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Multiple-Modality Exercise And Mind-Motor Training To Improve Mobility In Older Adults: A Randomized Controlled Trial

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Abstract

Objective: To investigate the effects of multiple-modality exercise with or without additional mind-motor training on mobility outcomes in older adults with subjective cognitive complaints.

Methods: This was a 24-week randomized controlled trial with a 28-week no-contact follow-up. Community-dwelling older adults underwent a thrice -weekly, Multiple-Modality exercise and Mind-Motor (M4) training or Multiple-Modality (M2) exercise with an active control intervention (balance, range of motion and breathing exercises). Study outcomes included differences between groups at 24 weeks and after the no-contact follow-up (i.e., 52 weeks) in usual and dual-task (DT, i.e., serial sevens [S7] and phonemic verbal fluency [VF] tasks) gait velocity, step length and cycle time variability, as well as DT cognitive accuracy.

Results: 127 participants (mean age 67.5 [7.3] years, 71% women) were randomized to either M2 (n = 64) or M4 (n = 63) groups. Participants were assessed at baseline, intervention endpoint (24 weeks), and study endpoint (52 weeks). At 24 weeks, the M2 group demonstrated greater improvements in usual gait velocity, usual step length, and DT gait velocity (VF) compared to the M4 group, and no between- or within-group changes in DT accuracy were observed. At 52 weeks, the M2 group retained the gains in gait velocity and step length, whereas the M4 group demonstrated trends for improvement (p = .052) in DT cognitive accuracy (VF).

Conclusions: Our results suggest that additional mind-motor training was not effective to improve mobility outcomes. In fact, participants in the active control group experienced greater benefits as a result of the intervention.

Keywords: Dual-task gait, community-dwelling, multiple-modality, group-based exercise.

1. Introduction

Older adults with subjective cognitive complaints (SCC) are at increased risk for future mobility impairment (Allali et al., 2016) and cognitive decline (Jessen et al., 2014; Kaup et al., 2015). Self-reported SCC may be the first indicator of underlying cognitive impairment (Amariglio et al., 2012; Chao et al., 2010; Jessen et al., 2010) and have been associated with poorer scores on objective cognitive assessments (Amariglio et al., 2011), as well as cortical and hippocampal atrophy (Saykin et al., 2006). In this perspective, SCC is a clinically-relevant phenomenon that can serve to identify individuals at-risk for more serious forms of cognitive impairment and dementia, and these cognitive complaints have been found to predict future neuropathological progression towards the establishment of dementia (Kaup et al., 2015). The current efforts to improve cognition and mobility in Alzheimer's disease and other dementias have been met with relatively little success (Brookmeyer et al., 2007; Sperling et al., 2011). Thus, directing interventions towards individuals who are at increased risk for future pathological cognitive decline (e.g., those with SCC) prior to the establishment of underlying neuropathological changes to the brain may provide the greatest clinical benefit (Livingston et al., 2017).

Cognitive deficits in older adults have been strongly associated with poor performance in several spatiotemporal gait characteristics, including slow velocity and increased stride time variability (Montero-Odasso et al., 2014). Moreover, slow gait velocity is an early indicator of cognitive impairment (Verghese et al., 2014) and is related to shortened life span (Studenski et al., 2011). Further, gait variability is associated with increased risk of falls (Beauchet et al., 2013, 2009), and higher gait variability is more apparent in those with a greater degree of cognitive impairment (Montero-Odasso et al., 2012). In fact, slower gait velocity and increased gait variability were linked to accentuated cognitive decline 25 years after baseline assessment in a recent retrospective investigation (MacDonald et al., 2017); however, the relationship between cognitive functioning and gait performance has yet to be fully understood. The relationship is thought to be mediated, at least in part, may be a result of poorer executive functioning (EF) (Hausdorff et al., 2008) among healthy individuals (Allali et al., 2013) and those with severe cognitive impairment (e.g., Alzheimer's disease) (Allali et al., 2007). The importance of preserved EF in the cognitive control of gait becomes more evident under dual-task (DT) conditions (e.g., walking and preforming a concurrent cognitive task) (Smith et al., 2016; Yogev-Seligmann et al., 2008), where individuals with poorer EF demonstrate the most dramatic gait impairments (Allali et al., 2010).

Early prevention strategies (prior to the establishment of permanent cognitive impairment) that effectively improve usual and dual-task gait performance in those at greater risk for cognitive impairment may preserve functional independence, reduce fall risk (Demnitz et al., 2016; Snijders et al., 2007), and attenuate the increasing burden on health care systems associated with mobility disability and dementia (Prince M, Wimo A, Guerchet M, 2015; Sperling et al., 2011). Thus far, increasing evidence has suggested that habitual participation in exercise programs may lead to improvements in usual and DT gait parameters (Dorfman et al., 2014; Hortobágyi et al., 2015), static and dynamic balance (Zanotto et al., 2014); with a greater effect on frail individuals (e.g., fallers, musculoskeletal disorders) and in those with neurological conditions (e.g., mild to moderate dementia) (Gobbo et al., 2014; Zanotto et al., 2014). For instance, in a recent laboratory-based investigation conducted by our research group, older adults with cognitive impairment, not dementia (CIND) (Plassman et al., 2011) who underwent a combined 26-week DT gait and aerobic exercise (AE) intervention (40 min/day, 3 days/week) demonstrated significant improvements in usual and DT gait velocity and step length (Gregory et al., 2017).

