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None declared.

Effects of combined Cognitive and Exercise Interventions on Post-stroke Cognitive Function: A Systematic Review and Meta-analysis

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Review question / Objective: **To investigate the cognitive-exercise the combined interventions reported in the research literature, and synthesize their effectiveness in improving cognitive function poststroke.**
Information sources: **We systematically searched the PubMed and Cochrane Library electronic databases and clinical trial registration websites, and screened clinical randomized controlled trials published in peer-reviewed journals.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 23 June 2021 and was last updated on 23 June 2021 (registration number INPLASY202160090).

INTRODUCTION

Review question / Objective: **To investigate the cognitive-exercise the combined interventions reported in the research literature, and synthesize their effectiveness in improving cognitive function poststroke.**

Condition being studied: **Post-Stroke Cognitive Impairment(PSCI) refers to a series of syndromes that meet the diagnostic criteria of cognitive impairment within 6 months after a stroke. This emphasizes the potential causality and importance of clinical management between stroke and cognitive impairment, including cognitive impairment caused by**

stroke as a result of key infarction, multiple infarctions, subcortical ischemic infarction, and cerebral hemorrhage. In this case, cognitive impairment includes executive dysfunction, memory dysfunction, attention disorder, orientation disorder, and perception disorder. Previous studies have demonstrated that more than 32% of stroke survivors showed cognitive dysfunction. According to the MMSE standard assessment, the incidence of cognitive dysfunction within 3 months of stroke is 24%～39% in the United Kingdom and Switzerland. A large-scale, multi-center, cohort study in South Korea recruited 620 patients with ischemic stroke that were assessed by MMSE. The results demonstrated that the prevalence of PSCI reached 69.8% in patients within three months of stroke. PSCI is associated with a decline in patients' life quality, ability to administer daily self-care, accelerated decline of body function, and increased risk of disability and death. Several strategies to improve cognition have been explored in both healthy individuals and patients with Alzheimer's disease. Extensive studies have demonstrated that cognitive training (including cognitive-behavioral training and computer-assisted cognitive training) and exercise training (including aerobic exercise and resistance exercise) can effectively improve cognitive function. A meta-analysis indicated that for PSCI patients, exercise training can positively impact global cognition, and that a combination of aerobic exercise and strength training produces the greatest cognitive benefits. Exercise can also improve cognitive function in patients with chronic stroke. There is a moderate improvement in treatment speed, and exercise training can be used as an intervention strategy to improve PSCI. Cognitive training is also essential for treating PSCI and is primarily divided into compensation training strategies and direct repair cognitive training. Direct repair cognitive training includes practical exercises, memory training (such as reciting acronyms or songs), or computer-aided cognition training. A systematic review of eight studies conducted by Lawla et al. demonstrated that the combined intervention can effectively improve cognitive function in the elderly with or without cognitive impairment. However, the mechanism behind how cognitive dysfunction affects stroke patients is still unknown. The purpose of this study is to review relevant evidence and evaluate the impact of the combined interventions on PSCI.

METHODS

Search strategy: We systematically searched the PubMed and Cochrane Library electronic databases and clinical trial registration websites, and screened clinical randomized controlled trials published in peer-reviewed journals from the earliest available record. We used the following keyword combinations to find relevant articles: (rehabilitation OR habilitation OR combine* interventions OR dual-task OR multi-modal) AND (exercise OR physical activity OR resistance training OR endurance training) AND (cognitive function OR cognition OR attention OR memory OR executive function OR neuropsychological test) AND (dementia*, vascular OR stroke OR cerebrovascular accident OR brain ischemia OR poststroke OR post-stroke OR vascular dementia* OR vascular cognitive impairment).

Participant or population: Patients over 18 years of age who were diagnosed with PSCI, excluding other types of vascular cognitive impairment and various nonvascular cognitive impairments related to strokepost-stroke cognitive impairment.

