Deep Brain Stimulation for Movement Disorders, OCD, and Depression

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Disclosures

• Nevro - Medical Advisory Board - Stock options

• Circuit Therapeutics - Chair, Medical Advisory Board - Stock options

• Medtronic - ad hoc consulting, Fellowship support (Stanford)

• Neuropace - Neurosurgical Advisory Board

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Deep Brain Stimulation

- Indications
- Targets
- Results
- Complications
Indications for DBS
Parkinson’s Disease

- Resting tremor
- Rigidity with or without cogwheeling
- Bradykinesia
- Gait disturbance
- Stooped posture
- Postural instability

*Note: all patients depicted in this presentation previously signed video / photography consent*
Selection Criteria

- Idiopathic PD
- Good response to Sinemet
- Wide “on-off” fluctuations
- No or minimal cognitive impairment
- Supportive family/environment
- No significant medical risk factors
- ?Age
Essential Tremor

- Tremor primarily with action
- Hereditary
- Slowly progressive
- Mainly appendicular, though may involve head/trunk/gait
- DBS primarily effective for appendicular component
Dystonia

- Heterogenous disease
- Primary vs. Secondary
- Generalized vs. Focal
- Hereditary (DYT-1 gene positive)
- Primary respond to DBS better than Secondary
- Mobile > fixed
Emerging Indications

- Tourette’s syndrome
- Cluster headache
- OCD
- Major depression
- Others in development
DBS Technique
Stereotactic Technique

- First developed for animal surgery
- XYZ coordinate system superimposed on brain
Stereotactic Technique

- Traditionally uses stereotactic head frame
- Allows precise positioning
- Modern stereotaxis based on MRI and CT
Head Frame Application
Frameless DBS

Frameless stereotaxy using bone fiducial markers for deep brain stimulation

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Clinical Motor Outcome of Bilateral Subthalamus Nucleus Deep-Brain Stimulation for Parkinson’s Disease Using Image-Guided Frameless Stereotaxy

BACKGROUND: Image-guided neuronavigation has largely replaced stereotactic frames when precise, real-time anatomic localization is required during neurosurgical procedures. However, some procedures, including placement of deep-brain stimulation (DBS) leads for the treatment of movement disorders, are still performed using frame-based stereotaxy. Despite the demonstration of comparable accuracy between frame-based and “frameless” image-guided approaches, the clinical efficacy of frameless DBS placement has never been reported.

OBJECTIVE: To analyze the outcomes of subthalamic nucleus (STN) DBS using the frameless technique for the treatment of Parkinson’s disease (PD).

METHODS: Of 31 subjects (20 men) with PD for 10 ± 4 years, 28 had bilateral STN DBS and 3 had unilateral STN DBS. The Unified Parkinson’s Disease Rating Scale (UPDRS) motor scale (III) and total medication doses were assessed before surgery on and off medication and off medication/ON DBS (off/ON) after 6 to 12 months of STN DBS.

RESULTS: There was a 58% improvement from bilateral STN DBS in the UPDRS III (40 ± 16 preoperatively off, 17 ± 11 off/ON 9.6 ± 1.9 months after surgery (P < .001). This compared favorably with the published outcomes using the frame-based technique. All motor subscores improved significantly (P < .01). The mean reduction in medication was 50%. No intraoperative complications occurred, but one subject with hypertension died of a delayed hemorrhage postoperatively. Two subjects developed postoperative infections that required lead removal and antibiotics.

CONCLUSIONS: Bilateral STN DBS for PD performed by an experienced team using a frameless approach results in outcomes comparable to those reported with the use of the frame-based technique.

KEY WORDS: Deep-brain stimulation, Frameless stereotaxy, Image-guided neurosurgery, Parkinson’s disease
Fiducial Placement

3-5 skull screws
? less discomfort than frame
Fiducial Identification

Choose point on images that will be identifiable in surgery, then "Store". Repeat for a total of at least four points.
Registration
Registration
NeXframe Tower
Registration
Re-assembly
Alignment
aim point

aiming reticle

target

Targeting Margin: 15 mm

StealthStation

- Check draping checkpoint
- Create accuracy checkpoints
- Navigate

Select the desired probe and press the footswitch to navigate.

