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Review

The Use of Repetitive Transcranial Magnetic Stimulations for the Treatment of Post-Traumatic Stress Disorder: A Scoping Review

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Abstract: Repetitive transcranial magnetic stimulation (rTMS) is a non-invasive procedure in which brain neural activity is stimulated by the direct application of a magnetic field to the scalp. Despite its wide and continuous usage for the management of psychiatric disorders, the use of rTMS for post-traumatic stress disorder (PTSD) is not well established and evaluated by researchers. This scoping review seeks to explore the relevant literature available regarding the use of rTMS as a mode of treatment for PTSD, to map evidence in support of the use of rTMS for PTSD, and recommendations on future clinical and research work. Five databases were searched (MEDLINE, CINAHL, Psych INFO, SCOPUS, and EMBASE) to identify empirical studies and randomized controlled trials aimed at the treatment of PTSD with rTMS. A total of 10 studies were eligible for this review. The search results are up to date as of the date of the electronic data search of 20 December 2020. The frequencies applied in the studies ranged from low (1 Hz) to high (10 Hz) at different thresholds. Nine reported significant positive outcomes and PTSD symptoms improvement. rTMS was reported as well tolerated with no significant side effects. The application of rTMS for PTSD looks promising despite the diversity in terms of its outcomes and its clinical significance. Studies with well-defined stimulation parameters need to be conducted in the future.

Keywords: repetitive transcranial magnetic stimulation; post-traumatic stress disorders; mental illness

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1. Introduction

Post-traumatic stress disorder (PTSD) is a common psychiatric condition that results in significant psychosocial dysfunction and presents through four distinct diagnostic clusters, namely: re-experiencing, avoidance, negative cognitions and mood, and arousal [1,2]. The prevalence of specific traumatic events varies geographically. Thus, compared to developing countries, developed countries have a greater number of individuals (28 to 90% of people) with at least exposure to a traumatic event [3]. Studies suggest that most adults will experience some form of traumatic situation at some point in their lives irrespective of their geographical location [3].

About 7% of the population of the United States of America will experience PTSD during their lifetime [4]. Furthermore, 48% to 71% of veterans are exposed to more traumatic situations during their service days, 15% of whom are diagnosed with PTSD [5,6]. About 25–40% of patients with PTSD are expected to recover within a year, but the rate of remission for most persons can require longer durations. The mean duration of symptoms is 6 years across the various trauma types. Symptoms from combat-associated PTSD have a mean duration of 13 years [7,8]. The treatment of choice for PTSD currently is psychotherapy and antidepressant medications [9]. Despite receiving these treatments, about 50% of patients continue to experience significant symptoms [10,11]. This highlights the need to continue

therapeutic development research for PTSD and to consider the role of machine-based interventions, such as transcranial magnetic stimulation (TMS).

TMS is a non-invasive neuromodulatory tool that stimulates neural activity by the use of rapidly alternating magnetic fields. TMS operates through Faraday's law of electromagnetic induction, where the rapidly alternating electric current in the stimulating coil placed over the scalp generates a magnetic field that moves across the skull and produces electric currents in the neural tissue underneath [12]. This magnetic field has the ability to penetrate the bone of the skull to stimulate activity in the cortical neurons beneath. The pulse can be delivered in a repeated manner to induce a long-term effect on neural activity [13]. Anthony Berker originally introduced TMS in 1985 as a safer and painless means of studying the central nervous system to stimulate the motor cortex and to assess the human central motor pathways [14].

Repetitive transcranial magnetic stimulation (rTMS) is a new TMS technique that alters brain activity via repeated changes of the coil's magnetic field. The modulation effect is capable of reaching the cortex and subcortical areas, and depending on whether high (>1 Hz) or low (1 Hz) frequency, rTMS can either decrease or increase cortical excitability [15,16]. rTMS has become an integral research tool in psychiatry treatment as a result of its ability to give rise to explicit effects on a range of measures of brain function [17,18]. rTMS is considered a safe and non-invasive treatment modality [19,20]. rTMS has been evaluated extensively as a major therapeutic tool for several psychiatric disorders, such as bipolar disorders, psychotic disorders, anxiety disorders, obsessive-compulsive disorders and PTSD [21].

