


Effects of Combined Aerobic Exercise and Cognitive Training on Verbal Fluency in Older Adults

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Abstract

We have previously shown that aerobic exercise improves measures of verbal fluency in older adults, and such an improvement is correlated with improved cardiovascular reserve (i.e., estimates of VO_2). Due to increasing popularity in computer-based cognitive training, we explored whether the addition of cognitive training to aerobic exercise would further enhance the beneficial cognitive impact of exercise. Therefore, this study sought to test the hypothesis that a cognitive training regimen alone would directly improve executive function and that this effect would be potentiated with the addition of aerobic exercise. The interventions lasted 12 weeks, and cognitive assessments were taken immediately prior to and after the interventions. We found that only the groups employing aerobic exercise showed improvements in verbal fluency (semantic and letter) and cardiovascular fitness with no other executive functions being significantly impacted. Cognitive training alone was associated with decreased verbal fluency. These data replicate previous findings which indicate that aerobic exercise may have a remedial or mitigating effect of cognitive decline. In addition, they provide evidence that the addition of concurrent cognitive training to an aerobic exercise program does not provide synergistic improvement in executive functions.

Keywords

active life/physical activity, experimental geriatrics/gerontology, prevention, rehabilitation, cognition

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Introduction

Due to the growing aging population within the United States, there is considerable interest in identifying behavioral interventions that can enhance physical functioning and/or mitigate cognitive decline. Declining cognitive health is a primary component of the expected 25% growth in health care costs associated with the aging crisis in the United States (Courtney-Long et al., 2015). Notably, impairments of executive function are of particular concern in older adults, as these changes may be early indicators of neurological pathology (Blicher et al., 2015; Rentz et al., 2014). Approaches to mitigate these declines over the past 20 years have largely been focused (at least monetarily) on pharmacological interventions, which have not yielded proportional returns for subsequent improvement in cognitive capacity (Honig et al., 2018; Salloway et al., 2014). Behavioral interventions to improve aging-related cognitive declines offer significant potential as inexpensive and highly accessible programs of activity in older adults of varying physical capacity. Physical activity and cognitive training programs are

being tested with increasing frequency to attempt to improve executive functions long associated with declines in older adults. However, often times these interventions are often considered in isolation of one another instead of as complementary to each other. The present research attempts to test the combination of interventions involving physical activity and brain training in comparison to the effects of these interventions individually over a 12-week program.

Over the last few years, considerable research has demonstrated that aerobic exercise can improve cognitive performance in older adults in an array of age-susceptible frontally mediated cognitive-executive

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functions. In our own work, we have shown that introducing an aerobic exercise regimen in previously sedentary older adults improves semantic fluency over a period of 12 weeks (Nocera et al., 2015, 2017). In addition, we have shown that these behavioral changes are associated with changes in patterns of cortical activity during functional neuroimaging (McGregor, Crosson, Krishnamurthy, et al., 2018; Nocera et al., 2017). Despite the growing evidence that participating in structured physical activity can mitigate negative health-related outcomes, American adults continue to exhibit low engagement in regular physical exercise (Chodzko-Zajko et al., 2009; Lachman et al., 2018). This is most evident in the older population, which is the most sedentary age group and the age group most prone to frailty and poor health outcomes (Bauman et al., 2016; McPhee et al., 2016). Furthermore, prolonged sedentary behavior is especially high among older adults living with cognitive dysfunction (i.e., memory loss or dementia), exacerbating the rate of adverse health outcomes in this population (Ekelund et al., 2016; Siddarth et al., 2018). Therefore, identifying complementary approaches and/or alternative approaches to exercise to improve physical function and maintain cognitive abilities is of growing interest.

One activity that has been increasingly promoted as having positive effects on cognitive outcomes is the use of cognitive training (“brain training”) programs. Independent, computer-based cognitive training targeting incipient cognitive impairment is becoming increasingly available and marketed, particularly using mobile device “App” presentation formats (Ten Brinke et al., 2019). The rapid growth of brain training applications provides increased accessibility to this approach, though the clinical significance of brain training remains a topic of debate. In cases of mild cognitive impairment (MCI), the combination of aerobic exercise with cognitive training has been shown to improve specific forms of memory (Combourieu Donnezan et al., 2018). In healthy older adults, experimental evaluations of cognitive training platforms have shown that cognitive training can improve older adults’ performances on specific aspects of executive function (Ten Brinke et al., 2019). However, the functional, “real-world” benefit is not without controversy, as gains are typically noted in areas closely related to the specific training protocols (Sala & Gobet, 2019). A recent Cochrane review has reported little to no improvement in any cognitive performance across eight randomized controlled trials involving more than 1,100 reportedly healthy adults more than the age of 65 years (Gates et al., 2019). However, additional work is warranted to test if cognitive training can augment improvements in executive function associated with lifestyle interventions such as increased physical activity (Colcombe et al., 2006; McGregor, Crosson,

Mammino, et al., 2018; Nocera et al., 2015, 2017; Zlata et al., 2015).

The combination of aerobic exercise with concomitant cognitive training is currently not well studied and reviews offer conflicting reports. For example, Karr et al. (2014) reported cognitive training as having a larger effect size than aerobic exercise with respect to improvements in executive function (Karr et al., 2014). These results, however, are challenged by more recent work in the Aerobic and Cognitive Exercise Study (ACES), which found a stronger effect for physical exertion on measures of executive function than that of cognitive training (Anderson-Hanley et al., 2018). As such, more work is needed to assess the specific cognitive domains that may be differentially sensitive to combined aerobic and cognitive interventions, as well as modifications of existing cognitive training regimens that could potentially improve outcomes (i.e., group training, training duration). In the current study, we contrast cognitive training without aerobic exercise to cognitive training with aerobic exercise to test whether a computerized brain training regimen would improve measures of executive function. We compare these data with an aerobic exercise control group that did not receive cognitive training.

In the present study, we randomized older participants into a cognitive training + physical exercise regimen ($n = 13$) versus a cognitive training ($n = 12$) alone programs. We compared these groups with another group of older participants ($n = 12$) that enrolled in an aerobic exercise intervention alone without a cognitive training component. We hypothesized that cognitive training would improve executive functions and specifically verbal fluency. Given our previous work showing selective improvements in executive function with aerobic exercise, we hypothesized that the addition of cognitive training would further enhance executive function in consideration of previous reports of improvements in executive function using this technology (Borella et al., 2010; Brehmer et al., 2012; Eggenberger et al., 2015; Mahncke et al., 2006).

