The Effect of Aerobic Exercise on Cognition and Brain Atrophy in Alzheimer's Disease

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Background

- Alzheimer's Disease (AD) is a progressive and fatal neurodegenerative disorder affecting 5.8 million people in the United States[1].
- AD is the most common cause of dementia, accounting for 60-80% of all dementias[6].
- Almost two-thirds of those affected by AD are women and the major risk factor is increasing age[1].
- Key pathology in AD involves extracellular protein fragments amyloid beta, intracellular truncated and phosphorylated tau, and loss of synapses and neurons[6].
- Family history and acquired risk factors such as hypertension, dyslipidemia, cardiovascular disease, and altered glucose metabolism play key roles in the development of AD[3].
- The nature of AD takes a devastating toll on caregivers, requiring substantial emotional, physical, and financial sacrifices as the disease progresses.
- The standard of care for AD includes symptomatic treatment with cholinesterase inhibitors and NMDA glutamate receptor antagonists, which are non-disease modifying therapies[7].
- Potential disease-modifying therapies have shown a lack of clinically relevant effects in people with AD, emphasizing the growing need for research on non-pharmacological interventions, such as exercise training programs[8].

PICO

- **Do individuals with Alzheimer's Disease who participate in aerobic exercise training exhibit less decline in cognitive function and brain atrophy?**

Methods

- **Search Engine:** PubMed MESH database
- **Time Frame of Interest:** 2010-Present
- **Search Terms:** "Alzheimer's disease," "aerobic exercise," and "therapy."
- **Study Designs Included:** Clinical trials, randomized control trials (RCTs), and systematic reviews
- **Study Exclusions:** Participants with other neurologic disorders such as non-Alzheimer's dementia or head trauma
- **Search Results:** 45
- **Selection and Analysis:** 3 articles (references 4,8, and 10)

Study Designs

- The articles selected are randomized control trials consisting of community-dwelling participants, aged 50 years and older, with a diagnosis of mild or early Alzheimer's Disease.
- Each of the studies organized participants into one of two groups: an intervention group or a control group. All intervention groups received approximately one hour of aerobic exercise training three to five times per week.
- The primary outcome measures focused on various aspects of cognition and memory. Secondary outcome measures included caregiver questionnaires, additional cognitive tests, physical tests, and analysis of high-intensity subpopulations from the intervention group.

