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REPETITIVE TRANSCRANIAL MAGNETIC STIMULATION (RTMS) AS A TREATMENT FOR POST-CONCUSSION SYNDROME

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ABSTRACT

As part of an ongoing study, a small group of volunteers with post-concussion syndrome (PCS) were given either real or sham rTMS treatment. Thirteen treatment sessions over three weeks applied 20 Hz rTMS to the left dorsolateral prefrontal cortex. Assessments to determine cognitive ability, memory, depression symptoms, and PCS symptom burden were done before and after treatment, and twice following up at one and two months post-treatment. Significant improvements were found at two months post-treatment in the measurement of symptom burden using the Rivermead Post Concussion Symptoms Questionnaire. This result suggests that rTMS may be an effective treatment for some of the symptoms of post-concussion syndrome.

INTRODUCTION

Repetitive Transcranial Magnetic Stimulation (rTMS) is a technology that may have the potential to help improve the symptoms of post-concussion syndrome (PCS). rTMS technology has already been shown to be effective in the treatment of various neurological and psychiatric disorders, such as depression, schizophrenia, and Parkinson's disease [1]. There are several reports of case studies that show beneficial effects of rTMS treatment on patients with severe traumatic brain injury (TBI) [2, 3]. Also, a pilot study by our lab has shown encouraging improvements in cognitive and memory deficits of Alzheimer's patients [4]. The ongoing study presented here evaluates a similar rTMS treatment protocol as that used in our Alzheimer’s treatment study for people with PCS.

Concussion or mild TBI (mTBI) is the most common form of traumatic brain injury. Concussion is more frequent in teenagers, young adults, males and people who are engaged in high impact physical activities [5, 6]. Individuals who usually sustain mTBI develop neuropathological, neurophysiological, and neurocognitive changes, which result in physical, cognitive, and emotional symptoms. If these symptoms persist long after the mTBI, it is referred to as PCS. These symptoms, if not treated, can last for months and years and may be permanent and cause disabilities [7, 8].

Given that TBI imposes substantial medical and socio-economic burden on patients and the healthcare system [9-11], there is an urgent need to develop an effective treatment strategy. The current treatments for PCS include medications [12] and psychological treatments [13-15]. However, the effectiveness of these treatments is still in dispute [16].

The principle behind rTMS is the application of a rapidly changing magnetic field to the brain [17], which induces electrical fields and ion currents. This causes neurons within a limited area on the surface of the brain to either depolarize or hyperpolarize. When applied over the cortex, depending on the frequency of pulses, rTMS can affect the excitability of the region. It is believed that high frequency (>5 Hz) pulses of rTMS are able to increase cortical excitability in a similar way to the effects of Long-Term Potentiation [18, 19]. The procedure is non-invasive and easy for patients to tolerate.

STUDY DESIGN

Recruitment

Seventeen participants with diagnoses of PCS from a physician (Authors B.M. and J.S.) due to a concussion within the past five years were recruited for this study. Eight of them were randomly assigned to receive active rTMS treatment, while the remaining nine participants received sham rTMS treatment.

Schedule

Participants of each of the active and sham groups received 2 weeks (5 days/week) of either active or sham rTMS treatments, plus an additional 3 treatments on following week (Monday, Wednesday, and Friday). This amounted to 13 treatment sessions over a 3-week period.

Cognitive assessments were done every 4 weeks on Wednesdays. The baseline assessment was done on the Wednesday before the first treatment, and the post-treatment assessment was done on the Wednesday following the final treatment. The 1-month and 2-month follow-up assessments were scheduled 4 and 8 weeks after the post-treatment assessment, respectively.

rTMS Protocol

Using a standard figure-8 coil, the left dorsolateral prefrontal cortex was stimulated. The pulse rate was set to 20 Hz, with each burst consisting of 30 pulses over 1.5 seconds. There was a 28.5 second delay between each burst, and a total of 25 bursts were applied each day for a total of 750 pulses.

The intensity of the stimulator was set to be equal to 100% of the resting motor threshold of each participant, which was measured once on the first day of the treatment.

Cognitive Assessments

Three cognitive assessments (described below) were performed to evaluate the effect of treatment; they were run 4 times as explained in Schedule section.

The Montreal Cognitive Assessment (MOCA) [20] was used to assess visual, language, memory, and cognitive skills. This score uses a positive scale, where higher results indicate improvement.