Materials and Methods

Participants

In this 12-week randomized controlled trial, 37 participants were randomized using a computerized algorithm (Urbaniak & Plous, 2013) prior to study enrollment into either an aerobic exercise plus cognitive training group (AE+Cog) or a nonaerobic exercise (stretching and balance) plus cognitive training control group (Cog) to equalize contact and monitoring. Due to participant attrition over the 12 weeks (three in AE+Cog, four in Cog), data from 25

completers of the interventions are presented in this report. An additional 12 participants enrolled in a separate study involving only aerobic exercise. These participants underwent the same aerobic training regimen in the same environment (structurally and socially) as the AE+Cog and Cog, but did not receive any cognitive training (this group will be referred to as the aerobic exercise group [AE]). Participants in the AE group were randomized to that group as compared with an alternative exercise condition beyond the scope of this report (attrition for these groups were as follows: AE = 3, alternative intervention = 3). Recruitment procedures were similar across studies. Project personnel explained the purpose and potential risks of the studies and completed the informed consent process with each participant. This consent process abides by protocols approved by XXX University's Institutional Review Board (IRB) in compliance with the Helsinki Declaration.

Participants were recruited from a volunteer database that included individuals aged 60 years and above. To meet inclusion criteria, participants had to be between the age range of 60 and 89 years, report being sedentary (defined as not engaging in structured physical activity and/or not accumulating 20 min or more of moderate physical activity during the week), have no history of major neurological disease, including Parkinson's disease, Alzheimer's disease, and multiple sclerosis or stroke, report being a native English speaker. All participants were required to obtain physician's written approval to participate in the study regardless of group assignment. Exclusion criteria included failure to provide informed consent, hospitalization within the past 6 months, and significant cognitive-executive impairment, which is defined as a score on the Montreal Cognitive Assessment (MoCA) of <24. If the MoCA score was below 24, but above 19, a second cognitive screen, the American National Adult Reading Test (ANART) was administered with more than 15 errors as an exclusion value (Grober & Sliwinski, 1991).

Interventions

Aerobic exercise and cognitive training (AE+Cog). For this arm of intervention, randomized participants ($n = 13$) attended both exercise training sessions and cognitive training sessions demonstrated to facilitate physiological changes. The aerobic training protocols were developed to follow the guidelines provided by the American College of Sports Medicine for optimizing cardiovascular fitness (American College of Sports Medicine, 2013). Participants in the aerobic exercise group completed 36 sessions over 12 weeks on stationary exercise bicycles. Group exercises were led by a trained instructor who monitored and modified training sessions to ensure that the intensity of exercise fell

within the parameters of the study (Nocera et al., 2015, 2017). Sessions started at 20-min duration and increased by 1 to 2 min each session as needed until a maximum length of 45 min was achieved. Exercise intensity began at low levels (50% of maximal heart rate reserve [HRR]) and increased by 5% every week (if the instructor deemed it appropriate) to a maximum of 75% maximal HRR.

Maximal HRR was determined using the Karvonen method (Karvonen et al., 1957) and is widely used in clinical trials. Target exercise HR is calculated by subtracting the participant's age from 220. Resting heart rate is then subtracted from this number. The result is then multiplied by the target percent (50%–75%) and the product is added back to resting heart rate to provide the target exercise session heart rate.

The cognitive training component for this group immediately followed the cool down activity (light stretching) of the aerobic intervention. The commercially available Mindfit program was utilized for the cognitive training. The Mindfit was selected based on its mainstream usage and its demonstrated effectiveness and adherence (>90%) in previous studies (Verghese et al., 2010). Each training session included a mixture of 21 visual, auditory, and cross-modality tasks aimed at executive functions as well as other cognitive processes. Each training session lasted approximately 20 min and progressed on three levels of difficulty as specified by the manufacturer: easy, moderate, and hard. Based on performance throughout the intervention, these levels were titrated to the participant's progress. The algorithm for this titration was proprietary and was not disclosed to investigators.

Cognitive training control group (Cog). For this intervention group, 12 randomized participants followed the same guidelines as the cognitive component of the AE+Cog group but did not partake in aerobic exercise. However, to equalize contact/monitoring of the groups, this group met for the same total duration time as the AE+Cog group, but instead of aerobic exercise before the cognitive training, this group participated in individual, progressive whole-body stretching and toning exercises designed for individuals 65 years and above. "Stretching" control groups have been utilized in previous studies examining cognition and aerobic exercise and have not been shown to result in improvements in cognitive function (Colcombe et al., 2006; Erickson et al., 2011; Jonasson et al., 2017; Voelcker-Rehage et al., 2011; Voss et al., 2010).

Aerobic exercise (AE). The aerobic exercise alone (AE) group ($n = 12$) completed the same exercise intervention using the same inclusion and progression parameters as denoted for the AE in the AE+Cog group. This group was enrolled in a separate study, but whose exercise regimen and class schedule were completed

alongside the 25 participants denoted above. The Research Center in which the groups performed the intervention has an exercise core with standardized interventions and exercise staff that are involved in multiple interventions. The AE group belonged to a study that used similar outcome measures. However, due to a different research focus for the study, some assessments completed for the Cog and AE+Cog groups were not completed in the AE alone group. These are denoted as appropriate.

Assessments

All participants were evaluated prior to beginning the interventions and again at the conclusion of the study. All assessments were done no more than 5 days before the start of or 5 days after the conclusion of the 12-week intervention period.

Physical Assessments

Physical measures of function include gait speed (single- and dual-task) as measured by a GaitRITE mat (GaitRite, Franklin, NJ), the Timed Up and Go (TUG) test (Podsiadlo & Richardson, 1991), and the Short Physical Performance Battery (SPPB; Guralnik et al., 1994).

Gait speed. Participants walked on the 6.10-m GaitRite for four trials: two single-task walking only trials and two dual-task walking while talking trials following a practice trial. The order of the walks was randomized. For the dual-task trials participants were asked to recite alternating letters of the alphabet. The primary outcome for each walk was gait speed for each of the two walks of both the single and dual-task trials. Of note, gait speed was only performed in the AE group using a 4-m walk time instead of the GaitRite. Dual-task measures were not assessed in this group.

TUG test. The TUG test was administered using a standard armless chair with a seat height of 46 cm. Participants were asked to rise from a seated position and ambulate around a cone placed 3 m in front of the chair's location and return to a seated position in the chair. Time to complete in seconds is the outcome measure. Three trials were averaged for each session.

