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TREATMENT

Three studies explore the role of TMS in the treatment of PTSD

Transcranial magnetic stimulation (TMS) is a non-invasive form of brain stimulation that is FDA-approved for the treatment of major depression. In addition to depression, TMS has been increasingly studied as a treatment for PTSD (see [NCPTSD PTSD Research Quarterly Volume 29, Issue 2](#)). Three new articles provide information about this potential use.

A multisite VA Cooperative Study, CSP #556, randomized 164 Veterans with medication-resistant major depression to receive either active or sham TMS daily for up to six weeks. Approximately half of the participants had comorbid PTSD. Participants randomized to active TMS received high frequency (10 Hz) TMS applied to the left dorsolateral prefrontal cortex. Nearly 25% of the participants did not complete the study, which is higher than the percentage seen in previous TMS studies. Compared to sham, active TMS did not have statistically significant effects on depression or on PTSD severity in those with PTSD. However, the overall remission rate (about 40%) was relatively high in both groups. Secondary analyses suggested that participants with comorbid PTSD showed a less robust response and were less likely to remit, potentially contributing to the negative findings in this study.

Read the article: <https://doi.org/10.1001/jamapsychiatry.2018.1483>

In a separate study focused on treating PTSD with TMS, investigators at the Atieh Clinical Neuroscience Center in Iran randomized 65 male Veterans with PTSD to: (1) 20 Hz TMS delivered to the right dorsolateral prefrontal cortex followed by 20 Hz TMS delivered to the left dorsolateral prefrontal cortex (bilateral treatment arm); (2) 20 Hz delivered to the right dorsolateral prefrontal cortex (unilateral treatment arm); or (3) sham TMS. Ten treatment sessions were delivered over two weeks. PTSD severity was assessed using the PCL-M. Both the bilateral and unilateral TMS groups had greater reductions in PTSD severity compared to the sham group, but the two active TMS groups did not differ from one another.

Read the article: <https://doi.org/10.1016/j.brainresbull.2018.06.001>

In another study of TMS added to trauma-focused psychotherapy (see the [April 2018 CTU-Online](#)), investigators at the Medical University of South Carolina conducted a small feasibility pilot combining TMS with PE for Veterans with PTSD. This study differs from other TMS for PTSD studies in that treatments were given weekly (in conjunction with up to 5 sessions of PE) rather than daily. Eight participants were randomized to one of four groups: (1) 10 Hz active TMS applied to the left dorsolateral prefrontal cortex ($n = 3$); (2) sham TMS applied to the left dorsolateral prefrontal cortex ($n = 2$); (3) 10 Hz active TMS applied to the right dorsolateral prefrontal cortex ($n = 2$); or (4) sham TMS applied to the right dorsolateral prefrontal cortex ($n = 1$). All randomized participants completed the treatment protocol. PTSD severity on the CAPS for DSM-IV decreased by 55% in the active TMS groups and 40% in the sham TMS groups, which was not a statistically significant difference. The active TMS groups showed greater improvement in depression after four and five weeks of treatment. Given its small size, this study does not permit conclusions regarding the clinical utility of combined TMS and PE, although it does help confirm the feasibility of combining focal non-invasive brain stimulation with behavioral interventions for the treatment of PTSD.

Read the article: <https://www.ptsd.va.gov/professional/articles/article-pdf/id50583.pdf>

These three studies highlight how clinical research on TMS is expanding to include a focus on PTSD and the Veteran population. In general, the literature on TMS as a treatment for PTSD suggests efficacy, but it is not yet clear how TMS should be optimally used. The published studies on TMS for PTSD have used a variety of stimulation parameters, including which part of the brain is targeted for stimulation, stimulation frequency, and number of sessions. In the few studies that have directly compared different sets of TMS parameters, a benefit is typically seen with active TMS, but no difference is seen between different active TMS parameter sets. CSP #566, which did not demonstrate a beneficial effect for TMS on depression or PTSD severity, used treatment parameters different from those used in most other studies of TMS for PTSD (including the second study summarized above). More work is needed to clarify which patients are most likely to benefit from TMS and what the optimal treatment parameters should be. Also, it is intriguing to consider how TMS might be used to augment other evidence-based treatments for PTSD, such as PE; more research examining whether TMS can make these treatments work more quickly or effectively is indicated.

