

Q. What is repetitive transcranial magnetic stimulation?

A. Repetitive transcranial magnetic stimulation (rTMS) is a noninvasive neuromodulation therapy. The U.S. Food and Drug Administration (FDA) has approved the use of rTMS for the treatment of major depressive disorder, but has not approved rTMS for treatment of posttraumatic stress disorder (PTSD). rTMS involves placing a magnetic field generator, or “coil,” over the brain region of interest (most often the dorsolateral prefrontal cortex for PTSD patients). The coil produces magnetic pulses that pass through the skull and create small electrical currents that stimulate neurons within that region of the brain (McClintock et al., 2018). The procedure typically takes between 30 to 60 minutes and does not require anesthesia. rTMS interventions can vary by pulse frequency used (high-frequency vs. low-frequency) and by coil location (left, right, bilateral). More novel forms of rTMS therapy can involve accelerated, deep, and synchronized rTMS (Brunoni et al., 2016).

Q. What are the potential mechanisms of action underlying rTMS for the treatment of PTSD?

A. rTMS induces a magnetic field that causes the depolarization of neurons in brain tissue beneath the area where the coil has been placed, as well as in downstream circuits (Liston et al., 2014). Although the biological mechanisms through which rTMS exerts clinical effects are not well understood (Cirillo et al., 2017), proposed theories suggest that neuromodulation of the cortex modulates changes in targeted brain regions and neural systems associated with mood and anxiety (Cho & Strafella, 2009; Keck et al., 2002; Strafella, Paus, Barrett, & Dagher, 2001). Trials have demonstrated that both high-frequency and low-frequency rTMS impact PTSD outcomes (Cohen et al. 2004; Kozel et al., 2019; Leong et al., 2020). PTSD patients show increased activation in the right prefrontal cortex, which may lead to hyperarousal and anxiety. By decreasing cortical excitability, low-frequency rTMS decreases hyperarousal symptoms (Osuch et al., 2009). The mechanism by which high-frequency rTMS impacts PTSD outcomes is unclear. One possibility is that it might activate the medial prefrontal cortex, which is one part of the impaired stress-induced fear circuitry (Shin & Handwerker, 2009).

Q. Is rTMS recommended as a treatment for PTSD in the Military Health System (MHS)?

A. **No.** The 2017 VA/DoD Clinical Practice Guideline for the Management of Posttraumatic Stress Disorder and Acute Stress Disorder states that there is insufficient evidence to recommend for or against rTMS as a treatment for PTSD.

The MHS relies on the VA/DoD clinical practice guidelines (CPGs) to inform best clinical practices. The CPGs are developed under the purview of clinical experts and are derived through a transparent and systematic approach that includes, but is not limited to, systematic reviews of the literature on a given topic and development of recommendations using a graded system that takes into account the overall quality of the evidence and the magnitude of the net benefit of the recommendation. A further description of this process and CPGs on specific topics can be found on the VA clinical practice guidelines website.

Q. Do other authoritative reviews recommend rTMS as a treatment for MDD?

A. **No.** Other authoritative reviews have not substantiated the use of rTMS for PTSD.

Several other recognized organizations conduct systematic reviews and evidence syntheses on psychological health topics using similar grading systems as the VA/DoD CPGs. These include the Agency for Healthcare Research and Quality (AHRQ) and Cochrane.

- AHRQ: No reviews were found on rTMS as treatment of PTSD.
- Cochrane: No reviews were found on rTMS as treatment of PTSD.

Q. Is there any recent research on rTMS as a treatment for PTSD?

A. There have been several recent systematic reviews evaluating the effectiveness of rTMS for PTSD (Belsher et al., under review; Kan, Zhang, Zhang, & Kranz, 2020; McGirr et al., 2020). The systematic reviews consistently found that rTMS treatment targeting the dorsolateral prefrontal cortex was more effective in improving PTSD symptoms compared to sham treatment. Both low-frequency and high-frequency rTMS were associated with a greater PTSD symptom decreases compared to sham. The quality of this evidence was rated as very low due to small samples sizes, treatment heterogeneity, inconsistent results, and an imprecise pooled effect that included wide 95% confidence intervals (Belsher, under review).

Q. What conclusions can be drawn about the use of rTMS as a treatment for PTSD in the MHS?

A. Because there is insufficient evidence that rTMS is effective in the treatment of PTSD, rTMS is not recommended by current guidelines or authoritative reviews.

