Summer 7-2015

The Healthy Mind, Healthy Mobility Trial: A Novel Exercise Program For Older Adults

Dawn P. Gill  
*Western University*

Michael A. Gregory  
*Western University*

Guangyong Zou  
*Western University*

Teresa Liu-Ambrose  
*University of British Columbia*

Ryosuke Shigematsu  
*Mie University*

See next page for additional authors

Follow this and additional works at: [https://ir.lib.uwo.ca/petrellateampub](https://ir.lib.uwo.ca/petrellateampub)

Part of the [Community Health and Preventive Medicine Commons](https://ir.lib.uwo.ca/hnhs), [Rehabilitation and Therapy Commons](https://ir.lib.uwo.ca/hnhs), and the [Sports Sciences Commons](https://ir.lib.uwo.ca/etit)

Citation of this paper:

Gill, Dawn P.; Gregory, Michael A.; Zou, Guangyong; Liu-Ambrose, Teresa; Shigematsu, Ryosuke; Hachinski, Vladimir; Fitzgerald, Clara; and Petrella, Robert, "The Healthy Mind, Healthy Mobility Trial: A Novel Exercise Program For Older Adults" (2015). *Lifestyle Research Team*. 3.
[https://ir.lib.uwo.ca/petrellateampub/3](https://ir.lib.uwo.ca/petrellateampub/3)
Authors
Dawn P. Gill, Michael A. Gregory, Guangyong Zou, Teresa Liu-Ambrose, Ryosuke Shigematsu, Vladimir Hachinski, Clara Fitzgerald, and Robert Petrella
The Healthy Mind, Healthy Mobility Trial: A Novel Exercise Program for Older Adults

Dawn P. Gill\textsuperscript{1,2}, Michael A. Gregory\textsuperscript{3}, Guangyong Zou\textsuperscript{4,5}, Teresa Liu-Ambrose\textsuperscript{6,7}, Ryosuke Shigematsu\textsuperscript{8}, Vladimir Hachinski\textsuperscript{9}, Clara Fitzgerald\textsuperscript{10}, and Robert J. Petrella\textsuperscript{1,2}

\textsuperscript{1}Department of Family Medicine, Western University, London, ON, Canada; \textsuperscript{2}Aging, Rehabilitation & Geriatric Care Research Centre, Lawson Health Research Institute, London, ON, Canada; \textsuperscript{3}School of Health and Rehabilitation Studies, Western University, London, ON, Canada; \textsuperscript{4}Department of Epidemiology & Biostatistics, Western University, London, ON, Canada; \textsuperscript{5}Robarts Clinical Trials of Robarts Research Institute, Western University, London, ON, Canada; \textsuperscript{6}Department of Physical Therapy, University of British Columbia, Vancouver, BC, Canada; \textsuperscript{7}Djavad Mowafaghian Centre for Brain Health, Vancouver, BC, Canada; \textsuperscript{8}Faculty of Education, Mie University, Japan; \textsuperscript{9}Department of Clinical Neurological Sciences, Western University, London, ON, Canada; \textsuperscript{10}Canadian Centre for Activity and Aging, Faculty of Health Sciences, Western University, London, ON, Canada

Corresponding Author:
Robert J. Petrella, MD, PhD
Centre for Studies in Family Medicine
Western Centre for Public Health and Family Medicine, Second Floor
Western University
1151 Richmond St.
London, ON
N6A 3K7
Phone: 519-661-2111 ext. 20658
Fax: 519-858-5114
E-mail: petrella@uwo.ca

Running head: Healthy Mind, Healthy Mobility Trial

This study was supported by an Operating Grant from the Canadian Institutes of Health Research (Grant number: 130474), a Team Grant from the Canadian Institutes of Health Research (Grant number: 201713) and by the Fellowship in Care of the Elderly Research, a training award through the Aging, Rehabilitation, and Geriatric Care Research Centre of the Lawson Health Research Institute in partnership with the St. Joseph’s Health Care Foundation. The study authors have no relevant conflicts of interest to report. Results of this study do not constitute endorsement by the American College of Sports Medicine.
Abstract

**Background:** More evidence is needed in order to conclude that a specific program of exercise and/or cognitive training warrants prescription for the prevention of cognitive decline. We examined the effect of a group-based standard exercise program for older adults, with and without dual-task training, on cognitive function in older adults without dementia. **Methods:** We conducted a proof-of-concept, single-blinded, 26-week randomized controlled trial whereby participants recruited from pre-existing exercise classes at the Canadian Centre for Activity and Aging in London, Ontario were randomized to the intervention group (exercise + dual-task; EDT) or the control group (exercise only; EO). Each week (2 or 3 days/week), both groups accumulated a minimum of 50 minutes of aerobic exercise (target 75 minutes) from standard group classes and completed 45 minutes of beginner-level Square Stepping Exercise (SSE). The EDT group was also required to answer cognitively challenging questions while doing beginner-level SSE (i.e., dual-task training). The effect of interventions on standardized global cognitive function (GCF) scores at 26 weeks was compared between the groups using the linear mixed effects model approach. **Results:** Participants [n = 44; 68% female; mean (SD) age: 73.5 (SD 7.2) years] had on average, objective evidence of cognitive impairment [Montreal Cognitive Assessment scores, mean (SD): 24.9 (1.9)] but not dementia [Mini-Mental State Examination scores, mean (SD): 28.8 (1.2)]. After 26 weeks, the EDT group showed greater improvement in GCF scores compared to the EO group [difference between groups in mean change (95% CI): 0.20 SD (0.01 to 0.39), p = 0.04]. **Conclusion:** A 26-week group-based exercise program combined with dual-task training improved GCF in community-dwelling older adults without dementia. **Trial Registration:** ClinicalTrials.gov Identifier: NCT01572311