The use of rTMS in PTSD was investigated as early as 1998 [22]. Studies since then have suggested rTMS as a potentially effective treatment modality for PTSD [23–26]. Consequently, there has been increasing use of rTMS in the treatment of PTSD [27,28]. However, despite the increasing use of rTMS for the treatment of psychiatric disorders, the therapeutic use of rTMS is still largely in the domain of major depressive disorder (MDD) [29]. Much less is known about how rTMS is used in the management of PTSD [30]. This scoping review aims to bridge this gap in the literature.

2. Methods

The study methods have been published previously in a related paper [31]. In summary, an operationalized search strategy was employed to electronically search five research databases (MEDLINE, CINAHL, Psych INFO, SCOPUS, and EMBASE) using identified keywords and index terms across all the databases to identify evidence-based studies and randomized controlled trials. Keywords included: repetitive transcranial magnetic stimulation, obsessive-compulsive disorder, post-traumatic stress disorders, bipolar disorders, and treatment. This is a larger search strategy involving results for the use of rTMS for the treatment of three major mental disorders (OCD, PTSD, and bipolar disorders), but this paper specifically reports only on and discusses the results for PTSD. The related paper reported on the results related to the use of TMS for OCD [31]. The search results are up to date as of the date of the electronic data search of 20th December 2020. Table 1 shows a sample of the search strategy on Medline. Thematic classifications were done by the first reviewer (MA), with decisions analyzed by the second reviewer (EE). Where conflicts in classification existed, the article in question was scrutinized and a consensus was reached between the two reviewers.

Inclusion and Exclusion Criteria

This study included completed randomized controlled trial (RCT) of rTMS as a treatment intervention for PTSD and open-label trials on PTSD using rTMS as a treatment intervention. The review only covered full-text articles and studies published in English. Studies involving rTMS as a form of treatment for conditions other than PTSD and studies with rTMS treatment involving PTSD patients but targeting comorbidities were also excluded. Studies with rTMS as combined therapy with pharmacotherapy or any other

interventions were excluded. Systematic reviews, meta-analysis and study protocols, and experiments of rTMS that are not designed for treatment for PTSD were not involved.

Through the search strategy, we identified a total of 2373 studies from the electronic databases searched. The Covidence software (Melbourne, VIC, Australia) automatically screened and removed 872 studies as duplicates. The remaining items (1501) were screened against the eligibility criteria set by the authors based on the title and abstract only, yielding 182 remaining records for full-text screening. The remaining items were full text screened by the two reviewers and excluded 172 studies from the records. A total of 10 studies were then eligible for inclusion for this scoping review as shown in Figure 1. All studies examined rTMS as a stand-alone treatment intervention for PTSD with most of them comparing the use and efficacy of rTMS to sham treatment. The key findings are summarized from the various studies and presented in Table 2.

Table 1. Medline Search Strategy.

Search Strategy	Number of Articles Found
exp * Stress Disorders, Post-Traumatic/or (PTSD or ((posttraumatic or post-traumatic or combat or war or trauma *) adj1 (stress * or neurosis or neuroses or nightmare *)) or ((traumatic or acute) adj (stress disorder * or stress symptom *)) or shell shock * or shellshock *).mp.	46,596
exp obsessive-compulsive disorder/ or Biplar Disorder/	54,776
(Bipolar or bi-polar or manic-depress * or mania or obsessive-compulsive disorder * or OCD).mp.	102,961
1 or 2 or 3	147,991
Transcranial Magnetic Stimulation/	11,653
(repetitive transcranial magnetic stimulation or rTMS).mp.	5423
5 or 6	13,372
4 and 7	492

NB: * = Truncation.

