International Platform of Registered Systematic Review and Meta-analysis Protocols

INPLASY

Meta-analysis of the effects of aerobic exercise interventions on cognitive function in older adults

INPLASY202470016
doi: 10.37766/inplasy2024.7.0016
Received: 05 July 2024
Published: 05 July 2024

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ADMINISTRATIVE INFORMATION

Support - Ministry of Education of Guangxi Zhuang Autonomous Region of China funded by the Chinese government（22YJA89019）.

Review Stage at time of this submission - Completed but not published.

Conflicts of interest - None declared.

INPLASY registration number: INPLASY202470016

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 05 July 2024 and was last updated on 05 July 2024.

INTRODUCTION

Review question / Objective Is there any difference in the degree of influence of aerobic exercise on cognitive function in the elderly under different cognitive states?

Rationale The objective of this study was to provide evidence for the prevention of cognitive impairment and enhancement of cognitive function in elderly individuals with different cognitive statuses. A systematic search was conducted using PubMed, ScienceDirect, Web of Science, and CNKI to identify randomized controlled trials focusing on the effects of aerobic exercise on cognitive function in the elderly. The Cochrane risk of bias tool was used for literature evaluation, and statistical analysis was performed using RevMan 5.4.1 software and encompassed tests for heterogeneity, effect size pooling, and subgroup analysis.

Condition being studied The spectrum of cognitive decline in older adults spans from normal age-related cognitive changes to subjective cognitive impairment (including routine cognitive complaints on screening tests), mild cognitive impairment, and ultimately dementia. Previous studies have suggested that interventions for age-related dementia in older adults are often ineffective, which hints at the challenge of reversing cognitive decline once it has progressed. However, other studies have proposed that the progressive decline in cognitive function from the initial stages of cognitive decline to early AD in elderly individuals may be reversible or present potential opportunities for reversibility and treatment.

Subjective memory impairment, also known as subjective memory complaints, signifies the presence of cognitive problems related to daily memory, irrespective of whether objective test

results indicate abnormal deficits. These symptoms, considered the initial stage of potential cognitive decline, may be associated with mild cognitive impairment and the progression to AD. MCI is characterized by subjective cognitive complaints and objectively impaired cognitive function and represents an intermediate state between normal aging and dementia. Some researchers have suggested that MCI is likely to progress to dementia, particularly in the direction of AD, while others believe that this progression is inevitable and irreversible.

Vascular cognitive impairment, which encompasses one or more cognitive disorders that affect executive function, attention, memory, language, and visuospatial functions, spans the spectrum from MCI to dementia. VCI is the second most prevalent form of cognitive impairment worldwide. VCI significantly contributes to cognitive impairment in approximately one-third of the at-risk population, and its associated pathology is closely linked to that of dementia. Small-vessel disease, particularly mild subcortical ischemic vascular cognitive impairment, has been identified as a leading cause of VCI. Retrospective studies by Vermeer and Román et al. have demonstrated a connection between mild SIVCI and executive function, which highlights the increased risk of executive function decline in affected patients.

AD is characterized by irreversible neurodegeneration and markedly impacts the daily activities and social functioning of affected individuals. Mild AD represents the primary cause of dementia and contributes to 50-70% of all cases. Given the profound impact of advanced cognitive decline on the daily lives of elderly individuals with limited recovery potential postintervention, early and aggressive intervention upon the onset of signs of cognitive decline is crucial for slowing or potentially reversing this decline.

