Systematic Review

A Systematic Review on the Effectiveness of rTMS for Management of Pain, cognitive Dysfunction, and Depression in Traumatic Brain Injury

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Abstract

Background: The objective is to evaluate the effectiveness of repetitive transcranial magnetic stimulation (rTMS) for improving cognitive dysfunction, pain, and depression following traumatic brain injury (TBI). **Material and Methods:** A systematic literature search was conducted in PubMed, Scopus, Web of Science, and the Directory of Open Access Journals from database inception to May 2025. Randomized controlled trials evaluating rTMS in patients with TBI were included. Two reviewers independently screened studies, extracted data, and assessed methodological quality using the Cochrane Risk of Bias 2 tool. Outcomes of our systematic reviews were cognitive improvement, depression and pain, which were qualitatively compared across studies. **Results:** Twelve randomized controlled trials involving 305 participants were included, comprising 158 participants receiving active rTMS and 147 receiving sham/control stimulation. Cognitive outcomes were assessed in 5 studies; 1 study demonstrated significant improvement, whereas 4 studies found no significant benefit, indicating heterogeneous cognitive effects. Pain outcomes were evaluated in 5 studies, of which 3 demonstrated significant improvement and 2 showed no statistically significant benefit. Depression was assessed in 7 studies; 2 demonstrated significant improvement, whereas 5 reported no significant between-group benefit. Improvements in some outcomes were observed immediately after treatment, but benefits were not consistently maintained during follow-up. **Conclusion:** rTMS is a non-invasive neuromodulatory intervention for TBI, however, improvement in cognition, pain and depression following TBI remain inconsistent among studies. Heterogeneity in stimulation parameters, patient characteristics, outcome measures, and follow-up duration limits definitive conclusions. Larger, well-designed multicenter randomized trials with standardized protocols and longer follow-up are warranted.

Keywords: cognitive dysfunction, depression, pain, transcranial magnetic stimulation, traumatic brain injury.

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Introduction

Traumatic brain injury (TBI) as defined by the Centers for Disease Control and Prevention (CDC) refers to a mechanical injury to the brain caused by a collision, blow, or bump.[1] Annually above 50 million people sustain TBI, contributing to 30% to 40% one-third to two-fifths of all injury-related mortality.[2] As per the latest Global Burden of Disease, the number of incident and prevalent cases of TBI were 20.84 million and 37.93 million, respectively in the world in 2021.[3] TBI has emerged as major health issue globally because of the complications related to it.[1]

Individuals recovering from TBI usually have impairment in motor cognition and behaviour. Cognitive impairment, major clinical consequence of TBI, commonly presents as deficit in memory, attention, memory, and executive functioning.[4] Impaired consciousness, manifested as coma or vegetative state, develops in above half of the patients and is related to prolonged cognitive impairment.[5] TBI leads to impairments in memory and executive function, making recovery challenging. These cognitive deficits significantly affect rehabilitation, thereby reducing quality of life of patients.[6]

Chronic headache is also related to moderate TBI, with prevalence reported as high as 75%, which presents in the form of recurrent or enduring pain lasting above 3 months and related to significant mental and functional impairment.[7] Apart from this, depression after trauma remains a significant mental disease seen in 9% to 30% individuals.[8]

Post-trauma, it becomes important to adjudge the morbidity associated with trauma and provide management for early recovery and better outcomes for the patients.

Currently, rehabilitation remains the cornerstone of management for neurological deficits following TBI. However, complete neurological recovery is often not achieved, highlighting the need for adjunctive therapeutic strategies. In this context, repetitive transcranial magnetic stimulation (rTMS) has emerged as a promising non-invasive neuromodulatory technique. By

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generating electromagnetic fields that induce electrical currents within targeted cortical regions, rTMS modulates neuronal excitability and promotes neuroplasticity, thereby improving cognitive function. This painless and well-tolerated intervention has shown therapeutic potential across a range of neurological and psychiatric disorders.[9] High-frequency rTMS (≥5 Hz) is particularly associated with cognitive enhancement, and stimulation of the dorsolateral prefrontal cortex (DLPFC) has been shown to improve cognitive performance by strengthening cortico-hippocampal connectivity and facilitating neural network reorganization.[10-12]

Multiple different studies and analyses have been done that assessed the therapeutic efficacy of rTMS in TBI patients, 2,13-28 and we tried to club it into one systematic review.

