Review Articles

Review of the Effectiveness of Transcranial Magnetic Stimulation for Post-traumatic Stress Disorder

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A B S T R A C T

Background: Post-traumatic stress disorder (PTSD) is a psychiatric condition with significant morbidity and limited treatment options. Transcranial magnetic stimulation (TMS) has been shown to be an effective treatment for mental illnesses including major depressive disorder.

Objective: Review effectiveness of TMS for PTSD.

Methods: Literature review with descriptions of primary studies as well as meta-analysis of studies with a control group.

Results: Eight primary studies were identified and three studies met criteria for meta-analysis. All studies suggest effectiveness of TMS for PTSD. Additionally, right-sided may be more effective than left-sided treatment, there is no clear advantage in high versus low frequency, and the treatment is generally well tolerated. Meta-analysis shows significant effect size on PTSD symptoms that may be correlated with total number of stimulations.

Conclusions: TMS for PTSD appears to be an effective and well-tolerated treatment that warrants additional study to further define treatment parameters, course, and side effects.

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Introduction

Post-traumatic stress disorder (PTSD) is a psychiatric condition that can occur in individuals who have sustained or witnessed “an event or events that involve actual or threatened death or serious injury, or a threat to the physical integrity of self or others” [1].1 PTSD is an anxiety disorder characterized by three symptom clusters — re-experiencing, avoidance, and hypervigilence — that result in significant social or occupational dysfunction. Symptoms must be present for at least one-month but may last many years. Epidemiologic studies estimate 7.8% of the United States population experiences PTSD in their lifetime [2]. PTSD often results in significant psychosocial impairment; for example, PTSD-related work impairments are estimated to cost in excess of $3 billion in annual productivity loss in the United States [3].

Although medications and psychotherapy have been shown to help reduce symptoms, there remains no definitive treatment for PTSD. Selective serotonin reuptake inhibitors (SSRIs), anticonvulsants, atypical antipsychotics, and noradrenergic antidepressants have all been shown effective in clinical trials [4]. Psychotherapy modalities with demonstrated efficacy in clinical trials include a number of cognitive behavioral approaches (e.g. prolonged exposure and cognitive processing therapy) and eye movement desensitization and reprocessing (EMDR) [5]. Despite these available treatments, it is estimated that symptoms do not remit in up to one-third of patients [2].

Transcranial magnetic stimulation (TMS) uses an electromagnetic field to non-invasively stimulate cortical neurons [6]. High-intensity current through a magnetic coil placed on the scalp generates a time-varying magnetic field that penetrates the cranium to cortical tissue [7]. Conventional descriptions based on electrophysiologic studies suggest that low frequency TMS (<1 Hz) inhibits and high frequency TMS (>1 Hz) excites neurons within the stimulated field [8]. The majority of research regarding TMS has been as a treatment of major depressive disorder [9–11]. In addition, there is some research supporting TMS use in bipolar

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1 All reviewed studies used DSM-IV-TR.
disorder, schizophrenia, obsessive-compulsive disorder, and pain syndromes [12].

Neurobiologic research suggests that PTSD is characterized by a dysregulated fear response [13]. Several imaging studies have demonstrated a hyperactive amygdala in people with PTSD compared to healthy subjects [14]. In addition, areas involved in modulation of the amygdala, namely the hippocampus and medial prefrontal cortex, have been demonstrated to have decreased activity to fearful cues in functional magnetic resonance imaging studies [15]. Particularly germane to treatment research, animal models demonstrate that ventral medial prefrontal cortex activation is critical in extinguishing fearful response [16]. Neuro-modulation of prefrontal structures using TMS has been hypothesized to have potential usefulness in treatment of PTSD. Many of these studies have targeted the dorsolateral prefrontal cortex (DLPFC), which resides within a mood regulatory network that includes the amygdala, hippocampus and ventromedial prefrontal cortex. Repetitive TMS applied to the DLPFC has demonstrated antidepressant efficacy via presumed activity changes throughout this distributed network [10,17].

Research regarding the effectiveness of TMS to treat PTSD is accumulating and evolving. Published studies have used various TMS treatment parameters [18–25]. To date, results from these diverse trials have not been adequately summarized. Using semi-quantitative analysis, this paper aims to describe the findings of these trials, compile available data, compare effectiveness of different TMS techniques, and offer suggestions for future research.

