



## Multiple-modality exercise and mind-motor training to improve mobility in older adults: A randomized controlled trial<sup>☆</sup>



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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 = 0.052) 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.

### 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

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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., 2009, 2013), 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 performing 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 et al., 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](http://ClinicalTrials.gov) on 29 April 2014

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