Clinical Rehabilitation

# Dual Task Training in Persons with Multiple Sclerosis: A Feasibility Randomized Controlled Trial

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| Abstract: | Objective: To determine the feasibility of dual task training in persons with Multiple Sclerosis.<br>Design: Randomized, single-blinded controlled trial.<br>Setting: University research laboratory.<br>Participants: 234 individuals inquired about the investigation. After screening, 20 individuals with multiple sclerosis who self-reported problems with multitasking and were ambulatory volunteered for the investigation. 14 participants completed the post-assessment following the 12-week intervention.<br>Intervention: Participants were randomly assigned to either single task training program which focused on balance and walking function (n=6) or dual task training program that incorporated cognitive tasks in balance and walking training (n=8).<br>Measures: Before and after the 12-week interventions participants underwent assessments of walking; dual task walking; balance (Berg Balance Scale and balance confidence) and cognition as indexed by the Brief International Cognitive Assessment for MS.<br>Results: There was an 8.5% recruitment rate, a 70% retention rate, and a 100% adherence rate. There was a trend for dual task gait speed to improve in the dual task training group following the intervention (Pre: task 1: 109.8±39, task 2: 104.2±34.1; Post: task 1:127.6±40.1, task 2: 122.8±37.4; p=0.14; η2 = 0.24). There was also a trend for the dual task training group (28.1) to have greater performance than the control group (24.7) on visuospatial memory (p=0.10; η2= 0.23). There were no changes in cognitive performance during walking trials.<br>Conclusions: The study procedures were found to be feasible and improvements should be made in recruitment efforts going forward. Further examination of dual task training programs in individuals with multiple sclerosis is warranted. |

## Abstract

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**Results:** There was an 8.5% recruitment rate, a 70% retention rate, and a 100% adherence rate. There was a trend for dual task gait speed to improve in the dual task training group following the intervention (Pre: task 1: 109.8±39, task 2: 104.2±34.1; Post: task 1:127.6±40.1, task 2: 122.8±37.4; p=0.14; $\eta^2 = 0.24$). There was also a trend for the dual task training group (28.1) to have greater performance than the control group (24.7) on visuospatial memory (p=0.10; $\eta^2$= 0.23). There were no changes in cognitive performance during walking trials.

**Conclusions:** The study procedures were found to be feasible and improvements should be made in recruitment efforts going forward. Further examination of dual task training programs in individuals with multiple sclerosis is warranted.

INTRODUCTION:

Simultaneous performance of a motor and cognitive task results in cognitive-motor interactions.[1] Typically, these interactions result in a change in performance in one or both domains.[2] In neurological populations, such as multiple sclerosis, declines in the simultaneous performance of cognitive and motor function are commonly observed.[3] Cognitive motor interference during walking is of practical and clinical importance. It has been hypothesized to exacerbate walking and cognitive performance particularly in those with pre-existing ambulatory and cognitive impairments.[4, 5] Further, it has been linked to decreased community mobility[6] and a greater risk of falls in various populations in multiple sclerosis, stroke, Parkinson's disease (PD), and the elderly. This underscores the importance of rehabilitation strategies for cognitive-motor interference in individuals with neurological conditions, including multiple sclerosis.[1]

Researchers suggest that exposing individuals to attention diverting situations (i.e. dual task training) allows them to develop appropriate motor control strategies.[7] Currently, there is very limited evidence for the effect of rehabilitation strategies on dual task gait and cognitive performance in persons with multiple sclerosis.[8] Indirectly, the benefits of rehabilitation on walking and cognition independently suggest that performance on these tasks in persons with multiple sclerosis can be improved with targeted interventions – specifically dual task training.[9] In line with this proposal, evidence from other special populations (geriatric, dementia and Parkinson's disease) suggests that motor and cognitive deficits can be minimized with targeted dual task training.[10] Indeed, a recent review highlighted the promise of a dual task training approach on walking and cognition in persons with multiple sclerosis.[11]

Prior to undertaking a large scale investigation examining dual task training in multiple sclerosis a feasibility study is needed. The current investigation examined the feasibility of dual

task training on walking, cognition and dual task performance in participants with multiple sclerosis.