Right STN
Length: 82.4 mm

Set Entry
Set Target

2.5 mm past target
2.2 mm off plan

Drive Z-depth
- Use Cameras For Navigation

Guide Frame-DT
Passive Spine Frame
Alignment

A.

B.
Parkinson’s - STN

11-12 mm lateral
3-4 mm posterior
4-5 mm inferior
Parkinson’s - STN

11-12 mm lateral

3-4 mm posterior

4-5 mm inferior
Movement-Related Cells

Movement-Related Cells

Stimulator Placement
Stimulator Placement
Stimulator Placement
Tremor - Vim/Vop

13-15 mm lateral
6-8 mm posterior
at AC-PC plane
Tremor - Vim/Vop

13-15 mm lateral

6-8 mm posterior

at AC-PC plane
Microrecording Pass #1 - Posterior

- Sensory thalamus- "Vc"
- Look for tactile responses
- Extremely low thresholds for producing tingling sensation with stimulation
Microrecording Pass #1 - Posterior

- Sensory thalamus-“Vc”
- Look for tactile responses
- Extremely low thresholds for producing tingling sensation with stimulation
Microrecording Pass #2

- Middle track – Vc Vim junction
- Tremor cells
- Joint position cells
- Muscle spindle responses
Microrecording Pass #2

- Middle track – Vc Vim junction
- Tremor cells
- Joint position cells
- Muscle spindle responses
Microrecording Pass #3

- Target track – motor thalamus - “Vim/VOp” junction
- Many tremor cells
- Tremor suppression with stimulation
Microrecording Pass #3

- Target track – motor thalamus - “Vim/VOp” junction
- Many tremor cells
- Tremor suppression with stimulation
DBS Placement
DBS Placement
Dystonia - GPi

19-22 mm lateral

2-3 mm anterior

4-5 mm inferior
Dystonia - G Pi

- 19-22 mm lateral
- 2-3 mm anterior
- 4-5 mm inferior
Dystonia - GPi

19-22 mm lateral

2-3 mm anterior

4-5 mm inferior
OCD - Anterior Limb of Internal Capsule
OCD - Anterior Limb of Internal Capsule
OCD - Anterior Limb of Internal Capsule
DBS Results and Complications
Complications

- **Hemorrhage - 1.5%**
- **Infection - 3-5%**
- **Stimulation side effects - common**
  - Tingling, muscle contractions, diplopia, speech difficulties
  - Can be mitigated by reprogramming
<table>
<thead>
<tr>
<th>Type of Adverse Event</th>
<th>Transient</th>
<th>Permanent</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>First three postoperative months (n=49)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Related to procedure</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ballism</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Asymptomatic bleeding detected on MRI</td>
<td>8</td>
<td>0</td>
</tr>
<tr>
<td>Intracerebral hemorrhage</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Head trauma (fall in hospital)</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Contusion</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>Dementia</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Delirium</td>
<td>12</td>
<td>0</td>
</tr>
<tr>
<td>Seizures</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>General health complications</td>
<td>6</td>
<td>0</td>
</tr>
<tr>
<td>Wound healing problem</td>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td>Related to device</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Skin erosion with infection</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Stimulator repositioning</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Related to treatment</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Disabling dyskinesia</td>
<td>NA</td>
<td>4</td>
</tr>
<tr>
<td>Weight gain</td>
<td>NA</td>
<td>41 (Mean, 3 kg; maximum, 5 kg)</td>
</tr>
<tr>
<td>Eyelid-opening apraxia</td>
<td>0</td>
<td>15</td>
</tr>
<tr>
<td>Depression</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Apathy</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Impulsive aggressive behavior</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Hypomania</td>
<td>4</td>
<td>1</td>
</tr>
</tbody>
</table>
From three months until five years after surgery (n=42)\textsuperscript{\textcircled{\texttildelow}}:

