

Effectiveness of exercise on cognitive impairment and Alzheimer's disease

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Abstract: Physical activity has a protective effect on brain function in older people. Here, we briefly reviewed the studies and results related to the effects of exercise on cognitive impairment and Alzheimer's disease. The main findings from the current body of literature indicate positive evidence for structured physical activity (cardiorespiratory and resistance exercise) as a promising non-pharmacological intervention for preventing cognitive decline. More studies are needed to determine the mechanisms involved in this preventative effect, including on strength, cardiorespiratory, and other types of exercise. Thus, the prevention of Alzheimer's disease may depend on healthy lifestyle habits, such as a structured physical fitness program.

Keywords: randomized controlled trial, memory disorders, healthy lifestyle habits, physical activity

Introduction

Alzheimer's disease (AD) is a multifactorial and progressive neurodegenerative disease. Aspects of AD, such as increased oxidative state, amyloid plaque deposition, and neurofibrillary tangles of tau protein in the central cortex and the limbic system of the brain, have been associated with the disease.¹ The incidence of AD doubles after the age 65 years, with 1.275 new cases diagnosed annually for every 100,000 individuals over the age of 65. It is expected that the incidence of AD will continue to rise, impacting both social and economic aspects of the world's health systems.² Therefore, it is imperative that potential prevention and/or treatment strategies are thoroughly researched to prepare medical professionals for an increase in AD cases.

The risk of heart disease, coronary artery disease, type 2 diabetes, some forms of cancer, and all-cause mortality is negatively associated with physical activity.³⁻⁵ Further, several observational studies have indicated that individuals who are more physically active accrue protective benefits against dementia, especially AD.^{6,7} Thus there is a need to investigate the effectiveness of non-pharmacological prescriptive strategies as regular structured exercise programs for preventing or reversing cognitive impairment as well as attenuating the progression of dementia. Therefore, the purpose of this brief review was to assess from the current body of literature the effects of structured physical fitness programs including cardiorespiratory and resistance exercise on the cognitive response in elderly subjects with AD.

Methods

For this review, MEDLINE, Google Scholar, IndexCat, PsycARTICLES®, and SPORTDiscus™ databases were searched up to November 2012 using MeSH

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database terminology. The two criteria for the inclusion of articles were: (1) studies retrieved using the controlled keywords “cognitive impairment” or “Alzheimer’s disease” combined with (2) studies retrieved on any of the following themes: physical fitness, aerobic exercise, cardiorespiratory fitness, cardiovascular training, aerobic capacity, aerobic conditioning, muscle strength, exercise, exercise training, strength training, resistance training, resistance exercise, performance, exercise capacity, functional capacity, and physical exercise. A survey was taken of the indexed publications in the searched databases. The effects of regular exercise on cognitive responses reported from these studies are summarized in Table 1.

Functional capacity and cognitive decline in AD

Functional capacity is recognized as a classic marker of cognitive impairment (CI) and AD.^{8–12} For instance, Eggermont et al¹³ conducted a comparative analysis between three groups: those without CI, those with CI, and patients with AD. They compared functional capacity through the following tasks: 4 m walk, sitting and standing for 30 seconds, and the timed up-and-go test. The results suggested an inverse association between CI and lower-limb functional capacity.

Several studies^{8–12} have examined differences in the functional capacity of the lower limbs in people with CI and/or adults who were cognitively healthy or had AD;

Table 1 Studies that reported results with randomized controlled trials involving regular exercise and effects on cognitive responses

