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Effects of ExoTMS stimulation on sleep quality: a sham-controlled study

Georgine Nanos[1*], Melinda Silva[2] and Charmi Patel[3]

Abstract

Background Sleep disturbances are prevalent and linked to adverse neurological outcomes. While conventional transcranial magnetic stimulation (TMS) shows promise, protocols typically require high intensities and prolonged courses. ExoTMS is a novel technology targeting cortical regions involved in sleep regulation.

Aim To evaluate ExoTMS efficacy in improving subjective sleep quality in individuals with sleep disturbances.

Methods In this multicenter, single-blinded, sham-controlled study, 43 adults were assigned to an active ($n=31$, 70% motor threshold (MT)) or a sham ($n=12$, 5% MT) group. Subjects underwent six sessions targeting the left dorsolateral prefrontal cortex (dlPFC). Outcomes were assessed at baseline and a 3-month follow-up via Pittsburgh Sleep Quality Index (PSQI), Perceived Stress Scale (PSS-10), Sleep and Stress Assessment, Subject Satisfaction Questionnaire, and Therapy Comfort Questionnaire.

Results At baseline, active subjects demonstrated poor sleep (average PSQI 9.7 ± 3.4). At 3 months, the active group showed a significant reduction (-4.7 points, $p < 0.0001$), with 48.3% of subjects achieving the minimal clinically important difference and 55.2% reaching clinical remission. Active stimulation was particularly effective in reducing sleep onset latency by 46.3 min in subjects with prolonged baseline latency. Additionally, 82.1% of active subjects reported improved stress coping, compared to 63.6% in the sham group. ExoTMS treatment was well tolerated, with all subjects reporting "0" on the Numerical Analog Pain Scale.

Conclusion These findings suggest that ExoTMS may represent a promising and well-tolerated non-invasive intervention for improving sleep quality.

Trial registration NCT07027657 (ClinicalTrials.gov), registered on June 11, 2025.

Keywords Transcranial magnetic stimulation, TMS, Sleep quality, Neuromodulation, Non-invasive, Sleep disturbances

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Introduction

Sleep quality is a multidimensional indicator reflecting the depth and restorative capacity of sleep, incorporating aspects such as sleep onset latency, total sleep duration, frequency of nocturnal awakenings, and subjective sleep satisfaction upon awakening (Zhang et al. 2024). Disruptions across these dimensions are clinically relevant, as extensive evidence indicates that poor sleep quality and insufficient sleep duration adversely affect multiple physiological systems, including neurological, psychiatric, cardiovascular, metabolic, and immune functioning (Lanza et al. 2023; Herrero Babiloni et al. 2021). Epidemiological studies suggest that 20—45% of individuals in Western populations experience recurrent difficulties initiating or maintaining sleep, underscoring the widespread public health burden of sleep disturbances (Herrero Babiloni et al. 2021).

Moreover, psychological stress is a well-recognized contributor to impaired sleep quality, with higher stress levels associated with delayed sleep onset, increased nocturnal awakenings, and non-restorative sleep. Conversely, insufficient or fragmented sleep can further exacerbate stress, reflecting a bidirectional relationship between these processes (Vandekerckhove and Cluydts 2010; Reis et al. 2024).

Current treatment approaches to poor sleep quality primarily include pharmacological interventions and cognitive behavioral therapy (CBT) (Sun et al. 2021; Morin 2017). While the latter is established as the first-line treatment, it is often limited by its time-consuming nature (Morin 2017). Pharmacological treatments may provide short-term symptom relief but are generally unsuitable for long-term use due to side effects such as residual sedation and cognitive impairment (Giblin and Clift 1983). Consequently, there is a critical need for therapeutic alternatives that are effective, safe, and accessible (Sun et al. 2021).

Emerging evidence highlights the central role of cortical networks in sleep regulation, with particular emphasis on the left dorsolateral prefrontal cortex (dlPFC) (Minichino et al. 2014; Kim et al. 2022). The dlPFC is involved in the top-down modulation of arousal systems and the regulation of sleep–wake transitions, mechanisms that are frequently disrupted in individuals with sleep disorders (Cools and Arnsten 2022). Neuroimaging and electrophysiological studies suggest that altered dlPFC activity and impaired cortical inhibition may contribute to difficulties in sleep initiation and maintenance (Sun et al. 2017; Feng et al. 2019). These findings provide a neurobiological rationale for targeting the dlPFC in interventions aimed at improving sleep quality.

Transcranial magnetic stimulation (TMS) is a noninvasive neuromodulation technique capable of altering cortical excitability through the application of time-varying magnetic fields (Lanza et al. 2023; Sun et al. 2021; Gao et al. 2023). The effects of TMS are frequency-dependent: low-frequency stimulation (≤ 1 Hz) typically suppresses neuronal firing (inhibition), while high-frequency stimulation (≥ 5 Hz) facilitates excitatory neuronal function. (Herrero Babiloni et al. 2021; Somaa et al. 2022; Sheng et al. 2023; Siebner et al. 2022) By inducing electric currents within targeted cortical regions, TMS can modulate neuronal firing patterns and network-level activity (Sun et al. 2021). Previous research indicates that TMS may influence sleep architecture, enhance restorative sleep quality, and improve subjective sleep quality, with effects that can persist beyond the stimulation period (Ding et al. 2024; Lanza 2020). These characteristics suggest that neuromodulation may offer advantages over chronic pharmacotherapy.

Optimizing stimulation parameters and tolerability is essential for maximizing the clinical utility of neuromodulation. ExoTMS technology was designed to address several technical limitations of conventional TMS systems. Unlike standard devices that deliver rectangular pulses, ExoTMS employs ramp-up shaped pulses designed to reduce peripheral nerve activation. This pulse configuration may allow for higher-intensity stimulation of target cortical neurons while minimizing sensory discomfort, a factor that can influence treatment adherence. Furthermore, the device incorporates a dual-core coil with parallel wiring to enhance magnetic field efficiency, along with an integrated air-cooling system that supports stable performance during higher pulse delivery within shorter treatment sessions.