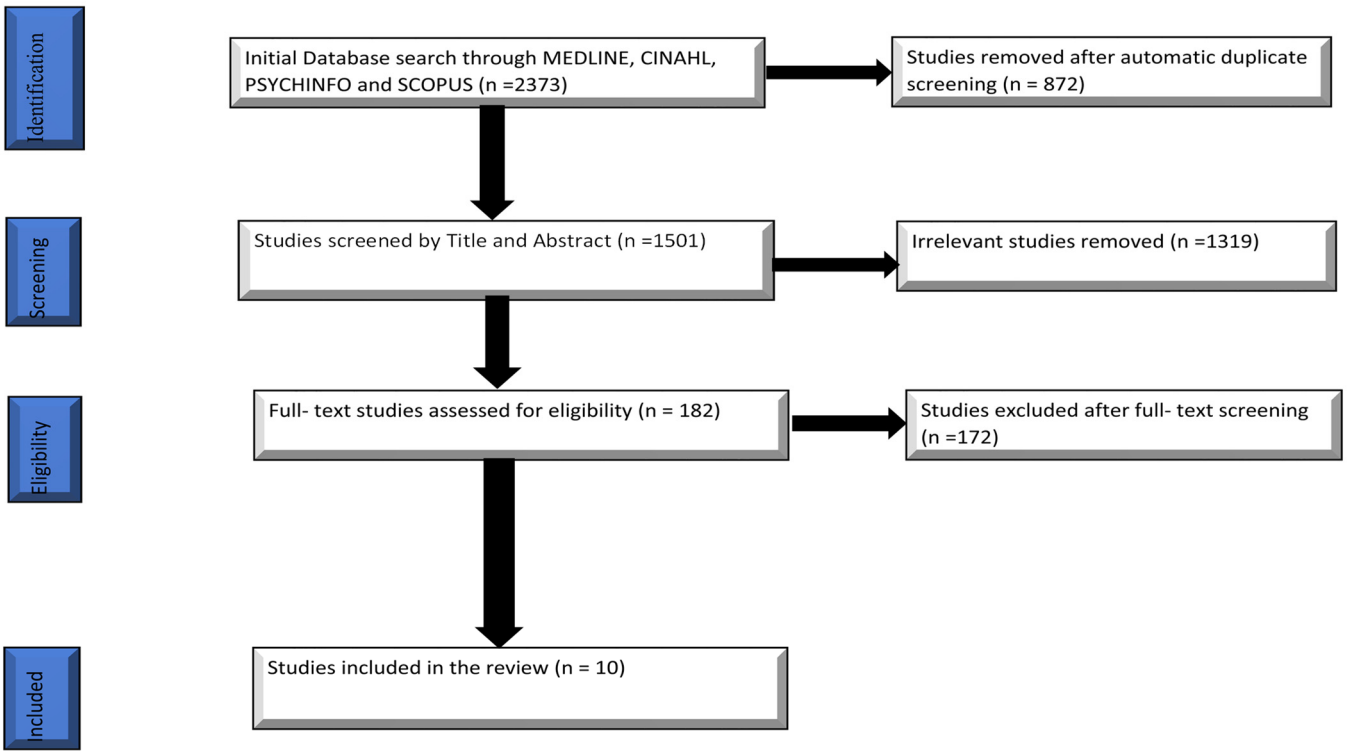

Figure 1. Prisma Flow Diagram Summarizing Search Process and Results.

Table 2. Summary of studies using rTMS for the treatment of PTSD.

