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Continuous Theta Burst Transcranial Magnetic Stimulation in Treating Post-Stroke Insomnia Monitored by Polysomnography: A Case Report

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Abstract: The incidence of stroke has been increasing in recent years, and post-stroke insomnia, a common complication, also bothers many stroke patients. Post-stroke insomnia not only affects the quality of sleep and daily functioning of stroke patients, but it can also impacts stroke recovery and potentially lead to anxiety and depression disorders. This case report presents the case of a 47-year-old man who exhibited symptoms of early awakening, easy awakening, and daytime fatigue after suffering from a hypertensive cerebral hemorrhage. These symptoms occurred more than three times per week and persisted for six months. After giving treatments such as acupuncture and medication, this patient's sleep quality did not significantly improve. Considering the availability of noninvasive brain stimulation techniques, we opted to utilize continuous theta burst stimulation for the patient's treatment. The stimulation was administered to the dorsolateral right frontal lobe, with an intensity set at 30% of resting motor thresholds. The treatment spanned 10 days, with one session per day lasting 48seconds. Following a single session, the patient's sleep quality and sleep structure showed improvement, and he did not experience any discomfort during this treatment. In conclusion, continuous theta burst stimulation proves to be an effective and safe therapeutic approach for patients with post-stroke insomnia.

Keywords: Post-Stroke Insomnia, Continuous Theta Burst Stimulation, Polysomnography

1. Introduction

Post-stroke insomnia (PSI) is a common complication of stroke, with a prevalence that can reach as high as 69% [1]. Compared with the normal population, post-stroke patients tend to experience poor sleep quality, low sleep efficiency, short total sleep duration, disrupted sleep continuity, and a reduced percentage of slow-wave sleep [2]. Insomnia is associated with the development of cardiovascular disease, and addressing insomnia not only helps prevent recurrent strokes but also improves the overall prognosis for stroke patients [3, 4].

Currently, the most common approaches for treating insomnia are medication and cognitive behavioral therapy. However, medication often fails to achieve long-term effects, and cognitive behavioral therapy also has potential problems such as high cost and poor patient compliance. We urgently need to look for a brand-new, secure, and long-term effective therapeutic approach [5, 6].

Transcranial magnetic stimulation (TMS), as an emerging non-invasive brain stimulation technology, has been widely used in various rehabilitation treatments for stroke, including speech rehabilitation and motor rehabilitation. In several years, more and more people have been investigating TMS for the therapy of PSI, and the efficacy of low-frequency

(1Hz) repetitive transcranial magnetic stimulation (rTMS) for the treatment of PSI is worthwhile affirmed [7, 8]. Continuous theta burst stimulation (cTBS), a novel modality of rTMS, has the advantages of short duration and low intensity compared to other non-invasive brain stimulation. Therefore, it is worth investigating the effectiveness of cTBS in individuals with PSI. This case report aims to explore the efficacy and related mechanisms of cTBS in the treatment of PSI. Additionally, it will assess the impact on sleep quality using the Pittsburgh Sleepiness Scale and polysomnography. These assessments will be conducted before and after a 10-day course of cTBS treatment [9].

2. Clinical Information

The patient, a male, 47 years old, had a cerebral hemorrhage in the right basal ganglia region due to hypertension in June 2022, with a hemorrhage volume of about 55 ml. He was diagnosed with PSI according to the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-V). The patient received treatment in the hospital from the Department of Psychiatry and Traditional Chinese Medicine. Despite undergoing intermittent treatment for a period of 5 months, the patient's insomnia symptoms persisted, and he continued to report frequent awakening, early awakening, and daytime fatigue. The patient was provided with a detailed explanation of the experimental steps and rationale, and he provided informed consent by signing a consent form prior to initiating the treatment.

3. Methods

3.1. Continuous Theta Burst Stimulation Therapy

In this case, the patient underwent treatment using a CCY-1 TMS stimulator from Wuhan Yiruide Company, with device section of an "8" coil. Considering the patient's limb movements, the patient was positioned in a seated posture and instructed to minimize trunk movement during the treatment. The Yiruide-provided positioning cap was used for localization, targeting the right dorsolateral prefrontal lobe. The stimulation intensity was set st 30% of resting motor thresholds. The stimulation parameters were as follows: intra-cluster frequency: 50Hz; stimulation time: 0.06s; intra-cluster counts: 3; inter-cluster frequency: 5Hz; stimulation time: 40s; inter-cluster counts: 200; intervals: 8s; and total number of stimuli: 600. The cTBS treatment was administered once a day for 48 seconds for 10 consecutive days. The main efficacy indicators were evaluated using the Pittsburgh Sleep Quality Index (PSQI) and polysomnography.