SPPB. The SPPB is based on a timed short distance walk (4 m), repeated chair stands, and tests of balance. The primary outcome was the total score (out of 12). This assessment is often used to characterize fall risk in older adults.

Estimated VO_2 . To evaluate change in cardiovascular fitness following the interventions, participants

performed a submaximal exercise test on a cycle ergometer test (YMCA) before and after the intervention. The test was controlled via computer with a Monark 928 electronically braked cycle ergometer (Monark, Sweden). VO_2 in mL/kg/min was the primary outcome for the analysis.

Cognitive Assessments

The cognitive test battery consisted of components of the Delis-Kaplan Executive Function System (D-KEFS; Delis et al., 2001), computerized n-back, and digit span forwards/backwards. These outcomes were chosen to isolate specific components of executive function and working memory that have previously been shown to decline with age (Lauenroth et al., 2016; Melby-Lervåg et al., 2016; Nocera et al., 2015; Wingfield et al., 1988; Zlatar et al., 2013). In addition, these aspects of cognition have been demonstrated to improve in older adults following a physical activity intervention designed to enhance aerobic fitness (Baniqued et al., 2018; Colcombe et al., 2006; Erickson et al., 2011; Loprinzi et al., 2017; Nocera et al., 2015; Verghese et al., 2010). Each of the tasks below had a practice session to allow the participant to acclimate and understand the directions. Alternate forms/version from pre to post were utilized to limit practice effects.

D-KEFS Tests

Trail making test. The trail making test assesses flexibility of thinking using a visual sequence tracking task. Participants are timed as they connect numbers and letters in ordered sequences. Outcome measure is time to complete for each section.

Verbal fluency. Comprising subcomponents, the verbal fluency assessment tests letter fluency (recall as many words beginning with a specific letter) and semantic fluency (recall as many members of a category as possible). The participant had 60 s to generate as many items as possible. Verbal fluency is susceptible to age related decline and generally considered a measure of a verbal component of executive function (Spren, O., y Strauss, 1998).

Color word interference. Also known as the Stroop paradigm, this test is a commonly used executive function task which requires participants to inhibit a dominant response or switch from inhibition of the response to an automatic response. Scores reflect a combination of errors and time to complete each section of the examination (Color = C, Word = W, Color-Word = CW). Score is total time plus $+(total\ time/100) \times uncorrected\ errors$ in the CW task.

Additional Working Memory Assessments

N-back task. The n-back task is a continuous performance working memory task (Kirchner, 1958). Both accuracy and latency of response were recorded. The n-back task employed four load factors (0-back to 2-back). Letters were presented in serial order asking the participant to denote YES (Keypad Button 1) if the digit was the target or NO (Keypad Button 2) if not target. The test was progressive (starting at 0-back) and adaptive ceasing if the participant performed below 50% accuracy on a given load factor. Of note, the AE group did not complete the n-back task.

Digit span forward/backward. Participants are asked to recall increasingly long strings of digits in order (forward) or reverse order (backward) of presentation. Digits are presented verbally to the participant at a rate of 1/s. Two exemplars of a given digit depth (e.g., -23,517 and 38,294) are presented and the test continues to the next digit depth if the participant correctly recalls at least one of the exemplars. The maximum digit span for this test was 14 digits. Outcome measure is total digit span depth prior to failure to complete two exemplars of the same depth.

Statistical Analysis

We completed a split-plot analysis of variance (ANOVA) testing differences between pre- and postsessions among groups. For this analysis, we employed a random effects maximum likelihood design with participants held as a random effect. We controlled for violations of sphericity using a Greenhouse–Geisser correction for within-participants variance.

In addition, we tested change scores (post–pre measures) to evaluate group differences in behavioral measures due to treatment condition: the aerobic training alone, aerobic condition + cognitive (AE+Cog) training or the cognitive training alone (Cog). An ANOVA ($df = [2, 35]$) was completed across the three groups on test of each change score to evaluate overall difference between pre–post across groups. For pairwise group comparisons, a between groups *t* test (single factor ANOVA) was used to test for group differences. In addition, we correlated change in physical function (estimated VO_2) with changes in cognitive measurements. Due to the influence of outliers in change score, we performed a Dixon *Q* test to denote if outliers were significant. If this were the case, we then performed a secondary Fisher’s exact test between groups setting the binary values of performance improvement or decrement after the intervention. We set the significance level at .05 with a Bonferroni

Table 1. Overall Participant Demographics at Study Enrollment.

Participant Variable	AE+Cog	Cog	AE
Age	72.1 (1.6)	73 (1.7)	69.5 (1.6)
N/Gender	13/9 female	12/9 female	12/8 female
Education	15.1 (0.9)	16.3 (0.9)	14.5 (0.7)
BMI	29.4 (3.3)	26.7 (2.7)	27.4 (3.1)
e VO_2 max	19.2 (2.6)	20.2 (2.4)	20.5 (2.5)
MoCA	27.9 (0.54)	27.5 (0.52)	26.8 (0.75)
SPPB	9.1 (0.45)	8.9 (0.46)	11.3 (0.2)
Gait speed ^a (cm/s)	100.7 (4.7)	104 (5.1)	106 (5.2)
TUG (s)	11.7 (0.75)	10.7 (0.78)	10.2 (0.61)

Note. Cell values denote group means. Parentheses indicate standard error within cell. Bracket indicates range. No significant differences between groups except for SPPB, where AE alone had higher scores as compared with both AE+Cog and Cog. AE = aerobic exercise; BMI: body mass index; e VO_2 max = estimate of VO_2 max in mL/min/kg; MoCA = Montreal Cognitive Assessment; SPPB = Short Physical Performance Battery; TUG = Timed Up and Go test.

^aGait speed was measured over 6.71 m for AE+Cog and Cog groups, but measured over 4 m for AE group.

correction for family-wise error. The software JMP13 (SAS Institute, Cary, NC) was used for all statistical analyses.

Results

Table 1 shows demographic data of participants prior to interventions. No significant differences were shown between the AE+Cog and the cognitive training alone groups. There were significant differences respective of the SPPB in the AE alone group at baseline with AE alone participants having lower risk of mobility impairment. Ethnicity of participants was also denoted. The study groups included both African Americans (AA) and Caucasians (Cau) with a roughly equivalent representation between groups. These were AE+Cog (4 AA, 9 Cau), Cog (4 AA, 8 Cau), and AE (6 AA, 6 Cau).

