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Effectiveness of non-invasive brain stimulation in improving sleep quality in insomnia: a systematic review

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Abstract

Introduction Insomnia, a prevalent sleep disorder, significantly impairs cognitive, emotional, and physical health, affecting millions worldwide. Traditional treatments, such as pharmacotherapy, often have limited efficiency and pose risks of dependency and adverse effects. Non-invasive brain stimulation (NIBS), including rTMS, tDCS, and tACS, shows promise in improving sleep quality. This systematic review evaluates the effectiveness and safety of NIBS in treating insomnia.

Methods We systematically searched PubMed, Web of Science, and Scopus for studies published from inception to December 2024. A total of 43 studies were included after rigorous screening, featuring diverse designs, sample sizes, and outcome measures. Data were extracted and assessed using the Joanna Briggs Institute (JBI) critical appraisal tool for experimental and quasi-experimental studies.

Results rTMS showed the strongest evidence, with most of studies reporting significant improvements in sleep parameters. High-frequency rTMS targeting the dlPFC improved sleep and mood. Also, other cortical areas targeted included the posterior parietal cortex, angular gyrus, and primary motor cortex can also enhance sleep quality, particularly in patients with comorbid insomnia and other psychiatric disorders. tDCS and tACS demonstrated potential, with tDCS enhancing deep sleep and tACS improving sleep onset through neural entrainment. NIBS was safe and well-tolerated.

Conclusion NIBS techniques represent a safe and effective non-pharmacological approach to improving sleep quality in insomnia patients. While rTMS has demonstrated strong efficiency, the potential of tDCS and tACS warrants further investigation. Future research should focus on protocol standardization, long-term effects, and personalized interventions.

Keywords Insomnia disorder, Sleep disturbances, Non-invasive brain stimulation, Transcranial direct current stimulation (tDCS), Transcranial alternating current stimulation (tACS), Repetitive transcranial magnetic stimulation (rTMS)

Introduction

Non-invasive brain stimulation (NIBS) has emerged as a powerful and promising therapeutic tool for the treatment of a wide range of neurological and psychiatric disorders. These techniques, including transcranial direct current stimulation (tDCS), transcranial alternating current stimulation (tACS), transcranial magnetic stimulation (TMS), and repetitive transcranial magnetic

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stimulation (rTMS), work by modulating cortical excitability through the application of electrical or magnetic fields to specific areas of the brain (Aderinto et al. 2024; Nitsche & Paulus 2009). NIBS has been widely investigated for its potential to enhance cognitive performance, alleviate symptoms of depression, anxiety, and other mood disorders, and even aid in improving sleep regulation and quality in sleep disturbances such as insomnia (Aderinto et al. 2024; Mitchell & Loo 2006; Tang et al. 2024; Young et al. 2023).

Insomnia, a disorder characterized by difficulty falling or staying asleep, affects approximately 10–30% of the adult population worldwide (Hirshkowitz et al. 2015). It is often associated with a wide range of negative consequences, including cognitive impairment, mood disturbances, reduced quality of life, and an increased risk of developing other psychological and physical health conditions, such as depression, anxiety, cardiovascular disease, and obesity (Riemann et al. 2015). Although pharmacological treatments have traditionally been used to manage insomnia, their efficacy is limited, and they are often associated with side effects, dependency, and long-term health risks (Riemann et al. 2015). Cognitive-behavioral therapy for insomnia (CBT-I) is considered an effective non-pharmacological intervention; however, access to trained therapists and the time commitment required for treatment can be barriers to its widespread use (Morin et al. 2006; Rossman 2019; D. Xu et al. 2024a, b). As such, there is a growing interest in identifying alternative treatments that are both effective and minimally invasive.

Non-invasive brain stimulation techniques, which directly target the neural circuits responsible for regulating sleep, have garnered significant attention as potential interventions for improving sleep quality (Aderinto et al. 2024). The mechanisms through which NIBS influences sleep are multifaceted, involving modulation of brain activity, alteration of cortical excitability, and the potential to enhance synaptic plasticity (Vallat et al. 2019). Specifically, tDCS and tACS have been shown to affect the oscillatory activity of the brain, particularly in the theta and delta frequency bands, which are known to be involved in the regulation of sleep and sleep-related processes (Di Lazzaro et al. 2013). Similarly, TMS and rTMS can affect cortical networks implicated in sleep regulation, with studies demonstrating the potential for these techniques to enhance sleep onset, and sleep continuity (Krone et al. 2023).

Despite the promising nature of these techniques, the evidence regarding their effectiveness in improving sleep quality remains inconsistent. Studies on the effects of NIBS on sleep quality in insomnia patients have yielded mixed results, with some demonstrating significant improvements in sleep parameters, while others report no change or minimal effects (Herrero Babiloni et al. 2021). Several factors contribute to this variability, including differences in study design, participant characteristics, NIBS protocols (e.g., stimulation site, intensity, duration, and number of sessions), and outcome measures (e.g., subjective sleep assessments vs. objective measures like polysomnography) (Brunoni et al. 2019). These inconsistencies highlight the need for a comprehensive synthesis of the existing literature to clarify the potential role of NIBS in the treatment of insomnia.

This systematic review evaluates the evidence on using non-invasive brain stimulation (NIBS) to improve sleep quality in individuals with insomnia. By applying strict criteria, it aims to clarify the efficacy, safety, and mechanisms of NIBS in sleep enhancement, including its effects on brain regions, sleep stages, and subjective quality. The findings could guide evidence-based treatment protocols, offering a non-invasive alternative for managing chronic insomnia while addressing research gaps and future directions.

Methods

Inclusion and exclusion criteria

Studies were considered eligible for inclusion if they met the following criteria: (1) Population: Adult participants ($\geq$ 18 years) diagnosed with insomnia (2) Intervention: Utilization of at least one non-invasive brain stimulation (NIBS) technique, including tDCS, tACS, TMS, or rTMS. (3) Outcome Measures: sleep quality assessments, using either subjective (e.g., validated questionnaires) or objective (e.g., polysomnography) measures, were reported. Exclusion criteria were applied to eliminate studies that did not meet the following standards: (1) Case reports and single-case studies. (2) Non-English language publications. (3) Animal studies. (4) Systematic reviews, meta-analyses, or non-primary research articles.

Search strategy

A comprehensive literature search was conducted across three major electronic databases: PubMed, Web of Science, and Scopus, covering the period from inception to December 1, 2024. The search strategy included a combination of Medical Subject Headings (MeSH) terms and keywords related to sleep disturbances and NIBS techniques. The specific syntaxes used for each database are detailed in Fig. 1. The initial search identified a total of 9,348 articles. All retrieved citations were imported into EndNote for reference management, where 4,617 duplicate entries were automatically removed. The remaining 4,731 articles were then uploaded to Rayyan, a web-based systematic review platform, for title and abstract screening.

("Sleep disorder*" OR insomnia OR "Chronic Insomnia" OR "insomnia disorder" OR "paradoxical insomnia" OR "sleep latency" OR "sleep quality" OR "sleep duration" OR "Secondary Insomnia" OR "Transient Insomnia" OR "Primary Insomnia") AND ("non-invasive brain stimulation" OR "noninvasive brain stimulation" OR "NIBS" OR "Transcranial Electrical Stimulation" OR "tES" OR "transcranial magnetic stimulation" OR "TMS" OR "repetitive transcranial magnetic stimulation" OR "rTMS" OR "transcranial direct current stimulation" OR "tDCS" OR "transcranial direct current stimulation" OR "tACS" OR "Electroencephalography" OR "EEG")

Fig. 1 Syntaxes

Screening and study selection

Screening and study selection were conducted in multiple stages as illustrated in Fig. 2, the flow chart of the systematic review process. Initially, the titles and abstracts of the 4,731 articles identified after duplicate removal were screened independently by reviewers using the predefined inclusion and exclusion criteria. Following the initial screening, 122 articles were identified as eligible for full-text review. These articles were meticulously assessed to determine their relevance and compliance with the study's eligibility criteria. During the full-text review stage, articles that failed to meet the criteria, such as incomplete reporting of outcomes or small sample size, were excluded. Ultimately, 43 studies were included in the final analysis, forming the basis for the systematic review and subsequent synthesis of findings. The detailed process of screening and selection is depicted in Fig. 2, highlighting the progressive narrowing of the dataset and the systematic application of inclusion and exclusion criteria.

