Brain Stimulation 7 (2014) 151–157

Contents lists available at SciencePlus

Brain Stimulation

journal homepage: www.brainstimjrnl.com

Review Articles

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

Ethan F. Karsen [a,*], Bradley V. Watts [a,b], Paul E. Holtzheimer [a,c]

[a] Department of Psychiatry, Geisel School of Medicine at Dartmouth, One Medical Center Drive, Lebanon, New Hampshire, USA
[b] Department of Psychiatry, Veterans Affairs National Center for Patient Safety, White River Junction, Vermont, USA
[c] Department of Surgery, Geisel School of Medicine at Dartmouth, Lebanon, New Hampshire, USA

ARTICLE INFO

Article history:
Received 7 July 2013
Received in revised form
18 October 2013
Accepted 23 October 2013

Keywords:
Repetitive transcranial magnetic stimulation
Transcranial magnetic stimulation
Post-traumatic stress disorder

ABSTRACT

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.

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

Financial disclosures: Dr. Karsen and Dr. Watts have no conflicts of interest to report.

Dr. Holtzheimer receives grant funding from the National Institutes of Health, Cervel Neurotech and Otsuka Pharmaceutical; he receives consulting fees from Cervel Neurotech and St. Jude Medical Neuromodulation.

* Corresponding author. Tel.: +1 603 650 5000x3575.
E-mail address: Ethan.Karsen@hitchcock.org (E.F. Karsen).

[1] All reviewed studies used DSM-IV-TR.

1935-861X/$ – see front matter © 2014 Elsevier Inc. All rights reserved.
http://dx.doi.org/10.1016/j.brs.2013.10.006

Table 1
Characteristics of seven primary studies of transcranial magnetic stimulation (TMS) for post-traumatic stress disorder (PTSD).

Paper	N	Gender	Age	Inclusion	Years since trauma	Trauma type
McCann et al., 1998	2	2 women	29 42	PTSD/MDD PTSD	18 2.5	Developing country Shooting
Grisaru et al., 1998	10	7 men 3 women	47	PTSD	5.5	Accident [7] Combat [2] Assault [1]
Rosenberg et al., 2002	12	12 men	54.8	PTSD MDD Taking medications Ham D >17	N/A	N/A
Cohen et al., 2004	24	17 men 7 women	41.7	PTSD	5.4	Combat [4] MVC [11] Sexual abuse [2] Assault [2] Work accident [2] Death of a relative [1]
Osuch et al., 2009	9	1 man 8 women	41.4	Treatment-resistant PTSD >2 years (all had concurrent MDD)	22.3	N/A
Boggio et al., 2010	30	9 men 21 women	44.5	PTSD	3.9	Assault [6] Sexual abuse [5] Death/disease of a relative [15] Perceived threat of harm [4]
Watts et al., 2012	20	18 men 2 women	55.9	PTSD CAPS >50	39.8	Combat [8] Sexual abuse [1] Assault [1] Multiple [10]
Isserles et al., 2013	26	20 men 6 women	43.4	PTSD treatment failure with antidepressant or trauma-focused therapy	15.8	Military [15] Other [11]

N = number of participants included in each study; MDD = major depressive disorder; CAPS = Clinician-administered PTSD Scale; N/A = data were not included in the published results.
Ages are in years and represent the mean age of patients, except where multiple ages are included which represent individual patients.
Trauma types are followed by the number of patients included in each study with each characteristic.

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]. Neuromodulation 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 DPLFC 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 with TMS, a placebo/sham comparison group, and pre- and post-assessments for PTSD symptoms, were included in the meta-analysis. Primary outcome data on continuous scale measures of PTSD and depression symptom severity were used to calculate effect sizes. Effect sizes and pooled estimates of effects for the studies were calculated with the Comprehensive Meta-Analysis software package [26]. In studies in which mean difference standard deviations were not reported, we imputed values using correlation coefficients calculated from the comparison studies. We calculated effect size as the standardized mean difference in pre-post change using Hedges *g* correction for small samples. Effect size was plotted against total number of pulses to assess for correlation.

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

Table 2
Treatment parameters for seven primary studies of TMS for PTSD.