The Montgomery-Asberg Depression Scale (MADRS) [21] was used to investigate the

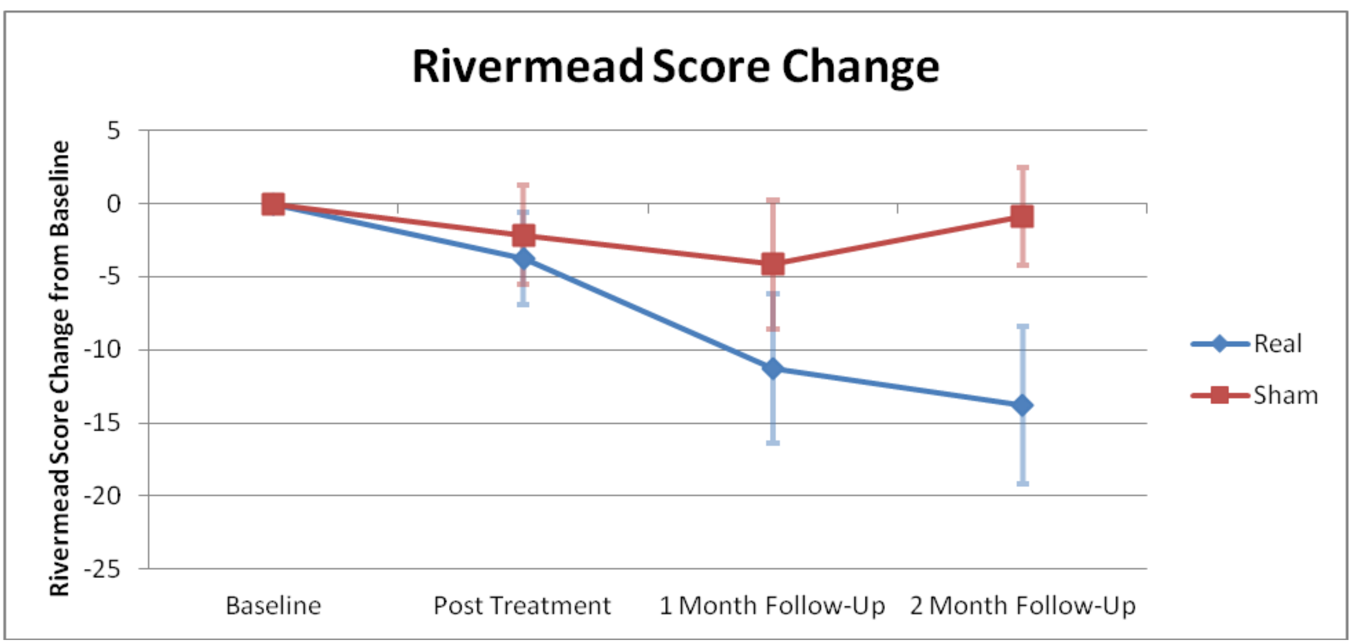

Figure 1: Change in score on the Rivermead Post Concussion Symptoms Questionnaire

Table 1: Change in Assessment Scores from Baseline

	MoCA		MADRS		Rivermead	
	Real	Sham	Real	Sham	Real	Sham
Post Treatment	0.25	0.67	-2.75	-2.33	-3.79	-2.16
1 Month Follow-Up	0.75	0.63	-2.38	-5.50	-11.28	-4.16
2 Month Follow-Up	1.00	0.71	-5.14	-4.57	-13.78	-0.90

effect of confounding variable (depression improvement) on treatment efficacy. Higher scores in this measurement indicate greater depression symptoms.

Finally, the Rivermead Post Concussion Symptoms Questionnaire [22], which is a questionnaire that allows participants to self-report a variety of symptoms, was used to evaluate specific PCS symptoms. Higher scores in this assessment indicate more burden from PCS symptoms. This measure was normalized to a maximum score of 64 for analysis (open-ended questions allow varying maximum scores).

RESULTS

By the time of writing this paper, 14 participants (7 in active and 7 in sham treatment groups) have completed the study. Thus, the results presented here are based on those 14 study subjects.

There were non-significant improvements in MADRS and MoCA scores in both active and sham treatment groups (Table 1).

On the other hand, the Rivermead scores were similar between active and sham treatment groups immediately post-treatment, but over the next few months the active treatment group improved dramatically, while the sham group returned to baseline (Figure 1).

The difference between Rivermead scores of the active and sham groups at the 2 month follow-up assessment was statistically significant ($p = 0.0443$) using a one-tailed t-test.

DISCUSSION

Non-significant MADRS scores between the two treatment groups indicate that the depression was not a confounding variable in this treatment protocol. The MADRS scores of both active and sham treatment groups improved after the treatment. Since the improvement occurred in both groups, then it is likely a placebo effect, and not due to the treatment effect of rTMS on depression [23].

The MoCA measurements likely suffered from ceiling effects. Most participants scored near the maximum score at baseline; thus, there was little room to show improvement. As MoCA is generally used as a diagnosis tool for Alzheimer's Disease, this is not surprising.

The significant response in the Rivermead scores in the follow up assessment is quite interesting. The delayed response shown in the Rivermead scores may indicate that rTMS does not improve symptoms immediately after the treatment, but rather aids in long-term recovery of PCS symptoms. If this is truly the case, then this technology would have significant potential for concussion treatment.

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