDSS 5 needed to hold a walking stick during the exercise for safety, and all but one participant increased the difficulty level of the Stepmania game. Figure 3 shows the duration and frequency of exercise for a typical participant. No adverse events related to step training were reported. However, one participant in the intervention group had to cease training due to a relapse of MS that required treatment in hospital.

Effects of the intervention

ANCOVAs revealed significant between-group differences at re-assessment for the two primary outcome measures: CSRT total time ($p = 0.031$) and

Table 1. Participant characteristics ($n=50$).

Participants ($n=0$)	Characteristics	
	Intervention group ($N=28$)	Control group ($N=22$)
Gender	F/M=21/7	F/M=17/5
Age	53.4 (SD=10.7)	51.4 (SD=12.8)
Duration of MS	11.6 (SD= 9.1)	13.4 (SD=6.9)
EDSS	4.1 (SD=1.4)	4.2 (SD=1.2)
Type of MS		
Relapse-remitting	15	11
Secondary progressive	5	7
Primary progressive	8	2
Unknown	0	2
Disease steps	*N* (percentage)	*N* (percentage)
Disease step 1	4 (14.3)	6 (27.3)
Disease step 2	6 (21.4)	3 (13.6)
Disease step 3	8 (28.6)	8 (36.4)
Disease step 4	8 (28.6)	2 (9.1)
Disease step 5	2 (7.1)	3 (13.6)
Disease modifying drugs	*N* (percentage)	*N* (percentage)
None	4 (14.3)	4 (18.2)
Interferon Beta-1a intramuscular	2 (7.1)	2 (9.1)
Interferon Beta-1a sub-cutaneous	2 (7.1)	1 (4.5)
Interferon Beta-1b	2 (7.1)	2 (9.1)
Glatarimer acetate	3 (10.7)	2 (9.1)
Natalizumab	1 (3.6)	5 (22.7)
Fingolimod	11 (39.3)	3 (13.6)
Oral corticosteroid	1 (3.6)	2 (91)
Others	2 (7.1)	1 (4.5)

SST performance ($p=0.011$) in favour of the intervention group. Compared with the control group, participants in intervention group also demonstrated faster CSRT decision ($p=0.041$) and movement ($p=0.039$) time components, less postural sway with eyes open ($p=0.023$), quicker 10-meter gait speed ($p=0.023$) and reduced 9-HPT times ($p=0.001$). There was also a significant improvement in intervention group compared with the control group in the level of disability measured by MSFC ($p=0.001$).

In addition, there were significant covariate-by-group interactions for TUG dual task (TUG-DT), 9-HPT and MSFC, suggesting that differences at re-assessment depended on baseline scores (Figure 4). For these outcome measures (TUG-DT, 9-HPT and MSFC), those participants with poorer baseline performance improved more than the control group as shown by the non-overlapping confidence intervals. There were no between-group differences for the remaining outcome measures (Table 3).

During the six-month follow up, participants in the intervention group reported fewer falls (78 falls; $n=23$) than those in the control group (95 falls; $n=21$), but this difference was not statistically significant – IRR=0.75 (95% confidence interval=0.38–1.5).

Discussion

We found that a 12-week home-based step training programme produced improvements in primary outcome measures (CSRT and SST), secondary outcome measures associated with falls in people with MS (TUG-DT, ten-metre walk, sway eyes open and 9-HPT) and overall functional performance as manifest by improved MSFC scores. The step training system proved feasible, and all but one participant played both games and changed the game difficulty levels. Those participants who needed support during training completed the intervention period, and no adverse events were reported, suggesting that with appropriate instruction step training is a safe mode of exercise for people with MS with moderate disability.

Table 2. Baseline measures of participants in each group.