Despite promising evidence, the specific components of an exercise intervention that would impart the greatest benefit to mobility impairments in older adults are yet to be defined (Young et al., 2015). Furthermore, evidence is insufficient to conclude that a specific program of cognitive training and/or exercise warrants prescription in individuals with SCC (Snowden et al., 2011). Although the administration of exercise with (Plummer et al., 2015) or without (Hortobágyi et al., 2015) additional DT gait training in previous exercise studies has been associated with improved usual and DT gait performance, several aspects of these investigations may raise concerns regarding the feasibility of exercise protocols administered in such laboratory settings (i.e., translation to community settings). Further, most studies have failed to comply with current guidelines for exercise in older adults with regards to exercise intensity, frequency and duration (Hortobágyi et al., 2015; Plummer et al., 2015). These guidelines also emphasize the importance of multiple-modality exercise programs over single-modality exercise programs to enhance overall health and quality of life in the general population of older adults (Chodzko-Zajko et al., 2009; Gregory et al., 2013), although evidence is still limited in more specific groups (e.g., individuals with SCC). In addition, exploring the combination of multiple-modality exercise with alternative, and perhaps more feasible (e.g., group-based, low-cost, and easily administered), forms of mind-motor training (simultaneous cognitive and physical engagement) on mobility outcomes may provide further support for optimal exercise interventions in older adults at risk for cognitive and mobility impairment (Gregory et al., 2013).

Square-stepping exercise (SSE) is a group-based, low-intensity exercise program that has been associated with improvements in lower extremity functional fitness and reduced fall risk in older adults at high risk of falling (Shigematsu et al., 2008a). The SSE intervention is best characterized as a visuospatial working memory task with a stepping response on a gridded floor mat, and thus, may be considered as a novel form of mind-motor training (Gill et al., 2016). Recent evidence suggests that SSE may yield improvements in global and domain-specific cognitive functioning, including EF subdomains (i.e., attention and mental flexibility) in older adults free of dementia (Shigematsu, 2014; Teixeira et al., 2013). Nonetheless, the additive effects of SSE on usual and DT spatiotemporal gait characteristics in combination with multiple-modality exercise warrants further investigation.

Hence, the purpose of this study was to examine the influence of group-based, multiple-modality exercise combined with mind-motor training (i.e., SSE), in comparison to multiple-modality exercise with additional balance, range of motion and breathing exercises on spatiotemporal gait characteristics in community-dwelling older adults with SCC. We hypothesized that the addition of a mind-motor component to the multiple-modality exercise intervention would lead to greater improvements in the study outcomes compared to multiple-modality exercise alone, particularly by influence of SSE on neural control of gait.

2. Methods

2.1. Study design

The M4 Study was a two-arm randomized controlled trial (RCT) implementing a 24-week intervention program with a 28-week no-contact follow-up (Gregory et al., 2016). Assessments were performed at baseline, 24 weeks (intervention endpoint) and 52 weeks (study endpoint). After baseline assessments, participants were randomized to either the multiple-modality exercise with mind-motor training intervention group (Multiple-Modality, Mind-Motor [M4]) or to the multiple-modality exercise active control group (Multiple-Modality [M2]). The randomization sequence was computer generated, and concealed envelopes were used to assign group status. All assessors were blinded to group assignment.

2.2. Participants

Details of the M4 study participants and eligibility criteria have been published (Boa Sorte Silva et al., 2017; Gregory et al., 2016). Briefly, the study included community-dwelling older adults aged 55 years or older, who self-reported a cognitive complaint (defined answering positively to the question "Do you feel like your memory or thinking skills have got worse recently?") (Barnes et al., 2013). Subjective cognitive complaints are defined as a subjective perception of cognitive deterioration by an individual or their peers, even though the individual may seem to perform well in neuropsychological tests, and may not demonstrate signs of objective cognitive impairment (Amariglio et al., 2012; Chao et al., 2010; Jessen et al., 2010). As well, we included individuals who were fully independent in functional activities (maximum score in the Lawton-Brody Instrumental Activities of Daily Living scale [8/8]) (Lawton and Brody, 1969). Individuals were excluded if they self-reported a diagnosis of dementia and/or scored < 24 on the Mini-Mental State Examination (MMSE) (Folstein et al., 1975), had major depression, recent history of severe cardiovascular conditions, any neurological and/or psychiatric disorders, or were unable to comprehend the study letter of information.

The study was registered with ClinicalTrials.gov on 29 April 2014 (Identifier: NCT02136368). The Western University Health Sciences Research Ethics Board approved this project and all participants provided written informed consent prior to taking part in the study.

2.3. Multiple-modality exercise intervention

Participants in both groups received 45 minutes of group-based, standardized, multiple-modality exercise, described in detail elsewhere (Gregory et al., 2016). The M4 group performed an additional 15 minutes of mind-motor training (i.e., SSE), whereas the M2 group underwent 15 minutes of training focused on balance, range of motion and breathing exercises (i.e., active control condition). In total, participants in both groups exercised 60 minutes/day, 3 days/week for 24 weeks.

The multiple-modality exercise intervention incorporated a 5-minute warm-up, 20-minute aerobic exercise (AE), 5-minute cool down, followed by 10 minutes of resistance training (see Table e-1) and 5 minutes of stretching. AE intensity was prescribed via target heart rates (HR) determined at baseline using the STEP™ tool (Stuckey et al., 2012). During the AE component, participants were encouraged to keep their HR at 65-85% of their predicted maximum HR (HRmax) and/or at a rating of 5-8 on the 10-point modified Borg Rating of Perceived Exertion (RPE) scale (Chodzko-Zajko et al., 2009). HR monitoring was conducted part way through and at the end of the AE component during each exercise session. Participants were instructed to record HR and RPE immediately after each monitoring in a training log provided by the research team. Target HR were recalculated at 12 weeks to adjust for progression in the AE training.

2.3.1. Active control intervention

The active control group underwent an additional 15 minutes of balance, range of motion and breathing exercises, prior to the 5 minutes of stretching. This component of the intervention was focused on low-intensity exercises without use of any additional loading (e.g., hand weights or resistance bands), with HR maintained below target zone, and were deemed as a suitable active control condition (Gregory et al., 2016). Participants performed 10 minutes of static (e.g., postures in narrow stance, tandem stance and single leg stance), dynamic (e.g., walk tandem line on heels or toes) and functional balance (e.g., changing direction on cue, walking with head turns). The session ended with 5 minutes of range of motion exercises (e.g., shoulder, hip and wrist circles) and accompanied by either standing or sitting breathing exercises.

