Research Article

Synergistic Effects of Cognitive Training and Physical Exercise on Dual-Task Performance in Older Adults

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Abstract

Background: Studies report benefits of physical exercise and cognitive training to enhance cognition in older adults. However, most studies did not compare these interventions to appropriate active controls. Moreover, physical exercise and cognitive training seem to involve different mechanisms of brain plasticity, suggesting a potential synergistic effect on cognition.

Objective: This study investigated the synergistic effect of cognitive training and aerobic/resistance physical exercise on dual-task performance in older adults. Intervention effects were compared to active controls for both the cognitive and the exercise domain.

Method: Eighty-seven older adults completed one of 4 different combinations of interventions, in which computer lessons was active control for cognitive training and stretching/toning exercise control for aerobic/resistance training: (a) cognitive dual-task training and aerobic/resistance training (COG+/AER+), (b) computer lessons and aerobic/resistance training (COG–/AER+), (c) cognitive dual-task training and stretching/toning exercises (COG+/AER–), and (d) computer lessons and stretching/toning exercises (COG–/AER–). The primary outcome was performance in an untrained transfer dual task. Stepwise backward removal regression analyses were used to predict pre- versus post-test changes in groups that have completed the dual-task training, aerobic/resistance or both interventions.

Results: Participation in AER+ did not predict improvement in any dual-task outcomes. Participation in COG+ predicted reduction in dual-task cost and participation in COG+/AER+ predicted reduction in task-set cost.

Discussion: Results suggest that the combination of cognitive and physical training protocols exerted a synergistic effect on task-set cost which reflects the cost of maintaining multiple response alternatives, whereas cognitive training specifically improved dual-task cost, which reflects the ability of synchronizing concurrent tasks.

Keywords: Cognitive training, Combined intervention, Divided attention, Dual-task abilities, Physical exercise

Age-related decline in the ability to manage concurrent tasks has often been reported (Fraser and Bherer, 2013; Verhaeghen and Cerella, 2002), and can greatly impact activities of everyday life. This ability is assessed using dual-task paradigms. Performances in dual-task paradigms have demonstrated predictive validity for everyday hazardous situations, such as automobile accidents and fall rates, that are common among older adults. Age-related decline in dual-task performance can be the result of a decrease in processing speed, a reduced ability to maintain and prepare response alternatives in working memory, and a decline in the ability to execute/manage simultaneous responses (Fraser and Bherer, 2013; Kramer and Kray, 2006; Kramer and Madden, 2008). Brain imaging studies also suggest that an age-related shift in dual-task strategy can take place such that younger adults use a more proactive strategy while older adults tend to rely on reactive processing (Braver et al., 2007).

Cognitive training studies suggest that dual-task performance can be improved in older adults (Bherer et al., 2005, 2006, 2008; Kramer et al., 1995, 1999; Lussier et al., 2012). These studies reported that improvement was related to increased processing speed, as well as enhanced ability to maintain multiple response alternatives in working memory and to synchronize the execution of multiple tasks. Although the extent to which cognitive training gains can transfer to untrained and everyday tasks is still unclear, it appears that training-related benefits can be observed in untrained tasks (Lussier, Brouillard, and Bherer, 2017; Lussier, Bugaïska, and Bherer, 2017), supporting the notion that albeit limited, training-related gains can transfer to new situations (Li et al., 2010).

Physical activity and exercise can also lead to improvement in dual-task performance. Hawkins et al. (1992) were among the first to show that a 10-week aquatic aerobic fitness program showed improved performances in dual-but not in single-task performance. In contrast, Madden et al. (1989) did not find any beneficial effects on dual-task performance in older adults aged between 60 and 83 after a 12-week aerobic intervention, but Kramer et al. (1999) did report improved task-switching following 6 months of aerobic exercise training in older adults. Together, these results of exercise interventions suggest that they can lead to improved dual-task performances.

