Brain stimulation shows promise in treating severe depression

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For years, electrodes implanted in the brain have helped people control the tremors of Parkinson’s disease. A new study has found encouraging results against severe depression. – Benedict Carey

For more than a decade, doctors have been using brain-stimulating implants to treat severe depression in people who do not benefit from medication, talk therapy or electroshock sessions. The treatment is controversial — any psychosurgery is, given its checkered history — and the results have been mixed. Two major trials testing stimulating implant for depression were halted because of disappointing results, and the approach is not approved by federal health regulators.

Now, a team of psychiatric researchers has published the first long-term results, reporting Friday on patients who had stimulating electrodes implanted as long ago as eight years. The individuals have generally fared well, maintaining their initial improvements. The study, appearing in the American Journal of Psychiatry, was small, with just 28 subjects. Even still, experts said the findings were likely to extend interest in a field that has struggled.

“The most impressive thing here is the sustained response,” said Dr. Darin Dougherty, director of neurotherapeutics at Massachusetts General Hospital. “You do not see that for anything in this severe depression. The fact that they had this many people doing well for that long, that’s a big deal.”

The implant treatment is known as deep brain stimulation, or DBS, and doctors have performed it for decades to help people control the tremors of Parkinson’s disease. In treating depression, surgeons thread an electrode into an area of the brain that sits beneath the crown of the head and is known to be especially active in people with severe depression. Running electrical current into that region, known as Brodmann Area 25, effectively shuts down its activity, resulting in relief of depression symptoms in many patients. The electrode is connected to a battery that is embedded in the chest. The
procedure involves a single surgery; the implant provides continuous current from then on.

In the early and mid-2000s, Dr. Helen Mayberg, a neurologist then at the University of Toronto, discovered the importance of Area 25 and was involved in the first experimental trials of DBS treatments to target it, though her work isolating Area 25 extends well back into the 1990s.

In the new analysis, Mayberg, now at the Icahn School of Medicine at Mount Sinai in Manhattan, and Dr. Andrea Crowell of Emory University in Georgia led a consortium of researchers from several institutions who evaluated the mental health and history of 28 people who had received DBS for depression at Emory. About a third experienced full remission of symptoms in the months after surgery, and half reported measurable, noticeable reduction in their distress. They were doing just as well years later, the report found.

“The bottom line is that if you get better, you stay better,” Mayberg, a professor of neurology, neurosurgery, psychiatry and neuroscience, said. “You don’t lose the effects over time. You wear the device like a pacemaker, and you stay well.”

Of the 28 subjects, 14 completed at least eight years of follow-up appointments, and 11 completed at least four years. Three patients had the implant removed, although they had been doing well with it, the report found. Most of the patients were on antidepressant drugs when they had the surgery, and they continued on the medications.

The researchers found no adverse effects related to the performance of the device. Seven subjects had received a diagnosis of bipolar depression, a severe distress that alternates with periods of high-energy mania. There was concern that deep-brain stimulation might prompt manic episodes in those individuals. That did not happen, the authors reported.

The most common complications came from underlying mental disorders and the surgical procedure itself. Over the years of follow-up, there were five suicide attempts in three subjects — a lower-than-average rate for people with this kind of severe depression, although the numbers were too small to be conclusive. In addition, there were 19 adverse events during the surgical procedures, including failure of the device and infection. That rate is roughly typical of DBS surgery for movement disorders like Parkinson’s.
Several of the participants had surgery more than once, as the implant’s battery power faded over time, reducing the effect on mood. The technology has since improved and the devices are now rechargeable wirelessly, Mayberg said; the surgical techniques also have been refined in recent years. Mayberg retains a share of the intellectual property patent on the treatment approach.

The new report notwithstanding, gaining federal approval of deep-brain stimulation for depression will require time, money and commitment, as well as more evidence. In the mid-2010s, two device makers, Medtronic and St. Jude Medical, ran U.S. Food and Drug Administration-approved trials of DBS for depression. Both trials were halted early, within the first six months, because the results were underwhelming.

In a recent review of the evidence to date, which included case reports, small samples and the larger trials, a team led by Dr. Steve Kisely of the University of Queensland in Australia, concluded that “DBS may show promise for treatment-resistant depression but remains an experimental treatment until further data are available.”

Dougherty said, “The most important thing this report can do is encourage device manufacturers to retrial these interventions. We can think whatever we want; there’s no way we get FDA approval without good trials.”