Methods

We conducted a literature search in PubMed, CINAHL, and PsycINFO using the terms “transcranial magnetic stimulation” or “TMS,” in combination with “post-traumatic stress disorder” or “PTSD,” and reviewed results through July 2013. We examined the reference section of each paper for additional trials.

We identified eight primary studies that were reviewed in detail. Data regarding patient characteristics and treatment parameters were abstracted from the manuscripts. Two studies did not present all required data in the published manuscript. Osuch et al. were contacted and provided requested data. Boggio et al. presented data in bar graphs, and requests to the authors for numerical data could not be accommodated, therefore we estimated values using the published graphs.

Clinical trials that included randomization, a treatment group or trauma-focused therapy against total number of pulses to assess for correlation. Using Hedges’ g correction for small samples. Effect size was plotted as the standardized mean difference in pre-post change values using the published graphs.

Results

We identified eight published articles that have studied TMS for PTSD (Tables 1 and 2). Three studies met criteria for inclusion in meta-analysis: Cohen et al., Boggio et al., and Watts et al. [22–24]. The eight studies identified are summarized below, followed a report on meta-analysis results for the three included studies.

McCann et al. described two case studies using low frequency (1 Hz) right frontal TMS for PTSD. PTSD symptoms, rated on a modified PTSD checklist (PCL) significantly improved during
treatment with return to baseline levels by one month after treatment discontinuation. Scores on anxiety and depression scales did not show significant change with treatment. No side effects were reported by either study participant. These case reports were not included in the meta-analysis.

Grisaru et al. conducted an open trial involving ten patients with PTSD. The patients received one session of low frequency (0.3 Hz) stimulation; intratrial exposure was 151000 minutes. There was no change in short recall memory on the University of Southern California Repeatable Episodic Memory Test at any follow up point. As this study was an open design, it was not included in the meta-analysis.

Cohen et al. compared high (10 Hz) versus low (1 Hz) frequency TMS over the right prefrontal cortex in a double-blind placebo-controlled trial in twenty-four patients with PTSD. Scores post-treatment on PCL significantly improved for high (20.4% improvement) versus low (10.4%) frequency. Clinician Administered PTSD Scale (CAPS) scores also showed significant improvement in all three symptom clusters (re-experiencing, avoidance, and hyperarousal) for high versus low frequency treatment. Decreases in Ham-D scores after treatment were found not to be significant for both treatment groups. Fourteen patients reported headache, with a total of 21 reported headaches out of 250 treatment sessions, an incidence of 8%. Two patients receiving high-frequency TMS reported neck and