Emerging research is now investigating the effects of combining cognitive and physical training on cognition. The rationale for this is based on the notion that both types of interventions have been associated with different mechanisms of brain plasticity. In fact, animal studies have identified mechanisms of neuroplasticity activated by both cognitive enrichment and exercise, supporting the notion that both interventions could have a synergistic effect (Fabel et al., 2009). Physical exercise studies in animal models have reported increased angiogenesis (new blood vessels grow from preexisting) and neurogenesis in the hippocampus in elderly rats, as well as exercise-induced

synaptogenesis (see Lista and Sorrentino, 2010). The molecular mechanisms supporting these effects could involve exercise-associated changes in molecular growth factors such as brain-derived neurotrophic factor (BDNF), which plays a crucial role in neuroplasticity and neuroprotection, and increased production of insulin-like growth factor 1 (IGF-1), which is involved in both neurogenesis and angiogenesis. Moreover, neurotransmitter systems also seem to be modulated through exercise. In human, studies report increased BDNF concentration in the blood following 1 year of aerobic exercise (Erickson et al., 2011; Heijnen et al., 2015) and 2 months of motor skill training (Grégoire et al., 2019). These changes might support the transient and permanent changes at the structural and functional levels in the aging brain reported in some studies following exercise (Bherer et al., 2013). Although purely speculative at this point, these effects would facilitate brain plasticity induced by a cognitive stimulation protocol. In fact, evidence of brain plasticity mechanisms has been reported after cognitive training in human, such as structural modifications (increased brain volume and cortical thickness) and functional changes (increased task-related brain activation in fMRI and PET) in older adults (Belleville and Bherer, 2012). Of specific interest for the present study, cognitive dual-task training was associated with change in prefrontal regions in older adults (Erickson et al., 2007). It thus seems that physical exercise and cognitive training would lead to cognitive improvement through different mechanism of brain plasticity, supporting the hypothesis that both types of intervention might have a synergistic effect on cognition, one potentializing (exercise) the effect of another (cognitive training).

Results from intervention studies in human are still unclear as to whether combined interventions lead to larger gain than either intervention alone. Some studies have shown synergistic effects of combining interventions as compared with passive control conditions (Fabre et al., 2002; Zhu et al., 2016), but others using active control interventions failed to reported advantages of combining interventions (Desjardins-Crépeau et al. 2016). Moreover, in a recent meta-analysis, Gheysen et al. (2018) reported that a combined intervention generally showed greater effects on cognition than physical training alone but no advantage compared with cognitive training alone. Potential benefits of combining exercise and cognitive training on cognition should be investigated further.

This study examined the effects of cognitive dual-task training, physical exercise, and a combination of both trainings on dual-task performance. While benefits of combined physical exercise and cognitive training could potentially be observed in a variety of cognitive domains and functions, we opted to explore the effects on dual-task performance based on previous research showing improvement in dual-task performances following cognitive training (Lussier, Brouillard, and Bherer, 2017; Lussier, Bugaïska, and Bherer, 2017) and aerobic exercise (Bherer et al., 2019) performed

alone. By doing so, we ensure that the outcome of interest was sensitive to each individual intervention, which seems to be a prerequisite to test the synergistic effects of combining them. All training conditions were compared to active controls, computer lessons for cognitive training, stretching and toning exercises for aerobic training. This enables isolating the impact of the active ingredient in both the cognitive and exercise training interventions.

Method

Participants

Eligible participants were recruited from the Institut Universitaire de gériatrie de Montréal research center, newspaper ads, and flyers posted in community centers and libraries. Out of 182 eligible community-dwelling individuals, 136 agreed to take part in the study (see Figure 1). Inclusion criteria were being a non-smoker and aged 60 years and older. Participants were excluded if they had progressive neurological diseases, contraindications to take part in physical activity, very limited mobility, cognitive impairment (score equal or lower than 24 on 30 on the Mini-Mental State Examination [MMSE]) (Folstein et al., 1975), or severe perceptual deficits.