Materials and Methods

This systematic review was conducted as per the Cochrane Handbook for Systematic Reviews of Interventions and reported following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.29

Literature Search Strategy: This review was conducted using a comprehensive literature search from database inception to 31 July 2026. The search identified relevant studies on the use of rTMS in TBI rehabilitation. The search strategy involved querying multiple electronic databases, including PubMed, Scopus, Web of Science, and DOAJ. Keywords used in the search included combinations of "repetitive transcranial magnetic stimulation," "rTMS," "traumatic brain injury," "TBI," "rehabilitation," "neurostimulation," and "neurorehabilitation." The search was restricted to peer-reviewed articles published in English, with no limitations on publication date to capture both early and recent studies.

Inclusion and Exclusion Criteria

Studies were included if they met the following criteria:

1. Focused on the application of rTMS in TBI rehabilitation.
2. Included human participants with TBI.
3. Randomized controlled trials (RCTs).
4. Reported on the therapeutic outcomes of rTMS, such as cognitive, motor, or behavioral improvements, depression or pain.

Studies were excluded if they:

1. Were case series, observational studies, reviews, or meta-analyses.
2. Did not specifically address the application of rTMS in TBI.
3. Lacked sufficient methodological details or outcome data.

Data Extraction: Data from the selected studies were extracted independently by two reviewers using a standardized form. The reference lists of relevant articles and systematic reviews were manually screened for identifying additional studies. Two reviewers independently screened titles and abstracts after duplicate removal. Eligible full texts were then assessed independently. Disagreements were resolved through consultation with a third reviewer. Extracted information included study design, sample size, participant characteristics (e.g., age, TBI severity), rTMS protocols (e.g., frequency, intensity, duration), and outcome measures. Any discrepancies in data extraction were resolved through discussion or consultation with a third reviewer.

Data Synthesis: A narrative synthesis was conducted to summarize the findings from the included studies. Given the heterogeneity in study designs, rTMS protocols, and outcome measures, a meta-analysis was not feasible. Instead, results were grouped by key outcome domains, including cognitive function, motor recovery, and emotional regulation. The efficacy of different rTMS protocols was compared, and safety profiles were analyzed, particularly concerning adverse effects like seizures. Patients demographic characteristics (age, gender), intervention details, comparator, follow-up duration, and outcome measures. were extracted. The outcomes of our systematic reviews were cognitive improvement, improvement in depression and pain. As no meta-analysis was done, publication bias was not evaluated.

Ethical Considerations: As this review involved the analysis of previously published studies, no ethical approval was required. However, the review adhered to ethical standards for systematic reviews, including transparency in reporting and minimizing potential biases in study selection and data synthesis.

Results

A total of 107 records were identified through database searching, including 90 from PubMed, 3 from Scopus, 2 from Web of Science, 5 from DOAJ, and 7 from other sources. Following duplicate removal, 47 records underwent title and abstract screening. Twenty were excluded as irrelevant. Of the remaining 27 articles assessed for eligibility, 15 were excluded due to unavailable results or insufficient data. Thus, 12 RCTs met the predefined criteria [Figure 1]