<table>
<thead>
<tr>
<th>Related to device</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Stimulator repositioning</td>
<td>1</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Related to stimulation</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Eyelid-opening apraxia</td>
<td>0</td>
</tr>
<tr>
<td>Disabling dyskinesia</td>
<td>5</td>
</tr>
<tr>
<td>Weight gain</td>
<td>0</td>
</tr>
<tr>
<td>Tetanic muscle contraction</td>
<td>0</td>
</tr>
<tr>
<td>Dysarthria</td>
<td>2</td>
</tr>
<tr>
<td>Hilarity</td>
<td>1</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Related to treatment or disease</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Depression</td>
<td>7</td>
</tr>
<tr>
<td>Suicide attempts</td>
<td>3</td>
</tr>
<tr>
<td>Hallucinations</td>
<td>2</td>
</tr>
<tr>
<td>Psychosis</td>
<td>1</td>
</tr>
<tr>
<td>Dementia</td>
<td>0</td>
</tr>
<tr>
<td>Apathy</td>
<td>2</td>
</tr>
</tbody>
</table>

* Data are expressed as numbers of complications; some patients had more than one adverse event. MRI denotes magnetic resonance imaging, and NA not assessed.

\textsuperscript{\textcircled{\textdagger}} Ballism is severe dyskinesia of the proximal limbs. Disabling dyskinesia is defined as a score on the dyskinesia disability item of the Unified Parkinson’s Disease Rating Scale that is greater than 2 (range, 0 to 4), indicating interference with motor function, as assessed at baseline, three months, one year, three years, or five years. Transient worsening of dyskinesia after changes in medication or stimulation were not systematically assessed. Eyelid-opening apraxia refers to an involuntary forceful closure of the eyelids. Tetanic muscle contraction indicates tonic muscle contractions that can be restricted to a single muscle or that include larger muscle groups leading to an abnormal posture. (This side effect is related to diffusion of the current to the pyramidal tract. Dysarthria, similarly, can be related to diffusion of the current to corticobulbar fibers.)

\textsuperscript{\textcircled{\textdagger\textdoublecircled{}}} Three patients died during the follow-up period, and four were lost to follow-up.
Side Effects Related to Spread of Electrical Fields

-1V Stimulation

-3V Stimulation

Contact 2; 90 \( \mu \text{s} \); 150 Hz

Contact 2; 90 \( \mu \text{s} \); 150 Hz

Stimulation Side Effects
Stimulation Side Effects

- Thalamus
- Zona Incerta
- Substantia Nigra - Reticulata
- Red Nucleus
- Internal Capsule
Muscle contractions, dysarthria, “dystonia”
Muscle contractions, dysarthria, "dystonia"

Tremor reduction without change in akinesia

STN Stimulation Side Effects
Stimulation Side Effects

Tremor reduction without change in akinesia

Muscle contractions, dysarthria, “dystonia”

Diplopia, ocular deviation, mydriasis, postural disturbance
Muscle contractions, dysarthria, “dystonia”

Tremor reduction without change in akinesia

Diplopia, ocular deviation, mydriasis, ?postural disturbance

?Inhibition of L-dopa effect with increased akinesia; depression

STN
Results - Tremor

- 50-75% of patients obtain complete tremor relief
- 75-100% achieve significant tremor reduction
- Comparable to thalamotomy with fewer complications
Results - Dystonia

• DYT-1 positive - average 55.6% improvement in Burke-Fahn-Marsden Dystonia Score

• DYT-1 negative - average 35.1% improvement

• Cervical dystonia - variable improvement

Results - Dystonia

• DYT-1 positive - average 55.6% improvement in Burke-Fahn-Marsden Dystonia Score