Pre–Post Analysis

Assessment scores pre and post are summarized in Table 2. These include both pre- and postexercise and cognitive measures. Within group changes (pre–post) are denoted by bold type. Stylized font denotes differences between groups at post as denoted in the table footer. Significant differences existed between groups at pre for SPPB (due to inclusion criteria differences).

Table 2. Pre/Postintervention Scores on Assessments.

Assessment	AE+Cog		Cog		AE	
	Pre	Post	Pre	Post	Pre	Post
VO ₂ (mL/min/kg)	19.2 (3.1)	23.6 (2.9)	20.25 (3.3)	19.7 (3.9)	20.3 (2.0)	<u>24.1 (2.2)</u>
SPPB	9 (1.47)	10 (1.26)	8.9 (1.78)	9.3 (1.67)	11.2 (0.2)	<u>11.3 (0.2)</u>
Single gait	100.7 (6.1)	100.1 (7.9)	104.1 (5.1)	101.1 (7.2)	110 (2.7)	111 (2.8)
Dual gait	82.2 (6.5)	85.2 (6.3)	80.1 (8.2)	81.5 (8.1)	—	—
Letter fluency	37.3 (5.6)	41.6 (7.9)	39.6 (7.7)	37.7 (3.1)	38.6 (4.2)	<u>41.6 (3.9)</u>
Sem. fluency	12.6 (2.5)	15.6 (2.1)	13.3 (3.1)	11.5 (2.1)	12.9 (2.5)	<u>15.7 (2.4)</u>
N-back acc.	80.2 (9.1)	90.7 (4.4)	88.7 (2.9)	85.5 (3.2)	—	—
N-back speed	961 (9.4)	987 (9.6)	977 (8.4)	906 (8.8)	—	—
Stroop	265.4 (8.4)	259.4 (8.9)	278.5 (6.5)	266 (5.8)	270 (6.2)	274 (7.9)
Trails A	38 (2.3)	38.5 (4.6)	36.8 (3.1)	36.1 (1.5)	40.1 (3.5)	39.2 (3.1)
Trails B	79.3 (6.0)	75.8 (7.2)	73.6 (4.1)	76.5 (8.1)	76.9 (4.3)	76.1 (5.2)
Digit forward	5.2 (1.5)	5.2 (1.2)	5.2 (2.3)	5.2 (1.8)	4.8 (2.4)	5.0 (3.2)
Digit back	6.1 (1.5)	6.7 (1.8)	5.2 (1.8)	7.1 (1.5)	6.2 (3.1)	6.5 (2.6)

Note. Units are denoted as appropriate. Parentheses denote standard error of the mean. Units provided as appropriate. Bold indicates within-participants (WITHIN GROUP) difference comparing pre–post at $p < .05$. — denotes test was not completed in this group. Italics denotes differences at post between AE+Cog and Cog. Underline denotes differences at post between AE only and Cog. AE = aerobic exercise; VO₂ = estimated VO₂max; SPPB = Short Physical Performance Battery; Single gait = gait speed; Dual gait = gait speed during dual task; Letter fluency and semantic fluency portion of D-KEFS verbal fluency.

Change Score Comparisons

All subsequent analyses were performed on change scores measuring post–pre. We have added comparisons of the AE alone group as a control.

VO₂ change. Changes scores in estimates of VO₂ significantly differed between AE+Cog and Cog groups ($t(24) = 3.17, p < .01$). On average, the AE+Cog group improved by 4.4 mL/min/kg as compared with .91 mL/min/kg in the Cog group. Significant outliers were reported in the VO₂ change data for both groups. A Fisher's exact test confirmed that members of the AE+Cog showed increased VO₂ capacity after the intervention as compared with Cog only: $p < .001$, Fisher's exact test. In addition, the AE group had improved VO₂ change as compared with Cog, $t(23) = 2.9, p < .01$. No difference in VO₂ change was shown between AE and AE+Cog, $t(24) = 1.25, n.s.$

Gait speed. We found no differences in change scores between groups after the interventions, $F(2, 35) = 1.5, n.s.$, in gait speed. In comparisons between AE+Cog and Cog, no differences were shown for the single-task gait speed change, $t(24) = 0.20, n.s.$, and dual-task gait speed change, $t(24) = 0.27, n.s.$ No significant outliers were reported. Of note, gait speed assessments in AE were done over 4 m, and dual-task gait was not attempted in this group.

TUG. Change scores on the TUG test did not show group differences after the interventions: $t(24) = 0.26, n.s.$ Significant outliers were shown across samples. The Fisher's exact test comparing increased or decreased speed post intervention showed that the AE+Cog group

improved on TUG as compared with the Cog intervention: $p < .03$, Fisher's exact test. Cog only group showed worse performance on TUG in postsession compared with pre. In addition, no differences were shown in change scores between the AE and other groups.

N-back tasks. Accuracy but not speed improved in the AE+Cog group in n-back testing. The AE+Cog group performed significantly more accurately post intervention than the Cog group: $t(24) = 2.19, p < .05$. As stated previously, the n-back was not attempted in the AE only group.

Digit span. We found significant differences between groups in backwards digit span. The AE+Cog group performed significantly better when comparing change scores on digit span backwards: $t(24) = 2.55, p < .05$. Due to outliers, we performed a Fisher's exact test on digits span forwards. We found the Cog intervention to have improved performance on forwards digit span as compared with both the AE+Cog and the AE alone: $p < .03, p < .05$, Fisher's exact test. The maximum digit span in the samples was 14 for the forward and 7 for the backward. The AE alone group did not differ from the AE+Cog group.

Letter fluency. We found significant differences in change scores in letter fluency between groups. AE+Cog had larger improvements in letter fluency as compared with the Cog intervention: $t(24) = 2.7, p < .02$. In addition, the AE only group showed improvements in letter fluency similar to the magnitude in the AE+Cog group. These were significantly greater than the Cog intervention: $t(23) = 2.9, p < .01$.

Semantic fluency. Semantic fluency showed improvement in AE+Cog. These were significantly higher than the Cog intervention: $t(24) = 2.7, p < .01$. Significant outliers necessitated a contingency analysis both within and between groups. The contingency analysis within-groups is a binomial test where the expected p value is set to .5. We found the Cog group showed consistent decreases in change score indicating worse performance after the intervention: $p < .01$, Fisher's exact test. This is contrasted to improvements in the AE+Cog group as compared with the Cog intervention: $p < .01$, Fisher's exact test. As outliers were confined to AE+Cog group, we completed a standard t test between AE alone and Cog condition on change score. This test showed significant differences between groups: $t(23) = 2.8, p < .01$.