METHODS

Search strategy

The primary author conducted a comprehensive computerized search across various databases, including the China National Knowledge Infrastructure (CNKI), VIP Database, PubMed, ScienceDirect, Web of Science, and Google Scholar. The search spanned from January 2014 to January 2023. The Chinese keywords utilized were "有氧运动" (aerobic exercise), "认知功能" (cognitive function), and "老年人" (elderly). For PubMed, the search strategy included the following terms: ((((((((((("Exercise"[Mesh]) OR (Physical Activity[Title/Abstract])) OR (Exercises[Title/Abstract])) OR (Physical Activities[Title/Abstract])) OR (Physical Exercise[Title/Abstract])) OR (Physical Exercises[Title/Abstract])) OR (Aerobic Exercise[Title/Abstract])) OR (Aerobic Exercises[Title/Abstract])) OR (Acute Exercise[Title/Abstract])) OR (Acute Exercises[Title/Abstract])) AND (("Aged"[Mesh]) OR (Elderly))) AND ((("Cognition"[Mesh]) OR (Cognitive Function)) OR (Cognitive Functions)) AND ((Randomized Controlled Trial [Filter]) AND (2014:2023[Date])). For Google Scholar, the key terms were "Aerobic exercise," "Physical exercise," "Cognitive function," and "Aged." The searches were limited to studies involving humans, and RCTs. Only peer-reviewed articles were included, and gray literature such as dissertations, proceedings, and government reports has been excluded.

Participant or population Including: Participants included healthy elderly individuals, those with mild cognitive deficits such as mild cognitive impairment or mild Alzheimer's disease, all aged 60 years or older.

Excluding: Patients with other psychiatric disorders, like Parkinson's disease and depression, are excluded. This is primarily because the current understanding of Parkinson's disease is not comprehensive, and the exercise options for Parkinson's patients are relatively limited. Moreover, the exercise intervention methods differ significantly from those used for other cognitive disorders. Depression research is excluded mainly due to its association with patients having MCI and AD. The relationship between depression and cognitive function in MCI and AD patients varies. To maintain the study's integrity, research related to Parkinson's disease and depression was not included.

Intervention The exercise was performed at least once a week for a minimum of 4 weeks, and the type of exercise (e.g., walking, treadmill, dancing) was considered immaterial.The experimental group, whose baseline data matched the control group in terms of age, sex, and education level, engaged in aerobic exercise.The experimental group, whose baseline data matched the control group in terms of age, sex, and education level, engaged in aerobic exercise.

Comparator Control group: The control group did not undergo specific exercise interventions. Participants in the control group maintained their usual physical activity, engaged in recreational activities, daily care, or participated in sham exercises (e.g., stretching and balance).

Study designs to be included Including randomized controlled studies that assessed the impact of aerobic exercise interventions on cognitive function in elderly individuals, encompassing both published and unpublished articles.Exclusing studies that were duplicates, those of poor quality, or those that provided insufficient information, rendering them unusable.

Eligibility criteria The inclusion criteria were as follows: Results: Studies assessed overall cognitive ability, as measured by neuropsychological tests or other objective measures, or evaluated specific cognitive domains, including memory, attention, verbal fluency tasks, or executive function. Subjects lacking available data were excluded.
The inclusion criteria were as follows: Unusable literature: Literature that lacked necessary outcome indicators for inclusion in the final meta-analysis.

Information sources China National Knowledge Infrastructure (CNKI), VIP Database, PubMed, ScienceDirect, Web of Science, and Google Scholar.

Main outcome(s) Two experienced researchers conducted a comprehensive database search, which yielded a total of 2,654 articles. After a detailed review of the article titles and abstracts and excluding those without full-text availability, 102 eligible articles remained. Additionally, through a meticulous examination of meta-analyses and review articles pertaining to the research topics, five secondary articles were identified. Subsequent scrutiny of the full text led to the exclusion of 45 articles that did not align with the inclusion criteria for functional outcome indicators, as well as 28 articles that used interventions outside the specified criteria. Furthermore, 15 articles that did not contain relevant data and for which the full text was unavailable were excluded. Notably, two papers with identical original data sources were identified. Ultimately, 17 papers satisfied the criteria for inclusion in this meta-analysis. The search spanned from January 2014 to January 2023.

