

Neuromodulation for Treating Depression

ELECTRICAL AND MAGNETIC STIMULATION OFFER NEW WAYS TO TREAT DEPRESSION

SANDEEP RAVINDRAN

I

magine feeling constantly tired and sad, being unable to concentrate, and losing interest in activities you previously enjoyed. These are just some of the symptoms of depression, a disorder that affects about 15 million people in the United States at any one time.

Left untreated, depression can have severe consequences, affecting work and personal relationships, and potentially contributing to suicide. Although antidepressant medication and psychotherapy can be effective at treating depression, up to a third of patients fail to respond even after multiple courses of medication.

There is hope for patients with treatment-resistant depression, in the form of neuromodulation, which uses electrical or magnetic stimulation to modify brain circuitry. "Neurons use electricity to communicate, and we can modulate that without the use of medication," said Veronica Slootsky, M.D., RESD '15, assistant professor of psychiatry and behavioral sciences at the George Washington University School of Medicine and Health Sciences (SMHS).

Some of these neuromodulatory therapies have been used for decades; others are still experimental. With current advances in neuromodulation, these treatments provide useful alternatives for patients for whom antidepressants and psychotherapy aren't sufficient. "It's nice to have another tool in our toolbox," Slootsky said.

Neuromodulation Has Come a Long Way

Neuromodulation encompasses a wide range of techniques. Although all of them use either electrical or magnetic stimulation to affect the brain, the precise mechanism by which they work is still not completely understood. There are several hypotheses for how the stimulation works: It may alter levels of signaling molecules in the brain, or cause the release of certain hormones, or increase levels of growth factors that promote the growth and survival of neurons.

Regardless of the specifics, some of these therapies affect the whole brain, whereas others are used to target particular regions. "The reason that we choose these different regions is that prior studies using functional MRI have determined that those regions are implicated in certain disorders, such as depression," said Slootsky.

Probably the best-known neuromodulation technique is electroconvulsive therapy (ECT), which has been used to treat psychiatric illnesses since 1938. ECT uses electric currents passed through the brain to trigger a brief seizure, and can quickly reverse symptoms of some mental illnesses.

Current ECT treatments use low doses of electricity in conjunction with modern anesthesia and muscle relaxants, reducing the risk of side effects such as memory loss or confusion. "In general, it's a very safe treatment, and for many patients it can be lifesaving," said Slootsky.

Despite being one of the most effective and safe treatments for severe mental illnesses, ECT still has negative associations due to its early incarnations, which used high doses of electricity and were administered without anesthesia. "This is a great, great method,

"Neurons use electricity to communicate, and we can modulate that without the use of medication."

VERONICA SLOOTSKY, M.D.

FEELING BLUE

Depression is a disorder that affects about 15 million people in the United States at any one time.

which unfortunately suffers from a lot of stigma, so it's really underutilized," Slootsky said.

ECT is very useful for treating patients with severe depression, especially those who have failed to respond to other treatments. "For patients with depression with psychotic seizures, it can be up to 95 percent effective, which is huge," said Slootsky. The therapy generally provides much quicker relief than medications, and is therefore helpful in patients who are at acute risk of suicide or are catatonic. "For some disorders it's really one of the best treatments we have, and it's often the only treatment."

Slootsky recalls an early experience witnessing the difference ECT can make on a severely depressed patient. Before the treatment the patient was "minimally interactive, was cognitively very slow and dull, and had a lot of the typical symptoms of very severe depression," she said. "After two weeks, she was like a different person when I saw her. She was joking around; she was smiling, interactive; she just looked much more animated, and it was a marked difference."

Different Ways to Stimulate Brain Circuitry

ECT is invaluable for treating severe depression, but those with mild depression can use two other neuromodulatory techniques that utilize much weaker electrical currents: transcranial direct current stimulation (TDCS) and transcranial alternating current stimulation (TACS). These therapies are cheaper, safer, and easier to administer than ECT. "These are things that people can probably do at home if they buy the unit with a doctor's prescription and direction," said Slootsky.

TDCS delivers very mild electrical currents through electrodes placed on the scalp, and can excite or reduce neuronal activity in specific brain regions. The technique is still experimental and has not yet been FDA-approved, but has shown promising results. TACS uses the same principle, but with alternating current instead of direct current, and is FDA-approved for treating depression.

Slootsky is preparing a study to test the effectiveness of a TACS technology called Alpha-Stim on women with postpartum depression. The condition is "extremely common, and some women don't want to take medication," said Slootsky. The Alpha-Stim technology consists of cellphone-sized units with electrodes attached. "They can actually take these units home, and the electrodes are clipped to their earlobe," she said. "This could be a great method for patients who have postpartum depression and would like some treatment."

Not all neuromodulation techniques are quite as easy to use; some require a pacemaker-like device to be surgically implanted in patients. One such technique is called vagal nerve stimulation (VNS), and it uses the implanted pacemaker to deliver electrical signals to the vagus nerve. VNS has been shown to improve mood, and the method is FDA-approved for treating chronic depression.

Another technique, called deep brain stimulation, uses the pacemaker-like device to deliver a current to electrodes

implanted in specific brain regions, to control excessive or abnormal electrical activity. This method has been used successfully in patients for whom multiple attempts at treatment have failed. However, the technique is not yet FDA-approved.

Some neuromodulation techniques use magnets rather than electrodes. One of them, transcranial magnetic stimulation (TMS), uses a large electromagnetic coil placed against the scalp to generate an electric field and stimulate brain cells. TMS is able to target certain brain structures and improve the symptoms of depression.

"TMS is currently FDA-approved for people who have failed their medication for depression," said Slootsky. Unlike ECT, TMS requires no anesthesia and has no cognitive side effects, but it is also not as effective for people who have found multiple antidepressant treatments unsuccessful, she said. "It's being [thoroughly] researched right now to see if we can make it more effective for those kinds of patients."

For treating severe depression, another technique, called magnetic seizure therapy, has emerged over the last decade and a half. Magnetic seizure therapy is similar to ECT, but uses strong magnetic fields instead of electricity to induce electrical currents in the brain. It is still experimental, but appears to have the same benefits as ECT, with fewer side effects.

A Bright Future

As noted, several of these neuromodulatory therapies are currently FDA-approved for treating different types of depression, and others are still experimental but appear very promising. SMHS is currently working on getting new ECT and TMS machines, and Slootsky hopes to begin her Alpha-Stim research study in the near future. Physicians will soon have a variety of neuromodulation tools at their disposal, and more research will help them understand how best to administer these therapies, Slootsky said. Further studies will also help uncover the mechanisms behind neuromodulation.

Slootsky wants to use neuromodulation in conjunction with other treatments to help patients with treatment-resistant depression. "We're constantly improving psychotherapy and medication management techniques as well, and I think that we have to use a multimodal approach, and we're refining everything," said Slootsky. "So I think that the future looks pretty bright."

"Electroconvulsive therapy is a very safe treatment, and for many patients it can be lifesaving."

VERONICA SLOOTSKY, M.D.