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Hemodynamic changes resulting from non-invasive neuromodulation: a systematic review protocol

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ADMINISTRATIVE INFORMATION

Support - Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES - Brazil) and National Council for Scientific and Technological Development (CNPq - Brazil).

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 21 August 2025 and was last updated on 21 August 2025.

INTRODUCTION

Review question / Objective To synthesize the available evidence on hemodynamic changes associated with non-invasive neuromodulation.

Rationale Transcranial electrical stimulation (tES) and repetitive Transcranial Magnetic Stimulation are non-invasive and painless techniques that have been associated with beneficial outcomes in various clinical conditions, such as pain management, cognitive enhancement, and improved performance and recovery in athletes. However, little is known about the hemodynamic repercussions induced by this stimulation, as the few studies published in this field have used different methodologies and stimulation protocols. Thus, it is necessary to systematically review the literature and try to summarize the results obtained until now, to understand the potential hemodynamic effects of those neuromodulatory techniques.

Condition being studied Human Studies (Healthy individuals or those with a health condition), Clinical Trials, or Observational Studies (Cross-Sectional, Longitudinal). Studies investigating hemodynamic changes after the use of tES or rTMS in the healthy population and participants with any health conditions.

METHODS

Search strategy (((Transcranial magnetic stimulation) OR (TMS) OR (tDCS) OR (transcranial direct current stimulation) OR (nibs)) AND ((blood flow) OR (hematology)) AND ((fNIRS) OR (fMRI) OR (tomographic angiography))).

Participant or population Healthy individuals or those with some health condition.

Intervention Transcranial Magnetic Stimulation (TMS), and transcranial Electrical Stimulation such as transcranial Direct Current Stimulation (tDCS), transcranial Alternating Current Stimulation (tACS),

transcranial Random Noise Stimulation (tRNS) and transcranial Pulsed Current Stimulation (tPCS).

Comparator Sham intervention (sham rTMS or sham tDCS), control group without any intervention.

Study designs to be included Clinical Trials or Observational Studies (Cross-Sectional, Longitudinal).

Eligibility criteria Inclusion criteria: Human Studies, clinical trials or observational studies (cross-sectional, longitudinal), studies that investigated hemodynamic changes after the use of tES or rTMS. Exclusion criteria: Animal studies, studies involving neuromodulation methods other than tES or rTMS (focal ultrasound, LASER, DBS), articles that do not use noninvasive neuromodulation, and articles that did not investigate hemodynamic changes.

Information sources Electronic databases: pubmed, medline, embase, web of science; contact with authors; references of the included articles.

Main outcome(s) Cerebral blood flow, cerebral perfusion, BOLD activity.

Data management Extracted data included the name of the first author, name of the article, publication year, parameters of intervention protocol, participants, number of participants in each group (active and sham), methods, outcome measures, number of sessions, adverse events, results, conclusions.

Quality assessment / Risk of bias analysis To assess the risk of bias of the included studies, we will use the Cochrane Risk of Bias 2 (RoB 2) tool. To assess the quality of the evidence the Grading of Recommendations Assessment, Development and Evaluation (GRADE) system will be used.

Strategy of data synthesis The standardized mean difference and 95% confidence intervals will be used to assess continuous variables. The χ^2 and I^2 statistical tests will be applied to confirm heterogeneity. A p-value of less than 0.1 will be considered statistically significant for the heterogeneity calculation. The results of the meta-analysis will be presented using a forest plot.

Subgroup analysis If significant heterogeneity is identified, subgroup analyses will be performed to investigate its causes. But a subgroup divided by the presence or absence of disease should exist.

Sensitivity analysis Leave-One-Out Analysis: Studies will be removed, one at a time, from the meta-analysis, and then the pooled result will be recalculated. If the overall finding remains stable, it suggests robustness; if it changes drastically, it indicates the removed study had a significant influence.
Varying Inclusion/Exclusion Criteria: The impact of different criteria for including or excluding studies will be evaluated to see if the conclusions change.
Adjusting for Methodological Assumptions: Sensitivity analysis can be used to change statistical assumptions or address methodological choices to evaluate their impact on the results.
Handling Missing Data: The impact of missing data will be assessed to determine the potential impact of data limitations on the pooled estimates.

Language restriction There is no restriction on language.

Country(ies) involved Brazil and Spain.

Other relevant information None

Keywords non-invasive brain stimulation, cerebral blood flow, fMRI, NIRS.

Dissemination plans Publishing at peer review journals, and preseting in scientific meetings.

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