Variable	Intervention group ($n=28$) (mean±SD)	Control group ($n=22$) (mean±SD)
Age	53.4±10.6	51.4±12.8
N years with MS	11.6±9.1	13.4±6.9
EDSS	4.1±1.4	4.2±1.2
N Falls past 12 months	4.7±5.4	5.1±5.3
Main outcomes		
CSRT response time (s)	2.4±0.275	2.39±0.258
SST (s)	72.0±25.8	71.1±25.2
Secondary outcomes		
Balance tests		
CSRT decision time (s)	0.99±0.12	0.98±0.12
CSRT movement time (s)	1.40±1.70	1.40±1.60
Sway eyes open (mm)	97.3±11.4	131.2±12.8
Sway eyes closed (mm)	243±162	284±142
Mobility tests		
10-m walk (s)	12.5±5.0	11.4±4.3
6-minute walk (m)	277±18	295±19
TUG single task (s)	13.1±5.5	12.1±3.9
Cognitive tests		
TUG dual task (s)	15.8±7.3	17.1±8.0
SDMT	38.1±10	42.2±9.7
TMT B-A (s)	62.6±39.7	57.3±34.2
Upper limb function and multiple sclerosis functional composite score (MFSC)		
9-hole Peg test (s)	30.4±9.0	27.5±9.2
MSFC	0.42±2	−0.5±2

EDSS: expanded disability status scale; CSRT: choice stepping reaction time; SST: Stroop stepping test; TUG: time – up-and-go test; SDMT: simple digit modality test; TMT B-A: difference between Trail making test B and A; MSFC: multiple sclerosis functional composite score, calculated by averaged Z scores of 10-m walk test, SDMT and 9-hole Peg test; thus MSFC values are between −1 and 1, with negative values indicating less disability.

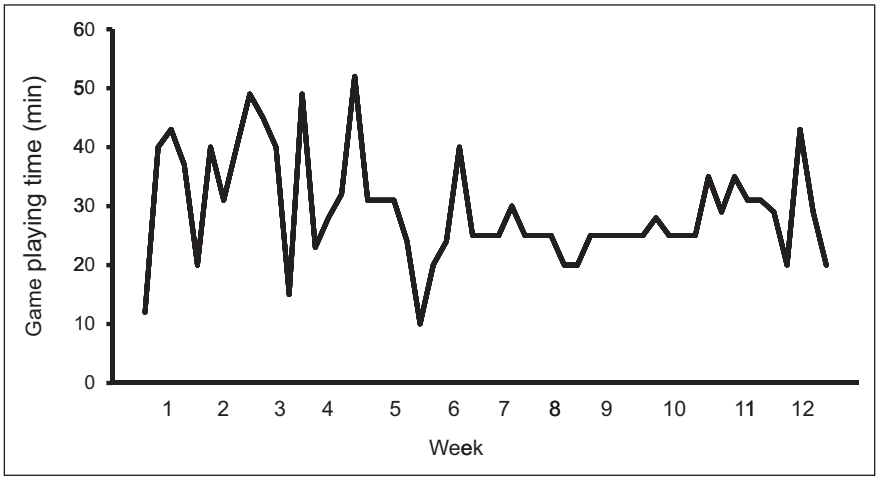

Figure 3. Number of training sessions and duration of each session are recorded for a typical participant during the intervention period.

