Repetitive Transcranial Magnetic Stimulation for Major Depressive Disorder

PHCoE
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Q: What is repetitive transcranial magnetic stimulation?

A: Repetitive transcranial magnetic stimulation (rTMS) is a noninvasive neuromodulation therapy approved by the U.S. Food and Drug Administration (FDA) for the treatment of major depressive disorder (MDD). The FDA specifies the use of rTMS "in adult patients who have failed to achieve satisfactory improvement from one prior antidepressant medication at or above the minimal effective dose and duration in the current episode" (FDA, 2011). rTMS involves placing a magnetic field generator, or "coil," over the brain region of interest (most often the prefrontal cortex for MDD 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 MDD?

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). Long-term, rTMS can produce lasting effects on neural function (Liston et al., 2014). Although the exact mechanism by which rTMS alleviates depressive symptomatology is not known, rTMS may relieve depressive symptoms by modulating functional connectivity within and between cortical networks (Liston et al., 2014). Neuroimaging studies conducted with humans before and after rTMS over the dorsolateral prefrontal cortex (dlPFC) have found changes in frontal or temporal lobe function, activity, or connectivity after rTMS, including normalizing abnormal connectivity (Eshel et al., 2020). Preclinical studies in recent years have explored a variety of mechanisms and signaling pathways (Luan et al., 2020).

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

A: Yes. The 2022 *VA/DoD Clinical Practice Guideline for the Management of Major Depressive Disorder* suggests offering treatment with rTMS during a major depressive episode in patients with treatment-resistant MDD with a "weak for" strength of recommendation.

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. Recommendations for or against a treatment may be characterized as strong or weak based on a variety of factors (e.g., confidence in the quality of the evidence, weight of treatment benefits versus risks, feasibility). The CPGs also state if there is insufficient evidence to develop a 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: Yes. Authoritative reviews published by other organizations recommend the use of rTMS for MDD.

Other recognized organizations conduct systematic reviews and evidence syntheses on psychological health topics using grading systems similar to the VA/DoD CPGs. Notable among these is Cochrane, an international network that conducts high-quality reviews of healthcare interventions.

- Cochrane: A 2001 systematic review found no strong evidence for benefit from using transcranial magnetic stimulation (TMS) to treat depression (Rodriguez-Martin et al., 2001). However, the majority of TMS trials were conducted after this review, which has not been updated.

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

A: Evidence supports the use of rTMS during a major depressive episode in patients with treatment-resistant MDD. Limitations of the evidence base include lack of a standard definition of treatment-resistant depression, heterogeneity of the population and interventions, and few head-to-head studies with other non-pharmacologic and pharmacologic interventions. For additional guidance on selecting a treatment for MDD, please visit the PHCoE Clinician Resources section of the intranet and navigate to clinical support tools.

References

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