This clinical study aims to evaluate whether targeted stimulation of the left dlPFC using the ExoTMS technology can modulate cortical activity associated with sleep regulation and improve sleep quality in individuals with sleep disturbances.

Methods

This multi-center, sham-controlled, single-blinded study design aimed to evaluate the efficacy of the ExoTMS therapy in improving sleep quality. Additionally, the study assessed the therapy's impact on stress, safety profile, and subject satisfaction and comfort. The study was approved by the institutional review board, Advarra, and adhered to the principles of the Declaration of Helsinki. It was registered on the clinicaltrials.gov site under NCT07027657. Written informed consent was obtained from each subject, using a personally signed and dated consent form, prior to the initiation of any study-related procedures.

Forty-three subjects ($n = 43$) were enrolled in the study. While eleven ($n = 11$) subjects reported a history of psychiatric disorders, all were free of any current psychiatric diagnosis at the time of enrollment. Subjects were

allocated to either the active treatment group (Group A) or the sham group (Group B) in a 3:1 ratio. Thirty-one subjects were assigned to the active group ($n = 31$, 22—64 years, 6 males, 25 females), and twelve to the sham group ($n = 12$, 27—65 years, 6 males, 6 females).

Group allocation was performed using a block randomization scheme. The randomization sequence was generated prior to study initiation using a computerized random number generator. Allocation concealment was maintained by implementing the randomization sequence through a centralized assignment process, whereby group allocation was determined at the time of enrollment without prior access to future assignments by study personnel.

The study employed a single-blinded design in which subjects were unaware of their group allocation. Blinding was maintained by ensuring that the sham procedure closely replicated the active intervention in terms of device appearance, treatment duration, and operator-patient interaction. Treating clinicians were not blinded due to the nature of the intervention.

To meet the inclusion criteria, subjects were required to be over 22 years of age, have a baseline pre-treatment Pittsburgh Sleep Quality Index (PSQI) score of ≥ 5, indicating the presence of self-reported sleep disturbance, and be willing to abstain from any interventions, other than the study procedure, aimed at improving sleep quality during the study period. Subjects were instructed to maintain their usual diet and exercise routines throughout the trial. Women of childbearing potential were required to use appropriate birth control measures, and a determinable motor threshold was necessary for inclusion.

Exclusion criteria included the presence of metallic or magnetically sensitive implants in or near the head, implanted medical devices such as drug pumps or pacemakers, and any severe or unstable medical condition. Subjects with significant cardiovascular, pulmonary, renal, or hematologic disorders; active malignancy; fever; active obsessive–compulsive disorder or active post-traumatic stress disorder; active major depression; or ongoing pregnancy were also excluded.

Subjects underwent six treatment sessions using the EXOMIND device (BTL Industries, Boston, MA, USA) with the ExoTMS technology, administered to the left dlPFC. At the baseline visit, the motor threshold (MT) was determined and defined as the lowest stimulation intensity that elicited a visible motor response in the fingers of the right hand in at least 50% of delivered pulses.

Stimulation intensity in the active group was gradually increased to a maximum of 70% of each individual's MT. This intensity was selected to ensure effective neuromodulatory engagement while maintaining a favorable safety and tolerability profile. In the sham group, stimulation was delivered at 5% of MT. Although this intensity is below the threshold required to induce cortical depolarization, it preserves the auditory and mild somatosensory characteristics of active stimulation. The use of low-intensity output, rather than no stimulation, was intended to enhance subject blinding by mimicking aspects of the active treatment without eliciting a biologically meaningful neuromodulatory effect.

Each treatment session lasted 24.5 min, with intervals of 3 to 7 days between treatments. The investigator examined the treatment area after each session to monitor for potential adverse events. The follow-up visit was conducted 3 months (± 14 days) after the final treatment session.

The primary outcome of the study was a change in subjective sleep quality, as measured by the PSQI. Secondary outcomes included Perceived Stress Scale (PSS-10), as well as subject-reported satisfaction and treatment tolerability evaluated using the Subject Satisfaction Questionnaire (SSQ) and Therapy Comfort Questionnaire (TCQ), respectively. Exploratory outcomes included results from the Sleep and Stress Assessment Questionnaire, item-level analyses of PSQI and PSS-10, and subgroup analyses.

Sleep quality over the previous month was assessed using the PSQI, administered at baseline and at the 3-month follow-up visit. The PSQI is a 19-item questionnaire comprising seven components, each scored on a 0—3 scale, with lower scores indicating better sleep quality. Global scores (0—21) were analyzed as continuous data, with scores > 5 indicating poor sleep quality. For further analysis, scores were stratified into four severity categories: good sleep quality (0—5), and mild (6—10), moderate (11—15), or severe (16—21) sleep disturbance (Sharma et al. 2015). Clinical remission was defined as achieving a global score < 5 at the follow-up. This cutoff is supported by validation studies of the PSQI, in which a threshold of 5 was shown to reliably differentiate individuals with and without clinically significant sleep disturbance (Shahid et al. 2011). The clinical significance of the treatment effect was evaluated using the minimal clinically important difference (MCID) threshold of 4.4 points (Longo et al. 2021).

The PSS-10 was administered at the same time points as the PSQI to evaluate perceived stress during the previous month. Each item is rated on a 0–4 scale (0 = never; 4 = very often), with lower scores reflecting lower perceived stress. Scores on the PSS-10 can range from 0 to 40; a score of 10 or greater signifies moderate to high levels of perceived stress (Xiao et al. 2023).

Subject satisfaction with treatment outcomes was assessed at the 3-month follow-up visit using the 19-item

SSQ, which evaluates perceived changes in sleep quality and stress management. Responses were rated on a 5-point Likert Scale (1 = strongly disagree; 5 = strongly agree).

