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Optimizing tDCS Parameters for Post-Stroke Upper Limb Recovery: A Systematic Review and Meta-Analysis Protocol

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ADMINISTRATIVE INFORMATION

Support - No.

Review Stage at time of this submission - Preliminary searches.

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 4 February 2025 and was last updated on 4 February 2025.

INTRODUCTION

Review question / Objective The primary objective of this systematic review and meta-analysis is to evaluate the efficacy and safety of transcranial direct current stimulation (tDCS) in improving upper limb motor impairments in stroke patients, with a focus on identifying optimal stimulation parameters and intervention targets.
PICOS Framework:
Population (P):
Adult patients diagnosed with stroke who have upper limb motor impairments. Patients will be included regardless of stroke type (ischemic or hemorrhagic), provided they have measurable upper limb motor dysfunction assessed using validated tools such as the Fugl-Meyer Assessment (FMA), Brunnstrom Rating Scale (BRS), Action Research Arm Test (ARAT), Wolf Motor Function Test (WMFT), Modified Ashworth Scale (MAS), and Box and Block Test (BBT).
Intervention (I):
Transcranial direct current stimulation (tDCS) applied to the scalp, including anodal, cathodal, and bipolar tDCS. The intervention will vary in terms of stimulation parameters such as current density (<0.057 mA/cm^2), stimulation.

Condition being studied 1.Stroke and Upper Limb Motor Impairments:
Stroke, a cerebrovascular accident, is a leading cause of death and long-term disability worldwide. It occurs when blood flow to a part of the brain is interrupted or reduced, depriving brain tissue of oxygen and nutrients. This can result from either a blocked blood vessel (ischemic stroke) or a ruptured blood vessel (hemorrhagic stroke). The global burden of stroke is substantial, with over 13 million new cases reported annually. The economic impact is significant, with the estimated global cost of stroke exceeding US$721 billion, equivalent to 0.66% of the global GDP.

2. Upper Limb Motor Impairments Post-Stroke:

Upper limb motor impairments are common sequelae of stroke, affecting approximately 65% of stroke survivors. These impairments significantly limit essential activities of daily living (ADLs), such as dressing, eating, and personal hygiene, thereby reducing independence and overall quality of life. The recovery of upper limb function is particularly challenging due to the large cortical projection area of the upper limbs, which contributes to a slower recovery process compared to lower limbs. Only 5% to 20% of patients regain full upper limb motor function within one year after stroke onset. This highlights the critical need for effective rehabilitation strategies to address upper limb motor impairments post-stroke.

3.Current Rehabilitation Challenges :
Traditional rehabilitation methods, such as repetitive task-specific training, occupational therapy, and physical therapy, have been used to address upper limb motor impairments post-stroke. However, these approaches face several challenges. The efficacy of traditional rehabilitation varies significantly among individuals, with some patients experiencing slow and incomplete recovery. These methods also demand high patient engagement, which can be difficult to maintain due to cognitive impairments or lack of motivation in stroke survivors. Moreover, traditional rehabilitation primarily relies on repetitive limb training and lacks direct modulation of cortical neuroplasticity, making it difficult to achieve precise neural functional remodeling.

4.Transcranial Direct Current Stimulation (tDCS):
tDCS is a non-invasive neuromodulation technique that applies a weak direct current to the scalp to modulate cortical neural activity. It has been shown to promote neural plasticity and functional recovery in stroke patients. The anodal stimulation enhances cortical excitability, inducing depolarization, while cathodal stimulation reduces excitability, inducing hyperpolarization. tDCS is repeatable, cost-effective, and can be integrated with conventional rehabilitation to amplify therapeutic effects. However, the optimal parameters for tDCS, including current intensity, stimulation duration, and target location, remain to be determined. Current research suggests that current densities of 0.029, 0.057, and 0.080 mA/cm^2 are effective, but the relative efficacy of different parameters and intervention targets is still a matter of debate.