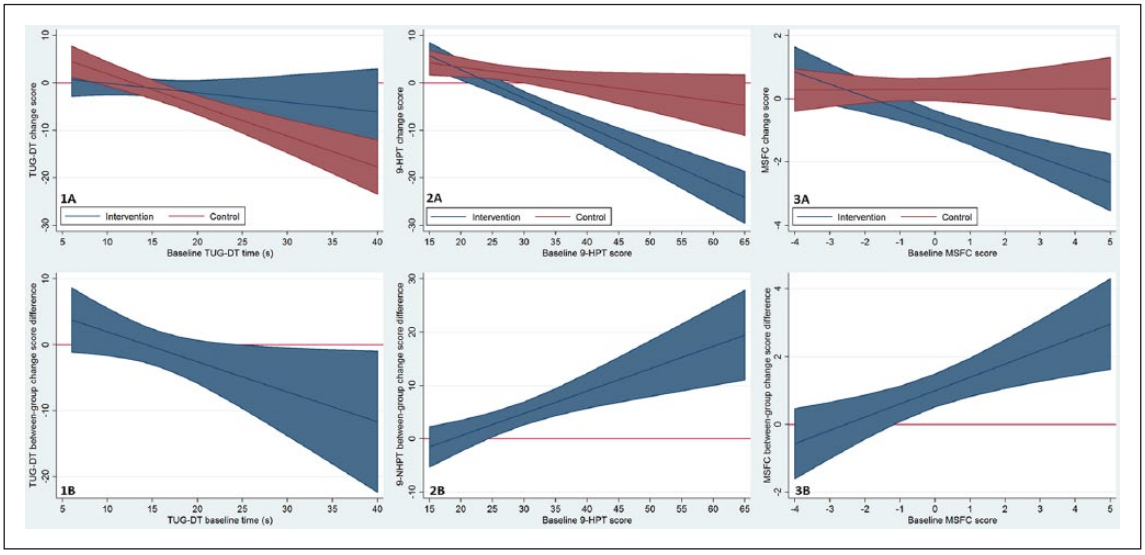

Figure 4. Top row shows significant covariate-by-group interactions for TUG dual task (1A), 9-HPT (2A) and MSFC (3A), suggesting that differences at re-assessment depended on baseline scores. Bottom row shows the mean difference in change scores between intervention and control groups. The central lines represent the means and shaded areas the 95% confidence intervals.

Table 3. Effects of the step training programme on primary and secondary outcome measures.

Outcome measure	Group				Effect size § (Cohen's f)	*P* value
	Intervention		Control			
	Baseline	Reassessment	Baseline	Reassessment		
Main outcomes						
CSRT total time (s)	2.4±0.3	2.1±0.3	2.4±0.3	2.5±0.7	0.35	0.031
SST (s)	72±25.8	52.6±16.6	71.1±25	69±22	0.41	0.011
Secondary outcomes						
Balance tests						
CSRT decision time (s)	0. 99±0.12	0.89±0.11	0.98±0.12	0.98±0.18	0.33	0.041
CSRT movement time (s)	1.4±1.7	1.26±1.7	1.4±1.6	1.5±5.2	0.33	0.039
Sway eyes open (mm)	97±46	62±30	131±75	128±101	0.33	0.040
Sway eyes closed (mm)	243±162	214±161	285±142	305±193	0.25	0.118
Mobility tests						
10-m walk task (s)	12.5±5.0	10.5±4	11.4±4.3	11.1±4.9	0.37	0.023
6-minute walk (m)	277±18	279±97	295±19	308±108	0.16	0.326
TUG single task (s)	13.1±5.5	12.3±4.3	12.1±3.9	11.7±4.6	0.07	0.659
Cognitive tests						
TUG dual task (s)	15.8±7.3	13.8±4.8	17.1±8	14.5±5.5	–	0.036#
SDMT (number of corrects answers)	38.1±10	40.3±10.1	42.2±9.7	41.3±11.1	0.14	0.384
TMT B-A (s)	62.6±39.7	57.4±33.4	57.3±34.2	50.3±33.3	0.11	0.489
Upper limb function and Multiple Sclerosis Functional Composite score						
9-hole Peg test (s)	30.4±9.0	26.8±5.4	27.5±9.2	29.6±8.3	–	0.001#
MSFC	0.42±2	−0.61±1.4	0.5±2	−0.27±2.3	–	0.001#

CSRT: choice stepping reaction time; SST: Stroop stepping test; TUG: Time – up-and-go test; SDMT: simple digit modality test (with written responses); TMT B-A: difference between Trail making test B and A; MSFC: multiple sclerosis functional composite score, calculated by averaged Z scores of 10-m walk test, SDMT and 9-hole Peg test; thus MSFC values are between −1 and 1 with negative values indicating less disability. #: significant group-by-covariate interaction (effect sizes not presented). §: values of 0.10, 0.25 and 0.40 indicate small, medium and large effect sizes, respectively.