2.3.2. Mind-motor training intervention

In addition to the multiple-modality exercise intervention, participants within the M4 group also performed SSE training (Shigematsu et al., 2008a), prior to the 5 minutes of stretching. The SSE program is a group-based intervention performed on a gridded floor mat (2.5 m × 1 m) containing 10 rows with 4 equal-sized squares per row. The training protocol entails the reproduction of previously demonstrated complex stepping patterns on the SSE mat (see Figure 1). The stepping patterns are demonstrated by an instructor and participants are expected to memorize, and further attempt to reproduce each stepping pattern by memory. Instructors could not physically intervene, but in instances where participants were having difficulty reproducing the SSE patterns, they were provided oral cues. There are more than 200 stepping patterns created for SSE (Shigematsu et al., 2008a), and the complexity of these stepping patterns is given according to the number of steps per pattern, as well as the order and direction of foot placement across the SSE mat. In our study, the SSE sessions were carried out in groups of no more than 6 participants per mat. To ensure equal group progression throughout the program, the complexity of the stepping patterns within each session was increased only when the majority of participants (i.e., 75%) had successfully performed a given stepping pattern at least four times. The goal was to progress through as many SSE patterns as possible over the 24-week intervention period. Additionally, to create a positive social atmosphere, participants were encouraged to assist each other, as necessary, by providing cues to accurately perform the stepping patterns.

Figure 1. Participants performing stepping patterns during a square-stepping exercise session.

2.4. Data collection

2.4.1. Baseline variables

Baseline assessments were performed after obtaining written informed consent and prior to participant randomization. Neuropsychological assessments were performed using the MMSE, the Montreal Cognitive Assessment (MoCA), (Nasreddine et al., 2005) and the Centre for Epidemiological Studies Depression Scale (Lewinsohn et al., 1997). Participant clinical and demographic data included: age, sex, race, medical history, weight, height, body mass index (BMI), and 24-hour blood pressure. Additionally, cardiorespiratory fitness was assessed at baseline (predicted maximal oxygen consumption [pVO_2 max]) using the STEP tool (Stuckey et al., 2012).

2.4.2. Study outcomes

The primary objective of the M4 Study was to investigate changes in global and domain-specific cognitive functioning via the Cambridge Brain Sciences cognitive battery (Hampshire et al., 2012), following the 24-week intervention period and a 26-week no-contact follow-up. The focus of this article, however, is to report findings of our secondary outcome in which we investigated changes in spatiotemporal gait characteristics. Please see Gregory et al., (2016) for further details regarding the M4 Study.

Spatiotemporal gait characteristics were collected using a portable electronic walkway system (GAITRite® System, 580 × 90 × 0.63 cm (L × W × H), scanning frequency of 60 Hz, Software Version 4.7.1, CIR Systems, Peekskill, NY, USA). The GAITRite® is valid and reliable for gait assessment in various populations, including older adults with and without mobility impairment (Bilney et al., 2003; Montero-Odasso et al., 2009). Participants completed two usual walking trials (i.e., walking at usual pace), followed by two separated walking trials under DT conditions (i.e., phonemic verbal fluency [VF] and serial sevens [S7] tasks) at a self-selected walking velocity. In the DT gait VF task, participants were instructed to name as many animals (baseline), vegetables (24 weeks), and countries (52 weeks) as possible. For the S7 task, participants were instructed to perform subtractions by sevens starting at 100 (baseline), 90 (24 weeks), and 80 (52 weeks). No instructions to prioritize gait performance or responses to the cognitive tasks during the DT conditions were given to the participants. In each trial, participants were instructed to start walking 1 m before and continue to walk until 1 m beyond the electronic walkway, in order to measure steady-state walking. Gait performance over two walking trials were averaged and used for analysis. The measures of interest were usual and DT (VF and S7) gait velocity (cm/s), step length (cm), and cycle time variability (coefficient of variation [%]) (Montero-Odasso et al., 2014).

In addition, we were interested in cognitive performance under the DT gait conditions (i.e., accuracy). As such, following previous methods (Maclean et al., 2017a), DT cognitive accuracy while dual-tasking was measured based on the number of correct cognitive responses (ccr) provided by each participant during the two DT gait assessments. This number was then divided by the time (s) taken for each individual DT condition. To adjust for performance errors, ccr/s was finally multiplied by the ratio of correct responses to total responses. We discarded repeated answers during each trial and did not consider answers that were deemed to be inappropriate or incorrect (e.g., naming ‘cities’ instead of ‘countries’ during the DT gait VF trial at 52 weeks).

2.5. Sample size calculations

The sample size included in this study was calculated based on the primary outcome from the larger RCT (i.e., difference between groups at 24 weeks in global cognitive functioning derived from the computer-based Cambridge Brain Sciences cognitive battery) (Gregory et al., 2016; Owen et al., 2010). Briefly, results from a previous meta-analysis indicated that exercise could improve cognition with an moderate effect size ($d = 0.48$) (Colcombe and Kramer, 2003). Although our study has a different design (e.g., intervention and outcome), we decided to take this number into account. Therefore, a sample size of 52 participants per group would have an 80% power at the 5% significance level to detect a moderate effect size of 0.55 in cognition. Considering a dropout rate of 20% during the 24-week intervention period, our final sample size was estimated at 130 participants (65 in each group). In a recent meta-analysis (Hortobágyi et al., 2015), multiple-modality exercise was associated with improvements in usual gait velocity in healthy older adults with an effect size of $d = .77$. Thus, if gait velocity were used to estimate the study sample size as the primary outcome, considering an 80% power at 5% significance level and a dropout rate of 20%, we would need only 25 participants per group (50 participants in overall) to detect a significant treatment effect.