Data extraction

Data from the included studies were systematically extracted into an Excel spreadsheet. The recorded variables included the title of the study, authors, and publication year; the type of non-invasive brain stimulation (NIBS) used, such as tDCS/tACS or TMS, along with details on electrode placement or stimulation site and the stimulation protocol, including intensity, duration, and number of sessions. The study design was categorized as randomized controlled trials (RCTs), crossover designs, or other relevant formats. Information about the population was extracted, including sample size, demographic characteristics such as age and sex, and the primary population studied, such as individuals with insomnia. Outcome measures were documented based on the type of sleep assessments, whether subjective (e.g., questionnaires) or objective (e.g., polysomnography). Finally, the key findings of each study were noted, specifically focusing on the results related to the impact of NIBS on sleep quality.

Quality assessment

The quality of the included studies was evaluated using the Joanna Briggs Institute (JBI) (Moola et al. 2015) critical appraisal tool for experimental and quasi-experimental studies. This evaluation framework ensures a systematic and objective assessment of the methodological rigor and reliability of the studies included in the systematic review. The quality assessment is provided in Table 1, and the detailed criteria used are outlined below.

Each study was scored based on the following eight criteria: (1) Criteria for inclusion: Whether the criteria for including participants in the sample were clearly defined, ensuring the study population was appropriately selected for the research objectives. (2) Description of subjects and setting: Whether the study subjects and the context of the study (e.g., clinical or experimental settings) were described in sufficient detail to facilitate reproducibility and generalizability. (3) Validity and reliability of exposure measurement: Whether the intervention, such as the specific type of non-invasive brain stimulation (e.g., tDCS or rTMS), was measured and reported in a valid and reliable manner. (4) Use of objective, standardized criteria: Whether the outcome

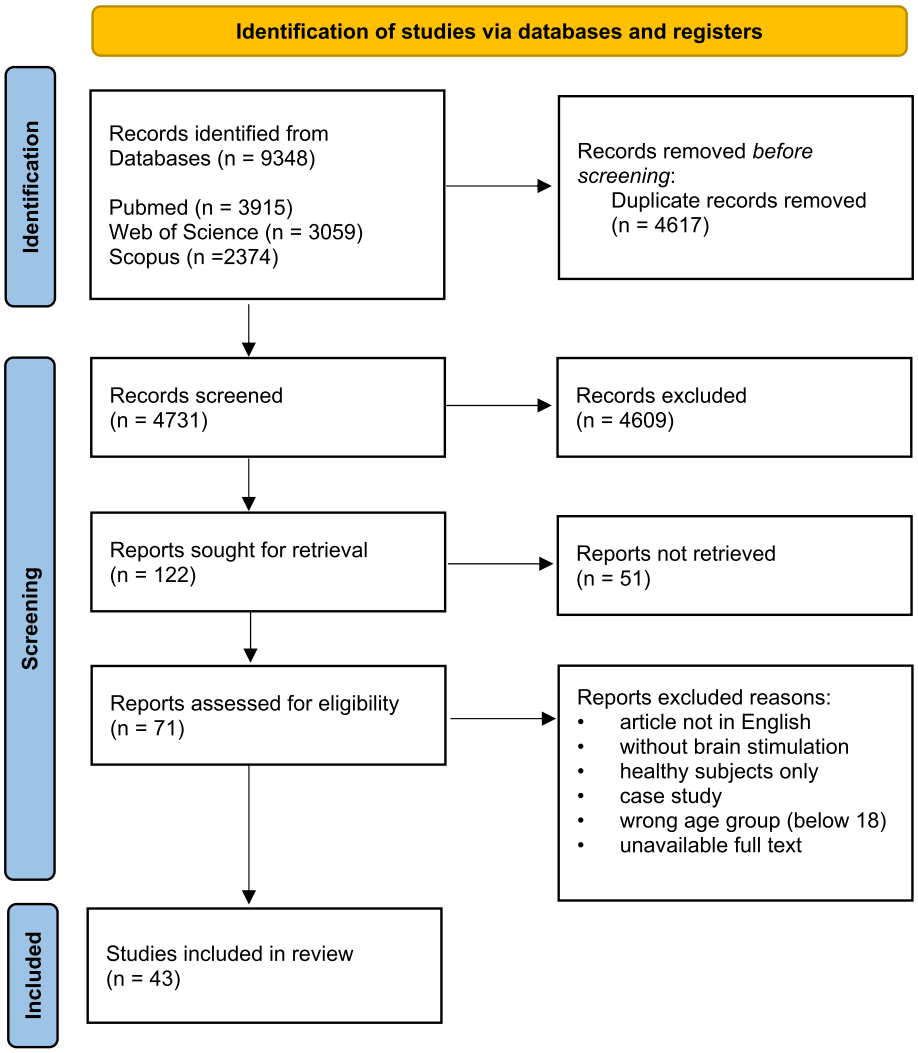
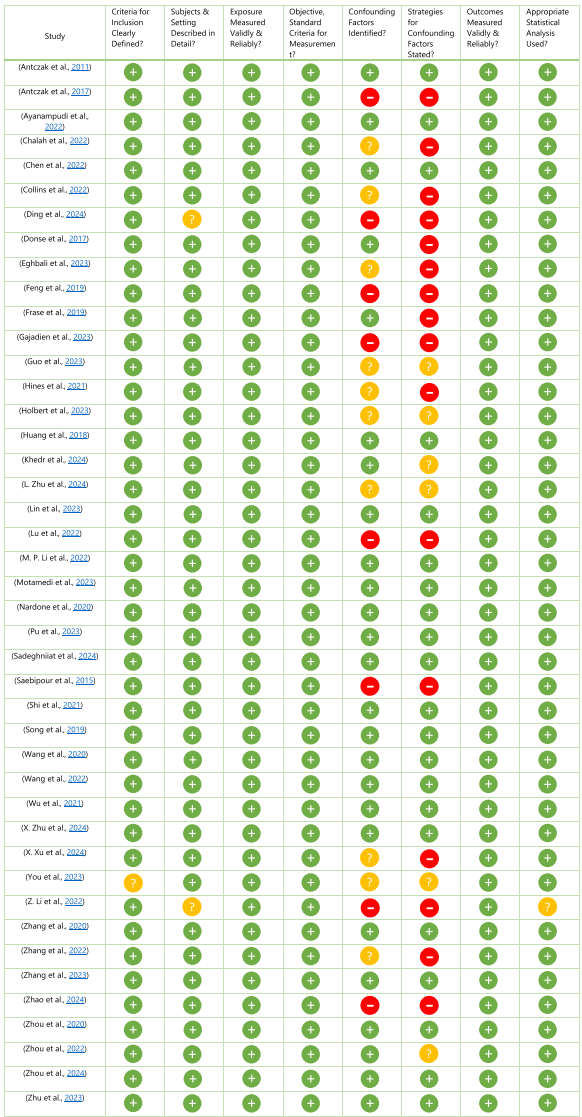


Fig. 2 The PRISMA flowchart of the systematic review process

measures, such as sleep quality assessments, used standardized and validated tools to ensure consistency and objectivity. (5) Identification of confounding factors: Whether potential confounding factors, such as demographic differences or baseline sleep quality variability, were identified. (6) Strategies to address confounding factors: Whether the studies described strategies to control or account for these confounding variables, such as through randomization or statistical adjustments. (7) Validity and reliability of outcome measurement: Whether the outcomes, particularly sleep-related metrics, were assessed using valid and reliable methods, including objective measures (e.g., polysomnography) and/or subjective measures (e.g., validated sleep questionnaires). (8) Appropriate statistical analysis: Whether statistical methods were suitable for the study design and research question, including the use of power analysis to justify sample size, and whether appropriate statistical tests were applied for data analysis (Moola et al. 2015).

Each criterion was scored as "Yes," indicate low risk of bias, "No," indicate high risk of bias and "Unclear," indicate uncertainty. The overall quality of each study was determined by the proportion of criteria met. Studies that met all or majority of the criteria (8 questions) were classified as high quality, while those with significant limitations, such as unclear outcome reporting were rated lower. These assessments were crucial in evaluating the reliability of the findings, as shown in Table 1. By using the JBI tool, this review ensures that only studies with strong methodological rigor contribute to the synthesis of evidence on non-invasive brain stimulation's impact on sleep quality.

