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Non-invasive Neuromodulation Interventions for Post-Stroke Emotional Symptoms and Quality of Life: An Umbrella Review and Evidence Mapping of Systematic Reviews and Meta-Analyses

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ADMINISTRATIVE INFORMATION

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 20 June 2026 and was last updated on 20 June 2026.

INTRODUCTION

Review question / Objective This umbrella review aims to systematically identify, summarize, and critically appraise existing systematic reviews and meta-analyses evaluating the effects of non-invasive neuromodulation interventions on post-stroke emotional symptoms and quality of life. The primary objective is to assess the effectiveness and certainty of evidence for non-invasive neuromodulation in improving emotional symptoms, including depressive and anxiety symptoms, in stroke survivors. The secondary objective is to summarize the evidence regarding quality of life and safety outcomes. An evidence map will be developed to visualize the distribution, direction, and certainty of evidence across different neuromodulation techniques and outcome domains.

Condition being studied The condition being studied is post-stroke emotional symptoms and quality of life impairment among stroke survivors. Emotional symptoms after stroke include depressive symptoms, anxiety symptoms, and related mood or affective symptoms assessed using validated clinical scales. Quality of life impairment refers to reduced health-related quality of life or stroke-specific quality of life after stroke. Stroke includes ischemic stroke, hemorrhagic stroke, or mixed stroke populations.

METHODS

Participant or population The target population will be adult patients, aged 18 years or older, with a clinical diagnosis of stroke, including ischemic stroke, hemorrhagic stroke, or mixed stroke populations. Reviews including patients at any stage after stroke, including acute, subacute, and chronic phases, will be eligible. Reviews involving mixed neurological populations will be included only if stroke-specific data can be extracted separately.

Intervention Eligible interventions will include non-invasive neuromodulation techniques used for post-stroke rehabilitation or symptom

management. These may include repetitive transcranial magnetic stimulation, transcranial magnetic stimulation, theta burst stimulation, transcranial direct current stimulation, transcranial alternating current stimulation, transcranial random noise stimulation, and transcutaneous vagus nerve stimulation, including transcutaneous auricular vagus nerve stimulation. Studies evaluating invasive neuromodulation, such as deep brain stimulation, implanted vagus nerve stimulation, or spinal cord stimulation, will be excluded. Electroacupuncture, conventional acupuncture, robot-assisted therapy, virtual reality, and neuromuscular electrical stimulation will not be considered eligible unless they are explicitly combined with one of the predefined non-invasive neuromodulation interventions and the effect of the neuromodulation component can be identified.

Comparator Eligible comparators may include sham stimulation, placebo stimulation, usual care, conventional rehabilitation, no intervention, pharmacological treatment, psychological intervention, or other active non-invasive neuromodulation techniques. Reviews comparing different non-invasive neuromodulation protocols will also be considered if they report relevant emotional symptom or quality-of-life outcomes.

Study designs to be included This umbrella review will include published systematic reviews and meta-analyses of randomized controlled trials or controlled clinical studies. Network meta-analyses and overviews of reviews will also be considered if they meet the eligibility criteria and provide extractable data relevant to post-stroke emotional symptoms or quality of life. Narrative reviews, scoping reviews without systematic methods, primary clinical trials, observational studies, case reports, editorials, letters, conference abstracts, animal studies, and in vitro studies will be excluded.

Eligibility criteria Studies will be eligible if they meet the following criteria:

The study is a systematic review, meta-analysis, network meta-analysis, or overview of reviews.
The population consists of adult stroke survivors, or stroke-specific data are available from a mixed population.
The intervention includes at least one predefined non-invasive neuromodulation technique, such as rTMS, TMS, TBS, tDCS, tACS, tRNS, tVNS, or taVNS.
The review reports at least one relevant outcome related to emotional symptoms, including depressive symptoms, anxiety symptoms, mood symptoms, or psychological distress, or quality of life.
The review reports sufficient methodological information to allow quality appraisal using AMSTAR 2.

Studies will be excluded if they focus only on motor function, swallowing, cognition, aphasia, pain, sleep, or activities of daily living without reporting emotional symptom or quality-of-life outcomes. Reviews involving invasive neuromodulation, electroacupuncture alone, acupuncture alone, neuromuscular electrical stimulation alone, functional electrical stimulation alone, robot-assisted therapy alone, or virtual reality alone will be excluded unless the predefined non-invasive neuromodulation component can be separately evaluated.

Information sources The following electronic databases will be searched from inception to the date of search: PubMed/MEDLINE, Embase, Web of Science Core Collection, Cochrane Library, PsycINFO, China National Knowledge Infrastructure, and Wanfang Database. Reference lists of included reviews and relevant articles will also be manually searched to identify additional eligible studies. Search terms will include combinations of terms related to stroke, non-invasive neuromodulation, emotional symptoms, depression, anxiety, quality of life, systematic review, and meta-analysis.

