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CURRENT PRACTICE OF USING TMS AS AN ADJUNCT IN THE MANAGEMENT OF SLEEP APNEA: A SYSTEMATIC REVIEW

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ABSTRACT This systematic review evaluates the efficacy of transcranial magnetic stimulation (TMS) as an adjunctive tool in the management and treatment of sleep apnea. The study provides insights into applying TMS as a diagnostic and therapeutic intervention among physiotherapy professionals for individuals suffering from sleep apnea. A comprehensive review of databases including PubMed, ResearchGate, and Google Scholar was conducted for studies published between 2014 and 2023. A total of 28 articles were identified, out of which 6 met the inclusion criteria (3 focused on evaluation and 3 on treatment). Data extraction was guided by PRISMA guidelines, and quality was assessed using the PEDro scale. Findings from the reviewed articles suggest that TMS effectively reduces corticospinal excitability, leading to decreased activity in critical muscles such as the diaphragm, genioglossus, and tongue muscles. As a treatment modality, TMS was associated with improved cognitive function, highlighting its therapeutic potential. The review emphasizes TMS as a safe, non-invasive tool with applications in both motor and cognitive domains. TMS shows promising potential as an adjunctive approach in managing sleep apnea, warranting further large-scale studies to establish its efficacy and safety.

KEYWORDS : Transcranial Magnetic Stimulation, Sleep Apnea, Cognitive Function, Non-Invasive Therapy, Corticospinal Excitability

INTRODUCTION

Sleep apnea is a prevalent sleep disorder characterized by recurrent episodes of partial or complete obstruction of the airway, leading to intermittent hypoxia and fragmented sleep patterns [1]. Affecting millions worldwide, obstructive sleep apnea (OSA) has significant implications for cardiovascular, metabolic, and cognitive health, contributing to increased morbidity and mortality rates [2]. Despite advancements in therapeutic modalities, conventional treatment options such as continuous positive airway pressure (CPAP) often encounter limitations, including poor patient compliance and comfort [3]. This has prompted a growing interest in exploring adjunctive and innovative approaches for managing OSA, one of which is transcranial magnetic stimulation (TMS).

TMS, a non-invasive neuromodulation technique, has emerged as a promising tool in various neurological and psychiatric conditions, including depression, chronic pain, and stroke rehabilitation [4]. It involves the application of electromagnetic pulses to specific regions of the brain to modulate cortical activity. Recent evidence suggests that TMS may have therapeutic potential in addressing OSA, particularly in targeting corticospinal excitability and enhancing the neuromuscular control of upper airway muscles [5]. By facilitating changes in motor cortex function, TMS holds the promise of complementing existing therapies to improve airway patency and mitigate the cognitive deficits commonly associated with sleep apnea [6].

The pathophysiology of OSA is multifactorial, involving an interplay between anatomical, neurological, and functional components. The collapse of the pharyngeal airway during sleep is exacerbated by the reduced activity of dilator muscles, such as the genioglossus and diaphragm, contributing to airflow obstruction [7]. Neuroplasticity plays a critical role in the adaptive and maladaptive responses of the central nervous system to these physiological disturbances. Studies have demonstrated that OSA patients exhibit altered corticospinal excitability and impaired motor control, which may be amenable to intervention through neuromodulatory techniques like TMS [8]. This approach not only addresses the neuromuscular deficits but also offers potential cognitive benefits by improving cortical connectivity and executive function [9].

Current evidence for TMS in OSA remains limited but compelling. Early studies have highlighted its efficacy in reducing corticospinal excitability, which correlates with a decrease in pharyngeal collapsibility and improved respiratory stability [10]. Additionally, TMS has shown promise in alleviating the cognitive impairments commonly reported in OSA patients, such as memory deficits and reduced attention span [11]. These findings underscore the dual role of TMS in addressing both the respiratory and neurocognitive dimensions of the disorder. Importantly, TMS is a safe, non-invasive, and well-tolerated intervention, making it a suitable candidate for long-term management of chronic conditions like OSA [12].

In clinical practice, the integration of TMS as an adjunctive modality requires a deeper understanding of its mechanisms of action, optimal parameters, and therapeutic outcomes. Unlike traditional therapies that primarily focus on mechanical airway patency, TMS offers a neuromodulatory perspective that targets the root causes of impaired muscle activation and cortical dysfunction in OSA [13]. This novel approach aligns with the growing emphasis on precision medicine, which advocates for tailored interventions based on individual pathophysiology and clinical profiles [14]. Moreover, the versatility of TMS in modulating different cortical areas opens avenues for personalized therapy, addressing the diverse needs of OSA patients [15].