Table 1 Risk of Bias (ROB); Green (+) circles indicate low risk of bias, red (-) circles indicate high risk of bias, and yellow (?) circles indicate uncertainty. (Antczak et al., 2011); (Antczak et al., 2017); (Ayanampudi et al., 2022); (Chalah et al., 2022); (Chen et al., 2022); (Collins et al., 2022); (Ding et al., 2024); (Donse et al., 2017); (Eghbali et al., 2023); (Feng et al., 2019); (Frase et al., 2019); (Gajadien et al., 2023); (Guo et al., 2023); (Hines et al., 2021); (Holbert et al., 2023); (Huang et al., 2018); (Khedr et al., 2024); (L. Zhu et al., 2024); (Lin et al., 2023); (Lu et al., 2022); (M. P. Li et al., 2022); (Motamedi et al., 2023); (Nardone et al., 2020); (Pu et al., 2023); (Sadeghniiat et al., 2024); (Saebipour et al., 2015); (Shi et al., 2021); (Song et al., 2019); (Wang et al., 2020); (Wang et al., 2022); (Wu et al., 2021); (X. Zhu et al., 2024); (X. Xu et al., 2024); (You et al., 2023); (Z. Li et al., 2022); (Zhang et al., 2020); (Zhang et al., 2022); (Zhang et al., 2023); (Zhao et al., 2024); (Zhou et al., 2020); (Zhou et al., 2022); (Zhou et al., 2024); (Zhu et al., 2023)



Results

The overall quality of the data was assessed using the Joanna Briggs Institute (JBI) critical appraisal tool for experimental and quasi-experimental studies. Based on the evaluation provided in Table 1, the majority of the studies demonstrated strong methodological rigor, meeting most or all of the eight evaluation criteria. Specifically, these studies provided clear inclusion criteria, detailed descriptions of subjects and settings, valid and reliable measurement of both exposures and outcomes, and appropriate statistical analyses. These strengths contributed to the high overall quality of the evidence included in this review. However, some limitations were identified, particularly in the open-label studies. These studies exhibited higher risks of bias due to inadequate strategies to address confounding variables, and reliance on subjective measures without proper validation. Additionally, a significant limitation of the non-RCT studies is the lack of sham controls, which reduces their ability to account for placebo effects and weakens the reliability of their results. Despite these issues, the comprehensive application of the JBI framework ensures the reliability of the overall findings, supporting the conclusion that the majority of studies are of good quality, with a few exceptions.

As demonstrated in Table 2, a total of 43 studies were included in this systematic review, encompassing a diverse range of non-invasive brain stimulation (NIBS) techniques such as rTMS, tDCS, and tACS. The studies utilized varied designs, including randomized controlled trials (RCTs), sham-controlled trials, single-arm pilot studies, and open-label trials. Sample sizes ranged from 6 to 157 participants, with populations including individuals diagnosed with primary or chronic insomnia, comorbid insomnia and depression, generalized anxiety disorder, Alzheimer's disease and Parkinson's disease. While subjective measures such as the Pittsburgh Sleep Quality Index (PSQI) and Insomnia Severity Index (ISI) were the most commonly employed tools, approximately 40% of studies incorporated objective assessments such as polysomnography (PSG) or electroencephalography (EEG) and actigraphy. Participants'demographic characteristics varied widely, with mean ages ranging from early 20 s to late 70 s and a female predominance in most studies. Stimulation protocols exhibited notable heterogeneity in terms of frequency, duration, and site of stimulation. This variability highlights the diverse approaches adopted to optimize NIBS outcomes and the necessity of standardizing protocols in future research.

Table 2 Features and results of the studies included

STUDY	TYPE	DESIGN	SAMPLE SIZE	AGE/SEX	POPULATION	MEASUREMENT	ELECTRODE PLACEMENT	PROTOCOL	MAIN RESULTS
(Zhou et al. 2024)	tDCS + rTMS	randomized, double-blind, parallel-group, controlled trial	157	(Mean age 44.59 ± 13.49; 101 females)	chronic insomnia	PSQI, HAMD and HAMA	anode over F3 and the cathode over F4	20 sessions for 4 weeks/2 mA/1 Hz/20 min	combined tDCS and rTMS significantly improved sleep quality and reduced depression and anxiety in chronic insomnia patients, with effects lasting up to 3 months and no adverse events reported
(Eghbali et al. 2023)	tDCS	randomized parallel double-blind	60	(Mean age: 33.52 ± 3.37, 22 females)	TBI-induced insomnia	PSQI, ISI and GCS	cathode electrode over the right DLPFC (F4)/anode electrode over the left shoulder	15 sessions (1.5 mA/15 min)	tDCS significantly improved sleep quality and reduced insomnia severity in TBI-induced insomnia, with more pronounced and lasting effects in younger participants and men, suggesting the need for gender- and age-specific protocols
(Chalah et al. 2022)	tDCS	pilot randomized sham-controlled crossover study	7	(Mean age: 43.14 ± 10.01,6 females)	multiple sclerosis	ESS, SOL, TST, WASO, actigraphy	Anode left dlPFC/ Cathode right dlPFC	15 sessions/2 mA/20 min	bifrontal tDCS significantly reduced daytime sleepiness in patients with multiple sclerosis but had no effect on objective sleep measures. The intervention was well-tolerated, with no serious side effects reported
(Z. Li et al. 2022a, b)	tDCS	Double-Blinded, Randomized, Placebo-Controlled	37	(Mean age: 44.79 ± 15.25, 13 females)	MDD	Hamilton-24 and Montgomery scales, PSG	anode over F3 and the cathode over F4	10 sessions/2 mA/30 min	daytime tDCS significantly decreased the complexity of REM sleep EEG signals in depressed patients, indicating potential improvement in sleep quality. However, it did not affect sleep structure or depression severity scores

Table 2 (continued)

STUDY	TYPE	DESIGN	SAMPLE SIZE	AGE/SEX	POPULATION	MEASUREMENT	ELECTRODE PLACEMENT	PROTOCOL	MAIN RESULTS
(Zhou et al. 2020)	tDCS	randomized, sham-controlled, parallel, double-blinded	90	(Mean age: 40.45 ±8.31, 11 females)	MDD	SDS, SAS, PSQI, PSG	left dlPFC—right dlPFC	20 sessions/2 mA/30 min/4 weeks	tDCS improved both depressive symptoms and sleep quality in patients with MDD and insomnia. Active tDCS significantly reduced anxiety and depression scores, enhanced sleep efficiency, and increased total sleep time, suggesting it as a potential adjunct treatment for these patients
(Frase et al. 2019)	tDCS	randomized, sham-controlled, cross-over	19	(Mean age 43.8 ±15.1; 13 females)	Insomnia	PSQI, BDI, ESS, PSG, EEG	FP1/FP2 – P3/P4	3 sessions/2 mA/20 min	No tDCS effects were found on sleep in ID patients, who showed higher arousal levels compared to healthy controls. Increased arousal predicted the lack of tDCS effects, suggesting the need for modified tDCS protocols
(Saebipour et al. 2015)	tDCS	randomized sham-control	6	(Mean age 34 ±7; 2 females)	Insomnia	PSG, ISI	Anodes on F3 and F4 and cathodes on the mastoids	0.75 Hz, four non-consecutive nights/25 min	Slow oscillatory transcranial direct current stimulation improved sleep in insomnia patients by increasing stage 3 sleep duration, sleep efficiency, and transitions to deeper sleep while reducing stage 1 sleep and wake time after sleep onset, demonstrating a sleep-stabilizing effect

Table 2 (continued)

