▪ Headache Medicine 2026, Supplement ▪ p-ISSN 2178-7468, e-ISSN 2763-6178

Headache Medicine

ID: 366

Non-invasive motor cortex stimulation for migraine: time to consider it as a prophylactic adjunctive treatment? A systematic review and meta-analysis

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Introduction
Migraine is one of the most prevalent neurological conditions, and a significant proportion of patients remain refractory to conventional treatments. Non-invasive brain stimulation (NIBS) targeting the motor cortex (M1) has emerged as a promising alternative. However, it is important to have a better understanding of the effectiveness of non-invasive M1 stimulation for the prophylactic treatment of migraine.

Objective
This systematic review and meta-analysis investigates the efficacy of non-invasive brain stimulation of the motor cortex (M1) for the treatment of migraine.

Methods
Following PRISMA guidelines, we searched PubMed, Web of Science, Embase, Cochrane Central, PsycINFO, and Scopus using the combined terms "migraine", "tDCS", "rTMS" and "NIBS". It was included randomized controlled trials, published in English, Portuguese, or Spanish adults diagnosed with migraine according to ICHD criteria; submitted to tDCS or rTMS; compared to sham; with outcomes reporting efficacy with extractable quantitative data. Exclusion criteria comprised invasive brain stimulation, other NIBS modalities (e.g., tACS), combined interventions without isolation of NIBS effect, non-RCT designs. Screening was performed by two independent reviewers, with disagreements resolved by a third reviewer. Statistical analysis was performed using R software. For continuous outcomes, standardized mean difference (SMD) was calculated using a random-effects model. Heterogeneity was assessed using the I^2 statistic.

Results
A total of 2,600 articles were screened, and 13 studies comprising 451 patients were included in the meta-analysis, all targeting the motor cortex (M1), of which 8 studies used tDCS and 5 studies used rTMS. For the M1 target, statistically significant reductions favoring NIBS were observed for headache days (SMD -0.78; 95% CI -1.19 to -0.37; p<0.001), migraine frequency (SMD -0.68; 95% CI -1.11 to -0.25; p=0.002), medication use (SMD -0.32; 95% CI -0.53 to -0.10; p=0.004), and pain duration (SMD -0.74; 95% CI -1.28 to -0.21; p=0.006). No significant differences were found for headache frequency (SMD -1.04; 95% CI -2.64 to 0.56; p=0.20), MIDAS score (SMD -0.35; 95% CI -1.14 to 0.45; p=0.39), or pain intensity (SMD -0.43; 95% CI -1.17 to 0.31; p=0.25). Substantial heterogeneity was observed for headache frequency (I^2=87%), pain duration (I^2=77.1%), and pain intensity (I^2=88.8%). No deaths were reported.

Conclusion
Non-invasive brain stimulation of the motor cortex (M1) appears to be an effective intervention for migraine, with significant reductions in headache days, migraine frequency, medication use, and pain duration. However, no significant differences were observed for headache frequency, MIDAS score, or pain intensity. The safety profile was acceptable, with no deaths reported. Further large-scale randomized controlled trials are needed to strengthen these findings.

Keywords:
Migraine
rTMS
Motor cortex
Non-invasive brain stimulation
tDCS

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