Reflections on using Deep Brain Stimulation (DBS) to treat neuropsychiatric disorders

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Deep brain stimulation (DBS) has been used to treat diverse neuropsychiatric disorders, ranging from Parkinson's Disease to OCD. Credit: Saad Faruque

One of my most fascinating experiences as a doctoral student of neuroscience began with an early morning trip to the university hospital. Upon arrival, my laboratory colleagues and I met with one of the clinical neurologists, who introduced us to a patient suffering from advanced Parkinson's Disease. Medications were no longer working effectively, and the patient's motor symptoms were severe and debilitating. The day that we arrived, the patient was to have electrodes implanted deep into the brain circuitry that was misbehaving in his disease, the first step in a revolutionary therapeutic approach known as deep brain stimulation (DBS).

What is Deep Brain Stimulation?

DBS is an increasingly well-utilized therapeutic tool for many neurological diseases, predominantly movement disorders. With this therapy, high frequency electrical stimulation is chronically delivered to a target brain region, powered by a battery source implanted near the patient's clavicle. In Parkinson's Disease, the effects of DBS can be dramatic and immediate—resting tremors (shakiness at rest) dissolve, rigid muscles loosen, and many more benefits may be immediately observed. Although the mechanisms of action are poorly understood, DBS therapy works well when targeted to brain regions in which surgical lesions are also effective. This may suggest that DBS acts to provide a "functional lesion" in brain circuitry, with the added benefits of being reversible and modifiable. If the therapy doesn't work, or side effects are intolerable, clinicians can try to adjust the stimulation parameters, or as a last step, remove the electrodes.

Not Just for Movement Disorders

An early hint that DBS therapy would be useful in treating other types of brain disorders came in a small case report published in 2002 by Mallett

and colleagues, describing two patients that received DBS for Parkinson's Disease. In addition to their Parkinson's, these patients suffered from a neuropsychiatric disease termed Obsessive-Compulsive Disorder (OCD). OCD is characterized by recurring, unwanted obsessions and compulsions (e.g., excessive hand-washing, other ritualistic behaviors), symptoms that can be incredibly debilitating and prevent many sufferers from engaging in everyday tasks. Standard treatments for OCD include medication and psychotherapy, which generally work well together to treat disease symptoms. But in a substantial number of cases, these therapies are ineffective.

Mallet's patients were unable to alleviate their OCD symptoms through medication and psychotherapy, but after using DBS to treat their Parkinson's Disease, the stimulation came with an unexpected and much-desired side effect—alleviation of their OCD symptoms. According to one patient, the decrease in OCD symptoms was even more satisfying than the alleviation of Parkinson's symptoms.

Although psychosurgical approaches have a long and contentious history in neuropsychiatry, reports such as this one rekindled enthusiasm for surgical interventions in otherwise treatment-resistant psychiatric patients. Clinical trials for neuropsychiatric DBS therapy have exploded, with a large number of brain targets and diseases under investigation. In 2009, the Food and Drug Administration (FDA) approved the standard clinical use of DBS therapy in treatment-refractory OCD patients, under a Humanitarian Device Exemption Act.

Challenges and Opportunities for Neuropsychiatric DBS Therapy

The challenges associated with DBS therapy are not trivial, particularly for neuropsychiatric diseases. One of the major associated hurdles

concerns the identification of optimal therapeutic targets and stimulation parameters (e.g., voltage and frequency). When I shadowed a DBS electrode implantation surgery in a Parkinson's Disease patient, I noticed that he was kept awake (only lightly sedated) throughout the entire procedure. Although there are no pain receptors in brain, this was surely an uncomfortable experience. However, by being awake, he could provide feedback about how the DBS stimulation tests were working, guiding the final electrode placement deep in the brain. With optimal electrode positioning, the motor symptoms in a Parkinson's patient may be instantaneously alleviated by DBS. Similarly, stimulation parameters can be readily altered to optimize therapeutic efficacy. This level of clinical feedback cannot be so readily provided in DBS surgery for neuropsychiatric diseases, where symptom alleviation is observed on a timescale of weeks or months, not seconds. Indirect, predictive measures of DBS efficacy have been reported, including smiling and laughter in OCD patients.

The future of neuropsychiatric DBS therapy is bright. At present, most is known about the efficacy of DBS for OCD and treatment-resistant depression, which often target emotional/limbic structures such as the nucleus accumbens. Available data suggests that about half of the patients respond well to this therapy. This is not to say that DBS therapy does not have the potential to work for a greater percentage of patients, or generate larger symptom reductions in responders. New targets and stimulation patterns are actively being tested, and it is exceedingly probable that optimal parameters have not yet been worked out. The ability to implement patient-specific stimulation parameters is a major strength of DBS therapy, and better patient categorization methods (e.g. by subsets of symptoms or biological measurements such as MRI scans), may also help to identify optimal DBS configurations on a more personalized basis.

My visit to the neurology clinic to witness a DBS surgery ended in

disappointment. The patient responded suboptimally to the procedure, and the electrodes were not put in place for chronic stimulation on that day. As the neurobiology and clinical insights guiding this therapy become increasingly sophisticated, it is my hope that the number of DBS responders will increase in time. I look forward to the day when no brain disease patient is left without therapeutic options.

More information: References:

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