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CASE REPORTS

Transcranial magnetic stimulation combined with transcranial direct current stimulation in patients with chronic insomnia: a case report

Qi Zhou, MD[1]; Zhiwang Liu, BA[1]; Shengnan Zhao, MD[1]; Jia Yu, BA[1]; Dongsheng Zhou, MD[1]; Weiqian Xu, BA[2]; Yuanyuan Zhang, MD[1]

[1]Department of Psychiatry, Ningbo Kangning Hospital, Affiliated Mental Health Center of Ningbo University, Ningbo, Zhejiang, China; [2]Taizhou Second People's Hospital, Taizhou, Zhejiang, China

Long-term insomnia affects the normal life and work of individuals and increases the risk of various health problems, including mental illness. Therefore, there is an urgent need for an efficient and safe treatment for improving sleep. In this study, we report the case a 52-year-old woman who received repetitive transcranial magnetic stimulation (rTMS) combined with transcranial direct current stimulation (tDCS) after agreeing to publish her case. In order to evaluate the quality of sleep and the stability of emotional symptoms, clinical evaluations were conducted at baseline, after 10 treatment sessions, after 20 treatment sessions, and 1 month after the end of treatment. After completing rTMS combined with tDCS, the patient showed an overall clinical improvement, with clinical changes mainly observed in the Pittsburgh Sleep Quality Index, Hamilton Depression Scale, Hamilton Anxiety Scale scores and polysomnography, and this improvement was maintained 1 month after the intervention. This case provides the first evidence for the feasibility, tolerability, and safety of combined rTMS and tDCS in a patient with chronic insomnia.

Clinical Trial Registration: Registry: Chinese Clinical Trial Registry; Name: Clinical study of repetitive transcranial magnetic stimulation combined with transcranial direct current stimulation in the treatment of chronic insomnia; URL: http://www.chictr.org.cn/edit.aspx?pid=57440&htm=4; Identifier: ChiCTR ChiCTR2100052681.

Keywords: transcranial magnetic stimulation, transcranial direct current stimulation, chronic insomnia, polysomnography

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INTRODUCTION

Insomnia is a subjective experience of dissatisfaction with one's sleep time and/or quality despite appropriate sleep opportunities and sleep environment, and it affects daytime social function. Chronic insomnia is defined as frequent nocturnal and daytime insomnia symptoms that persist for at least 3 months.[1] The incidence of chronic insomnia in the general population is approximately 6–10%.[2] Long-term insomnia affects the normal life and work of individuals and increases the risk of various health problems, including mental illness.[3,4] With the progress of modern society, people's work and life pressures are increasing, so the demand for high-quality sleep is also increasing. Therefore, there is an urgent need for an efficient and safe treatment for improving sleep.

Drug therapy and psychotherapy are the most common treatment modalities for chronic insomnia, but newer nondrug interventions, such as repetitive transcranial magnetic stimulation (rTMS) and transcranial direct current stimulation (tDCS), have shown promising results.[5,6] rTMS is a safe and noninvasive physical therapy technology for brain function intervention. rTMS treatment improves sleep quality by modulating neuronal excitability and affecting the metabolism of neurotransmitters in the brain.[7,8] tDCS effects on psychiatric disorders are the result of the induction of synaptic plasticity that occurs during and after treatment and modulates the dysfunctional neuroplasticity of these disorders.[9] For patients with long-term chronic insomnia, simple rTMS stimulation or simple tDCS stimulation have certain curative effects, but the onset is slow and the effect is not very satisfactory. Both rTMS stimulation and tDCS stimulation are used as physical therapy techniques, with different mechanisms of action. Therefore, it is considered to combine the 2 physiotherapies to explore the clinical efficacy of rTMS combined with tDCS in the treatment of insomnia.

