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# The role of transcranial magnetic stimulation in treating depression after traumatic brain injury

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Traumatic brain injury (TBI) is defined as the brain dysfunction occurring after an individual sustains trauma to the cerebrum [1]. Various incidents may cause TBI, such as motor vehicle accidents (MVA), sports injuries, or violent events [1]. Depending on the location and severity of impact, patients may experience relatively mild, to severe, lifelong symptoms. The presence of symptoms following TBI may be diagnosed as post-concussion syndrome (PCS) [2]. Many patients have acute depression symptoms after TBI which persist as medication refractory post-concussion depression. TBI survivors are at increased life-time risk of developing pharmaco-resistant major depressive disorder, bipolar disorder, dysthymia, or other psychiatric disorders along with increased risk of seizures.

Repetitive transcranial magnetic stimulation (rTMS) is a non-invasive, outpatient therapy that is FDA approved to treat major depressive disorder (MDD) [3]. Whereas rTMS therapy has been growing in the field of psychiatry, there is limited research on the use of rTMS for treatment of neurological issues, such as post-concussion syndrome.

Low-frequency right-sided rTMS, an inhibitory protocol, has demonstrated a mild, positive impact on TBI-related depression [4]. To our knowledge, the current study is the first to assess excitatory rTMS of the left dorsolateral prefrontal cortex as a treatment for depression in individuals who experienced TBI and PCS. We hypothesize that the rTMS protocol will significantly improve depression symptoms in patients.

In this retrospective, open-label, uncontrolled study, the utility of rTMS in patients suffering from TBI was examined. The study was approved by the Texas Christian University Institutional Review Board. Adults diagnosed with TBI or PCS and treated using rTMS between January 1, 2015 and August 31, 2022 were included in the study.

Prior to rTMS treatment, a Patient Health Questionnaire-9 (PHQ-9) was administered to assess severity of depression [5]. The TMS devices used in this study were the 2017 Neurosoft Cloud TMS and the 2016 Magstim Rapid 2. Patients underwent a series of either 15 to 16 or 30 to 38 rTMS sessions determined by their authorization status. The FDA-approved DASH excitatory protocol (10 Hz) was used for all patients with 11 second rest times after each 4 second treatment [6]. One session lasted 18.5 minutes. The total number of pulses per session was 3000. The magnet was positioned at the left dorsolateral prefrontal cortex. The power setting was 120% of the patient's motor threshold. Patients underwent five rTMS sessions per week, followed by a tapering schedule for the last six sessions. After completion of the full treatment series, PHQ-9 was used to measure post-rTMS depression. The Hamilton Rating Scale for Depression (HAM-D) and Beck's Depression Inventory-II (BDI-II) were administered as further confirmation of post-test diagnosis. Data was analyzed using Statistical Package for the Social Sciences statistics software by International Business Machines.

Fifty-nine patients were included in the study. Average age was 47 years (SD = 12), and 44% (n = 26) were male. All patients were diagnosed with TBI or PCS and had PHQ-9 data. Over half (n = 34) of patients had brain magnetic resonance imaging (MRI) performed prior to rTMS treatment. All patients with brain MRI results displayed findings consistent with TBI. Of the 59 patients, 27 had 30 to 38 rTMS sessions, whereas 32 had 15 to 16 rTMS sessions.

On average, PHQ-9 indicated moderately severe depression in patients prior to TMS treatment and mild to moderate depression after rTMS treatment. Likewise, BDI-II and HAM-D scores indicated mild depression after treatment. PHQ-9 scores decreased significantly in the 15 to 16 session cohort from baseline ($M = 15.67$, $SD = 5.65$) to the final session ($M = 9.05$, $SD = 6.37$, $t(38) = 5.82$, $p < 0.001$) (Fig. 1). The effect size of the mean difference was large ($d = 0.93$). A similar outcome occurred in the 30 to 38 session cohort. Depression scores decreased from baseline ($M = 17.41$, $SD = 4.64$) to their final session ($M = 10.26$, $SD = 6.43$, $t(26) = 5.36$, $p < 0.001$) (Fig. 1). The effect size of this mean difference was also large ($d = 1.03$).

An independent-samples *t*-test was conducted to determine differences in change of PHQ-9 between the 15 to 16 session cohort to the 30 to 38 session cohort as well as between male and female patients. The results indicated a non-significant difference between

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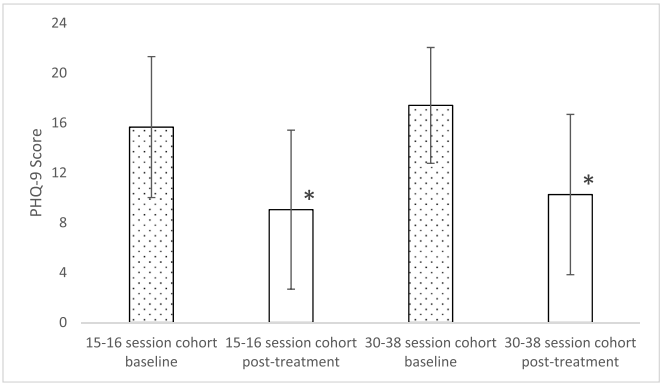


**Fig. 1.** PHQ-9 score before and after TMS treatment. (* = significant $p < 0.001$).

the 15 to 16 session cohort ($M = 28$, $SD = 8.57$) and 30 to 38 session cohort ($M = 31$, $SD = 10.16$), [$t(57) = -0.918$, $p = 0.362 > 0.01$].

To determine whether there were any sex or age-group related differences in depression at any time during the study, independent samples-t-tests were computed on baseline, 15 to 16 session, 30 to 38 session, and final PHQ-9 scores. None of the mean differences in sex or age groups were statistically significant.

This study analyzed an excitatory rTMS protocol as a treatment for post-concussion depression following TBI. Primary results supported the hypothesis that TBI patients experienced decreased depression following rTMS treatment. With a Cohen's d of 0.932 in the 15 to 16 session group and 1.031 in the 30 to 38 session group, effect was large.

Results suggested that rTMS was an effective treatment for depression in patients with PCS. rTMS is minimally invasive and safe relative to pharmaceutical and electroconvulsive therapies.

It is important to note limitations that arise from the retrospective, open-label, uncontrolled nature of this study. The ongoing assessment of rTMS as a treatment for post-concussion depression would benefit from a controlled study comparing patients undergoing rTMS treatment to patients undergoing alternative treatments or no treatment. With the only longitudinal measure of depression in this study being PHQ-9, a future study could include surveying of other aspects of PCS.

This study suggests that rTMS is a potential treatment option for depression following TBI. Both 15 to 16 session and 30 to 38 session cohorts showed significant decreases in depression as measured by PHQ-9 following rTMS treatment. These findings support the use of rTMS in post-concussion depression treatment and highlight the need for more research on rTMS therapy following TBI.

## Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Author Dr. Harpreet Singh owns the medical practice where the study took place. He declares no other financial conflicts of interest. All other authors declare no financial conflicts of interest.

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