References

- Belsher, B. E., Beech, E., Reddy, M., Smolenski, D. J., Rauch, S. A. M., Kelber, M., ... Bisson, J. I. (under review). Repetitive transcranial magnetic stimulation for posttraumatic stress disorder: A systematic review. *Journal of Psychiatric Research*.
- Brunoni, A. R., Chaimani, A., Moffa, A. H., Razza, L. B., Gattaz, W. F., Daskalakis, Z. J., & Carvalho, A. F. (2016). Repetitive transcranial magnetic stimulation for the acute treatment of major depressive episodes: A systematic review with network meta-analysis. *JAMA Psychiatry*, *72*(4), 143–152.
- Cho, S. S., & Strafella, A. P. (2009). rTMS of the left dorsolateral prefrontal cortex modulates dopamine release in the ipsilateral anterior cingulate cortex and orbitofrontal cortex. *PLoS One*, *4*(8), e6725.
- Cirillo, G., Di Pino, G., Capone, F., Ranieri, F., Florio, L., Todisco, V., ... Di Lazzaro, V. (2017). Neurobiological after-effects of non-invasive brain stimulation. *Brain Stimulation*, *10*(1), 1–18.
- Cohen, H., Kaplan, Z., Kotler, M., Kouperman, I., Moisa, R., & Grisar, N. (2004). Repetitive transcranial magnetic stimulation of the right dorsolateral prefrontal cortex in posttraumatic stress disorder: A double-blind, placebo-controlled study. *American Journal of Psychiatry*, *161*(3), 515–524.
- Department of Veterans Affairs/Department of Defense. (2017). *VA/DoD clinical practice guideline for the management of posttraumatic stress disorder and acute stress disorder. Version 3.0*. Washington, DC: Department of Veterans Affairs/Department of Defense.
- Kan, R., Zhang, B., Zhang, J., & Kranz, G. S. (2020). Non-invasive brain stimulation for posttraumatic stress disorder: A systematic review and meta-analysis. *Translational Psychiatry*, *10*(1), 168.
- Keck, M. E., Welt, T., Müller, M. B., Erhardt, A., Ohl, F., Toschi, N., ... Sillaber, I. (2002). Repetitive transcranial magnetic stimulation increases the release of dopamine in the mesolimbic and mesostriatal system. *Neuropharmacology*, *43*(1), 101–109.
- Kozel, F. A., Van Trees, K., Larson, V., Phillips, S., Hashimie, J., Gadbois, B., ... Catalano, G. (2019). One hertz versus ten hertz repetitive TMS treatment of PTSD: A randomized clinical trial. *Psychiatry Research*, *273*, 153–162.
- Leong, K., Chan, P., Ong, L., Zwicker, A., Willan, S., Lam, R. W., & McGirr, A. (2020). A randomized sham-controlled trial of 1-Hz and 10-Hz repetitive transcranial magnetic stimulation (rTMS) of the right dorsolateral prefrontal cortex in civilian post-traumatic stress disorder. *Canadian Journal of Psychiatry*, *65*(11), 770–778.
- Liston, C., Chen, A. C., Zebley, B. D., Drysdale, A. T., Gordon, R., Leuchter, B., ... Dubin, M. J. (2014). Default mode network mechanisms of transcranial magnetic stimulation in depression. *Biological Psychiatry*, *76*(7), 517–526.
- McClintock, S. M., Reti, I. M., Carpenter, L. L., McDonald, W. M., Dubin, M., Taylor, S. F., ... Lisanby, S. H. (2018). Consensus recommendations for the clinical application of repetitive transcranial magnetic stimulation (rTMS) in the treatment of depression. *Journal of Clinical Psychiatry*, *79*(1), 16cs10905.
- McGirr, A., Devoe, D. J., Raedler, A., Debert, C. T., Ismail, Z., & Berlim, M. T. (2020). Repetitive transcranial magnetic stimulation for the treatment of post-traumatic stress disorder: A systematic review and network meta-analysis. *The Canadian Journal of Psychiatry*. Advance online publication.
- Osuch, E. A., Benson, B. E., Luckenbaugh, D. A., Geraci, M., Post, R. M., & McCann, U. (2009). Repetitive TMS combined with exposure therapy for PTSD: A preliminary study. *Journal of Anxiety Disorders*, *23*, 54–59.
- Shin, L. M. & Handwerker, K. (2009). Is posttraumatic stress disorder a stress-induced fear circuitry disorder? *Journal of Traumatic Stress*, *22*, 409–415.
- Strafella, A. P., Paus, T., Barrett, J., & Dagher, A. (2001). Repetitive transcranial magnetic stimulation of the human prefrontal cortex induces dopamine release in the caudate nucleus. *Journal of Neuroscience*, *21*(15), RC157.

