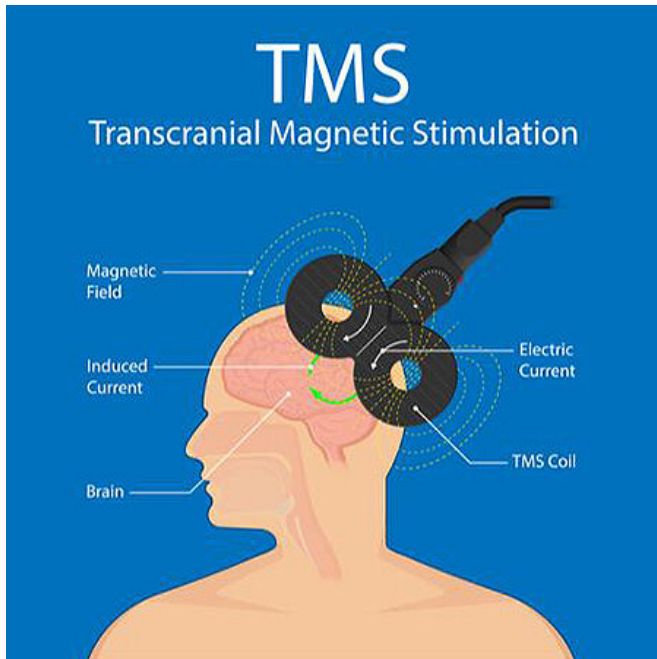


# New neuroimaging technique studies brain stimulation for depression

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A small coil positioned near the scalp generates repetitive, pulsed magnetic waves that pass through the skull and stimulate brain cells (neurons) to relieve symptoms of depression. A typical rTMS session lasts 30 to 60 minutes and does not require anesthesia. Credit: University of South Florida

Repetitive transcranial magnetic stimulation, or rTMS, was FDA approved in 2008 as a safe and effective noninvasive treatment for severe depression resistant to antidepressant medications. A small coil positioned near the scalp generates repetitive, pulsed magnetic waves that pass through the skull and stimulate brain cells to relieve symptoms of depression. The procedure has few side effects and is typically prescribed as an alternative or supplemental therapy when multiple antidepressant medications and/or psychotherapy do not work.

Despite increased use of rTMS in psychiatry, the

rates at which patients respond to therapy and experience remission of often-disabling symptoms have been modest at best.

Now, for the first time, a team of University of South Florida psychiatrists and biomedical engineers applied an emerging functional neuroimaging technology, known as [diffuse optical tomography](#) (DOT), to better understand how rTMS works so they can begin to improve the technique's effectiveness in treating depression. DOT uses near-infrared light waves and sophisticated algorithms (computer instructions) to produce three-dimensional images of soft tissue, including [brain tissue](#).

Comparing depressed and healthy individuals, the USF researchers demonstrated that this newer optical imaging technique can safely and reliably measure changes in [brain](#) activity induced during rTMS in a targeted region of the brain implicated in mood regulation. Their findings were published April 1 in the *Nature* journal *Scientific Reports*.

"This study is a good example of how collaboration between disciplines can advance our overall understanding of how a treatment like TMS works," said study lead author Shixie Jiang, MD, a third-year psychiatry resident at the USF Health Morsani College of Medicine. "We want to use what we learned from the application of the diffuse optical tomography device to optimize TMS, so that the treatments become more personalized and lead to more remission of depression."

DOT has been used clinically for imaging epilepsy, breast cancer, and osteoarthritis and to visualize activation of cortical brain regions, but the USF team is the first to introduce the technology to psychiatry to study brain stimulation with TMS.

"Diffuse optical tomography is really the only modality that can image brain function at the same time that TMS is administered," said study principal

investigator Huabei Jiang, Ph.D., a professor in the Department of Medical Engineering and father of Shixie Jiang. The DOT imaging system used for USF's collaborative study was custom built in his laboratory at the USF College of Engineering.

The researchers point to three main reasons why TMS likely has not lived up to its full potential in treating major depression: nonoptimized brain stimulation targeting; unclear treatment parameters (i.e., rTMS dose, magnetic pulse patterns and frequencies, rest periods between stimulation intervals), and incomplete knowledge of how nerve cells in the brain respond physiologically to the procedure.

Portable, less expensive, and less confining than some other neuroimaging equipment like MRIs, DOT still renders relatively high-resolution, localized 3-D images. More importantly, Dr. Huabei Jiang said, DOT can be used during TMS without interfering with treatment's magnetic pulses and without compromising the images and other data generated.

DOT relies on the fact that higher levels of oxygenated blood correlate with more brain activity and increased cerebral blood flow, and lower levels indicate less activity and blood flow. Certain neuroimaging studies have also revealed that [depressed people](#) display abnormally low brain activity in the prefrontal cortex, a brain region associated with emotional responses and mood regulation.

By measuring changes in near-infrared light, DOT detects changes in [brain activity](#) and, secondarily, changes in blood volume (flow) that might be triggering activation in the prefrontal cortex. In particular, the device can monitor altered levels of oxygenated, deoxygenated, and total hemoglobin, a protein in red blood cells carrying oxygen to tissues.

The USF study analyzed data collected from 13 adults (7 depressed and 6 healthy controls) who underwent DOT imaging simultaneously with rTMS at the USF Health outpatient psychiatry clinic. Applying the standard rTMS protocol, the treatment was aimed at the brain's left dorsolateral prefrontal

cortex—the region most targeted for depression.

The researchers found that the depressed patients had significantly less brain activation in response to rTMS than the healthy study participants. Furthermore, peak brain activation took longer to reach in the depressed group, compared to the healthy control group.

This delayed, less robust activation suggests that rTMS as currently administered under FDA guidelines may not be adequate for some patients with severe depression, Dr. Shixie Jiang said. The dose and timing of treatment may need to be adjusted for patients who exhibit weakened responses to brain stimulation at baseline (initial treatment), he added.

Larger clinical trials are needed to validate the USF preliminary study results, as well as to develop ideal treatment parameters and identify other dysfunctional regions in the depression-affected brain that may benefit from targeted stimulation.

"More work is needed," Dr. Shixie Jiang said, "but advances in neuroimaging with new approaches like diffuse optical tomography hold great promise for helping us improve rTMS and depression outcomes."

**More information:** Shixie Jiang et al, Neuroimaging of depression with diffuse optical tomography during repetitive transcranial magnetic stimulation, *Scientific Reports* (2021). [DOI: 10.1038/s41598-021-86751-9](#)

Provided by University of South Florida

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