2.6. Statistical Analysis

We conducted linear mixed models for repeated measurements (Fitzmaurice et al., 2011) to assess differences between groups in mean change from baseline to 24 weeks. Within the models, we also examined differences between groups from baseline to 52 weeks, and differences within groups from baseline to 24 and 52 weeks. The terms included in the models were: group, time, and group × time. Time was modeled categorically using two indicator variables representing each time point (baseline as reference category). All analyses were performed using the intent-to-treat approach, including all randomized participants, regardless of compliance with the program and follow-up assessments (Fitzmaurice et al., 2011). An advantage of the mixed effects regression modeling approach is that it does not require each participant to have the same number of measurements provided data are missing at random (i.e., after taking observed data into account, there are no systematic differences between participants with complete data as compared to those with missing data). This is also an assumption made by most multiple imputation methods (Fitzmaurice et al., 2011). We also performed a sensitivity analysis including only those who completed the study assessments at all time points. As well, for the main outcomes of the study, we conducted analyses adjusting for global cognitive functioning at baseline (MoCA scores). Interpretation of study results were primarily based on mean estimation and associated 95% confidence intervals. All analyses were performed using IBM® SPSS® Statistics for Mac, Version 21 (Armonk, NY: IBM Corp).

3. Results

3.1. Enrollment, randomization, and adherence

This study was conducted between January 13, 2014 and March 14, 2016. Participants were enrolled in 4 waves of assessments and intervention over a period of 14 months. During the screening process, 169 individuals were assessed for eligibility; 11 did not meet the inclusion criteria and 31 declined to participate. Thus, 127 participants were included and randomized to either the M2 (n=64) or M4 (n=63) groups,109 participants attended assessments at 24 weeks, and 102 returned for the final assessments at 52 weeks (see Figure 2). Participants had completed the study and the average attendance to the exercise sessions was 72% for the M2 group (52 out of 72 sessions) and 68% for the M4 group (49 out of out of 72 sessions). A two-sided independent samples t-test revealed no significant differences between groups in participant average attendance ($p = .3$). At the end of the intervention period, participants in the M4 group had achieved the Advanced Level 3 of the SSE program, with stepping patterns ranging from 12 to 16 steps, and with steps performed in a broader range of directions (backwards, diagonal, and backwards diagonal), as well as with stepping patterns incorporating wider and longer steps (3 to 5 squares between feet). Considering attendance level and program achievement, the SSE program was shown to be feasible in this specific population (i.e., older adults with SCC) and no study-related adverse events were recorded.

Table 1 provides the baseline descriptive characteristics of the 127 participants. In overall, the study participants were mostly Caucasian, highly educated and presented with sings of cognitive deterioration based on mean MoCA scores. Further observation of the domain-specific MoCA scores revealed that participants in both groups showed low scores in the delayed-recall memory composite, which indicate memory loss possibly underlying the nature of the self-reported SCC. As well, even though participants involved in the study were high-functioning and lived independently in the community, pVO_2max assessment yielded classification of ‘poor’ to ‘fait’ cardiorespiratory fitness compared to age and gender reference values (Heyward and Gibson, 2014).The study outcomes at baseline are presented in Table 2, participants demonstrated high gait velocity and low cycle time variability for age, indicating preserved function (Studenski et al., 2011).