Protocol and Measures

Pre- and post-test sessions

Participants completed three sessions of pre-test and post-test assessment within a 2-week period prior to and after the intervention. Research assistants and professional performing the assessment were not blinded to participants'

group assignment. Both assessments were identical except for the medical examination and the cognitive screening session which were done in pre-test assessment only.

Session 1: The medical examination and cognitive screening session took 2 hr. A geriatrician performed a complete medical examination, which included an overview of medical history and a review of the following systems: cardiovascular, musculoskeletal, pulmonary, and gastrointestinal. Participants then completed a set of neuropsychological screening tests to characterize cognitive functioning. The MMSE was used to obtain a measure of global cognitive functioning. The following subtests of the Wechsler Adult Intelligent Scale (WAIS-III) were also administered: Similarities, Digit Span, and Digit Symbol Substitution. These tests, respectively, assess verbal abstraction, short-term and working memory, and speed of processing. Each participant also completed the Geriatric Depression Scale (30 questions) (Yesavage et al., 1982) and questions about audition and vision.

Session 2: A computerized dual-task task different from the one used for training was administered at pre- and post-test. The dual-task was considered a within-modality near-transfer task (Lussier et al., 2017) since response modality (manual) was the same as in the cognitive training but the stimuli differed. The dual-task consisted of two visual discrimination tasks performed alone and concurrently: a letter discrimination task (A, B, or C), required pressing the corresponding keys (A, S, and D) with the left hand, and an arrow discrimination task (up, left, or right), involved pressing the corresponding keys (K, L, and “;” keys) with the right hand. The task included four different blocks: (a) single-pure letters block (18 trials), (b) single-pure arrows block (18 trials), (c) single-mixed block (48 trials) involving the letter or the arrow tasks performed alone (six response alternatives), and (d) dual-mixed block (48 trials) in which the letter and arrow tasks had to be performed simultaneously. In the dual-mixed block, participants were instructed to avoid prioritizing one task over the other, and to answer as quickly and as accurately as possible to both tasks. The task had the following structure: single-pure letter, single-pure arrow, single-mixed, dual-mixed, dual-mixed, single-mixed, single-pure letter, and single-pure arrow. The use of the three trial types allowed the calculation of two attentional costs associated with different cognitive processes involved in dual-task situations. Task-set cost is the ratio between single-mixed trials and single-pure trials. It reflects the ability to maintain different response alternatives in memory and to prepare to answer to multiple tasks. Second, the ratio between reaction time in dual-mixed trials and single-mixed trials provides a dual-task cost, which is thought to reflect the ability to synchronize two concurrent tasks while minimizing the effects of response preparation (Bherer et al., 2005). An increased

Figure 1. Participants sample flowchart. Full color version is available within the online issue.

task-set cost and dual-task cost, suggesting poorer performances, is reflected by an increased ratio in reaction time and a decreased ratio in accuracy.

Session 3: The physical fitness assessment lasted about an hour and characterized: functional physical capacity (*physical performance test* [Reuben and Siu, 1990]), mobility (*6-min walk test* [Bautmans et al., 2004] and *timed up and go* [Podsiadlo and Richardson, 1991]), grip strength, leg and forearm flexion, and flexibility. Body mass index (BMI) was calculated from the participants' weight and height.

Intervention

The intervention involved a combination of cognitive and physical interventions that could be training or active control, depending on group assignment. Cognitive dual-task training (COG+) and aerobic/resistance (AER+) training were used as cognitive and physical training, respectively. Computer lessons (COG-) and stretching and toning exercises (AER-) were used as active control conditions. The four potential combinations of training were: (a) cognitive dual-task training and aerobic/resistance training (COG+/AER+), (b) computer lessons and aerobic/resistance training (COG-/AER+), (c) cognitive dual-task training and stretching/toning exercises (COG+/AER-), and (d) computer lessons and stretching/toning exercises (COG-/AER-). Physical exercise sessions occurred twice a week (on Mondays and Fridays) and cognitive/computer sessions occurred once a week (on Wednesdays) for 12 weeks, for a total of 24 physical and 12 cognitive/computer sessions. Each session lasted about 60 min. The study was carried out in waves of 16–32 participants randomly assigned to one of the four intervention combinations using the website [randomization.com](https://www.randomization.com). The intervention took place in subgroups of four to eight participants from the same intervention combination at a time, for both the exercise and the cognitive/computer session and participants from different intervention groups did not interact.

