Clinical Neurophysiology Practice 8 (2023) 194–196

Contents lists available at ScienceDirect

Clinical Neurophysiology Practice

journal homepage: www.elsevier.com/locate/cnp

Case report

Short-term effect of coil handle orientations on fMRI-guided rTMS on insomnia: A case report

Zi-Jian Feng [a,b,1], Qiu-Ying Song [c,1], Yu Han [b], Zi-Yu Wei [b], Cong Fu [a,*], Yu-Feng Zang [a,b,*]

[a] TMS Center, Deqing Hospital of Hangzhou Normal University, Deqing, China
[b] Center for Cognition and Brain Disorders, The Affiliated Hospital of Hangzhou Normal University, Hangzhou, China
[c] Department of Neurology, The Affiliated Hospital of Hangzhou Normal University, Hangzhou, China

ARTICLE INFO

Article history:
Received 3 August 2023
Accepted 10 August 2023
Available online 6 September 2023

Keywords:
Repetitive transcranial magnetic stimulation
Coil handle orientation
Resting-state functional magnetic resonance imaging
Functional connectivity-guided
Short-term effect
Insomnia

ABSTRACT

Introduction: The coil handle orientation plays a pivotal role in the therapeutic efficacy of repetitive transcranial magnetic stimulation (rTMS). However, there is currently no consensus on the optimal individualized coil handle orientation, especially for non-motor areas.

Case presentation: The present case reported a short-term effect of functional connectivity (FC)-guided rTMS with coil handle posterior-anterior 45° (PA45°) and posterior-anterior 135° (PA135°) on a patient with insomnia. Notably, in this case, the PA45° orientation was nearly perpendicular to the adjacent sulcus, while the PA135° orientation was almost parallel to it. Local brain activity and functional connectivity were assessed using resting-state functional magnetic resonance imaging (RS-fMRI). Additionally, motor evoked potentials (MEPs) were captured both pre and post-rTMS sessions.

Findings: The coil handle orientation PA45° outperformed the PA135° in both RS-fMRI and MEP outcomes. Moreover, a 9-day rTMS treatment led to discernible improvements in symptoms of depression and anxiety, complemented by a modest enhancement in sleep quality.

1. Introduction

Studies have suggested that insomnia and depression may share a common genetic background and biological mechanisms involving abnormal dorsolateral prefrontal cortex (DLPFC) activities. The FDA-approved Stanford Accelerated Intelligent Neuromodulation Therapy (SAINT) repetitive transcranial magnetic stimulation (rTMS) protocol has been effective in alleviating depression by targeting the area most anticorrelated with the subgenual anterior cingulate cortex (sgACC) within the DLPFC. In a recent study, researchers investigated the feasibility of SAINT protocol to patients with insomnia and reported improvements in sleep quality, depression, and anxiety symptoms following the treatment (Qi et al., 2022). Despite various clinical treatment methods proposing precise localization of individualized targets, the specific coil handle orientation during treatment has not been explicitly defined. Previous research has demonstrated that rTMS applied to the prefrontal cortex with varying coil handle orientations leads to distinct blood oxygenation changes (Thomson et al., 2013). However, there is currently no consensus on the optimal individualized coil handle orientation, especially for non-motor areas.

Here we reported a short-term effect of functional connectivity (FC)-guided rTMS with coil handle posterior-anterior 45° (i.e., occipital to forehead longitudinal fissure at 45° to coil handle, PA45°) and posterior-anterior 135° (PA135°) on an insomnia patient. In this patient, PA45° was nearly perpendicular to an adjacent sulcus, while PA135° was nearly parallel (Fig. 1A). Study approved by local ethics committees (Affiliated Hospital of Hangzhou Normal University) and registered at Chinese Clinical Trial Registry (ChiCTR2200060725).

2. Case presentation

The patient is a 32-year-old male outpatient who provided a written informed consent. He had been experiencing insomnia symptoms for over 2 years, primarily difficulty falling asleep each night without any medication. Clinical assessments were conducted before and after treatment, as well as during a one-month follow-up, including the 17-item Hamilton Depression Rating Scale

* Corresponding authors at: TMS Center, Deqing Hospital of Hangzhou Normal University, Deqing 313200, Zhejiang, China (C. Fu), Center for Cognition and Brain Disorders, The Affiliated Hospital of Hangzhou Normal University, Hangzhou 311121, Zhejiang, China (Y.-F. Zang).

E-mail addresses: 112022010391@mail.ccmu.edu.cn (C. Fu), zangyf@hznu.edu.cn (Y.-F. Zang).