Ahmadizadeh, M.-J., & Rezaei, M. (2018). Unilateral right and bilateral dorsolateral prefrontal cortex transcranial magnetic stimulation in treatment post-traumatic stress disorder: A randomized controlled study. *Brain Research Bulletin*, 140, 334–340. PILOTS ID: 50480

Fryml, L. D., Pelic, C. G., Acierno, R., Tuerk, P., Yoder, M., Borckardt, J. J., . . . George, M. S. (2018). Exposure therapy and simultaneous repetitive transcranial magnetic stimulation: A controlled pilot trial for the treatment of posttraumatic stress disorder. *The Journal of ECT*. Advance online publication. PILOTS ID: 50583

Yesavage, J. A., Fairchild, J. K., Mi, Z., Biswas, K., Davis-Karim, A., Phibbs, C. S., . . . for the VA Cooperative Studies Program Study Team. (2018). Effect of repetitive transcranial magnetic stimulation on treatment-resistant major depression in US veterans: A randomized clinical trial. *JAMA Psychiatry*. Advance online publication. PILOTS ID: 50587

RCT of mantram repetition for PTSD shows positive results

Many complementary and alternative treatments for PTSD have been proposed but are lacking strong research evidence. A previous RCT showed that mantram repetition added to usual care for PTSD was superior to usual care alone (see the [April 2012 CTU-Online](#)). A team led by investigators at VA San Diego recently compared mantram repetition to Present-Centered Group Therapy (PCGT). A total of 173 Veterans recruited from two VA facilities were randomized to 8 weekly 1-hour individual sessions of either mantram repetition or PCGT. Mantram repetition involves slowing down thoughts and directing attention by repeating a personalized, meaningful word or phrase. The mantram repetition program included education in the mantram skills, *in vivo* skills practice, homework, and discussion of obstacles to practicing mantram. Veterans in the mantram group showed greater improvements than Veterans who received PCGT in PTSD symptoms measured with the CAPS at post-treatment ($d = .49$) and at the 2-month follow-up ($d = .46$). The mantram group also reported greater improvements than the PCGT group in insomnia. Effects were not related to the frequency of mantram practice. While these findings are promising, one caveat is that the study includ-

ed 8 sessions of PCGT, a smaller dose than has previously been shown to be effective.

Read the article: <https://doi.org/10.1176/appi.ajp.2018.17060611>

Bormann, J. E., Thorp, S. R., Smith, E., Glickman, M., Beck, D., Plumb, D., . . . Elwy, A. R. (2018). Individual treatment of posttraumatic stress disorder using mantram repetition: A randomized clinical trial. *American Journal of Psychiatry*. Advance online publication. PILOTS ID: 50584

Residual symptoms after completing PE or CPT

Although PE and CPT are two of the most effective treatments for PTSD, residual symptoms may persist even after a successful course of therapy. A study led by investigators from the VAMC in Milwaukee examined which symptoms remained after PE or CPT. This secondary analysis included 108 female rape survivors who completed PE or CPT as part of a randomized clinical trial. The investigators calculated the percentage of participants endorsing each symptom of PTSD as reported on the CAPS, as well as secondary symptoms, at posttreatment and long-term follow-up 5-10 years after treatment. Overall, prevalence of all PTSD symptoms was decreased after treatment and at follow-up, but distress related to trauma reminders, inability to recall the trauma, hypervigilance, and insomnia remained in 30-40% of the sample regardless of treatment modality. About half of the sample also reported residual secondary symptoms, including self-blame, body image concerns, fatigue, lack of satisfaction, self-hate, irritability, social withdrawal, and sleep problems. The presence of guilt dropped to less than 30% in the sample. This study is the first to explore residual comorbid symptoms beyond just PTSD following CPT and PE. Findings suggest that thinking about recovery beyond PTSD remission might be necessary to optimize outcomes for trauma survivors.

Read the article: <https://doi.org/10.1037/tra0000384>

Larsen, S. E., Fleming, C. J. E., & Resick, P. A. (2018). Residual symptoms following empirically supported treatment for PTSD. *Psychological Trauma: Theory, Research, Practice, and Policy*. Advance online publication. PILOTS ID: 50586

