

Deep Brain Stimulation Targets

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In 1987, it was discovered that stimulation of deep brain structures during surgery could halt tremor symptoms of Parkinson's disease (PD) or other movement disorders. (1) In 1997, the FDA approved deep brain stimulation of the ventral intermedius nucleus (VIM) of the thalamus for treating tremor-dominant PD or other tremor disorders such as essential tremor (ET).

The exact method by which stimulation achieves its beneficial clinical effects is not completely understood. In PD it is believed that the lack of dopaminergic activity results in abnormal firing patterns in networks within the basal ganglia, and that these are disrupted by stimulation, restoring normal function to a degree.

Several other brain targets have been discovered, either from basic research or from lesional neurosurgery experience in movement disorders. Two commonly used targets, also approved by the FDA, are the internal segment of the globus pallidus (GPi) and subthalamic nucleus (STN).

FDA-Approved Brain Stimulation Targets

Anterior limb of Internal Capsule – A deep brain stimulation (DBS) target that is approved under a Humanitarian Device Exemption for medically resistant obsessive-compulsive disorder.

Globus Pallidus internus (GPi) – Located in the basal ganglia on either side of the thalamus, the globus pallidus is one of two main targets for akinetic-rigid PD. The GPi is also used as a deep brain stimulation target for dystonia.

There are a number of common, or emerging, deep brain stimulation therapeutic targets

Subthalamic Nucleus (STN) – Situated in the basal ganglia above the substantia nigra, the subthalamic nucleus is the most commonly used deep brain stimulation target for akinetic-rigid PD. Symptoms are generally improved by 50-70%, often with significant medication reduction. Due to some stimulation of nearby structures, side effects of this target can include problems with speech and swallowing, or weakness or cramping in the face or hand.

Ventral Intermedius Nucleus (VIM) – This area of the thalamus has been the target of choice for controlling tremor in essential tremor, tremor-dominant Parkinson's disease, or other movement disorders. If bilateral stimulation of VIM is used, patients may experience difficulty with speech, swallowing, or fine motor control. Patients may choose to switch between pre-set stimulation programs, depending on their activity, to strike a balance between tremor control and adverse effects. (2)

Other Emerging, Investigational Brain Stimulation Targets

Anterior Nucleus of the Thalamus – An investigational DBS target for medically refractory epilepsy

Hippocampus – Another deep brain stimulation target under study for some epilepsies

Medial Thalamus – One target used for deep brain stimulation in the treatment of medically resistant obsessive-compulsive disorder

Nucleus Accumbens – An investigational deep brain stimulation target in treatment of medically resistant depression, and potentially also for obesity and anorexia nervosa

Pedunculopontine Nucleus (PPN) – This investigational target for deep brain stimulation treatment of movement disorders is thought to help control posture and gait (3)

Posterior Hypothalamus (PHypTh) – A target for medically refractory chronic cluster headache. This may be highly effective. Unusually, stimulation is ipsilateral to symptoms.

Subgenual Cortex (Brodmann area 25) – A potential target for the treatment of medically refractory depression

Ventromedial Nucleus of the Hypothalamus – May become a deep brain stimulation target for treatment of obesity and anorexia nervosa

Emerging Neurostimulation Capabilities

New devices are released onto the market frequently. Some of the recent developments include:

- **Directional DBS leads:** these give greater flexibility in the way stimulation is delivered to the brain and may allow shaping of the stimulation field to maximize beneficial effects while minimizing side effects. Studies evaluating these systems are ongoing.
- **MRI conditional systems:** DBS systems are increasingly being tested for safety in MRI scanners. At present some systems on the market are safe in MRI scanners subject to certain restrictions in the nature of the scanning, while others are not.
- **Better rechargeable batteries:** Batteries are now available that are expected to last 25 years. Given that PD commonly arises later in life, this may mean that in many cases the IPG never needs replacing.

It is anticipated that the nature of the stimulation itself may change in coming years; all DBS so far has employed simple regular square wave pulse trains, and alternative waveforms are waiting to be explored. There has also long been interest in developing closed-loop systems that can adjust stimulation based on feedback about changing conditions detected by integrated sensors.

Please note: *This information should not be used as a substitute for medical treatment and advice. Always consult a medical professional about any health-related questions or concerns.*

For further information see:

WIKISTIM at <https://www.wikistim.org> – This free-to-use collaborative, searchable wiki of published primary neuromodulation therapy research was created in 2013 as a resource for the global neuromodulation community to extend the utility of published clinical research. The goals of WIKISTIM are to improve patient care and the quality of research reports, foster education and communication, reveal research needs, and support the practice of evidence-based medicine.