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### Table 2

<table>
<thead>
<tr>
<th>Paper</th>
<th>Study type</th>
<th>Coil</th>
<th>Placement (active)</th>
<th>Motor threshold</th>
<th>Course</th>
<th>Treatment parameters</th>
<th>Pulses</th>
</tr>
</thead>
<tbody>
<tr>
<td>McCann et al., 1998</td>
<td>Case study</td>
<td>Figure 8 coil</td>
<td>Right frontal</td>
<td>80%</td>
<td>3–5/week</td>
<td>1 Hz Unreported interval but appears to be continuous</td>
<td>1200/day 20,400/total 36,000/total 30 total</td>
</tr>
<tr>
<td>Grisaru et al., 1998</td>
<td>Open label</td>
<td>Angular-shaped coil 14 cm diameter</td>
<td>C3/C4 left and right hemispheres</td>
<td>100%</td>
<td>1 session</td>
<td>0.3 Hz 15 stimulations 1 min rest interval 15 stimulations</td>
<td>Group 1 (1 Hz, 40 s stim, 20 s int, 15 min) Group 2 (5 Hz, 8 s stim, 52 s int, 15 min)</td>
</tr>
<tr>
<td>Rosenberg et al., 2002</td>
<td>Open label</td>
<td>Figure 8 coil</td>
<td>Left dorsolateral prefrontal cortex</td>
<td>90%</td>
<td>10 consecutive weekdays</td>
<td>Group 1 (1 Hz, 5 s stim, 55 s int, 20 min) Group 2 (10 Hz, 2 s stim, 58 s int, 20 min) Sham</td>
<td></td>
</tr>
<tr>
<td>Cohen et al., 2004</td>
<td>Randomized double-blind placebo-controlled</td>
<td>9 cm circular coil</td>
<td>Right dorsolateral prefrontal cortex</td>
<td>80%</td>
<td>10 working days</td>
<td>Group 1 (1 Hz, 5 s stim, 55 s int, 20 min) Group 2 (10 Hz, 2 s stim, 58 s int, 20 min) Sham</td>
<td></td>
</tr>
<tr>
<td>Osuch et al., 2009</td>
<td>Alternate assignment to consecutive patients Double-blind placebo-controlled cross-over</td>
<td>Figure 8 coil</td>
<td>Right dorsolateral prefrontal cortex</td>
<td>100%</td>
<td>3–5/week Two 20 session treatments 2 week washout period prior to cross-over</td>
<td>Each group received option of systematic exposure Group 1 (1 Hz, continuous stimulation) Group 2 (sham stimulation)</td>
<td></td>
</tr>
<tr>
<td>Boggio et al., 2010</td>
<td>Stratified randomization (medication type) Double-blind Placebo-controlled</td>
<td>Figure 8 coil</td>
<td>Right or left dorsolateral prefrontal cortex</td>
<td>80%</td>
<td>10 consecutive working days 20 min/day</td>
<td>Group 1 (left, 20 Hz, 2 s stim, 28 s int, 20 min) Group 2 (right, 20 Hz, 2 s stim, 28 s int, 20 min)</td>
<td></td>
</tr>
<tr>
<td>Watts et al., 2012</td>
<td>Randomized Double-blind Placebo-controlled</td>
<td>Figure 8 coil</td>
<td>Right dorsolateral prefrontal cortex</td>
<td>90%</td>
<td>10 consecutive working days</td>
<td>Sham Group 1 (1 Hz, 20 s stim, 40 s int, 20 min) Group 2 (1 Hz, 20 s stim, 40 s int, 20 min) Sham</td>
<td></td>
</tr>
<tr>
<td>Isserles et al., 2013</td>
<td>Randomized Double-blind Placebo-controlled cross-over phase</td>
<td>H-coil</td>
<td>Bilateral medial prefrontal cortex</td>
<td>120%</td>
<td>3/week 4 weeks</td>
<td>Group 1 (traumatic then neutral script, 20 Hz, 2 s stim, 20 s int, 42 total stim) Group 2 (positive then neutral, 20 Hz, 2 s stim, 20 s int, 42 total stim) Group 3 (traumatic then neutral script, sham stimulation)</td>
<td></td>
</tr>
</tbody>
</table>

$s =$ seconds; $stim =$ stimulation; $int =$ interval; $min =$ minutes.
muscle pain in the area of stimulation. Another reported an exacerbation of previously existing dizziness. One patient in each treatment group developed manic episodes after the third session. Two patients reported ear discomfort lasting less than 1 min. This study met criteria to be included in the meta-analysis.

Osuch et al. used low frequency (1 Hz) TMS over the right prefrontal cortex combined with exposure therapy in nine patients with treatment-resistant PTSD (symptoms not responsive to medications for over two years) in a placebo-controlled crossover study with twenty sessions in each phase. Each session began with 5 min of TMS or sham. For the next 5 min, all patients had the option to speak on a topic from a personalized hierarchy of distressing topics. Importantly each patient had the ability to limit how far up the hierarchy they went, and thus could control how distressing the topic. For the remaining 20 min, TMS or sham continued, with option to continue with exposure if desired. Results did not show significant differences in symptom reduction between TMS plus exposure versus sham plus exposure, but did show a trend toward improvement in hyperarousal symptoms on CAPS scores. Adverse events were not reported. This study was not included in the meta-analysis because it did include a true control group. The comparison group included exposure, a potentially active treatment condition.

Boggio et al. compared right versus left prefrontal cortex stimulation using high frequency (20 Hz) TMS over ten sessions in a double-blind placebo-controlled trial involving thirty patients with PTSD. There was a significant benefit in PTSD symptoms on PCL in both right- and left-sided treatment compared to sham treatments. Right-sided treatment (48.6%) showed significant improvement over left-sided treatment (22.8%) at post-treatment follow up. Symptom improvement became statistically significant at day five and sustained significance at day 94 after treatment. Of note, scores on anxiety symptoms improved only with right-sided treatment and scores on depressive symptoms improved only with left-sided treatment. Cognitive function, as measured by several tests, showed non-statistically significant improvement, save for the Control Oral Word Association Test, which showed significant results with right-sided treatment only. Mild adverse effects, including headache, neck pain, sleepiness and dizziness, were reported similarly in the three treatment groups. This study met criteria to be included in the meta-analysis.

