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Case Report OMICS International

Long Term Repetitive Transcranial Magnetic Stimulation Improve Task Performance in a Patient

Wang Fana[1] **, Zhao Yan-ping**[2]**, Wu Shuanga**[1]**, Feng Feng**[2] **and Cui Li-yinga**[1]

[1]*Department of Neurology, Peking Union Medical College Hospital, Beijing, P.R. China*

[2]*Deptartment of Radiology, Peking Union Medical College Hospital, Beijing, P.R. China*

[*]**Corresponding author:** Wang Han, Department of Neurology, Peking Union Medical College Hospital, Beijing, P.R. China, Tel: 86-10-18600044179; Fax: 86-10-69156371; E-mail: wanghanpumch@163.com

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Abstract

Multiple system atrophy (MSA) is a sporadic neurodegenerative disorder characterized by a combination of Parkinsonism, cerebellar ataxia, and autonomic dysfunction. Patients with predominant parkinsonian features are defined as MSA-P, which is similar to Parkinson's disease (PD), except that they are not well responsive to levodopa. Based on the facts that there is no effective treatment for MSA-P.

Keywords: Multiple System Atrophy; Magnetic Stimulation

Introduction

We previously conducted a pilot RCT study [1,2]. It showed that patients with MSA-P who received real rTMS would show increased activation in specific brain areas by fMRI, such as cerebellum, and the improvement of motor scale.

Transcranial magnetic stimulation (TMS) is a non-invasive technique based on the principle of electro- magnetic induction of an electric field in the brain. TMS could be delivered either in single pulse to produce motor evoke potential (MEP), or repetitively in sessions of various patterns. When TMS pulses are delivered repetitively, they can modulate (increase or decrease) the cortical excitability by depolarizing or hyperpolarizing neurons continually. Therefore, changes in cortical regions underneath the stimulation coil and within functionally connected cortical or subcortical regions will be induced as local effect or remote effects, and outlast the period of stimulation. The rTMS technique has been firstly introduced to the treatment of PD in 1994 by Pascual et al. [3], in which they found that the sub threshold 5Hz rTMS could improve the pegboard performance both in reaction time and in movement time in 10 PD patients comparing to normal controls. Presently, rTMS could be used as an alternative non-invasive method to alleviate motor symptoms of PD [4,5]. The underlying therapeutic mechanism of rTMS is not clearly understood. However, functional imaging and electrophysiological studies [6-9] have suggested that cortical plasticity might play a role. As one of the main electrophysiological methods, central motor conduct time (CMCT) of MEP is therefore used to evaluate the effect of rTMS.

Herein, we present a case report showing the positive response to long-term 5Hz rTMS intervention evaluated by CMCT.

Case Report

A 61-year-old right-handed woman developed bradykinesia and rigidity in her left extremities at the age of 57. The symptom progressed and involved the right side gradually. Within two years after onset, axial symptoms were present including dysarthria, dysphagia, and loss of equilibrium. Rest or postural tremor was absent. She also complained difficult empting, urinary incontinence, constipation and sweating dysfunction. The symptoms are not responsive to Madopar (the maximum amount was 375 mg per day), Sinemet-CR (200 mg per day), and Selegiline at al. Her family reported she often had nightmare, shouting and frequently waking up during night for eight years before she came to see doctors. On neurological examination, she had blurred speech, masked face, and mild rigidity on right side and moderate on the left, with bilateral positive Chaddock's sign. Eye movements were normal. Tasks such as finger tapping, pronation-supination alternating and heel tapping could not be performed on the left and clumsy on the right. She could stand from the chair by herself. The repetitive blood pressure was 120/80 mmHg on supine and 110/80 mmHg on standing. Brain MRI showed pons atrophy with hot cross bun and "slit-like" hypotensity of putamen on T2 (Figures 1 and 2).

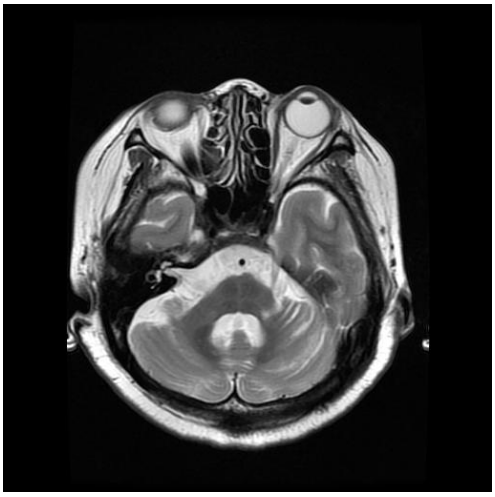

Figure 1: Pons atrophy with "hot-cross bun" sign on T2.