5.Clinical Implications and Future Directions:
Given the potential benefits of tDCS in enhancing upper limb motor recovery post-stroke, a systematic evaluation of its efficacy and safety is essential. This study aims to provide comprehensive and up-to-date evidence on the therapeutic potential of tDCS, guiding clinical practice and future research. Identifying optimal stimulation parameters and intervention targets will help clinicians tailor tDCS interventions to maximize therapeutic outcomes. Future research should focus on conducting high-quality randomized controlled trials to validate the efficacy of tDCS and further explore its mechanisms of action, particularly its impact on neural plasticity and long-term functional recovery.

11. Search strategy

We will conduct the literature search using medical subject headings (MeSH) and relevant keywords. Specifically, the search terms will include "Stroke[MeSH]", "Cerebrovascular Disorders[MeSH]", "Upper Extremity[MeSH]", "Motor Activity[MeSH]", "Rehabilitation[MeSH]", "Transcranial Direct Current Stimulation[MeSH]", "tDCS[MeSH]", "Neurorehabilitation[MeSH]", "Motor Skills[MeSH]", "Motor Function[MeSH]", "Motor Recovery[MeSH]", and their various synonyms and related terms. Additionally, we will use free-text terms such as "stroke*", "cerebrovascular accident*", "upper limb*", "motor function*", "rehabilitation*", "tDCS*", "neurorehabilitation*", "motor skill*", "motor recovery*", and similar variations. To ensure comprehensiveness, we will also search the reference lists of retrieved articles to identify additional relevant studies.

METHODS

Participant or population This systematic review and meta-analysis will focus on adult patients who have experienced a stroke and subsequently developed upper limb motor impairments. The inclusion criteria for participants are as follows:

1.Diagnosis of Stroke: Patients must have a confirmed diagnosis of stroke, which can be either ischemic or hemorrhagic, as determined by clinical presentation and imaging studies (e.g., CT or MRI).

2.Upper Limb Motor Impairments: Participants must exhibit significant upper limb motor impairments, as assessed by validated clinical tools such as the Fugl-Meyer Assessment (FMA), Brunnstrom Rating Scale (BRS), Action Research Arm Test (ARAT), Wolf Motor Function Test (WMFT), Modified Ashworth Scale (MAS), and Box and Block Test (BBT). These tools will be used to evaluate the presence and severity of upper limb motor dysfunction.

3.Age: Participants will be adults aged 18 years or older, as tDCS interventions and their effects may differ significantly in pediatric populations.

4.Post-Stroke Phase: The study will include patients in both the acute, subacute, and chronic phases of stroke recovery to provide a comprehensive understanding of tDCS efficacy across different stages of rehabilitation.

Exclusion Criteria: Patients with severe cognitive impairments that prevent their participation in the study protocol, those with contraindications to tDCS (e.g., severe skin conditions, pacemakers), and those who have received other forms of non-invasive brain stimulation concurrently with tDCS will be excluded to minimize confounding variables.

Intervention Interventions will be transcranial direct current stimulation (tDCS), including anodal, cathodal, and bipolar tDCS.

Comparator Comparators will include placebo stimulation, conventional rehabilitation, or other non-tDCS interventions.

Study designs to be included
To decrease the risk of bias in individual studies, only randomized controlled blind/double-blind studies (RCTs) which reported the interest outcomes were included in this meta-analysis.

Eligibility criteria In addition to the PICOS framework, the following inclusion and exclusion criteria will be applied to ensure the rigor and relevance of the studies included in this systematic review and meta-analysis:

Additional Inclusion Criteria:
1.Publication Language: Studies published in English or Chinese will be included to ensure a comprehensive review of both international and regional research.
2.Study Completeness: Only studies with complete data on stimulation parameters (e.g., current density, stimulation duration, target location) and outcome measures (e.g., upper limb motor function scores, activities of daily living) will be included. This ensures that the analysis is based on robust and complete datasets.
3.Peer-Reviewed Studies: Only studies published in peer-reviewed journals will be included to ensure the quality and validity of the research.

