Short-term effects of continuous theta burst stimulation in treating a young patient affected by post-ischemic hemidystonia

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INTRODUCTION

Post-ischemic Hemidystonia is a rare clinical manifestation, often showing minimal response to medical treatment and frequently accompanied by significant side effects due to structural damage in the basal ganglia (1). Transcranial magnetic stimulation (TMS), a non-invasive technique capable of inducing long-term potentiation or inhibition in the cortex, presents a potential adjunctive therapeutic option for managing such cases (2).

CASE REPORT

We describe the case of a 23-year-old male patient with no prior medical history. In January 2020, at the age of 19, after a Sars-Cov-2 infection, the patient started showing signs of rapidly progressive akinetic-rigid Parkinsonism on the right side of the body. Six months later, the clinical picture shifted to a prominent severe right hemidystonic syndrome affecting both the arm and the leg, whereas the hemiparkinsonism signs showed marked improvement. Upon stabilization of symptoms, the patient was able to maintain basic activities of daily living (eating and drinking, dressing up, managing personal hygiene) but was limited or unable to perform more complex tasks (driving, writing). Additionally, the patient developed a a tendency toward social withdrawal and apathy, further negatively impacting his quality of life. Brain MRI, , performed two months after the onset of the symptoms, showed asymmetry of the supratentorial ventricular system with prevalence of the left lateral ventricle and contextual presence of hemosiderin degradation products (Figure 1, Panel A), suggesting previous basal ganglia ischemic stroke with secondary hemorrhagic infarction. DatScan showed a severe uptake deficit in the left striatum (Figure 1, Panel B). Genetic testing for parkinsonism and dystonia showed no relevant mutations. A diagnosis of post-ischemic hemiparkinsonism with hemidystonia was made. He started medical therapy with Trihexyphenidyl 2mg twice/day, Tizanidine 2mg twice/day, Levodopa 350mg/day, and Rasagiline 1mg/day, with little clinical benefit.

METHODS

The patient came to our attention 50 months after the onset of the symptoms. We proposed a non-invasive neurostimolatory approach to treat hemidystonia. Repetitive TMS (rTMS) sessions, using continuous theta burst stimulation (cTBS), were performed over 10 consecutive days. Each session was divided into two parts: stimulation of the motor cortex of the right arm and stimulation of the motor cortex of the right leg. The two parts were separated by a 20-minute waiting period to avoid possible conflicting excitatory effects. Clinical features were evaluated using the Unified Dystonia Ranking Scale, and corticospinal and intracortical excitability were assessed at baseline and 24 hours after the last cTBS session.

Corticospinal excitability measures (Resting motor threshold (RMT), Active motor threshold (AMT), and stimulation intensity for 1mV MEP) were determined using single-pulse-TMS (sp-TMS) in both the arm and the leg at the beginning of every session. EMG activity was recorded from the right first interosseus (FDI) and the right tibialis anterior (TA). Moreover, we assessed short-interval intracortical inhibition (SICI) and intracortical facilitation (ICF) using paired-pulse TMS (pp-TMS) with a supra-threshold test stimulus (1mV MEP) and a subthreshold conditioning stimulus (90% of the AMT). The interstimulus interval (ISI) between conditioning and test stimuli was 1-2-3-4-5-6 for SICI and 10-15ms for ICF (3).

After that, cTBS stimulation protocol was performed. The stimulation consisted of bursts containing three pulses at 50Hz (20ms between each stimulus), repeated at 5Hz intervals (200ms inter-stimulus interval [ISI]), and applied continuously for 40s, providing a total of 600 pulses. Each stimulus was performed at 80% of AMT.

RESULTS AND CONCLUSION

The clinical effect was assessed by comparing UDRS scores before and after treatment: UDRS score calculated at baseline was 13 (Duration: 4; shoulder and proximal right arm: 1; distal right arm and hand: 3; Pelvis and proximal right leg: 1; Distal leg and foot: 4). UDRS score calculated after 10 days of rTBS was 11 (Duration: 4; shoulder and proximal right arm: 1; distal right arm and hand: 2; Pelvis and proximal right leg: 1; Distal leg and foot: 3). This score reduction reflected an up to 25% improvement in the movement amplitude of the affected areas. This differential response may stem from the deeper location of the leg's motor cortex, making it harder to stimulate. Moreover, a significant retraction of the right Achilles tendon likely contributed to the limited leg movement recovery.