Watts et al. compared right-sided low frequency (1 Hz) TMS to sham treatment in a double-blind placebo-controlled preliminary study. Significant improvement was found on PTSD symptoms for the TMS group post-treatment on two PTSD scales (33.9, 25.0%) with effect waning but remaining statistically significant at one and two months. Significant improvement was also found in depressive symptoms in the treatment group (30.6%) post-treatment. There was no change in cognitive function with treatment as measured by the Brief Neurobehavioral Cognitive Examination. Adverse effects were not reported, but no subjects dropped out of the study. This study met criteria to be included in the meta-analysis.

Isserles et al. conducted a trial using an H-coil at high frequency (20 Hz) combined with brief exposure in a double-blind crossover study of patients with refractory (failure with antidepressant or trauma-focused psychotherapy) PTSD with hypothesis that excitatory stimulation of medial prefrontal cortex could facilitate extinction of the fear response in traumatic memory recall. Thirty patients were divided into three groups: 1) deep transcranial magnetic stimulation (DTMS) after brief exposure to a traumatic event with script-driven imagery, 2) DTMS after brief exposure to a positive event, 3) sham stimulation after brief exposure to a traumatic event. Patients were exposed to script-driven imagery as follows: 30 s of instructions, 60 s of silence, 30 s of either traumatic or positive script (control) with 30 s of imagery and then a 30 s neutral script followed by 30 s of imagery. “Consecutive” to the script procedure, the subject then received either TMS or sham treatment, depending on assigned group. Statistical analysis showed significant improvement only in intrusion component of CAPS for group 1. Ten patients who crossed over into group 1 showed significant improvement in mean CAPS scores. In all patients who received TMS plus exposure either in first or second phase, improvement in CAPS scores persisted at two weeks and two months after treatment. Additionally, those patients in group 1 showed significant attenuation of heart rate responses to the traumatic exposure. The authors reported that most patients reported no side effects; a few complained of mild headaches. Two patients in the exposure plus TMS group withdrew; one complained of increased anxiety and the other of unease during treatment. Another patient in this group had a tonic-clonic seizure. One patient in the exposure plus sham group withdrew due to increased anxiety. Although this study used randomization, it was not included in the meta-analysis due to its lack of a true comparison group. Each of the three groups received at least one intervention with exposure or TMS. Without the data to describe the effect of the script-driven exposure on PTSD symptoms, we cannot evaluate the specific effects of TMS.

Results from meta-analysis are shown in Tables 3 and 4. All treatment groups included in the meta-analysis, except the low frequency group in Cohen et al., showed statistically significant effect sizes on PTSD and depression scales. The effect size on PTSD symptoms ranged from 0.73 to 3.78 and for depressive symptoms from 0.83 to 3.6. Pooled data showed significant effect sizes for both PTSD and depressive symptoms (2.67, 2.82). Correlation between effect size and total number of pulses suggests a trend but did not reach statistical significance with a P-value of 0.061 (Fig. 1).

### Table 3
Forest plot showing effect size calculated as Hedges g for TMS on PTSD symptom scales.

<table>
<thead>
<tr>
<th>Study</th>
<th>Effect size</th>
<th>CI lower</th>
<th>CI upper</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cohen (low)</td>
<td>0.73</td>
<td>−0.36</td>
<td>1.82</td>
</tr>
<tr>
<td>Cohen (high)</td>
<td>1.84</td>
<td>0.64</td>
<td>3.04</td>
</tr>
<tr>
<td>Boggio (right)</td>
<td>3.78</td>
<td>2.32</td>
<td>5.25</td>
</tr>
<tr>
<td>Boggio (left)</td>
<td>2.68</td>
<td>1.47</td>
<td>3.88</td>
</tr>
<tr>
<td>Watts</td>
<td>1.99</td>
<td>0.92</td>
<td>3.06</td>
</tr>
<tr>
<td>Pooled</td>
<td>2.67</td>
<td>1.11</td>
<td>4.23</td>
</tr>
</tbody>
</table>