**Key Words:** exercise; cognition; community-based; prevention; older adults
Introduction

The incidence of cognitive impairment without meeting the diagnostic criteria for dementia (i.e., cognitive impairment, not dementia; CIND), is currently two-fold greater than the incidence of Alzheimer’s disease and related dementias (33). Consequently, early prevention strategies for ameliorating cognitive decline should be directed towards persons who are at elevated risk and prior to the establishment of significant objective cognitive impairment or dementia, in order to observe the best clinical outcomes (20).

A recent editorial (23) suggested that the identification of modifiable risk factors associated with specific cognitive deficits is a significant priority in cognitive research and clinical practice. Numerous observational studies have demonstrated that those who are more physically active are less likely to experience cognitive decline and dementia in later life (3, 4). Aerobic exercise training can facilitate heightened task-related cortical activity, improve performance on executive function (EF) tasks (8), and increase hippocampal volume (12) in cognitively healthy older adults, as well as promote increased hippocampal volume (46), improve neural efficiency and task performance during semantic memory retrieval tasks (42), and improve global cognitive functioning (24) in older adults with mild cognitive impairment (MCI). Despite these initial observations, the effects of exercise training on cognitive functioning appears to be dependent upon a number of factors (i.e., the type of exercise program, the duration and frequency of exercise training, and participant demographics), and remains incompletely understood (16, 25).

In 2011, an expert panel concluded that due to the low quality of the existing evidence, there was insufficient evidence to support the association of any modifiable risk factors (including cognitive and physical activities) with risk of cognitive decline (10).
Engaging in cognitively challenging activities requires the organization and direction of numerous neurological processes, including EF, processing speed, and memory (21), and has been found to stimulate neuroplasticity in aging (22). Dual-task training is a multi-dimensional cognitive training intervention that combines cognitive and motor tasks to directly train the EF networks of the brain (32) and evidence suggests that the associated dual-task neurological control processes are plastic and can be modified with training (11). A recent meta-analysis highlighted the cognitive and functional benefits of dual-task training (25); however, there were a limited number of articles included in the analysis (n=8) and few studies investigated the effects of dual-task training among older adults with indications of cognitive impairment.

Observational studies have also implicated social and cognitive disengagement as modifiable risk factors associated with cognitive impairment and dementia (37). Group-based senior’s fitness programs can help alleviate these concerns by providing an atmosphere that involves socialization with peers of similar age. Although recent evidence has highlighted the cognitive benefits of group-based exercise training (30, 36, 50), these studies were limited by small sample sizes, a lack of standardized socialization components between study groups, heterogeneity in the interventions between studies, and the omission of active control comparisons or longitudinal follow-up.

Square Stepping Exercise (SSE) is a low-cost and easily administered group-based exercise intervention that involves replicating a previously demonstrated stepping pattern in order to progress across a gridded floor mat. Although SSE was originally designed and deemed effective for improving lower extremity functional fitness and reducing falls risk factors in high-risk elderly fallers (41), recent results suggest that SSE may improve cognition [i.e., memory, and EF (39), and global cognition, attention, and mental flexibility (45)]. The excellent long-term
adherence to SSE (i.e., regular participation over a 4-year longitudinal follow-up) is driven by a number of factors, including the simplicity of the exercise program and the facilitation of the development of friendship and social communication between peers of similar age (40). These preliminary observations suggest that SSE may be an effective avenue to address multiple important risk factors for cognitive decline (i.e., cognitive and social disengagement) and that the incorporation of SSE within group-based exercise programs might provide additive cognitive benefits. Furthermore, the incorporation of a dual-task component and the associated additional level of difficulty to the cognitive requirements of beginner-level SSE may provide cognitive benefits above and beyond that which could be expected from the practice of beginner-level SSE alone.

The current evidence is insufficient to conclude that a specific program of physical exercise and/or cognitive training warrants prescription for older adults to prevent future cognitive decline (15, 25). The purpose of this study was to examine the effect of combining a group-based exercise program with dual-task training on cognitive function in active older adults with indications of CIND. Our primary objective was to examine the difference between groups (group-based exercise with dual-task training versus group-based exercise alone) on change in global cognitive functioning (GCF) following a 26-week program. We hypothesized that the combination of group-based exercise with dual-task training would improve GCF to a greater extent than group-based exercise alone.

**Methods:**

**Participants**

Participants were recruited from pre-existing exercise classes at the Canadian Centre for Activity and Aging (CCAA) (5) in London, Ontario via fliers, class announcements, and class rosters. All
participants were aged 55 to 90 years, were current and active members of CCAA exercise programs, demonstrated preserved instrumental activities of daily living (Lawton-Brody instrumental Activities of Daily Living scale $>6$) (26), and scored $\leq 27$ on the Montreal Cognitive Assessment (MoCA) (29). The MoCA score cut-off used in this study is slightly above the traditional cut-off indicative of cognitive impairment ($<26$) (29). The relatively healthy, highly educated, and ethnically uniform nature of the participants in this study (compared to participants used to inform normative data) (29), suggests that it may be warranted to use a higher cut-off to indicate subtle underlying cognitive difficulties and to identify individuals who may be at increased risk for future cognitive decline (35).