At baseline, sp-TMS stimulation parameters were: FDI RMT 40%, AMT 35%, 1mV-MEP 48%; TA RMT 48%, AMT 44%, 1mV-MEP 53%. After cTBS, we observed an increase of sp-TMS stimulation parameters: FDI RMT 42%, AMT 38%, 1mV-MEP 50%; TA RMT 51%, AMT 46%, 1mV-MEP 56%. We also observed significant reductions post-cTBS compared to the baseline in the values of conditioned MEPs at ISI 1-2-3-4-5-6ms. No significant differences were found at ISI 10-15ms (Figure 2).

The observed therapeutic effects of cTBS can be explained by considering two main features in the physiopathology of dystonia: loss of inhibition in the central nervous system and maladaptive plasticity8. These changes result in abnormal cortical excitability, which cTBS can mitigate. Consistently, the patient demonstrated a lack of cortical inhibition at 1-6ms ISI, which reversed post-cTBS in alignment with its inhibitory effects.

In conclusion, the patient's response to non-invasive neurostimulation, while variable between the arm and leg, demonstrates the potential of cTBS in addressing the abnormal cortical excitability associated with dystonia.

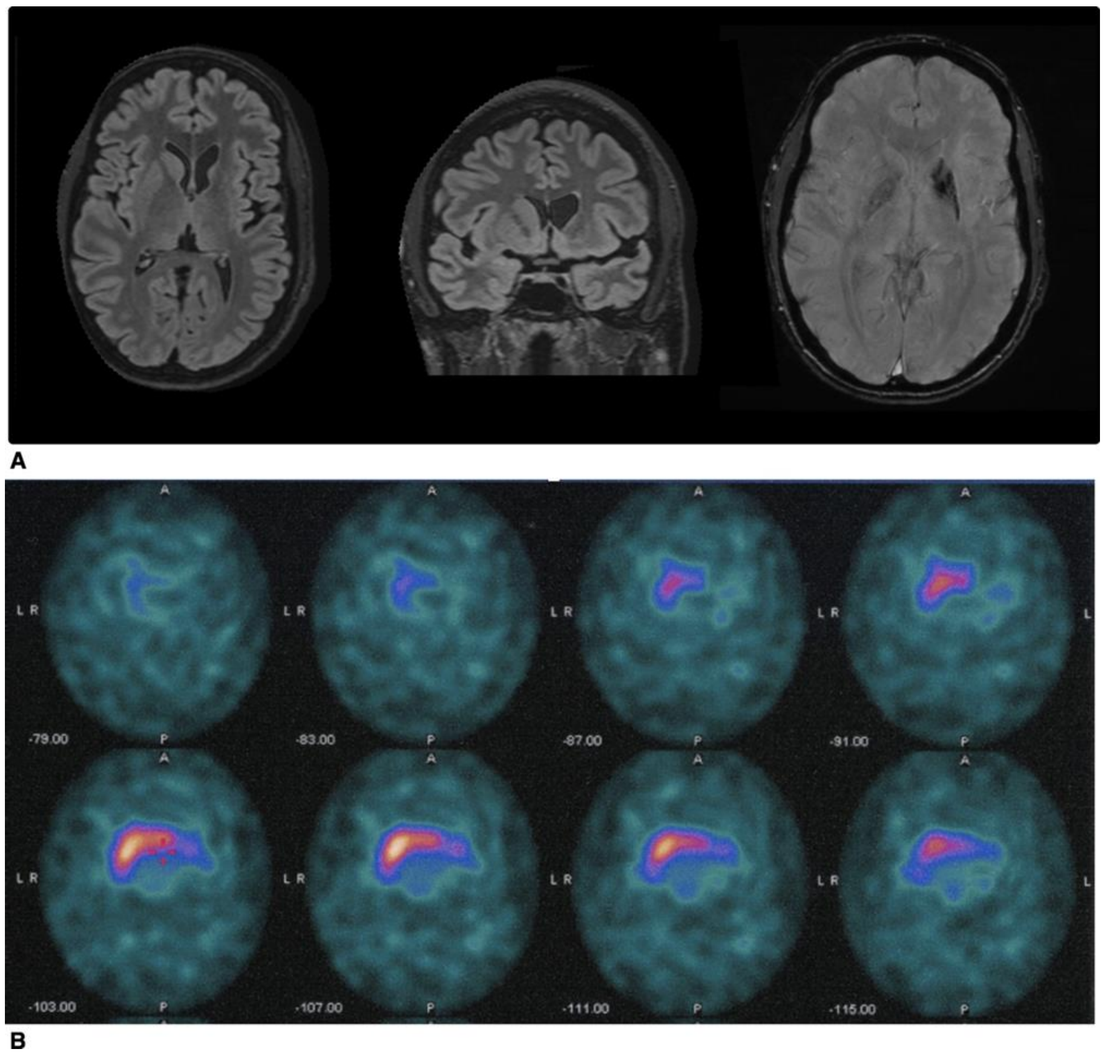

Figure 1: Panel A, from left to right: Axial FLAIR-T2 MRI, Axial SWI MRI - **Panel B**: DatScan

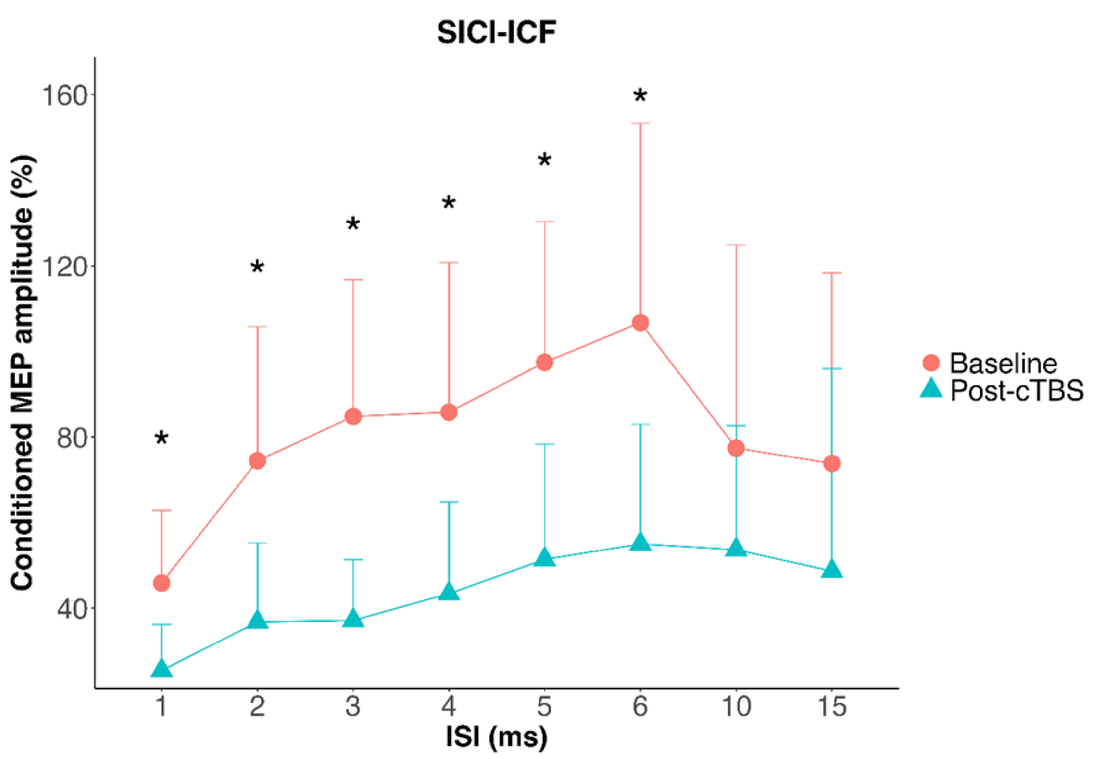

Figure 2: SICI and ICF of the study population at baseline and post-cTBS conditions

SCAN FOR VIDEO

References

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