STUDY	TYPE	DESIGN	SAMPLE SIZE	AGE/SEX	POPULATION	MEASUREMENT	ELECTRODE PLACEMENT	PROTOCOL	MAIN RESULTS
(X. Zhu et al. 2024a, b)	tACS	randomized, double-blind, parallel-group, placebo-controlled	120	(Mean age 48.93 ± 12.78; 37 females)	chronic insomnia	PSQI, HAMD and HAMA	one electrode over the forehead (Fpz, Fp1, and Fp2), and two electrodes over the mastoid areas	20 sessions/4 weeks (40 min, 77.5 Hz, 15 mA)	tACS improved sleep quality and duration in chronic insomnia, particularly in older patients, with lasting effects and reduced depressive and anxiety symptoms
(Motamedi et al. 2023)	tACS	randomized, sham-controlled, single-blind crossover	9	(Mean age 50.2 ± 10; 9 females)	chronic insomnia	PSG, SOL, WASO	simultaneously and bilaterally at F3/M1 and F4/M2	2 sessions/0.75 mA, 0.75 Hz, 5-min	tACS improved arousals, sleep quality, duration, efficiency, and daytime sleepiness in chronic insomnia patients, though reductions in sleep latency and wake after sleep onset were not statistically significant
(Ayanampudi et al. 2022)	tACS	cross-over design	25	(Mean age: 46.3 ± 12.4, 15 females)	Insomnia	ISI	frontal-lobe sites of Fp1 and Fp2 using a bipotential reference electrode at Fpz	15 min pre-sleep tACS stimulation (theta/alpha frequency bands)	Personalized tACS significantly improved sleep quantity and reduced sleep onset time compared to Fixed stimulation and Control, with the greatest benefit observed in individuals with clinical insomnia, supporting its potential as a sleep therapeutic
(Wang et al. 2020)	tACS	Randomized, Double-Blind, Parallel-Group, Placebo-Controlled Clinical Trial	62	(Mean age 52.5 ± 10.7; 47 females)	chronic insomnia	PSQI, ISI, SOL, TOT	forehead (Fpz, Fp1, and Fp2)—mastoid areas	20 daily 40-min, 77.5-Hz, 15-mA sessions/4 weeks	tACS significantly improved response rates, PSQI scores, SOL, TST, sleep efficiency, and sleep quality in chronic insomnia patients with benefits lasting up to 4 weeks post-treatment. No adverse events occurred, supporting its safety and effectiveness

Table 2 (continued)

STUDY	TYPE	DESIGN	SAMPLE SIZE	AGE/SEX	POPULATION	MEASUREMENT	ELECTRODE PLACEMENT	PROTOCOL	MAIN RESULTS
(Ding et al. 2024)	rTMS	single-blind, randomized sham-controlled trial	39	(Mean age: 23.55 ± 2.76, 29 females)	Insomnia	ISI, PSQI, MFI, BAI	left dlPFC	1 Hz/25 min/7 days	rTMS targeting the left dorsolateral prefrontal cortex significantly improved conflict control and sleep quality in insomnia patients, with no significant changes in the sham group
(Khedr et al. 2024)	rTMS	Randomized, sham-controlled, clinical trial, parallel	24	(Mean age: 61.82 ± 3.48, 11 females)	Parkinson's Disease	PDSS, BDI, PSG, MDS-UPDRS	the right then left parietal areas (P4 and P3)	10 sessions, 20 HZ/5 times-week/2 weeks	Ten sessions of 20 Hz rTMS over the parietal cortex improved sleep quality and reduced periodic leg movements in Parkinson's disease patients, with improvements in sleep parameters correlating with better UPDRS and BDI scores
(Zhao et al. 2024)	rTMS	non–sham-controlled	52	(Mean age: 43.27 ± 2.09, 9 females)	26 Insomnia/26 Halthy	PSQI, ISI, BDI, BAI, PSG, EEG	left dlPFC	20 sessions/1 Hz/30 min/5 times-week/4 weeks	Insomnia disorder patients showed abnormal EEG power in delta, beta, and gamma bands during sleep. rTMS treatment improved delta and beta power in NREM2 sleep, correlating with better sleep efficiency and reduced depression, suggesting rTMS may help restore EEG abnormalities in ID
(Sadeghniiat et al. 2024)	rTMS	open-label	25	(Mean age 41.2 ± 5.8; 10 females)	treatment- resistant depression	ISI, PSQI, BDI-II, HDRS	left dlPFC	15 sessions/10 Hz/18.5 min/3 weeks	Routine rTMS improved sleep duration, depressive symptoms, and quality of life in TRD patients in the short term, but benefits decreased over time. rTMS also independently reduced the time taken to fall asleep, regardless of depression resolution

Table 2 (continued)

STUDY	TYPE	DESIGN	SAMPLE SIZE	AGE/SEX	POPULATION	MEASUREMENT	ELECTRODE PLACEMENT	PROTOCOL	MAIN RESULTS
(Xu et al. 2024a, b)	rTMS	randomized, sham-controlled	90	(Mean age 58.15 ± 11.28; 51 females)	poststroke depression with insomnia	HAMD, PSQI, NIHSS, MBI	1 Hz: right dlPFC 10 Hz: left dlPFC	10 sessions each group/1 Hz – 10 Hz/5 times a week/2 weeks	Low-frequency rTMS combined with paroxetine improved insomnia symptoms, while high-frequency rTMS with paroxetine was more effective for depressive symptoms. Both treatments enhanced neurofunctional deficits and daily living activities
(L. Zhu et al. 2024a, b)	rTMS	single-arm open-label	36	(Mean age 49.04 ± 10.9; 22 females)	chronic insomnia	rsEEG, PSQI	right dlPFC (F4)	10 sessions/1 Hz/5 days-week/2 week	Baseline theta connectivity in rsEEG effectively predicted rTMS response in chronic insomnia patients, with lower connectivity at the stimulated site linked to greater improvement, supporting its use as a predictive marker for treatment outcomes
(Pu et al. 2023)	rTMS	randomized, sham-controlled, open-label, parallel-group	100	(Mean age: 35.24 ± 5.12, 59 females)	Mild to moderate depressive disorder (DD)	HAMD-17, PSQI, PSG	left dlPFC	20 sessions/10 Hz/5 times-week/4 weeks	High-frequency rTMS combined with agomelatine improved sleep quality and depressive symptoms in mild to moderate DD patients, with better sleep parameters and higher levels of norepinephrine and BDNF in the treatment group
(You et al. 2023)	rTMS	Single bind, Control group	34	(Mean age: 67.33 ± 7.22, 23 females)	Alzheimer (18 with ID, 16 without ID)	MMSE, MoCA, PSQI, ISI, ESS	the left angular gyrus	20 sessions/20 Hz/5 times-week/4 weeks	rTMS targeting the left angular gyrus improved sleep-related network activity and memory in AD spectrum patients with insomnia, enhancing sleep quality and memory through the hippocampus-cortical circuit

Table 2 (continued)

STUDY	TYPE	DESIGN	SAMPLE SIZE	AGE/SEX	POPULATION	MEASUREMENT	ELECTRODE PLACEMENT	PROTOCOL	MAIN RESULTS
(Zhu et al. 2023)	rTMS	single-arm, open-label	37 insomnia/40 healthy	(Mean age: 46.1 ± 9.4, 22 females)	Insomnia/healthy	PSQI, rsEEG, HAMA, HAMD	right dlPFC	10 sessions/1 Hz/2 weeks	Low-frequency rTMS improved sleep quality in chronic insomnia by enhancing lower alpha band connectivity. Changes in connectivity involving the left insula correlated with PSQI improvements, suggesting functional connectivity as a potential indicator for rTMS outcomes
(Guo et al. 2023)	rTMS	randomized, sham-controlled, parallel	60	(Mean age: 43.93 ± 10.93, 28 females)	Insomnia	PSQI, ISI, ESS, BDI, BAI, MMSE, and MoCA, EGG, PSG	left dlPFC	1 Hz/30 min/20 sessions/five times-week/4 weeks	Phase-amplitude coupling was weaker in insomnia patients, but improved after rTMS treatment, correlating with better sleep quality. This suggests phase-amplitude coupling as a potential marker for insomnia severity and rTMS effectiveness
(Gajadien et al. 2023)	rTMS	open-label	61	(Mean age: 37.83 ± 13.60, 18 females)	OCD	PSQI, HSDQ and actigraphy, Y-BOCS	SMA/right dlPFC	30 sessions/1 Hz SMA or 1 Hz SMA + DLPFC, combined with CBT	In OCD patients, sleep disturbances, particularly subjective sleep quality, sleep latency, and daytime dysfunction, predicted response to rTMS treatment. These factors may help personalize rTMS treatment
(Lin et al. 2023)	rTMS	randomized, double-blind, sham-controlled, parallel	49	(Mean age 53.5 ± 18.5; 38 females)	Insomnia	PSG, PSQI	left dmPFC	10 sessions/1 Hz/30 min/5 times-week/2 weeks	Low-frequency rTMS of the left DMPFC reduced wake after sleep onset and improved sleep efficiency in insomnia patients, but similar improvements were observed in the sham group, indicating a strong placebo effect. Nonetheless, rTMS may be a safe, non-invasive adjunctive therapy for insomnia