METHODS:

The investigation was single-blinded randomized control trial examining the feasibility of 12-weeks of dual-task (i.e., experimental condition) and single-task (i.e., control condition) training on walking, cognition and dual task walking outcomes (NCT#02274935). All procedures for the investigation were approved by the University of Illinois at Urbana-Champaign's institutional review board (#15002).

Participants:

Prospective participants were recruited through the North American Research Committee on Multiple Sclerosis patient registry, the online newsletter of the greater Illinois Chapter of the national Multiple Sclerosis Society, local newspaper, electronic newsletters and social media during the summer of 2014 (June-August). Individuals with multiple sclerosis who were between the ages of 18-64 were recruited. To be included in this study, participants were required to have a neurologist confirmed diagnosis of multiple sclerosis, been relapse free for the previous 30 days, ability to read and comprehend English, physician approval to engage in the investigation, and self-reported concerns with attention and/or multitasking while walking. Participants were excluded if they did not meet inclusion criteria or were unable to walk either with or without an assistive device for a distance of 25 feet. To ensure that participants could understand instructions participants were also required to score greater than 20 on the Modified Telephone Interview for Cognitive Status.[12]

Procedures:

Participants initially completed a baseline outcome assessment, followed by a 12-week

intervention period, and a post-intervention assessment within 7 days of the termination of the 12-week intervention period (i.e., immediate follow-up). Following baseline assessment, participants were randomized into single task or dual task training arms. Randomization was completed using sequentially numbered, opaque sealed envelopes by the study project coordinator who was not involved in intervention delivery or outcome assessment (e.g. blinded). Identical assessments were completed at baseline and immediate follow-up. The assessors remained blinded to the participant's training group and trainers were not involved in outcome assessment.

After arriving at the laboratory, all participants were given a verbal explanation of study procedures and the opportunity to ask questions about the study. Once all inquiries regarding the investigation were addressed, participants provided written informed consent. After providing consent, participants also provided self-reported multiple sclerosis subtype, disability level and years since diagnosis. Self-reported disability was assessed with the self-administered Kurtzke questionnaire.[13]

Measures:

Primary outcome measures of this investigation were gait velocity in various conditions and cognitive task performance. To assess gait performance, participants completed four walking trials at a comfortable walking speed covering 9 m. The central portion of the walk was covered with a 4.9m GAITRite™ (CIR Systems Inc, Franklin NJ) pressure sensitive walkway. Two of the walking trials were completed with no additional task and two were completed while simultaneously performing a cognitive task. Participants were instructed to pay equal amount of attention to both tasks. All participants completed the single task walking trials before the dual

task walking trials. Gait performance was indexed by gait velocity (cm/s) under both single and dual task conditions.

Two cognitive tests were used during dual task conditions. The first was an alternating letters task. Participants recited alternating letters of the alphabet from a predetermined starting letter (e.g. N, P, R). The alternating letters task is an executive control and selective attention task.[14] Additionally, a serial 7s subtraction task (e.g. 99, 92, 85) was used. The serial subtraction task is a mental tracking task.[15] Both tasks are widely used during dual task testing to investigate cognitive motor interference.[3] Prior to any dual task trials, both cognitive tasks were first performed in a seated condition to determine single task performance. Cognitive task performance was indexed by a combined measure of correct response rate (CRR) by multiplying frequency by accuracy.[16]

Cognition was measured with the Brief International Cognitive Assessment for MS [17], which consists of the Symbol Digit Modalities Test[18], first 5 learning trials of the California Verbal Learning Test-II[19], and the first 3 learning trials of the Brief Visuospatial Memory Test-Revised[20].