All participants were free of dementia [based on self-reported physician diagnosis or Mini-Mental State Examination (MMSE) score $<24$] (14), major depression (based on scoring Centre for Epidemiological Studies-Depression Scale (34) $>16$ combined with clinical judgment by the primary study physician), and other neurological or psychiatric disorders. Furthermore, participants who were unable to comprehend study procedures, or those with significant orthopaedic conditions, a recent history of severe cardiovascular conditions, or those who currently demonstrated blood pressure unsafe for exercise (47), were also excluded. The Western University Health Sciences Research Ethics Board approved this study and all participants provided written informed consent.

**Study Design**

We conducted a proof-of-concept, single-blinded, 26-week randomized controlled trial with a 26-week, no-contact follow-up. Assessments were performed at baseline (V0), 12 weeks (V1), 26 weeks (V2), and 52 weeks (V3). After V0, participants were randomized 1:1 (in one block) to either the intervention group (exercise + dual-task; EDT) or the control group (exercise only;
EO). The randomization sequence was computer-generated and concealed envelopes were used to assign group status. All assessors were blinded to group assignment.

**Interventions**

Over 26 weeks, participants took part in either a group-based exercise program alone [control group: exercise only (EO)] or with the addition of a dual-task training program [intervention group: exercise + dual-task (EDT)].

Participants in both groups continued to attend their CCAA group-based exercise classes for older adults that were led by certified CCAA Seniors’ Fitness Instructors (6) and involved aerobic exercise (largest component), as well as strength, balance, and flexibility training.

Participants attended the structured 60-minute or 75-minute group-based exercise classes, 2 or 3 times per week. Our focus was on keeping the prescribed aerobic exercise similar between groups; participants performed a minimum of 50 minutes (classes 2 days/week) to a maximum of 75 minutes (classes 3 days/week) of aerobic exercise from the classes. For those who only attended classes 2 days/week, these participants were instructed to log an additional 25 minutes of aerobic exercise each week outside of class (using a paper log provided). Individualized exercise training intensities were provided as part of the CCAA exercise program through one of two avenues: i) from performance on an annual maximal exercise stress test, or ii) following recommendations by Tanaka et al., (44) for those who abstained or were unable to complete the maximal exercise stress test. Participants were required to monitor and record their exercise intensity, before, at the mid-point, and immediately following the aerobic exercise portion of each class, and were instructed to try to meet their target heart rate (70-85% maximum heart rate). Thus, the amount of aerobic exercise performed per week was balanced between groups.
Immediately following exercise classes, participants took part in beginner-level SSE (41) (45 minutes per week, over 2 to 3 days/week). The SSE is a low-cost, indoor group exercise that was specifically developed to improve lower extremity functioning and prevent related disability in older adults (41). The SSE can be conceptualized as a visuospatial working memory task that requires a stepping response; however, the cognitive demands of the SSE are dependent upon the level of difficulty of the foot placement patterns being performed and progression through the stepping protocols. Both groups performed beginner SSE protocols only, requiring participants to observe and memorize an instructor-led demonstration of a specific stepping pattern involving simple forward, lateral and diagonal foot placements on a gridded mat (see Figure, Supplemental Digital Content 1, depiction several beginner SSE foot placement patterns). After adequate demonstration, participants were organized into groups of 6 or less, and were required to walk at a normal pace while replicating the previously demonstrated pattern. The beginner protocols were retained throughout the duration of the intervention, as they were not considered to provide a cognitive training stimulus on its own, and served as a lower extremity coordination exercise shared by both groups.

To provide the dual-task stimulus, participants in the intervention (EDT) group were also required to respond to cognitively challenging questions (i.e., semantic and phonemic verbal fluency tasks; randomly generated arithmetic) while participating in SSE. Specifically, participants were required to respond to verbal cognitive tasks during the dual-task SSE sessions as follows: i) seven minutes of randomly generated arithmetic (i.e., a two-digit number subtracted from, or added to a three-digit number); ii) one minute break (i.e., no dual-task component); iii) seven minutes of verbal fluency tasks (i.e., semantic or phonemic categories that were rotated every 90 seconds). Responses to questions were not recorded, but participants were
encouraged to perform correct arithmetic and to avoid repeating previous responses. The control (EO) group did not perform dual-task training (i.e., participants in this group were not required to answer verbal fluency or arithmetic tasks while performing the SSE). Participants in both groups performed the same amount of aerobic exercise each week, and interacted with study investigators at the same frequency and relative intensity, with the only difference being the verbal fluency and arithmetic tasks that were added to the SSE component in the EDT group (see Table, Supplemental Digital Content 2, overview of the interventions). Thus, the intervention was aimed at determining the cognitive benefit of incorporating a dual-task component to beginner level SSE compared to the active control (sham) condition of SSE alone, while also controlling for the social benefits that accompany group-based exercise training among aerobically-active older adults.

Attendance was recorded at all sessions, which was used to calculate compliance to the intervention. After the 26-week intervention, participants continued with their regular activities with no intervention by the research team for the 26-week no-contact follow-up and until the completion of the 52-week study period.