Participants in the intervention group improved both their decision and movement times in CSRT and the time to complete the SST, indicating improved central processing and movement velocity. The mean improvement of 300ms for CSRT total response time appears clinically meaningful as this is similar to the difference in CSRT times of 400ms between multiple fallers and non-multiple fallers that we identified in a previous study.[9] Also, the mean improvement of 300ms found in this study was much higher than that reported in a similar study that used the same training system in the elderly (117ms).[11] The difference perhaps was partly due to the difference in the age of participants with the MS group being much younger than the elderly (mean age 53 vs 77 years) and partly due to the difference in the training durations (12 weeks for people with MS vs eight weeks for the elderly). We also found a significant difference between groups for the SST, a test of combined stepping and inhibition. The SST has been suggested to detect small impairments due to its ecological validity.[15] This suggests that stepping exercises, with their inherent cognitive requirements, may also improve aspects of cognitive functioning in people with MS.

Of interest, there was a significant improvement in the ten-metre walk test, but not in the TUG single-task. This finding suggests the intervention may have been more efficacious in improving gait speed than it was for improving the other main aspects of the TUG test (i.e. standing up from and sitting back down on a chair). It is also possible that the intervention improved capacity to dual task, as evident in the TUG test that comprised this, but not separate tests of TUG or cognitive performance.

The finding that the intervention improved 9-HPT (a test that requires arm and hand function) is also of interest, given the training included only the execution of lower limb movements. It has been shown that slow performance in the 9-HPT is associated with abnormalities in the corpus callosum in people with MS[28] and with abnormalities in the inter-hemispheric white matter pathway, connecting bilateral supplementary motor areas and other areas involved in planning and movement control.[29] There is also evidence that 9-HPT scores are associated cerebellar white matter volume in patients with primary progressive MS, independent of cerebellar grey matter volume.[30] In addition, there is evidence that selective grey matter atrophy and widespread white matter tract damage are associated with functional impairment of upper-limb motion (9-HPT) and cognition.[31] This suggests that the association between slow 9-HPT performance and frequent falls in MS may be related, at least partially, to cortical, sub-cortical and cerebellar damage.

It is possible that the cognitive load of the stepping games resulted in changes in underlying physiological factors associated with improved central processing and subsequently improved 9-HPT performance. A recent study by Prosperini et al.[32] showed that a 12-week home-based training programme with a balance board system (Nintendo® Wii Balance Board) might be accompanied by transient white matter structural plasticity specifically involving the superior cerebellar peduncles. While these structural changes following balance training need to be confirmed, the improvement in 9-HPT following step training is clinically meaningful because poor performance in 9-HPT has been shown a significant and independent predictor of frequent falls in people with MS.[9]

Previous studies have found that other exergames (Nintendo® Wii Balance Board with Wii Fit® exergames) have beneficial effects for balance in people with MS.[33–36] However, all but one of these studies[36] was conducted in a rehabilitation setting and required supervision.[29–31] In the study that was conducted in the home setting, Prosperini et al.[32] reported that Wii Balance Board training improved measures of static and dynamic balance, but that game play resulted in a number of knee and back pain adverse events. It is also possible that improved balance resulting from balance board training may not transfer to daily life when balance is threatened and requires quick and well placed steps to regain balance and avoid a fall. With our step training system, trainees could play the Stepmania exergame at different levels. No participants were able to play the most difficult level with faster drifting speeds and more complex stepping patterns, suggesting that there was no ceiling effect that may have limited effectiveness or adherence. Given that over 80% of participant completed the trial and average gameplay exceeded one hour per week, the system might provide a viable long-term exercise option for people with MS.

The intervention group reported fewer falls (78 falls; $n=23$) than those in the control group (95 falls; $n=21$). However, while the difference was not significant and this study was not powered for falls as an outcome measure, the result is encouraging and suggests that, in an appropriately powered study, this intervention may be effective in preventing falls in people with MS. Based on the fall rate from our previous study[9] we estimate that a sample of 500 will be needed for determining clinically significant differences between the groups for falls as an outcome measure.

We acknowledge the following study limitations. First, the sample comprised primarily reasonably high-functioning people with MS (physically and cognitively), so the findings cannot be generalized to people with more disabling MS. Second, the SDMT test was administered as a pen and paper test, which might have been influenced by poor manual dexterity. Third, we did not formally screen for cognitive functioning with a standardized assessment. However, we ensured all participants could understand and follow instructions during baseline testing and appreciate the requirements of the intervention. In addition all participants could complete the Symbol Digit Modality and Trail Making neuropsychological tests within normal ranges. Finally, the sample size was too small to detect group differences in falls and possibly not large enough or the intervention period (three months) too short to detect changes in some of the secondary outcome measures including the tests of cognitive functioning and walking capacity (six-minute walk test).

