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MAKING WAVES

Richard Holbert, MD, demonstrates use of the transcranial magnetic stimulation device on a mock patient.

PROVIDING RELIEF FROM DEPRESSION

Magnetic Stimulation

WRITTEN BY MICHELLE CERULLI MCADAMS | PHOTOGRAPHY COURTESY OF UF PSYCHIATRY

Clinically diagnosed (major) depression affects roughly 15 million adults in the U.S. per year, according to the Anxiety and Depression Association of America.

The debilitating disease — which is characterized by persistent sadness, a loss of interest in regular activities, trouble sleeping and lack of energy, among other symptoms — takes a toll not only on the individuals experiencing it but also on their families and friends and costs the U.S. $210 billion each year.

Depression is a difficult disease to treat, and many patients must try a number or combination of different medications, such as antidepressants, before they experience relief. Even still, not everyone suffering from the serious mood disorder responds to medication.

That's where a pioneering therapy called transcranial magnetic stimulation (TMS) comes in. The noninvasive treatment stimulates a part of the brain that is under-functioning in people with depression and has

Richard Holbert, MD, director of TMS in UF's Department of Psychiatry, has treated about 100 patients with the therapy since UF first started providing it in 2009.

been shown to be effective for many patients who don't respond to antidepressants or psychotherapy.

"The ideal person is an individual who has failed to have a response from antidepressant medications," said Richard Holbert, M.D., director of TMS in UF's Department of Psychiatry. "You may have someone age 40 to 50 who is depressed, not sleeping well, has very poor energy and is not able to enjoy things in life or may be having thoughts of not wanting to live, and he or she hasn't responded to Prozac. That is an ideal patient. Or a person 50 to 60 or 25 to 35 with similar symptoms; they would also be very good candidates."

During TMS therapy, an insulated electromagnetic coil is placed on a person's scalp above the left dorsolateral prefrontal cortex — the part of the brain that is under-functioning — and an electric current is transmitted through the coil. The current produces a pulsating magnetic field that penetrates the scalp and tissue and stimulates neurons in the brain.

Patients typically don't feel anything during the outpatient treatment, though some experience discomfort during the first few sessions, Holbert said. A typical TMS treatment plan is five days per week for four to six weeks, with each treatment taking fewer than 40 minutes.

"The unique and innovative thing about TMS is that it's a treatment that can change brain function noninvasively," Holbert said. This means that the treatment doesn't require any kind of incision or operation.

From trials to treatment

TMS was developed in 1985 by the English medical physicist Anthony Barker, Ph.D., and his colleagues. The team created a small machine that could produce a spasm or twitch in a specific part of study participants' hands by applying TMS to the area of the brain that controlled the movement of that hand muscle. The groundbreaking discovery? TMS could pinpoint and stimulate a specific area of the brain without producing pain in participants, who were awake during the experiment.

After years of studies seeking to prove the effectiveness of TMS as a clinical therapy, the Food and Drug Administration (FDA)

cleared TMS as treatment for major depression in 2008.

There are multiple research studies going on around the country to assess TMS's effectiveness in other conditions, said Holbert, who first learned about TMS during the latter part of his residency at UF in the mid- to late-1990s.

In UF's Department of Psychiatry, researchers are investigating TMS as a treatment for obsessive-compulsive disorder (OCD) and insomnia, as well as for smoking cessation. The department is also running a research study assessing its effectiveness in people age 13 to 21 since the FDA only cleared TMS for people age 22 and older.

As an example of the power and precision of TMS, Holbert said that putting the electromagnetic coil over the area of the brain that controls speech and giving low-frequency TMS — which inhibits neurons instead of stimulating them like high-frequency TMS — will prevent a person from forming words.

"Once you take it off, you're completely fine and able to form words again," he said. "It's incredible."

But how does it work?

UF Psychiatry first began providing TMS therapy in July 2009. Since then, Holbert has treated more than 100 patients with the therapy.

During the initial TMS treatment session, a patient sits down in a chair in an exam room, where a psychiatrist determines the correct location for coil placement and the right intensity.