**CI** = confidence interval.

### Table 4
Forest plot showing effect size calculated as Hedges g for TMS on MDD symptom scales.

<table>
<thead>
<tr>
<th>Study</th>
<th>Effect size</th>
<th>CI lower</th>
<th>CI upper</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cohen (low)</td>
<td>0.83</td>
<td>−0.27</td>
<td>1.93</td>
</tr>
<tr>
<td>Cohen (high)</td>
<td>1.23</td>
<td>0.14</td>
<td>2.33</td>
</tr>
<tr>
<td>Boggio (right)</td>
<td>2.04</td>
<td>1.19</td>
<td>3.04</td>
</tr>
<tr>
<td>Boggio (left)</td>
<td>3.6</td>
<td>0.96</td>
<td>3.12</td>
</tr>
<tr>
<td>Watts</td>
<td>1.1</td>
<td>0.15</td>
<td>2.05</td>
</tr>
<tr>
<td>Pooled</td>
<td>2.82</td>
<td>1.99</td>
<td>3.65</td>
</tr>
</tbody>
</table>

**CI** = confidence interval.
Discussion

Eight studies with a total of 132 participants have examined the effectiveness of TMS in the treatment of PTSD. The main variables studied have been left or right-sided treatment and stimulation frequency (0.3, 1, 5, 10 and 20 Hz). All studies targeted prefrontal regions. Most studies used a frequency (0.3, 1, 5, 10 and 20 Hz). All studies targeted prefrontal areas and the stimulation parameters varied widely, in the randomized trials from 1000 to 20,160 total treatment pulses. The treatment was generally well tolerated with reports of mild adverse effects of headaches and dizziness, one seizure, and no major adverse effects reported.

Three of the eight published studies were included in our meta-analysis, which included five intervention arms, to assess for effect size for PTSD and depression measures. Depression measures were included in our analysis to help assess any laterality differences between TMS treatment of MDD and PTSD. All treatments showed significant effect size on PTSD and depression measures except for the low frequency arm in the Cohen et al. trial (Tables 3 and 4). Lack of response in this arm may reflect the lower number of total pulses. Of note, Boggio et al. and Watts et al. showed the TMS treatment effect for PTSD remained present at follow up assessment of 94 days and two months, respectively.

The main variables studied included: anatomic site of stimulation, stimulation frequency, total number of stimulation pulses, and the combination of TMS with exposure. Both right- and left-sided stimulation showed significant effects on PTSD symptoms. In the only direct comparison, Boggio et al. showed right-sided treatment to be more effective than left-sided in reducing core symptoms. Though not included in the meta-analysis, Rosenberg et al. supports this trend in that the study showed that left-sided treatment was effective for depressive symptoms but not PTSD symptoms. Several animal and human studies indicate right-sided brain laterality in fear circuitry. One study used PET to show increased blood flow in right-sided limbic and paralimbic regions in patients with PTSD when presented with traumatic scripts compared to neutral scripts [27]. Another showed decreased N-acetyl-l-aspartic-acid/creatin ratio in right medial temporal lobe relative to left in combat veterans with PTSD when compared to healthy controls [28]. Though further study on stimulation site is warranted, these preliminary clinical results and neuroimaging studies show that right-sided structures may be the most relevant targets for direct modulation in patients with PTSD.

Despite the previously described opposing effects on cortical activity, both high and low frequency stimulation have been shown here to be effective in alleviating PTSD symptoms. Explaining this result is difficult, especially when considering the current neurobiologic models for PTSD. As discussed in the introduction, medial prefrontal cortex hypoactivity and limbic and paralimbic hyperactivity is the currently accepted dysregulation responsible for PTSD symptoms. However, how stimulation of the dorsal prefrontal cortex affects this circuit is not well understood. The studies included in our meta-analysis come to different conclusions about the mechanism of action for TMS on PTSD: right-sided high frequency stimulation activates right dorsolateral prefrontal cortex, which activates the hypothalamic-pituitary-adrenal (HPA) axis, inhibits excessive autonomic response and suppresses amygdala activity (Cohen et al.); right-sided high frequency stimulation activates right dorsolateral prefrontal cortex that inhibits left-sided structures involved in memory retrieval networks (Boggio et al.); right-sided low frequency stimulation inhibits right dorsolateral prefrontal cortex, suggesting hyperactive right prefrontal cortex in patients with PTSD. Considerable caution should be taken when attempting to use results from these small studies to explain underlying neurobiology. How TMS modulation of neural circuitry or monoamine release may be playing a role in reducing PTSD symptoms is not clear. One explanation for how high and low frequency TMS may reduce PTSD symptom severity is that the different frequency stimulations affect different elements of the underlying neural network based on the direct increased or decreased excitability of the prefrontal cortex. While we might still hypothesize that both frequencies may be beneficial for PTSD, one frequency may have greater, and perhaps more lasting, efficacy compared to the other.