Main outcome(s) The primary outcomes will be post-stroke emotional symptoms, analyzed separately as depressive symptoms and anxiety symptoms. Depressive symptoms may be assessed using validated scales such as the Hamilton Depression Rating Scale, Beck Depression Inventory, Patient Health Questionnaire-9, Self-Rating Depression Scale, Hospital Anxiety and Depression Scale-depression subscale, Montgomery–Åsberg Depression Rating Scale, or other validated depression scales. Anxiety symptoms may be assessed using validated scales such as the Hamilton Anxiety Rating Scale, Self-Rating Anxiety Scale, State-Trait Anxiety Inventory, Generalized Anxiety Disorder-7, Hospital Anxiety and Depression Scale-anxiety subscale, or other validated anxiety scales.

The secondary outcome will be quality of life, including health-related quality of life or stroke-specific quality of life, assessed using validated instruments such as the Stroke-Specific Quality of Life Scale, Stroke Impact Scale, Short Form-36, Short Form-12, EuroQol-5 Dimension, WHOQOL-BREF, or other validated quality-of-life measures.

Safety outcomes, including adverse events and tolerability, will be extracted and summarized when reported. When multiple time points are available, post-intervention outcomes will be prioritized. Follow-up outcomes will be extracted separately and summarized narratively.

Quality assessment / Risk of bias analysis Two reviewers will independently assess the methodological quality of included systematic reviews and meta-analyses using AMSTAR 2. The overall methodological quality will be classified as high, moderate, low, or critically low according to AMSTAR 2 guidance. The risk of bias of included reviews will be assessed using ROBIS when sufficient information is available. The certainty of evidence for key outcomes will be evaluated using the GRADE approach, considering risk of bias, inconsistency, indirectness, imprecision, and publication bias. Any disagreements between reviewers will be resolved through discussion or consultation with a third reviewer.

Strategy of data synthesis A narrative synthesis will be conducted to summarize the characteristics and findings of included reviews. Extracted information will include author, publication year, number of included primary studies, total sample size, stroke type and phase, intervention type, stimulation parameters, comparator, outcome measures, effect estimates, confidence intervals, heterogeneity, adverse events, AMSTAR 2 rating, ROBIS assessment, and GRADE certainty.

Results will be organized by intervention type and outcome domain. Emotional symptoms will be analyzed separately as depressive symptoms and anxiety symptoms rather than combined into a single pooled outcome. Quality-of-life outcomes will be summarized separately. The direction of effect will be categorized as beneficial, no significant effect, harmful, or inconsistent based on the statistical significance, direction, and consistency of findings reported by the included reviews.

An evidence map will be developed to display the distribution of evidence across intervention types and outcome domains. Where possible, effect estimates such as standardized mean differences, mean differences, risk ratios, odds ratios, and 95% confidence intervals will be extracted. Due to expected overlap among primary studies included in different reviews, a new quantitative meta-analysis of review-level estimates will not be performed as the primary synthesis. The degree of overlap among primary studies will be assessed using the corrected covered area method when sufficient data are available.

Subgroup analysis If sufficient data are available, subgroup analyses will be conducted according to intervention type, including rTMS, TBS, tDCS, tACS, tRNS, tVNS, and taVNS; outcome type, including depressive symptoms, anxiety symptoms, and quality of life; stroke phase, including acute, subacute, and chronic stroke; stimulation target or protocol, such as high-frequency versus low-frequency stimulation, anodal versus cathodal stimulation, and stimulation of M1, DLPFC, or other targets; comparator type, including sham stimulation, usual care, conventional rehabilitation, or active treatment; and methodological quality of included reviews.

Sensitivity analysis Sensitivity analyses will be performed when data are sufficient. These may include restricting analyses to reviews rated as high or moderate quality by AMSTAR 2, excluding reviews with high risk of bias according to ROBIS, excluding reviews with critically low methodological quality, restricting analyses to reviews including only randomized controlled trials, excluding reviews with substantial overlap of primary studies, and prioritizing the most recent, most comprehensive, or highest-quality review when multiple reviews address the same intervention-outcome comparison. Sensitivity analyses may also be conducted by excluding network meta-analyses or reviews with mixed populations when stroke-specific evidence is limited.

Country(ies) involved China.

Keywords Stroke; post-stroke; non-invasive neuromodulation; non-invasive brain stimulation; repetitive transcranial magnetic stimulation; transcranial direct current stimulation; theta burst stimulation; transcutaneous vagus.

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