Treatment tolerability was evaluated immediately after the final session using the TCQ, which includes a 5-point Likert Scale and a Numerical Analog Pain Scale (range 0—10), where 0 denotes no pain, and 10 indicates the worst possible pain.

The Sleep and Stress Assessment Questionnaire was used to obtain information on sleep and stress medication use and overall stress levels. The baseline version includes 5 items, whereas the version administered at the 3-month follow-up includes 6 items. The baseline form includes information on the use of sleep and stress supplements and the reported cause of any stress. The 3-month follow-up form gathers comparable information regarding sleep and stress supplements, alongside details on whether stress levels had changed and if the therapy had improved the ability to cope with stress.

Statistical analyses were performed. Descriptive statistics, including means and standard deviations, were calculated. Changes over time within groups were assessed using Friedman's test. Given the pilot nature of the study and the limited sample size, the study was not powered for formal between-group comparisons, therefore, differences between the active and sham groups are presented descriptively. Baseline demographic and clinical characteristics were compared between the active and sham groups using Welch's t-test for continuous variables and Fisher's exact test for categorical variables, given the small and unequal group sizes. Effect sizes were reported alongside *p*-values to characterize the magnitude of within-group change. Significance level was set at $\alpha = 0.05$.

Given the pilot nature of the study, no formal sample size calculation was performed. Subjects who withdrew from the study were not included in the final analysis. The analysis was conducted on a per-protocol population, including only subjects who completed the study and had evaluable outcome data.

Table 1 Baseline demographic and clinical characteristics of subjects included in the analysis

Characteristic	Active ($n = 29$)	Sham ($n = 11$)	*P* value
Age (years)	45.0 ± 12.7	46.1 ± 11.8	0.80
Female, n (%)	24 (82.8%)	5 (45.5%)	0.04
Male, n (%)	5 (17.2%)	6 (54.5%)	0.04
Psychiatric history, n (%)	9 (31.0%)	2 (18.2%)	0.69
PSQI score (baseline)	9.7 ± 3.4	9.0 ± 3.0	0.56
PSS-10 score (baseline)	18.7 ± 6.6	16.4 ± 6.4	0.33

Data are presented as mean ± standard deviation (SD) or number (percentage), as appropriate

Results

Baseline demographic and clinical characteristics of subjects included in the analysis are summarized in Table 1.

PSQI

At baseline, subjects in the active group demonstrated poor sleep quality, with an average PSQI score of 9.7 ± 3.4. By the 3-month follow-up, 86.2% (25/29) of active subjects experienced significantly improved sleep ($p < 0.0001$, Cohen's d = 1.0), with a 4.7-point reduction in the average PSQI score to 5.0 ± 3.6. The average baseline PSQI score in the sham group was 9.0 ± 3.0 (Cohen's d = 1.9). At the 3-month follow-up, there was a 3.7-point reduction in the average score of 5.3 ± 3.2. A higher proportion of subjects in the active group achieved the MCID (48.3%, [14/29]) compared to the sham group (18.2%, [2/11]). Notably, 55.2% (16/29) of subjects achieved full remission (PSQI < 5), compared to the sham group, which showed a 45.5% (5/11) remission rate.

Exploratory item-level analysis demonstrated improvements among subjects with non-zero baseline scores in the affected domains, specifically item 6 (overall sleep quality) and item 9 (daytime enthusiasm). Within this subgroup, a higher percentage of the subjects in the active group showed improvement compared to the sham arm. At the 3-month follow-up, 62.1% of the active group subjects exhibited improved overall sleep quality (item 6) compared with 36.4% in the sham group. Similarly, for item 9, 72.0% of the active group reported improved daytime enthusiasm, versus 50.0% in the sham arm.

The average sleep onset time in the active group was 40.5 ± 45.7 min. At the 3-month follow-up, the time was reduced by 16.2 min (40.0%) to an average sleep onset time of 24.3 ± 28.2 min. In the sham group, the baseline sleep onset time was 36.4 ± 28.9 min. This time was reduced by 11.9 min (32.7%) to an average time of 24.5 ± 33.1 min at the 3-month follow-up.

Subjects in the active group with initial prolonged sleep latency (> 30 min) demonstrated a progressive decrease in sleep latency over time. In this subgroup, the average sleep latency decreased by 46.3 ± 33.9 min (55.8%) from a baseline value of 83.0 ± 57.3 min. In contrast, the sham group showed a more limited response, with an average reduction of 23.3 ± 42.3 min (33.9%) from a baseline of 68.8 ± 20.2 min (Fig. 1).

PSS-10

At the 3-month follow-up, a greater proportion of subjects in the active group experienced a reduction in overall perceived stress compared with the sham group (41.4% [12/29] vs 18.2% [2/11]), representing a 2.3-fold higher response rate. Average PSS-10 scores in the active group changed from 18.7 ± 6.6 at baseline to 19.8 ± 3.1 at follow-up (Cohen's d = 0.2), while average scores in