Another explanation for this apparent paradox is that, for the treatment of PTSD, stimulation frequency may be less relevant than other stimulation factors. For example, total number of stimulation pulses may be more important than the frequency at which these are delivered. In Fig. 1, there appears to be a correlation between number of pulses and effect size, though the relationship does not reach statistical significance. What is responsible for this possible effect neurobiologically is unclear, especially considering the complexities of frequency discussed above.

Though not included in the meta-analysis, the studies that used exposure plus TMS (Osuch et al. and Isserles et al.) offer an intriguing approach to the treatment of PTSD. This combination may affect symptoms of PTSD through several different mechanisms implicated in the disorder. One possibility is that TMS enhances activation of the ventral medial prefrontal cortex in fear extinguishing circuitry. Additionally, it may be possible to disrupt retrieved memories [29] as shown in a trial that gave a single dose of propranolol to patients with PTSD after describing a traumatic experience and showed reduced physiologic signs of fear a week later on re-exposure [30]. Finally, new learning requiring activation of glutamatergic NMDA receptors appears to be a component of extinguishing fear memories. To the extent that TMS may play a role in affecting these processes, it may be a potentially useful treatment in combination with exposure. Despite this potential, the two studies that we reviewed showed modest results. Though showing a trend toward efficacy, calculated effect sizes in the two studies using exposure plus TMS for PTSD symptoms were significant for subscales of PTSD measures only (the overall effect on PTSD was not significant); in Osuch et al. the CAPS D (hyperarousal)
subscale 0.72 (0.16–1.29) and Isserles et al. effect size for CAPS B (intrusion) 3.16 (1.75–4.58). Limitations in these studies may have impacted results include the small sample size and the absence of a true control group (as previously discussed).

Our analysis of TMS for PTSD is limited by several factors. As described, there are only four published randomized control trials, with heterogenous study designs, and each with a relatively small sample size. Standardized mean differences used immediate post-treatment scoring, and effect size is most likely falsely elevated. In some cases, as mentioned, we did not have access to primary data, and our estimates for results may be inaccurate. Additionally there may be studies that we did not capture in our search that would contribute to overall results.

There are many aspects of TMS treatment that require clarification through future studies. Although right-sided treatment appears superior to left-sided for PTSD, this issue is far from settled by past studies. Though the current neurobiological model for PTSD focuses on dysfunction of frontal and paralimbic structures, no study to date has targeted other brain regions. Both high and low frequency have been effective in reducing PTSD symptoms. Future studies should use comparison groups of varying frequencies to investigate potential advantages. Given the increased risk for the small sample size [31], finding the lowest effective frequency should be the goal of future research. Further, treatment intensity has ranged from 80 to 120% of resting motor threshold. Although effective intensity has been established over a wide range of settings for MDD [32], given the small number of patients studied in these trials, this conclusion cannot yet be reached for PTSD. Number of pulses, either per day or total, may also be an important factor in the treatment’s effectiveness. Studies so far have shown symptoms returning to baseline severity over the course of a few months after treatment. The optimal number of sessions during the initial course is not clear. The role of repeated series of treatment or maintenance therapy has yet to be assessed. Overall, more attention and study of side effects and tolerability are warranted. Finally, using neuroimaging such as positron emission tomography or functional magnetic resonance imaging in pre and post-assessment may help elucidate the effects of TMS on the neurobiology of PTSD.

Future study in the combination of exposure plus TMS should be mindful of the effect of the exposure on the outcome. Using standardized exposure techniques may be helpful in this regard. A comparison group with no exposure should be included in order to control for effects of exposure. The timing of TMS to the exposure merits further study, i.e. concurrent, consecutive, or other. Finally, what parameters of TMS, including placement, frequency, intensity and number of sessions, and whether this differs from TMS without exposure as discussed above, will need further research.

Conclusion

Review of eight studies suggests that TMS may be effective in treating the symptoms of PTSD. Some tentative trends on TMS for PTSD can be drawn from these studies: right-sided may be more effective than left-sided treatment, there is no clear advantage in high versus low frequency, and the treatment is generally well tolerated. TMS should continue to be studied as a treatment modality for PTSD, and future research is needed to continue to hone the treatment parameters, course, and side effects.

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References

[28] Freeman TW, Cardwell D, Karson CN, Komoroski RA. In vivo proton magnetic resonance spectroscopy of the medial temporal lobes of subjects with