Author (Year)	Country of Origin	Study Design	Number of Participants	Targeted Brain Region	Targeted Symptom	Measurement	Duration	Coil/ rTMS Parameters /Stimulation Method	Outcome/Significant Improvements	Assessment and Follow-Up	Conclusion	Side Effects
K. Leong et al. (2020) [32]	Canada	Randomized sham-controlled trial	31 patients	Right -DLPFC	Change in severity of PTSD symptoms	CAPS-IV. GAD-7 PCL-C	2 weeks	Double 70 mm Air Film Coil model 3910-00. 120% RMT. 1-Hz with 2250 pulses over 37.5 min, whereas those assigned to 10-Hz received 3000 pulses over 37.5 min (4-s stimulation train with 26 s intertrain interval). 2 weeks of daily treatments (10 treatments).	Low-frequency 1-Hz rTMS results in greater improvements in PTSD symptoms relative to sham (Hedges' g = −1.07). but not in the 10-Hz group.	At baseline, at treatment end, and 3-month follow-up.	Low-frequency rTMS is efficacious in the treatment of civilian PTSD.	Suicidal ideation
F.A. Kozel et al. (2019) [33]	USA	A random-ized clinical trial	44 patients	Right DLPFC	PTSD and depressive symptoms	CAPS, PCL-5, IPF	6 weeks	110% of MT. 1 Hz rTMS. 40 min for a total of 2400 pulses/session. 10 Hz, rTMS was 4 s on and 36 s off for 40 min for a total of 2400 pulses/session.	Although both groups demonstrated significant improvement in PTSD and depression symptoms, a significant advantage for either the 1 Hz or 10 Hz frequency group on any of the scales acquired was not demonstrated. (IPF 1 Hz—($p = 0.075$)) and IPF 10 HZ—($p = 0.008$)).	After every 5 treatments for the first 30 treatments, at the end of treatment taper, and 1- and 3-month posttreatment follow-ups.	Although both groups demonstrated significant improvement in PTSD and depression symptoms, a significant advantage for either the 1 Hz or 10 Hz frequency group on any of the scales acquired was not demonstrated.	Nil
Fryml et al. (2019) [34]	USA	A prospective, random-ized, double-blinded, active sham-controlled design	12 patients	Left or right DLPFC	Mood and PTSD symptoms	CAPS, HDRS, PCL-C	5 weeks	Figure-eight solid core coil at 120% MT, 10 Hz, 5-s train duration, and 10-s intertrain interval for 30 min (6000 pulses) weekly for 5 weeks (30,000 stimuli).	Results from this study suggest that delivering rTMS to PTSD patients while they simultaneously receive PE is feasible.	Baseline and weekly throughout the treatment	The study demonstrates the safety and feasibility of rTMS delivery to PTSD patients.	Nil
F.A. Kozel et al. (2018) [35]	USA	A random-ized clinical trial	103 patients	Right -DLPFC	Reduction in symptoms of PTSD	CAPS, QIDS, SCID, SC-Q	12 weeks	Double 70 mm Air Cooled Coil 110% MT at 1 Hz rTMS for 30 min for a total of 1800 pulses.	Improved symptom reduction in combat veterans with PTSD. $t(df \geq 325) \leq -2.01$, $p \leq 0.023$, one-tailed and $t(df \geq 303) \leq -2.14$, $p \leq 0.017$, one-tailed, respectively.	Baseline repeated session-5, session-9,1-month post-treatment, 3- and 6-months post-treatment.	Combining CPT with rTMS led to improved symptom reduction in combat veterans with PTSD.	Headaches