**Baseline Variables**

Participant demographic and clinical characteristics were collected at baseline and included: age, sex, race, education, medical history, self-reported cognitive complaint, objectively measured body mass index (BMI), and fitness level [i.e., predicted maximal oxygen uptake (VO₂ max)]. Predicted VO₂ max was determined via the Step Test and Exercise Prescription (STEP) tool (43), which involves stepping up and down a set of standardized steps 20 times at a self-selected pace. As there were no modifications to the aerobic exercise component of the CCAA group-based exercise classes, improvements in cardiorespiratory fitness were not
anticipated; however, the STEP test was repeated at follow-up assessments for the sole purpose of providing a better understand our study findings (i.e., not to be used as an outcome measure).

**Outcomes**

The primary outcome of the study was 26-week change in global cognitive function (GCF) based on a composite score from a neuropsychological battery that covered four cognitive domains. The selected battery included reliable and well-validated (17) measures of executive function/mental flexibility [Trail-Making Tests, Part A and Part B (Trails A and Trails B)], processing speed [Digit-Symbol Substitution Test (DSST)], verbal learning and memory [Auditory Verbal Learning Test (AVLT)], and verbal [category: semantic (animal naming)] and phonemic [letter: Controlled Oral Word Association (COWA) Test] fluency. Secondary outcomes were 12- and 52-week changes in GCF, as well as, 12-, 26-, and 52-week changes in composite scores for executive function/mental flexibility (EF), processing speed (PS), verbal learning and memory (VLM), and verbal fluency (VF).

For all tests except Trails A and Trails B, a low score indicated poor performance. In order to make the tests more comparable for creating the GCF composite, observed scores from Trails A and B were subtracted from maximum scores observed in our study (71 and 200, respectively) following previously published methods (27). Due to non-normal distributions, for the examination of Trails A, Trails B and the EF composite separately, log transformations were applied prior to standardization. Composite scores were then derived by first converting all individual outcomes from neuropsychological tests to standardized z scores (subtracting baseline group mean from raw score and dividing by the baseline group SD). Next, standardized scores were averaged within each domain (e.g., standardized scores for AVLT number of words learned and AVLT number of words recalled were averaged to created a single standardized VLM
composite score). Finally, domain-specific composite scores were averaged to create the GCF score, ensuring the four cognitive domains were weighted equally.

**Power and Sample Size**

We estimated that a total of 48 participants (24 participants per group) would be a reasonable sample size for this proof-of-concept RCT. Specifically, with 20 participants per group, our study would have 80% power to detect a large effect size of 0.9 for standardized GCF change at 26 weeks, at the 5% significance level. We assumed a dropout rate of 20%, which increased our calculation to 24 participants per group. Since we recruited 44 participants, we can conclude that our study had 80% power at the 5% significance level to detect an effect size of 0.95, while accounting for a dropout rate of 15% that we observed in this study at 26 weeks. We were unable to reach our goal of 48 participants primarily due to competing time demands or lack of interest.

**Statistical Analysis**

Baseline scores for all individual outcomes from the neuropsychological tests were compared between groups. We used a mixed model for repeated measurements to examine differences between groups at 26 weeks in GCF. We retained the baseline value as part of the outcome vector and constrained the group means as equal to reflect balance of baseline values due to randomization; time was modelled categorically using indicator variables. All analyses were based on the intent-to-treat principle. Thus, all randomized participants \( n = 44 \) were included in analyses according to the group they were randomized and regardless of compliance with the intervention and data at follow-up. An advantage of the mixed effects regression modeling approach is that it does not require each subject to have the same number of measurements, provided the data are missing at random which is an assumption made by most multiple imputation methods (13). The same modeling approach was carried out for all individual
standardized cognitive outcomes from neuropsychological tests and for the standardized
cognitive domain-specific composite scores. The mixed effect model approach was also adopted
to examine differences between groups in mean change from baseline to 12 and 52 weeks. In
addition, two sensitivity analyses were performed for each outcome: 1) analyses additionally
adjusted for age, sex, baseline fitness and type 2 diabetes status at baseline; and 2) analyses were
restricted to all-completers (i.e., only the 37 of the 44 participants who completed the 26-week
intervention and follow-up assessment were included). Results from adjusted analyses and “all-
completer” analyses were similar (i.e., conclusions did not change) and thus not presented. Two-
sided P-values less than 0.05 were claimed as statistically significant. Analyses were performed