Table 2 (continued)

STUDY	TYPE	DESIGN	SAMPLE SIZE	AGE/SEX	POPULATION	MEASUREMENT	ELECTRODE PLACEMENT	PROTOCOL	MAIN RESULTS
(Holbert et al. 2023)	rTMS	open label pilot trial	20	21–65 (NA)	Insomnia	PSQI, ISI, ESS	dlPFC	15 sessions/3 weeks/1 Hz	Bifrontal low-frequency rTMS reduced PSQI scores and improved insomnia symptoms in 52.6% of participants, showing promise despite the lack of a sham control
(Zhang et al. 2023)	rTMS	double-blind, randomized sham-control	50	(Mean age 45.65 ± 2.57; 30 females)	Insomnia	ISI, PSQI, MMSE, MOCA, BDI, BAI	Left DLPFC	20 sessions of treatment with 1 Hz/4 weeks (5 times/week)	rTMS improved sleep quality in insomnia disorder patients by modulating abnormal EEG coherence, particularly in theta and alpha bands. Baseline EEG coherence in specific frequency bands showed potential as indicators for predicting rTMS treatment outcomes
(Wang et al. 2022)	rTMS	randomized, Open-label	50	(Mean age: 40.15 ± 13.23, 31 females)	GAD	HAMA, HAMD, PSQI	right dlPFC (F4)/right PPC (P4)	10 sessions/1 Hz/2 weeks	Dual-site rTMS (rds-ccPAS) with 1500 pulses improved anxiety, depression, and insomnia symptoms more than single-site rTMS in GAD patients, with better response rates and lasting benefits
(Collins et al. 2022)	rTMS	open-label	21	(Mean age 43.9 ± 14.8; 14 females)	MDD	PSQI, PHQ-9	left dlPFC	30 sessions/10 Hz/37.5 min	rTMS improved both sleep quality and mood independently in patients with major depressive disorder. Changes in sleep quality and depression severity were not correlated, suggesting that rTMS has direct effects on both sleep and mood

Table 2 (continued)

STUDY	TYPE	DESIGN	SAMPLE SIZE	AGE/SEX	POPULATION	MEASUREMENT	ELECTRODE PLACEMENT	PROTOCOL	MAIN RESULTS
(Chen et al. 2022)	rTMS	randomized parallel, single-blind, sham-controlled	136	(Mean age: 50.221 ± 1.820, 65 females)	MDD	HAMD-17, sleep disorder (HAMD-SLD), sleep onset latency	left DLPFC/right DLPFC	15 sessions/10 Hz	bilateral rTMS over the DLPFC significantly reduced depressive symptoms and improved sleep disorders in patients with MDD after 3 weeks. The reduction in depressive symptoms correlated with decreased plasma ACTH levels, suggesting ACTH as a potential predictor of rTMS efficiency
(M. P. Li et al. 2022a, b)	rTMS	double-blind, sham-controlled	44	(Mean age: 43.8 ± 10.3; 28 females)	Insomnia	PSQI, ISI, PSG	left DLPFC	20 sessions/1 Hz/four weeks	The main results showed therapeutic improvement in sleep and potential underlying mechanisms of 1HZ rTMS therapy over the left DLPFC in insomnia disorders, which were associated with the modulation of the left DLPFC centered pathway
(Lu et al. 2022)	rTMS	parallel study	51/42	(Median age 57.0 ± 14.1)	51 insomnia/42 healthy	PSQI	right dlPFC	20 sessions/1 Hz/five times per week/four weeks	The study used machine learning to analyze functional connectivity (FC) in insomnia disorder (ID). Responders to rTMS and pharmacotherapy showed a decrease in FC anomalies, especially in the Default Mode Network, suggesting FC changes as potential diagnostic and therapeutic targets
(Zhou et al. 2022)	rTMS	randomized, double-blind, parallel, sham-controlled pilot study	70	(Mean age 74; 44 females)	Alzheimer	PSQI, ADAS-Cog	left and right dlPFC (between F3 and F7 and between F4 and F8)	20 sessions/left DLPFC: 10 Hz. right DLPFC: 1 Hz/5 times-week/4 weeks	rTMS significantly improved sleep quality and cognitive function in AD patients, with effects persisting at 8 weeks, but did not affect daily living activities

Table 2 (continued)

STUDY	TYPE	DESIGN	SAMPLE SIZE	AGE/SEX	POPULATION	MEASUREMENT	ELECTRODE PLACEMENT	PROTOCOL	MAIN RESULTS
(Zhang et al. 2022)	rTMS	randomized, double-blind, sham	40	(Mean age 51.78 ±11.22; 25 females)	Insomnia	ISI	Left DLPFC	(A) 14 sessions of 1 Hz real rTMS; (B) 14 sessions of sham rTMS	rTMS significantly reduced insomnia severity and increased GABA +/Cr levels in the left DLPFC of chronic insomnia patients, though changes in GABA +/Cr were not associated with symptom improvement
(Shi et al. 2021)	rTMS	single-arm, open-label design	25	(Mean age 48.5 ±11.6; 16 females)	Insomnia	PSQI, HAMD, HAMA	right dlPFC	10 sessions/1 Hz/25 min/5 days per week, 2-week	Low-frequency rTMS improved sleep and depressive symptoms in insomnia patients. Weaker baseline connectivity in specific brain regions predicted a better response to treatment, suggesting electroencephalographic connectivity as a potential indicator for outcomes
(Hines et al. 2021)	rTMS	pilot, prospective, non–sham-controlled	20	(Mean age: 32.2 ±6.61, 9 females)	Depression	PHQ9, ESS, ISI, PSG	left dlPFC	20 sessions/10 Hz/5 times-week/4 weeks	rTMS increased REM sleep and improved depression symptoms. Total sleep time improved in responders, with reductions in insomnia severity and enhancements in mental health metrics, suggesting rTMS benefits for both sleep and mood

Table 2 (continued)

STUDY	TYPE	DESIGN	SAMPLE SIZE	AGE/SEX	POPULATION	MEASUREMENT	ELECTRODE PLACEMENT	PROTOCOL	MAIN RESULTS
(Wu et al. 2021)	rTMS	sham-controlled, parallel study	70	(Mean age 55.4 ±6.27; 39 females)	Insomnia	PSQI, HAMD and HAMA	right dlPFC	daily sessions of 1 Hz rTMS for parietal lobe (CPZ)	rTMS improved sleep and mental health in intractable insomnia, with two consecutive treatment courses offering lasting benefits at 3 months, while one course showed no sustained effect
(Zhang et al. 2020)	rTMS	randomized sham-control	72	(Mean age 49.7 ± 8.4; 33 females)	post-stroke insomnia	PSQI, SAS, SDS	right dlPFC	1 Hz/5 times-week/4 weeks	Combining Governor Vessel-unblocking and mind-regulating acupuncture with rTMS was more effective than rTMS alone in improving sleep quality, anxiety, and depression in post-stroke insomnia patients
(Nardone et al. 2020)	rTMS	randomized, sham-controlled	20	(Mean age 48.8 ± 9.8; NA)	10 chronic insomnia/10 healthy	PSQI, ISI, ESS, HAM-D, HAM-A, EMG, MEPs	primary motor cortex (M1)	20 trains of 50 stimuli at 1 Hz, a 30-s inter-train interval	Low-frequency rTMS reduced MEP amplitudes, but the effect was significantly less pronounced in primary insomnia patients, indicating impaired cortical plasticity and altered GABAergic inhibitory mechanisms in their motor cortex
(Song et al. 2019)	rTMS	randomized crossed design	20	(Mean age 49.2 ± 9.4; 8 females)	Insomnia	PSQI, ISI, ESS	right posterior parietal cortex	14 days of 1 Hz/20 min	rTMS targeting the right posterior parietal cortex significantly improved primary insomnia symptoms, with effects lasting at least one month. It also regulated abnormal brain network connectivity, particularly in the left temporal and frontal mid-line regions

Table 2 (continued)

