Deep Brain Stimulation Targets

In 1987, it was discovered that stimulation of deep brain structures during surgery could halt tremor symptoms of Parkinson's disease 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 Parkinson's disease or other tremor disorders.

The stimulation is believed to reduce the abnormal excitability of neural networks, thereby reducing excessive release of neurotransmitters and calming unusual firing patterns.

Since that time, other brain targets were suggested either from basic research or neurosurgery experience in movement disorder.

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 target that is approved under a Humanitarian Device Exemption for medically resistant obsessive-compulsive disorder.

Globus Pallidus (GPi) – Located in the basal ganglia on either side of the thalamus, the globus pallidus communicates with the substantia nigra (the loss of cells in the substantia nigra leads to dopamine depletion in Parkinson's disease). The GPi is also used as a deep brain stimulation target for dystonia.

Subthalamic Nucleus (STN) – Situated in the basal ganglia above the substantia nigra, the subthalamic nucleus is frequently used as a deep brain stimulation target to reduce symptoms of rigidity, tremor and slowness of movement (bradykinesia). Those 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 a target of choice for controlling tremor in essential tremor, 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 potential target for movement disorders that may also be used in medically refractory cluster headache

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 may be designed in the future with different electrodes, stimulation patterns, and improved rechargeable batteries. (1)

It is anticipated that types of stimulation will vary too, using new waveforms, changing sequences over time, pulses to reset the phase, and either constant current or constant voltage systems. Closed-loop systems will adjust stimulation based on feedback about changing conditions detected by integrated sensors.

Finally, other methods to alter nerve cell function will be tried, such as using light as a stimulus through optogenetics or other tools, potentially incorporating nanotechnology.

References:

1. ifess2012.com. Deep Brain Stimulation - Where did we start from, where are we, what did we learn, where are we heading to? http://ifess2012.com/papers/oral/plenary_2/deep_brain_stimulation_-_where_did_we_start_from_where_are_we_what_did_we_learn_where_are_we_heading_to_.html (accessed Oct. 2, 2012).

2. Virginia.edu. There are three targets approved for DBS. http://people.virginia.edu/~rf3y/Elias/DBS_Targets.html (accessed Oct. 2, 2012).
3. Riley J, Boulis N. Emerging Targets for Stimulation-Refractory Movement Disorders. The Open Neurosurgery Journal, 2011, 4, (Suppl 1-M5) 53-61. Review. http://benthamscience.com/open/toneurosj/articles/V004/SI0028TONEUROSJ/53TONEUROSJ.pdf (accessed Oct. 2, 2012).

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Hong Yu, MD
Member, International Neuromodulation Society
Clinical Assistant Professor
Department of Neurosurgery, Stanford University
Stanford, California, USA