[1] These authors have contributed equally to this work and share first authorship.

https://doi.org/10.1016/j.cnp.2023.08.004
2467-981X/

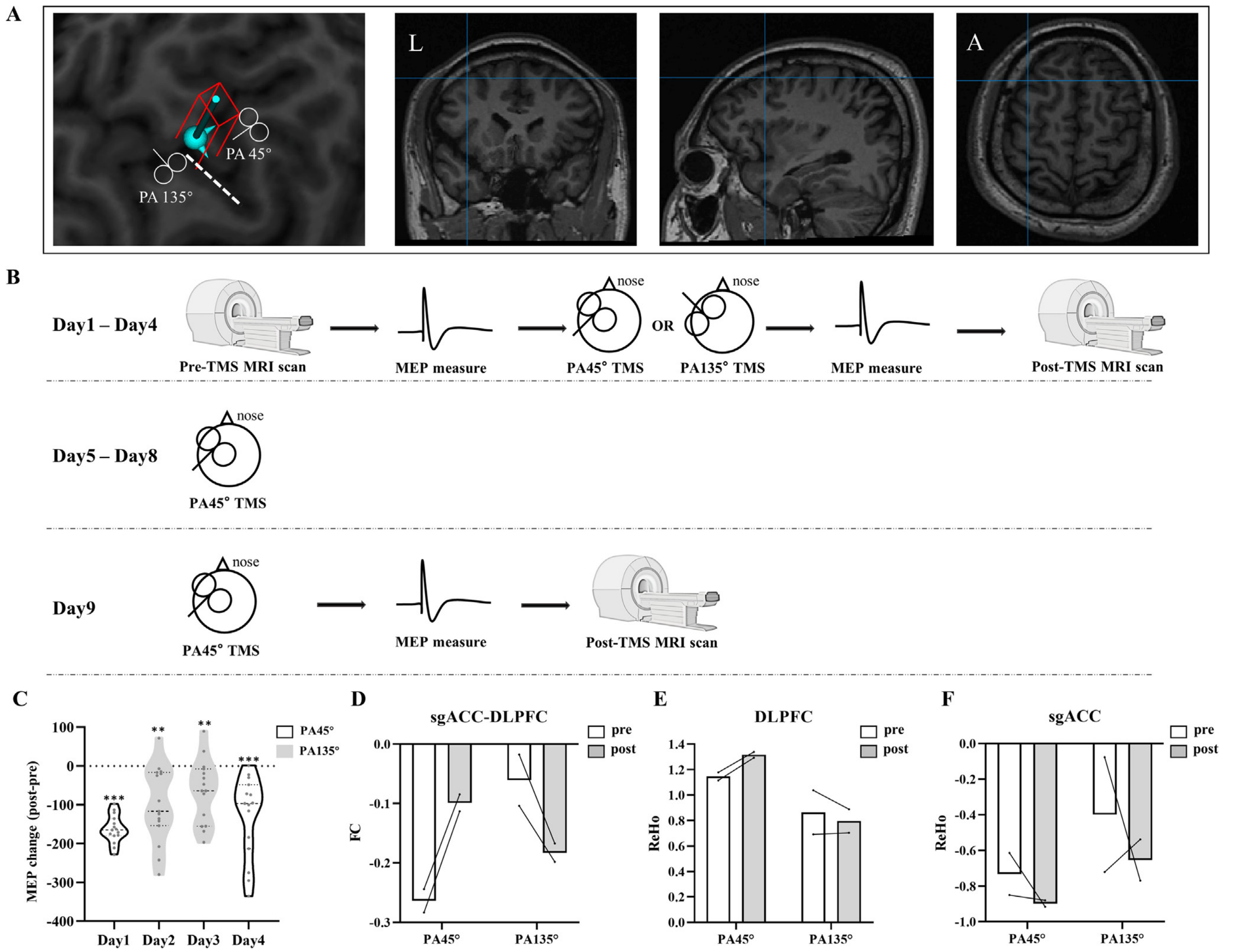

Fig. 1. Case protocol and results. (A) Stimulation target on the surface, along with the coronal, sagittal, and axial views. (B) Experimental protocol. (C) MEPs change after Day1 (PA45°), Day2 (PA135°), Day3 (PA135°) and Day4 (PA45°) TMS. (D) FC between DLPFC and sgACC in PA45° and PA135° TMS. (E) Pre-TMS and Post-TMS ReHo within DLPFC in PA45° and PA135°. (F) Pre-TMS and Post-TMS ReHo within sgACC in PA45° and PA135°. PA45°: occipital to forehead longitudinal fissure at 45° to coil handle; PA135°: occipital to forehead longitudinal fissure at 135° to coil handle; FC: functional connectivity; ReHo: regional homogeneity; DLPFC: dorsolateral prefrontal cortex; sgACC: subgenual anterior cingulate cortex. *** $p < 0.001$; ** $p < 0.01$.

(HAMD-17), the 14-item Hamilton Anxiety Rating Scale (HAMA-14), and the Pittsburgh Sleep Quality Index (PSQI). The patient's baseline scores for mood symptoms and sleep quality were as follows: HAMD 8, HAMA 11, and PSQI 15.

Intermittent theta-burst stimulation (iTBS) was administered by delivering 1,800 pulses at 90% of the resting motor threshold (RMT) daily for nine consecutive days to the left DLPFC. The stimulation was conducted using a MagStim Rapid2 system (Magstim Company Ltd., UK) with a 70-mm figure-8 coil, navigated by the neuro-navigation system (Brainsight, Rogue Research, Canada). The target for stimulation was determined by the maximum anti-correlation of the 5 mm sgACC seed (x = 0, y = 16, z = −10). During the first four days of stimulation, two coil handle orientations were alternated: PA45° and PA135°, while the remaining five days used PA45° exclusively. The RMT was determined based on evoked MEPs (>50 μV) in 5 out of 10 trials of the right first dorsal interosseous muscle (Fig. 1B).