Conclusions

In summary, the step training system was safe and feasible to be administered at home without supervision, and effective in improving stepping, standing balance, coordination and functional performance in people with MS. Future studies with larger samples need to confirm these findings and determine whether other relevant outcomes, such as fatigue and fear of falling, can be improved, and whether step training can prevents falls in this group.

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Conflict of interest

None declared.

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References

1. Frzovic D, Morris ME and Vowels L. Clinical tests of standing balance: performance of persons with multiple sclerosis. *Arch Phys Med Rehabil* 2000; 81: 215–221.
2. Nilsagård Y, Gunn H, Freeman J, et al. Falls in people with MS-an individual data meta-analysis from studies from Australia, Sweden, United Kingdom and the United States. *Mult Scler* 2015; 21(1): 92–100.
3. Peterson EW, Cho CC, von Koch L, et al. Injurious falls among middle aged and older adults with multiple sclerosis. *Arch Phys Med Rehabil* 2008; 89: 1031–1037.
4. Peterson EW, Cho CC and Finlayson ML. Fear of falling and associated activity curtailment among middle aged and older adults with multiple sclerosis. *Mult Scler* 2007; 13: 1168–1175.
5. Finlayson ML, Peterson EW and Cho CC. Risk factors for falling among people aged 45 to 90 years with multiple sclerosis. *Arch Phys Med Rehabil* 2006; 87: 1274–1279.
6. Kasser SL, Jacobs JV, Foley JT, et al. A prospective evaluation of balance, gait, and strength to predict falling in women with multiple sclerosis. *Arch Phys Med Rehabil* 2011; 92: 1840–1846.
7. Matsuda PN, Shumway-Cook A, Bamer AM, et al. Falls in multiple sclerosis. *PM R* 2011; 3: 624–632.
8. Cameron MH and Lord S. Postural control in multiple sclerosis: implications for fall prevention. *Curr Neurol Neurosci Rep* 2010; 10: 407–412.
9. Hoang PD, Cameron MH, Gandevia SC, et al. Neuropsychological, balance, and mobility risk factors for falls in people with multiple sclerosis: a prospective cohort study. *Arch Phys Med Rehabil* 2014; 95: 480–486.
10. Sherrington C, Whitney JC, Lord SR, et al. Effective exercise for the prevention of falls: a systematic review and meta-analysis. *J Am Geriatr Soc* 2008; 56: 2234–2243.
11. Schoene D, Lord SR, Delbaere K, et al. A randomized controlled pilot study of home-based step training in older people using videogame technology. *PLoS One* 2013; 8: e57734. Doi: 10.1371/journal.pone.0057734.
12. Mansfield A, Peters AL, Liu BA, et al. Effect of a perturbation-based balance training program on compensatory stepping and grasping reactions in older adults: A randomized controlled trial. *Phys Ther* 2010; 90: 476–491.
13. Schoene D, Lord SR, Verhoef P, et al. A novel video game–based device for measuring stepping performance and fall risk in older people. *Arch Phys Med Rehabil* 2011; 92: 947–953.
14. Polman CH, Reingold SC, Banwell B, et al. Diagnostic criteria for multiple sclerosis: 2010 revisions to the McDonald criteria. *Ann Neurol* 2011; 69: 292–302.

15. Schoene D, Smith ST, Davies TA, et al. A Stroop Stepping Test (SST) using low-cost computer game technology discriminates between older fallers and non-fallers. *Age Ageing* 2014; 43: 285–289.

16. Sturnieks DL, Arnold R and Lord SR. Validity and reliability of the Swaymeter device for measuring postural sway. *BMC Geriatr* 2011; 11: 63.

17. Podsiadlo D and Richardson S. The timed "Up & Go": a test of basic functional mobility for frail elderly persons. *J Am Geriatr Soc* 1991; 39: 142–148.