The application of TMS in OSA also raises important questions regarding its feasibility, cost-effectiveness, and integration into existing treatment paradigms. While initial studies have demonstrated promising results, larger randomized controlled trials are needed to establish its efficacy and long-term benefits [16]. The standardization of stimulation protocols, including frequency, intensity, and duration, remains a critical challenge in translating research findings into clinical practice [17]. Furthermore, the potential synergistic effects of combining TMS with conventional therapies such as CPAP or mandibular advancement devices warrant exploration to optimize therapeutic outcomes [18].

In addition to its therapeutic implications, TMS offers valuable insights into the neurophysiological underpinnings of OSA. By mapping cortical excitability and connectivity, TMS can serve as an evaluation tool to identify OSA severity [19]. This dual evaluation and therapeutic capability underscores the transformative potential of TMS in reshaping the management of sleep apnea. However, addressing the gaps in knowledge and overcoming logistical barriers are essential to realize its full potential [20].

TMS represents a novel and promising adjunctive intervention for managing OSA, with potential benefits extending beyond respiratory stability to cognitive enhancement and neuroplasticity. As a non-invasive and versatile modality, it aligns with the evolving paradigm of precision medicine and holds the potential to complement existing therapies in addressing the multifaceted challenges of OSA. This systematic review aims to provide a comprehensive evaluation of the current evidence on TMS in OSA, focusing on its efficacy, safety, and integration into clinical practice.

Methodology

Search Strategy

A comprehensive literature search was conducted to identify relevant studies evaluating transcranial magnetic stimulation (TMS) as an adjunct in managing obstructive sleep apnea (OSA). The search included peer-reviewed articles published between 2014 and 2023 across databases such as PubMed, Google Scholar, and ResearchGate. Keywords used in the search included combinations of "transcranial magnetic stimulation," "sleep apnea," "obstructive sleep apnea," "TMS in sleep disorders," "neuromodulation," and "airway patency." Boolean operators (AND, OR) were applied to refine the search strategy. Articles published in the English language were included to ensure accessibility and clarity.

Inclusion And Exclusion Criteria

Studies were included based on the following criteria:

- **Study Type:** Randomized controlled trials (RCTs) and crossover trials.
- **Population:** Adult patients diagnosed with obstructive sleep apnea (OSA) using standardized diagnostic criteria, such as polysomnography.
- **Intervention:** Use of TMS either as an evaluation or therapeutic tool in managing OSA.
- **Outcome Measures:** Polysomnography (EEG, EOG, EMG, flow sensor, and oximetry), Pnematochrograph.
- **Publication Timeline:** Studies published between 2014 and 2023.

Exclusion Criteria Included:

- Studies focusing exclusively on central sleep apnea or other sleep disorders without mentioning OSA.
- Non-human studies or experimental models.
- Non-peer-reviewed articles, conference abstracts, or review papers.

Study Selection

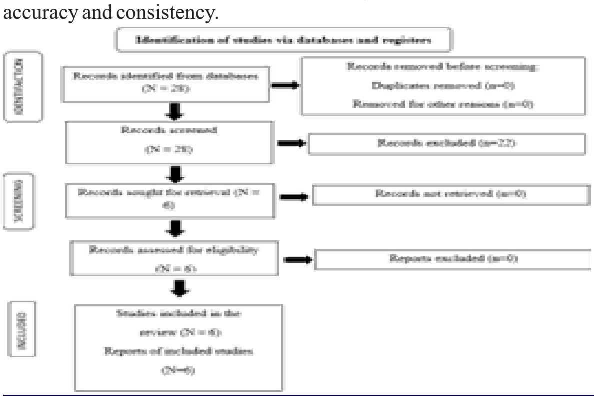
The study selection process adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. After removing duplicates, titles and abstracts of all identified studies were screened independently by two reviewers. Full-text articles of potentially eligible studies were retrieved and assessed for inclusion using the predefined criteria. Discrepancies in selection were resolved through discussion and, when necessary, consultation with a third reviewer.

Data Extraction

Data extraction was performed independently by two reviewers using a standardized data extraction form. Extracted data included:

1. Study design and year of publication.
2. Sample size and demographic characteristics of participants.
3. Details of TMS intervention, including parameters (e.g., frequency, intensity, duration).
4. Outcome measures (e.g., improvement in airway patency, changes in corticospinal excitability, cognitive improvements).
5. Results and conclusions.
6. Assessment of risk bias and study quality.

