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Structured Exercise Does Not Stabilize Cognitive Function in Individuals with Mild Cognitive Impairment Residing in a Structured Living Facility

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Abstract

Exercise has been shown to have positive effects on the brain and cognition in healthy older adults, though no study has directly examined possible cognitive benefits of formal exercise programs in persons with mild cognitive impairment (MCI) living in structured facilities. Thirty one participants completed neuropsychological testing and measures of cardiovascular fitness at baseline and after 6 months of a structured exercise program that included aerobic and resistance training. While exercise improved cardiovascular fitness in persons with mild cognitive impairment, there was no improvement in cognitive function. Rather, mild cognitive impairment patients in this sample declined in performance on several tests sensitive to Alzheimer's disease. Examined in the context of past work, it appears exercise may be beneficial prior to the onset of MCI, though less helpful after its onset.

Keywords

mild cognitive impairment; exercise; cognitive functioning; older adults; neuropsychology; cardiovascular fitness

There is growing evidence that physical activity is associated with better neurocognitive outcome in older adults. Both cross sectional and prospective studies demonstrate that older adults engaging in regular physical activity show improved performance on neuropsychological testing and fewer pathological changes on neuroimaging (Colcombe, et al., 2003; Colcombe et al., 2006; Kramer, Colcombe, McAulley, Scalf, & Erickson, 2005).One large prospective study found that older adults with self-reported memory problems exhibited improved cognition after completing an exercise program

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Declaration of Interest
The authors report no conflicts of interest.

(Lautenschlager et al., 2008) and a meta-analysis found a medium effect (d = 0.48) of fitness training on cognitive tasks in sedentary older adults (Colcombe & Kramer, 2003).

The results of exercise studies in individuals with known neurological impairment have been mixed. Exercise has been found to reduce agitation in patients in a nursing home setting (Aman & Thomas, 2009)as well as improve mood and affect in similar patients (Williams & Tappen, 2007). In terms of cognitive function, some studies reported no change (McMurdo & Rennie, 1993; Mulrow et al., 1994; Schnell et al., 1996), while others have found slight improvements (Molloy, Beerschoten, Borrie, Crilly, & Cape, 1988; Powell, 1974). A recent study examined the effects of aerobic exercise in community-dwelling persons with mild cognitive impairment (MCI) (Baker et al., 2010). Baker and colleagues (2010) randomized 33 individuals with MCI into a 6-month aerobic exercise or stretching control group. Individuals in the aerobic exercise group exercised for 45–60 minutes per day, four days per week exerting 75–85% of heart rate reserve while those in the stretching control group completed stretching activities on the same schedule, but exerting 50% of less of heart rate reserve. Results indicated that aerobic exercise had beneficial gender-specific effects on cognition. Specifically, women in the aerobic exercise group (N = 10) showed cognitive benefits, with improved performance on tasks of executive function (Baker et al., 2010).

Given these promising findings, the current study examined the possible cognitive benefits of a 6-month aerobic and resistance training exercise program in persons with MCI residing in a structured living facility. Implementation of this program into a living facility was chosen based on the growing number of individuals living in these communities and their importance in promoting health in a number of innovative ways. Based on the above findings, it was hypothesized that exercise would stabilize or even improve cognitive function in the sample. Cognitive testing, physical fitness levels, and blood markers were assessed at baseline and after completion of the 6-month program.

Method

Participants

Study participants were 31 English-speaking residents of a structured living facility offering assisted and independent living arrangements. Participants were recruited through flyers posted at the living facility and one recruitment talk. Individuals who then approached the researchers were included in the study. All participants included had a global Clinical Dementia Rating (CDR; Morris, 1993) score of 0.5 (questionable dementia or Mild Cognitive Impairment) rated by an experienced neuropsychologist and were receiving some level of assistance in activities of daily living. Table 1 shows medical characteristics of the sample. Potential participants were excluded if they (1) demonstrated a CDR rating above or below 0.5, (2) could not participate in exercise sessions due to physical limitations, (3) were younger than 55 years of age, or (4) could not independently provide informed consent. There were no participant refusals. Thirty-five participants were initially recruited. One individual did not meet CDR criteria and was excluded; three participants later dropped out of the study.

Measures

Neuropsychological battery—Participants completed a battery of well-validated measures that assessed cognitive functioning both at baseline and at the end of the study. Specifically, participants completed measures of memory, executive function, attention, language, visuospatial, and motor skills. These measures included the following:

Modified Mini Mental Status Examination (3MS): This test is a brief screening measure of global cognitive function. It is comprised of several short tasks, including orientation, similarities, animal fluency, learning and brief and delayed recall of a short list of target words, and a copy of a simple geometric figure (Teng & Chui, 1987).