Study	Training program, age in years (standard deviation or range)	Results
Lautenschlager et al ¹⁸	Group 1: had 85 CI; trained 6 months, varied exercises program; 150 min per week or 10,000 steps/day – age: 68.6 (8.7) Control group: had 85 CI; daily living activities – age: 68.7 (8.5)	Group 1: ADAS-Cog = NS
Baker et al ¹⁹	Group 1: had 23 CI; trained 6 months walking, 75%/85% MHR 4 days week; 45/60 min – age: 70.0 (8.5) Control group: had 10 CI; did stretching – age: 68.7 (8.5)	Group 1: executive activities = @ (only in women)
Rolland et al ²⁰	Group 1: had 67 AD; trained 6 months, varied exercises (not reported); 3 days week; 60 min – age: 83 (62–103) Control group: had 67 AD; daily living activities – age: 83 (62–103)	Group 1: MMSE = NS
Hernandez et al ²¹	Group 1: had 9 AD; trained 6 months, varied exercises, 60%/80% FCM; 2 days week; 60 min – age: 78.5 (6.8) Control group: had 7 AD; daily living activities – age: 78.5 (6.8)	Group 1: MMSE = NS Control: significant decline in MMSE compared with the baseline
Liu-Ambrose et al ²⁸	Group 1: had 52 EI; strength training; 6 months, 2 days week; 6/8 reps; 2 sets; 60 min – age: 69.4 (3.0) Group 2: had 54 EI; strength training; 6 months, 1 day week; 6/8 reps; 2 sets; 60 min – age: 69.5 (2.7) Control group: had 49 EI; did balance 2 days week – age: 70.0 (3.3)	Group 1 and 2: executive cognitive activities = @
Nagamatsu et al ²⁹	Group 1: had 28 CI; strength training; 6 months, 2 days week; 6/8 reps; 2 sets; 60 min – age: 73.9 (3.4) Group 2: had 30 CI; cardiorespiratory training; 6 months, 2 days week; 70%/80% HRR; 60 min – age: 75.6 (3.6) Control group: had 28 CI; did balance 2 days week – age: 75 (3.6)	Group 1: executive cognitive activities = @
Cassilhas et al ²⁶	Group 1: had 20 EI; strength training; 6 months, 3 days week; 80% 1 RM; 2 sets; 60 min – age: 67.0 (0.5) Group 2: had 19 EI; strength training; 6 months, 3 days week; 50% 1 RM; 2 sets; 60 min – age: 69.0 (1.1) Control group: had 23 EI; did stretching 1 day week – age: 68.4 (0.6)	Group 1 and 2: †cognitive tests = @
Venturelli et al ⁴	Group 1: had 11 AD; 4 months of walking, moderate intensity; 4 days week; 30 min – age: 83.0 (6) Control group: had 10 AD; daily living activities (bingo/patchwork sewing/music therapy) – age: 85.0 (6.0)	Group 1: MMSE = @ Control: significant decline in MMSE (compared with the baseline)

Notes: @, significantly higher average values than the control group; †cognitive tests, Wechsler Adult Intelligence Scale III (similarities: assessing central executive/digit span, forward and backward: assessing short-term memory), Wechsler Memory Scale–Revised (Corsi block-tapping task, forward and backward: assessing visual modality of short-term memory), Toulouse–Piéron’s concentration attention test – assessing attention, and Rey–Osterrieth complex figure (form A – Rey figure and form B – Taylor alternative version) assessing long-term episodic memory.

Abbreviations: 1 RM, one-maximum repetition; AD, Alzheimer’s disease individuals; ADAS-Cog, Alzheimer Disease Assessment Scale – Cognitive subscale; CI, cognitive impairment individuals; EI, elderly independent individuals; NS, no significant difference between the groups in the aspects evaluated; HRR, heart rate reserve; min, minutes; MHR, maximum heart rate; MMSE, mini-mental state examination; reps, repetitions.

however, these analyses have methodological limitations (the use of different study populations, diagnostic criteria, sample sizes, and motor function measurements). Notably, several possible moderating factors can affect the functionality of the lower limbs, such as osteoporosis^{8,11} and parkinsonian signs,^{9,10,12} and these were not uniformly considered in all studies. However, Eggermont et al¹³ addressed these methodological biases and indicated the extent of physical dysfunction independently associated with CI in their study.

Other studies have shown a greater impairment in lower limb function in individuals with AD compared with controls.^{8–12} Moreover, Venturelli et al¹⁴ recently investigated the effect of moderate intensity walking on cognitive response and functional capacity in elderly patients with AD. This randomized controlled trial (RCT) indicated that a 4-month walking intervention (moderate intensity) improved the distance covered in the 6-minute walk test (6WT), as well as activities of daily living (ADL) evaluated by the Barthel index. However, scores on the mini-mental state examination (MMSE) decreased 13% over the intervention period in the experimental group. Nevertheless, the control group (who did not undergo the walking intervention) demonstrated significantly greater decline in all the tests: –20% in the 6WT, –23% in ADL, and –47% in the MMSE. This study reveals the positive effects of a walking program on physical function and in attenuating the decline of cognitive function for AD patients.

Effect of cardiorespiratory exercise and varied exercise programs on CI and AD

Currently, studies have focused on the effects of cardiorespiratory exercise on symptoms associated with CI.¹⁵ Possibly due to the inverse relationship between CI and cardiovascular fitness,^{15,16} For example, Burns et al demonstrated that subjects who had higher levels of cardiorespiratory fitness (VO₂ peak) displayed lower levels of brain atrophy.¹⁷

Some RCTs have evaluated the effect of cardiorespiratory exercise in older adults with AD. Lautenschlager et al¹⁸ conducted an intervention in elderly patients for a period of 6 months followed by another 18 months of follow-up, after which they reported no significant difference in cognitive responses – as assessed by the Alzheimer Disease Assessment Scale – Cognitive subscale (ADAS-Cog) and ADL – between the exercise group and the control group. In another study, Baker et al¹⁹ evaluated the effect of a

6-month cardiorespiratory exercise intervention and found that improved cardiovascular fitness was accompanied by an increased efficiency in activities – such as executive control processing, multitasking, and efficiency of information processing and selective attention. However, when the results were adjusted for sex, a significant difference occurred only in women with increased oxygen consumption (VO₂ peak) and improvements in cognitive activities.

