Review Article

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Effect of Contralesional rTMS on Hand Function in Chronic Stroke: Case Series

Vivek Sharma*, Harraman Kaur*, Divya Gupta**

Abstract

Repetitive transcranial magnetic stimulation (TMS) is a non-invasive technique to stimulate the cortical regions of the brain. rTMS can be used as a therapeutic adjunct to improve motor recovery following stroke, because of its potential to modulate cortical excitability. Depending on essential parameters of the stimulation frequency and number of trains of stimuli, rTMS can produce lasting up or down- regulation of the corticospinal system. At lower frequency (1-Hz) rTMS can suppress the excitability of the motor cortex causing an inhibitory effect; whereas at higher frequencies (>1 Hz) rTMS can increase cortical excitability causing facilitation. Many studies suggest that following stroke, there is exaggerated interhemispheric inhibition of the ipsilesional hemisphere, by the contralesional hemisphere. We report findings of a few stroke patients, where rTMS was given over the contralesional hemisphere to see its effect on the affected hand function.

Keywords: rTMS; Repetitive transcranial magnetic stimulation; Stroke; Ipsilesional hemisphere; Contralesional hemisphere; Hand function.

Introduction

Transcranial magnetic stimulation (rTMS) is a non-invasive technique to stimulate the cortical regions of the brain. The term rTMS means repetitive transcranial magnetic stimulation as it is delivered at regular intervals. A number of forms of brain stimulation, in particular rTMS, have been studied for improving post-stroke deficits. However, the ability of rTMS to modulate cortical excitability makes its as a therapeutic adjuvant that may enhance motor recovery following stroke.[1,2,3] The technique of rTMS is purely based on the Faraday's law of magnetism, which states "when an electric current passes along a wire a magnetic field is induced in the surrounding space" and this magnetic field induces depolarisation in the neurons stimulated. Depending on essential parameters of the stimulation frequency and number of trains of stimuli, rTMS can produce lasting up or down- regulation of the corticospinal system. At lower frequency (1-Hz) rTMS can suppress the excitability of the motor cortex causing an inhibitory effect; whereas at higher frequencies (>1 Hz) rTMS can increase cortical excitability causing facilitation.[3,4]

Stroke may affect the balance of transcallosal inhibitory pathways between primary motor areas in both hemispheres: the ipsilesional hemisphere not only gets disrupted by stroke itself but also by the resulting asymmetric inhibition from the contralesional hemisphere. This exaggerated interhemispheric inhibition of the ipsilesional hemisphere, in particular primary motor area (M1), by contralesional M1 can lead to down regulation of excitability in neurons that have survived the stroke. Therefore, it is believed that contralesional M1 virtual lesion by using rTMS at low frequency causes paradoxical functional facilitation of the affected hand in

Author Affilation: *Consultant Physiotherapist, **Clinical Research Associate, Department of Neurorehabilitation, VIMHANS, Delhi, India.

Reprint Request: Dr. Vivek Sharma, Consultant Physiotherapist, Department of Neurorehabilitation, VIMHANS, Delhi, India.

E-mail: viveksharma607@gmail.com

Table 1: Demographic Details and Scores of Patients

S. No	Age (years)	Gender	Diagnosis	Side of hemiplegia	Time since onset (months)				
						Pre FMA	Post FMA	Pre BI	Post BI
1	72	Male	Periventricular infarct	Right	24	8	8	75	75
2	55	Male	Middle cerebral artey infarct	Right	12	8	10	75	75
3	27	Male	Traumatic brain injury	Left	36	38	38	100	100
4	35	Male	Stroke	Left	50	27	27	100	100
5	45	Male	Basal ganglia bleed	left	13	2	3	35	35

stroke patients.[4,5] Many studies using rTMS suggest that inhibitory rTMS over the contralesional hemisphere may be a more effective method of enhancing paretic limb function, although ipsilesional stimulation is still beneficial.[2]

Cases Summary

Informed consent was taken from the patient/immediate family member. Protocol of rTMS was cleared by the institutional ethical board. Patients with uncontrolled seizures, implanted defibrillator, pacemaker, pre-morbid neurological insult, metal implants in head, uncontrolled migraine were excluded from the study.A total of 5 patients were recruited for the pilot study, between December 2013 and January 2014 at Vidyasagar Institute of Mental Health ,Neuro & Allied Sciences (VIMHANS),Delhi.Four of them had stroke and one had hemiplegia following traumatic brain injury. All patients were male ranging in age from 27 to 72 years. All patients were right hand dominant before stroke. 2 of them had right sided hemiplegia and 3 had left sided hemiplegia. The time since onset of hemiplegia ranged between 1 to 4 years. All the patients were ambulatory with or without the use of assistive aid.