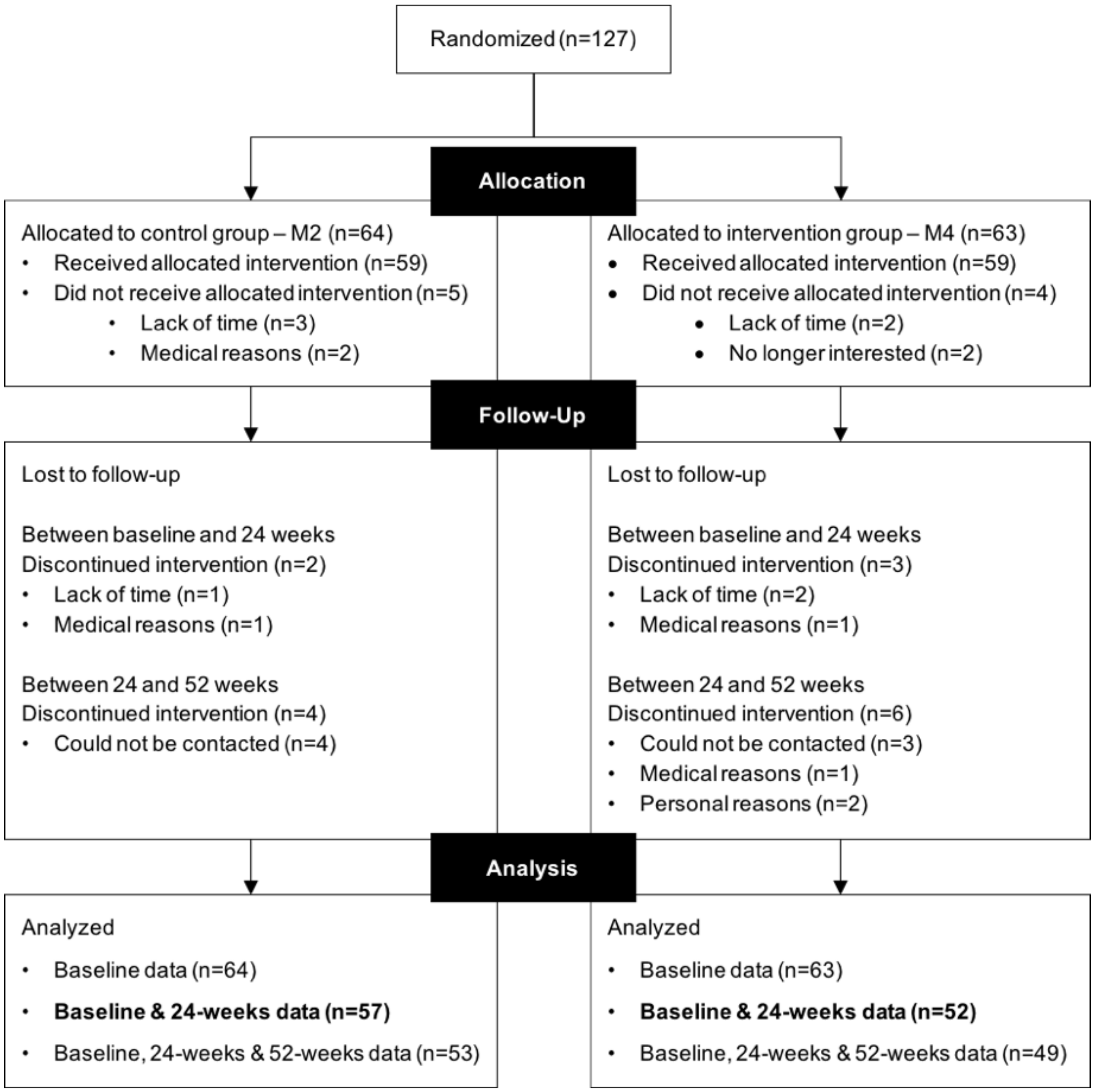

Figure 2. Flow of participant in the 24-week randomized controlled trial with a 28-week no-contact follow-up. For the M4 group, data from 4 participants were missing at 24 weeks and, therefore, not included in analyses.

Table 1. Baseline demographics and clinical characteristics.

Variables [a,b]	M2 (n = 64)	M4 (n = 63)
Demographics		
Age, yr	67.4 (7.2)	67.6 (7.5)
Females	46 (71.9%)	44 (69.8%)
Caucasian	62 (98.4)	61 (96.8)
Education, yr	13.8 (3)	13.3 (2.7)
MoCA, score (/30) [c]	25.6 (2.4)	25.3 (2.7)
Visuospatial/Executive (/5)	4 (2)	4 (2)
Naming (/3)	3 (0)	3 (0)
Attention (/6)	6 (1)	6 (1)
Language (/3)	3 (0)	3 (0)
Abstraction (/2)	2 (0)	2 (0)
Delayed recall (/5)	3 (2)	3 (2)
Orientation (/6)	6 (0)	6 (0)
≤ 12 years of education	19 (30%)	15 (24%)
MMSE, score	29.2 (1)	29 (1.2)
CES-D, score	9.4 (7.4)	10 (8.9)
24-hour systolic BP, mmHg	129.6 (15.2)	126.5 (11.3)
24-hour diastolic BP, mmHg	74.2 (8.3)	72.2 (8.1)
Weight, kg	80.8 (17.7)	80 (13.8)
Height, m	1.65 (0.1)	1.65 (0.1)
BMI, kg/m^2	29.7 (6.2)	29 (4.1)
pVO_2max, ml/kg/min	26.8 (8)	27.1 (7.9)
Medical history, *n* (%)		
Hypertension	32 (50%)	36 (57.1%)
Hypercholesterolemia	23 (35.9%)	28 (44.4%)
Type 2 diabetes	5 (7.8%)	7 (11.1%)
Myocardial infarction	4 (6.3%)	5 (7.9%)
Atrial fibrillation	-	3 (4.8%)
Angina/coronary artery disease	1 (1.6%)	2 (3.2%)
Aneurysm	1 (1.6%)	2 (3.2%)
Former smoker	28 (44.4%)	29 (46%)
Current smoker	1 (1.6%)	1 (1.6%)

Abbreviations: M2, multiple-modality group; M4, multiple-modality, mind-motor group; MMSE, Mini-Mental Status Examination; MoCA, Montreal Cognitive Assessment; CES-D, Centre for Epidemiological Studies Depression Scale; BP, blood pressure; pVO_2max, predicted maximal oxygen consumption.

[a] Data presented either as mean (standard deviation) or no. (%) where applicable.

[b] There were no differences between groups in any of the baseline measurements.

[c] Domain-specific MoCA scores presented as median and interquartile range.

Table 2. Baseline study outcomes

Outcomes [a,b]	M2 (n = 64)	M4 (n = 63)
Usual gait		
Gait velocity, cm/s	116.5 (16.7)	116.6 (20.9)
Step length, cm	64.7 (7.9)	64.03 (9.8)
Cycle time variability, %, Mdn (IQR)	1.8 (1.5, 2.3)	2.08 (1.5, 2.8)
DT Gait (VF)		
Gait velocity, cm/s	97.6 (23.5)	94.6 (26.7)
Step length, cm	61.2 (8.7)	59.7 (10.8)
Cycle time variability, %, Mdn (IQR)	3.8 (2.3, 7)	4 (2.1, 8.1)
DT Gait (S7)		
Gait velocity, cm/s	88.9 (26.7)	85.4 (28.2)
Step length, cm	59.9 (10.2)	58.4 (10.6)
Cycle time variability, %, Mdn (IQR)	5 (2.7, 8.1)	4.6 (3, 7.1)
Secondary outcomes		
DT cognitive accuracy (VF), ccr/s	1.16 (.33)	1.02 (.33)
DT cognitive accuracy (S7), ccr/s	.40 (.35)	.37 (.36)

Abbreviations: M2, multiple-modality group; M4, multiple-modality, mind-motor group; Mdn, median; IQR, interquartile range, VF, verbal fluency task; S7, serial sevens task; CCR, rate of correct cognitive responses.

[a] Data presented as mean (standard deviation) or otherwise indicated.

[b] There were no differences between groups at baseline in any of the study outcomes.

3.2. Study outcomes

Table 3 shows differences between groups in estimated mean change from baseline to 24 and 52 weeks in the study outcomes. At 24 weeks, the M4 group demonstrated inferior performance in usual gait velocity, usual step length, and DT gait velocity (VF) compared to the M2 group. Differences between groups in usual gait velocity remained significant and 52 weeks, favouring the M2 group. No other differences were seen in the remaining outcomes; however, the M4 group demonstrated a trend for higher DT cycle time variability (VF) at 24 weeks ($p = .054$) compared to the M2 group.

Regarding within-group analyses, Figure 3 shows the estimated mean change from baseline to 24 and 52 weeks. At 24 weeks, improvements were observed in usual gait velocity and usual step length among participants in the M2 group; whereas the M4 group demonstrated decline in DT step length (VF) at the same time point. Lastly, the M4 group demonstrated a trend for increased DT cognitive accuracy (VF) at 52 weeks (p = .052).