Color word interference. We did not find any significant differences in the Stroop paradigm after the interventions.

Trails making test. No differences were shown in completion time after the interventions of Trails A or B.

Discussion

This study examined whether cognitive training would improve executive function across a battery of neuropsychological tests, and whether those findings could be potentiated in a group undergoing cognitive training plus aerobic exercise over 12-week interventions. We hypothesized that cognitive training alone would improve performance on executive function and that the impact would in fact be enhanced with the addition of aerobic exercise. Our results did not demonstrate a significant benefit of cognitive training in isolation. However, as we have shown in previous work (Nocera et al., 2015), an aerobic exercise intervention demonstrated improved cardiovascular fitness, improved TUG time, and improved performance in verbal executive function. In aggregate, these results are in support of the literature suggesting that executive functions in aging are susceptible to improvements via aerobic exercise.

The unsupported hypothesis of improved performance via cognitive training alone was suggested based on a body of research supporting various cognitive training paradigms that have demonstrated large and durable effects on cognitive functioning in older adults (Ball et al., 2002; Ten Brinke et al., 2019). In addition, the study by Ball et al. demonstrated cognitive interventions targeting memory, reasoning, and speed of processing were effective to the magnitude equivalent to the amount of decline expected in older persons without dementia over a 7- to 14-year interval. However, despite some promising results, cognitive training paradigms and related studies are more often mixed with the effectiveness of relatively short-term cognitive training described as "limited." For example, Owen and colleagues examined cognitive training tasks designed to improve

reasoning, memory, planning, visuospatial skills, and attention in more than 11,000 participants. The researchers found improvements in each of the cognitive tasks trained; however, "no evidence was found for transfer effects to untrained, 'real-world?' tasks, even when the tasks were cognitively closely related" (Owen et al., 2010). Findings from the present study are limited with respect to the scope of the test battery administered, but though the cognitive training program included a verbal flexibility component, this did not appear to impact verbal fluency outcomes as measured in the current work. However, the dosing of the present study was limited to 12 weeks, and this may simply not be long enough to show effect on our rather small study cohort. Additional work with longer cognitive training interventions may provide more promising outcomes.

That the aerobic exercise with cognitive training group in addition to the aerobic exercise only group improved executive function and, more specifically, semantic verbal fluency is in line with our previous work documenting enhanced verbal fluency following a 12-week spin intervention (Nocera et al., 2015, 2017). Importantly, based on the finding of limited impact of cognitive training alone, we believe the documented effects were due mostly to the aerobic exercise component. Our group has previously shown spin exercise in isolation resulted in a 15% improvement in semantic verbal fluency compared with a 2% improvement for the control group in a cohort of sedentary older adults. In the current study, we saw an improvement of 18% in semantic verbal fluency and a letter fluency improvement of 10%. Taken together, these studies support the selective improvement hypothesis which suggests that tasks supported by the frontal and prefrontal regions of the brain are selectively improved by aerobic exercise (Kramer et al., 2006). Furthermore, the hypothesis suggests improvements are relegated to areas most impacted by "normal" cognitive aging. That is, in aging, cognitively normal older adults demonstrate faster and earlier decline in executive functions, and importantly, that cognitive decline in these domains may be able to be reversed, or slowed, with exercise therapy. In the context of our findings, this suggests that verbal fluency may demonstrate the greatest age-related decline and may be most malleable to improvements brought on by an aerobic intervention (Amieva et al., 2005; Clark et al., 2009; Mueller et al., 2016). More broadly, our results further add to the current body of literature, which suggests improvements of various executive functions among healthy older adults who undergo aerobic exercise training.

Evidence from animal models and early human work has demonstrated several possible mechanisms that may underlie the ameliorative effects of aerobic exercise on cognitive function in aging. Both the animal model and human studies of brain morphology have suggested that aerobic activity positively influences cortical structure

with the greatest neuroprotective effects localized to the frontal and prefrontal areas of the human brain (Colcombe et al., 2006; Erickson et al., 2014; Kramer et al., 2006). More specifically, research has shown that older adults who participated in 6 months of aerobic training significantly increased brain volume in both gray and white matter with no such change being demonstrated in older adults who participated in stretching or toning (nonaerobic) exercise. These findings are especially meaningful because frontal areas typically demonstrate the greatest age-related decline (Colcombe et al., 2006). The documented enhancement in frontal integrity is supportive of the previously described behavioral research demonstrating that aerobic fitness has the greatest impact on frontally mediated executive functions.

Neuroimaging studies show that aerobically trained individuals have increased functioning of key aspects of the attentional circuitry during cognitive tasks. In line with this, and to better understand the behavioral findings via aerobic exercise, our group recently examined changes in cortical activation patterns following an aerobic (spin) intervention. It is important to note that older adults, in comparison with younger adults, typically exhibit greater bilateral hemispheric BOLD activation patterns across the inferior frontal cortex while performing an fMRI verbal fluency paradigm. Critically, this increased bilateral activity has been repeatedly documented to be associated with worse performance on the verbal fluency task when compared with younger individuals who evidenced more left lateralized (Meinzer et al., 2012; Nocera et al., 2017). In this previous exercise study, and in support of the current findings, when comparing right lateral frontal activity and verbal fluency performance across all participants pre-exercise, there was a strong negative correlation between positive BOLD activity in the right hemisphere and exemplar output. That is, the more likely the individuals were to recruit right inferior frontal gyrus during verbal fluency tasks, the worse their verbal output was. Interestingly, the spin group exhibited less BOLD activity following the spin intervention in right frontal regions while simultaneously demonstrating improvement in verbal fluency output. The findings suggest that an aerobic spin intervention might facilitate a more efficient recruitment array during verbal fluency task and support the current study's findings of improved verbal fluency following aerobic exercise.

However, there are limitations in the present study. The relatively low number of participants makes extrapolation of the current findings toward the general population somewhat challenging. It may be that cognitive training alone could show benefits in verbal fluency or other executive functions with a higher participant inclusion. Future work would be improved by increasing the number of participants assessed over the intervention.