Trail Making Test A and B: In the Trail Making A task, participants are asked to connect a series of 25 numbered dots in ascending order as quickly as they can (e.g. 1–2–3, etc.). Trail Making B adds a set-shifting component and requires participants to alternate between numbers and letters in ascending order (e.g. 1-A-2-B, etc.) (Reitan, 1958).

Digit Symbol Coding: This test asks participants to transpose a coded sequence. They are provided with a code at the top of the page (e.g. a '1' means '+') and asked to complete as many of the blank items as possible in 120 seconds (Wechsler, 1997).

Frontal Assessment Battery: This test employs several short tasks to assess frontal system executive function. More specifically, participants are asked to identify similarities among two words (e.g. automobile, boat), name as many words as they can that start with a target letter (e.g. words that begin with 'M'), complete frontal-motor hand movements, and tap patterns with their right and left hands (Dubois, Slachevsky, Litvan, & Pillon, 2000).

Letter Number Sequencing: This test is a measure of complex attention and working memory. Participants are read strings of numbers and letters of increasing length, and asked to reorganize the numbers and letters according to predetermined rules (Wechsler, 1997).

Hopkins Verbal Learning Test-Revised (HVLT-R): The HVLT-R requires participants to learn and remember a list of 12 words. Participants are read the list of words and asked to recall as many as they can. After 20-minute delay during which other tasks are completed, participants are asked to recall as many words from the list as possible. Finally, they are asked to identify the words from a list of targets and foils (Brandt, 1991).

Animal Naming: This test is a measure of semantic verbal fluency. Participants are asked to name as many different kinds of animals as they can in 60 seconds (Eslinger, Damasio, & Benton, 1984).

Boston Naming Test: This test is a measure of confrontation naming and language abilities. Participants are shown pictures and asked to name the depicted item. Items difficulty increases from high-frequency objects (e.g. bed) and lower-frequency objects (e.g. trellis) (Kaplan, Goodglass, & Weintraub, 1983).

Cardiovascular fitness—Cardiovascular endurance was assessed with a 2-minute step test (Rikli & Jones, 2001). Participants were asked to march in place for two minutes bringing each knee up to a marked target on the wall set at each individual's own midpoint between their hip and knee. The number of times the right knee met this point was counted.

Blood markers—Fasting blood draws were conducted and all serum levels of β-amyloid 1–38, β-amyloid 1–40, and β-amyloid 1–42 were determined using the MSD 96-Well Multi-Spot Human (6E10) Abeta Triplex Assay during a single batch run. The manufacturer's directions were followed and specimens were tested in duplicate.

Procedure

This study was approved by the Kent State University institutional review board and informed consent was provided by all participants before beginning any part of the study.

Prior to beginning the exercise program, participants completed the neuropsychological test battery, cardiovascular fitness measure, and blood draws. Participants took part in a structured exercise sessions 2 times per week. Each session lasted approximately 60 minutes and included a combination of aerobic (e.g. marching in place, knee lifts) and non-aerobic (e.g. resistance training, flexibility) exercises that were tailored to the group and varied from session to session. Exercise sessions were supervised by a certified exercise physiologist and conducted over a 6-month period. Upon completion of the exercise program, all participants were re-assessed using the same measures. Three participants were lost to follow up.

Analyses

Analyses included repeated measures ANOVA and MANOVA with posttests to examine changes over time in each cognitive domain, cardiovascular fitness, and blood markers. Missing data was excluded pairwise. See Table 2.

Results

Change in Cognitive Performance

Global cognitive function—Repeated measures ANOVA revealed that performance on the 3MS declined over time [$\lambda = .86$, $F(1,29) = 4.61$, $p = .04$, $d = .28$]. See Table 2 for all descriptive statistics.

Memory—Repeated measures MANOVA indicated no overall changes in memory performance from pre- to post-exercise intervention [$\lambda = .87$, $F(3,27) = 1.38$, $p = .27$, $\eta_p^2 = .13$]. However, when examined individually, a trend emerged for decline on HVLT-delayed recall [$F(1,29) = 3.54$, $p = .07$, $d = .27$].

Attention and executive function—Repeated measures MANOVA revealed no change as a whole in attention and executive function performance over time [$\lambda = .82$, $F(5,24) = 1.10$, $p = .41$, $\eta_p^2 = .18$]. However, with examination of individual tests, a significant decline in performance on Trails B was noted [$F(1,28) = 4.84$, $p = .04$, $d = .29$].

Language—Repeated measures MANOVA indicated a significant change in overall language performance over time [$\lambda = .79$, $F(2,28) = 3.62$, $p = .04$, $\eta_p^2 = .21$]. Specifically, there was a decline in animal naming [$F(1,29) = 6.19$, $p = .02$, $d = .30$], though confrontation naming on the BNT did not change [$F(1,29) = 1.82$, $p = .19$, $d = .15$].

