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SAFETY, EFFICACY, AND TOLERABILITY OF INTERMITTENT THETA-BURST RTMS OF THE DORSOMEDIAL PREFRONTAL CORTEX FOR REFRACTORY MAJOR DEPRESSION

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rTMS is an emerging treatment for major depressive disorder (MDD) refractory to medications and psychotherapy. The conventional target for rTMS in MDD is the dorsolateral prefrontal cortex (DLPFC). However, convergent evidence from lesion, stimulation, and neuroimaging studies suggests that the dorsomedial prefrontal cortex (DMPFC) may play a more central role in emotion regulation. We have recently demonstrated robust and potentially superior antidepressant properties for excitatory rTMS of the DMPFC. However, one of the enduring limitations of rTMS is the long duration of each treatment session under conventional protocols, which require ~40 minutes per day over 20-30 sessions for maximum efficacy using conventional 10 Hz stimulation. More recent studies have suggested that theta-burst stimulation (TBS) protocols can achieve stronger and more durable effects in markedly less time. Intermittent theta-burst stimulation (iTBS) generates robust and long-lasting excitatory effects with 600 pulses over ~3 min. Pilot studies have previously reported antidepressant effects with TBS over the DLPFC. However, TBS over the DMPFC has not previously been studied. Here we report robust antidepressant effects for a 7 min course of iTBS, administered bilaterally over the DMPFC with MRI-guidance at 120% resting motor threshold, over 20-30 sessions, in an open-label series of 40 patients with refractory MDD. Safety, efficacy, and tolerability are comparable to a 10 Hz rTMS protocol requiring 30-40 min of treatment. iTBS of the DMPFC may effectively reduce the duration (and cost) of rTMS >4-fold, thus increasing patient capacity per clinic and improving the overall accessibility of rTMS in refractory MDD.

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