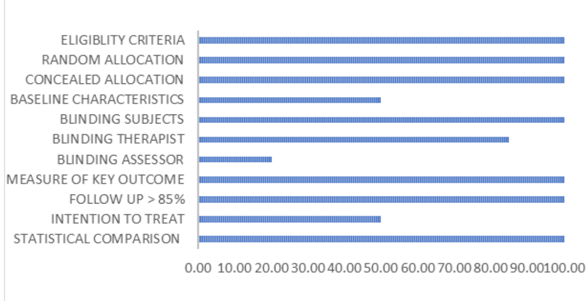
The extracted data were cross-verified by the reviewers to ensure accuracy and consistency.



Risk Of Bias And Quality Assessment

The methodological quality of included studies was assessed using the PEDro scale, a reliable tool for evaluating the quality of randomized controlled trials. This assessment involved scoring studies based on 11 criteria, including randomization, allocation concealment, blinding, and follow-up rates. Studies scoring ≥6 were considered of high quality. Two reviewers independently analyzed risk of bias across studies, and disagreements were resolved through discussion.

PEDro Rating: 2 trials (9 – 10) – Excellent and 4 trials (6 – 8) – Good



Data Synthesis

A narrative synthesis of the findings was conducted due to the heterogeneity in study designs, interventions, and outcome measures. Key findings were grouped into two categories:

1. TMS as an Evaluation Tool: Studies that investigated the effects of TMS on corticospinal excitability, muscle activity, and diagnostic insights.

2. TMS as a Treatment Tool: Studies assessing the therapeutic effects of TMS on improving respiratory stability, airway patency, and cognitive function.

Where appropriate, descriptive statistics were reported, and the trends in findings were summarized to provide a comprehensive understanding of TMS's role in OSA management.

RESULTS

A total of 6 studies published between 2015 and 2023 were included in the final analysis. These studies explored the application of single-pulse, paired-pulse, or repetitive transcranial magnetic stimulation (rTMS) in patients with obstructive sleep apnea (OSA). Study designs included observational, interventional, and exploratory physiological studies.

Cortical Excitability And Inhibition In OSA

Two studies evaluated cortical excitability and inhibition in individuals with OSA using TMS:

- **Borel et al. (2016)** investigated corticomotor excitability of the diaphragm and genioglossus muscles in response to hypercapnia. No significant differences in excitability were observed between OSA patients and healthy controls, suggesting preserved responsiveness to CO_2 in this population.
- **Rogić Vidaković et al. (2020)** used navigated TMS (nTMS) with MRI guidance to assess resting motor threshold (RMT) and short-latency afferent inhibition (SAI). OSA patients exhibited impaired afferent inhibition and elevated RMT, confirming cortical sensory-motor integration deficits.

These findings collectively support altered cortical excitability and impaired inhibition mechanisms in OSA, which may reflect compensatory or pathological adaptations in central motor pathways.

Effects Of TMS On Upper Airway Muscle Control

Three studies investigated whether TMS or rTMS could improve upper airway motor control or dynamics in OSA patients:

- **Rousseau et al. (2015)** assessed the mechanical effects of rTMS on upper airway muscle function during wakefulness. Although corticomotor facilitation during expiration was observed, rTMS did not significantly improve inspiratory flow or upper airway mechanics.
- **Rousseau et al. (2016)** extended their work into NREM sleep and found that rTMS during sleep did not improve inspiratory flow in flow-limited breaths. Notably, rTMS did not trigger arousals in most subjects, suggesting tolerability during sleep.
- **Iida et al. (2020)** examined the effect of a jaw protrusion training task on corticomotor excitability of the masseter and tongue

muscles. The training induced neuroplastic changes as evidenced by increased motor-evoked potentials, suggesting that task-specific orofacial training may enhance upper airway muscle control.

These studies indicate that while rTMS alone may not improve airway patency during sleep, it can enhance corticomotor responsiveness and could support adjunct behavioral or physical therapy strategies.

Cognitive Function And Cortical Oscillations

One study explored the neurocognitive effects of TMS in OSA:

Han et al. (2023) applied rTMS to the left dorsolateral prefrontal cortex (DLPFC) and assessed its impact on cognitive performance and EEG oscillations. TMS was associated with significant improvements in attention, working memory, and visual memory. EEG analysis revealed modulation of cortical oscillations post-intervention, suggesting enhanced neurocognitive processing.