Aerobic/resistance training (AER+).—Each session started with a 5-min warm-up on a machine selected by the participant (elliptical, treadmill, or recumbent bicycle), followed by a muscle-strengthening portion targeting different lower body muscle groups (quadriceps, hamstrings, hip extensors and flexors, ankle plantar flexors, etc.). Muscle-strengthening exercises were performed with elastics and the objective was to gradually increase elastic resistance throughout training sessions. Sit to stand was also performed with participants being asked to perform as many as possible in a given time, also increasing gradually with training. Training sessions ended with a cardiovascular portion lasting about 30 min. Participants were instructed to walk on a treadmill at a pace reflecting a medium to high intensity on the Borg Scale of Perceived Exertion (Borg, 1998). Intensity and duration both increased progressively from one training session to the next. When needed, the

slope of the treadmill was augmented to increase intensity. This was followed by a 5-min cool-down period. Certified kinesiologists supervised the training and constantly monitored participants' condition (e.g., level of effort, tiredness, etc.), in order to adjust exercise intensity accordingly.

Stretching/toning exercises (AER-).—Participants assigned to the active control condition of the physical training took part in stretching sessions supervised by a kinesiologist. The exercises were devoted to improving flexibility without improving cardiorespiratory capacity. The session started with a 5-min warm-up on the machine of their choice. This was followed by 50 min of stretching exercises that targeted the entire body, one joint at a time, from head to toes. Exercises were performed in a seated position as much as possible. The program was based on one developed by Stanziano et al. (2009). Sessions ended with 5 min of relaxation on a yoga mat.

Cognitive dual-task training (COG+).—Cognitive training took place in a room containing 10 computer stations and was supervised by a student in neuropsychology. Participants were trained on a visual dual-task following the same task design as the one performed during pre- and post-test sessions, but with different visual discrimination tasks. The two visual discrimination tasks consisted of a number discrimination task (3, 5, 8) and a shape discrimination task (circle, square, diamond). The structure of the task was similar to pre-test, but more trials were executed: a total of 72 single-pure trials, 240 single-mixed trials, and 864 dual-mixed trials. More importantly, the training task included continuous performance feedback during the dual-mixed block. Feedback was provided via a histogram that changed color (green, yellow, red) to inform participants of their response speed. The color was determined by the average reaction time of the last three trials of the dual-mixed block and was compared to the median reaction time of the single-pure blocks. The goal was to maintain the histogram bar in the green zone and to avoid it becoming red. In addition to on-line feedback, global feedback was provided at the end of the session, informing participants on their mean reaction time and accuracy for sessions performed so far. Both types of feedback were used to foster participants' motivation.

Computer lessons (COG-).—The active cognitive control took place in the same computer room as the cognitive training and was also conducted by students in neuropsychology. Each computer lesson consisted of introductory exercises to computers (Windows operating Software), to common software (e.g., Word, Excel), and to common websites (e.g., search engines, news, games).

Data and Statistical Analyses

Z-score changes were calculated for all dual-task outcomes (single-pure, single-mixed, dual-mixed, task-set

cost, and dual-task cost) for reaction time and accuracy. Z-score change provides a reliable measure of the intervention effect size, which allows comparison of experimental groups using a standardized method. Z-scores were computed on raw scores by subtracting individual scores to global mean (pre and post combined), divided by the global standard deviation (pre and post combined). Z-score changes were then calculated by subtracting Z-score pre to Z-score post.