In addition, the sensitivity analysis, which included only participants who completed the study, did not change the main findings, except that it confirmed the trend for increased DT cycle time variability (VF) at 24 weeks (p = .049) in the M4 group compared to the M2 group (see Supplemental Table 1). As well, there results remained the same when adjusting for global cognitive functioning at baseline (MoCA scores).

Table 3. Differences between groups in the study outcomes

	Difference between groups in estimated mean change (95% CI) [a]					
Outcomes [b]	24 weeks	*p* Values		52 weeks	*p* Values	
Usual gait						
Gait velocity, cm/s	–10.1 (–15.8 to –4.4)	<.001*	.001**	–6.7 (–13.4 to –.05)	.048*	.044**
Step length, cm	–2.9 (–4.8 to –1)	.003*	.003**	–2.1 (–4.2 to .1)	.06	.06**
Cycle time variability, % [c]	.02 (–.08 to .11)	.74	.72	–.01 (–.11 to .09)	.86	.89
Dual-task gait (VF)						
Gait velocity, cm/s	–7.9 (–15.5 to –.3)	.043*	.039**	–4.8 (–14.7 to 5)	.33	.32
Step length, cm	–1.8 (–4 to .5)	.11	.11	–.4 (–3 to 2.2)	.76	.74
Cycle time variability, % [c]	.15 (–.002 to .29)	.054	.052	.11 (–.06 to .27)	.19	.18
DT gait (S7)						
Gait velocity, cm/s	–7.3 (–15.9 to 1.2)	.09	.085	–7.5 (–17 to 1.9)	.11	.11
Step length, cm	–1.5 (–4 to 1)	.23	.22	–2.2 (–4.7 to .3)	.09	.085
Cycle time variability, % [c]	.11 (–.05 to .27)	.17	.15	.1 (–.07 to .27)	.23	.21
Secondary outcomes						
DT cognitive accuracy (VF), ccr/s [d]	–.05 (–.23 to .14)	.62	.58	.13 (–.04 to .31)	.14	.16
DT cognitive accuracy (S7), ccr/s [d]	–.04 (–.22 to .13)	.62	.64	.02 (–.16 to 19)	.86	.84

Reference category = M2.

Abbreviations: 95% CI, confidence interval; M2, multiple-modality group; M4, multiple-modality, mind-motor group; DT, dual-task; VF, verbal fluency task; S7, serial sevens task; CCR, rate of correct cognitive response.

[a] Calculated from linear mixed effects regression models that included group (M2 or M4), time (baseline, 24 and 52 weeks), and group × time interaction terms. A total of 13 models were conducted, corresponding to each outcome listed in the first column.

[b] M4 group: baseline, n=63; 24 weeks, n=52; 52 weeks, n=49. M2 group: baseline, n=64; 24 weeks, n=57; 52 weeks, n=53.

[c] Log transformation applied.

[d] Square root transformation applied.

* Significant differences between groups in estimated mean change from baseline.