Secondary measures included measures of clinical and self-report indexes of balance. The Berg Balance Scale was the clinical measure of balance.[21] It is a 16-item test that targets functional balance and is scored from 0-56 points, with higher scores indicating lower performance. The Activities-specific Balance Confidence Scale is self-report measure of balance confidence when performing 16 different daily mobility activities. Scores range from 0-100 and a low score indicates a subject is not confident in his/her ability to maintain balance during daily activities.[22]

Feasibility outcomes include recruitment, adherence and retention rates, and ability to

collect primary and secondary outcomes.[23] Recruitment rate was calculated as the percentage of potential participants that contacted the research laboratory and were enrolled in the investigation. Adherence rate was calculated as the percentage of total number of training sessions completed by the participants in each intervention arm. Retention rate was calculated as the percentage of enrolled participants that completed immediate follow-up assessments. Ability to collect outcome assessments was operationalized as the percentage of possible outcome measures that were completed at baseline and follow-up assessments.

Interventions:

Participants were randomly assigned to one of two 12-week intervention arms: a single task training condition or a dual task training condition. Briefly, the single task arm involved balance and gait training, whereas the dual task arm involved balance and gait training while performing cognitive tasks. Both arms involved initially completing an introductory session where participants were familiarized with all balance and gait training exercises and procedures. Additionally, the dual task group was introduced to the cognitive tasks during the introductory session. For both arms, training took place twice per week (1 hour/session).

Both groups received the individualized progressive regimen of balance and gait exercises. The balance training consisted of 10 exercises that have been shown to improve balance and stability in multiple sclerosis.[24] Balance training was done during the first 30 minutes of the session and each balance exercise was performed twice. The dual task group performed a cognitive task during the second set of balance exercises. The difficulty of the exercises was matched to the abilities of the individual participants. Specifically, after each exercise participants reported their perceived difficulty on a 1-10 scale with 10 being extremely difficult. Balance tasks that met a difficulty score of 7/10 were prescribed to each participant on

a weekly basis. If a task was too easy or too hard, predetermined modifications were made to each exercise to maintain a difficulty level of 7 (See Appendix A).

The second half of the training session consisted of walking on a treadmill for up to 30 minutes. The dual task group performed a cognitive task for half of the walking training. They alternated one minute of walking with a cognitive task and one minute walking without a cognitive task throughout the session. Initial treadmill walking speed was determined based on the participant's comfortable walking speed recorded at baseline assessment. The walking speed and duration were alternatively progressed on a weekly basis. Walking speed was determined from their recorded comfortable pace during the baseline assessment. In the first training session, participants walked for a total of 10 minutes and worked up to walking for 30 minutes by the end of the 12 weeks. Walking speed was increased in ~10% increments and duration in 5 minute intervals every other week in an alternating fashion. For safety, participants wore a harness during treadmill training.

The cognitive tasks targeted verbal fluency, discrimination and decision making, working memory, mental tracking, and visuospatial cognition. All domains were chosen due to previously demonstrated impairment in the multiple sclerosis population.[25] Moreover, these cognitive tasks have been shown to elicit cognitive motor interference in persons with neurological impairment.[26, 27] Cognitive difficulty level was based on task accuracy. Difficulty levels were set for each participant to maintain an accuracy of 70%. Although subtraction tasks were utilized during training, participants did not receive 7s as a stimuli. The alternating letters task was not part of the intervention training.

Statistical Analysis:

RESULTS

Participant flow through recruitment and enrollment is outlined in Figure 1. A total of 234 individuals with MS who met the inclusion criteria were assessed for eligibility. After screening, a total of 20 individuals enrolled in the investigation and underwent baseline assessment.

Following enrollment, 6 individuals withdrew post-randomization. One withdrew due to moving out of state, 2 withdrew due to health concerns (unrelated to the interventions), and 3 participants withdrew because of time commitments. Data from these participants were excluded from analyses (See Figure 1). A total of 14 participants completed the post-intervention assessment (n = 6 control; n=8 dual task training).

The 14 participants who finished the intervention completed 100% of the prescribed exercise sessions. The 6 participants who dropped out of the intervention (e.g. withdrew prior to follow-up intervention) completed a total of 85% of sessions prior to dropping out.