Change in Cardiovascular Fitness

A repeated measures ANOVA revealed significant improvement on the two-minute step test over time [$\lambda = .77$, $F(1,26) = 7.86$, $p = 0.01$, $d = .54$].

Change in Blood Markers

Repeated measures MANOVA showed no change in β-amyloid blood markers over time [$\lambda = .92$, $F(3,28) = .83$, $p = .50$, $\eta_p^2 = .08$].

Discussion

The current study examined the impact of an aerobic and resistance training program on cognitive function in individuals with MCI who reside in a structured living facility. While exercise improved cardiovascular fitness levels, decline was observed in aspects of cognitive function and β-amyloid levels remained unchanged. Several aspects of these findings warrant brief discussion.

Although a growing number of studies have shown that physical activity may reduce risk for developing Alzheimer's disease or memory loss, few have directly examined the effectiveness of exercise intervention in neurological populations. In the current study, persons with MCI exhibited significant improvements in cardiovascular fitness following a six-month exercise program. These findings are consistent with past work showing benefits of exercise in persons with neurological conditions. For example, exercise intervention in persons with AD has been linked to better maintenance of functional abilities, reduced depressive symptoms, as well as better strength, balance and fitness levels (Rolland et al., 2007; Santana-Sosa, Barriopedro, López-Mojares, Pérez, & Lucia, 2008; Williams & Tappen, 2008).Given that persons with early AD generally have intact capacity for cardiorespiratory fitness (Burns, Mayo, Anderson, Smith, & Donnelly, 2008), interventions to improve physical activity levels are encouraged, even independent of any possible cognitive benefits. Recent studies have provided guidelines for possible intervention (Pérez & Cancela Carral, 2008) and additional work is much needed to clarify its potential benefits

Despite improvements in cardiovascular fitness levels, participants declined on several key tests of cognitive function. Past research has shown cognitive benefits of exercise in healthy older adults (Colcombe & Kramer, 2003; Lautenschlager et al., 2008), with improvements commonly found in domains such as memory and executive functioning. A recent study found exercise improved executive function in small sample of women with MCI ($N = 10$), while men with MCI ($N = 9$) only showed improvement on a single task. (Baker et al., 2010). In the current study, no cognitive benefits emerged and performance declines were noted in cognitive domains frequently associated with Alzheimer's disease and vascular dementia (Lezak, 1995; Pirttilä, Erkinjuntti, & Hachinski, 2003). For example, participants exhibited an average decline of 2.2 points on the 3MS during the 6-month intervention. Although there are no universally accepted standards for change, a recent longitudinal study investigating 3MS changes found a 5-point change over the course of 10 years to be clinically meaningful (Andrew & Rockwood, 2008). That the current sample approximated half this degree of decline in a substantially shorter period of time suggests that the 3MS was sensitive to changes in cognition and that this decline is likely clinically meaningful for this sample. If replicated, the overall findings are consistent with the mixed pattern for cognitive benefits of exercise in persons with neurological conditions (e.g. Baker et al., 2010; Molloy et al., 1988; Schnell et al., 1996) and raise the possibility of a disease threshold that, once passed, limits the benefits of exercise on cognitive functioning. Consistent with this notion, the rapid rate of decline seen in the current sample appears more consistent with conversion from MCI to AD rather than age-related cognitive changes in persons with MCI. If so, early intervention would be key to maximizing the cognitive benefits of exercise, as persons with subjective memory complaints have been shown to benefit from an exercise program (Lautenschlager et al., 2008) but the window of opportunity may be passed once the diagnosis of MCI has been met. With an estimated conversion rate of 41% to Alzheimer's disease (AD) after the first year and 64% after 2 years of MCI diagnosis (Geslani, Tierney, Herrman, & Szalai, 2005), it is important that research focuses on finding effective interventions in delaying progression in persons with MCI.

Previous research has found that increased levels of β-amyloid are associated with poorer performance on neuropsychological tasks in both healthy older adults (Gunstad et al., 2008) and cognitively impaired individuals (Luis et al., 2009). Despite the positive association between exercise and cognitive functioning seen in previous work (Colcombe & Kramer, 2003; Lautenschlager et al., 2008), no change in β-amyloid levels were found in the current study, despite improved fitness levels and reductions in cognitive test performance. Such findings suggest that the association among these factors is more complicated than typically

believed and that future research is needed to elucidate the association among exercise, cognitive functioning, and β-amyloid levels.