** Significant differences between groups in estimated mean change from baseline adjusted for MoCA scores.

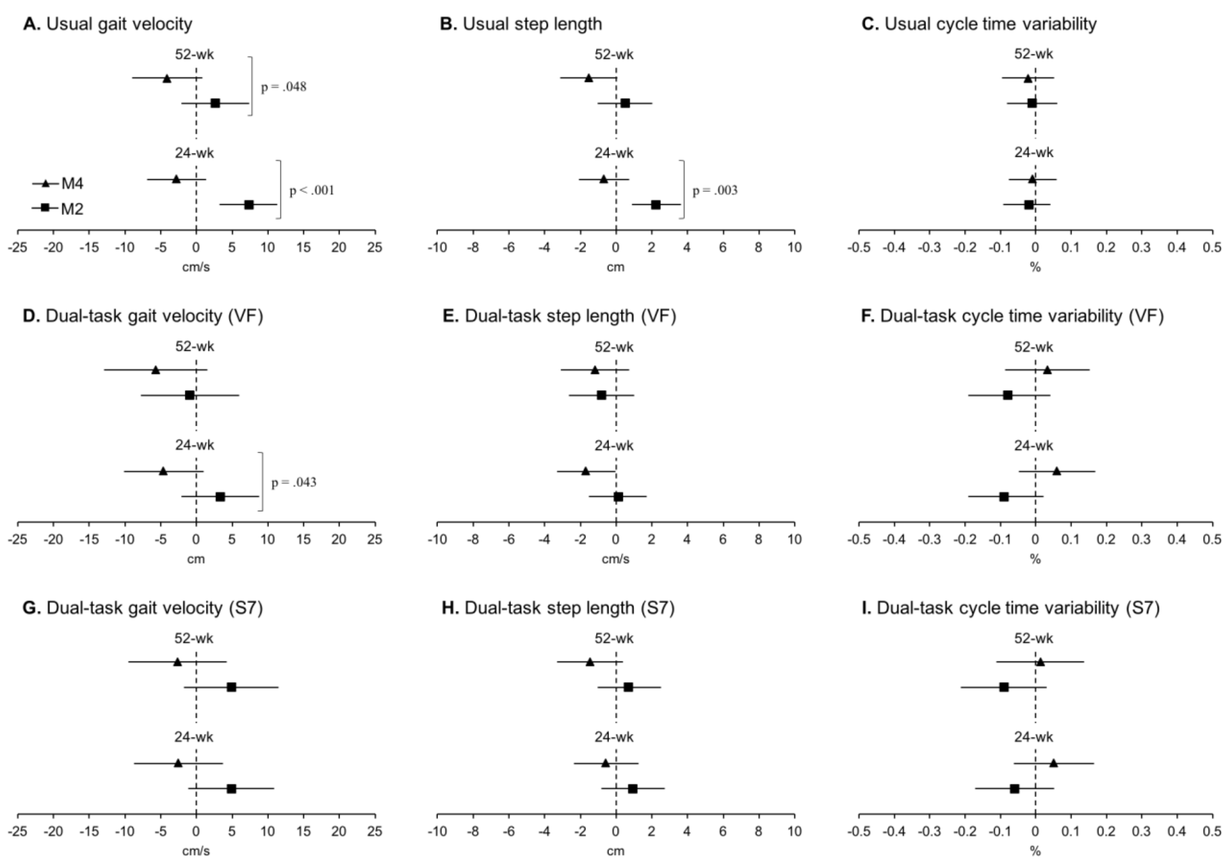

Figure 3. Within-group estimated mean changes from baseline in the study primary outcomes. Solid squares (M2) and triagles (M4) represent point estimated group mean change from baseline; bars represent associated 95% confidance intervals. Confidence intervals not including zero (i.e., not crossing the vertical dotted line) indicate significant differences from baseline. P value indicates significant differences between groups in estimated mean change from baseline (see supplemental table 2 for specific). Abbreviations: M2, multiple-modality group; M4, multiple-modality, mind-motor group. 24-wk, intervention endpoint; 52-wk, study endpoint

4. Discussion

The results of the current study indicated that the addition of mind-motor training (i.e., SSE) to a standardized multiple-modality exercise intervention did not yield further improvements in spatiotemporal gait characteristics and DT cognitive accuracy. Nonetheless, the multiple-modality exercise intervention with additional balance, range of motion and breathing exercises (i.e., M2) did impart improvements to usual gait velocity, step length, and DT gait velocity (VF) at 24 weeks, and did retain the gains in usual gait velocity at 52 weeks. The changes observed in the M2 group are in accordance with previous investigations (Hortobágyi et al., 2015; Plummer et al., 2015). Results from a systematic review and meta-analysis indicated that multiple-modality exercise interventions may yield clinically significant changes in gait velocity in older adults (mean change 0.09 m/s or 8.4%) similar to our findings (0.07 m/s or 6.25%) (Hortobágyi et al., 2015).

A surprising finding of the current study is that despite the fact that SSE was developed to promote improvements in lower extremity functioning in at-risk older fallers (Shigematsu et al., 2008a), it did not provide additional benefits to gait performance when added to the M2 exercise component. From a neuromuscular point of view, the lack of improvement within the M4 group may indicate that the specific biomechanical and/or physical requirements of SSE are not intrinsically associated with the mechanisms underlying exercise-induced changes in gait dynamics in older adults (Hausdorff et al., 2001a). Further, the fact that M2 group received additional balance exercises may account for the superior gait performance in comparison to the M4 group. Indeed, positive changes in gait performance following balance training in older adults have been widely reported in the literature (Hortobágyi et al., 2015), and have been associated with reduced risk for mobility impairment and falls (Sherrington et al., 2011). Taking this perspective, even though previous studies (Shigematsu et al., 2008a, 2008b; Shigematsu and Okura, 2006) indicated that SSE improved balance in older adults–which was the basis of our hypothesis that SSE would impart similar or greater benefits than the additional balance exercises–we failed to report such improvements.

It is important to mention, however, that the SSE program encompasses gradual progression in complexity to perform the stepping patterns; this complexity is determined by the number of steps performed, as well as the direction and length of the steps. Therefore, at a certain point in the program (advanced phase), participants did perform stepping patterns requiring wider and lengthier steps and thus, improvements in spatiotemporal gait characteristics could be expected. As the key component of SSE is its simultaneous cognitive-physical demand, we argue that it was a valid hypothesis to expect favourable changes in the study outcomes, particularly with regards to DT gait measures.

In addition, it was hypothesized that the specific requirements of the SSE exercise would not directly train the specific gait outcomes that were considered for this study, but would act more specifically to train the control of gait on a more global scale. Among healthy populations, the control of gait is rather automatic and very little attention and/or effort is needed for habitual daily ambulation (Woollacott and Shumway-Cook, 2002). However, the SSE removes the habitual automatic walking response, and forces participants to actively modify their gait to successfully complete the task. This active modification of gait was also thought to be the key to the potential effectiveness of the SSE among relatively pre-clinical patient populations; a conscious modification of gait would potentially serve to strengthen the neural control of global gait performance.

Exercise-induced improvements in gait performance are primarily attributed to gains in muscle strength and neuromuscular control of the lower extremities (Hausdorff, 2005; Hausdorff et al., 2001a, 2001b; Zhuang et al., 2014), especially with respect to gait velocity (Hortobágyi et al., 2015). For instance, gains in gait velocity over a 22-week exercise intervention program were associated with increased muscle strength in the hip flexors and ankle dorsiflexors muscles (Lord et al., 1996). In the SSE sessions, the main goal was to complete the stepping pattern accurately, however, time to complete the tasks was not a main priority of the program. In this scenario, participants were expected to observe and retain information about the stepping patterns, then proceed to their execution in order to maintain forward gait, at a relatively slow gait velocity, regardless of participants' individual abilities. This may be understood as a lower-intensity set of stimuli that did not reach the threshold to impart muscle adaptions and induce gains in gait performance compared to the M2 group, which received additional balance exercises. Additionally, the SSE stepping patterns were executed in a way that does not necessarily correspond to the configuration of normal walking (e.g., backwards, lateral, and diagonal steps) and may have negatively influenced the results within the M4 group, ultimately indicating task-specific effects of the SSE intervention unrelated to normal walking.

Looking at our findings from a neurological/cognitive perspective, it was also expected that SSE would improve DT gait parameters to a greater extent in the M4 group compared to the M2 group. Previous studies reported that SSE has been associated with improvements in EF subdomains (i.e., attention and mental flexibility) (Shigematsu, 2014; Teixeira et al., 2013), which are understood as primary cognitive functions and/or brain networks involved in DT gait functioning (Yogev-Seligmann et al., 2008). Therefore, it was believed that even though SSE is of lower physical intensity, it would enhance DT gait parameters by benefiting EF, via a more neurological/cognitive pathway as opposed to a neuromuscular pathway, due to its high cognitive demand. In reality, we observed that the M4 group showed a decay in one of the DT gait velocity (VF) outcomes after the intervention, which leaded to statistically significant differences between groups at 24 weeks.

