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Application of Transcranial Magnetic Stimulation in Mania

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Mini Review

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Abstract

In the literature, few studies have established therapeutic effect of transcranial magnetic stimulation (TMS) in manic episodes. To date, only one randomized study has suggested the potential benefit of a TMS protocol over the right DLPFC for mania.

Keywords: Transcranial; Magnetic Stimulation; Noninvasive; Magnetic Pulses

Background

Transcranial magnetic stimulation (TMS) is a relatively new, noninvasive therapeutic option that involves the application of magnetic pulses on hyperactive or hypoactive cortical brain areas with the aim of modulating brain networks [1]. To administer TMS, the clinician places an electromagnetic coil on a prespecified region of the patient's scalp. Magnetic pulses from the coil travel through the skull toward a target cortical area, resulting in neural activation changes. To date, TMS has received the most consistent clinical and research application in treatment-resistant depression [2-4]. In the past several years, studies have explored the application of TMS in other psychiatric disorders.

The aim of this review is to explore the existing literature on the application of TMS across symptomatic manic episodes.

Methods

We searched PubMed for relevant articles using the following search terms: "Transcranial magnetic stimulation" AND "bipolar disorder, "TMS" And "bipolar disorder", "Transcranial magnetic stimulation "AND" mania", "TMS" and "mania". All search fields of the databases were included to maximize inclusivity. The research took place in December 2019, and no time restriction was placed on any of the database searches. Only articles published in English in peer-reviewed journals were eligible. Case studies with fewer than five patients, review papers, and theoretical articles were excluded.

Results

In studies of TMS for mania, nearly all protocols have targeted the right prefrontal region. We found four randomized studies and two open-label studies conducted in TMS for patients with manic episodes (Table 1).

The first randomized clinical trial was conducted by Grisaru, et al., in which 16 manic patients were randomly assigned to 10 sessions of right prefrontal or left prefrontal high frequency (20 Hz) TMS over a two week period. At post treatment, patients receiving right prefrontal TMS demonstrated significantly greater improvement in YMRS and the CGI scores relative to patients receiving left prefrontal TMS [5].

Following up to their initial study, Kaptan and al., randomly assigned 19 patients to receive 10 sessions of right-sided, high frequency (20 Hz) prefrontal TMS versus sham treatment over the course of two weeks. They didn't found differences between right-sided TMS and sham TMS

[6].

The third randomized study conducted by Praharaj, et al., in 41 patients with mania receiving 10 sessions of high frequency (20 Hz) rTMS over the right DLPFC compared with patients with sham treatment found significant reductions in YMRS scores favoring active group [7]. However, in a follow-up study employing an identical protocol in an adolescent sample found no significant differences in mania outcomes between the active and sham groups. The authors suggest that the discrepant findings between the two studies may be accounted for by metabolic differences between adults and children. Adult patients with mania may have decreased metabolism on the right side of their brain and increased metabolism on the left side. Thus, in adults, an rTMS protocol over the right DLPFC may help account for these metabolic discrepancies [7].

For the open-label studies, using high frequency right-sided magnetic stimulation, authors found significant reduction in mania assessment scales [9-10].

Table I shows open-label and RCTs studies of efficacy of rTMS in mania.

	Authors	Design	Sample size	sessions	Notable outcomes
Randomized Studies	Grisaru, et al. (1998) [5]	right-sided, high frequency Vs left-sided high frequency TMS	16	10	Greater reduction in YMRS and CGI scores favoring right-sided group, notably low response in left-sided group
	Kaptsan et al. (2003) [6]	right-sided, high frequency TMS Vs sham	19	10	No differences between groups
	Praharaj et al. (2009)[7]	Right-sided, high frequency rTMs Vs sham	41	10	Significant reduction in YMRS scores favoring active group
	Pathak et al. (2015) [8]	Right-sided, high frequency rTMS Vs sham	26	10	No significant differences between groups
Open Studies	Michael et al. (2004) [9]	Right-sided, rapid TMS	9	8	Reduction in Bech-Rafaelsen scores
	Saba et al. (2004) [10]	Right-sided, high frequency TMS	8	10	Significant reduction in Mania Assessment scales and CGI

Table 1: Open-label and RCTs studies of rTMS in mania.

Discussion

Transcranial magnetic stimulation represents an important, largely understudied avenue of intervention research and clinical care in bipolar disorders. This review synthesizes data from the few clinical trials that have explored TMS as a treatment for patients with manic episodes. To date, most research has focused on rTMS for patients in a bipolar depressive episode and most of them found significant improvement in depressive symptoms.

TMS for mania has been the focus of fewer clinical trials and yielded more inconsistent findings with only two randomized, controlled trial suggesting the benefit of rTMS over a sham treatment and the benefit effect of right sided high frequency compared to let-sided high frequency [5,7]. Open-label studies of TMS for bipolar mania have also delivered promising findings using high frequency in right prefrontal dorsolateral cortex [9-10]. To date, only one randomized study has suggested the potential benefit of a TMS protocol over the right DLPFC for mania compared to patient receiving sham.

Conclusion

To date, only one randomized study has suggested the potential benefit of a TMS protocol over the right DLPFC for mania compared to patient receiving sham. There are some important limitations associated with existing clinical trials of TMS in mania. Among the few studies that have evaluated TMS as a treatment for mania, many are limited by small samples with most studies including less than 20 patients. Additional randomized studies with a large sample of bipolar patients with manic episodes are needed to understand active mechanism of TMs in those symptoms.

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