INPLASY

INPLASY202460035 doi: 10.37766/inplasy2024.6.0035 Received: 10 June 2024

Published: 10 June 2024

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Potential Therapeutic Effects of Exercise-Induced Brain-Derived Neurotrophic Factor Modulation on Geriatric Depression: A Network Meta-Analysis of Randomized Controlled Trials

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ADMINISTRATIVE INFORMATION

Support - Wei Gong Memorial Hospital.

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

Conflicts of interest - None declared.

INPLASY registration number: INPLASY202460035

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 10 June 2024 and was last updated on 10 June 2024.

INTRODUCTION

Review question / Objective This network meta-analysis follows the PICO model (Population, Intervention, Comparison, Outcome) guidelines: Population - elderly patients with depression; Intervention - exercise therapy; Comparison - any control group or alternative nonpharmacological interventions; Outcome standardized assessments of depression in the elderly.

Condition being studied This study aims to investigate the therapeutic effects of exercise on geriatric depression, focusing on its impact on depressive symptoms and Brain-Derived Neurotrophic Factor (BDNF) levels in elderly individuals. Through a network meta-analysis (NMA) of randomized controlled trials (RCTs), various exercise interventions will be compared to identify the most effective types for improving depressive symptoms in the elderly population. The study will include a range of exercise modalities, and the results will provide valuable

insights into non-pharmacological approaches to managing depression in older adults.

METHODS

Search strategy In the review, we will include the following terms and brief information about relevant electronic databases: Exercise, Depression, Elderly. We will search relevant literature in major medical electronic databases such as PubMed, Embase, and Cochrane Library.

Participant or population In this review, we will focus on the following population: elderly individuals aged sixty years and above with depression.

Intervention The content of the exercise intervention will vary depending on the specific studies included in the review. However, typical components of exercise interventions for elderly individuals with depression may include various types of physical activities such as aerobic exercises (e.g., walking, jogging, swimming), strength training, flexibility exercises (e.g., yoga, tai chi), balance exercises, and functional exercises. The duration, frequency, and intensity of the exercise sessions may also vary across studies. Additionally, some interventions may include supervised exercise programs conducted in a group setting, while others may involve homebased or self-directed exercise programs.

Comparator The comparison will involve evaluating the effects of the exercise intervention on elderly individuals with depression compared to a control group who do not receive any exercise intervention. The control group may receive standard care or participate in activities unrelated to exercise, such as social activities or relaxation techniques. The comparison will focus on assessing changes in depressive symptoms and Brain-Derived Neurotrophic Factor (BDNF) levels between the intervention group and the control group over a specified period.

Study designs to be included The included study designs will primarily consist of randomized controlled trials (RCTs).

Eligibility criteria The eligibility criteria we will use are as follows: Participants: Elderly individuals aged sixty years and above with depression. Intervention: Receipt of exercise intervention. Control group: Control group receiving no exercise intervention. Study design: Randomized controlled trials. Literature type: We will include published original studies and studies employing NMA methodology for analysis. These eligibility criteria will help ensure that the selected studies align with the theme of the review and provide sufficient data for NMA.

Information sources The information sources will primarily include four major databases: PubMed, Embase, Cochrane Library, and Web of Science. These databases are widely recognized for their comprehensive coverage of biomedical and psychological literature, making them suitable sources for identifying relevant studies on exercise interventions for elderly individuals with depression.

Main outcome(s) The primary outcomes will include ranking the effectiveness of various exercise interventions in alleviating depressive symptoms among elderly individuals. These interventions will be assessed based on their ability to reduce depressive symptoms as measured by standardized depression assessment scales. The ranking will help identify the most effective types of exercise interventions for managing depression in the elderly population.

Quality assessment / Risk of bias analysis We conducted quality assessment and risk of bias analysis using the ROB 2 (Risk of Bias 2) tool. This tool assesses various domains of bias, including randomization process, deviations from intended interventions, missing outcome data, measurement of the outcome, and selection of the reported result. Each domain is evaluated to determine the overall risk of bias for each included study, allowing for a comprehensive assessment of study quality and potential biases.

Strategy of data synthesis Our data synthesis strategy involved using Metalnsight (version 5.2.1), developed by the Complex Reviews Support Unit funded by the National Institute for Health Research (NIHR) in London, UK. Additionally, we utilized the netmeta package integrated into the online NMA platform in R for statistical analysis. This approach allowed us to conduct network meta-analysis (NMA) to compare multiple interventions simultaneously and assess their relative effectiveness in improving depressive symptoms among elderly individuals.

Subgroup analysis NA.

Sensitivity analysis We conducted two different sensitivity analyses to verify the reliability of the results.

Firstly, we performed a sensitivity analysis by sequentially removing each study to assess whether any single study disproportionately influenced the overall results. This involved stepwise removal of each study and subsequent evaluation of how these removals impacted the final conclusions and the comparative effects of the interventions.

Secondly, another sensitivity analysis focused on exploring the correlation coefficient applied in the pre- and post-assessments of cognitive function. Initially, we used the correlation coefficient of 0.8 as recommended in the Cochrane Handbook (Higgins, Li, et al., 2019). To further verify the results, we conducted sensitivity analyses using different correlation coefficients, particularly varying between 0.5 and 0.8 (Pearson & Smart, 2018). In this analysis, we recalculated the effect size of cognitive function changes using a lower correlation coefficient of 0.5 (Pearson & Smart, 2018), to assess how changes in the correlation coefficient influenced the direction and magnitude of the results, statistical significance, and the comparative effects of the interventions.

Language restriction There were no language restrictions imposed in our study.

Country(ies) involved Taiwan.

Keywords geriatric, depression, exercise, network meta-analysis.

Contributions of each author

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