Analyses were conducted with IBM SPSS 21.0. Multivariate 2×2 ANOVAs (COG+/COG- $\times$ AER+/AER-) were performed on baseline characteristics to determine if all groups were comparable. To assess the synergistic effect of combining exercise and cognitive training versus one of the two trainings alone, stepwise backward removal regression analyses was used to predict the Z-score change in each dual-task outcome for both reaction time and accuracy, based on participation in cognitive training (COG+) without physical activity, participation in aerobic training (AER+) without cognitive training, and participation in both aerobic and cognitive training (COG+/AER+) to isolate the potential synergistic effect of both interventions.

Results

Participants

From the initial 136 participants, 11 withdrew before the study started (see Figure 1). Participants were considered as having completed the intervention program if they attended

a minimum of 75% of the sessions for both cognitive and physical interventions, that is a minimum of 18 physical and 9 cognitive training sessions.

Baseline Comparisons

Baseline characteristics of the groups are presented in Table 1. The groups were comparable for age, education, scores on the Geriatric Depression Scale, medical variables, and cognitive screening tests as shown by the absence of a group effect or an interaction. There were more females than men in all intervention groups. However, no between-group differences were found regarding the sex of the participants ($\chi^2 = 5.748$, $p = .125$). Moreover, additional analyses were performed to determine whether sex moderated the intervention effects found in the present paper. No significant moderation effect was found. However, the small number of males in all intervention groups did not allow for exploring the specificity of each sex regarding the physical and cognitive training effects on cognition. Finally, the four groups were comparable on most physical performance tests; groups differed only regarding chair-stands, $F(1,86) = 4.21$, $p < .05$. At baseline, the COG+/AER+ group performed more chair-stands than the COG+/AER- group, $p < .05$. All groups showed equivalent improvements in measures of functional mobility but those that did AER+ showed larger effect size in lower body strength, independently of cognitive training. A complete description of the participants' profile has been published previously and can be found in Desjardins-Crpeau et al. (2016).

Table 1. Demographic and Baseline Characteristics of Participants According to the Type of Intervention

	COG+		COG-	
	AER+	AER-	AER+	AER-
Characteristics	$n = 26$	$n = 23$	$n = 20$	$n = 18$
Age (years), $M \pm SD$	71.85 ± 7.16	74.17 ± 6.71	70.75 ± 6.90	72.50 ± 6.96
Education (years) $M \pm SD$	14.85 ± 2.84	14.09 ± 4.17	15.65 ± 2.39	14.06 ± 3.80
Sex, $F (M)$	17 (9)	19 (4)	11 (9)	15 (3)
Hypertension, $n (%)$	9 (34.6)	12 (52.2)	11 (55)	11 (61.1)
Diabetes mellitus, $n (%)$	6 (23.1)	3 (13)	1 (5)	3 (16.7)
Dyslipidemia, $n (%)$	9 (34.6)	9 (39.1)	8 (40)	3 (16.7)
Thyroid disease, $n (%)$	8 (30.8)	9 (39.1)	1 (5)	5 (27.8)
Arthritis, $n (%)$	11 (42.3)	14 (60.9)	9 (45)	12 (66.7)
Osteoporosis, $n (%)$	6 (23.1)	9 (39.1)	2 (10)	3 (16.7)
Number of medications, $M \pm SD$	4.34 ± 2.68	6.09 ± 4.10	4.25 ± 2.94	3.88 ± 3.16
MMSE, $M \pm SD$	28.88 ± 1.21	29.17 ± 1.03	28.85 ± 1.04	28.50 ± 1.38
Digit Span Forward, $M \pm SD$	6.23 ± 1.24	6.13 ± 1.25	6.10 ± 1.16	5.94 ± 1.35
Digit Span Backward, $M \pm SD$	4.50 ± 1.18	4.91 ± 1.62	4.85 ± 0.93	4.67 ± 1.14
Similarities, $M \pm SD$	23.15 ± 4.95	21.70 ± 4.61	22.45 ± 5.38	22.28 ± 5.68
Digit Substitutions, $M \pm SD$	57.32 ± 13.14	54.13 ± 12.63	58.25 ± 17.63	57.00 ± 14.88
GDS, $M \pm SD$	5.38 ± 4.28	4.32 ± 4.38	5.80 ± 4.68	2.72 ± 2.93
Quality of life, $M \pm SD$	3.70 ± 3.60	2.68 ± 3.47	3.47 ± 2.40	3.05 ± 2.44

Note: AER+ = aerobic/resistance training; AER- = stretching/toning exercises; COG+ = dual-task training; COG- = computer lessons; GDS = Geriatric Depression Scale; MMSE = Mini-Mental State Examination.