This study supports the potential role of TMS in ameliorating the cognitive impairments commonly associated with OSA, likely through modulation of prefrontal cortical networks.

Domain	Key Findings
Cortical Excitability	Altered motor cortex inhibition and impaired afferent inhibition in OSA; possible biomarkers for disease.
Motor Function	rTMS alone does not improve upper airway mechanics during sleep but can facilitate motor cortex activation.
Neuroplasticity	Jaw protrusion training enhanced corticomotor excitability, indicating neuroplastic potential in OSA therapy.
Cognition	TMS improved cognitive function and modulated EEG activity, indicating therapeutic value beyond respiratory function.

DISCUSSION

This systematic review evaluates the role of transcranial magnetic stimulation (TMS) in the management of obstructive sleep apnea (OSA), a chronic condition marked by recurrent upper airway (UA) obstruction during sleep. By synthesizing evidence from recent studies, we examine the neuromodulatory mechanisms of TMS and its potential for influencing both physiological and cognitive aspects of OSA. The findings offer valuable insights into the utility of TMS as both a diagnostic and therapeutic modality.

Cortical Excitability in OSA

Altered cortical excitability has emerged as a characteristic neurophysiological feature of OSA. Lanza et al. (2015) reported that OSA patients exhibit heightened motor cortex inhibition relative to individuals with other sleep disorders, such as restless legs syndrome and insomnia. This increased inhibitory tone may reflect maladaptive plasticity resulting from chronic intermittent hypoxia and disrupted sleep architecture. Such changes may compromise the central regulation of UA dilator muscles, thereby contributing to airway collapsibility during sleep. These findings underscore the potential of TMS to modulate abnormal cortical excitability in OSA patients.

TMS and Upper Airway Muscle Function

The mechanical influence of repetitive TMS (rTMS) on UA muscle function has been explored in both wakefulness and sleep. Rousseau et al. (2015) found that rTMS did not significantly improve UA mechanical properties during wakefulness, but it did facilitate corticomotor activity, particularly during expiration. This suggests a priming effect on UA dilator muscles, which, while insufficient as a standalone intervention, could enhance the efficacy of adjunctive therapies such as continuous positive airway pressure (CPAP) or mandibular advancement devices (MADs).

In a complementary study, Borel et al. (2016) investigated the effects of hypercapnic stimulation on the corticomotor excitability of the diaphragm and genioglossus muscles in OSA patients. While CO_2 stimulation normalized diaphragmatic responsiveness, it failed to restore genioglossus excitability, indicating a selective impairment in UA muscle control. These findings support the hypothesis that targeted neuromodulation using TMS could potentially restore balance in respiratory muscle activation pathways.

Repetitive TMS During Sleep

Extending their investigation into the sleep state, Rousseau et al. (2016) examined the effects of rTMS on UA function during non-REM sleep. Although rTMS did not yield consistent improvements in airflow among OSA patients, it did not provoke cortical or autonomic arousals, highlighting its safety and tolerability during sleep. This is clinically relevant, as minimizing sleep fragmentation is critical in OSA management. The findings suggest that while rTMS may be safely administered during sleep, further optimization of stimulation parameters—such as intensity, frequency, and duration—is necessary to achieve therapeutic benefits.

Neuroplasticity And TMS

TMS has shown promise in inducing neuroplastic changes relevant to OSA. Iida et al. (2020) investigated the effects of a jaw protrusion training task on corticomotor excitability. Their results demonstrated significant post-training increases in motor-evoked potentials in the masseter and tongue muscles. This supports the hypothesis that task-specific training, when paired with TMS, can enhance neural control of UA muscles. Such interventions could be integrated with mechanical therapies like MADs to improve functional outcomes, especially in patients with orofacial muscular deficits.

TMS and Cognitive Function in OSA

Cognitive dysfunction is a well-established consequence of OSA, frequently involving deficits in attention, memory, and executive functioning. These impairments are believed to stem from disrupted cortical connectivity and repeated hypoxic insult. Rogić Vidaković et al. (2020) utilized navigated TMS (nTMS) to assess cortical excitability and afferent inhibition, revealing reduced short-latency afferent inhibition (SAI) and increased motor thresholds in OSA patients. These markers of cortical dysfunction may serve both diagnostic and prognostic purposes.

Further supporting the cognitive potential of TMS, Han et al. (2023) demonstrated that stimulation of the dorsolateral prefrontal cortex (DLPFC) improved performance across multiple cognitive domains, including sustained attention, working memory, and visual memory. These improvements were accompanied by increased theta and beta EEG oscillatory activity, indicative of enhanced cortical connectivity. These findings highlight TMS as a promising strategy for addressing neurocognitive sequelae in OSA, particularly in patients with prominent cognitive complaints.

