DEEP BRAIN STIMULATION FOR PARKINSON’S DISEASE

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The reversible lesion hypothesis also fit well with the prevailing model of basal ganglia function. The cortical-basal ganglia-thalamo-cortical loop had been divided into a direct pathway (cortex-striatum-GPi/SNr-thalamus), which functioned to initiate and facilitate voluntary movement, and an indirect pathway [cortex-striatum-globus pallidus externus (GPe)-STN-GPi/SNr-thalamus] that inhibits movement (Parent and Hazrati 1995a, 1995b; Penney and Young 1983) (Fig. 3). D1-receptor-expressing striatal medium spiny neurons (MSNs) project primarily to the direct pathway, and D2-receptor-expressing MSNs project primarily to the indirect pathway (Alexander and Crutcher 1990). Dopaminergic input from the substantia nigra pars compacta (SNc) to the striatum increases activity in the direct pathway via D1 receptors and decreases activity in the indirect pathway via D2 receptors, facilitating movement (Gerfen et al. 1990). In addition to the motor system, multiple parallel circuits exist that are thought to subserve oculomotor, limbic, and associative functions but maintain this same fundamental organization (Alexander et al. 1986, 1990; Hoshi et al. 2005; Jung et al. 2014; Kelly and Strick 2004; Middleton and Strick 2000; Postuma and Dagher 2006).

Over the years, additional, functionally important pathways were recognized. The hyperdirect pathway consists of a direct excitatory input from the cortex to the STN (Nambu et al. 2000; Tokuno and Nambu 2000) and is thought to function in conflict-related response inhibition (Frank et al. 2007). The PPN is a part of the mesencephalic locomotor region that has reciprocal connections with the STN, GPe, GPi, and thalamus (Mena-Segovia et al. 2004) and is an experimental target of...
(BRIEF) HISTORY OF DBS

• 1930s: Wilder Penfield mapped human brain with stimulation
• 1950s-70s: Small studies of electrical stimulation to treat pain, spasticity, epilepsy, multiple sclerosis and psychiatric disease
• 1950s-60s: Pallidotomy and thalamotomy in use for PD
• 1987: Alim Benabid demonstrates Vim DBS for PD & ET tremor
• 1994: STN DBS improves PD bradykinesia, rigidity and tremor
• 2010-2013: Two studies, GPi & STN DBS w/ similar benefit
• 2013-2014: Two studies, DBS beneficial in “early” PD
• 2015: Over 140,000 DBS implants worldwide
EXPANDING INDICATIONS

• Essential tremor
• Parkinson’s Disease
• Dystonia
• Obsessive-Compulsive Disorder (HDE)

• Future:
  • Depression
  • Tourette Syndrome
  • Epilepsy
  • Appetitive Disorders
PARKINSON’S DISEASE SYMPTOMS

• Motor
  • Resting tremor (80% of patients)
  • Hypophonia
  • Micrographia
  • Rigidity
  • Bradykinesia
  • Shuffling gait
  • Balance difficulty
PARKINSON’S DISEASE SYMPTOMS

• Non-motor
  • Mood disturbance (depression, anxiety, apathy)
• Cognitive
  • Frontal lobe dysfunction
  • Memory difficulty
  • Dementia
• Sleep disturbance
• Autonomic dysfunction
  • Sexual
  • Digestive
  • Orthostatic
PD PROGRESSION

- ~5 years after starting therapy
- Dyskinesias (involuntary dance-like movements)
- On-Off fluctuations
  - rapid loss of benefit from medications
  - reduced mobility, gait/balance difficulty, tremor and rigidity
- Carbidopa-Levodopa resistance
  - motor, swallowing, cognitive
WHEN TO SEEK REFERRAL

• When you and (or) your doctor feel like you:
  • have troublesome medication side effects (dyskinesia)
  • develop refractory tremor (not improving with medications)
• want to learn more about DBS
SURGICAL OPTIONS

- Lesion Surgery - destruction of a particular area of brain
- Thalamotomy (VIM) - reduce tremor
- Pallidotomy & Subthalamotomy - reduce tremor, rigidity, and bradykinesia (slowness)
- Not reversible, high complication rate
- Fallen out of favor in DBS era
SURGICAL OPTIONS

- Deep Brain Stimulation (DBS)
- Electrodes (metal contacts and wires) implanted in specific brain regions
- Pulse generator and battery implanted in chest
## DBS Symptom Response

<table>
<thead>
<tr>
<th>Improves a lot</th>
<th>Improves some</th>
<th>Does not improve or worsens</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tremor</td>
<td>Speech</td>
<td>Dementia</td>
</tr>
<tr>
<td>Rigidity</td>
<td>Balance</td>
<td>Atypical Parkinsonism</td>
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<tr>
<td>Bradykinesia</td>
<td>Freezing of gait</td>
<td>Psychosis</td>
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<tr>
<td>Dyskinesias</td>
<td></td>
<td>Autonomic symptoms</td>
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<td>Dystonia</td>
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<td>Levodopa-related motor fluctuations</td>
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DBS EXTENDS “ON” PERIOD

Deuschl 2006

![Graph showing outcomes of DBS surgery](image)