Summary of Results

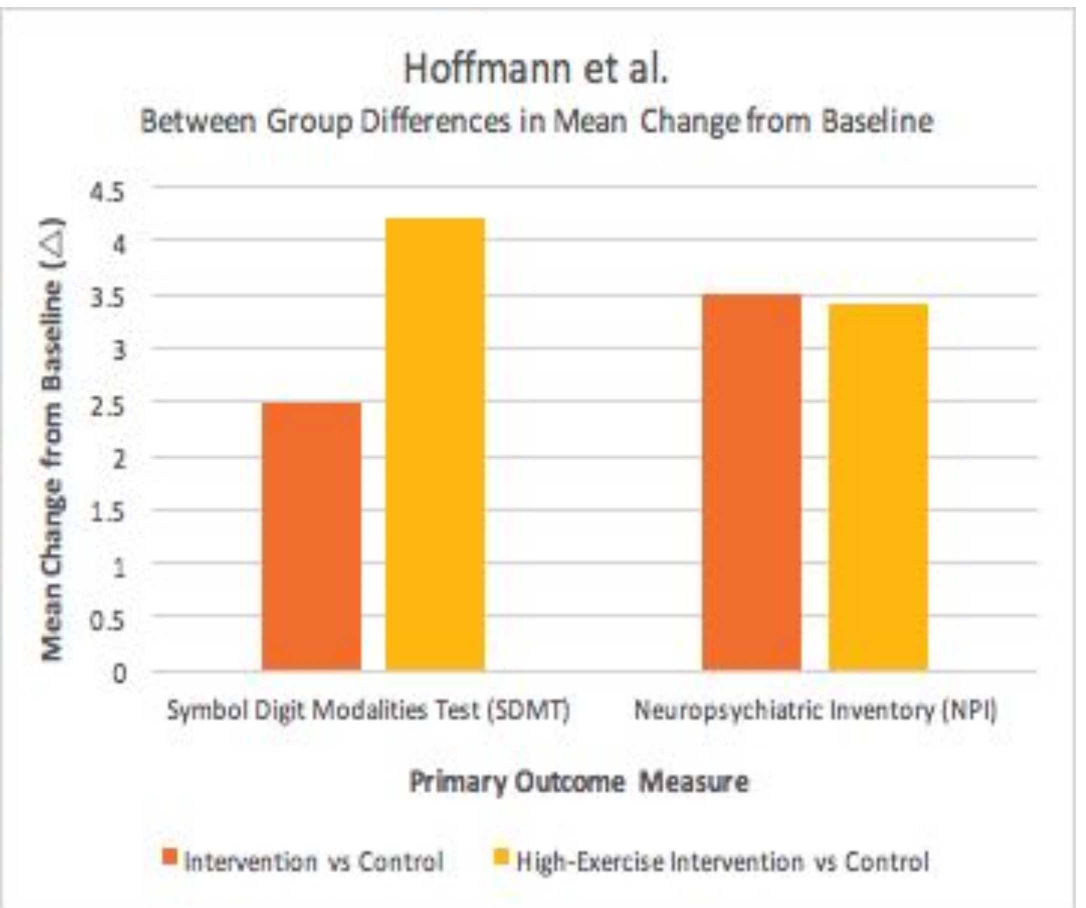

Figure 1. *Between group differences in the mean change from baseline to 16-week follow up in the study by Hoffmann et al.*
Scores on the Symbol Digit Modalities Test showed no significant mean change from baseline in the intervention versus the control group ($p=0.179$), but significant mean change from baseline in the high-exercise intervention (adherence >80% and intensity >70%) versus the control group ($p=0.028$).
Scores on the neuropsychiatric inventory showed significant mean change from baseline in both the intervention versus control group ($p=0.002$) and in the high-exercise intervention group versus control group ($p=0.007$).