STUDY	TYPE	DESIGN	SAMPLE SIZE	AGE/SEX	POPULATION	MEASUREMENT	ELECTRODE PLACEMENT	PROTOCOL	MAIN RESULTS
(Feng et al. 2019)	rTMS	open-label trial	32	(Mean age 44.8 (25–62); 20 females)	Insomnia	PSQI	30 min (first 15 min over left DLPFC, and then 15 min over right DLPFC)	10 daily sessions of sequential bilateral 1 Hz rTMS	A sequential bilateral low-frequency rTMS over DLPFC significantly im-proves primary insomnia probably by increas-ing the level of BDNF and GABA in the brain and reducing cortical excitability
(Huang et al. 2018)	rTMS	randomized, double-blind, sham controlled pilot study	36	(Mean age 38.8 (9.4); 20 females)	comorbid GAD and insomnia	HRSA, PSQI	right posterior parietal cortex (P4) superior parietal lob-ule (SPL), intraparietal sulcus (IPS)	10 sessions/1 Hz/10 consecutive days	1 Hz rTMS to the right parietal lobe significantly improved both anxi-ety and insomnia symptoms in the active group compared to the sham group, and that these improvements were positively correlated with each other
(Antczak et al. 2017)	rTMS	open study	13	(Mean age 50.6 ±13.9; 11 females)	bipolar or unipolar depression	CGI, HDRS, AIS, sleep diary and actigraphy	left dlPFC	20 daily sessions of 10 Hz rTMS	While rTMS improved mood in depression, its effect on sleep quality was limited, with only mod-est improvements in insomnia-related measures, suggesting the need for additional interventions or pro-tocol adjustments to address insomnia
(Donse et al. 2017)	rTMS	open-label design	22	(Mean age: 39.3 ±13.5,9 females)	OCD	Y-BOCS, BDI-II-NL, PSQI, Actigraphy	Bilateral SMA and right dlPFC	10 sessions/1 Hz with/without psy-chotherapy	CRSD was more com-mon in OCD patients, especially in rTMS non-responders, and could predict treatment non-response, highlighting its potential as an indi-cator for personalized OCD treatment

Table 2 (continued)

STUDY	TYPE	DESIGN	SAMPLE SIZE	AGE/SEX	POPULATION	MEASUREMENT	ELECTRODE PLACEMENT	PROTOCOL	MAIN RESULTS
(Antczak et al. 2011)	rTMS	sham-controlled, parallel study	11	(Mean age 64.2; 5 females)	Parkinson's disease (PD)	PSG, PDSS, UPDRS, the 9 Hole Peg Test	bilaterally over the primary motor areas	10 daily rTMS sessions at 15 Hz	The study found that 15-Hz rTMS over both PMCs significantly improved sleep quality by reducing arousal frequency and Non-REM stage 1 sleep, as well as enhancing subjective sleep assessments

Abbreviation: *rTMS* Repetitive transcranial magnetic stimulation, *tDCS* Transcranial direct current stimulation, *tACS* Transcranial Alternating Current Stimulation, *PSQI* Pittsburgh Sleep Quality Index, *HAMD* Hamilton Depression Scale, *HAMA* Hamilton Anxiety Scale, *CGI* Clinical Global Impression, *HDRS* Hamilton Depression Rating Scale, *AIS* Athens Insomnia Scale, *dlPFC* dorsolateral prefrontal cortex, *DMPFC* left dorsal medial prefrontal cortex, *PSG* Polysomnography, *PDSS* Parkinson's Disease Sleep Scale, *UPDRS* Unified Parkinson's Disease Rating Scale, *ISI* Insomnia Severity Index, *GCS* Glasgow Coma Scale, *ESS* Epworth Sleepiness Scale, *OCD* Obsessive–Compulsive Disorder, *Y-BOCS* the Yale-Brown Obsessive–Compulsive Screening, *BDI-II-NL* The Beck Depression Inventory, *CRSD* Circadian Rhythm Sleep Disorders, *SMA* Supplementary Motor Area, *HAMD-17* Hamilton Depression Rating Scale, *HRSA or HAMA* The Hamilton Rating Scale for Anxiety, *ADAS-Cog* the Alzheimer's Disease Assessment Scale-Cognitive section, *MOCA* Montreal Cognitive Assessment, *BDI* Beck Depression Index, *BAI* Beck Anxiety Index, *SAS* self-rating anxiety scale and *SDS* self-rating depression scale, *MDD* Major Depressive Disorder, *GAD* Generalized Anxiety Disorder, *rsEEG* resting-state electroencephalography, *SOL* Sleep onset latency, *WASO* wake after sleep onset, *TST* Total Sleep Time, *HAM-D* Hamilton Depression Scale, and *HAM-A* Hamilton Anxiety Scale, *MEPs* the motor evoked potentials, *EMG* Electromyographic, *NIHSS* National Institutes of Health Stroke Scale, *MBI* Modified Barthel Index, *PHQ-9* Patient Health Questionnaire-9, *Y-BOCS* Yale-Brown Obsessive–Compulsive Scale, *SMA* Supplementary Motor Area, *GAD* Generalized Anxiety Disorder, *PPC* Posterior Parietal Cortex, *BAI* Beck Anxiety Inventory, *PDSS* Parkinson's Disease Sleep Scale, *MDS-UPDRS* Movement Disorder Society-Sponsored Unified Parkinson's Disease Rating Scale, *SDS* Self-rating Depression Scale, *SAS* Self-rating Anxiety Scale, *MFI* Multidimensional Fatigue Inventory

tES (tDCS & tACS)

The studies analyzed in this review utilized various electrode placements targeting regions implicated in sleep regulation. The most commonly targeted area was the dorsolateral prefrontal cortex (DLPFC). For instance, in the study by Eghbali et al. (2023), the cathode electrode was positioned over the right DLPFC (F4) while the anode was placed on the left shoulder. Similarly, Chalah et al. (2022) applied bifrontal stimulation with the anode over the left DLPFC and the cathode over the right DLPFC. Li et al. (2022a, b) and Zhou et al. (2020) targeted the left DLPFC by positioning the anode over F3 and the cathode over F4, whereas Saebipour et al. (2015) adopted a broader approach with anodes on both F3 and F4 and cathodes on the mastoids and Frase et al. (2019) targeted frontoparietal regions with anode electrodes placed at FP1/FP2 and cathode on P3/P4.

The intensity of stimulation varied across studies, with most employing a current of 2 mA. Exceptions included Eghbali et al. (2023), who used a lower intensity of 1.5 mA, and Saebipour et al. (2015), who applied slow oscillatory stimulation at 0.75 Hz. Session durations ranged from 15 to 30 min, with most protocols including daily or near-daily sessions. The total number of sessions also varied, from as few as 3 sessions (Frase et al. 2019) to 20 sessions (Zhou et al. 2020). Eghbali et al. (2023) and Chalah et al. (2022) conducted 15 sessions, Li et al. (2022a, b) employed 10 sessions, and Saebipour et al. (2015) used 4 non-consecutive sessions over several days.

The effects of tDCS on sleep quality and insomnia-related parameters were inconsistent across studies. Eghbali et al. (2023) reported significant improvements in sleep quality and reductions in insomnia severity among patients with TBI-induced insomnia, as assessed by the Pittsburgh Sleep Quality Index (PSQI) and Insomnia Severity Index (ISI). These effects were more pronounced in younger participants and males, suggesting potential demographic influences on treatment efficacy. Chalah et al. (2022) observed significant reductions in daytime sleepiness among multiple sclerosis patients, as measured by the Epworth Sleepiness Scale (ESS). However, no significant changes were noted in objective sleep measures, including sleep onset latency (SOL), total sleep time (TST), or wake after sleep onset (WASO). Zhou et al. (2020) showed improved both depressive symptoms and sleep quality in patients with MDD and insomnia after 20 sessions of 2 mA tDCS over left dlPFC. However, Li et al. (2022a, b) reported a reduction in the complexity of REM sleep EEG signals in patients with major depressive disorder, indicating a potential improvement in sleep efficiency. However, this study found no significant effects on overall sleep quality or depression severity. Frase et al. (2019) found no significant effects of tDCS on sleep quality in patients with insomnia, who exhibited higher baseline arousal levels compared to healthy controls. Increased arousal was identified as a potential barrier to the effectiveness of tDCS, highlighting the need for modified stimulation protocols in this population. Saebipour et al. (2015) demonstrated that slow oscillatory tDCS improved sleep by increasing stage 3 sleep duration, enhancing sleep efficiency, and promoting transitions to deeper sleep stages. Concurrently, it reduced stage 1 sleep and wake time after sleep onset.

