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Effects Of Combined Exercise Interventions on Cognition In Older Persons With or Without Mild Cognitive Impairment: A Systematic Review And Meta-Analysis

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ADMINISTRATIVE INFORMATION

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Review Stage at time of this submission - Data analysis.

Conflicts of interest - None declared.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 11 September 2025 and was last updated on 11 September 2025.

INTRODUCTION

Review question / Objective a) What are the effects of the combined exercises with cognitive training compared to physical exercise alone on overall cognition, and cognition-related blood biomarkers in older persons with or without mild cognitive impairment (MCI)?
b) Do the effects of combined exercises with cognitive training on overall cognition differ across exercise types in older persons with or without MCI?

Rationale A growing aging population with a sedentary lifestyle may cause an increase in the incidence of neurodegenerative diseases such as dementia. Exercise is among the most effective strategies against cognitive decline with age and a sedentary lifestyle. In addition, cognitive training may facilitate neural connections and preserve cognitive functions. Therefore, a combination of exercise and cognitive training may have more pronounced effects for preserving cognitive function in aging. Despite the number of studies that have analyzed the effects of combined exercise with cognitive training on cognitive function compared to the impact of exercise alone, in older persons with or without MCI, there is a lack of a more comprehensive approach. This systematic review and meta-analysis will allow us to identify the magnitude of the effect of different strategies, providing insights for investigators and clinicians.

Condition being studied The effects of combination of exercise with cognitive training, in comparison with exercise alone, on overall cognitive function and the influence of the type of exercise on those effects in persons with or without MCI remain unclear. The effects of combined exercise with cognitive training on different cognitive functions have been studied. However, the design of cognitive training and the type of exercise may influence cognitive outcomes and the cognitive domains that were assessed. Our study may contribute to the field by examining

different types of combined exercises and comparing the effects of combined exercises and cognitive training on overall cognitive function and their influence on neuroprotective and inflammatory blood markers.

METHODS

Search strategy Reviews and Meta-Analyses (PRISMA) guidelines by using the keywords and inclusion criteria defined by authors. The keywords that used in search strategy ((("Older persons" OR "MCI") AND (" Dual-Task" OR "Multimodal" OR " Cognitive Training" OR ("Physical Exercise" AND "cognitive stimulation") OR "Exergaming")) AND ("Physical Exercise" OR " Aerobic Exercise" OR " Resistance Exercise" OR " Multimodal Exercise" OR " Exercise" OR " Training")) AND ("Mental health" OR "Cognitive assessment" OR memory OR neurogenesis OR neuroplasticity OR "brain health" OR "BDNF" OR "IGF-1" OR "IL-6" OR "TNF-? " OR "VEGF" OR irisin OR cognition OR "MMSE" OR "MoCA") were searched in Web of Science, Scopus, PsychInfo and US National Library of Medicine National Institutes of Health (PubMED) without time restrictions. The last search performed in April 2025.

Participant or population Older persons, both male and female, with and without MCI, are included. We excluded supplement usage, the population with dementia, and the population with obesity.

Intervention We review studies that included both exercise intervention with cognitive training and exercise alone in the context of aerobic, resistance, and multicomponent exercise. We included all levels of exercise intensities.

Comparator Our comparator group is the group that performed only exercise without cognitive training. However, the type of exercise is the same as that of the combined intervention group.

Study designs to be included Randomized controlled trials.

Eligibility criteria The inclusion criteria for present SRMA were: (a) use human population older persons (>60) with or without MCI; (b) evaluate regular exercise effects; (c) studies that have intervention with both combined exercise (with cognitive training) and only exercise groups; (d) randomized controlled trials ; (e) use quantitative assessment tools (e.g. MoCA, MMSE, Stroop task, etc.) to measure cognitive functions; (f) reports published in English language.

The exclusion criteria were defined as: (a) Animal studies; (b) have intervention with acute exercise design; (c) inclusion of demented population; (d) studies that assessed supplement effects (e) low assessment score according to Modified Downs and Black Checklist; (f) studies only included combined (with cognitive training) exercise or only exercise groups; (g) cross-sectional studies; (h) studies compared motor learning or level of cognitive training; (i) studies that have different type of exercise in comparison group than combined intervention; (j) studies whose included biomarkers without evaluating cognitive outcomes.

Information sources US National Library of Medicine National Institutes of Health (PubMED), Web of Science, Scopus and PsycInfo.

Main outcome(s) Our outcome is overall effects of combined interventions on the cognitive performance and on the blood biomarkers in older persons with or without MCI. Therefore, multiple outcomes that reported in the studies were combined and presented as single effect size by using Comprehensive Meta-Analysis (CMA) software (Biostat, Englewood, NJ, USA, version 4.0) selecting the standard difference in means metric. In order to calculate effect sizes, we used data of sample size, pre-post combined intervention and only exercise group size, means and standard deviations (sd), effect direction, pre-post correlation and standardized by sd score changes. We utilized random effect model. Effect size was categorized as trivial ($d \leq 20$), small ($0.21 < d < 0.50$), moderate ($0.51 < d < 0.79$) and large ($d \geq 0.80$).

Data management Comprehensive Meta-Analysis 4.0; EndNote 20.2; Microsoft Word.

Quality assessment / Risk of bias analysis Methodological quality of the studies was assessed by using a modified version of the Downs and Black checklist for randomized and non-randomized designs of health care intervention.

Strategy of data synthesis The collected data was imported into EndNote 20.2 program. The imported references were screen to determinate eligibility for the study by using following screening strategy; (a) All duplicates removed; (b) articles were screened by title and abstract, and excluded if they did not include necessary information about topic; (c) full text articles whose did not meet our inclusion criteria were excluded; (d) Methodological quality of the studies was evaluated using the Modified Downs and Black

checklist. Data extraction and screening were performed according to the PRISMA guidelines.

Subgroup analysis Subgroup analyses were conducted to evaluate the different types of exercise.

Sensitivity analysis We did not perform Sensitivity Analysis.

Language restriction Only articles that were published in the English language are included.

Country(ies) involved Portugal.

Keywords Exercise; Aging; Cognitive Function; Mild Cognitive Impairment; Cognitive Training.

Contributions of each author

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