Additional Exclusion Criteria:
1.Non-Randomized Studies: Non-randomized controlled trials, including non-randomized concurrent control trials, before-after studies, and cohort studies, will be excluded to minimize bias and ensure the highest quality of evidence.
2.Animal Studies: Studies conducted on animal models will be excluded, as the focus is on human clinical outcomes.
3.Duplicate Publications: Studies that are duplicates or report the same data in multiple publications will be excluded to avoid redundancy and overrepresentation of the same data.
4.Incomplete Data: Studies with incomplete or unobtainable data on stimulation parameters or outcome measures will be excluded to ensure the accuracy and reliability of the meta-analysis.
5.Commentaries and Editorials: Commentaries, editorials, conference abstracts, meta-analyses, and letters will be excluded as they do not provide original data.
6.Specific Patient Exclusions: Patients with severe cognitive impairments that prevent their participation in the study protocol, those with contraindications to tDCS (e.g., severe skin conditions, pacemakers), and those who have received other forms of non-invasive brain stimulation concurrently with tDCS will be excluded to minimize confounding variables.

Information sources To identify all relevant studies, we will combine electronic and manual search strategies. We will search the following electronic databases: MEDLINE via PubMed, Cochrane Library, Web of Science, Embase, China National Knowledge Infrastructure (CNKI), and Wan fang Data (up to December 31, 2024). Additionally, we will search grey literature, including conference proceedings and unpublished studies, and contact study authors to obtain additional data.

Main outcome(s) Primary outcomes will be upper limb motor function scores (e.g., Fugl-Meyer Assessment). Secondary outcomes will include activities of daily living (ADL) scores and adverse event rates. These outcomes will be prioritized based on their importance and frequency in the literature.

Data management To efficiently manage and document the retrieved literature and data, we will utilize EndNote 21 software (Captivate Analytics, USA, version EndNote 21.4). This software enables systematic organization and storage of bibliographic information, ensuring the transparency and traceability of the research process. All search results will be imported into the EndNote library for preliminary screening and subsequent detailed evaluation.

Quality assessment / Risk of bias analysis The quality of the included studies will be assessed using the Cochrane Risk of Bias Tool (RoB 2.0) [18] . This tool evaluates five domains: the randomization process, deviations from intended interventions, missing outcome data, measurement of the outcome, and selection of the reported result. Each domain is assessed through a series of "signaling questions" that identify potential biases in the study design, implementation, and reporting. Based on the responses, the risk of bias in each domain can be categorized as "low risk," "some concerns," or "high risk." The assessment will be conducted independently by two researchers (LC and WW). Any discrepancies will be resolved through discussion, with consultation of a third researcher (ZCQ) if consensus cannot be reached.

Strategy of data synthesis In this study, quantitative synthesis will be performed using a random-effects model if data from included studies are suitable for meta-analysis. For continuous outcomes, effect sizes will be calculated as mean differences (MD) or standardized mean differences (SMD) with 95% confidence intervals (CI). For dichotomous outcomes, relative risks (RR) with 95% CI will be used. Heterogeneity will be assessed using the I^2 statistic, with $I^2 > 50\%$ indicating significant heterogeneity.

Subgroup analysis Subgroup analyses will explore the impact of stimulation parameters (e.g., current intensity, stimulation duration) and patient characteristics (e.g., stroke type, disease duration) on outcomes.

Sensitivity analysis Sensitivity analyses will be conducted by excluding lower-quality studies to assess the robustness of the results. Publication bias and selective reporting bias will be evaluated using funnel plots and Egger's test.

Country(ies) involved China.

Keywords stroke, upper limb motor impairments, transcranial direct current stimulation (tDCS), neurorehabilitation, meta-analysis.

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