

New Hope for Resistant Obsessive Compulsive Disorder

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High-frequency deep transcranial magnetic stimulation (dTMS) may offer new hope for patients with treatment-resistant obsessive-compulsive disorder (OCD), new research suggests.

Results of a 6-week, double-blind, placebo-controlled study showed daily high frequency dTMS (20 Hz) was safe and effective and achieved almost twofold reduction in OCD symptoms compared with sham treatment.

Study investigator Abraham Zangen, PhD, professor of neuroscience at Ben-Gurion University of the Negev in Israel, noted that the original assumption was to use low frequency dTMS to reduce the activity of the anterior cingulate cortex, based on the literature showing that it is overactive in OCD patients.

"We were surprised to find that actually, it was the high frequency that caused the effect," Zangen told *Medscape Medical News*.

The findings were [published online](#) May 21 in the *American Journal of Psychiatry*.

Poor Response Rate

OCD affects 2% to 3% of the US population. However, only 40% to 60% of these patients achieve partial response to treatment.

[As reported](#) by *Medscape Medical News*, the BrainsWay dTMS system (BrainsWay Ltd) received marketing approval from the US Food and Drug Administration (FDA) in August 2018 for treatment of OCD. The dTMS system treats patients through magnetic pulses administered to areas of the brain. In the current multicenter international study, dTMS targeted the cortico-striatal-thalamic-cortical loop circuit, specifically, the medial prefrontal cortex and anterior cingulate cortex.

A total of 94 patients with OCD between the ages of 22 and 68 years were randomized to receive either high frequency dTMS using the BrainsWay system once daily for 6 weeks (n = 47) or sham treatment (n = 47). The latter induced scalp sensations but without penetration of the electric field into the brain.

The study's primary outcome measure was change in baseline scores to post-treatment scores on the Yale-Brown Obsessive Compulsive Scale (Y-BOCS)

Secondary outcome measures included change in Y-BOCS score from baseline assessment to 1-month follow-up assessment. Rate of full response was defined as a reduction of $\geq 30\%$ on Y-BOCS score at the post-treatment assessment. Partial response was defined as $\geq 20\%$ from the baseline assessment to post-treatment assessment.

The dTMS treatment was provided as an adjunctive therapy to the patients' current treatment, whether maintenance medication such as a serotonin reuptake inhibitor or cognitive behavioral therapy (CBT). None of the patients was responsive to previous trials of medication.

Before each dTMS session, patients received 3 to 5 minutes of individualized provocation. For example, they might be told to "please keep thinking about that dirty handle," in order to activate their OCD circuitry. The dTMS treatment was immediately followed by CBT delivered via cellphone.

The study had a high completion rate: 89% in the dTMS group and 96% in the sham group.

Significant Symptom Reduction

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Significant between-group differences were maintained at follow-up. At 1-month post-treatment, the dTMS-treated patients had a full response rate of 45.2% vs. 17.8% in the placebo group ($P = .006$).

Partial response at the follow-up assessment was 59.5% vs 42.2%, respectively.

The researchers also compared secondary outcomes at 4 weeks post-treatment. The mean change in Y-BOCS score had declined at that assessment by 6.5 points (95% CI, 4.3 - 8.7) in the dTMS group and by 4.1 points (95% CI, 1.9 - 6.2) in the sham group ($P = .03$, for an effect size of 0.62).

In addition, 73% of the dTMS group and 69% of the placebo group reported adverse events, with headaches being the most frequently reported (by 37.5% vs 35.3%, respectively).

Rebuilding Brain Connections

"The mechanism of action is the stimulation of the areas in the brain that have been known for years to be implicated in the pathophysiology of OCD," Zangen said.

"Now, just stimulating these areas by itself creates a window for plasticity changes in the circuit. These areas of the brain are known to be malfunctioning in a general way in OCD patients," he added.

Zangen noted that one theory is that dTMS stimulation disrupts pathological brain circuitry. After patients are treated within a short window of about 10 minutes, they can rebuild brain connections because of neuroplasticity.

In addition, the results were enhanced by the addition of remotely delivered CBT immediately following dTMS.

"Once you learn something, you change the circuitry [and] then it's there. It's like a memory and even old people can create new memories," Zangen said.

"An alternative explanation is that this area is serving as a compensatory neural network for the symptoms of OCD and by exciting this area, we allow the brain to compensate better for the symptoms," he noted.

He added that this actually activates the pathological circuitry of the specific patient within the areas of the brain.

"We know that it's the anterior cingulate cortex that we target. These areas in the brain include many functions, but we activate the pathological circuitry by a provocation." Zangen said that repeating this process over 6 weeks produces a durable effect.

New Hope

Commenting on the findings for *Medscape Medical News*, Ryan Vidrine, MD, assistant clinical professor of psychiatry and director of the OCD Program at the School of Medicine at the University of California-San Francisco, called the findings exciting because dTMS "is a new tool for a disorder that hasn't had any new treatments in quite a time."

He noted that in the study, dTMS was used as an adjunctive treatment to existing treatment — which is the way he uses it in clinical practice to treat depression and OCD.

"The nice thing with TMS is that we can target circuits in the brain that we know are important in OCD based on years of research," said Vidrine, who was not involved with the current research. "We can target them without also having to target the rest of the body with the medication."

He added that many patients with OCD often choose to stop their medication because of side effects such as sexual dysfunction, sedation, or weight gain; but TMS seems to have "pretty minimal side" effects.

While there is a decade of research data on using TMS in depression, one theory is that TMS treatment boosts cognitive control in OCD patients, enabling them to control their symptoms better. It also seems helpful for people stuck in a plateau in therapy, Vidrine said.

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