

## Disclosure

The authors report no conflicts of interest.

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# Comment on “Transcranial magnetic stimulation of the medial prefrontal cortex for psychiatric disorders: a systematic review”

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In a recent issue, the *Brazilian Journal of Psychiatry* published a systematic review on transcranial magnetic stimulation of the medial prefrontal cortex for psychiatric disorders conducted by two of the authors of this letter (RCM and AC).<sup>1</sup> It has since come to our attention that a multicenter clinical trial of great relevance to the topic was not included in the review. This unfortunate oversight was due to the trial's publication taking place after acceptance of the review. Nonetheless, the importance of this trial is such that it would have influenced our overall analysis of the literature on medial prefrontal cortex transcranial magnetic stimulation (mPFC TMS), which motivated this correspondence.

The study in question, conducted by Carmi et al.,<sup>2</sup> is the largest randomized controlled trial to date investigating the use of mPFC TMS in the treatment of a psychiatric

disorder. In 11 centers across the United States, Canada, and Israel, the researchers tested the efficacy of 20 Hz mPFC TMS in 99 patients with obsessive-compulsive disorder (OCD). The main outcome measure was the Yale-Brown Obsessive Compulsive Scale (YBOCS). Repetitive TMS was performed with an H-coil, which produces deeper and larger stimulation volumes than those of regular coils. Before and during the TMS session, a personalized OCD symptom provocation technique was used to activate the relevant neural circuitry being targeted. The trial design and sample size were based on a pilot study previously completed by part of the same group.<sup>3</sup>

The intervention resulted in a significantly different decrease in YBOCS measures between the active and sham groups ( $p = 0.01$ ), with an effect size of 0.69. The between-group difference was maintained at 1-month follow-up, with a response rate of 45.2% in the active treatment group vs. 17.8% in the sham group. Had it been included in the review, this trial would have a low risk of bias according to the quality assessment tool. It would also have changed the tone of our conclusions, since it figures as the first high-quality mPFC TMS trial with a relatively large sample, offering solid evidence for the clinical application of this intervention, expanding on findings from pilot trials and smaller studies.

Other than the clinical importance of this publication, the successful therapeutic use of mPFC TMS emphasizes the value of a circuit-based approach to mental illness, and how neuromodulation interventions such as TMS can be effectively used for this purpose.<sup>4</sup> Greater understanding of the neurobiology of mental illnesses has guided a recent shift in attention in TMS research from regions more closely associated with cognition and executive functions (e.g., the dorsolateral prefrontal cortex) to areas involved in limbic processes and emotional regulation (e.g., the mPFC).<sup>5</sup> The results obtained by Carmi et al. are an important example of how this different approach can aid the development of new effective treatments for psychiatric disorders.

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