Use of Transcranial Magnetic Stimulation in Bipolar Disorder

To the Editor: Bipolar disorder is an episodic illness that affects 1.0%–1.8% of the population.[1] Challenges to its management include the limited number of pharmacologic and psychosocial interventions supported by evidence for both short- and long-term efficacy, and limitations to individual tolerance and adherence, and potential emergent mania.[2] However, advances in understanding of the neurobiology of mood disorders are guiding consideration of implicated brain regions and testing of potential new therapeutic interventions. For example, there are now 30 published randomized, controlled trials and 10 meta-analyses that have reported on the antidepressant effects of transcranial magnetic stimulation (TMS) in patients with unipolar depression.[3] In 2008, the U.S. Food and Drug Administration approved TMS for the treatment of unipolar major depression in adult patients who have failed to respond to a single adequate antidepressant medication trial.[3]

TMS affects neural activity at the site of stimulation and in distal regions that are interconnected and are implicated in mood disorders, such as the striatum, thalamus, and anterior cingulate cortex.[3] Imaging studies of mood disorders point to dysfunction of the limbic and prefrontal cortex activity.[1] Depression syndromes may be associated with low cortical activity (blood flow and metabolism), particularly on the left side, with relative increase on the right side.[1] On the basis of results of unipolar depression studies, it has been hypothesized that left-sided dorsolateral prefrontal cortex stimulation via TMS-induced neuronal depolarization may change brain activity and improve mood.[3] although the anatomopathophysiology of bipolar disorder may be somewhat different, affecting right- as well as left-sided systems, few studies have examined the therapeutic effects of TMS in bipolar depression. We searched the database of PubMed, Ovid MEDLINE, and ScienceDirect for reports concerning the TMS use in bipolar disorder. Our search yielded only 10 published papers.[4–13] There were five studies in bipolar depressed patients (total n: 66) and five studies in manic patients (total n: 74). These studies suggest the efficacy of TMS as an augmenting treatment during the acute and maintenance treatment of bipolar depression. Evidence concerning TMS benefits in bipolar depression as a monotherapy and in mania is conflicting. There are many methodological considerations that limit interpretation of this early bipolar TMS literature. These include the small number of patients, unequal randomization, lack of sham control, and differences in clinical features and treatment history. Stimulation parameters, treatment duration, and symptom assessment methods differed across the reports. It has been hypothesized that TMS could be effective in bipolar depression by stimulating the left prefrontal cortex or inhibiting the right prefrontal cortex.[11] It has been proposed that in bipolar mania there is decreased cortical activity in the right side, with a relative increase in left-sided activity.[12] Moreover, TMS might have therapeutic effects in mania when the right prefrontal cortex is stimulated.[12] It has been thought that high-frequency (>1 Hz) TMS induces cortical excitation, whereas low-frequency (<1 Hz) causes cortical inhibition.[14] TMS appears to be relatively safe and well tolerated. There is no post-procedure recovery period and no risk of anesthesia.[3,15] The most common side effects are headaches and pain at the site of the stimulation.[3] The estimated risk of TMS-induced seizures and memory impairment is reportedly low.[3,15] There are conflicting findings regarding TMS-induced mania. Three studies did not report a statistically significant increase in manic symptom ratings in bipolar depressed patients during TMS.(5,7,8) However, induction of hypomania and mania has been reported in healthy volunteers and in unipolar and bipolar depressed patients.[16] In summary, data on the safety and efficacy of TMS in bipolar disorder are preliminary but intriguing. They support the need to focus on such patients in exploratory studies and in adequately powered confirmatory studies.

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