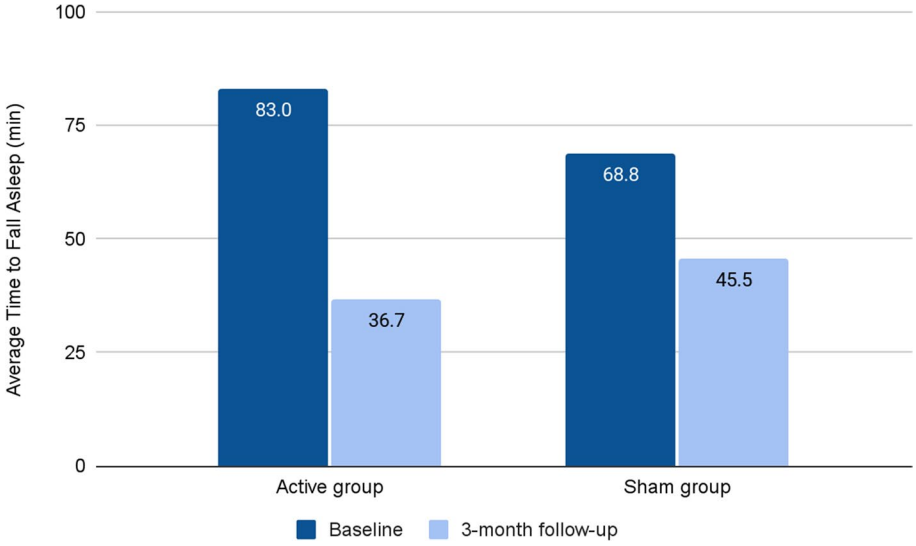

Fig. 1 Exploratory subgroup analysis: Average time to fall asleep (minutes) is shown for subjects with baseline sleep onset latency > 30 min. Sleep onset latency decreased by 46.3 min in the active group (83.0 to 36.7 min) and by 23.3 min in the sham group (68.8 to 45.5 min) at 3-month follow-up

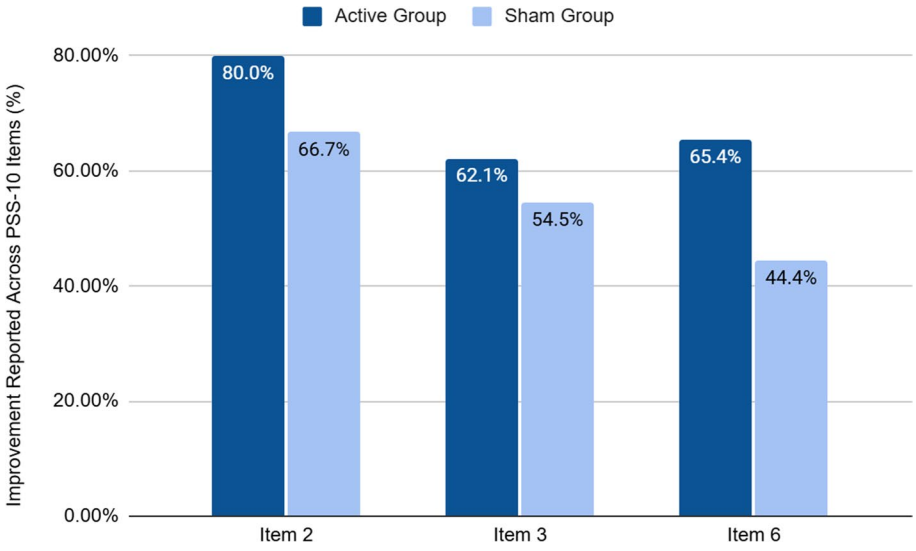

Fig. 2 Percentage of subjects reporting improvement from baseline to 3-month follow-up in PSS-10 Items 2, 3, and 6, stratified by treatment group (active vs. sham). Item 2 assesses perceived lack of control over important aspects of life; Item 3 assesses feelings of nervousness and stress; and Item 6 assesses perceived inability to cope with daily demands

the sham group increased from 16.4 ± 6.4 to 20.4 ± 2.8 (Cohen's d = 0.5).

Exploratory item-level analysis demonstrated improvements (Fig. 2) among subjects with non-zero baseline scores in items related to day-to-day stress and perceived control (items 2 and 3), as well as subjective stress and nervousness (item 6). Within this subgroup, a higher percentage of the subjects in the active group showed improvement than in the sham arm. Specifically, 80.0% of active subjects reported improved control over important life aspects (item 2) versus 66.7% in the sham group, while 62.1% reported feeling less stressed and nervous (item 3) compared with 54.5% in the sham group. For item 6, 65.4% of active subjects reported better coping with daily tasks, versus 44.4% in the sham arm.

Subject satisfaction and therapy comfort questionnaires

According to the SSQ, 86.2% (25/29) of the active group expressed satisfaction with the results at the 3-month follow-up (see Table 2 for details). The mean score for the active group across all SSQ items at the 3-month follow-up was 4.0 out of 5.0, compared to the score of 3.5 for the sham group.

Regarding specific domains, 76.4% of subjects in the active group agreed with statements concerning improved sleep quality, compared to 64.9% in the sham

Table 2 Percentage of subjects in the active and the sham group in agreement with statements of the SSQ

Statement	Subjects in agreement with the statement (3-month follow-up) (%)	
	Active group ($n=29$)	Sham group ($n=11$)
I find it easier to fall asleep after the treatments	**75.9%**	72.7%
I am able to sleep without restlessness at night after the treatments	**72.4%**	72.7%
I wake up less frequently during the night after the treatments	**75.9%**	54.5%
I wake up more refreshed in the morning after the treatments	**79.3%**	54.5%
I feel less drowsy during the day after the treatments	**82.8%**	72.7%
I feel more alert during the day (due to improvement in the quality of sleep) after the treatments	**69.0%**	63.6%
My overall sleep quality has improved after the treatments	**79.3%**	63.6%
I feel calmer after the treatments	**82.8%**	72.7%
I handle stressful situations better after the treatments	**82.8%**	36.4%
I feel more in control of my emotions after the treatments	**72.4%**	54.5%
My ability to cope with stress has improved after the treatments	**82.8%**	63.6%
I feel less tense throughout the day after the treatments	**79.3%**	63.6%
My mind feels clearer after the treatments	**69.0%**	72.7%
I am less irritable after the treatments	**72.4%**	54.5%
I have more mental energy after the treatments	**78.6%**	45.5%
I feel less anxious after the treatments	**75.9%**	63.6%
I feel relaxed after the treatments	**86.2%**	72.7%
My overall stress levels have decreased after the treatments	**69.0%**	63.6%
I am satisfied with the treatment results	**86.2%**	72.7%
OVERALL SATISFACTION	**77.5%**	62.7%

group. A higher proportion of subjects in the active group reported easier sleep onset, fewer nighttime awakenings, feeling more refreshed in the morning, and reduced daytime drowsiness than in the sham group.