Results:
Participants were enrolled starting on June 13, 2012 and data collection ended on May 5, 2014.
Figure 1 shows the flow of study participants. A total of 59 individuals were assessed for
eligibility and 15 were excluded from the study (13 did not meet inclusion criteria, primarily
because of high MoCA scores and 2 declined to participate). This left 44 individuals who were
enrolled and randomized to the EDT group (n = 23) or the EO group (n = 21). The slight
imbalance between groups is a result of the randomization sequence being generated in one large
block that corresponded with our intended sample size (n=48). In total, 7 (16%) were withdrawn
due to medical reasons unrelated to the study (n=4) or loss of interest (n=3) by the end of the 26-
week intervention, and one participant 8 (18%) was unwilling to attend final assessments
following the additional 26-week no-contact follow-up period (n = 4 withdrawn from each
group). In total, 2 participants (5%) experienced adverse events that were possibly or probably
study-related (bruising in 1 participant due to a study assessment procedure and cramping
following exercise in 1 participant). All participants recovered without further issues. Of the
participants who completed the intervention (37/44 participants), compliance was 78% or higher.
Participant characteristics were similar between groups (see **Table 1**). Participants had a mean
age of 73.5 (SD 7.2) years, just over two-thirds were female; most (98%) were Caucasian and all
participants were highly educated [mean years: 16.5 (SD 2.5)]. Slightly over half of all
participants reported that their memory was worse than five years earlier and on average,
participants had evidence of cognitive impairment [MoCA scores, mean (SD): 24.9 (1.9)] but not
dementia [MMSE scores, mean (SD): 28.8 (1.2)].
Baseline scores on all individual cognitive measures were also similar between groups (see **Table 2**). On average, study participants had better scores at baseline on Trails A and Trails B,
compared to mean scores from normative data for older adults of similar age and education (48).
When comparing to normative data for a slightly younger population but with similar education
levels, our sample performed similarly for number of words by category (in 1 minute) but worse
for number of words by letter (in 1 minute) (49). Performance at baseline on the remainder of the
measures was similar to normative data that has been compiled from other cognitively healthy
samples of older adults (18, 38).
The effect of our exercise intervention on change in standardized GCF at 26 weeks is shown in
**Figure 2.** At 26 weeks, there was greater improvement in standardized GCF in the EDT group
compared to the EO group (p = 0.04); this difference was not seen at 12 or 52 weeks (i.e., 26
weeks after the end of the intervention period). Specifically, the EDT group had mean
standardized GCF change scores that were 0.20 SD higher (95% CI: 0.01 to 0.39) when
compared to the EO group at 26 weeks (see **Table 3**).
At 26 weeks, the EDT group showed significant improvements in both standardized VLM and VF scores, but not standardized EF or PS scores, when compared to the EO group (see Figure 3). For instance, at 26 weeks, the EDT group had standardized VLM scores that were 0.30 SD higher (95% CI: 0.04 to 0.56) than the EO group. As shown in Table 3, the total number of words learned, rather than number of words recalled, accounted for much of this difference between groups for the standardized VLM score. At 26 weeks, the EDT group had VF standardized scores that were 0.62 SD higher (95% CI: 0.22 to 1.02), compared to the EO group.

**Discussion:**

Following 26 weeks of a group-based exercise program for older adults and dual-task training, we found improvements in global cognitive function, when compared to the group-based exercise program alone. These group differences were not seen by 12 weeks nor did they remain 26 weeks after the end of the intervention. We also found that these improvements were primarily driven by improvements in verbal fluency and verbal learning and memory.

Results from a recent meta-analysis suggest that exercise interventions impart a subtle but significant effect on verbal fluency outcomes and no consistent benefit to memory processes (15); however, the influence of exercise on verbal fluency and verbal learning and memory is inconsistent and appears to depend upon the specific components of the intervention (i.e., frequency, intensity, time, and type) and the cognitive status of the participants. For instance, short-term (i.e., 4 weeks) moderate to vigorous intensity multiple modality exercise training can improve verbal fluency (i.e., letter and category verbal fluency tasks) among previously sedentary older adults with healthy cognition (31), while it appears that longer duration (i.e., 6- to 12-months) aerobic (1) and multiple modality exercise training interventions are required to
improve verbal fluency (i.e., letter verbal fluency tasks only) among older adults with amnestic MCI.

Improved cardiorespiratory fitness appears to be an important mediator of improved cognition following physical exercise training (8) and the cognitive benefits imparted following cognitive training are traditionally highly domain-specific (9). Greater improvements in verbal fluency for the EDT group at 12 and 26 weeks are not surprising since this group had relatively preserved cognition, there were no modifications of the aerobic component of the exercise program nor were there any between group differences in the cardiorespiratory response to the intervention (data not shown), and the EDT participants performed verbal fluency tasks while doing square-stepping exercise (tasks that were different from those used during assessments).

Greater improvements in verbal learning and memory for the EDT group may be related to the fact that these participants had to both remember and execute square-stepping exercise patterns and answer questions where they were encouraged to actively remember and avoid repeating answers they had already provided.

Improved memory performance has not been consistently observed following aerobically based exercise training but has been linked with isolated resistance exercise training (15). Thus, the observed improvements in verbal learning and memory within the EDT group may be attributed to the memory requirements of the dual-task square-stepping exercise. Other studies, however, have suggested the potential for both aerobic and resistance training to improve memory performance in older adults with probable MCI (28) and stimulate increased hippocampal volume in older women with probable MCI (46). Further research on the impact of exercise on memory performance is required to elucidate the memory-related benefits of physical exercise training, among healthy older adults and those with indications of cognitive impairment.
While there were no group differences in processing speed, both groups demonstrated improvements following the intervention. These findings may be related to both groups participating in standard group-based exercise programs and beginner-level square-stepping exercise (i.e., similar processing speed requirements) and previous meta-analyses have reported only moderate effect sizes for the influence of exercise on processing speed (7). Since our participants were active prior to the initiation of our intervention and our intervention did not change the amount of aerobic exercise that participants were receiving, this may have contributed to the lack of observed improvement in executive function (8). This may also suggest that the observed improvements in global cognitive function within both groups occurred as a result of the cognitive stimulation provided by square-stepping exercise alone and even further by square-stepping exercise combined with cognitive tasks (45). Barnes and colleagues (2) conducted a factorial RCT and observed significant improvements in global cognitive function following 12 weeks of mental activity, exercise, or combined mental activity and exercise, but no differences between intervention and active control groups. It is likely that differences in study design contributed to discrepancies with our findings. For example, Barnes et al. (2) recruited ethnically diverse and previously sedentary older adults. As well, the intervention was 12-weeks in length and involved different types of cognitive training and active control groups. However, results for the executive function domain in the current study should be interpreted with caution; even after transformation, there was still a slight violation of normality. General conclusions should be based on our primary outcome, the standardized global cognitive functioning score at 26 weeks.

