Updates on Transcranial Magnetic Stimulation Therapy for Major Depressive Disorder

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KEYWORDS

• Noninvasive neuromodulation • Depression • Treatment-resistant depression
• Transcranial magnetic stimulation

KEY POINTS

- Transcranial magnetic stimulation is a noninvasive brain stimulation therapy developed for use in treatment-resistant depression.
- Metaanalyses and large, randomized, controlled trials largely support efficacy of transcranial magnetic stimulation targeting the dorsolateral prefrontal cortex for major depressive disorder.
- Transcranial magnetic stimulation for depression continues to advance, with studies focusing on refining parameters for treatment optimization, and identification of biomarkers related to treatment response.

INTRODUCTION

Major depression is a leading cause of disability; however, a subset of patients do not experience sufficient relief from existing first-line treatments[1] or have trouble tolerating the side effects of antidepressant medications. Thus, identifying alternative treatments

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Abbreviations	
DLPFC	Dorsolateral prefrontal cortex
DMN	Default model network
DMPFC	Dorsomedial prefrontal cortex
EEG	Electroencephalography
MDD	Major depressive disorder
MT	Motor threshold
rCBF	Regional cerebral blood flow
RCT	Randomized, controlled trial
sgACC	Subgenual anterior cingulate cortex
TMS	Transcranial magnetic stimulation
VMPFC	Ventromedial prefrontal cortex

has been an area of significant interest. Transcranial magnetic stimulation (TMS) has emerged over the last few decades as one such potential option for treatment-resistant depression.

TMS involves application of a strong, pulsed magnetic field to a targeted brain region. A coil generating an electromagnetic field is placed on the scalp, such that strong magnetic pulses are delivered to a relatively focal area of cerebral cortex, resulting in regional neuronal depolarization and generation of action potentials. In treatment protocols, TMS is typically delivered in bundles or "trains" of pulses, separated by periods of rest; this is called repetitive TMS (hereafter referred to as "TMS"). In 2008, the US Food and Drug Administration cleared the first TMS device to treat major depressive disorder (MDD); now multiple devices have regulatory approval in the United States and internationally.

The most common target for TMS for depression is the dorsolateral prefrontal cortex (DLPFC). Both high-frequency (eg, pulses delivered at 10 Hz)[2,3] TMS to the left DLPFC and low-frequency (1 Hz) TMS to the right DLPFC[4] have shown efficacy for pharmacoresistant depression, as well as bilateral TMS (a combination of these approaches).[5] Antidepressant efficacy has also been suggested for high-frequency TMS targeting broader prefrontal cortex.[6] In addition, open trial results show preliminary support for TMS to the dorsomedial prefrontal cortex (DMPFC)[7] for depression. Recent research has examined efficacy of TMS delivered using a pulse pattern called theta-burst,[8] a form of stimulation that has shown ability to promote synaptic plasticity in motor cortex; preliminary evidence suggests theta-burst TMS is as effective as a standard stimulation for MDD, but sessions are much shorter. Additionally, a small number of studies have investigated accelerated TMS protocols, delivering 2 or more TMS sessions per day, potentially shortening the number of weeks that comprise a course of TMS therapy. Preliminary findings suggest accelerated approaches may be efficacious,[9,10] although definitive trials have yet to be conducted.

The TMS for depression field depression is growing quickly, with new studies seeking to optimize parameters for delivery and to identify biomarkers of treatment response. Hereafter, we review efficacy data from controlled TMS trials for depression and discuss ongoing areas of research aimed at further improving this treatment, including research identifying neuroimaging and neurophysiologic biomarkers.

EVIDENCE FOR THE EFFICACY OF TRANSCRANIAL MAGNETIC STIMULATION FOR DEPRESSION

Over the past 20 to 30 years, studies of TMS for depression have shifted from small trials focused on safety, tolerability, and preliminary efficacy to larger multicenter trials and refinement of treatment parameters. Thus, many randomized, controlled trials

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