

# Brain Pacemakers Could Zap Psychiatric Diseases

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Called brain pacemakers, these tiny implants hold promise for fighting tough psychiatric diseases — if scientists can figure out just where in all that gray matter to put them. Deep brain stimulation, or DBS, has proved a powerful way to block the tremors of Parkinson's disease, but blocking mental illness isn't nearly as easy a task. However, a push is on to expand research into how well these brain stimulators tackle the most severe cases of depression, obsessive-compulsive disorder and Tourette's syndrome.

"It's not a light switch," cautions Dr. Michael Okun of the University of Florida. Unlike with tremor patients, the psychiatric patients who respond to DBS tend to improve gradually, sometimes to their frustration. And just because the tics of Tourette's fade or depression lightens, it doesn't mean patients can abandon traditional therapy. They also need help learning to function as much as recipients of hip replacements undergo physical therapy, says Dr. Helen Mayberg of Emory University.

"Once your brain is returned to you, now you have to learn to use it," she told the annual meeting of the American Association for the Advancement of Science. Roughly 70,000 people around the world have undergone deep brain stimulation for Parkinson's or other movement disorders when standard medications fail, says Okun, among leading researchers who gathered at that meeting last week to assess the field.

How does it work? Surgeons implant a wire deep in the brain. Tiny electrical jolts — running from a pacemaker-like generator near the collarbone up the neck to that electrode — disable overactive nerve cells to curb the shaking. Scientists figured out which spot to target based on surgery that sometimes helps worst-case Parkinson's patients by destroying patches of brain tissue. But with deep brain stimulation, the electrodes don't destroy that tissue. The electrical signals can be adjusted or even turned off if they don't help, or if they cause neurological side effects. (The surgery, however, does sometimes cause dangerous brain bleeding or infections.)

Psychiatric illnesses require a similar operation, but surgeons must implant the electrode into a different spot in the brain. There's the rub: It's not clear which spot is best for which psychiatric disease. In fact, two manufacturers — Medtronic and St. Jude Medical — have begun major studies of DBS' effects on depression. Each places the implant in a different region, based on promising pilot studies.

The Food and Drug Administration approved Medtronic's version in 2009 for a small group of obsessive-compulsive patients who get no relief from today's treatments,

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under a special program that lets devices for rare conditions sell before there's final proof that they work. Dr. Joseph Fins, medical ethics chief at New York Presbyterian Hospital, worries that may hurt efforts to get such proof. The more available the electrodes are, the more people may seek to try the \$30,000 surgeries without enrolling in strict trials.

How good is the evidence so far? The researchers are pushing for a registry to track DBS recipients to better tell, but overall they're cautiously optimistic. Just over 60 people with intractable obsessive-compulsive disorder have undergone DBS since 2000, says Dr. Benjamin Greenberg, a Brown University psychiatrist who is heading a major study funded by the National Institute of Mental Health. About three-fourths of the first few dozen patients studied significantly improved.

"You still have a burden, but you have a life," is how he describes the improvement. These are people who try to relieve fears or anxiety with obsessive behavior, such as washing their hands or checking locks repeatedly — many of whom never got out of the house because their daily rituals consumed so much time, Greenberg says. They'd failed behavior therapy designed to teach that whatever they fear doesn't happen if they skip the ritual.

But with the brain pacemaker, somehow that behavior therapy starts working, Greenberg says — maybe by enabling their brains to better remember the lessons. One big hurdle: The battery, tucked near the collarbone, tends to last less than two years. Changing it entails outpatient surgery, one reason that about one-third of studied patients stop getting zapped. So Greenberg just began testing a newer version that patients can recharge every few days.

Results on about 100 DBS patients with severe depression have been published so far, and roughly half improve regardless of which of the two targeted brain regions is zapped, says Emory's Mayberg, who shares a patent licensed to St. Jude. Separately, she's now studying what the successfully treated brains have in common that might help predict the best candidates, hoping to ease "a tremendous burden on the patients" as they decide whether to try these experiments.

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