Intervention Effects on Dual-Task Performances

Z-score changes for each trial type are presented in Table 2 and performance costs (task-set cost and dual-task cost) are shown in Figures 2 and 3 for Reaction Time and Accuracy, respectively.

Reaction time

A significant regression equation was found for Z-score change of reaction time in dual-mixed trials following cognitive training (COG+), which decreased by 0.535, indicating better performance: $-0.133 - (0.535 * \text{COG+})$ with an $R^2 = .088$, $F(1,85) = 8.24$, $p < .005$. Dual-task cost in reaction time also decreased by .911 following COG+, indicating improved performances: $0.180 - (0.911 * \text{COG+})$, $R^2 = .1442$, $F(1,85) = 14.33$, $p < .001$. Participation in physical exercise alone (AER+) or in combination with cognitive training (COG+/AER+) failed to predict Z-score change in the dual-task outcomes.

Accuracy

Z-score change of dual-mixed trials accuracy increased by 0.598 in participants following cognitive training alone (COG+), indicating an improved performance: $-0.271 + (0.598 * \text{COG+})$, $R^2 = .065$, $F(1,85) = 5.901$, $p = .017$. Participation in cognitive training alone (COG+) also predicted Z-score change in dual-task cost, with an improvement of 0.448: $0.297 + (0.448 * \text{COG+})$, $R^2 = 0.057$, $F(1,85) = 5.163$, $p = .0256$. Participation in physical exercise

intervention alone did not predict Z-score change in any outcome. However, participation in both conditions (COG+/AER+) predicted improved task-set cost in accuracy, while COG+ alone and AER+ did not: $0.297 + (0.448 * \text{COG+}/\text{AER+})$, $R^2 = 0.066$, $F(1,85) = 6.008$, $p = .0162$. Accuracy Z-score change in task-set cost increased by .448 in participants following combined training. This result suggests a synergistic effect of aerobic/resistance and cognitive dual-task training on the cost of maintaining different response alternatives in memory and preparing to respond.

Discussion

This study assessed the synergistic effects of exercise and cognitive training on dual-task abilities in older adults by comparing cognitive training or physical exercise training alone or in combination. Results showed that dual-task training alone (COG+) predicted improvement in dual-mixed trials and in dual-task cost, the cost of the synchronization of two concurrent tasks. Aerobic training alone (AER+) did not predict any of the dual-task outcomes. However, participation in both conditions (COG+/AER+) predicted improved task-set cost in response accuracy, while COG+ alone and AER+ alone were not significant predictors of task-set cost. This result suggests a synergistic effect of aerobic/resistance and cognitive dual-task training on task-set cost, the cost of maintaining different response alternatives in memory and preparing to respond. The task-set cost is

Table 2. Z-Score Change on Dual-Task Trial Types According to the Type of Intervention

	COG+		COG-	
	AER+	AER-	AER+	AER-
Reaction time				
Single-pure	-0.150 ± 0.789	-0.410 ± 0.849	-0.199 ± 0.821	-0.409 ± 0.639
Single-mixed	-0.400 ± 0.659	-0.285 ± 0.616	-0.332 ± 0.660	-0.397 ± 0.691
Dual-mixed	-0.628 ± 0.699	-0.715 ± 1.027	-0.049 ± 0.987	-0.228 ± 0.726
Accuracy				
Single-pure	-0.032 ± 0.826	0.415 ± 1.362	0.132 ± 1.409	0.585 ± 1.166
Single-mixed	0.055 ± 1.333	0.065 ± 0.774	-0.110 ± 1.368	0.276 ± 0.509
Dual-mixed	0.278 ± 0.567	0.384 ± 0.717	-0.513 ± 2.087	-0.001 ± 0.570

Figure 2. Reaction time Z-score change in task-set cost and dual-task cost according to type of intervention. Full color version is available within the online issue.