Previous studies found that patients with insomnia exhibited increased cortical excitability, decreased intracortical facilitation, and cortical hyperarousal during wakefulness and sleep compared with healthy participants.[10] Therefore, we hypothesized that sleep can be improved by modulating the excitability of the cerebral cortex in an individual, but since physical therapy techniques are not widely used in sleep disorders, the optimal regimen for improving sleep is unknown.

REPORT OF CASE

In this study, we report the case of a 52-year-old woman who was diagnosed with insomnia according to *International Classification of Sleep Disorders*, third edition, criteria for more than 10 years. In the past 3 years, the patient has repeatedly experienced difficulty in falling asleep, poor sleep quality, irritability, palpitations, restlessness, lack of energy during the day, and fatigue, with no mental or nervous system complications.

Table 1—Clinical outcomes.

	Baseline	Day 10	Day 20	Day 50
PSQI total score	20	14	9	8
Sleep quality	3	2	1	1
Sleep latency	3	2	1	0
Sleep duration	3	2	1	1
Sleep efficiency	3	2	2	2
Sleep disturbance	2	1	1	1
Sleep medication	3	3	2	2
Daytime dysfunction	3	2	1	1
HAMA score	38	22	14	15
HAMD score	37	25	14	12
Polysomnography				
Sleep continuity				
Sleep-onset latency (SOL), min	41	35.9	21.5	27
Total sleep time (TST), min	420	431	502.5	521
Sleep efficiency, %	65.4	67.8	82.9	87.7
Apnea-hypopnea index (AHI), events/h	8.6	5.1	5.2	4.6
Sleep architecture, % of total sleep time				
Stage 1 sleep	15.1	5.5	10	5.4
Stage 2 sleep	70.2	80.9	65.9	81.7
Slow-wave sleep	6.1	1.4	2.2	4.7
REM sleep	8.6	12.3	21.9	8.3
REM sleep parameters				
REM latency, min	214.5	221.5	116.5	111

HAMA = Hamilton Anxiety Scale, HAMD = Hamilton Depression Scale, PSQI = Pittsburgh Sleep Quality Index, REM = rapid eye movement.

In order to evaluate the quality of sleep and the stability of emotional symptoms, clinical evaluations were conducted at baseline, after 10 treatment sessions, after 20 treatment sessions, and 1 month after the end of treatment. Assessments included polysomnography, Pittsburgh Sleep Quality Index (PSQI), Hamilton Depression Scale (HAMD), and Hamilton Anxiety Scale (HAMA).

rTMS stimulation was performed first, and a single pulse of TMS was delivered to the motor cortex (M1) via an octagonal coil (Magstim Ltd, Oxford, UK) to confirm the resting motor threshold.

First, a low-frequency, 1-Hz rTMS stimulation of the dorsolateral right prefrontal cortex (midpoint of F4–FP2 according to the 10/20 electroencephalography electrode placement system) was selected. The intensity was 80% of the motor threshold, the stimulation time was 6 seconds, the interval time was 4 seconds, the continuous stimulation was performed 1,800 times, and the total number of pulses was 1,800. Afterward, tDCS stimulation was performed using a battery-powered microprocessor-controlled constant current stimulator (Foc.us Ltd, London, UK), and two 25-cm^2 sponge electrodes were used to soak the electrodes in saline. Two-milliampere stimulation (rise/fall of 30 seconds) was given once a day for 20 minutes. The anode was placed over the left prefrontal cortex (F3–FP1), and the cathode was placed over the right prefrontal cortex. The treatment mode was rTMS treatment first and tDCS treatment immediately after the end, once a day for 20 consecutive times, for a total of 20 days of treatment.