• DYT-1 negative - average 35.1% improvement

• Cervical dystonia - variable improvement

# Results - Parkinson’s

<table>
<thead>
<tr>
<th>Investigator (year)</th>
<th>Pts.</th>
<th>F/U</th>
<th>ADL</th>
<th>Motor</th>
<th>Dyskinesia</th>
<th>Med ↓ %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Krack et al. (1998)</td>
<td>8</td>
<td>6 mos</td>
<td>N/A</td>
<td>71</td>
<td>N/A</td>
<td>56</td>
</tr>
<tr>
<td>Limousin et al. (1998)</td>
<td>24</td>
<td>12 mos</td>
<td>58</td>
<td>60</td>
<td>N/A</td>
<td>50</td>
</tr>
<tr>
<td>Kumar et al. (1998)</td>
<td>7</td>
<td>12 mos</td>
<td>30</td>
<td>58</td>
<td>83</td>
<td>40</td>
</tr>
<tr>
<td>Moro et al. (2000)</td>
<td>7</td>
<td>16 mos</td>
<td>52</td>
<td>42</td>
<td>N/A</td>
<td>65</td>
</tr>
<tr>
<td>Houeto et al. (2000)</td>
<td>23</td>
<td>6 mos</td>
<td>66</td>
<td>67</td>
<td>77</td>
<td>61</td>
</tr>
<tr>
<td>DBS for PDSG (2001)</td>
<td>96</td>
<td>6 mos</td>
<td>44</td>
<td>51</td>
<td>70</td>
<td>37</td>
</tr>
<tr>
<td>Romito et al. (2002)</td>
<td>22</td>
<td>36 mos</td>
<td>68</td>
<td>50</td>
<td>N/A</td>
<td>69</td>
</tr>
<tr>
<td>Thobois et al. (2002)</td>
<td>18</td>
<td>12 mos</td>
<td>53</td>
<td>55</td>
<td>66</td>
<td>76</td>
</tr>
<tr>
<td>Krack et al. (2003)</td>
<td>49</td>
<td>5 years</td>
<td>49</td>
<td>54</td>
<td>N/A</td>
<td>63</td>
</tr>
</tbody>
</table>

**Mean Improvement %**

<p>| | | | | | | |</p>
<table>
<thead>
<tr>
<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>52</td>
<td>56</td>
<td>74</td>
<td>59</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Table 2. Effect of Bilateral Stimulation of the Subthalamic Nucleus on Off-Medication UPDRS Subscores.*

<table>
<thead>
<tr>
<th>Subscale</th>
<th>Range of Possible Scores</th>
<th>Base Line (N=49)</th>
<th>1 Year after Surgery (N=43)</th>
<th>3 Years after Surgery (N=42)</th>
<th>5 Years after Surgery (N=42)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Motor examination</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>0–108</td>
<td>55.7±11.9</td>
<td>19±11.1</td>
<td>22.8±11.6</td>
<td>25.8±12.3</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Tremor</td>
<td>0–28</td>
<td>5.2±4.8</td>
<td>1.3±1.8</td>
<td>0.9±1.5</td>
<td>1.3±1.7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Rigidity</td>
<td>0–20</td>
<td>13.4±3.4</td>
<td>3.6±3.5</td>
<td>3.5±2.0</td>
<td>3.9±3.0</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Akinesia</td>
<td>0–32</td>
<td>18.5±5.7</td>
<td>6.9±5.8</td>
<td>8.8±5.7</td>
<td>9.5±6.2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Speech</td>
<td>0–4</td>
<td>1.9±1.0</td>
<td>1.3±1.0</td>
<td>1.8±1.0</td>
<td>1.9±1.0</td>
<td>0.56</td>
</tr>
<tr>
<td>Postural stability</td>
<td>0–4</td>
<td>2.5±0.9</td>
<td>0.9±0.9</td>
<td>1.3±0.9</td>
<td>1.4±1.0</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Gait</td>
<td>0–4</td>
<td>3.1±0.8</td>
<td>1.0±1.0</td>
<td>1.2±1.1</td>
<td>1.5±1.1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Activities of daily living</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>0–52</td>
<td>30.4±6.6</td>
<td>10.3±6.9</td>
<td>14.8±6.0</td>
<td>15.6±8.5</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Writing</td>
<td>0–4</td>
<td>3.5±0.7</td>
<td>2.2±1.2</td>
<td>2.6±1.2</td>
<td>2.2±1.4</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Freezing of gait</td>
<td>0–4</td>
<td>2.6±0.2</td>
<td>0.7±1.0</td>
<td>1.3±1.2</td>
<td>1.4±1.2</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

* Plus–minus values are means ± SD. UPDRS denotes the Unified Parkinson's Disease Rating Scale. A reduction in scores indicates an improvement in function. Off-medication evaluations were performed when the patient had taken no antiparkinsonian medications for 8 to 12 hours. Writing and freezing of gait are complex motor functions that are not represented in the motor scores.
Results

- Tremor: 80
- Rigidity: 68
- Akinesia: 55
- Gait: 54
- Postural Stability: 60
Results - Parkinson’s

Pre-op

Post-op
Results - Parkinson’s

Pre-op  

Post-op
DBS for OCD

- Anterior limb of internal capsule
- Initial results promising
- Multi-center trial currently underway in US and Europe
- Decrease in compulsions and anxiety
- Currently approved under HDE
Three-Year Outcomes in Deep Brain Stimulation for Highly Resistant Obsessive–Compulsive Disorder