Table 2. *Cont.*

Author (Year)	Country of Origin	Study Design	Number of Participants	Targeted Brain Region	Targeted Symptom	Measurement	Duration	Coil/ rTMS Parameters /Stimulation Method	Outcome/Significant Improvements	Assessment and Follow-Up	Conclusion	Side Effects
M.-J. Ahmadizadeh, M. Rezaei (2018) [36]	Iran	A randomized controlled study	384 males patients	Bilateral DLPFC and right DLPFC (F4),	PTSD symptoms	SCID, PCL-M	4 weeks	70 mm figure-eight stimulation coil (air film coil). 100% MT. HF, 20 Hz rTMS Duration: 2 s Inter-train interval: 28 s Total train: 30 for bilateral Total pulse per session: 1200 for 15 min.	Significant PTSD symptom reductions in the bilateral group compared to the sham group in session five and endpoint. (effect of time: Wilks' Lambda = 0.22, $F_{(2,45)}$ = 81.50, p = 0.0001).	Baseline and after each session.	Findings suggest that bilateral and unilateral right rTMS are superior to sham rTMS but do not support the hypothesis that bilateral rTMS is more effective than unilateral high-frequency right-sided rTMS.	Headache
D.H. Nam, et al. (2013) [37]	Korea	A double-blind, sham-controlled study	18 patients	Right- PFC	Re-experiencing symptoms of PTSD	CAPS, SCID	3 weeks	A figure-of-8 coil 100% MT total, 18,000 pulses 3 weeks of 1 Hz for 20 min per weekday (for a total of 15 days).	The study showed low-frequency rTMS to be an effective and tolerable option for the treatment of PTSD. Treatment group effect (df = 1, F = 2.36, p = 0.147).	Baseline and at 2, 4, and 8 weeks	The study showed low-frequency rTMS to be an effective and tolerable option for the treatment of PTSD.	Headache, Dizziness
B.V. Watts et al. (2012) [38]	USA	A sham-controlled study	20 patients	Right -DLPFC	Changes in symptom measures	CAPS, BDI, STAI, BNCE	10 days	A figure-of-eight (MCB) 70 coil 90% MT. 1 Hz 20 min per day. Each 1 min cycle consisted of a 20-s stimulation train with a 40-s intertrain interval.	Statistically and clinically significant improvements in core PTSD symptoms CAPS (p = 0.009) and PCL (p = 0.0002) and depressive symptoms compared with sham treatments. (p = 0.03)	At baseline, after 10 rTMS sessions, 1 month after the last session, and 2 months after the last session.	This blinded sham-controlled trial supports the efficacy of 10 sessions of right DLPRC rTMS delivered at 1 Hz for the treatment of PTSD symptoms.	Nil
Boggio et al. (2010) [28]	USA	Double-blind, placebo-controlled phase II trial,	30 patients	L-DLPFC and right DLPFC	PTSD symptoms	PCL-5 HRSD HAMA	2 weeks	Figure-8 coil, 20 Hz at 80% MT 10 TMS, 1600 pulses per session, 5 days per week for 2 weeks.	Results show that both active conditions—20 Hz rTMS of left and right DLPFC—induced a significant decrease in PTSD symptoms.	Baseline, at day 5, at day 10, at day 24, at day 38, at day 66, and day 94 (12 weeks after treatment).	Results support the notion that modulation of the prefrontal cortex can alleviate the core symptoms of PTSD and suggest that high-frequency rTMS of R- DLPFC might be the optimal treatment strategy.	Nil