The majority of participants in our study were female, Caucasian, and highly educated, all of which will impact the generalizability of our findings. We did not perform a full clinical or
neurological evaluation of study participants and thus we have a lower degree of certainty related
to the cognitive status of our participants. The MoCA is highly sensitive in identifying
individuals who exhibit subtle declines in cognition that may not be significant enough to
warrant a dementia diagnosis, but may be indicative of underlying neurocognitive pathology
(available at www.mocatest.org). The MoCA test has been widely used to evaluate cognition
and screen for cognitive impairment; the MoCA is available in 46 different languages and
dialects, has been used in 100 countries worldwide, and is recommended as an appropriate
cognitive screening tool by the Canadian Consensus Conference for Diagnosis and Treatment of
Dementia Guidelines for Alzheimer’s disease and the National Institutes of Health and Canadian
Stroke Consortium for Vascular Cognitive Impairment. Although cut-off scores for probable
MCI have been established (29), these appear to be highly population specific. For instance,
there is evidence to suggest that demographic differences between the population that was used
to create the normative data and those within a given study, may contribute to the inaccurate
groupings (35). Thus, in our study, although we used a higher than standard cut-off on the
MoCA, we feel that due to other factors, participants included in our study may be at increased
risk for future cognitive decline. Other limitations of our study include that our
neuropsychological battery did not include any cognitive tests covering visuospatial functioning;
and the effect of our intervention on cognitive domains that have traditionally been found to
benefit from aerobic exercise (e.g., executive function) (7) might have been attenuated due to the
active nature of our participants at baseline. Finally, although the global cognitive function and
verbal learning and memory results are promising, it is possible that contextual cues present
during original learning (e.g., participants coming to the same location to meet the same
assessor) may have directly influenced subsequent memory performance (19).
Recent reviews (25) have drawn attention to the limited number of investigations on the effects of exercise in older adults that include active control group comparisons, and have recommended that future studies address this issue. Furthermore, the inclusion of an active control group similar to that used in our study (i.e., exercise only group), allows for the control of environmental factors (e.g., social interaction provided by exercise classes). Additional strengths of our study include the wide range of cognitively challenging questions that were used for the EDT group intervention, in order to maintain interest and avoid category-specific practice effects. Further, questions used during the intervention were not repeated as part of the assessments.

With the global population aging, there is a growing urgency to identify the most effective strategies to prevent cognitive decline. Results from our study indicate that 26 weeks of standard, group-based exercise for older adults combined with dual-task training (i.e., beginner-level square-stepping exercise with simultaneous cognitive challenges) can lead to greater improvements in global cognitive functioning, when compared to a standard group-based exercise program alone. Results from our study corroborate the safety of square-stepping exercise as an exercise program and contribute to its further definition as a cognitive training intervention for older adults.

Acknowledgments:

The study authors would like to thank study participants and staff at the Canadian Centre for Activity and Aging at Western University. In addition we would like to thank the following research staff: Joe DeCaria, Ashleigh De Cruz, Lee Gonzalez, Noah Koblinsky, Heather Morton, Stephanie Muise, and Shannon Belfry. The results presented herein are preliminary, and do not constitute an endorsement by the American College of Sports Medicine.
Funding:

This study was supported by an Operating Grant from the Canadian Institutes of Health Research (Grant number: 130474), a Team Grant from the Canadian Institutes of Health Research (Grant number: 201713) and by the Fellowship in Care of the Elderly Research, a training award through the Aging, Rehabilitation, and Geriatric Care Research Centre of the Lawson Health Research Institute in partnership with the St. Joseph’s Health Care Foundation.

Conflict of Interest:

The study authors have no relevant conflicts of interest to report. Results of the is study do not constitute endorsement by the American College of Sports Medicine.
References:


19. Hupbach A, Hardt O, Gomez R, and Nadel L. The dynamics of memory: context-


Figure Legends (with Titles)

Figure 1: Flowchart for the Healthy Mind, Healthy Mobility ($HM^2$) trial. Participant flow for the 26-week randomized controlled trial, with a 26-week follow-up period. This trial followed a parallel-groups design whereby participants were randomized (1:1) to either the exercise intervention (Exercise + Dual-Task) or exercise control (Exercise Only) group.

Figure 2: Effects of interventions on standardized Global Cognitive Function (CGF) composite score. From baseline (V0) to 26-weeks (V2), change in the standardized GCF score was significantly greater in the Exercise + Dual-Task group, compared to the Exercise Only group. This significant difference between groups was not present at 12-weeks (V1) or at 52-weeks (V3).