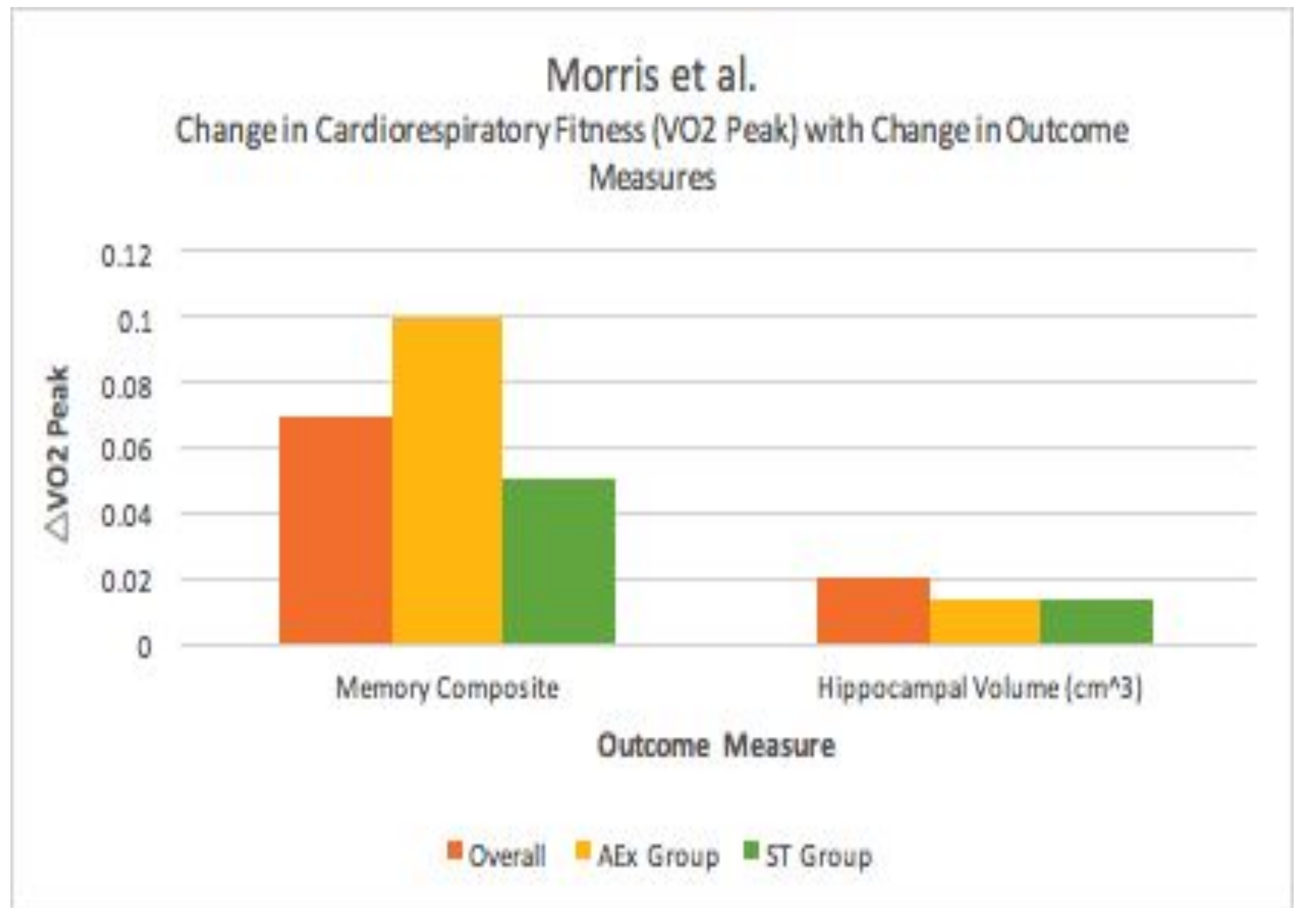

Figure 2. *Relationship of change in cardiorespiratory fitness (VO_2 peak) with changes observed in outcome measures among the overall group and within treatment groups in the study by Morris et al.*
For the overall group, change in peak VO_2 was associated with a significant change in memory composite score ($p=0.003$) and hippocampal volume ($p=0.03$).
For the AEx (aerobic exercise) group, change in peak VO_2 was associated with a significant change in memory composite score ($p<0.01$) and hippocampal volume ($p<0.05$).
For the ST (stretching and toning control) group, change in peak VO_2 was not associated with a significant change in memory composite score or hippocampal volume.

Outcome Measures	Intervention Group (mean ± SD)	Control Group (mean ± SD)	SDR
ADAS-Cog Score	1.0±4.6	0.1±4.1	2.3
Shuttle Walk Test (SWT) Distance	-52.3±91.2	81.3±83.3	37
6-Minute Walk Test (6MWT) Distance	-53.7±273.0	-151.6±244.6	121.1
VO2 Max	1.3±2.1	0.7±1.3	1.7

Table 1. *Interindividual differences in aerobic fitness and cognitive responses after 6-month aerobic exercise intervention among treatment groups in the study by Yu et al.*
The intervention (cycling) group had a greater standard deviation than the control (stretching) group on all 4 outcome measures.
True interindividual differences in aerobic fitness and cognitive responses were calculated as the standard deviation of change (SDR) in the outcome measures listed from baselines to 6 months. A substantially greater SDR in the outcome measures in the intervention group than in the control group is shown, demonstrating true interindividual differences are supported.

Limitations

- **Duration of Exercise Program:** Recent studies show at least six months of exercise training is necessary to induce cognitive changes. The study by Hoffmann et al had a treatment duration of only sixteen weeks, which is not long enough to accurately assess cognitive change.
- **Sample Size and Demographics:** The studies by Morris et al and Yu et al had sample sizes of less than 100 participants, which is difficult to generalize to larger populations and detect significant group effects. Additionally, the study by Yu et al lacked diversity in the study sample, as most participants were caucasian and had achieved a high-level of education.
- **Degree of Supervision during Exercise Program:** The studies by Hoffmann et al and Yu et al included supervised exercise sessions across the duration of the study to ensure consistency in the execution of exercises. The participants in the study by Morris et al were only supervised for six of the twenty-six week exercise training program, which could introduce variability in exercise execution, therefore affecting the outcome measures.

Conclusions and Future Directions

- The literature surveyed uses a variety of outcome measures to analyze the effect of aerobic exercise training on cognition and brain atrophy in adults with mild or early AD.
- The further analysis of high-intensity exercise subgroups and the relationship of change in cardiorespiratory fitness (peak VO_2) with changes observed in outcome measures helps to display fitness-specific effects of aerobic training on cognition.
- The study by Yu et al demonstrated the existence of true interindividual differences in aerobic fitness and cognitive responses to aerobic exercise training in adults with mild AD. These findings emphasize the need to apply a precision exercise approach in future AD exercise studies to account for individuals who do not respond to traditional aerobic fitness training, and who require other augmented and adaptive interventions.
- Additional research using MRI and other imaging techniques to analyze the effect of aerobic exercise training on the rate of brain atrophy in adults with AD would be useful to further assess this topic.

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