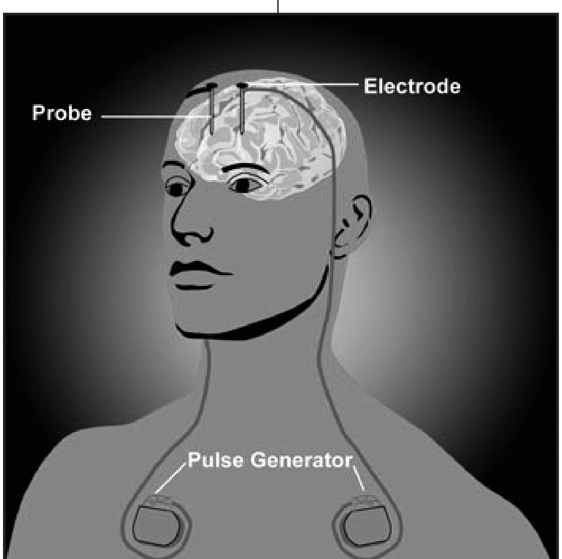
Deep Brain Stimulation

By Anirudh Penumaka

Just over fifty years after Ramon y Cajal's famously drew the architecture of the nervous system, neurosurgery transformed from a bold idea into a concrete, life-saving discipline. The human brain, with approximately one hundred billion neurons and one thousand trillion synapses, controls everything from heart beat and body temperature to emotions and personality (1). Neurosurgery was once a haphazard business, as was clearly demonstrated in the infamous psychosurgeries and lobotomies of the 1950s and 1960s which often did more harm than good (2). Since knowledge of the functions of different regions of the brain has expanded, neurosurgery is now performed not only to remove tumors, but also to treat pain, address Parkinson's disease and Tourette's syndrome, and even to improve symptoms of obsessive compulsive disorder and depression (3, 4). These latest developments have largely been made possible by a technique called Deep Brain Stimulation (DBS).



Credit:National Institute of Mental Health. <http://www.nimh.nih.gov>. Nov 2009.

Figure 1. The placement of electrodes and the location of the battery device and generator used for Deep Brain Stimulation.

Deep Brain Stimulation involves electrically stimulating small regions in the brain using thin electrodes to produce functional changes. The electrodes utilized for DBS, approximately one millimeter thick, are inserted through an opening in the patient's skull and are directed to a specific region of the brain depending on the disorder bring treated. The wires from the electrode are then placed underneath the scalp and connected subcutaneously to a battery device implanted underneath the collarbone. Stimulation parameters, such as frequency, voltage, and duration of pulses, are then modified specifically for each patient (5). Continuous electrical stimulation has been found to elicit benefits in the treatment of Parkinson's disease, as well as epilepsy, pain management, and affective disorders such as severe depression (6).

The details of the cellular mechanisms through which DBS alters disease pathology remain uncertain. Electrodes in DBS stimulate a localized region surrounding the electrode, yet they appear to impose large-scale changes in macroscopic circuits. Communication between neurons is mediated both electrically and chemically. Signals transmitted through electrical impulses, called action potentials, take place along the axons of neurons. Chemical signaling occurs at the junctions between neurons, or synapses. At these junctions, certain chemicals and amino acids act as neurotransmitters. Neurotransmitters are released from the end of an axon, travel across the synapse, and bind to receptors on a different neuron. Thus, DBS can act to alter either the production of action potentials or the binding and release of neurotransmitters. These are the two major hypotheses for the mechanism of action of DBS. One possibility is that DBS causes firing of action potentials along the axons of neurons emanating from the site of stimulation (7). Patients report improvements because firing neurons at the stimulation site blocks the transmission of abnormal signaling that takes place in the disorder. Consistent with this idea, several studies have shown that stimulation induces the release of various neurotransmitters, which in turn cause downstream neurons to fire (8, 9). On the other hand, it is known that stimulation in a different region, for example the Globus Pallidus, actually inhibits neurons from firing (10). The results of DBS stimulation appear to be intricate and regionally defined. They depend both on the region stimulated and on the frequency of the electrical stimulation; therefore, there is no single paradigm that can explain the mechanistic effects of DBS.

Previously, treatment for both locomotive and some psychological disorders involved performing irreversible surgical procedures to create lesions in regions of the brain thought to be affected by the disorder. These techniques were highly controversial, and were abandoned in favor of medications. However, there has been a resurgence of interest since the development of reversible surgical techniques to address neurological disorders. DBS for neuropsychiatric disorders is also being explored, and there have been some interesting results, especially in the treatment of depression. In all cases, patients were treated first with medications. Only those patients with severe, treatment-resistant forms of the disorder were recommended for DBS. In the long term, treatment-resistant depression, a team led by Dr. Helen Mayberg demonstrated in 2005 that DBS of the subgenual cingulate, found to be overactive in some depression patients, produced encouraging clinical improvements (11, 12, 17). In addition to depression, studies of DBS performed in order to treat chronic pain and affective disorders, such as obsessive compulsive disorder, reported moderate recovery (13, 14).

DBS has been studied in several clinical trials to treat various movement disorders such as Parkinson's disease, Dystonia, and Tourette's syndrome. These conditions share a common theme in that the important motor circuits responsible for motor control are disrupted. For instance, Parkinson's disease is characterized by slow movements, tremors, and stiff muscles. DBS treatment for Parkinson's disease is most commonly performed and correspondingly has been the most thoroughly studied. In this disease, there is a loss of a subset of neurons called dopaminergic neurons. Neuroimaging studies to indirectly observe the effects of DBS revealed that DBS resulted in greater activity in the primary motor area as measured by blood oxygen level. A clinical trial of DBS treatment for Dystonia in 22 patients published in 2005 showed improvements in roughly half of the patients (15). DBS for Tourette's syndrome is rare, but existing studies suggest enhanced control in the management of tics (usually random, involuntary movements), and analogous improvements were observed for DBS treatment for involuntary tremors (16).

The mechanisms though which DBS elicits these changes in brain function remain largely unknown, although DBS seems to be an effective treatment for a variety of neurological conditions. Future imaging and neurophysiological studies will reveal the effects of DBS on neurotransmitter release, the role of electric stimulation in the communication between neurons, and the transformations leading to changes in higher order brain function.

Surgery on the human brain was not always the precise science it is now. Neurosurgery has become routine and is an invaluable tool to treat systemic and complex conditions. Although surmounting many fundamental obstacles has permitted neurosurgery to become as successful as it is currently, there is still a great deal to learn about the coordination of activity among different regions of the brain and their participation in vital pathways and neural circuits. H

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