

Effect of Virtual Reality-Based Treatments on Cognition for Stroke Patients: An Updated Meta-Analysis and Systematic Review

INPLASY2024100106

doi: 10.37766/inplasy2024.10.0106

Received: 25 October 2024

Published: 25 October 2024

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ADMINISTRATIVE INFORMATION**Support** - National High Level Hospital Clinical Research Funding.**Review Stage at time of this submission** - Completed but not published.**Conflicts of interest** - None declared.**INPLASY registration number:** INPLASY2024100106**Amendments** - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 25 October 2024 and was last updated on 25 October 2024.**INTRODUCTION**

Review question / Objective This study aims to determine whether VR-based treatment of patients with stroke improves cognition and mental health compared with traditional rehabilitation alone. We aim to evaluate the effect of virtual reality (VR) based treatments on cognition in stroke patients.

Rationale Although there are several systematic reviews conducted on the contribution of VR-based interventions to cognition rehabilitation, no unified conclusion has yet been reached. A systematic review indicated that exercise-based VR interventions are potentially valuable as a support in improving psychological outcomes. Nonetheless, due to the diversity of study design and insufficient data, the authors only described their results and did not conduct a meta-analysis. Hence, the overall effect of VR-based therapies on improving cognition and mental health in patients with stroke remains unclear. The evidence is

sparse, and a comprehensive picture of the effects of VR-based therapies is needed. With ongoing advancements in VR, a plethora of original studies focused on cognitive recovery and mental health after stroke has been recently published.

Condition being studied Stroke-related cognitive deficits may interfere with functional recovery, the ability to (re-)acquire motor skills, and compromise independence, potentially exerting considerable influence on rehabilitation outcomes. Although stroke occurs as an acute event, it is a chronic condition that necessitates multidimensional and overwhelming treatment. The neurological trauma of stroke survivors is irreversible and devastating; hence, after a stroke, patients face various stressors, which may trigger different aspects of their health, especially their mental health. Mental health is defined as a state of complete happiness, which refers to our ability to enjoy life and cope with challenges. Depression, anxiety, and stress are particularly common and persistent psychological problems following a stroke, with a

high risk of relapse, even after a long period of remission. Systematic reviews carried out in this area have proved inconclusive, providing conflicting results. With underscored inadequacies of conventional rehabilitation, new high-tech innovations that use virtual reality (VR) are considered a potential avenue toward effective rehabilitation and may offer a supplementary platform to enhance the cognitive and psychological benefits after stroke. Management of VR-based neurorehabilitation for stroke is highly related to recovery, reorganization, and neuroplasticity. VR can also exploit a brain mechanism known as embodied simulation, encouraging the patients' motivation and participation by allowing physical and emotional interactions with the environment through the digital medium. In particular, VR offers a high level of flexibility and control over therapeutic tasks by automatically recording and tracking the user's performance, enabling the user to perform intensive training according to their ability and keeping the experience of interaction with therapeutic tasks enjoyable and compelling.

METHODS

Search strategy We searched MEDLINE (source, PubMed from 2005 to Dec. 2023), EMBASE (2005 to Dec. 2023), the Cochrane Controlled Clinical Trials Register Database (to Dec. 2023), CNKI, WanFang, VIP, SinoMed database and the ClinicalTrials.gov website (to Dec. 2023) using the terms "virtual reality", "stroke", "cognition", "mental", and "randomized trial". Manual reference checking of the bibliographies of all relevant articles was performed. No language restrictions were applied.

Participant or population Stroke patients.

Intervention Stroke patients undergoing VR-based rehabilitation.

Comparator Stroke patients not undergoing VR-based rehabilitation.

Study designs to be included Randomized controlled trials.

Eligibility criteria Studies without control groups, those that do not report cognitive outcomes, or studies with very small sample sizes (<20 participants) are excluded.

Information sources PubMed, Embase, Cochrane Library, Web of Science, and CNKI (Chinese databases).

Main outcome(s) Primary outcome is cognition assessed by Mini-Mental State Examination (MMSE), or Montreal Cognitive Assessment (MoCA).

Additional outcome(s) Secondary outcomes are the executive function, memory, visuospatial function, depression, quality of life, attention and verbal fluency.

Data management Two reviewers extracted data concerning patient characteristics, the VR-based treatment used, study quality, and clinical outcomes using a standard data-collection form. Disagreements were resolved by discussion.

Quality assessment / Risk of bias analysis The Preferred Reporting Items for Systemic Reviews and Meta-Analyses (PRISMA) statement[5] was followed. Two reviewers assessed the quality of the selected trials. Components used for quality assessment were means of generation of random sequence, allocation concealment, blinding of outcome assessment, and selective outcome reporting.

We used the GRADEpro GDT software to evaluate the certainty of evidence according to the GRADE guidelines for HDRS and rate of response based on areas of study design, risk of bias, inconsistency, indirectness, imprecision, and other considerations, such as publication bias, effect size, and potential confounding.

According to GRADE Working Group, grades of evidence were divided into (1) high quality: we are very confident that the true effect lies close to that of the estimate of the effect; (2) moderate quality: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different; (3) low quality: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect; (4) very low quality: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

Strategy of data synthesis Results were analyzed quantitatively with STATA 14.0 software (Stata Corp, California, USA) using the fixed-effects model[6]. We calculated the pooled relative risk (RR) for dichotomous outcomes and the standard mean difference (SMD), or weighted mean difference (WMD) for continuous data with 95% confidence intervals (CI).

Subgroup analysis Stratified by stroke type, VR type, and duration of treatment to explore sources of heterogeneity.

Sensitivity analysis Sensitivity analyses were conducted to determine the influence of individual trials on the overall pooled results.

Language restriction No language restrictions were applied.

Country(ies) involved China.

Keywords Virtual reality; Stroke; Cognition; Meta-analysis.

Contributions of each author

Author 1 - Ying Deng - 1. Responsible for the overall study design and planning, including formulating the research questions and objectives.

2. Conducted data searches, screening, and extraction, collaborating with the second author on data cleaning and validation.

3. Performed the meta-analysis, interpreted the results, and drafted the introduction, methods, results, and discussion sections of the manuscript. Coordinated.

Author 2 - Shan Huang - 1. Assisted in refining the study design and search strategy, contributing to defining the inclusion and exclusion criteria.

2. Collaborated with the first author in data extraction, cleaning, and preparing data for analysis.

3. Supported the statistical analysis and contributed to drafting the results and discussion sections, providing critical revisions and insights on.

Author 3 - Chao Sun - 1. Provided expertise in cognitive rehabilitation and stroke recovery, guiding the interpretation of findings within the clinical context.

2. Conducted a thorough literature review, identifying relevant studies and trends in VR and cognitive rehabilitation.

3. Reviewed and revised the manuscript critically for important intellectual content, ensuring accuracy and clarity in reporting findings.