Benjamin D Greenberg*,1,2, Donald A Malone3,4, Gerhard M Friehs1,2, Ali R Rezai3,4, Cynthia S Kibu3,4, Paul F Malloy1,2, Stephen P Salloway1,2, Michael S Okun5,6, Wayne K Goodman5,6 and Steven A Rasmussen1,2

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### DBS for OCD

**Table 3 Clinical Assessment of Functioning before and during Chronic DBS**

<table>
<thead>
<tr>
<th></th>
<th></th>
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<th></th>
<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td>BH1</td>
<td>No</td>
<td>Extreme slowness</td>
<td>No</td>
<td>Limited</td>
<td>Finished degree program</td>
<td>Yes</td>
<td>Yes</td>
<td>Good</td>
<td>38</td>
</tr>
<tr>
<td>BH2</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Minimal</td>
<td>Entered job training</td>
<td>Mainly</td>
<td>Yes</td>
<td>Limited</td>
<td>12†</td>
</tr>
<tr>
<td>BH3</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Minimal</td>
<td>No</td>
<td>Mainly</td>
<td>Yes</td>
<td>Limited</td>
<td>31</td>
</tr>
<tr>
<td>BH4</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Minimal</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Limited</td>
<td>12†</td>
</tr>
<tr>
<td>BH5</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Minimal</td>
<td>Entered technical training</td>
<td>Mainly</td>
<td>No</td>
<td>Limited</td>
<td>33</td>
</tr>
<tr>
<td>CC1</td>
<td>No</td>
<td>Total care</td>
<td>No</td>
<td>Minimal</td>
<td>No</td>
<td>Mainly</td>
<td>Limited VN services</td>
<td>Dating, brief engagement</td>
<td>39</td>
</tr>
<tr>
<td>CC2</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Limited</td>
<td>No</td>
<td>Mainly</td>
<td>Limited VN services</td>
<td>Dating, brief engagement</td>
<td>49</td>
</tr>
<tr>
<td>CC3</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
<td>Limited</td>
<td>Works FT</td>
<td>Yes</td>
<td>Yes</td>
<td>Dating</td>
<td>64</td>
</tr>
<tr>
<td>CC4</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
<td>Limited</td>
<td>Works FT</td>
<td>Yes</td>
<td>Yes</td>
<td>Engaged to marry</td>
<td>64</td>
</tr>
<tr>
<td>CC5</td>
<td>No; unable to leave room</td>
<td>No; assisted living room</td>
<td>No; assisted living room</td>
<td>Minimal</td>
<td>Travels alone to day program</td>
<td>Improved</td>
<td>No</td>
<td>Limited</td>
<td>35</td>
</tr>
</tbody>
</table>

*The two patients who discontinued stimulation before the 36-month end point.*

---

DBS for OCD

Figure 2 OCD severity (YBOCS) during long-term DBS.

Figure 4 Global functioning during long-term DBS.

DBS for Depression

- 6 patients
- Treatment refractory
- Severe depression scores
- Subgenual cingulate (area 25) targeted based on prior imaging work

DBS for Depression

### Table 2. Hamilton Depression Rating Scale, HDRS-17, Scores over Time for Each Subject

<table>
<thead>
<tr>
<th>Time</th>
<th>Hamilton Score&lt;sup&gt;a&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pt 1&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Preop baseline</td>
<td>29</td>
</tr>
<tr>
<td>1 week postop (acute stimulation)</td>
<td>5</td>
</tr>
<tr>
<td>2 weeks postop (DBS off)</td>
<td>9</td>
</tr>
<tr>
<td>1 month</td>
<td>10</td>
</tr>
<tr>
<td>2 months</td>
<td>13</td>
</tr>
<tr>
<td>3 months</td>
<td>2</td>
</tr>
<tr>
<td>4 months</td>
<td>4</td>
</tr>
<tr>
<td>5 months</td>
<td>5</td>
</tr>
<tr>
<td>6 months</td>
<td>5</td>
</tr>
</tbody>
</table>

<sup>a</sup>Clinical response: decrease HDRS score >50%. Clinical remission: absolute HDRS score <8.