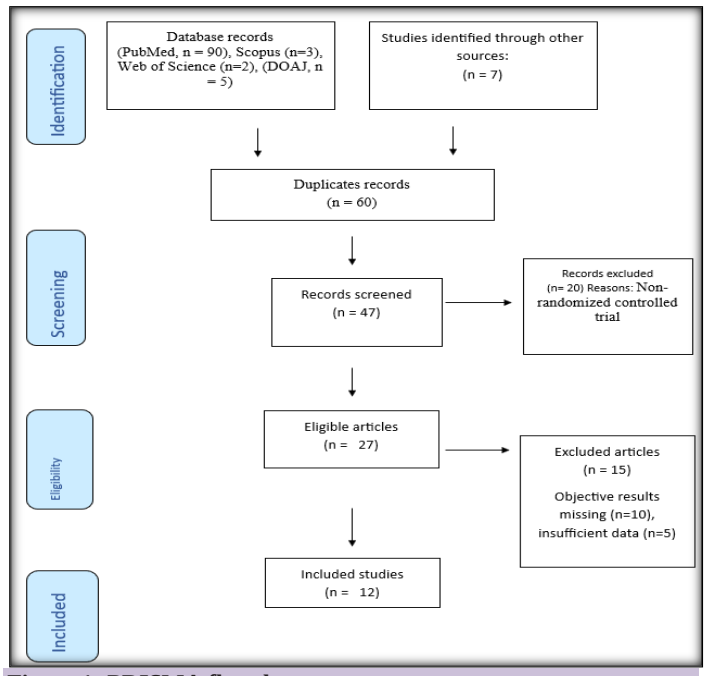


Figure 1: PRISMA flowchart

The extracted evidence comprised 12 studies, with 158 participants receiving active rTMS and 147 receiving sham/control stimulation. Most studies used double-blind designs, while one study used a single-blind design. Stimulation was most commonly applied over the DLPFC, although M1 was used in one study. Follow-up duration ranged from immediately after treatment to 16 weeks. [Table 1]

Table 1: Previous studies assessing effectiveness of rTMS for TBI

Author, year	Treatment (n, age, males)	Controls (n, age, males)	Study blinding	Area of rTMS	Cognition: Treat / Control (Mean ± SD)	Cognition: SMD (95% CI)	Pain: Treat / Control (Mean ± SD)	Pain: SMD (95 % CI)	Depression: Treat / Control (Mean ± SD)	Depression: SMD (95% CI)	Follow up
Leung et al, 2018	n=7	n=6	Double-blind	DLPFC	60.0±8.4 / 51.7±9.2 p>0.05	NR	3.6±2.0 / 4.7 ±1.7, P=0.002	NR	19.0±5.0 / 24.6±5.0, p=0.018	NR	4 weeks
Choi et al, 2018	n=12, 41 years, 83.33%	n=12, 41 years, 91.66%	Double-blind	M1 (10 Hz)	NR	NR	-27.5 ± 35.54 / 0.14 ± 27.43	-0.84 (-1.68, 0.00)	NR	-	NR
Lee et al, 2018	n=7, 42.42 years, 71.42%	n=6, 41.33 years, 66.67%	Single blind	Low-frequency DLPFC	NR	-	NR	-	-6.54 ± 4.76 / -10.27 ± 5.05	0.73 (-0.16, 1.62)	Immediately after rTMS
Rao et al, 2019	n=13, 39.8 years, 38%	n=17, 40.2 years, 65%	Double blind	Right DLPFC (1 Hz)	NR	-	NR	-	23.2 ± 4.4/ 23.7 ± 4.4	Small (Hedge's g=0.19) effect	16 weeks
Hoy et al, 2019	n=11, 41.27 years, 63.63%	n=10, 51.80 years, 30%	Double blind	Bilateral DLPFC	NR	-	-2.69 ± 8.86 / -0.85 ± 8.52	-0.21 (-0.95, 0.54)	-3.29 ± 10.65 / -2.03 ± 10.57	-0.12 (-0.86, 0.63)	4 weeks
Siddiqi et al, 2019	n=9	n=6	Double-blind	Bilateral DLPFC	NR	-	NR	NR	NR	MADRS 56% ± 14%/ 27% ± 25% (Cohen's d = 1.43)	NR
Moussavi et al, 2019	n=9, 46.7±15.3 years, 44.4%	n=9, 53.0 ± 8.8 years, 55.6%	Double-blind	Left DLPFC	NR	NR	NR	NR	11.6 ± 10.6 / 11.9 ± 9.2	NR	2 months
Neville et al, 2019	17, 32.62±12.81 years; 88.23%	13, 29.0±10.35 years; 92.3%	Double-blind	DLPFC	Executive functions: −0.99±0.56 / −0.93±0.58, P=0.838	NR	NR	NR	NR	NR	3 months
Rodrigues et al, 2020	16, 32.8±13.3 years, 87.5%	11, 31.6±11.3 years, 90.9%	Double-blind	DLPFC	Executive functions: −1.1±0.6 / 1.0±0.5, P=0.50	NR	NR	NR	BDI-II 8.4±9.0 / 4.9±5.5, P=0.54	NR	3 months
Stilling et al, 2020	n=10, 36 years, 10%	n=10, 36 years, 10%	Double-blind	DLPFC	-0.1± 2.8 / -0.1 ± 2.46	0.00 (-0.88, 0.88)	-5.6 ± 10.81 / -3.7 ± 4.14	-0.22 (-1.10, 0.66)	-4.3 ± 8.66 / -0.7 ± 7.94	-0.42 (-1.30, 0.47)	3 months
Franke et al, 2022	n=14, 45.07 years, 92.9%	n=14, 46.07 years, 78.6%	Double-blind	DLPFC	NR	-	-2.52 ± 0.81 / -0.01 ± 0.8	-2.88 (-4.68, -	NR	-	2 weeks