The current findings are limited in several ways. A primary limitation is the lack of a control group, as this exploratory study sought to determine the feasibility of a larger, blinded trial. However, the current group exhibited a rate of decline typical for persons with MCI, suggesting the pattern of findings would not have differed with a larger sample. For example, power analysis conducted with G*power (Faul, Erdfelder, Lang, & Buchner, 2007) showed that >8500 participants would have been necessary to detect cognitive improvement on Trail Making Test A, a measure on which exercise-related benefits would be expected. No power analyses could be conducted on several other tests that are important for understanding MCI, as test scores actually declined through the study period (e.g. Hopkins Verbal Learning Test, Animal Naming).

Another potential limitation is the nature of the exercise program itself. As noted above, the exercise program consisted of 60 minute sessions twice per week for six months. This schedule was chosen to enhance acceptability of study participants (no payment was provided for participation) and due to space considerations at the living facility. Additionally, the intensity of exercises was relatively low during early sessions, in response to the low levels of fitness exhibited by study participants (as evidenced by the poor performance at baseline on the 2-minute step test). In addition, we chose to use this exercise schedule in order to maximize the generalizability of our findings. We wanted to examine the feasibility of an exercise program that would be acceptable to older adults who are active, but who do not regularly engage in intense exercise. It is possible that more frequent exercises at a higher intensity for a longer duration may provide greater benefits. Future studies should consider this possibility, including matching the recommendations for aerobic exercise from the American College of Sports Medicine and the American Heart Association (i.e. 30 minutes of moderate intensity aerobic activity 5 days per week) (Nelson et al., 2007). Lastly, more detailed information regarding the individual's medical and family histories, genetic testing, and neuroimaging may provide additional information and insight into explaining the conflicting results in this important area.

In sum, the current study found that an exercise program containing aerobic and resistance training components improved cardiovascular fitness in a sample of older adults with MCI residing in a structured living facility, though cognition declined and β-amyloid levels were unchanged. Future studies are needed to clarify the potential benefits of exercise on cognitive outcomes in this population.

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Table 1

Participant Demographic and Clinical Characteristics.

Demographic Characteristics	Mean (SD)
Age (years)	83.71 (3.59)
Education (years)[a]	15.70 (3.34)
Female (%)	58.1
Clinical Characteristics	%
Hypertension	41.9
CABG	9.7
Myocardial Infarction	12.9
Diabetes	6.5

Note. CABG = Coronary Artery Bypass Graft Surgery.

[a] denotes N = 30.

Table 2

Baseline and 6-Month follow-up Neuropsychological Performance, Cardiovascular Fitness Level, and Blood Marker Levels.

	Baseline	6-Month				
Variable	***M* (SD)**	***M* (SD)**	***F***	***p***	***d***	**β**
Neuropsychological Performance						
Global Cognition[a]						
3MS	90.03 (7.14)	87.83 (8.53)	4.61	.04*	0.28	.99
Memory[a]						
HVLT-R Learning Trial	19.37 (5.74)	19.01 (5.96)	0.16	.70	0.05	.17
HVLT-R Delayed Recall	6.10 (3.23)	5.17 (3.56)	3.54	.07†	0.27	.95
HVLT-R Recognition	8.80 (2.93)	7.80 (3.58)	2.62	.12	0.31	.89
Attention/Executive Function[b]						
Trail Making Test A (sec)	50.24 (27.49)	50.14 (19.39)	<0.01	.97	<.01	.05
Trail Making Test B (sec)	134.48 (67.52)	156.66 (85.68)	4.8	.04*	0.29	.99
Frontal Assessment Battery	14.45 (1.97)	14.48 (1.92)	0.01	.92	0.02	.06
Letter-Number Sequencing	7.28 (2.85)	7.41 (2.67)	0.22	.64	0.05	.08
Digit Symbol Coding	46.66 (15.52)	47.62 (11.79)	0.08	.78	0.07	.16
Language[a]						
Boston Naming Test	53.93 (5.46)	54.73 (5.12)	1.82	.19	0.15	.73
Animal Naming	17.67 (6.16)	16.03 (4.81)	6.19	.02*	0.30	.99
Cardiovascular Fitness[c]						
2-minute Step Test	75.56 (17.97)	85.11 (17.58)	7.86	.01**	0.54	.99
Blood Markers[d] (pg/ml)						
β-amyloid 1–38	80.90 (162.51)	89.57 (194.23)	0.06	.81	0.05	.08
β-amyloid 1–40	274.52 (111.13)	302.84 (169.72)	1.12	.30	0.20	.58
β-amyloid 1–42	107.67 (193.45)	116.75 (204.52)	0.07	.80	0.05	.08

Note. 3MS = Modified Mini Mental Status Examination; HVLT-R = Hopkins Verbal Learning Test-Revised.

[a] denotes N = 30;

[b] denotes N = 29;

[c] denotes N = 27;

[d] denotes N = 31.

* $p < .05$;

** $p < .01$;

† $p < .10$.