Table 2. *Cont.*

Author (Year)	Country of Origin	Study Design	Number of Participants	Targeted Brain Region	Targeted Symptom	Measurement	Duration	Coil/ rTMS Parameters /Stimulation Method	Outcome/Significant Improvements	Assessment and Follow-Up	Conclusion	Side Effects
E.A. Osuch et al. (2009) [39]	USA	Double-blind, sham-controlled crossover design	9 patients	R-DLPFC	Exaggerated reactions individuals have in response to reminders of the traumatic event	CAPS, HDRS	2 weeks	Figure-8 shaped water-cooled coil. 100% MT. 1 Hz. total of 36,000 stimuli in each condition 20 rTMS sessions. 3 sessions per wk and no more than 5 per wk. Each for 30 min. 2 weeks interval between first and second conditions.	Reduction of the exaggerated reactions individuals have in response to reminders of the traumatic event or other stimuli through fear extinction. CAPS ($p = 0.87$) HDRS ($p = 0.92$)	At baseline (within 3 days before the first condition); on the final day of the first condition; on the day before the onset of the second condition; and on the last day of the second condition.	Reduction of the exaggerated reactions individuals have in response to reminders of the traumatic event or other stimuli through fear extinction.	Nil
Cohen et al. (2004) [40]	Israel	A double-blind, placebo-controlled study	24 patients	Right-DLPFC	Reexperiencing, avoidance	HDRS, PCL-C	2 weeks	Circular coil with a 9-cm diameter. (1 Hz) or (10 Hz) rTMS at 80% MT 20 min per days. 10 daily sessions over 2 weeks.	10 daily sessions of 10-Hz rTMS at 80% MT over the right DLPFC has therapeutic effects on PTSD patients active 10-Hz rTMS was significantly different from the sham ($p < 0.01$) and 1-Hz ($p < 0.002$) treatments.	Before TMS (baseline), at day 5, at day 10, and day 24 (14 days after the intervention).	Trial suggests that in PTSD patients, 10 daily sessions of right dorsolateral prefrontal rTMS at a frequency of 10 Hz have greater therapeutic effects than slow-frequency or sham stimulation.	Headache

MT = motor threshold; SMA = supplementary motor area; Y-BOCS = Yale–Brown obsessive-compulsive scale; Ham-D–24 = Hamilton Rating Scale for Depression–24-item; BDI–II, DLPFC = dorsal lateral prefrontal cortex; OFC = orbitofrontal cortex; RMT = resting motor threshold; CGI-I = Clinical Global Impression; HAMA = Hamilton Anxiety Rating Scale; HRSD = Hamilton Rating Scale for Depression; YMRS = Young Mania Rating Scale; GAF = Global Assessment of Functioning; MCCB = MATRICS Consensus Cognitive Battery; QIDS = Quick Inventory of Depressive Symptomatology; CAPS = Clinician-Administered PTSD Scale; BNCE = Brief Neurobehavioral Cognitive Examination; STAI = State-Trait Anxiety Inventory; SC-Q = Self-Administered Comorbidity Questionnaire; SCID = Structured Clinical Interview for DSM-IV; IPF = Inventory of Psychosocial Functioning; BRMAS = Bech–Rafaelsen mania scale; CRSD= circadian rhythm sleep disorder; SCL-90-R = Symptom Checklist-90-Revised.

3. Results

Out of the 10 studies on rTMS application and treatment included in this review, six (60%) were conducted in the United States of America. Iran, the Republic of Korea, Canada, and Israel, all had one paper conducted representing (10%) each. This suggests that studies on rTMS treatment in PTSD are not widely and evenly conducted across the different geo-graphical regions in the world. All 10 studies applied the randomized controlled trial method, but of different formats and forms, such as parallel, double-blind, open labels, and with single, two, or, four arms. The sample size for the various trials ranged from (n = 9 to n = 384). The participants in the various studies were all patients diagnosed with PTSD.

3.1. Outcome Measures

A wide range of scales were used to measure positive symptoms and reduction in symptoms scales including, for example, PCL- C, PCL-5, CAPS, and HDRS were the outcome measure in most of the studies. Safety outcomes included adverse event reporting, neurocognitive assessments, and vital signs assessments for the various studies.

3.2. Frequency, Intensity of Stimulation, Duration of Treatment, and Brain Target

The frequency of rTMS ranged from as low as 1 Hz to 20 Hz. The majority of the studies (6 out of 10) applied the 1 Hz frequency. The intensity of stimulation reviewed in the included studies also ranged from 80% to 120% motor threshold. The duration of active rTMS treatments in the included studies ranged from 2 weeks to 12 weeks. Regarding the number of magnetic pulses given per treatment session, there was a range varying from 1200 pulses up to 36,000 pulses. The studies were heterogeneous in terms of features of clinical variability, such as the severity of PTSD symptoms and duration of sickness. Out of the 10 studies included, seven used 70 mm figure-of-eight shaped coils, one study utilized the 9 cm circular coil design and two studies used the double 70 mm air cooled coil. In eight out of the ten studies extracted, the site of rTMS stimulation was targeted at the right-DLPFC [32,33,36–41], and the remaining two studies sought to compare the efficacy of the right-DLPFC and the left-DLPFC [28,34].