There are some explanations for the inequality between men and women regarding cognitive improvement in association with exercise. For example, it is speculated that estrogen may have a neuroprotective effect because many women after menopause are on hormone replacement therapy.¹⁵

Another RCT, which was performed in elderly residential institutions in France, investigated the effect of an exercise program on the ability of AD patients to perform ADLs, physical performance, and of behavioral disturbances and depression. In that study, Rolland et al²⁰ conducted an interventional exercise program for 12 months with 1 hour of exercise twice a week that included walking, exercise, muscle strength, balance and flexibility tasks, while the control group received only traditional health care. The intervention group performed significantly better in the 6 m walking speed test. However, no effect was observed for cognitive responses.

In a study conducted in Brazil,²¹ AD patients underwent a varied exercise program for 6 months that included various exercises, circuits, sport dance sequences, recreational activities, stretching activities, weight training, and relaxation. The results indicated that cognitive function (measured using the MMSE) was preserved during the interventional period, while the control group, whose members maintained their routine activities (no exercise), experienced a significant decline in MMSE score.

Another important point, regardless of sex, is that cardiorespiratory training is critical for a patient with AD, especially in the initial phase.²² Recently, Middleton et al²⁴ found that women who reported being physically active at any point over their life course had a lower likelihood of CI in later life.

Effect of strength training on CI and AD

In a cross-sectional study, Petrella et al²⁴ evaluated the relationship between quadriceps muscle strength and CI among frail

elderly patients and physically independent patients. An inverse correlation was found between muscle power and CI in the physically independent individuals – that is, as results from the power tests decreased for the quadriceps muscle, signs of CI increased. Similarly, Scherder et al²⁵ found that, in older women, quadriceps muscle strength was associated with an improvement in completing function activities, such as attention and working memory. Recently, Boyle et al²⁷ conducted a longitudinal study (3.6 years) and found that individuals with greater muscle strength had a lower risk of coronary heart disease. In addition, for each unit of increase in muscle strength acquired when CI begins, they observed a 43% reduction in the risk of conversion to AD. More importantly, this association with muscular strength persisted even after adjustments for covariates such as body mass index, physical activity, lung function, vascular risk factors, and genotypes of apolipoprotein E. Lastly, the increase in muscle strength was associated with a lower rate of decline in global cognitive function.

Despite this association between muscular fitness and cognitive function, few studies have examined independently the effect of strength training on cognitive responses. Cassilhas et al²⁶ studied the effect of 6 months of strength training on cognitive function in the elderly. The intervention compared different intensities of strength training and the sample was distributed between moderate intensity (50% one-maximum repetition), high intensity (80% one-maximum repetition), and a control untrained group. In terms of muscle strength, both experimental groups performed better than the control group, but no differences were noted between them. In both experimental groups (moderate and high intensity), positive changes were noted in cognitive function.

Further, Liu-Ambrose et al²⁸ investigated the effect of different frequencies of strength training (ie, once or twice weekly) or twice-weekly balance training on changes in cognitive function in older women. Their results demonstrated that 12 months of once- or twice-weekly strength training significantly improved Stroop test performance in cognitively healthy women aged 65–75 years.

Recently, Nagamatsu et al²⁹ demonstrated that 6 months of twice-weekly strength training improved selective attention/conflict resolution, associative memory, and regional patterns of functional brain plasticity compared with twice-weekly balance exercises. This study provided novel evidence that strength training can benefit multiple domains in those at risk for dementia.

Future research might assess the cost-effectiveness of the exercise interventions for the reduction of CI in AD;

in 2000, the cost of AD and CI treatment in the USA was estimated to be US\$100 billion. Although there is accumulating evidence for the effectiveness of exercise in combating cognitive decline, there is still a gap in the literature on the indirect and economic costs of physical exercise interventions for CI and AD.³⁰

Limitations

The results of this review must be interpreted with caution, as the studies reviewed are not conclusive regarding the potential for structured exercise to elicit positive changes in CI and AD. Moreover, another potential limitation of the studies included in this brief review is that most studies presented a small sample size.

Conclusion

Structured physical exercise (strength and cardiorespiratory exercise) appears to be a promising non-pharmacological strategy for preventing cognitive decline. Individuals with mild or moderate dementia should be more physically active to prevent major losses of physical fitness and function. More studies are needed to delineate the possible mechanisms involved with strength, cardiorespiratory, and other modes of exercise. In addition, future studies with well-controlled designs are needed to address questions regarding the benefits of physical exercise for the prevention and control of dementia.

Disclosure

The authors declare no conflicts of interest in this work.

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