

Post-Traumatic Major Depression (PTMD) among Repetitive Trans-Cranial Magnetic Stimulation (rTMS) and Sham controlled Traumatic Brain Injury (TBI) patients: A Systematic Review and Meta-analysis.

Introduction 33% of Traumatic Brain Injury (TBI) patients suffer from Post Traumatic Major Depression (PTMD) within a year (1). Unlike conventional interventions, low frequency repetitive Transcranial Magnetic Stimulation (rTMS) has emerged as a non-invasive treatment for PTMD.

Objectives To determine the effectiveness of low frequency rTMS for the treatment of PTMD in TBI patients.

Methods PubMed (n=9), Trip Medical Database (n=4), ClinicalTrials.Gov (n=13) & ICTRP (n=1) were searched for 'rTMS', 'TBI' & 'depression'. Studies from inception were imported to EndNote X9 Library and duplicates (n=3) were removed. RCTs conducted with TBI patients (≥ 18 years) having completed treatment with rTMS for PTMD compared against Sham controlled placebo groups were screened by Title & Abstract (n=23-12=11) and full text (n=11). Data extracted from 4 studies were included in the meta-analysis of Montgomery-Åsberg Depression Rating Scale (MADRS) Score and analysed in Review Manager 5.4.

Results Due to significant heterogeneity ($\text{Chi}^2 = 177.99$, $p < 0.000001$, $I^2 = 98\% > 75\%$), inverse variance random effect meta-analysis was done. MADRS scores of 63 patients from 4 studies revealed a pooled Mean Difference of 3.52 [CI 95%, -2.54, 9.58]. Test for overall effect indicates no statistically significant difference $Z = 1.14$ ($P = 0.26$) in the decrease in PTMD between Sham controlled and rTMS patients. Overall improvement in depression reached statistical significance ($Z = 5.11$ ($P < 0.00001$)) in sham controlled favouring sub-group (fixed effect meta-analysis ($I^2 = 76\%$)), while the only study

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favouring rTMS showed significant improvement in PTMD with $Z = 3.33$ ($P = 0.0009$).

Conclusion The pooled evidence suggests that there is no significant improvement in PTMD by rTMS compared to Sham control. While statistically significant improvement in PTMD was seen after treatment with both rTMS and Sham. The meta-analysis from our study shall guide treatment and future researchers.