Anal sphincter electromyography suggested neurogenic impairment. On psychological consultation before the rTMS

intervention, suicide tendency was recognized, the Hamilton's depression scale scored 16, suggesting a medium depression. The past medical history was unremarkable. There was no family history of tremor or Parkinson disease. She did not drink alcohol and denied toxin or drug exposure. The diagnosis of probable MSA-P was made.

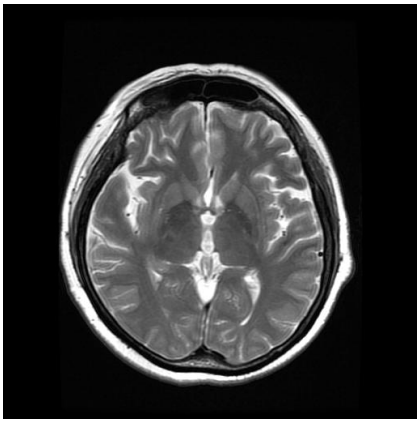

Figure 2: Slit-like hypotensity of putamen on T2.

After written consent obtained, she was treated with a 10-session-rTMS delivered to the primary motor cortex (MC) with a standard 65 mm figure-of-eight coil (MCF BF65) connected to a Medtronic MagPro Compact stimulator (Danmark). The ideal point to deliver the pulses was determined by moving the coil until the maximum MEP was found, which is also known as the hotspot. Rest motor threshold (RMT) was defined as the minimum stimulator output necessary to induce at least five MEPs of greater than 50 μV in ten consecutive stimulations in the contralateral relaxed abductor digiti minimi (ADM). The coil was positioned with the handle pointing 45 degree backwards perpendicular to the line of the central sulcus. Ten trains of 100 stimuli at 5-Hz frequency separated by 40 seconds of pause were delivered at 110% RMT for a total of 1000 pulses per day. A total of 10 sessions were given in 12 days (day 6 and day 7 for a rest). The motor part of the unified Parkinson's disease rating scale (UPDRS) was measured before, on the 5th day and 10th day after rTMS. During the period of rTMS intervention, the patient continued the Modopar treatment at the dosage of 375 mg divided into three times per day as before. rTMS were delivered at fixed time every day.

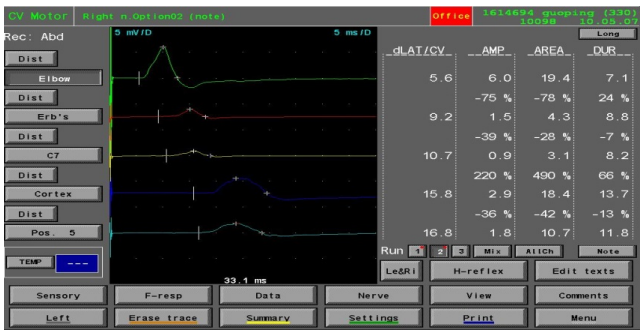

Figure 3: Right arm before stimulation.

No remarkable side effects were observed within the period of rTMS intervention. The performance of finger tapping (FT), hand alternating (HA) and heel tapping (HT) before and after rTMS administration (on the 12th day). The UPDRS motor score specified item score of FT, HA, and HT were shown as Table 1.

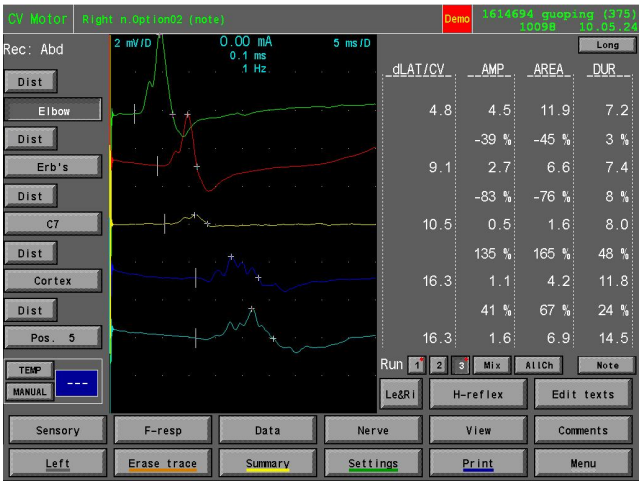

Figure 4: Right arm after stimulation.