Similarly, 77.4% of subjects in the active group agreed with statements related to improved stress management, compared to 59.1% in the sham group. Relative to the sham group, a higher proportion of subjects reported improved ability to cope with stress, reduced irritability and anxiety, and lower overall stress levels.

According to the TCQ, all subjects reported the treatment as comfortable. The comfort level was also supported by all subjects reporting "0" on the Numerical Analog Pain Scale, which indicates no perceived pain during the study procedure.

Sleep and stress assessment questionnaire

Exploratory analyses based on the Sleep and Stress Assessment Questionnaire indicated that at the 3-month follow-up, 82.1% (23/28) of subjects in the active group reported improved stress coping, compared to 63.6% (7/11) of subjects in the sham group.

The usage of sleep supplements at the baseline was reported by twelve subjects in the active group and four in the sham group, with melatonin and herbal supplements being the most frequently cited. At the 3-month follow-up, supplement use was reported by nine subjects in the active group and two in the sham group. Stress-specific supplements (tetrahydrocannabinol (THC) and cannabidiol (CBD) gummies) were used by one subject per group at baseline, though only the active group subject reported continued use at the 3-month follow-up. The most prevalent stressors reported by both groups were work and family/relationships.

Exploratory analysis of subjects with psychiatric history

An exploratory post hoc subgroup analysis was conducted in subjects with a documented history of psychiatric disorders. A total of eleven ($n=11$) subjects met this criterion, including nine ($n=9$) assigned to the active group and two ($n=2$) to the sham group. Reported diagnoses included generalized anxiety disorder (GAD; $n=6$), major depressive disorder (MDD; $n=2$), postpartum depression ($n=2$), posttraumatic stress disorder (PTSD; $n=2$), and unspecified depression ($n=1$). The time since diagnosis ranged from 5 to 31 years.

At baseline, the active group demonstrated poor sleep quality as measured by the PSQI, with a mean score of 10.8 ± 4.0. At the 3-month follow-up, the mean PSQI score decreased to 5.4 ± 3.0, corresponding to a 5.3-point reduction from baseline. In the sham group, the mean baseline PSQI score was 9.0 ± 1.4, with a mean reduction to 3.5 ± 2.1 points at 3 months. All active group subjects classified as having severe or moderate sleep disturbances at baseline improved to either the mild disturbance category or good sleep quality by 3 months, with 55.6% of active subjects categorized as having good sleep quality at follow-up (Fig. 3).

Regarding perceived stress, the mean PSS-10 score in the active group decreased from 21.1 ± 6.8 at baseline

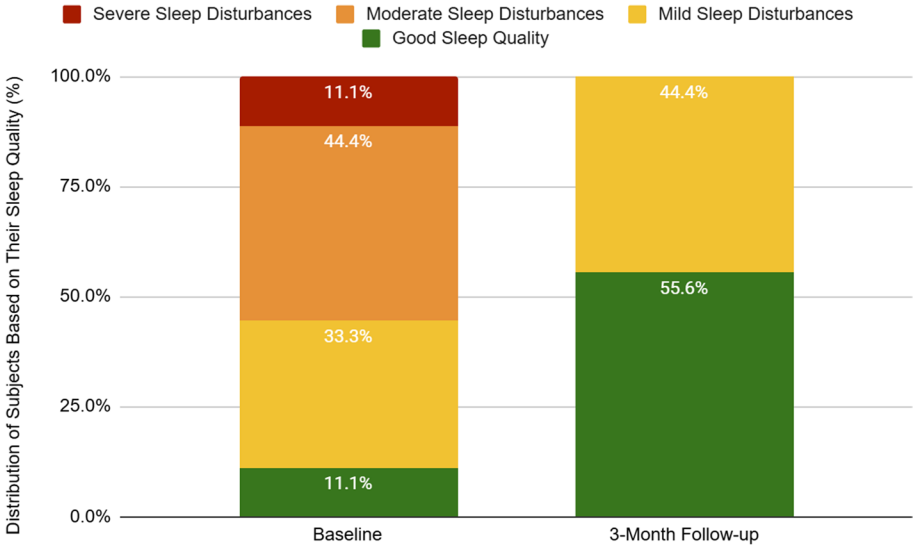

Fig. 3 Exploratory subgroup analysis: Distribution of subjects across sleep quality categories at baseline and at 3-month follow-up in the active group, based on PSQI global scores. Categories include good sleep quality, mild sleep disturbances, moderate sleep disturbances, and severe sleep disturbances

to 20.1 ± 2.8 at 3 months. In contrast, the mean score in the sham group increased from 19.0 ± 1.4 at baseline to 20.0 ± 1.4 at follow-up.

Regarding the Sleep and Stress Assessment, at the 3-month follow-up, 88.9% ($n = 8$) of subjects in the active group reported improved stress coping, compared to 50.0% ($n = 1$) of subjects in the sham group.

Safety

No adverse events were reported in the active treatment group. In the sham group, one subject ($n = 1$) experienced a mild headache after the third treatment, which led to study withdrawal. The event was transient, and no further intervention was required. Overall, three subjects were withdrawn from the study: two subjects from the active group, one ($n = 1$) at baseline due to not meeting the inclusion criteria, and one ($n = 1$) for personal reasons after the first treatment, and one from the sham group due to the adverse event described above.

Discussion

This study investigated the efficacy of ExoTMS stimulation on subjective sleep quality in individuals with sleep disturbances. The active treatment group demonstrated a substantial reduction in PSQI scores over the 3-month follow-up period, with mean scores decreasing by 4.7 points from 9.7 ± 3.4 at baseline to 5.0 ± 3.6 at the follow-up. This transition from mild sleep disturbance to normative sleep quality levels may reflect improved sleep regulation. All subjects reported comfort with the therapy and a high level of satisfaction with the treatment results.