All patients were assessed on Fugl Meyer Assessment scale (upper limb and hand component) and Barthel's Index, pre and post rTMS. The rTMS parameters used for each patient were 1-Hz frequency at 100% resting motor potential (RMP) with 30 trains of 30 pulses each and 5 sec interval between each train. The stimulation was applied for a period of 10 days, spread over a period of 2 weeks. During the procedure, patients were comfortably seated in an armchair. rTMS was given with a machine developed by Medicaid systems, Chandigarh, INDIA, the model of the machine used for our study was MedStim-MS30. Hand area of motor cortex in unaffected hemisphere was stimulated using figure-of-eight coil. Resting motor threshold (RMP) was determined for each patient by placing the coil tangentially over the motor cortex of unaffected hemisphere and moving until the smallest possible impulse produced a visible movement of the thumb or fingers of the contralateral hand in atleast half of 10 stimulations. Stimulation intensity was calculated as 100% of RMP for each patient. [6]

Results

Our results showed that 2 out of 5 patients improved on Fugl Meyer Assessment (FMA) of their affected hand and rest of them did not show any change. The change seen in FMA scores was very minor and non-significant; however, no statistical analysis was done due to small number of patients. None of the patients showed improvement on Barthel's

Index (BI) score.

Discussion

There is now growing evidence that contralesional hemisphere impairs, rather than facilitates motor performance in stroke patients. It has therefore been proposed by Ward and Cohen that a down regulation of the contralesional primary motor cortex might be effective for facilitation of motor recovery after a stroke.[5,7,8,9,10] In this study, we hypothesized that reducing the inhibition from the contralesional hemisphere by using 1-Hz rTMS might improve motor performance of the affected hand. Recovery from hemiplegia likely involves motor learning processes. At the cellular and molecular level, learning motor skills is associated with neural plasticity mediated in part by long term potentiation (LTP) and long term depression (LTD). LTP is defined as long lasting synaptic enhancement, where as LTD by the decrease of synaptic activity. LTP and LTD like changes can be induced in healthy and stroke patients using different rTMS protocols. For instance, application of low frequency rTMS (1-Hz) to the hand area of the M1 reduces the excitability of corticospinal projections from the site of stimulation. In addition, inhibitory 1-Hz rTMS to the M1 also increases regional blood flow in the contralateral M1 as detected by positron emission tomography.[1]

The rTMS parameters which we incorporated in this study have been used previously by Khedr *et al* in 2009. They conjectured that patients receiving contralesional 1-Hz rTMS showed more improvement relative to the other interventions (ipsilesional 3-Hz & sham stimulation) on simple motor tasks, stroke impairment and disability.[6] Although the only change in our study was, total number of sessions, khedr *et al* had used it for 5 days and we delivered rTMS for 10 days. Our results did not show much change after the 10 day treatment. As this was a pilot study, so we need to consider few things for our future trials, such as: more number of sessions so that more inhibition of contralesional cortex can take place as the patients are already in chronic stage of stroke, more accurate method of choosing cortical area of stimulation for rTMS, having more specific outcome measures for hand function assessment. For the reference, we would like to discuss some of the studies using contralesional rTMS.

Most of the clinical trials using low frequency rTMs applied to the unaffected hemisphere have demonstrated decreased interhemispheric inhibition of the affected hemisphere and improvement in motor performance. Boggio *et al* reported a case of a stroke patient with severe motor impairment who underwent sham and active repetitive transcranial magnetic stimulation (rTMS) of the unaffected hemisphere. They have shown that a chronic stroke patient with no movements in the affected hand was able to partially gain hand motor function after inhibitory 1-Hz rTMS was applied on the unaffected primary motor cortex.[11] Mansur *et al* investigated the use of low-frequency repetitive transcranial magnetic stimulation (rTMS) to the unaffected hemisphere for improving motor function in 8 patients within 12 months of a stroke. Of these patients, five had mild impairment and three had moderate impairment. Patients showed a significant decrease in simple and choice reaction time and improved performance of the Purdue Pegboard test with their affected hand after rTMS of the motor cortex in the intact hemisphere as compared with sham rTMS. [12] Takeuchi *et al* conducted a double blind study of real versus sham rTMS in 20 stroke patients. They reported an improvement in hand function (pinch acceleration) after giving to low frequency rTMS to the contralesional hemisphere. They also concluded that rTMS reduced the amplitude of motor evoked potentials in contralesional M1 and the transcranial inhibition (TCI) duration.[13] No patients with total paralysis participated in the above two studies.

In contrast, a study done by Werhahn *et al* on 5 stroke patients showed no improvement

in the motor function of the paretic hand after 1-Hz rTMS of the unaffected hemisphere. The inconsistent results may be explained by the patient selection, the type of lesion, the different tasks employed, dose and intensity of rTMS and placement of coil.[4]

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