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HOT TOPICS

PFC neuromodulation with theta burst stimulation to impact behavior and neural network activity in schizophrenia and bipolar disorder

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Theta Burst Stimulation (TBS) is a repetitive Transcranial Magnetic Stimulation (rTMS) neuromodulation protocol that employs short bursts (three, 50 Hz pulses) delivered at 5 Hz. Intermittent TBS (iTBS) increases, and continuous TBS (cTBS) decreases, cortical neuron excitability [1]. iTBS usually comprise 20, 2-s trains interleaved with 8 s of silence for 190 s, while cTBS blocks typically last 40 s. Both iTBS and cTBS are significantly shorter than rTMS paradigms, thereby allowing TBS to induce more rapid effects on neural activity and related clinical measures [2]. While TBS has been traditionally applied to the motor cortex, more recently both iTBS and cTBS paradigms have been employed over the prefrontal cortex (PFC) in healthy and psychiatric populations, including patients with Schizophrenia (SCZ) and Bipolar Disorder (BD). Specifically, in individuals with SCZ, TBS over PFC has been recently used to target negative symptoms (anhedonia, avolition), and cognitive deficits (attention, working memory) [3]. Regarding mood disorders, TBS of PFC has been primarily employed in Major Depressive Disorder individuals [4], and the safety and efficacy of iTBS was lately established in individuals with BD depression [5]. Yet, despite some promising initial results, there is a need to replicate these findings in larger groups of patients, ideally with the following methodological enhancements to establish treatment effectiveness in SCZ and BD.

First, symptom improvement is presently the goal/main outcome measure of double-blind, randomized clinical trials in psychiatric populations. However, identifying and modulating the neural circuits and mechanisms underlying these symptoms is critical to developing more targeted, effective interventions. Thus, some biological measures (e.g., resting-state fMRI connectivity), are and should be increasingly used both to guide treatment (i.e., target engagement trials) and assess treatment response. Future studies should also employ resting state and task-based fMRI, to locate neural regions to be targeted at the individual level, as well as to identify new regions for targeting based on understanding of underlying neural circuitry abnormalities associated with SCZ and BD. Second, EEG measures offer non-invasive, direct assessments of cortical regions, including PFC, that are critically altered in both SCZ and BD. Thus, EEG could be utilized to provide more precise PFC and other cortical region targets for TBS-based interventions. Third, TBS paradigms can acutely modulate neural circuitries and behavioral (e.g., task performance) outcomes in healthy individuals [6]. However, far less is known about the acute effects of TBS of PFC in psychiatric populations. Using TBS to acutely modulate PFC, which is implicated in several domains of treatment (e.g., cognition, psychosis, impulsivity), and examining the impact of such interventions on neural, clinical, and behavioral biomarkers, will clarify TBS effects on these domains, thus better informing subsequent neuromodulation-based chronic treatments in SCZ and BD patients. Finally, optimizing TBS parameters, including coil placement, intensity of stimulation, frequency/total number of sessions, and employing a set of universally accepted standards in treatment to enhance reliability and precision holds promise to improve the effectiveness of PFC neuromodulation with TBS paradigms in these patients.

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