Given that no changes in any other DT gait parameters (under either VF or S7 conditions) were noted, it is possible that this singular between-group difference in DT gait velocity (VF) could be explained by the same neuromuscular mechanisms described previously. That is, participants had slower DT gait velocity (VF) probably due the lack of an overall effect of SSE on gait, and thus, the DT component did not change that relationship. If SSE had a negative effect on the cognitive aspect of the DT, it would have likely appeared in the other DT gait parameters, particularly under the serial sevens condition (S7), since this task has been shown to be more cognitively demanding than the VF task (Li et al., 2014). Furthermore, the measures of cognitive accuracy recorded from both DT gait VF and S7 conditions did not differ between groups at 24 weeks, which supports this hypothesis.

Nonetheless, we observed a trend for increased DT cycle time variability (VF) in the M4 group that is worth discussing. Increased variability in gait parameters may indicative of impairment in cognitive control of gait, particularly EF (Springer et al., 2006), and has been associated with increased risk of falling (Hausdorff, 2005). Although this finding may indicate an adverse effect of SSE in the M4 group, it should be interpreted with caution. We did not measure EF in the current study, therefore it is unknown whether adverse changes in DT cycle time variability was associated with unfavorable changes in EF. Nonetheless, this assumption is unlikely given that SSE has been associated with improve EF in previous studies (Shigematsu, 2014; Teixeira et al., 2013). Rather, we argue that because of the above describe characteristics of the SSE program, increased gait variably would likely result from a more cautious gait pattern developed in response to performing stepping patterns requiring increased attention and concentration. In fact, increased gait variability is a marker of cautious gait in fallers (Herman et al., 2005). It is paramount, however, to bear in mind that the trends for increased DT cycle time variability were nonexistent at 52 weeks, suggesting that, if any, the adverse effects of SSE on gait variability would not permanent and would wear off after program session.

After the no-contact follow-up period, the M4 group demonstrated trends for improvements in DT cognitive accuracy (VF); this was not seen in the M2 group. Aerobic-based and multiple-modality exercise interventions have been shown to improve VF in this population under single task conditions (Baker et al., 2010; Suzuki et al., 2012); however, under DT conditions, exercise-induced changes in DT cognitive accuracy has not been fully explored. Thus, the trend for improved performance of the M4 group in the VF task may be indicative of delayed-treatment impact of the exercise intervention with additional SSE (Teixeira et al., 2013), although this requires further exploration particularly with regards to clinical meaningfulness of these measures. This finding would implicate superior efficiency in proper allocation of attention resources to the cognitive task while maintaining stable gait velocity, which may be an encouraging sign of improvements in EF, particularly in our sample of older adults with SCC (Maclean et al., 2017b).

In sum, we speculate that the lack of SSE superior effects to drive between-group differences in DT gait parameters may be due to two main reasons: 1) the short duration and different frequency in which the mind-motor component was administered compared to previous studies (Gill et al., 2016; Teixeira et al., 2013), along with the low-intensity aspect of the SSE component; and 2) SSE could target specific cognitive functions/brain networks different from those required under DT gait conditions and, therefore, a significant treatment effect could not be expected under these circumstances. Another relevant factor to be taken into account when interpreting our findings is participants' baseline characteristics. This is particularly important given that participant health and functional status prior to the beginning of any given exercise regimen can mediate the effect of exercise on gait performance (Hortobágyi et al., 2015). For instance, in a study including patients with objective cognitive impairment, poorer baseline motor performance was the only factor related to greater response to the exercise training (Hauer et al., 2012). In this study, we recruited high-functioning community-dwelling older adults who, despite reporting signs of early cognitive deterioration (i.e., SCC), already presented relatively higher gait velocity and lower gait variability before the program, compared to population parameters (Studenski et al., 2011). Consequently, the lack of improvement in the M4 group may also be due the high-functioning aspect of our sample that would limit the extent to which the relatively low-intensity SSE would impart additional benefits to gait performance (Hausdorff et al., 2001a; You et al., 2009). In other words, this could indicate a dose-response relationship, where a higher-intensity intervention would be necessary to observe significant changes in gait parameters in high-functioning older adults, even in those with SCC (Hortobágyi et al., 2015; Lopopolo et al., 2006). Moreover, past studies have shown that higher intensities of AE may yield functional and morphological alterations in brain regions associated with the cognitive control of gait (Berchicci et al., 2013) and improve usual gait and DT gait performance (Iuliano et al., 2015; Snowden et al., 2011).

This study presents several limitations. The lack of a non-exercising control group impaired our ability to control for the possible influence of external factors. Further, limitations regarding the DT assessments are also noted, including: 1) the task performance was not randomized (i.e., usual gait followed by DT gait VF, and then DT gait S7); 2) performance on the secondary cognitive tasks within the DT gait evaluation was not methodologically controlled (i.e., VF and S7 tasks isolated, without the walking task). Thus, our ability to determine whether changes in DT gait performance were similar to change in cognitive task (isolated VF and S7 tasks) is limited. In addition, AE intensity was controlled based on participants indirectly monitoring their own HR (i.e., via radial artery pulse), which could have created room for underestimations and participants may have exercised at different intensities from what was prescribed. In addition, due to our group-based intervention, we were not able to monitor progression in both exercise groups to an individual level; therefore, it cannot be concluded with high confidence that each individual performed at their optimal performance. Finally, individuals in this study were predominantly Caucasian, well educated, functionally independent, and relatively healthy; thus, results may not be generalized to other populations.

5. Conclusions

The current investigation explored the influence of multiple-modality exercise with either additional mind-motor training or an active control intervention (e.g., additional balance, range of motion and breathing exercise) on mobility outcomes in older adults with SCC. Our findings demonstrated that additional SSE training was not effective to improve usual and DT spatiotemporal gait characteristics compared an active control intervention. In fact, participants enrolled in the active control group experienced greater changes in usual gait velocity, step length and DT gait velocity after the 24-week intervention program.

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