After each treatment, the tolerability and safety of rTMS and tDCS, including itching, pain, and skin reactions, were monitored using the Treatment Emergent Symptom Scale.[11]

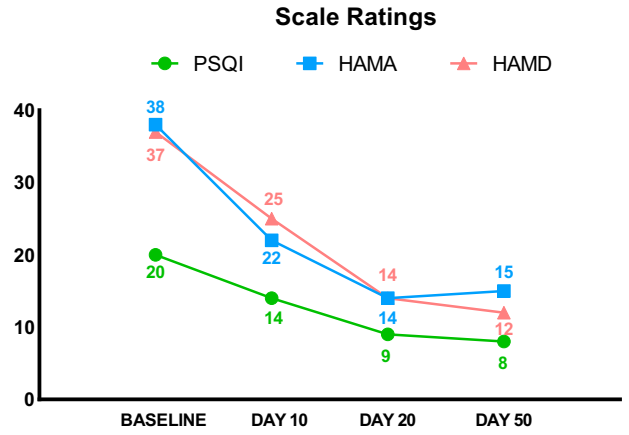
The study was approved by the Ethics Committee of Ningbo Kangning Hospital.

DISCUSSION

After completing rTMS combined with tDCS, the patient showed an overall clinical improvement, with clinical changes mainly observed in the PSQI, HAMD, HAMA scores and polysomnography, and this improvement was maintained 1 month after the intervention.

The subscore analysis of the 7 dimensions of the PSQI scale revealed the effects of rTMS combined with tDCS treatment on various aspects of sleep status. On the 5 dimensions of sleep quality, sleep onset time, sleep duration, sleep disturbance, and daytime dysfunction, the scores gradually decreased as the number of treatments accumulated and remained stable at one-month follow-up. After 10 days of intervention, the HAMA score decreased by 42% and the HAMD score decreased by 32%. After 20 days of intervention, the HAMA score decreased

Figure 1—Scale ratings.



HAMA = Hamilton Anxiety Scale, HAMD = Hamilton Depression Scale, PSQI = Pittsburgh Sleep Quality Index.

by 63% and the HAMD score decreased by 62%. After 30 days of follow-up at the end of treatment, the HAMA score decreased by 61% and the HAMD score decreased by 68%.

With the accumulation of the number of treatments, in the polysomnogram, we found that the sleep latency and rapid eye movement (REM) latency gradually shortened and the total sleep time and sleep efficiency gradually increased, which again confirmed the previous results of the PSQI scale (**Table 1** and **Figure 1**).

After all treatments, not only were the objective indicators, such as scale scores, improved but the patient also reported that her sleep conditions were significantly improved and her emotions were relieved. The patient had good tolerance for rTMS combined with tDCS, and no serious adverse reactions were reported. At the end of daily stimulation, only slight and transient skin redness was observed on the scalp, which subsided soon after the stimulation stopped.

This case provides the first evidence for the feasibility, tolerability, and safety of combined rTMS and tDCS in a patient with chronic insomnia. We also used the Treatment Emergent Symptom Scale to assess adverse reactions to ensure the safety of the treatment regimen.

This study found that the decrease in PSQI, HAMA, and HAMD scores and the change in sleep structure, which appeared to be similar to those reported in previous clinical trials.[12]

Our exploratory research provides a new perspective for the treatment of patients with simple insomnia so that follow-up research can further replicate this intervention. In future studies, we suggest adding more participants to explore different treatment modes, including the number of treatments, duration of treatment, and methods for assessing the effectiveness of treatment options.

ABBREVIATIONS

HAMA, Hamilton Anxiety Scale
HAMD, Hamilton Depression Scale
PSQI, Pittsburgh Sleep Quality Index
REM, rapid eye movement
rTMS, repetitive transcranial magnetic stimulation
tDCS, transcranial direct current stimulation

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Address correspondence to: Yuanyuan Zhang, MD, Department of Psychosomatic Medicine, Ningbo Kangning Hospital, Affiliated Mental Health Center of Ningbo University, Ningbo, Zhejiang, China; Email: lanxin2929@163.com; and Weiqian Xu, BA, Taizhou Second People's Hospital, Taizhou, Zhejiang, China; Email: zjttxwq@163.com

DISCLOSURE STATEMENT

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