Paper	Study type	Coil	Placement (active)	Motor threshold	Course	Treatment parameters	Pulses
McCann et al., 1998	Case study	Figure 8 coil	Right frontal (unreported region)	80%	3–5/week 17 sessions 30 sessions	1 Hz Unreported interval but appears to be continuous	1200/day 20,400/ total 36,000/ total
Grisaru et al., 1998	Open label	Angular-shaped coil 14 cm diameter	C3/C4 left and right hemispheres	100%	1 session	0.3 Hz 15 stimulations 1 min rest interval 15 stimulations	30 total
Rosenberg et al., 2002	Open label	Figure 8 coil	Left dorsolateral prefrontal cortex	90%	10 consecutive weekdays	Group 1 (1 Hz, 40 s stim, 20 s int, 15 min) Group 2 (5 Hz, 8 s stim, 52 s int, 15 min)	600/day 6000/total
Cohen et al., 2004	Randomized double-blind placebo-controlled	9 cm circular coil	Right dorsolateral prefrontal cortex	80%	10 working days	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	Group 1 100/day 1000/total Group 2 400/day 4000/total
Osuch et al., 2009	Alternate assignment to consecutive patients Double-blind placebo-controlled cross-over	Figure 8 coil	Right dorsolateral prefrontal cortex	100%	3–5/week Two 20 session treatments 2 week washout period prior to cross-over	Each group received option of systematic exposure Group 1 (1 Hz, continuous stimulation) Group 2 (sham stimulation)	1800/day 36,000/ total
Boggio et al., 2010	Stratified randomization (medication type) Double-blind Placebo-controlled	Figure 8 coil	Right or left dorsolateral prefrontal cortex	80%	10 consecutive working days 20 min/day	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) Sham	1600/day 16,000/ total
Watts et al., 2012	Randomized Double-blind Placebo-controlled	Figure 8 coil	Right dorsolateral prefrontal cortex	90%	10 consecutive working days	Group 1 (1 Hz, 20 s stim, 40 s int, 20 min) Sham	400/day 4000/total
Isserles et al., 2013	Randomized double-blind placebo-controlled cross-over phase	H-coil	Bilateral medial prefrontal cortex	120%	3/week 4 weeks	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)	1680/day 20,160/ total

s = seconds; stim = stimulation; int = interval; min = minutes.

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) with fifteen stimuli delivered to the right then left prefrontal areas. Overall there were no changes as measured by the Impact of Events Scale (IES). However, avoidance subscale scores significantly improved (39.3%) immediately after the treatment course was concluded. This improvement remained present seven days after treatment, but the symptoms levels returned to baseline twenty-eight days after treatment. Two adverse effects were reported: one patient reported a mild headache for several weeks following TMS, the other reported an increase in intrusive thoughts for a few days following treatment. Due to its open-label design and lack of a control group, this study was not included in the meta-analysis.

Rosenberg et al. compared high (5 Hz) versus low (1 Hz) frequency TMS over the left prefrontal cortex in twelve patients with co-morbid PTSD and major depressive disorder (MDD) in an open study. There was no statistically significant difference between results for the two groups on PTSD or MDD scales. PTSD symptoms improved statistically but minimally by 6% at two-month follow up on Mississippi Scale of Combat Severity scale. Depression measures showed significant improvement with over 50% reduction on Hamilton Depression Rating Scale (Ham-D) at post-treatment, one-month, and two-month follow up for both treatment groups. There was no change in short recall memory on the University of Southern California Repeatable Episodic Memory Test at any follow up point. The authors did not systematically report on non-cognitive side effects, but did report that one patient dropped out due to headaches. 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 (29.3%) 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

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.

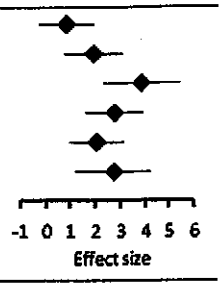
Boggio et al. compared right versus left prefrontal cortex stimulation using high frequency (20 Hz) TMS over ten sessions in a double-blind placebo-controlled trial involving thirty patients with PTSD. There was a significant benefit in PTSD symptoms on PCL in both right- and left-sided treatment compared 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.