18. Lezak M, Howieson D and Loring D. *Neuropsychological Assessment*. 4th ed. New York: Oxford University Press, 2004.

19. Smith A. *Sybol digit madalities test: Manual*. Los Angeles, CA: Western Psychological Services. 1982.

20. Rao SM, Leo GJ, Bernardin L, et al. Cognitive dysfunction in multiple sclerosis. I. Frequency, patterns, and prediction. *Neurology* 1991; 41: 685–691.

21. Hofheinz M and Schusterschitz C. Dual task interference in estimating the risk of falls and measuring change: a comparative, psychometric study of four measurements. *Clin Rehab* 2010; 24: 831–842.

22. Rudick RA, Cutter G, Baier M, et al. Use of the Multiple Sclerosis Functional Composite to predict disability in relapsing MS. *Neurology* 2001; 56: 1324–1330.

23. Rudick RA, Cutter G and Reingold S. The multiple sclerosis functional composite: a new clinical outcome measure for multiple sderosis trials. *Mult Scler* 2002; 8: 359–365.

24. Drake AS, Weinstock-Guttman B, Morrow SA, et al. Psychometrics and normative data for the Multiple Sclerosis Functional Composite: replacing the PASAT with the Symbol Digit Modalities Test. *Mult Scler* 2010; 16: 228–237.

25. Fischer JS, Jak AJ, Kniker JE, et al. for the National MS Society Clinical Outcomes Assessment Task Force. *Multiple sclerosis functional composite measure (MSFC): Administration and scoring manual*. Seattle, WA: National MS Society, revised October 2001.

26. Lamb SE, Jorstad-Stein EC, Hauer K, et al. Development of a common outcome data set for fall injury prevention trials: the Prevention of Falls Network Europe consensus. *J Am Geriatr Soc* 2005; 53: 1618–1622.

27. Perneger TV. What's wrong with Bonferroni adjustments. *BMJ* 1998; 316: 1236–1238.

28. Ozturk A, Smith SA, Gordon-Lipkin EM, et al. MRI of the corpus callosum in multiple sclerosis: association with disability. *Mult Scler* 2010; 16: 166–177.

29. Lowe MJ, Horenstein C, Hirsch JG, et al. Functional pathway-defined MRI diffusion measures reveal increased transverse diffusivity of water in multiple sclerosis. *Neuroimage* 2006; 32: 1127–1133.

30. Anderson VM, Wheeler-Kingshott CA, Abdel-Aziz K, et al. A comprehensive assessment of cerebellar damage in multiple sclerosis using diffusion tractography and volumetric analysis. *Mult Scler* 2011; 17: 1079–1087.

31. Sbardella E, Petsas N, Tona F, et al. Assessing the correlation between grey and white matter damage with motor and cognitive impairment in multiple sclerosis patients. *PLoS One* 2013; 8: e63250. Doi: 10.1371/journal.pone.0063250.

32. Prosperini L, Fanelli F, Petsas N, et al. Multiple sclerosis: changes in microarchitecture of white matter tracts after training with a video game balance board. *Radiology* 2014; 273: 529–538.

33. Brichetto G, Rinaldi S, Spallarossa P, et al. Efficacy of physical therapy in multiple sclerosis as measured with the modified fatigue impact scale and ambulation index: a retrospective study. *NeuroRehab* 2013; 33: 107–112.

34. Nilsagard YE, Forsberg AS and von Koch L. Balance exercise for persons with multiple sclerosis using Wii games: a randomised, controlled multi-centre study. *Mult Scler* 2013; 19: 209–216.

35. Nilsagard YE, von Koch LK, Nilsson M, et al. Balance exercise program reduced falls in people with multiple sclerosis - a single group pretest posttest trial. *Arch Phys Med Rehabil* 2014; 95: 2428–2434.

36. Prosperini L, Fortuna D, Gianni C, et al. Home-based balance training using the Wii balance board: a randomized, crossover pilot study in multiple sclerosis. *Neurorehabil Neural Repair* 2013; 27: 516–525.