Importantly, the clinical relevance of these changes was further supported by analysis using the established MCID for the PSQI. Nearly half of the subjects in the active group (48.3%) achieved or exceeded the MCID threshold, compared with fewer than one-fifth of subjects (18.2%) in the sham group. This distinction highlights the difference between group-level improvements and individual-level clinically meaningful change. While the sham group demonstrated an average PSQI reduction approaching the MCID, most sham subjects did not experience improvements large enough to meet this criterion. In contrast, the higher proportion of MCID responders in the active group indicates a greater likelihood of subject-relevant benefit, supporting the clinical relevance of the observed effects.

Both groups exhibited reductions in PSQI scores over time, which is consistent with known placebo, expectancy, and care effects commonly observed in sleep intervention studies (Gutiérrez-Romero et al. 2024; Potthoff and Schienle 2024). However, numerical differences between groups suggest that active stimulation may have targeted specific sleep-related domains more effectively than sham stimulation. This distinction was particularly evident in sleep onset latency. Among subjects with prolonged baseline sleep latency, active stimulation was associated with a marked reduction in time to fall asleep (46.3 min), exceeding the reduction observed in the sham group.

Improvements in nighttime sleep were accompanied by favorable changes in daytime functioning. Among active subjects who initially struggled to maintain enough enthusiasm during the day, 72.0% reported improvement at the 3-month follow-up, compared to 50.0% in the sham group. Unlike pharmacological sleep treatments, which may alleviate nighttime symptoms at the expense of residual daytime sedation, ExoTMS stimulation was

not associated with reported drug-related adverse effects and appeared to support both nocturnal and daytime outcomes (Madari et al. 2021). Moreover, the treatment exhibited improvements persisting three months post-treatment, suggesting that the effects of ExoTMS extend beyond the immediate treatment period. Although this does not represent long-term follow-up, the observed durability contrasts with the transient benefits often seen after short-term pharmacological treatment (Lanza et al. 2023; Lanza 2020). These sustained effects may be consistent with ongoing modulation of cortical networks involved in sleep regulation, a possibility that warrants further investigation using objective neurophysiological measures (Lanza et al. 2023).

An additional finding concerns the interaction between sleep quality and perceived stress. Although PSS-10 scores increased in both groups over the follow-up period, the magnitude of worsening was smaller in the active group (+1.1 ± 7.3 points) than in the sham group (+4.0 ± 7.0 points). In contrast, 82.1% of the active group subjects reported an improved ability to cope with stress based on the Sleep and Stress Assessment Questionnaire. This pattern suggests a potentially multidimensional response, in which perceived stress levels and subjective coping ability may not change in parallel. While external stressors persisted or increased, subjects in the active group reported improved ability to manage these stressors.

Given the bidirectional relationship between stress and sleep, these combined findings are consistent with the hypothesis that modulating prefrontal cortical networks may facilitate the regulatory processes necessary to maintain sleep under challenging conditions; however, this interpretation remains speculative in the absence of objective neurophysiological measures. These results align with evidence implicating the dlPFC in cognitive control and emotion regulation, raising the possibility that stimulation of this region may facilitate adaptive stress responses that protect sleep initiation and maintenance even in the presence of elevated perceived stress (Lo Martire et al. 2020; Pulopulos et al. 2020).

Consistent with previous research establishing the positive impact of TMS on sleep-related outcomes, the active group demonstrated an improvement in sleep quality (Lanza et al. 2023; Lanza 2020). Comparable reductions in PSQI scores have been reported in other rTMS studies employing substantially longer and more intensive treatment protocols. For example, Feng et al. (Feng et al. 2025) observed an improvement in sleep quality following 10 consecutive daily treatment sessions delivered at 90% of the resting MT, with mean PSQI scores decreasing from 14.4 to 11.5. In contrast, the present study achieved similar improvements using the ExoTMS device with only six treatment sessions, making the treatment more efficient (Magyarová et al. 2023). By condensing the therapeutic window, this approach may reduce treatment burden, minimize daily disruption, and lower the risk of treatment fatigue. Additionally, the protocol employed a maximum stimulation intensity of 70% of the resting MT, which is substantially lower than the conventional range of 80—120% used in previous studies (Magyarová et al. 2023). This reduced stimulation intensity likely contributed to improved subjects' comfort (Espinosa Mendoza et al. 2024). Analysis of the TCQ confirmed that, unlike standard high-intensity protocols associated with pain or discomfort, the ExoTMS treatment was well-tolerated and described as comfortable (Borckardt et al. 2006).

Notably, the improvement in sleep quality observed in subjects with a history of psychiatric disorders was comparable to that of the overall study population. This finding is clinically meaningful, as prior diagnoses such as PTSD or MDD are frequently associated with persistent or residual sleep disturbances, including insomnia, fragmented sleep, and trauma-related nightmares, even during clinical remission (Pruiksma et al. 2016; Zajecka 2013; Li et al. 2012). Such enduring sleep pathology is believed to reflect sustained alterations in arousal regulation and limbic-prefrontal circuity (Giudice et al. 2026). The observed treatment response, therefore, suggests that ExoTMS may modulate sleep-regulating neural networks despite underlying neurobiological vulnerability related to prior psychiatric illness (Pruiksma et al. 2016; Giudice et al. 2026; Geoffroy et al. 2014). These data support the potential clinical applicability of the intervention across populations with complex psychiatric histories. However, given the limited size of this subgroup, the findings should be interpreted with caution and require confirmation in larger, adequately powered cohorts designed to further elucidate the interaction between ExoTMS and chronic psychiatric vulnerability.