A distinguishing improvement of task performance could be observed, manifested by either speed increase or action amplitude increase. On self-evaluation, the patient reported she could use chopsticks with less difficulty than before. However, she did not feel remarkable change in her daily living after all.

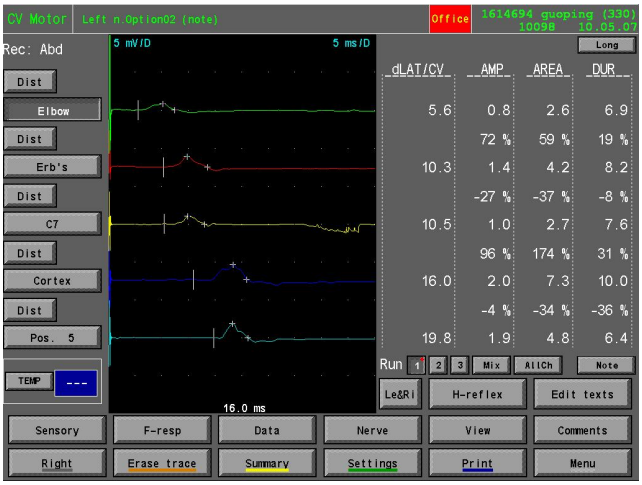

Figure 5: Left arm before stimulation.

MEP of both upper extremities was evaluated before and after rTMS. The central motor conduction time (CMCT) was calculated by subtracting the peripheral conduction time, which was obtained at 7th cervical motor root, from the total conduction time measured by MEP. It decreased after rTMS stimulation compared to baseline (Table 1, Figures 3-6). The RMT decreased from 70% at baseline to 65% on the 12th day.

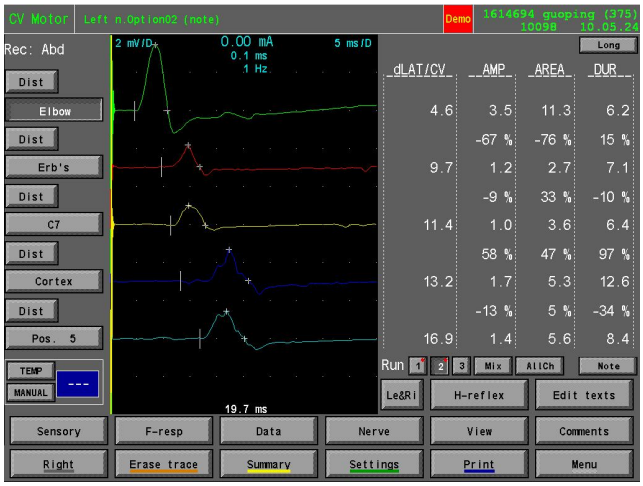

Figure 6: Left arm after stimulation.

	Left			Right
	Before	After	Before	After
FT	3	2	2	1
HA	3	2	2	1
HT	3	2	2	1
UPDRS-	21	16	17.5	11
CMCT (ms	4.5	1.8	3.5	3.3

Table 1: UPDRS including specified items and CMCT of both sides before and after rTMS intervention.

Comments

To our knowledge, this is the first case study to observe the treatment effects of long-term rTMS intervention measured by CMCT in a patient with MSA-P. After rTMS treatment, our case had a significant improvement in UPDRS-III and specific task performance, such as finger tapping, hand alternating and heel tapping. CMCT of both sides were shortened after rTMS compared to the baseline.

The mechanisms underlying the positive effects after rTMS treatment in our case are unknown. Studies concerning rMTS effects in PD patients and animal models suggested that it might act on the doparminergic circus and cause the striatum dopamine release [10,11]. But this could not reasonably explain the effect in MSA-P, because they did not respond to exogeneous levodopa as PD. The other mechanism related to rTMS efficacy is brain plasticity. In our case, the CMCT decrease might reflect the trans-synaptic efficiency improvement. Thus we presumed that rTMS might alter the excitability of motor cortex by regulating the brain plasticity in our patient.

Previous studies [12-15] applying MEP on patients with MSA-P suggested the abnormal inhibition within their motor cortex. Our current case report is in accordance with our previous pilot RCT study [1], both of which suggested that 5Hz rTMS might activate the brain inhibition in patients with MSA-P and therefore associate with motor improvement

Further RCT study with enlarged sample is warranted.

Funding

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