Intervention: Cognitive-exercise the combined intervention that includes both cognition and exercise, regardless of their order or if they were administered simultaneously (for example, memory training after walking on a treadmill or while walking on a treadmill).

Comparator: Any control group conducted at the same time was deemed acceptable, including no intervention/routine care, delayed intervention, sham intervention, and passive training.

Study designs to be included: Clinically administered random trials with controls.

Eligibility criteria: Inclusion criteria Trials were considered for this review if they met the following criteria: Research subjects: Patients over 18 years of age who were diagnosed with PSCI, excluding other types of vascular cognitive impairment and various nonvascular cognitive impairments related to stroke; Intervention: Cognitive-exercise the combined intervention that includes both cognition and exercise, regardless of their order or if they were administered simultaneously (for example, memory training after walking on a treadmill or while walking on a treadmill); Comparison: any control group conducted at the same time was deemed acceptable, including no intervention/routine care, delayed intervention, sham intervention, and passive training; Result: The use of any validated cognitive neuropsychological test to evaluate cognitive function as a primary or secondary result; Research design: Clinically administered random trials with controls. Exclusion criteria - Non-intervention research; - Theoretical articles or descriptions of treatment methods; - Review articles; - Unpublished studies, abstracts, or papers; - Articles that do not fully explain the intervention measures; - Non-peer-reviewed articles and book chapters; - Non-English articles.

Information sources: We systematically searched the PubMed and Cochrane Library electronic databases and clinical trial registration websites, and screened clinical randomized controlled trials published in peer-reviewed journals.

Main outcome(s): The score of scale.

Data management: 1. Basic information: research title, number, source of publication, and research funding; 2. Inclusion/exclusion criteria: research design, population sample, intervention type, implementation site, outcome indicators ; 3. Research methods and characteristics: Research period, sample scale, distribution sequence generation and hiding, blinding, and other related bias issues; 4. Subject characteristics: number of subjects, diagnostic criteria, age, gender, country; 5. Intervention/comparison: grouping, specific intervention measures, duration, frequency, intensity, and completeness of the intervention process; 6. Outcome measurement: all relevant cognitive results and measurement tools, and the measurement time point of outcome indicators; 7. Conclusion; two personnel cross-checked to extract data for each trial. Inconsistent results were determined by additional discussion or decided by a third examiner, if necessary.

Quality assessment / Risk of bias analysis: The Cochrane Risk of Bias assessment tool was used to independently assess the risk of bias in the included trials. The assessment scope includes the following parameters: random sequence generation, allocation concealment, blinding, incomplete data, and selective reporting. Each part was classified into three categories: low risk, unclear, and high risk. Each trial was classified using the following criteria: low risk of bias (all criteria are rated as low risk); medium risk of bias (one standard is rated as high risk, or two criteria are rated as unclear); high risk of bias (multiple criteria are rated as high risk, or more than two are rated as unclear). Two examiners conducted independent evaluations, and inconsistent results were determined by additional discussion or decided by a third examiner, if necessary.

Strategy of data synthesis: Cognitive results were grouped according to the cognitive domains that were evaluated (such as global cognition, executive function, and memory), and the baseline-endpoint difference of neuropsychological tasks was used to conduct a meta-analysis of related cognitive domains. The following correlation coefficient equation was used to calculate the baseline-endpoint SD change. SD1/change=√SD1/baseline 2+SD1/final2-(2*R1*SD1/baseline*SD1/final) R1=0.5 Review Manager (version 5.2) was used for the meta-analysis and data processing. The SMD of continuous variables and a 95% CI were used for

quantification. The heterogeneity between the experimental design schemes was unclear, so the fixed-effect model was chosen. Heterogeneity was measured by I2 statistics.

Subgroup analysis: **None.**

Sensitivity analysis: **None.**

Language: **Only randomized clinical trials published in English will be considered for inclusion English.**

Country(ies) involved: **China.**

Keywords: **post-stroke cognitive impairment; cognitive-exercise the combined intervention; cognitive function; systematic review.**

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