Figure 3: Effects of interventions on standardized Executive Function (EF), Processing Speed (PS), Verbal Learning and Memory (VLM) and Verbal Fluency (VF) scores. There were no significant differences between groups at any of the time points for EF and PS domain-specific scores. From baseline (V0) to 12-weeks (V1), 26-weeks (V2), and 52-weeks (V3), changes in the standardized VLM scores, as well as VF scores were significantly greater in the Exercise + Dual-Task group, compared to the Exercise Only group.
Supplemental Digital Content:

SDC 1- Figure: Schematic of Square-Stepping Exercise. Example beginner patterns are presented.

SDC 2- Table: Description of Interventions by Group. A description of the exercise + dual-task and exercise only interventions.
Table 1. Baseline Characteristics of 44 Study Participants by Randomization Groupa

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>EO Group (n = 21)</th>
<th>EDT Group (n = 23)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean (SD), y</td>
<td>74.5 (7.0)</td>
<td>72.6 (7.4)</td>
</tr>
<tr>
<td>Female sex, No. (%)</td>
<td>15 (71.4)</td>
<td>15 (65.2)</td>
</tr>
<tr>
<td>Education, mean (SD), y</td>
<td>15.8 (2.3)</td>
<td>17.1 (2.6)</td>
</tr>
<tr>
<td>Caucasian race, No. (%)</td>
<td>21 (100)</td>
<td>22 (95.7)</td>
</tr>
<tr>
<td>Memory worse (ref: 5 y ago)b, No (%)</td>
<td>11 (52.4)</td>
<td>13 (56.5)</td>
</tr>
<tr>
<td>MMSE score, mean (SD)</td>
<td>28.9 (1.3)</td>
<td>28.7 (1.0)</td>
</tr>
<tr>
<td>MoCA score, mean (SD)</td>
<td>24.7 (1.7)</td>
<td>25.1 (2.1)</td>
</tr>
<tr>
<td>Fitness (pVO2max) score, mean (SD)</td>
<td>27.6 (10.3)</td>
<td>27.8 (8.6)</td>
</tr>
<tr>
<td>Body mass index, mean (SD)</td>
<td>27.2 (3.9)</td>
<td>27.7 (4.4)</td>
</tr>
<tr>
<td>Medical history, No. (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>10 (47.6)</td>
<td>9 (39.1)</td>
</tr>
<tr>
<td>Hypercholesterolemia</td>
<td>8 (38.1)</td>
<td>10 (43.5)</td>
</tr>
<tr>
<td>Type 2 Diabetes</td>
<td>4 (19.0)</td>
<td>1 (4.3)</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>3 (14.3)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Angina/Coronary Artery Disease</td>
<td>2 (9.5)</td>
<td>2 (8.7)</td>
</tr>
<tr>
<td>Former smokerc</td>
<td>10 (47.6)</td>
<td>13 (56.5)</td>
</tr>
</tbody>
</table>

**Abbreviation:** EO, Exercise Only; ECM, Exercise + Dual-Task; MMSE, Mini-Mental Status Examination; MoCA, Montreal Cognitive Assessment; pVO2max, Predicted Maximal Oxygen Uptake

aData were missing for pVO2max score in 2 participants and for body mass index in 1. Percentages are calculated excluding missing values (where applicable).

bParticipants were asked to rate their memory on a scale of 5 (from much better to much worse)

cThere were no current smokers in the study.
Table 2. Baseline Cognitive Scores by Randomization Group

<table>
<thead>
<tr>
<th>Cognitive Test</th>
<th>EO Group (n = 21)</th>
<th>EDT Group (n = 23)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Executive Function/ Mental Flexibility</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trails A, sec to complete</td>
<td>36.8 (17.3)a</td>
<td>29.8 (16.4)a</td>
</tr>
<tr>
<td>Trails B, sec to complete</td>
<td>80.9 (35.0)a</td>
<td>65.3 (42.6)a</td>
</tr>
<tr>
<td><strong>Processing Speed</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DSST, no. correct</td>
<td>53.6 (12.2)</td>
<td>59.2 (12.3)</td>
</tr>
<tr>
<td><strong>Verbal Learning and Memory</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AVLT, no. of words learned</td>
<td>43.6 (13.7)</td>
<td>42.3 (9.2)</td>
</tr>
<tr>
<td>AVLT, no. of words recalled(^b)</td>
<td>7.7 (4.2)</td>
<td>8.2 (3.4)</td>
</tr>
<tr>
<td><strong>Verbal Fluency</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. of words, by category</td>
<td>19.5 (6.3)</td>
<td>19.7 (5.1)</td>
</tr>
<tr>
<td>No. of words, by letter</td>
<td>14.4 (4.2)</td>
<td>13.6 (3.9)</td>
</tr>
</tbody>
</table>

**Abbreviation:** EO, Exercise Only; EDT, Exercise + Dual-Task; DSST, Digit Symbol Substitution Test; AVLT, Auditory Verbal Learning Test

**Note:** Means (SD) are presented unless otherwise indicated.

\(^a\)Medians (Interquartile Range) presented due to skewness.

