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HEALTH

New Electrical Brain Stimulation Technique Shows Promise in Mice

By PAM BELLUCK JUNE 1, 2017

Pulses of electricity delivered to the brain can help patients with Parkinson's disease, depression, obsessive-compulsive disorder and possibly other conditions. But the available methods all have shortcomings: They either involve the risks of surgery, from implanting electrodes deep within the brain, or they stimulate from the skull's surface, limiting the ability to target electricity to the right brain areas.

Now, a team of neuroscientists and engineers has devised a method that might achieve the best of both worlds: skipping the surgery while reaching deep brain areas. The research, published Thursday in the journal Cell and led by a prominent neurobiologist at the Massachusetts Institute of Technology, was conducted in mice, and many questions remain about its potential application to people. But experts say if the method proves effective and safe, it could help a range of neurological and psychiatric disorders more cheaply and safely than current approaches.

"They have this clever new way to deliver current to a spot of interest deep in the brain and do it without invading the brain," said Dr. Helen Mayberg, a professor of psychiatry, neurology and radiology at Emory University, who was not involved in the study and who pioneered the still-experimental treatment of deep brain stimulation for depression. "If you didn't have to actually open up somebody's brain and put something in it, if it could do what we're doing now just as well — sign me up."

Edward S. Boyden, the study's senior author and co-director of the M.I.T. Center for Neurobiological Engineering, said he and his colleagues are already testing the method on people without disorders to see if it works in human brains. If those results are promising, at least one clinician, Dr. Alexander Rotenberg, a neurologist who directs the neuromodulation program at Boston Children's Hospital and Harvard Medical School, said he would collaborate with the team to evaluate the technique for epilepsy.

"This is something that many of us in the field have wished for for a long time," said Dr. Rotenberg, who said it might also eventually help tens of thousands of epilepsy patients for whom medications fail. Dr. Rotenberg and Dr. Mayberg said they could also envision the technique as a diagnostic tool to pinpoint the best brain location to target for electrical stimulation before surgically implanting electrodes for deep brain stimulation.

At a time when scientists are developing sophisticated technological approaches to look inside the brain and manipulate brain cells — including a celebrated technique called optogenetics that was created in part by Dr. Boyden — the new study uses a basic and long-established tool: electricity. But it adds a brand new twist.

"Rather than try to prove another way to modulate the brain, they take a very simple technology and are using it in a unique way," said Dr. Casey Harrison Halpern, an assistant professor of neurosurgery at Stanford University who uses deep brain stimulation for Parkinson's and O.C.D. and was not involved in the study. "Now we just have to see where it plays out best in the clinical arena. I could rattle off 10 potential ways that it could and should be tested."

The method, called temporal interference, involves beaming different electric frequencies, too high for neurons to respond to, from electrodes on the skull's surface. The team found that where the currents intersected inside the brain, the frequencies interfered with each other, essentially canceling out all but the difference between them and leaving a low-frequency current that neurons in that location responded to, Dr. Boyden said.

"Very high frequency electronic fields are much faster than the brain can actually follow for the same reasons that you and I can't hear sonar," he said. "But if you deliver 1,000 hertz and 1,001 hertz to the brain, the neuron will react as if you were delivering 1 hertz. And only the region where the two interfere is where you get the signal."

That means other regions would be unaffected by the electricity, in contrast to what happens with other surface techniques, like transcranial magnetic stimulation, a federally approved treatment for depression.

When the team used electricity to stimulate the hippocampus in mice, "there's no evidence whatsoever that the neurons were activated," in the cortex and other structures closer to the surface, said Li-Huei Tsai, director of M.I.T.'s Picower Institute for Learning and Memory, who led the mouse experiments.

"Before you see the results, you're like 'really?' " she said. "But we saw the extremely precise localized signal only in the region we stimulated."

To further test whether they could target the electricity, the researchers aimed at certain spots in the motor cortex causing mice to move forepaws, whiskers or ears. The technique caused no safety problems, Dr. Tsai said.

Several experts raised potential limitations and questions. Dr. Mayberg said it would have to deliver frequencies like 130 hertz, higher than those in the study, and would need to work among complex brain circuitry, like the white matter bundles her work involves.

Dr. Michael Okun, a neurologist at the University of Florida and medical director for the Parkinson's Foundation, said delivering electricity to people who need it occasionally or even once a day seemed more feasible than for people with "complex diseases like Parkinson's who have a need for near-continuous stimulation."

All the experts wondered about logistics: Would patients use a portable, wearable electricity-delivery device? And they emphasized a need to direct electricity to smaller, more precise brain locations, a limitation Dr. Boyden said he hoped could be addressed by using more electrodes.

"We've got to avoid areas of the brain that might cause motor contractions or weakness or problems with speech or vision," Dr. Okun said. "A couple of millimeters in brain space could be the distance between Florida and Australia."

Still, he said, so far "they've accomplished something that's fairly remarkable."

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