<sup>b</sup>Clinical responders.

<sup>c</sup>Clinical nonresponders.
DBS for Depression

• 5/6 patients considered “responders” at 2 months; 4/6 at study end

• 2 patients met criteria for remission

• Blinded stimulator deactivation for 4 weeks with sustained mood improvements

• 2 patients required explant for infection

DBS for Memory Enhancement

- Single case report
- Unexpected side effect during DBS for obesity
- Improved attention and verbal learning

Memory Enhancement Induced by Hypothalamic/ Fornix Deep Brain Stimulation

Clement Hamani, MD, PhD, 1 Mary Pat McAndrews, PhD, 2 Melanie Cohn, PhD, 2 Michael Oh, MD, 1 Dominik Zumsteg, MD, 3 Colin M. Shapiro, MD, PhD, FRCP, 4 Richard A. Wennberg, MD, FRCP, 3 and Andres M. Lozano, MD, PhD, FRCSC 1

Bilateral hypothalamic deep brain stimulation was performed to treat a patient with morbid obesity. We observed, quite unexpectedly, that stimulation evoked detailed autobiographical memories. Associative memory tasks conducted in a double-blinded “on” versus “off” manner demonstrated that stimulation increased recollection but not familiarity-based recognition, indicating a functional engagement of the hippocampus. Electroencephalographic source localization showed that hypothalamic deep brain stimulation drove activity in mesial temporal lobe structures. This shows that hypothalamic stimulation in this patient modulates limbic activity and improves certain memory functions.


Table 1. Neuropsychological Testing at Baseline before Surgery and after Chronic Hypothalamic Stimulation

<table>
<thead>
<tr>
<th>Test</th>
<th>Baseline</th>
<th>Postoperative</th>
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<tbody>
<tr>
<td>WAIS Full-Scale Intelligence Quotient(a)</td>
<td>125</td>
<td>134</td>
</tr>
<tr>
<td>WAIS Attention Index(a)</td>
<td>108</td>
<td>119(b)</td>
</tr>
<tr>
<td>Trail Making Test of processing speed (average Parts A and B)(c)</td>
<td>60</td>
<td>50</td>
</tr>
<tr>
<td>Verbal Fluency (average phonemic and semantic)(c)</td>
<td>43</td>
<td>50</td>
</tr>
<tr>
<td>California Verbal Learning Test (total learning)(c)</td>
<td>40</td>
<td>77(b)</td>
</tr>
<tr>
<td>California Verbal Learning Test (short-delay recall)(c)</td>
<td>40</td>
<td>70(b)</td>
</tr>
<tr>
<td>California Verbal Learning Test (long-delay recall)(c)</td>
<td>55</td>
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<tr>
<td>Spatial Associative Learning (trials to criterion)(c)</td>
<td>39</td>
<td>54(d)</td>
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<tr>
<td>Wechsler Memory Scale-III Face Recognition (Immediate)(c)</td>
<td>62</td>
<td>58</td>
</tr>
<tr>
<td>Wechsler Memory Scale-III Face Recognition (Delay)(c)</td>
<td>68</td>
<td>63</td>
</tr>
<tr>
<td>Behavioral Evaluation of Memory Figural Learning(c)</td>
<td>77</td>
<td>81</td>
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</tr>
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Postoperative scores were obtained after 3 weeks of continuous stimulation (bilateral stimulation, 2.8 volts, 130Hz, 60-microsecond pulse width, contacts 0 and 4 as cathodes, case as anode). Stimulation was initiated at the first postoperative office visit. The settings chosen did not produce any acute overt memory, behavioral, sensory, or autonomic effects.

\(a\)Scaled scores: mean = 100; standard deviation (SD) = 15.
\(b\)\(T\) scores: mean = 50; SD = 10.
\(c\)Measures in which pre-post change exceeds the 95% confidence interval for reliable change.
\(d\)Measures showed performance increase of greater than 1.5 SD units; normative test-retest data for reliable change computation are not available. WAIS = Wechsler Adult Intelligence Scale.
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Conclusions

• **DBS** well-established for the treatment of movement disorders

• Excellent results for tremor, dystonia, Parkinson’s

• Promising early results in OCD, major depression

• Improving technology will continue to expand indications