								1.07)			
Shen et al, 2023	n=33, 78.78%	n=33, 57.57%	Double blind	DLPFC	11 ± 12.13 / 2.5 ± 4	0.93 (0.42, 1.44)	NR	-	NR	-	NR

BDI: Beck Depression Inventory; MADRS: Montgomery–Åsberg Depression Rating Scale; NR: not reported.

Cognition: Cognitive outcomes were reported in five studies, although the outcome measures varied considerably. Leung et al,[19] reported a cognitive score of 60.0 ± 8.4 in the rTMS group compared with 51.7 ± 9.2 in the control group, with the between-group difference reported as non-significant (p > 0.05). Neville et al23 reported executive-function scores of −0.99 ± 0.56 and −0.93 ± 0.58 in the treatment and control groups, respectively (p = 0.838), indicating no significant cognitive benefit. Rodrigues et al27 similarly found no significant difference in executive-function scores between active rTMS and sham stimulation (−1.1 ± 0.6 vs. 1.0 ± 0.5; p = 0.50). In contrast, Shen et al28 reported a favorable standardized effect for cognition (SMD 0.93, 95% CI 0.42–1.44), with mean cognitive scores of 11.0 ± 12.13 versus 2.5 ± 4.0. Stilling et al,[15] found no difference (SMD 0.00, 95% CI −0.88 to 0.88).

Pain: Pain-related outcomes were reported in five studies. Leung et al19 observed significantly lower pain scores with rTMS (3.6 ± 2.0 vs. 4.7 ± 1.7; p = 0.002). Choi et al,[17] reported a favorable effect of rTMS on chronic central pain, with scores of −27.5 ± 35.54 compared with 0.14 ± 27.43 in controls (SMD −0.84, 95% CI −1.68 to 0.00). Hoy et al,[18] found no significant difference (−2.69 ± 8.86 vs. −0.85 ± 8.52; SMD −0.21, 95% CI −0.95 to 0.54). Similarly, Stilling et al15 reported −5.6 ± 10.81 vs. −3.7 ± 4.14, with an SMD of −0.22 (95% CI −1.10 to 0.66). Franke et al14 demonstrated favorable effect (−2.52 ± 0.81 vs. −0.01 ± 0.80; SMD −2.88, 95% CI −4.68 to −1.07).