Several limitations should be considered. First, the relatively small sample size and unequal group distribution limit the generalizability, and reliance on self-reported measures precludes objective assessment of sleep architecture or neurophysiological changes. The study was not powered to detect between-group differences, therefore, comparisons between the active and sham groups should be interpreted as descriptive. Furthermore, uncontrolled external stressors may have influenced the observed outcomes. Concomitant use of sleep and stress supplements, including melatonin, herbal supplements, and cannabinoids, was reported by a subset of subjects throughout the study period and was not controlled for. Although supplement use appeared to decrease at follow-up in both groups, its potential influence on sleep outcomes cannot be excluded and should be considered when interpreting the results. Future studies should incorporate larger

sample sizes and objective sleep and neurophysiological measures to further characterize treatment effects.

Despite these limitations, the study possesses notable strengths, including the presence of a sham control group, assessment of outcomes at 3 months, and high tolerability. Together, these findings support further investigation of ExoTMS as a non-invasive approach for improving sleep quality in individuals with sleep disturbances.

Conclusion

These findings suggest that ExoTMS may represent a feasible non-invasive approach associated with improvements in subjective sleep quality and stress coping capacity in individuals with sleep disturbances. Subjects in the active group demonstrated sustained improvements in sleep quality and stress coping ability through the 3-month follow-up, with high tolerability. Together, these results support further investigation of ExoTMS in larger, controlled studies incorporating objective sleep and neurophysiological measures.

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Authors' contributions
All authors contributed to the study conception and design. Material preparation and data analysis were performed by Georgine Nanos. Data collection was performed by Georgine Nanos, Melinda Silva, and Charmi Patel. All authors have read and approved the final manuscript.

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Data availability
The datasets generated and/or analyzed during the study are not publicly available due to confidentiality reasons, but are available upon reasonable request from the corresponding author.

Declarations

Ethics approval and consent to participate
The study was conducted in accordance with the Declaration of Helsinki and was approved by the Institutional Review Board Advarra (Pro00083009). Informed consent was obtained from all individual participants included in the study.

Consent for publication
Each patient provided consent for publication and signed a written informed consent form.

Competing interests
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References

Borckardt JJ, Smith AR, Hutcheson K, Johnson K. Reducing pain and unpleasantness during repetitive transcranial magnetic stimulation. J ECT. 2006. https://doi.org/10.1097/01.yct.0000244248.40662.9a.

Cools R, Arnsten AFT. Neuromodulation of prefrontal cortex cognitive function in primates: the powerful roles of monoamines and acetylcholine. Neuropsychopharmacology. 2022;47(1):309–28. https://doi.org/10.1038/s41386-021-01100-8.

del Giudice R, Stefanelli R, Donati F, et al. Elevated gamma activity in left frontotemporal regions preceding sleep signals emotional arousal in Bipolar Disorders: insights from a high-density EEG investigation. J Affect Disord. 2026;394:120517. https://doi.org/10.1016/j.jad.2025.120517.

Ding X, He L, Kang T, et al. The role of the left dorsolateral prefrontal cortex in conflict control during insomnia disorder. J Psychiatr Res. 2024;171:271–6. https://doi.org/10.1016/j.jpsychires.2024.02.010.

dos Reis LD, Pereira Generoso L, Pereira GS, et al. Effects of multisession prefrontal cortex tDCS or taVNS on stress, perceived stress and sleep quality: a double-blind, randomized controlled study. Front Psychol. 2024. https://doi.org/10.3389/fpsyg.2024.1343413.

Espinosa Mendoza TA, Oviedo Lara AR, Henk Jordan G, Sampieri-Cabrera R, Perez Martinez LE. Effects of low-intensity transcranial magnetic stimulation in neuropsychological development of pediatric subjects with autism spectrum disorder: a longitudinal retrospective approach. Cureus. 2024. https://doi.org/10.7759/cureus.76569.

Feng J, Zhang Q, Zhang C, Wen Z, Zhou X. The effect of sequential bilateral low-frequency rTMS over dorsolateral prefrontal cortex on serum level of BDNF and GABA in patients with primary insomnia. Brain Behav. 2019;9(2):e01206. https://doi.org/10.1002/brb3.1206.

Feng Z, Li M, Zheng Y, Ping W, Zhou Z. Efficacy of low-frequency repetitive transcranial magnetic stimulation in the treatment of sleep disorders in the early stage of Parkinson disease: a single-center double-blind controlled study. Medicine (Baltimore). 2025;104(38):e44780. https://doi.org/10.1097/MD.0000000000044780.

Gao J, Zhang L, Zhu J, et al. Prefrontal cortex hemodynamics and functional connectivity changes during performance working memory tasks in older adults with sleep disorders. Brain Sci. 2023. https://doi.org/10.3390/brainsci13030497.

Geoffroy PA, Boudebesse C, Bellivier F, et al. Sleep in remitted Bipolar Disorder: a naturalistic case-control study using actigraphy. J Affect Disord. 2014;158:1–7. https://doi.org/10.1016/j.jad.2014.01.012.

Giblin MJ, Clift AD. Sleep without drugs. J R Coll Gen Pract. 1983;33(255):628–33.

Gutiérrez-Romero SA, Torres-Narváez ES, Zamora-Gómez AC, et al. Effect of a nutraceutical combination on sleep quality among people with impaired sleep: a randomised, placebo-controlled trial. Sci Rep. 2024;14(1):8062. https://doi.org/10.1038/s41598-024-58661-z.

Herrero Babiloni A, Bellemare A, Beetz G, et al. The effects of non-invasive brain stimulation on sleep disturbances among different neurological and neuropsychiatric conditions: a systematic review. Sleep Med Rev. 2021;55:101381. https://doi.org/10.1016/j.smrv.2020.101381.

Kim SY, Lee KH, Lee H, et al. Neural activation underlying emotional interference of cognitive control in rotating shift workers: moderating effects of the prefrontal cortex response on the association between sleep disturbance and depressive symptoms. Sleep. 2022;45(11):zsac219. https://doi.org/10.1093/sleep/zsac219.