Interestingly, Combined tDCS-rTMS protocols demonstrated improved outcomes compared to separate approaches, although this finding is based on a single study. Zhou et al. (2024) conducted a large-scale randomized controlled trial involving 157 participants with chronic insomnia, reporting collaborative benefits of combined 20 sessions of 2 mA tDCS and 1 Hz rTMS over anode left and cathode right dlPFC. This approach not only improved subjective sleep measures such as PSQI but also reduced depressive and anxiety symptoms. Importantly, these benefits persisted for up to three months post-treatment, underscoring the potential for multimodal stimulation to achieve durable outcomes. These results highlight the variable efficacy of tDCS for improving sleep quality, with outcomes influenced by stimulation parameters, target populations, and individual differences. The findings underscore the need for further optimization of protocols to enhance treatment efficacy.

All studies reported good tolerability of tDCS with no serious adverse effects. Minor side effects, such as mild scalp tingling or discomfort at the electrode sites, were noted but did not affect adherence to the protocols.

The effectiveness of tACS in improving sleep quality and treating insomnia was evident across multiple studies, with differences in electrode placement, stimulation intensity, frequency, and session protocols influencing the outcomes. Zhu et al. (2024a, b) and Wang et al. (2020) utilized a forehead-to-mastoid protocol (Fpz, Fp1, Fp2, and mastoid areas) with high-intensity stimulation (15 mA, 77.5 Hz) in 20 daily 40-min sessions over four weeks. Both studies reported significant improvements in sleep quality, duration, sleep efficiency, and PSQI scores, with additional reductions in depressive (HAMD) and anxiety (HAMA) symptoms. These effects were most noticeable in older patients and persisted for up to four weeks post-treatment. Ayanampudi et al. (2022) explored a personalized pre-sleep stimulation protocol targeting Fp1 and Fp2 at theta/alpha frequency bands, demonstrating significant enhancements in sleep quantity and reduced sleep onset latency compared to fixed-frequency stimulation and control conditions. Motamedi et al. (2023), using

bilateral stimulation at F3/M1 and F4/M2 (0.75 mA, 0.75 Hz) in two sessions (5 min), found improvements in sleep quality, efficiency, and daytime sleepiness, though changes in sleep latency and wake after sleep onset were not statistically significant. Across all studies, tACS was well-tolerated with no reported adverse effects, emphasizing its safety. Collectively, these findings support the utility of tACS in improving sleep outcomes in insomnia, with individualized protocols showing particular promise for enhancing therapeutic efficacy.

rTMS

This systematic review includes findings from 33 studies that investigated the efficacy of rTMS in improving sleep quality across various populations, including individuals with primary insomnia, insomnia comorbid with psychiatric or neurological disorders, and healthy controls. The studies utilized different protocols, stimulation sites, and evaluation measurements, offering insights into the potential of rTMS as a therapeutic intervention.

The dorsolateral prefrontal cortex (dlPFC) was the most frequently targeted area, with both left and right hemispheres explored. Low-frequency stimulation (1 Hz) targeting the left dlPFC was employed in multiple studies, such as those by Ding et al. (2024), demonstrating significant improvements in subjective sleep measures like the Pittsburgh Sleep Quality Index (PSQI) and Insomnia Severity Index (ISI). Similarly, studies like Zhao et al. (2024) and Guo et al. (2023) confirmed the efficacy of 1 Hz stimulation over the left dlPFC in reducing sleep disturbances, enhancing EEG phase-amplitude coupling (which was weaker in insomnia patients before stimulation), and restoring normal sleep patterns in individuals with insomnia. The table also emphasized studies like Holbert (2023) where bifrontal low-frequency of 15 sessions rTMS (1 Hz) targeting the both right and left dlPFC demonstrated promising results in reducing insomnia symptoms, with improvements observed in over half of the participants.

High-frequency stimulation (10 Hz) targeting the left dlPFC was reported in studies investigating comorbid conditions such as depression (Pu et al. 2023; Collins et al. 2022). These studies demonstrated dual benefits, improving both sleep quality and depressive symptoms. Xu et al. (2024a, b) explored the efficacy of 10 sessions both 1 Hz and 10 Hz stimulation of the dlPFC in 90 post-stroke depression with insomnia patients, showing that low-frequency stimulation over right dlPFC was more effective for insomnia symptoms, while high-frequency stimulation over left dlPFC yielded greater reductions in depressive symptoms.

Other cortical areas targeted included the posterior parietal cortex (Song et al. 2019; Khedr et al. 2024), angular gyrus (You et al. 2023), and primary motor cortex (Nardone et al. 2020; Antczak et al. 2011). These studies highlighted that stimulation of non-frontal regions can also enhance sleep quality, albeit with fewer studies in this area, particularly in patients with comorbid insomnia. For instance, You et al. (2023) reported that targeting the angular gyrus with 20 sessions of 20 Hz rTMS, improved memory and sleep quality through hippocampal-cortical circuit enhancement in AD spectrum patients with insomnia. Moreover, Khedr et al. (2024) applied 20 Hz rTMS to parietal regions in Parkinson's disease patients in 10 sessions, resulting in reduced periodic leg movements and improved sleep efficiency and Parkinson's Disease Sleep Scale (PDSS) scores. Also, Antczak et al. (2011) used 10 sessions of 15 Hz rTMS bilaterally over primary motor areas in PD patients, reporting enhanced subjective sleep assessments.

The frequency of rTMS varied between studies, with low-frequency protocols (1 Hz) being more commonly employed for sleep-specific outcomes. The duration of individual sessions ranged from 18 to 37.5 min, and the total number of sessions varied from 10 to 30. For example, Shi et al. (2021) employed 10 sessions of low-frequency rTMS over the right dlPFC, achieving significant reductions in PSQI scores.

The reviewed studies assessed sleep quality using a variety of subjective and objective measures, including the PSQI, ISI, and polysomnography (PSG). Low-frequency rTMS was consistently associated with improved subjective sleep quality, as measured by the PSQI, across populations with chronic insomnia (Zhao et al. 2024; Zhu et al. 2023). Objective measurements, such as PSG and EEG, revealed enhanced sleep quality, including improved sleep efficiency and reductions in wake-after-sleep onset (Lin et al. 2023). In comorbid insomnia, studies by Xu et al. (2024a, b) and Pu et al. (2023) reported dual benefits in sleep quality and primary condition symptoms, such as depression or anxiety.

Across all studies, rTMS was well-tolerated with no severe adverse effects reported. Mild discomfort at the stimulation site was the most common side effect. Notably, tDCS and tACS exhibited fewer side effects compared to rTMS, likely due to their lower stimulation intensities. Long-term safety data are limited, but available evidence suggests that repeated sessions are not associated with adverse effects. These findings confirm the safety of NIBS as a non-pharmacological intervention for insomnia while emphasizing the need for future research to standardize protocols, explore long-term efficiency, and optimize treatment personalization.

Discussion

The exploration of brain stimulation techniques as potential treatments for insomnia has gained considerable attention in recent years, building on earlier investigations into electrical modulation of sleep. Historical attempts, such as studies in the mid-twentieth century on"electrosleep"therapy (Frankel et al. 1973), arranged the groundwork for the current wave of research into non-invasive brain stimulation (NIBS) techniques. Modern NIBS methods, including rTMS, tDCS, and tACS have demonstrated the capacity to modulate cortical activity, offering promising new paths for the treatment of insomnia. Most of the studies included in this review have been published in the past five years, reflecting the growing interest in the therapeutic potential of NIBS for sleep disorders. The majority of these trials investigated the effects of rTMS or transcranial electrical stimulation (tES, encompassing tDCS and tACS). These techniques have already been established as effective treatments for various neurological and psychiatric disorders, such as depression and anxiety. The findings from 43 studies highlight the therapeutic potential of these techniques, particularly rTMS, which demonstrated the most consistent results, reporting improvements in both subjective and objective sleep parameters. However, it remains unclear how stimulating diverse cortical targets, using various stimulation techniques and parameters, applied at different regions, consistently yields significant treatment effects for insomnia. In this review, studies employed rTMS, tDCS, and tACS with considerable variation in stimulation protocols, including frequency, intensity, duration, and the total number of sessions. Cortical targets ranged from the dlPFC to regions such as the angular gyrus, posterior parietal cortex, and primary motor cortex, yet improvements in subjective and objective sleep measures were observed across these diverse approaches. These findings suggest a complex interplay between cortical modulation and the neural mechanisms regulating sleep, which warrants further investigation to better understand the underlying processes driving these therapeutic outcomes. This discussion contextualizes the evidence within the broader landscape of insomnia treatment, addressing key implications, limitations, and directions for future research.