Depression: Depression outcomes were reported in several studies using different scales, predominantly the Beck Depression Inventory (BDI) or Montgomery–Åsberg Depression Rating Scale (MADRS). Leung et al,[19] demonstrated significantly greater improvement with rTMS (19.0 ± 5.0 vs. 24.6 ± 5.0; p = 0.018). Lee et al22 reported depression scores of −6.54 ± 4.76 versus −10.27 ± 5.05, with an SMD of 0.73 (95% CI −0.16 to 1.62). Rao et al,[20] found a small effect (Hedges' g = 0.19), while Siddiqi et al,[21] reported a larger effect (Cohen's d = 1.43). Hoy et al,[18] found no significant difference (−3.29 ± 10.65 vs. −2.03 ± 10.57; SMD −0.12, 95% CI −0.86 to 0.63). Similarly, Stilling et al,[15] reported an SMD of −0.42 (95% CI −1.30 to 0.47). Rodrigues et al,[27] found no significant between-group difference in BDI-II scores at 3 months (8.4 ± 9.0 vs. 4.9 ± 5.5; p = 0.54).

Discussion

The review provides an overall understanding of the effects of rTMS on cognitive dysfunction, pain, and depression or anxiety following TBI.

Cognitive dysfunction is a common and disabling consequence of TBI, particularly after moderate-to-severe injury, and may cause persistent functional limitations. Timely interventions are therefore essential to improve cognitive outcomes and reduce neuropsychiatric complications. Impaired consciousness and cognition may result from ischemic or hypoxic injury, disrupted neuronal activity, and impaired cortical-subcortical connectivity. Restoring network function supports neurological recovery.[2]

In the present review, only one study demonstrated a favourable effect of rTMS on cognitive function,28 whereas the remaining studies did not identify a significant between-group difference.[15,19,23,27] The findings corroborate with other systematic reviews and further supports this inconsistency. Aleid et al,[2] reported a significant improvement in cognition following rTMS, whereas Tsai et al,[13] found that the overall cognitive evidence remained limited and inconclusive. It was also observed that rTMS may have greater effects on specific cognitive domains, particularly visuospatial memory, while effects on processing speed and selective attention were less convincing. Zhang et al,[4] similarly reported improvements in memory and executive functioning accompanied by favourable changes in brain connectivity, whereas Li X et al,[16] did not observe significant improvement in cognitive measures. Thus, although rTMS appears promising for cognitive rehabilitation, its overall effectiveness remains uncertain.

The mechanism by which rTMS may show cognitive benefits may be from enhanced cortical excitability and neuroplasticity. High-frequency stimulation may promote neuronal repair, axonal regeneration, reactivation of silent neurons, and restoration of disrupted neural connectivity.[2] Moreover, rTMS can modulate cortico-cortical and cortico-subcortical networks, cerebral metabolism, blood flow, neurotransmitter release, and synaptic transmission, supporting functional reorganization and neurological recovery after TBI.[2,13] However, factors like severity of TBI and the protocol followed in RTMS may play a discretionary role in allowing for improvement in cognitive functions.

Pain is another frequent and debilitating consequence of TBI which was assessed for improvement following rTMS. Chronic central and neuropathic pain may develop following moderate-to-severe injury, and post-traumatic headache is a particularly common pain-related manifestation of post-concussion syndrome. Central pain following TBI may be associated with injury to the spinothalamic tract and deterioration of neuronal microstructures, resulting in impaired sensory processing and persistent pain.[2]

The findings from individual trials in the review suggest a potential analgesic effect of rTMS. Franke et al,[14] Leung et al,[19] and Choi et al,[17] reported reductions in pain following rTMS, particularly after high-frequency stimulation of the primary motor cortex. In contrast, Stilling et al,[15] and Hoy et al,[18] did not find significant improvements in pain. These findings indicate that although rTMS may provide analgesic benefits in some patients, the magnitude and consistency of the effect

remain variable.