None of the participants enrolled in the intervention reported adverse events directly associated with the interventions (e.g., carrying out exercises).

Sample characteristics as a function of group are reported in Table 1. There were no group differences in age, multiple sclerosis duration, gender composition, assistive device use or disability (p's > 0.05).

*Gait*

All gait variables are reported in table 2. Statistical analyses revealed no differences between groups in single task gait speed. [$F(1,13)=0.15$; $p=0.71$; $\eta^2=.01$] following the intervention when controlling for baseline values. There was a trend for the dual task training group to have greater dual task gait speeds with alternating letters [$F(1,13)=3.5$; $p=0.09$; $\eta^2=.24$]

and serial subtractions [F(1,13)=3.1; p=0.11; $\eta^2$=.22] following the intervention compared to the control group when controlling for baseline values.

*Cognition*

Cognitive performance measures during dual task trials are reported in table 3. Statistical analysis revealed no differences between groups in cognitive task performance (correct responses/s) on either seated letters [F(1,13)=0.04; p=.85; $\eta^2$=.004]; or serial sevens [F(1,13)=1.5; p=.25; $\eta^2$=.12]) following the intervention when controlling for baseline values.

Among all participants, Symbol Digit Modalities Test performance ranged from 16 to 96 with a mean of 58.4 at baseline. Performance on verbal learning test ranged from 46 to 74 with a mean of 55.4 at baseline. Visual memory performance ranged from 9 to 35 with a mean score of 23.2. Statistical analysis revealed no differences between groups in performance on the Symbol Digit Modalities Test [F(1,13)=0.6; p=0.47; $\eta^2$=.05]; and CVLT-II [F(1,13)=0.23; p=0.64; $\eta^2$=.02] following the intervention when controlling for baseline values. There was a trend for the dual task training group (28.1) to have greater performance than the control group (24.7) on the Brief Visuospatial Memory Test – Revised [F(1,13)=3.3; p=0.10; $\eta^2$=.23] following the intervention when controlling for baseline values.

*Balance*

Among all participants, balance as measured by Berg Balance Scale ranged from 26 to 56 with a mean of 49.6 at baseline. Self-reported balance confidence ranged from 33.75 to 100% with a mean of 80.2% at baseline. Statistical analysis revealed no differences between groups in balance [F(1,13)=1.2; p=0.30; $\eta^2$=.10] or balance confidence [F(1,13)=0.0; p=0.98; $\eta^2$=.0] following the intervention when controlling for baseline values.

DISCUSSION

The principal finding of this feasibility randomized controlled trial was that dual task (cognitive-motor) training is a safe approach to target dual task performance in persons with multiple sclerosis. There were concerns with recruitment and retention. Lessons learned from this feasibility investigation can maximize the success of larger rehabilitation interventions focusing on dual task performance. This investigation sets the stage for larger interventions focusing on rehabilitation of dual task performance in multiple sclerosis as well as research focusing on the impact of the improving dual task performance on ecologically valid outcomes.

Feasibility outcomes of the current investigation focused on recruitment, adherence and retention rates, and ability to collect primary and secondary outcomes.[23] Data on adverse events was also collected. Recruitment rate was less than 10% of eligible participants. Future investigations need to explore other recruitment strategies such as partnering with clinicians. Retention of participants over the 12-week intervention was 30%. The most common reason for withdrawing from the investigation was time commitment. Additional effort educating participants of importance of exercise for their general health and well-being may maximize retention. Overall there was a high level of adherence to the training program.
There was no difficulty in collecting the primary and secondary outcomes. Lastly, the program was found to be safe.

Additional outcomes that assessed gait, balance, and cognition demonstrated trends for the intervention group to improve on dual task gait speed and visuospatial memory. Balance function and balance confidence did not demonstrate changes between groups following the intervention. This could indicate that the prescribed balance exercises were not challenging enough or the intervention was too short to elicit changes in balance. However, these statistical

results should be taken with caution due to the small sample size and limited power.