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

Study	Effect size	CI lower	CI upper
Cohen (low)	0.73	−0.36	1.82
Cohen (high)	1.84	0.64	3.04
Boggio (right)	3.78	2.32	5.25
Boggio (left)	2.68	1.47	3.88
Watts	1.99	0.92	3.06
Pooled	2.67	1.11	4.23

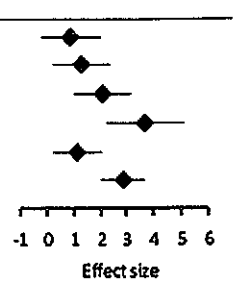


CI = confidence interval.

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

Study	Effect size	CI lower	CI upper
Cohen (low)	0.83	−0.27	1.93
Cohen (high)	1.23	0.14	2.33
Boggio (right)	2.04	2.19	5.04
Boggio (left)	3.6	0.96	3.12
Watts	1.1	0.15	2.05
Pooled	2.82	1.99	3.65



CI = confidence interval.

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 that 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 seizure at higher frequencies [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.

Acknowledgments

The authors would like to sincerely thank Elizabeth Osuch for her perseverance in providing her group's original data for this review.

References

[1] American Psychiatric Association. Diagnostic and statistical manual of mental disorders. 4th ed., text rev. Washington, DC: American Psychiatric Press; 2000.
[2] Kessler RC, Sonnega A, Bromet E, Hughes M, Nelson CB. Posttraumatic stress disorder in the National Comorbidity Survey. Arch Gen Psychiatry 1995 Dec;52(12):1048–60.
[3] Thomas JL, Wilk JE, Riviere LA, McGurk D, Castro CA, Hoge CW. Prevalence of mental health problems and functional impairment among active component and National Guard soldiers 3 and 12 months following combat in Iraq. Arch Gen Psychiatry 2010 Jun;67(6):614–23.
[4] Ballenger JC, Davidson JR, Lecrubier Y, et al. Consensus statement on posttraumatic stress disorder from the International Consensus Group on Depression and Anxiety. J Clin Psychiatry 2000;61(Suppl. 5):60–6.
[5] Bisson J, Andrew M. Psychological treatment of post-traumatic stress disorder (PTSD). Cochrane Database Syst Rev 2007 Jul 18;(3). CD003388.
[6] George MS, Nahas Z, Kozel FA, et al. Mechanisms and state of the art of transcranial magnetic stimulation. J ECT 2002 Dec;18(4):170–81.
[7] Post A, Keck ME. Transcranial magnetic stimulation as a therapeutic tool in psychiatry: what do we know about the neurobiological mechanisms? J Psychiatr Res 2001 Jul-Aug;35(4):193–215.
[8] Speer AM, Kimbrell TA, Wassermann EM, et al. Opposite effects of high and low frequency rTMS on regional brain activity in depressed patients. Biol Psychiatry 2000 Dec 15;48(12):1133–41.
[9] Fitzgerald PB, Brown TL, Marston NA, Daskalakis ZJ, De Castella A, Kulkarni J. Transcranial magnetic stimulation in the treatment of depression: a double-blind, placebo-controlled trial. Arch Gen Psychiatry 2003 Oct;60(10):1002–8.
[10] George MS, Lisanby SH, Avery D, et al. Daily left prefrontal transcranial magnetic stimulation therapy for major depressive disorder: a sham-controlled randomized trial. Arch Gen Psychiatry 2010 May;67(5):507–16.
[11] Gross M, Nakamura L, Pascual-Leone A, Fregni F. Has repetitive transcranial magnetic stimulation (rTMS) treatment for depression improved? A systematic review and meta-analysis comparing the recent vs. the earlier rTMS studies. Acta Psychiatr Scand 2007 Sep;116(3):165–73.
[12] Wassermann EM, Lisanby SH. Therapeutic application of repetitive transcranial magnetic stimulation: a review. Clin Neurophysiol 2001 Aug;112(8):1367–77.
[13] Parsons RG, Ressler KJ. Implications of memory modulation for post-traumatic stress and fear disorders. Nat Neurosci 2013 Feb;16(2):146–53.
[14] Etkin A, Wager TD. Functional neuroimaging of anxiety: a meta-analysis of emotional processing in PTSD, social anxiety disorder, and specific phobia. Am J Psychiatry 2007 Oct;164(10):1476–88.