Figure 3. Accuracy Z-score change in task-set cost and dual-task cost according to type of intervention. Full color version is available within the online issue.

thought to reflect the contribution of working memory, updating and response preparation. These results are consistent with Fabre et al. (2002) who demonstrated larger improvements in memory performance after 2 months of combined aerobic and cognitive training. The major contribution of the present study was to compare training types to matched active control conditions for both the physical and cognitive interventions, which had never been done in previous study. This is critical knowledge to further understand how multidomain intervention such as those used in large non-pharmaceutical trials can be optimized to better enhance cognition in healthy older adults and those with cognitive deficits (FINGER trial, Ngandu et al., 2015).

Future studies are needed to better understand the neural mechanisms by which exercise and cognitive interventions could synergistically act to enhance cognition. Studies suggest that aerobic and resistance training exercise activate biochemical and physiological cascades that play crucial role in brain plasticity, such as increase in blood flow and neurotrophic factor supporting neurogenesis. Cognitive training on the other hand has been associated with increased connectivity, brain volume, and task specific activation. These reports suggest that physical exercise and cognitive training involve different brain plasticity mechanisms, supporting the notion that they could have a synergistic effect when combined. Another important issue would be to document if patients that have already experienced cognitive decline, such as those with mild cognitive impairment, could benefit from combined intervention. Large clinical trials involving those patients (Montero-Odasso et al., 2018) are currently underway and will inform on the potential of these non-pharmaceutical interventions with clinical populations.

This study has a few limitations. First, the study design was such that physical and cognitive training sessions were performed on different days, which could have limited the extent of the synergistic effects. A recent meta-analysis suggest that simultaneous cognitive and physical training might have greater effects on cognition than sequential training (Gheysen et al., 2018; Tait et al., 2017). However, results of the present study suggest that synergistic effects of cognitive and exercise training can be observed with sequential training. Another limit was that cognitive training was only done once per week, possibly providing suboptimal volume for this intervention. Nevertheless, cognitive dual-task training alone led to gains on dual-task cost and dual-mixed trials, which is consistent with previous studies with more frequent cognitive training sessions (e.g., Bherer et al., 2005, Lussier et al., 2012). Another limitation of the present study was the small number of males in all intervention groups, which did not allow for exploring the specificity of each sex regarding the physical and cognitive training effects on cognition, which is an issue of high interest. In particular, sex has recently been suggested to moderate the relationship between different exercise training modalities and cognition (Barha et al. 2017). Further studies with larger sample size should determine

whether the synergistic effects of physical exercise and cognitive training differ between men and women in older adults. Finally, there was no follow-up assessment after the intervention, which could have revealed stronger gains in the combined intervention (see Rahe et al., 2015).

A major contribution of the present study was to test intervention effects against active control conditions, which allowed for a more systematic evaluation of the efficacy of different types of intervention. Notably, all groups, even groups including control conditions, had comparable intervention times. Moreover, active control conditions provide similar conditions with regards to social interactions, travelling three times a week to the research center, which could by themselves represent a significant change in lifestyle for previously sedentary individuals.

In conclusion, this study shows that two non-pharmacologic interventions, cognitive training and exercise training, can exert synergistic effects on cognition. Future studies comparing the effects of sequential and combined cognitive and physical training are warranted to better understand the extent of synergistic effects of these interventions on cognition. Studies integrating neuroimaging techniques could help shed light on the mechanisms underlying these synergistic effects.

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Conflict of Interest

None declared.

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This study was not preregistered. Data, analytic methods, and study materials can be made available upon request.

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