Although there is significant documentation of deficits during dual task performance in persons with multiple sclerosis,[26, 28] there has been limited examination of strategies to minimize it. The investigations that have examined interventions to reduce cognitive motor interference in multiple sclerosis have utilized exergaming or virtual reality based training. Peruzzi and colleagues[8] conducted an unblinded pilot investigation of virtual reality based-treadmill training in a small sample (n=8) of individuals with multiple sclerosis. Overall, it was found that participants not only improved standard walking but also improved their gait speed during dual task conditions by 18%. However, the promising results of the investigation need to be interpreted with caution given the methodological weakness (e.g. lack of control group, lack of blinding and small sample size). Another investigation with fewer methodological concerns revealed that 3 weeks of exergaming while undergoing balance training resulted in reductions in gait variability during dual task walking compared to traditional balance training in persons with multiple sclerosis.[29] In addition, a recent dual task balance training program, that trained participants 3 times a week for 4 weeks, demonstrated improvements in dual task walking performance, balance function, and balance confidence.[30] Collectively, these observations suggest that dual task performance in persons with MS is amendable with targeted interventions.

The current observation that a 12-week progressive dual task training program may alter dual task gait speed is consistent with these previous pilot investigations. In contrast to previous reports, no equipment beyond a treadmill was needed to implement the current protocol suggesting that this program could be easily implemented in various healthcare settings. The potential effective of the intervention is consistent with that observed by a recent systematic review of interventions targeting cognitive motor interference in neurodegenerative diseases.[10]

Despite the promising observations, this study did have several weaknesses. We note that the majority of these weaknesses are common in feasibility studies.[23] The small sample size limits the generalizability of the results and reduces the observed power. The sample had an average age of ~53 years of age and it is not clear how age impacted the observations. Based on the observations of this current investigation a sample of 40 with 20 participants per group would be needed to observe a significant changes in dual task performance. It should be noted that caution should be used when estimating sample sizes based on feasibility studies such as the current investigation.[31] Additional weaknesses included the relatively low level of disability within the current sample. It is possible that different intervention effects would have been observed in a sample with greater dual task impairments. During assessments, the dual task walking trials were not randomized. It is possible that participants could have experienced fatigue – although the same assessment order was utilized for all participants. Consequently, any impact would have been similar across groups. The intensity of the exercise prescription (based on comfortable walk speed) may have limited the effectiveness of the intervention.[32] The lack of change in single task gait speed indirectly supports the notion that the training intensity was relatively low. It is also possible that the difficulty of the cognitive tasks was not optimal to elicit effects. These limitations should be addressed in future investigations.

The completion of this feasibility randomized control trial has provided valuable information concerning the feasibility of dual task performance rehabilitation trials in MS samples. This is one of the first investigations to examine whether dual task training can be improved. This investigation sets the stage for larger interventions focusing on rehabilitation of dual task performance in MS as well as research focusing on the impact of the improving dual task performance on ecologically valid outcomes.

Clinical Messages

- A dual-task training intervention for people with multiple sclerosis who notice cognitive-motor interference is feasible.
- The size of the beneficial effect noticed suggests a trial recruiting over 40 people should have adequate power to detect benefit.
- An increase in training intensity would also be preferable.

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Conflict of Interest Statement

The authors declare there is no conflict of interest.

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Table 1. Descriptive statistics for demographic information

| | Intervention | Control | p |
|---|---|---|---|
| Age | 48.3±14.2 (28-64) | 56.8±7.1 (47-64) | t=.99; p = .34 |
| Gender | Female = 5, Male = 8 | Female = 5, Male = 1 | U=15.5; p=.45 |
| MS Subtype | RR = 7, B = 1 | RR = 5, PP = 1 | U=18.0; p=.73 |
| Year Singe Diagnosis | 11.9±11.7 (1-36) | 11.7±7.6 (4-24) | t=-0.32; p =.76 |
| $EDSS_{SR}$ | 1.75 (1-3) | 2.5 (2.5-5) | U=11.5, p=.18 |