Other previously conducted systematic reviews have provided some support for the analgesic effects of rTMS. Aleid et al,[2] and Li X et al,[16] reported significant reductions in pain and suggested that the beneficial effects on central pain may persist after treatment. However, Tsai et al,[13] found that rTMS was not superior to sham stimulation for post-concussion symptoms, suggesting that its effects on broader post-TBI symptomatology remain inconclusive. Evidence from study involving other clinical populations, i.e. post-traumatic stress disorder patients found limited improvement in symptom severity.[12] Therefore, evidence supporting the use of rTMS specifically for pain following TBI remains encouraging and may be explored further. The analgesic effects of rTMS mechanises from modulation of cortical and subcortical pain-processing networks. Primary motor cortex stimulation influences pain-related structures, including the thalamus, anterior cingulate cortex, and periaqueductal grey matter. Also, rTMS may activate descending inhibitory pathways, reduce nociceptive transmission, alter cerebral blood flow, and modulate endogenous opioid activity.[2]

Lastly, TBI may be associated with depression, which is another important neuropsychiatric consequence of TBI. Dysfunction of the DLPFC has been implicated in post-traumatic depressive symptoms because of its important role in emotional regulation and cognitive functioning.[2]

In terms of rTMS leading to improvement in depression, Leung et al,[19] Siddiqi et al,[21] and Lee et al,[22] reported significant improvements following rTMS, whereas other studies observed comparable post-treatment depressive symptoms between groups.[15,18,20,26,27] Among systematic reviews, Tsai et al,[13] and Li X et al,[16] reported a significant antidepressant effect immediately following treatment, however, it was seen that the benefit was not maintained during follow-up. In contrast, Aleid et al,[2] found no significant difference between rTMS and control groups. Hassanzadeh et al,[11] reported significant reductions in depressive symptoms in patients with major depressive disorder, although these findings may not be directly generalizable to the TBI population.

The antidepressant effects of rTMS, as seen in some studies may be explained by modulation of cortical excitability, cerebral metabolism, neural oscillations, and neurotransmitter systems. Prefrontal stimulation may enhance serotonin and dopamine neurotransmission while promoting neuroplasticity in emotion-regulation networks. These mechanisms may contribute to therapeutic benefits, although variability among studies warrants further investigation in patients with TBI.[13,16]

Overall, the review suggests that rTMS is a promising non-invasive neuromodulatory intervention for cognitive dysfunction, pain, and depressive symptoms following TBI, however, its efficacy may remain inconclusive and may not be a one-shot treatment for the patients.

Strengths of the Review: Detailed and recent synthesis of the available evidence is provided by this systematic review. Several electronic databases were systematically searched, and only RCTs and high-quality systematic reviews were included. Detailed assessment of cognitive dysfunction, pain, and depression was done, while critically comparing the consistency of evidence between studies.

Limitations of the Review: Most studies had small samples, limiting statistical power and generalizability. Comparisons were limited due to substantial heterogeneity in participant characteristics, TBI severity, stimulation parameters, treatment duration, outcome measures, and follow-up periods.

Future Recommendations: Future multicenter studies are needed to standardize rTMS protocols, including stimulation site, frequency, intensity, session duration, and treatment duration. Consistent outcome measures and longer follow-up are needed to assess effects on cognition, pain, and depression, while evaluating injury severity, timing, and patient characteristics influencing treatment response.

Conclusion

In conclusion, rTMS is a promising non-invasive neuromodulatory intervention for improving selected neurological and neuropsychiatric outcomes following TBI. The existing evidence indicates beneficial effects on cognitive function, specifically memory, and suggests a potential role in decreasing post-traumatic pain as well as depressive symptoms. However, the magnitude and consistency of these benefits differed between studies due to variation in patient populations, injury severity, stimulation protocols, outcome measures, and follow-up duration. Present evidence supports the safety and therapeutic potential of rTMS, however, it remains inadequate to establish standardized clinical recommendations.

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