3.3. Outcome Results

Nine out of the ten studies reported significant positive outcomes and significant PTSD symptoms improvement. One study that sought to evaluate the effectiveness between low and high frequencies failed to identify any superiority of one over the other. rTMS application was reported as well tolerated with no significant side-effects, although there were a few reports of mild side-effects, such as mild headache, dizziness, and scalp pain, across the studies.

4. Discussions

This review found that rTMS may be a clinically efficacious treatment modality for patients diagnosed with PTSD. There were consistent significant improvements in the condition of subjects across the studies despite the diverse nature of the outcomes. Many factors may have accounted for the differences in the effectiveness of rTMS application across the major domains. For example, rTMS treatment protocols and stimulation parameters vary across studies, with poorly defined application protocols. Again, the different measuring tools used for the evaluation of similar outcomes across studies make comparison and evaluation of results difficult. It also makes it difficult to identify which rTMS application protocols lead to the most significant treatment response. However, due to the differences in the presentation of patients' conditions in terms of severity and duration of illness, it may seem unrealistic to identify a single or even a standardized rTMS protocol that will work for studies of the different conditions even if they target similar or the same symptoms [42]. An essential aspect of rTMS as identified in this review is its versatility, making its application

have room for study-specific protocols addressing different symptoms and still coming out with potentially positive outcomes.

Although data suggest that rTMS may have some therapeutic effect in the management of PTSD [43], they mostly present without information about maintenance treatment or long-term outcomes [44]. The possible effect of rTMS may be through stimulation of the prefrontal cortex, especially the ventromedial aspects, and hence inhibiting the hyperactive amygdala and the overactive sympathetic system, which in turn may explain the reduction of hyperarousal symptoms in PTSD [43,44].

4.1. Targeted Brain Regions of rTMS

Post-traumatic stress disorder, according to neurobiological studies, is characterized by a dysregulated fear response and a hyperactive amygdala, as demonstrated by imaging studies. The regions involved in the modulation of the amygdala, thus, the medial prefrontal cortex and hippocampus, are deemed to have a reduced activity to fear cues in functional magnetic resonance imaging studies [45]. Considering the pathophysiology of PTSD, neuromodulation of prefrontal structures using rTMS has been hypothesized by many studies to have potential effects in the treatment of patients with PTSD [43,46]. Some studies have also suggested that rTMS induced significant changes in a monoamine receptor in the cerebral cortex and has a substantial and rapid effect on the monoamine neurotransmitters system [36,43]. Studies evaluating the use and efficacy of rTMS as a treatment intervention for PTSD are still accumulating and evolving [25]. In eight out of the ten studies extracted, the site of rTMS stimulation was targeted at the right-DLPFC [32,33,36–41] and the remaining two studies sought to compare the efficacy of the right-DLPFC and the left-DLPFC [28,34]. In a double-blind placebo-controlled study [38], the efficacy of a right-sided low-frequency rTMS to sham treatment in 20 patients diagnosed with PTSD was evaluated and found clinically significant improvements in PTSD symptoms and depressive symptoms compared with sham treatments. Though the improvement of depression symptoms by rTMS leads to improvement in the symptoms of PTSD, the majority of rTMS studies have sought to stimulate the R- PFC for PTSD versus L-PFC commonly targeted in MDD [33,41].

