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Experimental depression treatment is nearly 80% effective in controlled study

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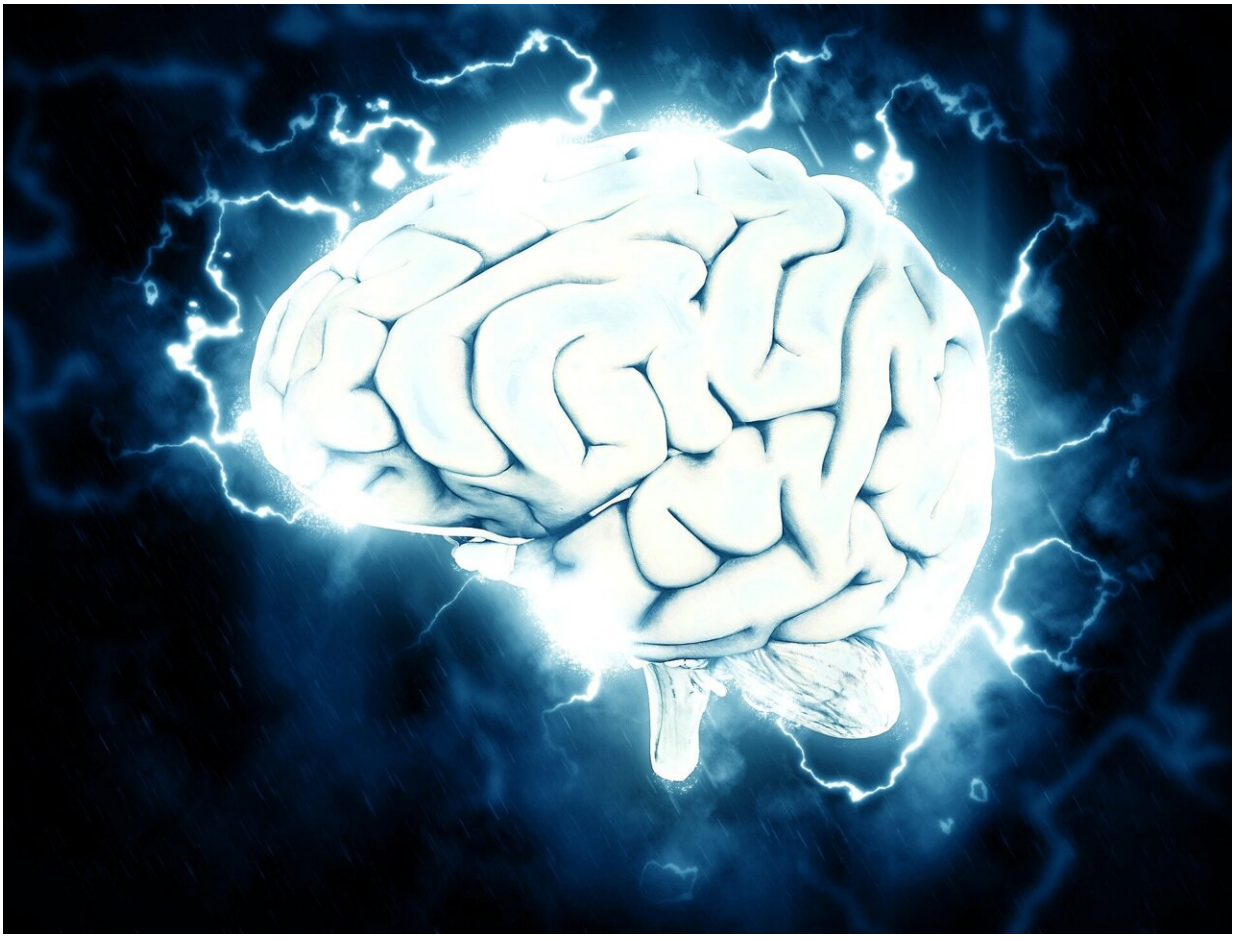

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A new type of magnetic brain stimulation brought rapid remission to

almost 80% of participants with severe depression in a study conducted at the Stanford University School of Medicine.

The treatment, known as Stanford accelerated intelligent neuromodulation therapy (SAINT) or simply Stanford neuromodulation therapy, is an intensive, individualized form of transcranial magnetic stimulation. In the study, remission typically occurred within days and lasted months. The only side effects were temporary fatigue and headaches.