3.2. Polysomnography Collection

An Australian Compumedics Grael 76-channel standard polysomnograph was used to collect nocturnal polysomnographic data from the subjects. The electroencephalograms were placed by the international 10-20 system of placing the electrodes (F3, F4, C3, C4, O1, O2), with bilateral mastoids used as reference electrodes. Additionally, body position, fingertip oxygen saturation (SPO2), and changes in the heart rate were simultaneously recorded. A sleep technologist in the field interpreted and analyzed the sleep monitoring charts, following the revised interpretation criteria issued by the American Academy of Sleep Medicine in 2013, which encompassed sleep staging and related events. The indicators include total record time (TRT), total sleep time (TST), wake after sleep onset (WASO), sleep latency (SL), sleep efficiency (SE), non-rapid eye movement sleep (NREM) stages (N1, N2, N3) and rapid eye movement sleep (REM) stages.

4. Results

4.1. Results of the Pittsburgh Sleep Quality Inventory

Following a 10-day course of cTBS sessions, the patient's insomnia significantly improved, and the patient achieved duration of up to 6.5 hours. Pre-treatment the patient's PSQI score was 12 (the cutoff value for non-insomnia symptoms), whereas post-treatment, the patient's PSQI score dropped to 7. Sleep duration, sleep efficiency, sleep disorders, and daytime dysfunction were all improved.

4.2. Results of Polysomnography

During polysomnography monitoring, the patient's sleep efficiency increased from 72.9% to 80.1%. Compared to the previous period, the percentage of stage N1 sleep decreased, the percentage of stage N3 sleep increased significantly, the percentage of stage R sleep increased, and the mean oxygen saturation also improved.

Table 1. *Basic data on polysomnography.*

	Bedtime (minutes)	Total sleep time (minutes)	wake after sleep onset	Number of wakes	sleep latency (minutes)	REM phase latency (minutes)	sleep efficiency
pre-treatment	578	390	137.5	29	7.5	90	72.9%
post-treatment	560.5	428	100.5	32	6.0	33.5	80.1%

Table 2. *Percentage of sleep by period.*

	Percentage of R-period	Percentage of N1-period	Percentage of N2-period	Percentage of N3-period
pre-treatment	7.3%	40.9%	45.1%	6.7%
post-treatment	16.8%	10.2%	49.6%	23.4%

Table 3. *Fingertip oxygen saturation (SPO2) during sleep.*

	Mean SpO2	Minimum SpO2
pre-treatment	95%	62%
post-treatment	96%	76%

Table 4. *Heart rate changes during sleep.*

	Average heart rate (beats/min)	Minimum heart rate (beats/min)	Maximum heart rate (beats/min)
pre-treatment	78	58	101
post-treatment	71	54	88

5. Discussion

The results of this study demonstrated a significant improvement in the patient treated with cTBS compared to drug therapy.

Prior to treatment, the patient's average heart rate was 78 beats per minute, with a maximum of 101 beats per minute. After treatment, a decrease in heart rate was observed. This finding may be attributed to the hyperarousal theory, which is a recognized pathophysiological mechanism of insomnia [10, 11]. The hyperarousal theory is primarily manifested on polysomnography by prolonged wakefulness after sleep onset, an increase in the N1 phase and a decrease in the N3 phase [2, 11, 12]. Normal people will gradually transition from N1 and N2 phases (light sleep phase) to N3 phase (deep sleep phase) after falling asleep. However, in patients with insomnia, the percentage of N3 sleep stage is significantly lower compared to N1 and N2 stages.

After a stroke, there is weakened cortical inhibition of sympathetic nerves and increased sympathetic nerve activity, resulting in a hyperactivated state during the night and disrupted cortical excitability. As a result, patients experience heightened arousal at bedtime and have difficulty entering a deep sleep period, spending most of their time in light sleep stages [13].

Theta burst stimulation induces changes in potential plasticity by generating electrical currents through varying magnetic fields, modulating the balance between excitation and inhibition in human cortical regions. In this study, cTBS was chosen to inhibit local cortical excitability and reduce the hyperaroused state in insomnia patients, aiming to increase slow-wave activity, and promote deeper sleep based on the theory of hyperarousal of insomnia [8, 14-16]. The results showed a reduction in wakefulness time after falling asleep, decreased sleep latency and REM phase latency, and a significant increase in the proportion of N3 sleep stage, indicating an optimization of sleep continuity and structure. We believe that cTBS is effective in ~~th~~e treating PSI, and no adverse effects such as dizziness, nausea, or vomiting were observed during the 10-day treatment period.

Of a certainty, sleep is closely intertwined with emotions and cognition, and the dorsolateral frontal lobe is also the most common target of stimulation for mood-related rTMS treatment [17-20]. While we evaluated the relevant depression and anxiety scales for this patient, no significant changes in mood were observed before and after treatment. Future studies should explore whether cTBS has an improvement effect on the mood of PSI patients in subsequent treatments.

6. Conclusion

There is no doubt that cTBS improves sleep quality in patients with PSI by prolonging sleep duration, decreasing patients' awakening duration, and increasing the proportion of N3 sleep stage.

7. Recommendations

Based on our findings, we can affirm the efficacy of cTBS in treating PSI. Compared to other treatments, cTBS offers a novel approach that is short, low-intensity and safe. Future studies on post-stroke insomnia should consider increasing the sample size and extending the treatment duration to further investigate the initial speculations presented in this report.

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