Integration of findings

rTMS demonstrated robust therapeutic potential for improving sleep quality in individuals with insomnia, as consistently reported across the studies included in this review. Both low-frequency (1 Hz) and high-frequency (10 Hz) rTMS targeting the dlPFC were associated with significant improvements in sleep parameters, although the mechanisms and extent of these effects differed depending on the stimulation protocol. Low-frequency (1 Hz) rTMS, predominantly applied over the left dlPFC, showed consistent benefits in enhancing subjective sleep quality and reducing insomnia severity (Ding et al. 2024; Zhao et al. 2024; Guo et al. 2023; Zhang et al. 2023; M. P. Li et al. 2022a, b).

High-frequency (10 Hz) rTMS over the left dlPFC demonstrated that high-frequency stimulation not only improved sleep but also alleviated depressive symptoms (Pu et al. 2023; Xu et al. 2024a, b) This dual benefit highlights the potential of rTMS to address overlapping pathways implicated in insomnia and mood disorders. Concurrently, low-frequency (1 Hz) rTMS over the right dlPFC also showed potential benefits in specific contexts, such as reducing insomnia symptoms and associated anxiety, as reported in studies like Wang et al. (2022), highlighting its capacity to modulate neural circuits involved in emotional and sleep regulation. Interestingly, targeting other cortical regions with rTMS also yielded improvements in specific populations. For instance, high-frequency stimulation of the angular gyrus improved sleep and memory in Alzheimer's spectrum patients (You et al. 2023), while parietal cortex stimulation reduced periodic leg movements and improved sleep efficiency in Parkinson's disease patients (Khedr et al. 2024). Stimulation of the primary motor cortex (M1) using low-frequency rTMS demonstrated limited but notable improvements in sleep quality, with studies such as Nardone et al. (2020) reporting reductions in cortical excitability and enhanced subjective sleep measures, particularly in patients with chronic insomnia. These findings underscore the versatility of rTMS in modulating neural circuits beyond the dlPFC to address sleep disturbances associated with diverse conditions. Overall, rTMS consistently demonstrated significant improvements in subjective and objective sleep measures across a range of protocols and target sites. The observed efficacy, coupled with its safety and tolerability, positions rTMS as a leading NIBS modality for insomnia treatment. However, the variability in stimulation parameters and target regions highlights the need for further research to optimize protocols and clarify the mechanisms underlying these effects.

The findings for tDCS were mixed but demonstrated promising potential in specific contexts. Several studies targeting the left dlPFC with 2 mA tDCS reported significant improvements in subjective sleep quality and reductions in sleep onset latency. For instance, Zhou et al. (2020) observed that 20 sessions of 2 mA tDCS improved both sleep quality and comorbid depressive symptoms in patients with major depressive disorder (MDD) and insomnia. Slow oscillatory tDCS also yielded notable results. Saebipour et al. (2015) reported that 0.75

Hz tDCS targeting the prefrontal areas increased stage 3 (deep) sleep duration and enhanced sleep efficiency. However, studies such as Frase et al. (2019) highlighted the variability in outcomes, with no significant effects observed in insomnia patients with high baseline arousal levels, indicating that individual differences may influence treatment response.

Although fewer studies focused on tACS compared to rTMS and tDCS, the results indicate its potential for improving sleep quality. Zhu et al. (2024a, b) and Wang et al. (2020) demonstrated significant improvements in sleep onset, duration, and efficiency following 20 sessions of high-frequency (77.5 Hz) tACS applied to the frontal regions. These studies also noted reductions in depressive and anxiety symptoms, suggesting that tACS may have broader therapeutic applications. Personalized tACS protocols, such as those employed by Ayanampudi et al. (2022), showed particular efficacy. By adapting stimulation frequencies to individual theta and alpha oscillations, the study achieved reductions in sleep onset latency and increases in total sleep time, further supporting the role of frequency-specific stimulation in optimizing sleep outcomes.

Clinical implications

The clinical implications of these findings are significant. First, NIBS offers a non-pharmacological alternative for insomnia treatment, addressing limitations such as dependency, tolerance, and side effects associated with conventional sleep medications. Second, its safety profile and tolerability make it easy to use by diverse populations, including older adults, individuals with neurodegenerative conditions, and those with contraindications to pharmacological interventions. Third, the demonstrated efficacy of personalized and multimodal stimulation protocols emphasizes the importance of adapting interventions to individual needs. The integration of NIBS into routine clinical practice could develop insomnia treatment. For example, patients with treatment-resistant insomnia or comorbid mood disorders could benefit from rTMS's dual effects on sleep and mood. Furthermore, the ability of combined protocols, such as tDCS with rTMS to enhance efficiency highlights the potential for multimodal approaches that maximize therapeutic benefits.

Limitations of the current evidence

Despite the encouraging findings, this review underlines several limitations that must be addressed. The heterogeneity in participant characteristics, including age, gender, and comorbid conditions, complicates the generalizability of results. Additionally, the reliance on subjective sleep quality measures in many studies limits the reliability of findings, emphasizing the need for greater integration of objective tools such as polysomnography (PSG) and actigraphy. The limited number of studies on tDCS and tACS compared to rTMS reflects the early stage of research on these modalities. While their initial results are promising, larger and more diverse cohorts are needed to confirm their efficiency and explore their broader applications. Moreover, the lack of standardized protocols across studies presents a significant barrier to clinical implementation. Future research must prioritize the development of standardized guidelines on stimulation parameters, session frequency, and duration. Another notable gap is the absence of long-term efficiency data. While short-term improvements are well-documented, the long-term effects of NIBS remain unclear. This raises questions about the potential need for maintenance sessions or booster treatments to sustain benefits over time.

Directions for future research

Advancing the field of NIBS requires addressing several important areas. To start, having standardized protocols is crucial by setting clear and consistent guidelines for how stimulation is applied, outcomes are measured, and results are reported, researchers can make studies more comparable and clinically useful. Another key step is developing reliable guidelines, which can help predict who will respond to treatment and allow for more personalized and effective interventions. It's also important to focus on long-term studies. These can show whether the benefits of NIBS last over time and whether follow-up treatments are necessary to maintain those effects. Combining NIBS with other approaches, such as behavioral therapy, medications, or other neuromodulation techniques, could increase its benefits, opening new possibilities for treatment. Expanding research to include more diverse groups is equally vital. For instance, studying people with neurodevelopmental disorders or severe insomnia can make findings more applicable to a wider range of individuals. At the same time, understanding the economic side, how cost-effective NIBS is, will be essential to determine whether it can be realistically implemented on a large scale in healthcare systems. Finally, sham-controlled and double-blind studies are critical. These ensure that the observed benefits come from NIBS itself, not just from people's expectations. By addressing these areas, we can take NIBS from promising research to a reliable tool for improving lives.

Conclusion

NIBS represents a revolutionary advancement in the treatment of insomnia, offering non-invasive, safe, and highly adaptable interventions that address both the

neural and psychological dimensions of sleep disorders. This review emphasizes the strong efficacy of rTMS, the emerging potential of tDCS and tACS, and the critical role of personalization in optimizing outcomes. To reach the full potential of NIBS, further research is needed to address current limitations, standardize protocols, and ensure diverse and inclusive studies. Advancing knowledge of its mechanisms and improving access to these treatments will help integrate NIBS into broader care strategies. This could mark a significant step forward in precision medicine, offering new hope for individuals worldwide who struggle with insomnia and its related challenges.

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M.khosravi: Writing, analysis, methodology, visualization, Conceptualizatio, and supervision R.khosravi: Writing, analysis, visualization, Conceptualization, and Editing.

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Data availability
The datasets generated and/or analyzed during the current study are available from the corresponding author upon reasonable request.

Declarations

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