The effectiveness of repetitive transcranial magnetic stimulation (rTMS) on improving sleep quality in adults without serious mental illness

Repetitive Transcranial Magnetic Stimulation (rTMS) is a non-invasive brain stimulation technique that uses magnetic fields to modulate neural activity in targeted brain regions. Over the years, rTMS has shown promise in treating various mental health conditions, including depression[1,2], obsessive-compulsive disorder (OCD)[3,4] and clinical insomnia[5,6,7].

Sleep is a fundamental component of overall health and well-being, playing a crucial role in cognitive function, emotional regulation, and physical health. However, sleep complaints are common, even among otherwise healthy adults, often leading to reduced quality of life and increased health risks. The prevalence of poor sleep quality can be attributed to a variety of factors, including stress, lifestyle habits, and environmental disturbances.

Prior research on rTMS and sleep has primarily focused on clinical populations, particularly individuals with insomnia or sleep disorders comorbid with other health conditions. While these studies have provided valuable insights, there is a burgeoning interest in exploring the effects of rTMS on sleep quality in the general population, specifically targeting those who report sleep complaints but do not meet the criteria for clinical insomnia.

This research proposal aims to investigate the effects of rTMS on sleep quality among healthy adults experiencing subclinical sleep issues. By focusing on this population, we hope to uncover the potential of rTMS as a preventive intervention, offering individuals a non-pharmacological option to enhance sleep without the side effects often associated with sleep medications.

Understanding the impact of rTMS on sleep in this demographic could pave the way for larger-scale studies and clinical applications, ultimately contributing to better sleep hygiene and enhanced quality of life for those affected by sleep complaints.

Methodology

Study Design

This open-label pilot study aims to evaluate the effectiveness of repetitive transcranial magnetic stimulation (rTMS) in improving sleep quality among healthy adults with sleep complaints.

An existing literature studying the effects of rTMS on sleep quality and mood in patients with major depressive disorder with similar outcome measures, has sample size of 21. Thus, this study will enrol 30 participants who meet the inclusion criteria.

Participants

30 participants will be recruited from the community through advertisement including universities based on the following criteria:

- Healthy adults aged 18-65
- self-reported sleep complaints

Exclusion criteria include serious mental illness other than primary insomnia, severe neurological conditions, and contraindications for rTMS.

Hypothesis

rTMS significantly improves sleep quality among healthy adults experiencing subclinical sleep issues.

Intervention setting

Participants will undergo a treatment protocol involving six sessions of rTMS using the EXOMIND™ device, administered once or twice a week. Each session will deliver 6,300 pulses at alternating frequencies of 12, 15, and 18 Hz, with a total duration of 24 minutes and 30 seconds. The target site would be left dorsolateral prefrontal cortex (DLPFC), determined by the most common used 5-cm rule. The procedure would be conducted in our research centre with medical staff supported.

Baseline Assessments

The subjects' basic demographic data, including age, gender, years of education, place of birth, marital status, number of children, financial condition, household income, family history of sleep difficulties will be collected upon study entry. Medical history in relation to mental illnesses and medications will also be assessed.

Outcome Measures

Assessments will be conducted at three time points: baseline (pre-intervention), post-intervention, and four weeks post-intervention.

Primary Outcome

Pittsburgh Sleep Quality Index (PSQI): Measures overall sleep quality.

Secondary Outcomes

- Perceived Stress Scale (PSS): Evaluates perceived stress levels.
- Patient Health Questionnaire-9 (PHQ-9): Assesses depressive symptoms.
- Home sleep monitoring: Collects data on sleep duration and sleep stages.

Adverse effects

A checklist of potential adverse effects from TMS administration will be referenced from existing literature to monitor tolerability and adverse events during each session. Blood pressure and heart rate will be recorded at the beginning and end of each session.

Statistical Analysis

Data will be analysed using SPSS version 26.0 or a similar statistical software package.

All the descriptive data including the age and educations will calculate means and standard deviations for continuous variables and frequencies and percentages for categorical variables. Repeated measures ANOVA will be used to assess changes in PSQI scores across the three time points (baseline, post-intervention, and 4 weeks post-intervention). Paired t-tests will be conducted to evaluate changes in PSS and PHQ-9 scores, as well as sleep duration and sleep stages recorded by the Apple Watch, between baseline and post-intervention, and between baseline and 4 weeks post-intervention. A p-value of <0.05 will be considered statistically significant.

Impact of the study

This study contributes to the growing body of literature on non-pharmacological interventions for sleep improvement. By focusing on a non-clinical population, it expands the understanding of how rTMS can benefit individuals experiencing everyday sleep disturbances. Results could pave the way for integrating rTMS as a preventive intervention in clinical practice, offering an alternative to traditional sleep medications. This could be particularly beneficial for individuals who are sensitive to medication side effects or those who prefer non-drug therapies. As a pilot study, this research sets the groundwork for larger, more comprehensive trials. Positive findings could lead to further exploration of rTMS applications across different populations and settings, encouraging innovation in sleep disorder treatments.

Handling and storage of personal data and study data

Personal data will be anonymized and kept in password protected computers during and after the study; raw data will be anonymized and kept in locked rooms. Only principal investigator and authorized research assistants will have access to and are responsible for safekeeping of the stored data.

Personal data will be kept for 5 years after completion of study and publications to keep track on potential side effects related to the intervention, and will be destroyed after completion of publications.

Compliance with the ICH-GCP

This study complies with ICH-GCP.

Compliance with Declaration of Helsinki

It declares that the research was conducted according to ethical standards, including the Declaration of Helsinki and its amendments.

Funding

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Conflict of Interest Statement

There are no conflicts of interest regarding the use of the rTMS machine in this study that influenced the design, implementation, or interpretation of the research.

References

1. Sabé, Michel, et al. "Transcranial magnetic stimulation and transcranial direct current stimulation across mental disorders: a systematic review and dose-response meta-analysis." *JAMA network Open* 7.5 (2024): e2412616-e2412616.
2. Voineskos, Daphne, et al. "Neurophysiological effects of repetitive transcranial magnetic stimulation (rTMS) in treatment resistant depression." *Clinical Neurophysiology* 132.9 (2021): 2306-2316.
3. Fitzsimmons, Sophie MDD, et al. "Repetitive transcranial magnetic stimulation for obsessive-compulsive disorder: A systematic review and pairwise/network meta-analysis." *Journal of affective disorders* 302 (2022): 302-312.
4. Liang, Kaili, et al. "Efficacy and tolerability of repetitive transcranial magnetic stimulation for the treatment of obsessive-compulsive disorder in adults: a systematic review and network meta-analysis." *Translational psychiatry* 11.1 (2021): 332.
5. Zhu, Lin, et al. "Functional connectivity changes are correlated with sleep improvement in chronic insomnia patients after rTMS treatment." *Frontiers in Neuroscience* 17 (2023): 1135995.
6. Ma, Haixia, et al. "Effectiveness of TES and rTMS for the treatment of insomnia: meta-analysis and meta-regression of randomized sham-controlled trials." *Frontiers in psychiatry* 12 (2021): 744475.
7. Sun, Nianyi, et al. "The effect of repetitive transcranial magnetic stimulation for insomnia: a systematic review and meta-analysis." *Sleep Medicine* 77 (2021): 226-237.