\(^b\)Data missing for 1 participant.
Table 3. Standardized Mean Change in Cognitive Scores at 26 weeks by Randomization Group

<table>
<thead>
<tr>
<th>Cognitive Test</th>
<th>EO Group (n = 21)</th>
<th>EDT Group (n = 23)</th>
<th>Difference Between groups</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Global Cognitive Function Composite</strong></td>
<td>0.22 (0.08 to 0.36)</td>
<td>0.42 (0.29 to 0.55)</td>
<td>0.20 (0.01 to 0.39)</td>
<td>0.04</td>
</tr>
<tr>
<td><strong>Executive Function/ Mental Flexibility</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trails A, sec to complete</td>
<td>-0.24 (-0.59 to 0.11)</td>
<td>-0.37 (-0.69 to -0.05)</td>
<td>-0.13 (-0.58 to 0.32)</td>
<td>0.56</td>
</tr>
<tr>
<td>Trails B, sec to complete</td>
<td>-0.19 (-0.64 to 0.26)</td>
<td>0.18 (-0.24 to 0.59)</td>
<td>0.37 (-0.23 to 0.96)</td>
<td>0.22</td>
</tr>
<tr>
<td>EF/MF Composite</td>
<td>-0.20 (-0.51 to 0.11)</td>
<td>-0.09 (-0.38 to 0.19)</td>
<td>0.11 (-0.31 to 0.52)</td>
<td>0.60</td>
</tr>
<tr>
<td><strong>Processing Speed</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DSST, no. correct (PS Composite)</td>
<td>0.39 (0.08 to 0.70)</td>
<td>0.33 (0.05 to 0.61)</td>
<td>-0.06 (-0.48 to 0.36)</td>
<td>0.78</td>
</tr>
<tr>
<td><strong>Verbal Learning and Memory</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AVLT, no. of words learned</td>
<td>0.56 (0.27 to 0.85)</td>
<td>1.19 (0.93 to 1.45)</td>
<td>0.63 (0.25 to 1.02)</td>
<td>0.002</td>
</tr>
<tr>
<td>AVLT, no. of words recalled</td>
<td>0.56 (0.22 to 0.89)</td>
<td>0.72 (0.41 to 1.02)</td>
<td>0.16 (-0.27 to 0.59)</td>
<td>0.45</td>
</tr>
<tr>
<td>VLM Composite</td>
<td>0.38 (0.18 to 0.58)</td>
<td>0.68 (0.50 to 0.86)</td>
<td>0.30 (0.04 to 0.56)</td>
<td>0.02</td>
</tr>
<tr>
<td><strong>Verbal Fluency</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. of words, by category</td>
<td>0.006 (-0.39 to 0.40)</td>
<td>0.54 (0.18 to 0.91)</td>
<td>0.54 (0.04 to 1.04)</td>
<td>0.04</td>
</tr>
<tr>
<td>No. of words, by letter</td>
<td>-0.01 (-0.38 to 0.36)</td>
<td>0.65 (0.31 to 0.99)</td>
<td>0.66 (0.17 to 1.15)</td>
<td>0.009</td>
</tr>
<tr>
<td>VF Composite</td>
<td>-0.03 (-0.33 to 0.27)</td>
<td>0.60 (0.32 to 0.87)</td>
<td>0.62 (0.22 to 1.02)</td>
<td>0.003</td>
</tr>
</tbody>
</table>

Abbreviation: EO, Exercise Only; EDT, Exercise + Dual-Task; EF/MF, Executive Function/ Mental Flexibility; DSST, Digit Symbol Substitution Test; PS, Processing Speed; AVLT, Auditory Verbal Learning Test; VLM, Verbal Learning and Memory; VF, Verbal Fluency

*a*Calculated from linear mixed effects regression models that included terms for time (0, 12, 26 and 52 weeks) and group x time interaction. P values reflect statistical significance of the group x time interaction at 26 weeks (i.e., difference between groups in mean change at 26 weeks).

*b*For comparability reasons with the other tests and cognitive domains, the Trails A and Trails B scores were reverse coded and then standardized for inclusion within the global cognitive functioning composite.

*c*Due to non-normality, original scores were log transformed prior to standardization.
Enrollment
Assessed for eligibility (n= 59)

Excluded (n= 15)
- Not meeting inclusion criteria (n= 13)
- Declined to participate (n= 2)

Randomized (n= 44)

Allocation
Allocated to Exercise Intervention (Exercise + Dual-Task) Group (n= 23)
- Received allocated intervention (n= 22)
- Did not receive allocated intervention due to failure to attend classes (n=1)

Allocated to Exercise Control (Exercise Only) Group (n= 21)
- Received allocated intervention (n= 20)
- Did not receive allocated intervention due to failure to attend classes (n=1)

Follow-Up
6-month intervention
Discontinued intervention (n= 2)
  - Medical reasons (n=1)
  - Personal reasons (n=1)

6-month follow-up period
Discontinued follow-up due to personal reasons (n= 1)

Analysis
Analysed (n=23)
- Baseline data (n= 23)
- Baseline & 3-mo. data (n=22)
- Baseline, 3-mo. & 6-mo. data (n=20)
- Baseline, 3-mo., 6-mo. & 12-mo. data (n=19)

Analysed (n=21)
- Baseline data (n= 21)
- Baseline & 3-mo. data (n=17)
- Baseline, 3-mo. & 6-mo. data (n=17)
- Baseline, 3-mo., 6-mo. & 12-mo. data (n=17)