

## Magnetic Relief For Depression?

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Steve Newman had suffered from major depression from the time he was 13. He tried innumerable treatments: psychotherapy and medications. Approaching 60, single by necessity and friendless by choice, he decided his train had only two stops left before suicide.

One option was shock therapy, formally known as electroconvulsive therapy, or ECT. The controversial technique has been shown to be effective in treating depression, but it involves inducing seizures in patients. Memory loss is a common side effect. Newman was not looking forward to it.

Newman was working in Florida as an insurance agent when he heard about the other option. It sounded like science fiction, or just kooky: Scientists in this country and overseas were experimenting with the use of high-power magnets to cure depression, using a technique known as transcranial magnetic stimulation, or TMS.



"I would have jumped into a volcano to get better; my life was just unbearable," Newman said. "I was at the point in my life where I did not have a lot of choice. I decided I would try TMS and then ECT, and if neither of them worked, I was going to consider suicide."

Newman gave up his job in Florida and in 2005 moved to Philadelphia, where he signed up for the magnetic therapy trial at the [University of Pennsylvania](#). Weeks after the treatments began, Newman said, he woke up one morning and found that his depression had vanished.

"It was like a light switch went on and I had my life back," said Newman, who now lives in Northwest Washington and works at the [National Institutes of Health](#).

In October, the [Food and Drug Administration](#) approved the magnetic therapy as a treatment for major depression. Many scientists believe that the technique is a harbinger of things to come. Already, researchers are probing its effects on schizophrenia, post-traumatic stress disorder and bipolar disorder, or manic depression.

The basic principle behind the treatment is less kooky than it sounds and comes not from psychiatry but physics -- specifically, the 19th-century discovery of the principle of electromagnetism. British physicist Michael Faraday and others found that when a magnet was suspended around a wire carrying an electric current, the magnet tended to rotate. Conversely, when a magnetic field moves around a coil, an electric current is induced in the wire. The principle of electromagnetism suggests that electricity and magnetism are linked phenomena.

TMS uses the principle of electromagnetism to induce small electric currents inside the brain. Patients such as Newman are seated in what looks like a dentist's chair and have a magnetic coil placed near the left side of their foreheads. A powerful, fluctuating magnetic field is then started.

Since neurons, or nerve cells, are electrochemical agents (they transmit bursts of energy in systematic patterns using chemical signaling), the magnetic field stimulates them. This, in turn, alters blood flow and metabolic activity in the brain. In the trial Newman participated in, patients received about 3,000 rapid magnetic pulses in just under 40 minutes. Doctors aimed the magnetic field at patients' left prefrontal cortex (around the left temple), a brain area that has been implicated in depression. Patients sometimes reported a tingling in their scalp or slight pain.

"When you think of psychiatric illnesses and the brain, therapy has been dominated by the use of chemicals, but when you give an antidepressant, the pill alters the electrochemical properties of the cell," said Mark Demitrack, chief medical officer at Neuronetics Inc., the Malvern, Pa., company that has developed the recently approved magnetic therapy device, called NeuroStar. "This is the flip side of the same coin. It is just a different way of getting at the same end effect: to change, restore or alter the functioning of nerve cells."

No one really knows what is specifically happening in the brain to cause depression, and no one really knows why TMS, psychotherapy and other treatments work. Like a host of psychiatric medications that have been discovered through serendipity, the effect of powerful magnetic fields on mood was discovered by chance. Doctors don't like this analogy, but a lot of psychiatric treatments for depression are somewhat akin to banging the side of a blurry TV; even if you don't know why it helps, it sometimes clears up the signal.

### **'It Makes You Jump'**

Newman's case is striking, but that does not mean it is representative. Indeed, many scientists think the jury is still out on the utility of TMS for depression.

The FDA wrestled with the approval of the magnetic device for years. In early 2007, an advisory committee said it was unimpressed with the results of the trial that Newman participated in. (Newman himself testified before the committee.)

The concern was not about safety -- it seemed clear that TMS was much safer than medication and ECT -- but whether it was really effective. Only about one in six patients who received the treatment were cured over six weeks. So were one in 20 patients who got sham treatment: the sound effects and drama of the magnetic therapy without the actual magnetic fields. The chairman of the FDA advisory committee, Thomas Brott, a [Mayo Clinic](#) neurologist in Florida, openly said that a reasonable person could question whether the study had found any benefit at all. Brott declined a request for an interview for this article.