Integrated CBT for PTSD and substance use in Veterans

Integrated CBT (ICBT) for PTSD and substance use is a 12-session protocol that uses non-exposure techniques to target both disorders. Although ICBT has shown promising results in community samples, a new study by investigators at the Providence VA suggests that this treatment may fall short in Veterans. The trial included 44 Iraq or Afghanistan-era Veterans (95% male) who met criteria for PTSD and SUD. During the study, all participants could continue their usual care in VA or the community, including medication or psychotherapy for PTSD, SUD, or other diagnoses. Half of the participants were randomized to 12 sessions of ICBT adapted for Veterans; the manual included Veteran-specific examples and sessions 5-12 were delivered in a group format. Most participants (ICBT: 64%, usual care: 82%) were receiving other individual PTSD therapy. At posttreatment, ICBT participants

showed significant reductions in PTSD symptoms and substance use—but usual care participants showed comparable gains. The investigators had expected that because it does not include exposure, ICBT would demonstrate good retention. However, only 38% of ICBT participants completed at least 8 sessions. Another integrated intervention that includes exposure (called COPE) has shown similarly low retention in a Veteran sample, but comparatively larger treatment effects (see the [June 2017 CTU-Online](#)). Future trials are needed to better understand whether exposure may be a necessary ingredient for effective SUD+PTSD treatment in Veterans.

Read the article: <https://www.ptsd.va.gov/professional/articles/article-pdf/id50582.pdf>

Capone, C., Presseau, C., Saunders, E., Eaton, E., Hamblen, J., & McGovern, M. (2018). Is integrated CBT effective in reducing PTSD symptoms and substance use in Iraq and Afghanistan veterans? Results from a randomized clinical trial. *Cognitive Therapy and Research*. Advance online publication. PILOTS ID: 50582

Mixed findings in RCT of spiritually-oriented group treatment for PTSD

Some individuals with PTSD experience distressing thoughts and feelings about their religious faith or spirituality. “Building

Spiritual Strength” (BSS), a manualized, spiritually-informed group intervention for PTSD, was previously shown to be superior to waitlist for reducing PTSD symptoms. In a new RCT, a team of investigators at the Minneapolis VA compared BSS to Present-Centered Group Therapy (PCGT). Veterans with full or subthreshold PTSD were randomized to 8 2-hour sessions of BSS ($n = 71$) or PCGT ($n = 67$), which were delivered by chaplains with mental health training. Participants in both groups showed reductions in PTSD at posttreatment on the CAPS, but there were no differences between groups. There were no improvements in either group in PTSD severity on the PCL. BSS was more effective than PCGT in reducing distress related to one’s relationship with a higher power. While interesting, findings should also be interpreted with caution because the authors only conducted analyses among Veterans who completed treatment (60% of BSS, 67% of PCGT), which can significantly bias estimates of treatment effects. Also, it is unknown whether there are specific advantages of BSS compared with treatments such as CPT or PE, which can also successfully treat guilt and shame.

Read the article: <https://doi.org/10.1016/j.psychres.2018.06.045>

Harris, J. I., Usset, T., Voecks, C., Thuras, P., Currier, J., & Erbes, C. (2018). Spiritually integrated care for PTSD: A randomized controlled trial of “Building Spiritual Strength.” *Psychiatry Research*, 267, 420–428. PILOTS ID: 50585

ASSESSMENT

Defining subthreshold PTSD continues to be a work in progress

In DSM-5, subthreshold PTSD—clinically-significant PTSD symptoms that do not meet the criteria for a PTSD diagnosis—can be classified as a “trauma- and stressor-related disorder,” either trauma-specified or unspecified. However, there are no criteria for the number, type, or intensity of symptoms needed for these diagnoses. A study led by investigators at the Southeast Louisiana VAMC explored how four definitions of subthreshold PTSD differed in estimates of prevalence and in distress or impairment. Male Veterans ($N = 171$) completed the CAPS-5 in routine clinical care. The subthreshold definitions were: (a) meeting criteria B and C and either D or E; (b) having 5 symptoms, including at least 1 symptom in every criterion (which means that meeting B and C was necessary); (c) meeting 3 out of 4 symptom criteria; and (d)

having 6 or more symptoms but not meeting full PTSD criteria. The two definitions requiring both B and C had lower prevalence (a, 37.8%; b, 30.6%) than the other two definitions (c, 54.9%; d, 57.5%). However, not meeting D was the most common reason participants failed to meet full criteria. The definitions were not associated with differences in distress and impairment, making it difficult to determine which definition is optimal. Looking at additional correlates, and comparisons with full PTSD, could help to determine how to best define subthreshold PTSD and what implications this may have for treatment of trauma-related disorders.

Read the article: <https://doi.org/10.1016/j.jad.2018.03.001>

Franklin, C. L., Raines, A. M., Chambliss, J. L., Walton, J. L., & Maieritsch, K. P. (2018). Examining various subthreshold definitions of PTSD using the Clinician Administered PTSD Scale for DSM-5. *Journal of Affective Disorders*, 234, 256–260. PILOTS ID: 50023



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