Another open-label and prospective trial, involving nine subjects conducted over the R-DLPFC [47] with treatment lasting for 4 weeks reported that right prefrontal rapid TMS is safe and efficacious in the treatment of PTSD. Similar studies of rTMS [32,33,37,39,40] applied over the R-DLPFC included in the study, all suggested the safety and efficacy of rTMS for the treatment of PTSD. Boggio et al. (2012), evaluated the clinical significance of right versus left PFC stimulation with high frequency (20 Hz) rTMS involving thirty subjects diagnosed with PTSD. Though the study achieved a significant improvement in symptoms of PTSD as measured on PCL in both right and left-D LPFC treatment against the sham treatments, R-DLPFC had a significant edge over the L-DLPFC at the post-treatment follow up. These results affirm the assertion that modulation of the prefrontal cortex can minimize the core symptoms of PTSD and suggest that high-frequency rTMS of R-DLPFC might be the optimal treatment strategy.

Ahmadizadeh et al. [36], in their study, summarized that both bilateral and unilateral rTMS are a safe and effective treatment for patients with PTSD as they are superior to sham rTMS, but does not support the hypothesis that bilateral rTMS is more clinically significant and effective than unilateral high-frequency right-sided rTMS.

4.2. Effects of High and Low Frequencies

The pattern drawn from the reviewed studies seems to suggest that there is no significant advantage in high versus low frequencies as both 1-Hz and 10-Hz protocols over L-DLPFC or R-DLPFC appeared effective, safe, and tolerable to participants.

4.3. Tolerability/Side Effects of rTMS

The overall importance of any treatment intervention must acknowledge both its efficacy as well as any safety and tolerability issues. rTMS is generally noted in the literature to be tolerable with minimal or no major side effects on the patients for which it is administered. Data from this review suggest the application was generally highly tolerated with minimal side effects, such as mild headache, dizziness, localized scalp pain, and, at times, stimulation of facial nerves during the administration of rTMS.

4.4. Limitations

There are several limitations to this scoping review. First, our search strategy considered only studies published in English and the results are up to date as of the date of the electronic data search of 20 December 2020. Secondly, although we carefully tried to identify all necessary studies for this study per our eligibility criteria, we still may have missed some relevant studies, with special emphasis on those published in other languages. Notwithstanding this limitation, the therapeutic potential of rTMS for treating PTSD as evidenced from the studies appears robust.

5. Conclusions

In summary, the review of these ten studies suggests that rTMS may be effective as a treatment intervention for the symptoms of PTSD. The study found significant heterogeneity concerning the sites and intensity of stimulation, as well as the outcomes of rTMS use in PTSD management. Findings from reviewed studies suggest that the application of rTMS to the right-DLPFC may be more effective than left-DLPFC. There seems to be no significant advantage in high versus low frequency, and concerning safety and tolerability, rTMS was generally well tolerated. Both 1-Hz and 10-Hz protocols over L-DLPFC or R-DLPFC appeared acceptable to participants. The treatment is generally well tolerated with mild side effects.

Despite limitations and concerns, the field of therapeutics in PTSD is currently progressing toward the use of innovative treatment approaches, such as rTMS. Though the data from the 10 studies reviewed are diverse in terms of their outcomes and clinical viability, there is enough evidence to show that rTMS is a promising treatment intervention in PTSD. However, the definitive conclusion of the clinical effectiveness of rTMS and its long-term treatment outcomes and use in maintenance treatment in PTSD is yet to be established. More studies, particularly systematic reviews of RCTs with well-defined stimulation parameters, must be conducted with large sample sizes to evaluate the true effect of rTMS in PTSD. For accuracy in pieces of evidence, it will be appropriate for researchers to find a robust and refined methodology that includes the risk of bias assessment, quantitative analysis, and evaluation of the reliability of findings across different outcomes by the use of the Grading of Recommendations Assessment, Development, and Evaluation, which is now applied in many major guidelines and is progressively being considered a universal standard method of providing a transparent and authentic estimate of evidence.

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