INPLASY PROTOCOL

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Conflicts of interest:
None.

Biomarkers for evaluating the effects of exercise interventions in people with MCI or dementia: A Systematic Review

Huang, XX[1]; Zhao, XY[2]; Li, B[3]; Wan, QQ[4].

Review question / Objective: **Which biomarkers have been used in studies with exercise-based interventions among people with MCI or dementia? What are the effects of exercise interventions on these biomarkers, and which are most responsive to exercise? Which factors may influence the effects of exercise on these biomarkers?**
Condition being studied: **In recent years, there are increasing studies in people with MCI and dementia, which adopt objective markers to evaluate the effects of exercise interventions on cognitive function and explore the potential mechanism. This study aims to synthesize the biomarkers in related studies and their responses to exercise interventions. It will be helpful to identify the sensitive biomarkers and clarify the potential mechanisms induced by exercise.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 27 April 2020 and was last updated on 27 April 2020 (registration number INPLASY202040198).

INTRODUCTION

Review question / Objective: **Which biomarkers have been used in studies with exercise-based interventions among people with MCI or dementia? What are the effects of exercise interventions on these biomarkers, and which are most responsive to exercise? Which factors may influence the effects of exercise on these biomarkers?**

Rationale: **Cognitive dysfunction has become a global public health concern and brought high burdens on patients, families and the whole society. Exercise, as a non-pharmacological therapy, has received considerable attention and showed**

favorable effects. But the exact mechanism is still unclear. Identifying the biomarkers responsive to exercise from previous studies is helpful to confirm the efficacy of exercise interventions on cognitive function and clarifying the potential mechanism.

Condition being studied: In recent years, there are increasing studies in people with MCI and dementia, which adopt objective markers to evaluate the effects of exercise interventions on cognitive function and explore the potential mechanism. This study aims to synthesize the biomarkers in related studies and their responses to exercise interventions. It will be helpful to identify the sensitive biomarkers and clarify the potential mechanisms induced by exercise.

METHODS

Search strategy: The search strategy in PubMed was as follows. #1 (((Dementia[MeSH Terms]) OR (cognition disorders[MeSH Terms])) OR (Alzheimer*[MeSH Terms])) OR (cognitive impairment[MeSH Terms]) #2 (exercise[MeSH Terms]) OR ((((((((((exercises[Title/Abstract]) OR physical activit*[Title/Abstract]) OR training*[Title/Abstract]) OR danc*[Title/Abstract]) OR yoga[Title/Abstract]) OR taichi[Title/Abstract]) OR wuqinxi[Title/Abstract]) OR baduanjin[Title/Abstract]) OR yijinjing[Title/Abstract]) #3 ((randomized controlled trial [pt] OR controlled clinical trial [pt] OR randomized [tiab] OR placebo [tiab] OR clinical trials as topic [mesh: noexp] OR randomly [tiab] OR trial [ti]) NOT (animals [mh] NOT humans [mh])) #4 #1 AND #2 AND #3 The search strategy has been reviewed by experts from the fields of cognitive impairment, sports specialty, and gerontological nursing.

Participant or population: The participants in our study include people with MCI or dementia. But people with cognitive impairment caused by Stroke, Parkinson's disease, Huntington's disease, Epilepsy, Multiple Sclerosis, Diabetes, cancer, and psychiatric illness (e.g. schizophrenia) will be excluded.

Intervention: The interventions include any types of exercise and physical activity, and no restrictions on the exercise intensity, exercise duration, setting or the supervision.

Comparator: The comparators include no intervention, usual care, knowledge education, sham exercise training or other forms of exercise.

Study designs to be included: All international studies will be included (including randomized controlled trials and non-randomized controlled trials).

Eligibility criteria: (1) International studies; (2) The participants are diagnosed with MCI or dementia; (3) The intervention group adopts exercise interventions; (4) The comparator receives no intervention, usual care, health education, sham exercise training or other forms of exercise; (5) The outcomes include biomarkers.

Information sources: We systematically searched different types of electronic database for relevant studies, including PubMed, Cochrane Central Register of controlled trials, Embase, Web of Science, PsycINFO, SPORTDiscus, CNKI, and Wanfang, without date restrictions.

Main outcome(s): The main outcomes include all the objective markers related to cognition, such as pathological markers (A, tau), neurotrophic factors, inflammatory cytokines, structural and functional changes in brain regions, and so on.

Quality assessment / Risk of bias analysis: Risk of bias will be assessed independently by two authors according to the Cochrane Collaboration's risk of bias tool, which includes random sequence generation, allocation concealment, blinding of outcome assessor, blinding of participants, incomplete data, selective reporting, and other sources of bias. Disagreement was resolved by the third author.

Strategy of data synthesis: The study characteristics and primary outcome variables will be summarized and

tabulated. The change or post-intervention values will be extracted for continuous variables. If data collected is enough, meta-analysis will be performed to obtain pooled estimates of the effects of exercise interventions on different biomarkers. The software of Stata and Rev Man will be used for analysis.

Subgroup analysis: Not planned.

Sensibility analysis: If necessary, sensibility analysis will be performed excluding studies with high risk of bias.

Language: Studies reported in English and Chinese will be included.

Country(ies) involved: China.

Keywords: Mild cognitive impairment; dementia; exercise; biomarker.

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