Another limitation of the study relates to the use of an aerobic only control condition. As this component was from a separate study, the total contact time with study personnel was lower in the aerobic only group. Despite this, this group showed significant changes with respect to measures of verbal fluency. Toward this, however, while this condition supports the contention that aerobic exercise shows benefits to certain measures of executive function, a more appropriate control may be a no-contact control via a wait-list condition. Future work may consider the inclusion of such a group. The present study is also limited in its time course. Other studies were able to find significant changes with a longer 6-month cognitive training intervention. In future studies, a longer time course might demonstrate more significant findings related to cognitive training in isolation. Future inquiries into the effect of aerobic and cognitive interventions can further explore imaging to shed light on the physiological mechanisms.

In summary, the deleterious effect of aging and its impact on cognitive status, mobility, and independence are well established. As the population continues to age, these issues and efforts aimed at remediation will only become more important. Herein, we aimed to examine whether cognitive training could be impactful and if the impact could be potentiated with aerobic exercise. The findings demonstrate a relatively low beneficial impact of cognitive training alone but add to the robust and undeniable systematic benefit of exercise. This study was performed with healthy adults but the impact of aerobic exercise could be even greater in populations with cognitive impairment and warrants further study.

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Author Contributions

JRN, KMM, BC designed project; JRN, YK, KMM, KM conducted experiment; JRN, KMM, KM, YK conducted intervention; JRN, KMM, KM performed data analysis; KMM, YK, JRN, WW, YK contributed to manuscript preparation.

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References

- American College of Sports Medicine. (2013). *ACSM's guidelines for exercise testing and prescription*. *The Journal of the Canadian Chiropractic Association*, *58*, 328. <https://doi.org/10.1007/s13398-014-0173-7.2>
- Amieva, H., Jacqmin-Gadda, H., Orgogozo, J.-M., Le Carret, N., Helmer, C., Letenneur, L., . . . Dartigues, J.-F. (2005). The 9 year cognitive decline before dementia of the Alzheimer type: A prospective population-based study. *Brain: A Journal of Neurology*, *128*(Pt. 5), 1093–1101. <https://doi.org/10.1093/brain/awh451>
- Anderson-Hanley, C., Barcelos, N. M., Zimmerman, E. A., Gillen, R. W., Dunnam, M., Cohen, B. D., . . . Kramer, A. F. (2018). The Aerobic and Cognitive Exercise Study (ACES) for community-dwelling older adults with or at-risk for mild cognitive impairment (MCI): Neuropsychological, neurobiological and neuroimaging outcomes of a randomized clinical trial. *Frontiers in Aging Neuroscience*, *10*, Article 76. <https://doi.org/10.3389/fnagi.2018.00076>
- Ball, K., Berch, D. B., Helmers, K. F., Jobe, J. B., Leveck, M. D., Marsiske, M., . . . Willis, S. L. (2002). Effects of cognitive training interventions with older adults: A randomized controlled trial. *Journal of the American Medical Association*, *288*, 2271–2281. <https://doi.org/10.1001/jama.288.18.2271>
- Baniqued, P. L., Gallen, C. L., Voss, M. W., Burzynska, A. Z., Wong, C. N., Cooke, G. E., . . . D'Esposito, M. (2018). Brain network modularity predicts exercise-related executive function gains in older adults. *Frontiers in Aging Neuroscience*, *9*, Article 426. <https://doi.org/10.3389/fnagi.2017.00426>
- Bauman, A., Merom, D., Bull, F. C., Buchner, D. M., & Fiatarone Singh, M. A. (2016). Updating the evidence for physical activity: Summative reviews of the epidemiological evidence, prevalence, and interventions to promote “active aging.” *Gerontologist*, *56*, S268–S280. <https://doi.org/10.1093/geront/gnw031>
- Blicher, J. U., Near, J., Næss-Schmidt, E., Stagg, C. J., Johansen-Berg, H., Nielsen, J. F., . . . Ho, Y. C. L. (2015). GABA levels are decreased after stroke and GABA changes during rehabilitation correlate with motor improvement. *Neurorehabilitation & Neural Repair*, *29*(3), 278–286. <https://doi.org/10.1177/1545968314543652>
- Borella, E., Carretti, B., Riboldi, F., & De Beni, R. (2010). Working memory training in older adults: Evidence of transfer and maintenance effects. *Psychology and Aging*, *25*, 767–778. <https://doi.org/10.1037/a0020683>
- Brehmer, Y., Westerberg, H., & Bäckman, L. (2012). Working-memory training in younger and older adults: Training gains, transfer, and maintenance. *Frontiers in Human Neuroscience*, *6*, Article 63. <https://doi.org/10.3389/fnhum.2012.00063>
- Chodzko-Zajko, W. J., Proctor, D. N., Fiatarone Singh, M. A., Minson, C. T., Nigg, C. R., Salem, G. J., & Skinner, J. S. (2009). Exercise and physical activity for older adults. *Medicine & Science in Sports & Exercise*. https://www.vub.be/GERO/Docs_Gero/Chodzko-Zajko%20MedSciSportsExerc%202009.pdf
- Clark, L. J., Gatz, M., Zheng, L., Chen, Y.-L., McCleary, C., & Mack, W. J. (2009). Longitudinal verbal fluency in normal aging, preclinical, and prevalent Alzheimer's disease. *American Journal of Alzheimer's Disease & Other Dementias*, *24*(6), 461–468. <https://doi.org/10.1177/1533317509345154>
- Colcombe, S. J., Erickson, K. I., Scalf, P. E., Kim, J. S., Prakash, R., McAuley, E., . . . Kramer, A. F. (2006). Aerobic exercise training increases brain volume in aging humans. *Journal of Gerontology*, *61*, 1166–1170. <https://doi.org/10.1093/gerona/61.11.1166>
- Comboureu Donnezan, L., Perrot, A., Belleville, S., Bloch, F., & Kemoun, G. (2018). Effects of simultaneous aerobic and cognitive training on executive functions, cardiovascular fitness and functional abilities in older adults with mild cognitive impairment. *Mental Health and Physical Activity*, *15*, 78–87. <https://doi.org/10.1016/j.mhpa.2018.06.001>
- Courtney-Long, E. A., Carroll, D. D., Zhang, Q. C., Stevens, A. C., Griffin-Blake, S., Armour, B. S., & Campbell, V. A. (2015). Prevalence of disability and disability type among adults—United States, 2013. *MMWR. Morbidity and Mortality Weekly Report*, *31*, 777–783.
- Delis, D. C., Kaplan, E., & Kramer, J. (2001). Examiner's manual for the Delis-Kaplan executive function system. *Child Neuropsychology*. <https://doi.org/10.1080/09297040490911140>
- Eggenberger, P., Schumacher, V., Angst, M., Theill, N., & de Bruin, E. D. (2015). Does multicomponent physical exercise with simultaneous cognitive training boost cognitive performance in older adults? A 6-month randomized controlled trial with a 1-year follow-up. *Clinical Interventions in Aging*, *10*, 1335–1349. <https://doi.org/10.2147/CIA.S87732>
- Ekelund, U., Steene-Johannessen, J., Brown, W. J., Fagerland, M. W., Owen, N., Powell, K. E., . . . Yi-Park, S. (2016). Does physical activity attenuate, or even eliminate, the detrimental association of sitting time with mortality? A harmonised meta-analysis of data from more than 1 million men and women. *The Lancet*, *388*, 1302–1310. [https://doi.org/10.1016/S0140-6736\(16\)30370-1](https://doi.org/10.1016/S0140-6736(16)30370-1)
- Erickson, K. I., Leckie, R. L., & Weinstein, A. M. (2014). Physical activity, fitness, and gray matter volume. *Neurobiology of Aging*, *35*, S20–S28. <https://doi.org/10.1016/j.neurobiolaging.2014.03.034>
- Erickson, K. I., Voss, M. W., Prakash, R. S., Basak, C., Szabo, A., Chaddock, L., . . . Kramer, A. F. (2011). Exercise training increases size of hippocampus and improves memory. *Proceedings of the National Academy of Sciences*, *108*, 3017–3022. <https://doi.org/10.1073/pnas.1015950108>
- Gates, N. J., Rutjes, A. W., Di Nisio, M., Karim, S., Chong, L.-Y., March, E., . . . Vernooij, R. W. (2019). *Computerised cognitive training for maintaining cognitive function in cognitively healthy people in midlife*. Cochrane Database of Systematic Reviews. <https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD012278.pub2/full>
- Grober, E., & Sliwinski, M. (1991). Development and validation of a model for estimating premorbid verbal intelligence in the elderly. *Journal of Clinical and Experimental Neuropsychology*, *13*, 933–949. <https://doi.org/10.1080/01688639108405109>
- Guralnik, J. M., Simonsick, E. M., Ferrucci, L., Glynn, R. J., Berkman, L. F., Blazer, D. G., . . . Wallace, R. B. (1994). A short physical performance battery assessing lower

