Deep Brain Stimulation Surgery for Parkinson’s Disease

Demystifying Medicine
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NINDS
Surgery for Parkinson’s Disease

Medically refractory PD

Thalamotomy (VIM/VOP)
  Tremor suppression
  Risks of speech impairment, memory loss, and hemiparesis

Pallidotomy (Posteroventral)
  Rigidity and bradykinesia
  Risks of visual deficit and speech impairment

FDA approved for:

- Parkinson’s Disease (2002)
- Essential Tremor (1997)
- Dystonia (2003)
- OCD (HDE 2009)
Basal Ganglia

- Putamen
- Globus pallidus (lateral part)
- Globus pallidus (medial part)
- Caudate nucleus
- Thalamus
- Subthalamic nucleus
- Substantia nigra
Basal Ganglia Circuitry
Parkinson’s Disease
Parkinson’s Disease

(a) Raw signal showing bursts of activity.

(b) Power spectrum with peaks at certain frequencies.

(c) Autocorrelation function of the spike trains.

(d) Time-frequency representation of LFP activity.

Parkinson’s Disease

Figure 2

Monkeys treated with the toxin MPTP show an increase in dopamine deficiency, which can lead to pathological activity in the basal ganglia networks. The STN, a key structure in these networks, is synchronized by both hyperdirect and indirect cortical pathways, which can explain the emergence of tremors or its higher harmonics. Both STN inactivation and reduction of 8–20 Hz oscillations in GPi support the amelioration of MPTP tremors and other motor symptoms.

Figure 3

The main analysis was performed from the 51 (out of 57) STN sides that showed complex spectral reactivity. Simple spectral reactivity, which was present in all cases, was associated with a higher frequency range than that observed in MPTP-treated rats. The frequency of synchronization in clinical studies of scalp electroencephalographic activity is broader than that observed in parkinsonian rats, which may be due to the fact that STN neurons can now be entrained by both the hyperdirect and indirect cortical pathways.

Correlation tests were considered significant if the 95% confidence limits between the suppression of 8–30 Hz STN LFP activity induced by dopaminergic therapy and the improvement in tremor scores were not normally distributed (Kolmogorov-Smirnov test). The data were analyzed with bivariate correlation for non-parametric data, and the statistical dependency of improvement in motor impairment on the maximal correlation was also correlated with the frequency of oscillations in local field potential (LFP) activity in the basal ganglia.

Reference:

Deep Brain Stimulation
Electrode Ablation

http://www.us.oup.com/us/companion.websites/0195171934/cases/ch33/?view=usa
Parkinson's Disease

Diagram showing the neural circuitry involved in Parkinson's Disease, including the striatum, STN, thalamus, SN, GPe, GPi, and cortex. The diagram illustrates excitatory and inhibitory connections. 

- **Striatum** with D1 and D2 subtypes
- **STN** (Subthalamic Nucleus)
- **Thalamus**
- **SN** (Substantia Nigra)
- **GPe** (Globus Pallidus External Segment)
- **GPi** (Globus Pallidus Internal Segment)

Connections are indicated with arrows, showing excitatory (bolded arrows), inhibitory (dashed arrows), and modulatory (thin arrows) pathways.
High frequency stimulation


Basal Ganglia

Courtesy of Kirk Finnis, Medtronic
Basal Ganglia

Cortex

Caudate nucleus

Putamen

Thalamus

Globus pallidus

Subthalamic nucleus

Substantia nigra

Hypothalamus
Basal Ganglia
Basal Ganglia

Caudate
Basal Ganglia

Caudate

Putamen, GP
Basal Ganglia

- Caudate
- Putamen, GP
- Internal Capsule
Basal Ganglia

- Caudate
- Putamen, GP
- Internal Capsule
- Red Nucleus

[Image of brain regions labeled]

