A surgically implanted brain stimulation device could help treat severe depression

Sarah had no options left. Over five years, she'd tried every possible treatment for her severe depression, and nothing had helped. "My daily life had become so restricted and impoverished by depression that I felt tortured by each day," the 36-year-old said.

But after undergoing an experimental procedure that implanted a device into her brain, she felt her depression lift for the first time in years. "It was like my lens on the world changed," Sarah, who is remaining anonymous because of the stigma around depression, said during a press briefing.

Sarah was the patient in a proof-of-concept trial of a new approach to treating severe, treatment-resistant depression, published today in the journal *Nature Medicine*. The findings open up another possible strategy for helping people with the disorder. The study only involved Sarah, and it's still not clear how well it might work in other people. The lessons from the trial, though, helped the researchers understand more about the nature of depression and could apply to other efforts to treat the disease.

"We identified through this trial some fundamental properties about the brain," said study author Katherine Scangos, a psychiatrist at the University of California San Francisco Weill Institute for Neurosciences, during the press briefing. "We think these findings about the brain will be available for the general public, and will help us develop new personalized depression treatments."

“depression is caused by faulty circuits”

The trial used a technique called deep brain stimulation, where electrodes implanted within the brain deliver electrical impulses in an attempt to change or regulate abnormal brain activity. It’s common for conditions like epilepsy and Parkinson’s disease. Research over the past decade has shown that it can sometimes help with depression, but the findings have been inconsistent. Most previous efforts delivered stimulation to individual regions of the brain thought to be involved in depression. This study, though, was targeted at regions that were part of specific brain *circuits* — interconnected parts of the brain that are responsible for specific functions.

“What we are increasingly realizing now is that depression is caused by faulty circuits,” Scangos says.

In addition, the circuits involved might be different for each person. So in this trial, the study team personalized the treatment approach to the specific patient’s depression. They mapped out the type of brain activity that occurred when Sarah’s depression symptoms flared. Then, they surgically implanted a device that could detect that brain activity and send stimulation to the circuit where the activity was happening.

For Sarah, the procedure was highly effective. Her scores on depression rating scales dropped the morning after the device was turned on. And perhaps more importantly, she felt dramatic changes in her mood. During her first time getting the stimulation, she laughed out loud in the lab. “And everyone in the room went, ‘Oh my god,’ because that’s the first time I spontaneously laughed and smiled, where it wasn’t faked, in five years,” she said.

Sarah’s depression circuit flares up hundreds of times a day, and each time, the implanted device delivers a brief stimulating pulse. In total, she gets around 30 minutes of

stimulation each day, Scangos says. Sarah can't feel the pulses, but she said she does have a general idea of when they're happening throughout the day. "There's a sense of alertness and energy or positivity that I'll feel," she said.

Despite the overwhelming success for Sarah, this trial was just a first demonstration of this approach. The device used in the trial isn't authorized to treat depression – it was originally designed to treat epilepsy and was used in the trial under an investigational device exemption from the FDA. "We have a lot of work ahead of us as a field to validate this result to see if it's actually something that will be enduring as a treatment option," said Edward Chang, an author on the study and the chairman of the department of neurosurgery at UCSF.

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If it proves to work for other people, it would likely be used only after trying all other options, Chang says. Surgery – especially brain surgery – is always a risk. For patients with Parkinson's and epilepsy, patients who go that route have generally tried every other treatment. "For now, a lot of these approaches we consider a last resort," Chang said. It's an expensive approach, as well – the device used in this study typically costs between $35,000 and $40,000.

But even just this demonstration could help push our general understanding of depression forward. The team was able to identify circuitry in the brain involved in at least one person's depressive symptoms, and that circuitry could be shared by other patients. Having foundational information about depression circuits could help develop non-surgical strategies that target similar areas. "Having this information and knowledge we think is going to go far beyond this application," Chang said.

Sarah thinks her success could also help cut through some of the stigma around depression. Going through the study helped

Sarah reframe her relationship with the disease, she said. For her whole life, she said she'd internalized some of the idea that she should be able to feel better if she picked herself up and tried hard enough. "We tried every treatment possible, and I had such a positive attitude through all of it, and none of it worked. And it just reinforced the depression, and made me feel like I was the world's worst patient, and that was my own personal moral failing," she said.

The trial changed that and helped the constant refrain from her doctors — that her depression was a disease in her brain — fully sink in. "By the end of this I went, 'Oh my god, this is no different than someone with Parkinson's,'" Sarah said.

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