Challenges

Despite the promising findings, several challenges remain in integrating TMS into routine OSA care. First, the variability in stimulation parameters across studies highlights the need for standardized protocols to optimize efficacy. For instance, differences in frequency, intensity, and duration of stimulation may account for the inconsistent results observed in studies such as Rousseau et al. (2016) [24]. Future research should focus on identifying the most effective stimulation parameters for different patient subgroups.

Second, the combination of TMS with existing therapies, such as CPAP or behavioral interventions, has not been extensively studied. Given the priming effects of rTMS on UA muscles observed by Rousseau et al. (2015) [22], exploring synergistic approaches could yield better outcomes. Similarly, integrating TMS with cognitive behavioral therapy (CBT) may enhance cognitive recovery in OSA patients with significant neurocognitive impairments.

Third, the cost and accessibility of TMS remain barriers to widespread adoption. While studies such as Han et al. (2023) [27] demonstrate its potential benefits, the economic feasibility of incorporating TMS into clinical practice needs to be evaluated. Addressing these challenges will require collaborative efforts between researchers, clinicians, and policymakers.

Clinical Implications

The integration of transcranial magnetic stimulation (TMS) into the clinical management of obstructive sleep apnea (OSA) offers significant potential for improving outcomes. Studies by Lanza et al. (2015) [21] and Rousseau et al. (2015) [22] demonstrate that TMS can modulate corticospinal excitability, offering a novel approach to addressing upper airway collapsibility—a hallmark of OSA. Lanza et al. (2015) [21] emphasized TMS's ability to highlight distinct cortical excitability profiles, which can guide personalized treatment plans. Meanwhile, studies such as Han et al. (2023) [27] suggest that TMS can also target the cognitive deficits often associated with OSA, such as memory and executive function impairment. These findings underline TMS's dual therapeutic and diagnostic value in OSA care.

Clinically, TMS may serve as an adjunct to conventional treatments like continuous positive airway pressure (CPAP) or mandibular advancement devices. Studies by Rousseau et al. (2015) [22] and Iida et al. (2020) [25] suggest that TMS-induced neuroplasticity could improve upper airway muscle responsiveness and cortical connectivity, thereby complementing mechanical therapies. Additionally, its application in cognitive rehabilitation, as shown by Han et al. (2023) [27], could address a key unmet need in OSA patients with persistent neurocognitive dysfunction.

However, clinical translation requires standardized protocols for stimulation parameters. Current studies, such as Rousseau et al. (2016) [24], report variability in outcomes based on frequency and intensity, making it crucial to establish optimized TMS protocols tailored to OSA's pathophysiology.

CONCLUSION

This systematic review highlights the potential of transcranial magnetic stimulation (TMS) as a promising adjunctive tool in the management of obstructive sleep apnea (OSA). TMS has demonstrated the ability to modulate corticospinal excitability, improve upper airway muscle function, and enhance cognitive performance in OSA patients. It offers a non-invasive and safe intervention that addresses both the respiratory and neurocognitive deficits associated with the disorder.

By targeting the pathophysiological mechanisms of OSA, such as impaired upper airway muscle activity and reduced cortical plasticity, TMS provides a novel therapeutic approach. Furthermore, its ability to improve cognitive outcomes, including working memory, attention, and executive function, highlights its broader clinical relevance. These dual benefits position TMS as a valuable addition to traditional therapies for OSA.

However, significant challenges remain in translating these findings into routine clinical practice. Variability in stimulation protocols, small sample sizes, and a lack of long-term data limit the generalizability of current evidence. Additionally, the potential for combining TMS with existing treatments, such as continuous positive airway pressure (CPAP) or mandibular advancement devices, has yet to be fully explored. Addressing these limitations is critical to unlocking the full potential of TMS.

Future research should focus on large-scale, randomized controlled trials to validate its efficacy and safety across diverse populations. Standardizing stimulation protocols and conducting longitudinal studies will be essential to determine the sustainability of TMS-induced improvements. Furthermore, exploring the synergistic effects of combining TMS with conventional therapies could enhance its clinical utility.

In conclusion, TMS offers a promising and innovative approach to managing OSA by addressing both its physiological and neurocognitive dimensions. With further research and optimization, TMS has the potential to become a transformative tool in the comprehensive care of OSA patients.

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