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Patients Seek Off-Label Depression Therapy

Magnetic Stimulation Shows Promise in Intractable Cases; Heading to Canada for Help

By **ELENA CHERNEY**
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Pediatrician Laura Schulman suffered from depression so severe that it forced her to stop practicing medicine five years ago. A string of drug cocktails over the years failed to help. Then she read about an experimental treatment called repetitive transcranial magnetic stimulation.

The treatment hadn't been approved for depression, but a clinic in Canada was offering it to U.S. residents, and would even help arrange travel and lodging. So last summer, the Seattle resident dipped into her savings and headed north to a MindCare Centers clinic in Vancouver, British Columbia, where three to four weeks of treatment costs nearly \$7,000.




Ron Wurzer/Getty Images
 Laura Schulman of Seattle went to Canada to get an experimental treatment for depression.

After a few sessions of rTMS, which delivers electromagnetic pulses to the brain via a magnetic coil held against the skull, Dr. Schulman says she felt her depression lifting. As she made her way around Vancouver she started finding it easier to manage everyday tasks that had once felt so burdensome -- such as buying a bottle of water at a corner store. "It was like putting on glasses for the first time if you've been myopic all your life," she says.

Dr. Schulman is one of many desperate patients leaving the U.S. to obtain rTMS after failing numerous antidepressant medications. And while some doctors are cautioning patients to wait for the Food and Drug Administration to weigh in, scores of other patients have traveled to U.S. clinics that offer the treatment on an "off label" basis. The technique is approved in the U.S. only for brain research, but doctors can use it to treat depression, just as other drugs and therapies can be used in applications other than those for which they are approved. In Canada, the rTMS device has limited federal approval for safety, but provincial health-insurance plans won't cover it, citing lack of evidence on its efficacy.

The therapy is showing promise in studies. In the first big multisite trial of rTMS, the method was shown to benefit about 42% of patients with treatment-resistant depression -- or severe depression that doesn't improve with medication. And side effects were considered mild, mostly consisting of headache. The 300-patient study, released last month, was sponsored by Neuronetics Inc., which

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is seeking Food and Drug Administration approval for use of its rTMS device in treating depression. A spokeswoman for the FDA declined to comment on the review process.

Many psychiatry experts say rTMS is likely to be approved soon in the U.S. But some doctors note that for now, the clinics in both Canada and the U.S. are operating without direct regulatory authority, and may not be following the same protocols in screening patients that researchers use in their clinical trials. So some patients who aren't appropriate candidates may be paying for pointless treatment, these doctors say, and failing to pursue the treatment that they do need. Since rTMS isn't covered by insurance, patients typically pay thousands of dollars out of pocket.

"The results are very promising, but standards need to be in place" before patients seek treatment, says Sarah H. Lisanby, a lead investigator on the Neuronetics study and a psychiatrist at the Brain Stimulation and Neuromodulation division of the New York State Psychiatric Institute.

Treating stubborn depression remains one of psychiatry's most puzzling problems. About 14 million people in the U.S. suffer from depression, and some 70% don't fully respond to the first antidepressant drug they try. At least one-third of patients still have symptoms after adding a second drug or switching to another medicine, according to recent studies by the National Institutes of Health. "These are people who've lived their lives in misery or have tried many medications," says Mark George, a psychiatrist at the Medical University of South Carolina, who is an investigator on the Neuronetics trial and has consulted for the MindCare clinics.

Nondrug Treatments

Only two nondrug treatments have been approved by the FDA for depression. Electroconvulsive therapy, or ECT, is considered the gold standard in hard-to-treat cases, based on its efficacy. But because it works by causing a seizure, it must be performed in a hospital. And it can have serious side effects, including memory loss and cognitive problems. Dr. Schulman of Seattle, for instance, said she didn't want to try ECT because of the risk of side effects.

Vagus nerve stimulation, approved last year, involves surgery to implant a device in the neck, but is only approved as an add-on to medication for chronic or recurrent depression.

In rTMS a strong magnetic field is directed through a coil held against the head for a series of sessions that last less than an hour each. The magnetic force stimulates a part of the brain believed to play a role in depression. The treatment doesn't require anesthesia and produces few side effects, though it doesn't work for as many people, or as effectively, as ECT.

The treatment does carry a small risk of seizure, and the American Psychiatric Association guidelines for research state that rTMS should be supervised by a licensed doctor. In research trials, patients are screened to make sure they don't have medical conditions that could put them at risk for having a seizure. Patients in the studies are also screened by a psychiatrist to make sure that they in fact are suffering from depression.

Atlanta psychiatrist Mark Hutto has treated about 100 patients with rTMS at his clinic, North Atlanta Psychiatric Associates, since 2001. Dr. Hutto says he has patients sign a consent form that explains that the treatment isn't FDA-approved for depression. He says he also requires patients to undergo physical and psychiatric exams to determine whether they are good candidates.

Dr. Hutto, who says he has trained a technician to do the treatment but is in the building when it's

done, wasn't able to get malpractice insurance for doing rTMS because it isn't approved for depression. But "I think it's a very safe procedure," says Dr. Hutto, who uses a Neuronetics device. "I'm not worried about it."

Dr. Hutto says he charges \$75 to \$150 per session, depending on a patient's income, since the treatment isn't covered by insurance. Most patients get 15 to 25 sessions, so their cost is about \$1,125 to \$3,750, he says. A course of ECT, which is covered by most insurers, can cost more than \$12,000, he says.

At the two MindCare clinics in Vancouver and Toronto, almost 400 people have been treated for depression since 2001, about half of whom traveled up from the U.S., says Chief Executive Officer Iain Glass. They charge \$4,500 to \$6,750 for a three-to-four-week course of treatment and cater to an international clientele by helping to arrange hotel accommodations for patients.

Mr. Glass has approval from the Canadian government to sell the device, which has been deemed safe for use. But while there is no rule that says the device cannot be used, neither is there an official sanction of its use in depression by provincial authorities. An Ontario government panel considered the evidence in 2004 and ruled there weren't yet enough data to warrant the government health system paying for the procedure. Mr. Glass says his technique is very similar to the one used in the Neuronetics study, but he uses a device made by a unit of **Medtronic Inc.**, Minneapolis.

The British Columbia College of Physicians and Surgeons, which licenses doctors in the province, says the device doesn't pose a risk of "direct harm" to patients, according to college registrar Morris Van Andel.

At the Toronto MindCare clinic, which occupies an examining room in a suburban walk-in clinic, treatment is administered by a technician who is trained as a surgeon in his native Ukraine, Mr. Glass says. He says a family doctor from the walk-in clinic supervises and assesses patients before treatment. The Vancouver clinic has a staff psychiatrist who does the exams, but that doctor isn't always in the room when patients are treated, Mr. Glass says.

Response Rates

The method won't help all patients with treatment-resistant depression. The randomized, controlled Neuronetics trial involved patients at 22 sites who had failed to respond to at least one drug during their current depressive episode, and had been depressed for at least six months. In the first phase of the study, only 25% of patients who received treatment showed a response. But that response rate was more than double the response of the patients in the placebo group, who received a sham treatment.

When the sham patients were offered active treatment, and more sessions were given to patients who hadn't improved on the active treatment, response rates rose to between 42% and 43%. "This is not a cure," says study investigator Dr. Lisanby. "It's not going to be for everyone. It did help a significant percentage of patients."

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