- extremity function: Association with self-reported disability and prediction of mortality and nursing home admission. *Journals of Gerontology*, *49*, M85–M94. <https://doi.org/10.1093/geronj/49.2.M85>
- Honig, L. S., Vellas, B., Woodward, M., Boada, M., Bullock, R., Borrie, M., . . . Siemers, E. (2018). Trial of solanezumab for mild dementia due to Alzheimer's disease. *New England Journal of Medicine*, *378*, 321–330. <https://doi.org/10.1056/NEJMoa1705971>
- Jonasson, L. S., Nyberg, L., Kramer, A. F., Lundquist, A., Riklund, K., & Boraxbekk, C. J. (2017). Aerobic exercise intervention, cognitive performance, and brain structure: Results from the Physical Influences on Brain in Aging (PHIBRA) Study. *Frontiers in Aging Neuroscience*, *8*, Article 336. <https://doi.org/10.3389/fnagi.2016.00336>
- Karr, J. E., Areshenkoff, C. N., Rast, P., & Garcia-Barrera, M. A. (2014). An empirical comparison of the therapeutic benefits of physical exercise and cognitive training on the executive functions of older adults: A meta-analysis of controlled trials. *Neuropsychology*, *28*, 829–845. <https://doi.org/10.1037/neu0000101>
- Karvonen, M., Kentala, K., & Musta, O. (1957). The effects of training heart rate: A longitudinal study. *Annals of Medicine and Experimental Biology*, *35*, 307–315.
- Kirchner, W. K. (1958). Age differences in short-term retention of rapidly changing information. *Journal of Experimental Psychology*, *55*, 352–358. <https://doi.org/10.1037/h0043688>
- Kramer, A. F., Erickson, K. I., & Colcombe, S. J. (2006). Neural changes associated with training exercise, cognition, and the aging brain. *Journal of Applied Physiology*, *101*. <https://doi.org/10.1152/jappphysiol.000500.2006>
- Lachman, M. E., Lipsitz, L., Lubben, J., Castaneda-Sceppa, C., & Jette, A. M. (2018). When adults don't exercise: Behavioral strategies to increase physical activity in sedentary middle-aged and older adults. *Innovation in Aging*, *2*. <https://doi.org/10.1093/geroni/igy007>
- Lauenroth, A., Ioannidis, A. E., & Teichmann, B. (2016). Influence of combined physical and cognitive training on cognition: A systematic review. *BMC Geriatrics*, *16*, Article 141. <https://doi.org/10.1186/s12877-016-0315-1>
- Loprinzi, P. D., Frith, E., Edwards, M. K., Sng, E., & Ashpole, N. (2017). The effects of exercise on memory function among young to middle-aged adults: Systematic review and recommendations for future research. *American Journal of Health Promotion*, *32*, 691–704. <https://doi.org/10.1177/0890117117737409>
- Mahncke, H. W., Connor, B. B., Appelman, J., Ahsanuddin, O. N., Hardy, J. L., Wood, R. A., . . . Merzenich, M. M. (2006). Memory enhancement in healthy older adults using a brain plasticity-based training program: A randomized, controlled study. *Proceedings of the National Academy of Sciences of the United States of America*, *103*, 12523–12528. <https://doi.org/10.1073/pnas.0605194103>
- McGregor, K. M., Crosson, B., Krishnamurthy, L. C., Krishnamurthy, V., Hortman, K., Gopinath, K., . . . Nocera, J. R. (2018). Effects of a 12-week aerobic spin intervention on resting state networks in previously sedentary older adults. *Frontiers in Psychology*, *9*, Article 2376. <https://doi.org/10.3389/fpsyg.2018.02376>
- McGregor, K. M., Crosson, B., Mammimo, K., Omar, J., García, P. S., & Nocera, J. R. (2018). Influences of 12-week physical activity interventions on TMS measures of cortical network inhibition and upper extremity motor performance in older adults—A feasibility study. *Frontiers in Aging Neuroscience*, *9*, Article 422. <https://doi.org/10.3389/fnagi.2017.00422>
- McPhee, J. S., French, D. P., Jackson, D., Nazroo, J., Pendleton, N., & Degens, H. (2016). Physical activity in older age: Perspectives for healthy ageing and frailty. *Biogerontology*, *17*, 567–580. <https://doi.org/10.1007/s10522-016-9641-0>
- Meinzer, M., Seeds, L., Fleisch, T., Harnish, S., Cohen, M. L., McGregor, K., . . . Crosson, B. (2012). Impact of changed positive and negative task-related brain activity on word-retrieval in aging. *Neurobiology of Aging*, *33*(4), 656–669. <https://doi.org/10.1016/j.neurobiolaging.2010.06.020>
- Melby-Lervåg, M., Redick, T. S., & Hulme, C. (2016). Working memory training does not improve performance on measures of intelligence or other measures of “far transfer”: Evidence from a meta-analytic review. *Perspectives on Psychological Science*, *11*, 512–534. <https://doi.org/10.1177/1745691616635612>
- Mueller, K. D., Kosciak, R. L., Turkstra, L. S., Riedeman, S. K., LaRue, A., Clark, L. R., . . . Johnson, S. C. (2016). Connected language in late middle-aged adults at risk for Alzheimer's disease. *Journal of Alzheimer's Disease: JAD*, *54*(4), 1539–1550. <https://doi.org/10.3233/JAD-160252>
- Nocera, J. R., Crosson, B., Mammimo, K., & McGregor, K. M. (2017). Changes in cortical activation patterns in language areas following an aerobic exercise intervention in older adults. *Neural Plasticity*, *2017*. <https://doi.org/10.1155/2017/6340302>
- Nocera, J. R., McGregor, K. M., Hass, C. J., & Crosson, B. (2015). Spin exercise improves semantic fluency in previously sedentary older adults. *Journal of Aging and Physical Activity*, *23*, 90–94. <https://doi.org/10.1123/JAPA.2013-0107>
- Owen, A. M., Hampshire, A., Grahn, J. A., Stenton, R., Dajani, S., Burns, A. S., . . . Ballard, C. G. (2010). Putting brain training to the test. *Nature*, *465*, 775–778. <https://doi.org/10.1038/nature09042>
- Podsiadlo, D., & Richardson, S. (1991). The timed “Up & Go”: A test of basic functional mobility for frail elderly persons. *Journal of the American Geriatrics Society*, *39*, 142–148. <http://doi.wiley.com/10.1111/j.1532-5415.1991.tb01616.x>
- Rentz, D. M., Papp, K. V., Mormino, E. C., Amariglio, R. E., Becker, J. A., Schultz, A. P., . . . Sperling, R. A. (2014). DETECTING COGNITIVE PROFILES IN THE BIOMARKER STAGES OF PRECLINICAL AD. *Alzheimer's & Dementia*, *10*(4), P276. <https://doi.org/10.1016/j.jalz.2014.05.092>
- Sala, G., & Gobet, F. (2019). Cognitive training does not enhance general cognition. *Trends in Cognitive Sciences*, *23*(1), 9–20. <https://doi.org/10.1016/j.tics.2018.10.004>
- Salloway, S., Sperling, R., Fox, N. C., Blennow, K., Klunk, W., Raskind, M., . . . Brashear, H. R. (2014). Two phase 3 trials of bapineuzumab in mild-to-moderate Alzheimer's disease. *New England Journal of Medicine*, *370*, 322–333. <https://doi.org/10.1056/NEJMoa1304839>
- Siddarth, P., Burggren, A. C., Eyre, H. A., Small, G. W., & Merrill, D. A. (2018). Sedentary behavior associated with reduced medial temporal lobe thickness in middle-aged