Lanza G. Repetitive TMS for sleep disorders: are we ready? Sleep Med. 2020. https://doi.org/10.1016/j.sleep.2020.03.001.

Lanza G, Fisicaro F, Cantone M, et al. Repetitive transcranial magnetic stimulation in primary sleep disorders. Sleep Med Rev. 2023;67:101735. https://doi.org/10.1016/j.smrv.2022.101735.

Li SX, Lam SP, Chan JWY, Yu MWM, Wing YK. Residual sleep disturbances in patients remitted from Major Depressive Disorder: a 4-year naturalistic follow-up study. Sleep. 2012;35(8):1153–61. https://doi.org/10.5665/sleep.2008.

Lo Martire V, Caruso D, Palagini L, Zoccoli G. Stress & sleep: a relationship lasting a lifetime. Neurosci Biobehav Rev. 2020. https://doi.org/10.1016/j.neubiorev.2019.08.024.

Longo UG, Berton A, De Salvatore S, et al. Minimal clinically important difference and patient acceptable symptom state for the Pittsburgh Sleep Quality Index in patients who underwent rotator cuff tear repair. Int J Environ Res Public Health. 2021;18(16):8666. https://doi.org/10.3390/ijerph18168666.

Madari S, Golebiowski R, Mansukhani MP, Kolla BP. Pharmacological management of insomnia. Neurotherapeutics. 2021;18(1):44–52. https://doi.org/10.1007/s13311-021-01010-z.

Magyarová E, Albrecht J, Buday J, Mareš T, Jirečková G, Anders M. Treatment of sleep disorders with repetitive transcranial magnetic stimulation. Cesk Slov Neurol Neurochir. 2023;86(6):375–82. https://doi.org/10.48095/cccsnn2023375.

Minichino A, Bersani FS, Spagnoli F, et al. Prefronto-cerebellar transcranial direct current stimulation improves sleep quality in euthymic Bipolar patients: a brief report. Behav Neurol. 2014;2014(1):876521. https://doi.org/10.1155/2014/876521.

Morin CM. Issues and challenges in implementing clinical practice guideline for the management of chronic insomnia. J Sleep Res. 2017. https://doi.org/10.1111/jsr.12639.

Potthoff J, Schienle A. Effects of (non)deceptive placebos on reported sleep quality and food cue reactivity. J Sleep Res. 2024;33(2):e13947. https://doi.org/10.1111/jsr.13947.

Pruiksma KE, Taylor DJ, Wachen JS, et al. Residual sleep disturbances following PTSD treatment in active duty military personnel. Psychol Trauma. 2016;8(6):697–701. https://doi.org/10.1037/tra0000150.

Pulopulos MM, Schmausser M, De Smet S, et al. The effect of HF-rTMS over the left DLPFC on stress regulation as measured by cortisol and heart rate variability. Horm Behav. 2020;124:104803. https://doi.org/10.1016/j.yhbeh.2020.104803.

Shahid A, Wilkinson K, Marcu S, Shapiro CM. Pittsburgh Sleep Quality Index (PSQI). In: Shahid A, Wilkinson K, Marcu S, Shapiro CM, editors. STOP, THAT and one hundred other sleep scales. New York: Springer; 2011. p. 279–83. https://doi.org/10.1007/978-1-4419-9893-4_67.

Sharma R, Das K, Randhawa HBNS. Sleep quality and its effect on activities of daily living among substance dependent subjects. Delhi Psychiatry J. 2015;18:11.

Sheng R, Chen C, Chen H, Yu P. Repetitive transcranial magnetic stimulation for stroke rehabilitation: insights into the molecular and cellular mechanisms of neuroinflammation. Front Immunol. 2023. https://doi.org/10.3389/fimmu.2023.1197422.

Siebner HR, Funke K, Aberra AS, et al. Transcranial magnetic stimulation of the brain: what is stimulated? – A consensus and critical position paper. Clin Neurophysiol. 2022;140:59–97. https://doi.org/10.1016/j.clinph.2022.04.022.

Somaa FA, de Graaf TA, Sack AT. Transcranial magnetic stimulation in the treatment of neurological diseases. Front Neurol. 2022. https://doi.org/10.3389/fneur.2022.793253.

Sun JJ, Liu XM, Shen CY, et al. Reduced prefrontal activation during verbal fluency task in chronic insomnia disorder: a multichannel near-infrared spectroscopy study. Neuropsychiatr Dis Treat. 2017;13:1723–31. https://doi.org/10.2147/NDT.S136774.

Sun N, He Y, Wang Z, Zou W, Liu X. The effect of repetitive transcranial magnetic stimulation for insomnia: a systematic review and meta-analysis. Sleep Med. 2021;77:226–37. https://doi.org/10.1016/j.sleep.2020.05.020.

Vandekerckhove M, Cluydts R. The emotional brain and sleep: an intimate relationship. Sleep Med Rev. 2010;14(4):219–26. https://doi.org/10.1016/j.smrv.2010.01.002.

Xiao T, Zhu F, Wang D, Liu X, Xi SJ, Yu Y. Psychometric validation of the Perceived Stress Scale (PSS-10) among family caregivers of people with schizophrenia in China. BMJ Open. 2023;13(11):e076372. https://doi.org/10.1136/bmjopen-2023-076372.

Zajecka JM. Residual symptoms and relapse: mood, cognitive symptoms, and sleep disturbances. J Clin Psychiatry. 2013;74(Suppl 2):9–13. https://doi.org/10.4088/JCP.12084su1c.02.

Zhang J, Li X, Tang Z, et al. Effects of stress on sleep quality: multiple mediating effects of rumination and social anxiety. Psicol Reflex Crit. 2024;37(1):10. https://doi.org/10.1186/s41155-024-00294-2.

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