"They certainly had questions about the magnitude of the effect," said Wayne Goodman, director of the Division for Adult Translational Research at the [National Institute of Mental Health](#), the federal institution charged with setting the nation's agenda on mental health treatment. Goodman listened to the entire deliberations of the advisory committee as a member of the audience. "The committee was not persuaded [that Neuronetics, which sponsored the trial Newman participated in,] had made the case."

"What has happened since then to change the mind of the FDA?" Goodman asked. "Why did they now decide to clear it?"

The FDA declined to make officials available for an interview. But in an e-mail, spokesman Scott McFarland said the agency had determined that the treatment seemed especially effective for a subset of patients.

Demitrack, at Neuronetics, said the FDA had told his company that the trial, which involved 301 patients at 23 sites, had shown a "signal" of efficacy and that the agency had asked the company to determine whether there were some patients for whom the magnetic therapy seemed especially effective. Patients who had unsuccessfully tried one antidepressant (as opposed to a large number of prior treatments) seemed most likely to respond to TMS. The FDA approval last month recommends the magnetic therapy for patients who have failed one round of prior treatment.

Demitrack also argued that there is a difference between results in clinical therapy, where both doctors and patients know that patients are getting actual treatment and not sham therapy, and in a clinical trial, where they do not.

Among patients who stayed on the therapy after the main study ended, Demitrack said, nearly one in three were cured after six weeks -- a measure, he said, of what patients might expect in real-world settings.

One such patient was Garrett Aguilar, 57, of Berwyn, Pa. (She and Newman were made available by a public relations firm representing Neuronetics.) Aguilar had also tried many treatments before signing up for the trial. But the TMS sessions did not seem to help her. After six weeks in the study, she said, she felt worse than she had at the start.

"I cried and cried," she said. "I would wander around and look at everything that needed to be done and say I was not capable of doing anything."

But at the end of the six-week period, Aguilar was told she had been in the group receiving the sham therapy. As was the case with all patients getting the sham treatment, she was offered a course of the real therapy. Four weeks into it, she said, she started to feel better.

"Within two months, I was feeling so excited about life again," she said.

John O'Reardon, an associate professor of psychiatry who headed the Penn trial and treated Newman and Aguilar, argued, like Demitrack, that the results of the study were not equivocal: "The fact you are giving people a novel treatment gives them a lot of hope, and hope itself is an antidepressant," he said. "It would make a lot of sense to do a course of talk therapy or a course of generic antidepressants, but if that does not work, you need to look for alternatives."

"You are not getting memory problems like you get with ECT, and you are not getting weight gain or sexual side effects like you may get with medications," O'Reardon said. The dropout rate in the study was very low, which suggests the side effects of the therapy are minimal.

Aguilar said the treatment caused a tapping feeling on her head that was uncomfortable but something she got used to: "You jump a little before you start and then it goes dit-dit-dit-dit-dit-dit-dit-dit," she said. "It does not really hurt, but it makes you jump."

O'Reardon said that some of the discomfort arose because the magnetic field was setting off electrical currents in the scalp, causing the muscles to tighten.

### **Not a Panacea**

Philip Janicak, a professor of psychiatry at Rush University in Chicago, who helped conduct the study, said the therapy added to physicians' armamentarium in treating depression.

"It is estimated 14 million patients will experience major depression annually," he said. "Half will be diagnosed, and only half of those will benefit from treatment. We clearly need other approaches to treat depression and need to improve safety and tolerability."

"Is it the new standard of treatment for depression that will replace all other treatments and resolve all the problems we have with depression? No, it is not," Janicak added. "We don't have a treatment like that yet."

With insurance unlikely to cover transcranial magnetic stimulation therapy right away, Janicak said a course of TMS treatment might run a patient \$6,000 to \$8,000.

Goodman, at the National Institute of Mental Health, said that in principle at least, magnetic therapy was appealing in that it appeared to have few side effects and could be highly targeted toward the brain, unlike a drug. The federal government is sponsoring a study into the therapy; this would provide independent and noncommercial data that Goodman said are essential for doctors making judgments about the utility and effectiveness of the procedure.

"It's attractive in that it is a relatively noninvasive and well-tolerated procedure," he said. "We have more to learn about the actual mechanism of action, which may tell us more about the underlying biology of depression. In addition to being a treatment, it may turn out to be a tool to understand depression."