The short-term effects of the stimulation were evaluated using three different assessments: MEPs to measure cortical excitability, FC to depict brain network integration, and regional homogeneity (ReHo) to reflect local brain activity. The results showed that both coil handle orientations reduced cortical excitability, with PA45° demonstrating a greater inhibitory effect than PA135° ($t = 3.10$, $p < 0.01$) (Fig. 1C). However, the effects on FC differed, with PA45° increasing sgACC-DLPFC FC and PA135° decreasing it (Fig. 1D). Moreover, ReHo in sgACC decreased significantly after PA45°, while the changes in ReHo were irregular after PA135°. In the DLPFC target, ReHo tended to increase after PA45°, but the changes were irregular after PA135° (Fig. 1E, 1F).

The sgACC-DLPFC FC-guided rTMS treatment significantly improved depression and anxiety over 9 days, with sustained benefits at the one-month follow-up. HAMD scores reduced from 8 to 6, and HAMA scores decreased from 11 to 8 immediately after treatment, both further decreasing to 6 at one month. Despite a slight improvement in the PSQI score (15 to 13), the patient still reported poor sleep quality. Additionally, MEPs significantly decreased after the 9-day rTMS treatment ($t = 12.6$, $p < 0.001$). RS-fMRI revealed decreased ReHo in both sgACC (from −0.85 to −1.13) and DLPFC (from 1.18 to 0.81), while sgACC-DLPFC FC increased after treatment (−0.24 to −0.09).

3. Discussion

This study is the first to investigate the brain mechanism of different coil handle orientations of rTMS guided by RS-fMRI FC.

Direction-specific effects play a crucial role in axonal depolarization, particularly in the motor area, where the impact of rTMS can be observed through the MEPs, showing significantly higher for PA45° compared to PA135°. However, there is a lack of clear evidence for different coil handle orientations in non-motor regions such as the DLPFC, one of the most commonly stimulated targets of rTMS. A previous review study reported inconsistent trends in MEP changes when rTMS targets the DLPFC (Nordmann et al., 2015), which may be attributed to the variability in coil handle orientations. Therefore, future research that controls for coil handle orientation is likely to advance our understanding of rTMS plasticity mechanisms.

Our RS-fMRI study yielded intriguing results on the effects of different coil handle orientations during rTMS. Specifically, PA45° rTMS increased sgACC-DLPFC FC, while PA135° led to a decrease. Interestingly, administering a nine-day treatment resulted in an overall increase in sgACC-DLPFC FC. These findings highlight the critical role of coil handle orientation in the direction of FC alterations induced by rTMS. A systematic review emphasized significant heterogeneity in FC changes after rTMS, even with the same target, frequency, and population, underscoring the urgent need to consider coil handle orientation in clinical rTMS research (Beynel et al., 2020). Furthermore, our observation of decreased ReHo of sgACC after PA45° rTMS supports the potential of rTMS in directly modulating diseases with abnormal deep brain region activity, as previously noted in our dACC-DLPFC FC-guided rTMS study (Feng et al., 2022).

To conclude, we revealed that the PA45° coil orientation outperformed the PA135° in both RS-fMRI and MEP measures. While the patient exhibited improvements in depression, anxiety, and slight sleep quality after nine days of rTMS treatment, the low dosage of rTMS may have limited the extent of sleep improvement. Further replication and extended follow-up are needed to explore the physical, neuropsychological, and molecular effects of TMS on insomnia.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

References

Beynel, L., Powers, J.P., Appelbaum, L.G., 2020. Effects of repetitive transcranial magnetic stimulation on resting-state connectivity: A systematic review. Neuroimage 211, 116596.

Feng, Z.J., Deng, X.P., Zhao, N., Jin, J., Yue, J., Hu, Y.S., et al., 2022. Resting-state fMRI functional connectivity strength predicts local activity change in the dorsal cingulate cortex: A multi-target focused rTMS study. Cereb. Cortex 32 (13), 2773–2784.

Nordmann, G., Azorina, V., Langguth, B., Schecklmann, M., 2015. A systematic review of non-motor rTMS induced motor cortex plasticity. Front. Hum. Neurosci. 9, 416.

Qi, S., Zhang, Y., Li, X., Sun, C., Ma, X., Li, S., et al., 2022. Improved functional organization in patients with primary insomnia after individually-targeted transcranial magnetic stimulation. Front. Neurosci. 16, 859440.

Thomson, R.H., Cleve, T.J., Bailey, N.W., Rogasch, N.C., Maller, J.J., Daskalakis, Z.J., et al., 2013. Blood oxygenation changes modulated by coil orientation during prefrontal transcranial magnetic stimulation. Brain Stimul. 6 (4), 576–581.