Data management All searched records were imported into the reference management software (Note Express V.2.0) to remove duplicate records. The full texts of the studies that potentially met the inclusion criteria were obtained for further evaluation of their eligibility. Any disagreements were resolved through discussion with the third reviewer. Data were extracted by one reviewer using a prepared form and checked for accuracy by another reviewer. The extracted information from eligible studies included participants' characteristics, sample size, study design, methodological information on study quality, experimental and control interventions, duration, frequency, intensity, and style of aerobic exercise, outcomes, and adverse events.RevMan 5.4.1 software (International Cochrane Collaboration Network) was used for the meta-analysis. First, heterogeneity among the included studies was tested at the OR = 0.05. When I2 was ≤50%, no significant statistical heterogeneity was considered, and a fixed-effects model was used. If any statistical heterogeneity was suggested among the studies, a random effects model was adopted. Sensitivity analysis or subgroup analysis could be performed for those with heterogeneity, whereas a meta-analysis of outcome measures was abandoned for those with significant clinical and methodological heterogeneity for general statistical description.

Quality assessment / Risk of bias analysis Data extraction was performed using a standardized extraction table and encompassed key information such as the first author's name, region, publication year, clinical study design, study subjects, intervention methods, intervention cycle, and outcome measures. The Cochrane risk bias assessment tool, which was used to evaluate the included literature, comprises the following seven criteria: random sequence generation, allocation concealment, blinding, loss to follow-up, completeness of outcome data, selective outcome reporting, and other potential biases. The original literature entries were assessed for the risk of low bias, high bias, or uncertainty based on their design and implementation.

Strategy of data synthesis RevMan 5.4.1 software (International Cochrane Collaboration Network) was used for the meta-analysis. First, heterogeneity among the included studies was tested at the OR = 0.05. When I2 was ≤50%, no significant statistical heterogeneity was considered, and a fixed-effects model was used. If any statistical heterogeneity was suggested among the studies, a random effects model was adopted. Sensitivity analysis or subgroup analysis could be performed for those with heterogeneity, whereas a meta-analysis of outcome measures was abandoned for those with significant clinical and methodological heterogeneity for general statistical description.

Subgroup analysis Various cognitive measurement tools were employed across the studies, including the Minimum Mental State

Examination (MMSE), the Montreal Cognitive Assessment (MoCA), and the Alzheimer's Disease Assessment Scale Cognitive Subscale (ADAS-Cog). These tools were utilized to assess four cognitive function subscales: memory, attention, executive function, and verbal fluency. It is noteworthy that different studies utilized distinct tools to evaluate the same cognitive domains.Besides, the studies were stratified based on longitudinal and transverse perspectives. In the longitudinal dimension, the duration of aerobic exercise was categorized into two phases: the first phase included interventions lasting ≥4 weeks and ≤3 months, and the second phase included interventions lasting >3 months and ≤6 months. For studies in which the experimental cycle extended beyond 6 months but less than 7 months, the interventions were also relegated to the second phase.In the transverse dimension, the participants included normal control elderly individuals and those with SMC, MCI, SIVCI, and AD. Upon reviewing their study, it was observed that older patients with SMC could be categorized with mild MCI during subject screening, whereas the analysis combined SMC and MCI into two groups.

Sensitivity analysis Firstly, assess the sensitivity of the influence of aerobic exercise on the overall cognitive function of the elderly. If the heterogeneity is relatively high, a random-effects model is adopted for further analysis first. If the analysis results do not improve significantly, the source of heterogeneity is identified initially through the method of sequential elimination. By eliminating some low-quality studies or those with different evaluation criteria for therapeutic effect and inclusion-exclusion criteria, a combined analysis is conducted and compared with the combined effect size before elimination to explore the influence of the excluded studies on the combined effect size.

Country(ies) involved China.

Keywords Aerobic exercise; Elderly; Cognitive function; Cognitive impairment.

Contributions of each author

Author 1 - Jin Wei Lu - designed the study, collected and selected articles, extracted data from the included studies, evaluated the risk of bias, performed meta-analyses, and drafted the manuscript.
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