[15] Shin LM, Rauch SL, Pitman RK. Amygdala, medial prefrontal cortex, and hippocampal function in PTSD. Ann N Y Acad Sci 2006 Jul;1071:67–79.
[16] Milad MR, Quirk GJ. Neurons in medial prefrontal cortex signal memory for fear extinction. Nature 2002 Nov 7;420(6911):70–4.
[17] O'Reardon JP, Solvason HB, Janicak PG, et al. Efficacy and safety of transcranial magnetic stimulation in the acute treatment of major depression: a multisite randomized controlled trial. Biol Psychiatry 2007 Dec 1;62(11):1208–16.
[18] McCann UD, Kimbrell TA, Morgan CM, et al. Repetitive transcranial magnetic stimulation for posttraumatic stress disorder. Arch Gen Psychiatry 1998 Mar;55(3):276–9.
[19] Grisaru N, Amir M, Cohen H, Kaplan Z. Effect of transcranial magnetic stimulation in posttraumatic stress disorder: a preliminary study. Biol Psychiatry 1998 Jul 1;44(1):52–5.
[20] Rosenberg PB, Mehndiratta RB, Mehndiratta YP, Wamer A, Rosse RB, Balish M. Repetitive transcranial magnetic stimulation treatment of comorbid posttraumatic stress disorder and major depression. J Neuropsychiatry Clin Neurosci 2002 Summer;14(3):270–6.
[21] Osuch EA, Benson BE, Luckenbaugh DA, Geraci M, Post RM, McCann U. Repetitive TMS combined with exposure therapy for PTSD: a preliminary study. J Anxiety Disord 2009 Jan;23(1):54–9.
[22] Cohen H, Kaplan Z, Kotler M, Kouperman I, Moisa R, Grisaru N. Repetitive transcranial magnetic stimulation of the right dorsolateral prefrontal cortex in posttraumatic stress disorder: a double-blind, placebo-controlled study. Am J Psychiatry 2004 Mar;161(3):515–24.
[23] Boggio PS, Rocha M, Oliveira MO, et al. Noninvasive brain stimulation with high-frequency and low-intensity repetitive transcranial magnetic stimulation treatment for posttraumatic stress disorder. J Clin Psychiatry 2010 Aug;71(8):992–9.
[24] Watts BV, Landon B, Groft A, Young-Xu Y. A sham controlled study of repetitive transcranial magnetic stimulation for posttraumatic stress disorder. Brain Stimul 2012 Jan;5(1):38–43.
[25] Isserles M, Shalev AY, Roth Y, et al. Effectiveness of deep transcranial magnetic stimulation combined with a brief exposure procedure in post-traumatic stress disorder–a pilot study. Brain Stimul 2013 May;6(3):377–83.
[26] Borenstein M, Hedges L, Higgins J, Rothstein H. Comprehensive Meta-analysis Version 2. Englewood NJ: Biostat; 2005.
[27] Shin LM, McNally RJ, Kosslyn SM, et al. Regional cerebral blood flow during script-driven imagery in childhood sexual abuse-related PTSD: a PET investigation. Am J Psychiatry 1999 Apr;156(4):575–84.
[28] Freeman TW, Cardwell D, Karson CN, Komoroski RA. In vivo proton magnetic resonance spectroscopy of the medial temporal lobes of subjects with

combat-related posttraumatic stress disorder. Magn Reson Med 1998 Jul;40(1):66–71.
[29] Nader K, Schafe GE, Le Doux JE. Fear memories require protein synthesis in the amygdala for reconsolidation after retrieval. Nature 2000 Aug 17;406(6797):722–6.
[30] Brunet A, Orr SP, Tremblay J, Robertson K, Nader K, Pitman RK. Effect of post-retrieval propranolol on psychophysiologic responding during subsequent script-driven traumatic imagery in post-traumatic stress disorder. J Psychiatr Res 2008 May;42(6):503–6.
[31] Green RM, Pascual-Leone A, Wasserman EM. Ethical guidelines for rTMS research. IRB 1997 Mar-Apr;19(2):1–7.
[32] Johnson KA, Baig M, Ramsey D, et al. Prefrontal rTMS for treating depression: location and intensity results from the OPT-TMS multi-site clinical trial. Brain Stimul 2013 Mar;6(2):108–17.