http://www.pharmainfo.net/reviews/parkinsons-disease
Basal Ganglia

Caudate

Putamen, GP

Internal Capsule

Red Nucleus

STN

http://www.pharmainfo.net/reviews/parkinsons-disease
Basal Ganglia
Basal Ganglia

Red Nucleus
Basal Ganglia

- STN
- Red Nucleus
Stereotactic Surgery

Victor Horsley & Robert Henry Clarke
1908
Stereotactic Surgery

The resurgence of surgical treatment for movement disorders

Although surgery for PD dropped off precipitously with the advent of L-dopa, many groups continued to perform thalamotomies for tremor of various etiologies (reviewed in reference 36). In 1991, both Benabid et al's 37 and Blond and Siegfried's 38 groups reported on thalamic DBS for tremor. Subsequent studies found that thalamic DBS was safer than thalamotomy and especially bilateral thalamotomy. These studies led to the approval of Medtronic's Activa system for thalamic DBS for essential tremor and tremor related to PD in 1997.

There was a gradual realization that L-dopa was not the magic bullet that it had initially seemed to be. Patients were requiring increased and more frequent dosing with motor fluctuations and L-dopa induced dyskinesias as their disease progressed. By the 1980s, groups in Sweden and Mexico were reporting transplantation of autologous adrenal tissue into the brains of patients with PD via both open craniotomy and stereotactic approaches. 39,40 Although the thalamus had been the preferred target for patients with PD prior to the introduction of L-dopa, Laitinen et al. 41,42 popularized pallidotomy as the principal procedure for patients with advanced, medically refractory PD.

Ernest Spiegel & Henry Wycis
1947
Stereotactic Neurosurgery
Stereotactic Neurosurgery
Anterior Commissure-Posterior Commissure
Anterior Commissure-Posterior Commissure
Anterior Commissure-Posterior Commissure
Anterior Commissure-Posterior Commissure

Anterior Commissure-Posterior Commissure
Stereotactic Neurosurgery
Stereotactic Neurosurgery
Microelectrode Recording (MER)
Microelectrode Recording (MER)

Microelectrode Recording (MER)
Deep Brain Stimulation

http://www.medtronic.com
Deep Brain Stimulation
### Efficacy PD


<table>
<thead>
<tr>
<th>Time</th>
<th>Best Medical Therapy (n = 134)</th>
<th>Deep Brain Stimulation (n = 121)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Baseline, Mean (SD)</td>
<td>6 mo, Mean (SD)</td>
</tr>
<tr>
<td>On, h/d</td>
<td>7.0 (2.9)</td>
<td>7.1 (3.3)</td>
</tr>
<tr>
<td>Without troublesome dyskinesia</td>
<td>4.2 (3.1)</td>
<td>3.9 (3.3)</td>
</tr>
<tr>
<td>Off, h/d</td>
<td>5.6 (2.9)</td>
<td>5.7 (2.8)</td>
</tr>
<tr>
<td>Asleep, h/d</td>
<td>7.1 (1.7)</td>
<td>7.3 (2.0)</td>
</tr>
</tbody>
</table>

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**Graph:**

![Graph showing UPDRS Motor Score](image-url)

- **UPDRS Baseline**
- **UPDRS Post-surgery**

**Significance:**

- **P < 0.05**
- **P < 0.01**
Efficacy

Subthalamic Nucleus
- Rigidity and bradykinesia; ~40% reduction of medication

Globus Pallidus
- Rigidity and bradykinesia

Ventral Intermediate Nucleus (Thalamus)
- Tremor suppression
Efficacy

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   Rigidity and bradykinesia; ~40% reduction of medication

Globus Pallidus
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Ventral Intermediate Nucleus (Thalamus)
   Tremor suppression

Pedunculopontine Nucleus
   Gait and postural instability
Deep Brain Stimulation

Fibres of posterior limb of internal capsule coursing anteromedially to STN

Zona incerta

STN

SNC

SNr

Red nucleus

CN III nerve roots

Oculomotor nucleus of CN III

Medial lemniscal pathway

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Courtesy of Kirk Finnis, Medtronic
Thank you