Note: Age and year since diagnosis is reported as mean±SD (range); $EDSS_{SR:}$ self-administered Kurtzke questionnaire is reported as median (IQR); RR: relapse remitting, B: benign MS, PP: primary progressive

Table 2. Descriptive statistics for gait performance

| | Intervention | | Control | | p |
|---|---|---|---|---|---|
| | Pre | Post | Pre | Post | |
| Single Task Gait Speed (cm/s) | 123.1±42.1 (64.9-173.6) | 128.1±43.3 (66.1-189.2) | 107.3±35.8 (65.6-147.1) | 111.0±30.9 (70.6-143.9) | .71; $\eta^2$=.01 |
| Dual Task Gait Speed Letters (cm/s) | 109.8±39.0 (56.9-164.7) | 127.6±40.1 (61.1-170.4) | 100.6±41.4 (59.2-162.1) | 100.0±28.9 (65.2-138.9) | .09; $\eta^2$=.24 |
| Dual Task Gait Speed 7s (cm/s) | 104.2±34.1 (51.3-141.9) | 122.8±37.4 (56.9-159.1) | 88.4±37.5 (47.3-145.2) | 87.9±36.6 (45.7-137.2) | .11; $\eta^2$=.22 |

Note: Values are reported as mean±SD (range)

Table 3. Descriptive statistics for cognitive performance

| | Intervention | | Control | | p |
|---|---|---|---|---|---|
| | Pre | Post | Pre | Post | |
| CRR Letters Seated (correct responses/s) | 87.5±26.0 (40.0-120.0) | 90.0±22.0 (50.0-120.0) | 65.0±13.8 (50.0-90.0) | 75.0±31.4 (20.1-110.0) | .85; η2=.004 |
| CRR Letters Walking (correct responses/s) | 86.1±25.9 (40.0-125.7) | 90.3±20.7 (57.6-122.2) | 65.2±25.2 (27.3-92.7) | 73.8±32.9 (18.2-107.1) | .93; η2=.001 |
| CRR 7s Seated (correct responses/s) | 42.5±21.2 (20.0-80.0) | 45.0±19.2 (20.0-80.0) | 35.0±21.7 (10.0-60.0) | 31.7±19.4 (0-60.0) | .25; η2=.12 |
| CRR 7s Walking (correct responses/s) | 37.8±16.2 (11.4-55.2) | 47.4±24.2 (15.0-79.5) | 24.8±16.3 (0-41.4) | 34.2±19.6 (7.5-55.0) | .61; η2=.03 |

Note: Values are reported as mean±SD (range)
CRR = correct response rate

Supplemental Table 1. Descriptive statistics for dual task cost of performance

| | Intervention | | Control | | p |
|---|---|---|---|---|---|
| | Pre | Post | Pre | Post | |
| DTC Gait Speed Letters (%) | 10.1±11.3 (6.6-26.6) | 1.8±18.2 (-41.7-13.7) | 7.8±11.4 (-10.2-24.7) | 12.4±18.7 (-13.8-36.7) | .21; η2=.14 |
| DTC Gait Speed 7s (%) | 13.8±15.9 (-21.1-26.8) | 17.5±23.4 (-53.6-18.30 | 19.5±9.6 (1.3-28.0) | 22.6±16.0 (4.6-48.7) | .13; η2=.20 |
| DTC CRR Letters (%) | 0.8±11.0 (-11.2-25.5) | -5.5±35.9 (-80.0-28.0) | -0.9±37.6 (-54.6-54.6) | 1.9±19.5 (-33.9-20.4) | .68; η2=.02 |
| DTC CRR 7s (%) | 4.7±42.9 (-66.7-44.8) | -11.2±55.3 (-104.9-62.4) | 16.1±64.6 (-65.6-100.0) | -6.4±43.3 (-77.6-38.5) | .73; η2=.01 |

Note: Values are reported as mean±SD (range); CRR = correct response rate; DTC is the percent change from single task to dual task performance

Figure 1. Consort Diagram