- and older adults. *PLoS ONE*. <https://doi.org/10.1371/journal.pone.0195549>
- Spreen, O., & Strauss, E. (1998). A compendium of neuropsychological tests: Administration, norms and commentary (2nd edition). New York: Oxford University Press.
- Ten Brinke, L. F., Best, J. R., Chan, J. L. C., Ghag, C., Erickson, K. I., Handy, T. C., & Liu-Ambrose, T. (2019). The effects of computerized cognitive training with and without physical exercise on cognitive function in older adults: An 8-week randomized controlled trial. *The Journals of Gerontology, Series A: Biological Sciences & Medical Sciences*. Advance online publication. <https://doi.org/10.1093/gerona/glz115>
- Urbaniak, G. C., & Plous, S. (2013). *Research randomizer* (Version 4.0) [Computer software]. <http://www.randomizer.org/>
- Verghese, J., Mahoney, J., Ambrose, A. F., Wang, C., & Holtzer, R. (2010). Effect of cognitive remediation on gait in sedentary seniors. *Journals of Gerontology, Series A: Biological Sciences & Medical Sciences*, *65*, 1338–1343. <https://doi.org/10.1093/gerona/g1q127>
- Voelcker-Rehage, C., Godde, B., & Staudinger, U. M. (2011). Cardiovascular and coordination training differentially improve cognitive performance and neural processing in older adults. *Frontiers in Human Neuroscience*, *5*, Article 26. <https://doi.org/10.3389/fnhum.2011.00026>
- Voss, M. W., Prakash, R. S., Erickson, K. I., Basak, C., Chaddock, L., Kim, J. S., . . . Kramer, A. F. (2010). Plasticity of brain networks in a randomized intervention trial of exercise training in older adults. *Frontiers in Aging Neuroscience*, *2*, Article 32.
- Wingfield, A., Stine, E. A. L., Lahar, C. J., & Aberdeen, J. S. (1988). Does the capacity of working memory change with age? *Experimental Aging Research*, *14*, 103–107. <https://doi.org/10.1080/03610738808259731>
- Zlatar, Z. Z., McGregor, K. M., Towler, S., Nocera, J. R., Dzierzewski, J. M., & Crosson, B. (2015). Self-reported physical activity and objective aerobic fitness: Differential associations with gray matter density in healthy aging. *Frontiers in Aging Neuroscience*, *7*, Article 5. <https://doi.org/10.3389/fnagi.2015.00005>
- Zlatar, Z. Z., Towler, S., McGregor, K. M., Dzierzewski, J. M., Bauer, A., Phan, S., . . . Crosson, B. (2013). Functional language networks in sedentary and physically active older adults. *Journal of the International Neuropsychological Society*, *19*, 625–634. <https://doi.org/10.1017/S1355617713000246>