The left side of the motor cortex of the brain controls movement on the right side, and vice versa, so to determine the location of the coil, the clinician searches the left part of the motor cortex for the area that makes the person's right thumb twitch, Holbert said.

"That gives us a landmark," he said. "The treatment location is — depending on the [TMS] machine you use — either 5.5 or 6 centimeters in front of that. Studies have shown that that is where the left dorsolateral prefrontal cortex is, and that area is not functioning the way it should."

The electromagnetic coil is then placed on that precise spot on the person's head, and the treatment begins. The patient remains awake; no sedatives or anesthesia is needed, and he or she is able to get up, drive home and go about his or her day after the therapy is over.

At UF, patients complete a depression rating scale with their psychiatrist once per week to monitor their progression. A TMS technician typically provides the therapy after the initial session, along with supportive counseling to patients. The team encourages patients to be active; walking is shown to be especially helpful for depression, Holbert said.

"I've had patients have resolution [of their symptoms] in as little as six treatments," Holbert said, while cautioning that timing and results are highly variable from patient to patient.

Since depression is often a recurring illness, TMS typically does not cure a person of depression, but rather, manages his

or her symptoms over time. It is not uncommon for people to receive additional TMS treatments later. Some insurance companies cover the treatment while others do not.

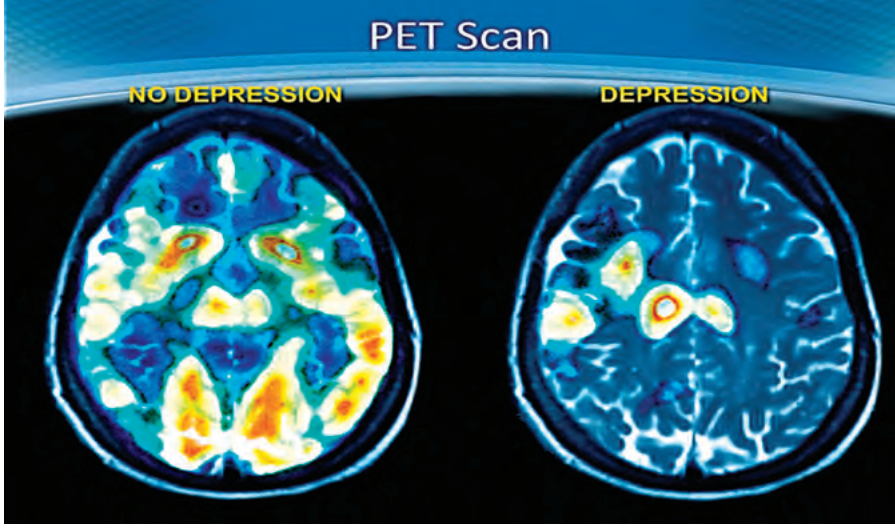
"Most people require 20 to 30 treatments, and patients often start being able to sense positive change in 10 to 15 treatments," Holbert said. "I've also had patients who have had no benefit at all for the first 25 treatments, and then all of a sudden, they see improvement."

According to the International Neuromodulation Society, "in open-label clinical trials, after four to six weeks of treatment, one out of two patients treated with TMS for depression experienced a reduction in symptoms of 50 percent or more, and one out of three experienced remission."

Holbert said that if no benefit or improvement is seen after 30 treatments, TMS is not considered effective for the patient and is not continued. There are some patients who don't respond to the treatment at all.

Though many patients experience no side effects, some people feel discomfort at the site of the electromagnetic coil.

"Sometimes for the first couple treatments, patients say it feels like a woodpecker is pecking at their head," Holbert said. "In eight years of doing this, I've had two people who couldn't tolerate the treatment, but for most people, discomfort resolves in two to three treatments, if they have discomfort" at all.



The brain scan shows that patients with depression (scan at right) have decreased activity in certain parts of their brain.

There is also a risk of headache, as well as eye twitching during the treatment and for certain patients there is a very low risk of seizure.

"I see TMS growing significantly to other psychiatric illnesses," Holbert said. "There is a very good chance we will see it FDA-approved for OCD and smoking cessation, and a good chance it will be utilized for those who have substance-use disorders. It may even be utilized for schizophrenia ... We're very, very early with TMS." **OT**