"It works well, it works quickly and it's noninvasive," said Nolan Williams, MD, an assistant professor of psychiatry and behavioral sciences. "It could be a game changer." Williams is the senior author of the study, which was published Oct. 29 in the *American Journal of Psychiatry*.

Twenty-nine people with treatment-resistant depression participated in the study: About half received SAINT, and the rest underwent a placebo procedure that mimicked the real treatment. After five days of treatment, 78.6% of the participants in the treatment group were no longer depressed, according to several standard methods of evaluation. "It's quite a dramatic effect, and it's quite sustained," said Alan Schatzberg, MD, the Kenneth T. Norris, Jr. Professor in Psychiatry and Behavioral Sciences, who was a co-author of the study.

A lifetime of depression

Tommy Van Brocklin, 60, has suffered from depression since he was 15. "In 1975, they didn't have the medication and understanding they do now," he said. "I was told I wasn't trying hard enough."

"I've functioned all these years, but it's been very difficult at times," the civil engineer added. Talk therapy helped "for about half a day after an

appointment." When selective serotonin reuptake inhibitors became available in the 1990s, he started on paroxetine, commonly sold under the brand name Paxil.

"It worked like a miracle drug," he said, but after 10 or 15 years it started to lose its effect. After 25 years, it stopped working entirely. He tried other medications, but none helped; one even made him suicidal.

His sister, who lives near Stanford, connected him with the researchers studying SAINT. He flew from his home in Memphis, Tennessee, and underwent the treatment in September. He felt nothing the first day; on day two, he began feeling emotional—"I felt the struggle of what I'd been through all these years."

"The next day, all of a sudden, it broke through," he said. "I felt so much better, and it's stuck with me."

Specialized magnetic stimulation

The transcranial magnetic stimulation treatment currently approved by the Food and Drug Administration requires six weeks of once-daily sessions. Only about half of patients who undergo the treatment improve, and only about a third experience remission from depression.

SAINT advances that treatment by targeting the magnetic pulses according to each patient's neurocircuitry and providing a greater number of pulses at a faster pace.

In the study, the researchers first used MRI to locate the best location to target within each participant's dorsolateral prefrontal cortex, which regulates executive functions, such as problem solving and inhibiting unwanted responses. They applied the stimulation in a subregion that has the strongest relationship with the subgenual cingulate, a part of the

brain that is overactive in people experiencing depression. The transcranial magnetic stimulation strengthens the connection between the two regions, facilitating dorsolateral prefrontal cortex control of the activity in the subgenual cingulate.

The researchers also used 1,800 pulses per session instead of 600. (The larger amount has been used safely in other forms of brain stimulation for neurological disorders such as Parkinson's disease.) And instead of providing one treatment a day, they gave participants 10 10-minute treatments, with 50-minute breaks in between.

For the control group, the researchers disguised the treatment with a magnetic coil that mimicked the experience of the magnetic pulse; both the control and active treatment groups wore noise-canceling earphones and received a topical ointment to dull sensation. Neither the researcher administering the procedure nor the participant knew whether the participant was receiving real treatment.

A hard-to-treat group

The trial participants ranged in age from 22 to 80; on average, they had suffered depression for nine years. They had tried medications, but either they had had no effect or they had stopped working. During the trial, participants who were on medication maintained their regular dosage; participants who weren't taking medications did not start any.

Within four weeks after treatment, 12 of the 14 participants who had received the treatment improved, and 11 of them met FDA criteria for remission. In contrast, only two of the 15 participants who had received the placebo met the criteria for remission.

Because the study participants typically felt better within days of starting SAINT, the researchers are hoping it can be used to quickly treat

patients who are at a crisis point. Patients who start taking medication for depression typically don't experience any reduction of symptoms for a month.

"We want to get this into emergency departments and psychiatric wards where we can treat people who are in a psychiatric emergency," Williams said. "The period right after hospitalization is when there's the highest risk of suicide."

Van Brocklin said that since he returned home following treatment, he's made some radical changes. "I have a really strong desire to get my life together," he said.

"I don't procrastinate anymore," he added. "I'm sleeping better. I completely quit alcohol. I'm walking my dog and playing the guitar again, for nothing more than the sheer joy of it."

Most importantly, he said, "I'm remaining positive and being respectful of others. These are big changes in my life."

More information: Eleanor J. Cole et al, Stanford Neuromodulation Therapy (SNT): A Double-Blind Randomized Controlled Trial, *American Journal of Psychiatry* (2021). DOI: 10.1176/appi.ajp.2021.20101429

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