Deep Brain Stimulation for Essential tremor and Parkinson’s disease

JL Houeto, MD, PhD University of Poitiers and Clinical Investigation Center- INSERM 802, Poitiers (France)
DBS

right electrode

left electrode

target

extension lead

Dual channel IPG

Kinetra
The targets?

The 3 main targets: Vim, GPi, STN
Which patients?

- the most suitable candidate
  - tremors
  - Parkinson’s disease
  - Quality of life

Surgical complications
- Misplacement
- Intracerebral bleeding
- Infection, rejection
- Material dysfunction
- Death

3–4%

Deuchl et al, 2006
Thalamic stimulation for tremor dominant PD

• Excellent effect on rest and postural tremor

• No effect on: Rigidity, akinesia, gait, dyskinesia or motor fluctuations
Thalamic stimulation

• **ET +++**
  – Distal upper limb postural tremor but minimal intention component
  – Risk of long-term tolerance
• **Tremor-dominant PD ±**
  – no effect on akinesia and rigidity

Pure anti-tremoric target
Parkinson’s disease

PD at time of diagnosis

With time and therapy, emergence of motor complications
STN stimulation for PD

- Effects of stimulation depend on
  - Appropriate patient
  - Accuracy of the targetting
    - anatomical
    - microrecording
    - intraoperative stimulation ++
  - Adequate medical postoperative management
Intraoperative recording and test stimulation
Effect of STN-stimulation therapy

- STN-stimulation provides a 60-90% improvement
  - Parkinsonian motor disability,
  - Motor complications
  - Reduction in antiparkinsonian drugs

Limousin et al., 1998; Moro et al, 1999; Houeto et al., 2000, Molinuevo et al., 2000, Romito et al., 2002, Krack et al., 2003….
STN stimulation for PD

• Persistence of a transient but major levodopa response: **excellent best on motor score**

• Absence of on-period levodopa-resistant symptoms

• Good cognitive and mental reserve

• Good general health

➤ Early onset PD after 5 to 15 years of chronic levodopatherapy
PREDICTORS OF EFFICACY

“AXIAL ON-SCORE”

- Axial symptoms
  - Gait
  - Speech and swallowing
  - Postural instability
  - Cognitive disorders

- Extent of non-dopaminergic lesions
- Correlate with age, disease duration and atrophy of the midbrain

Adapted from Welter et al., 2002
Postoperative medical problems

- Motor
  - Hypophonia
  - Freezing

- Psychiatry
  - Depression/apathy and withdrawal syndrome
Evolution of axial symptoms

- Develop with age and disease duration
  - Extent of non-dopaminergic pathology
- May counterbalance the benefit of the therapy

**Table 3. 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=40)</th>
<th>5 Years after Surgery (N=39)</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>14.3±7.0</td>
<td>11.4±8.9</td>
<td>15.3±9.5</td>
<td>21.1±12.2</td>
<td>0.003</td>
</tr>
<tr>
<td>Tremor</td>
<td>0–34</td>
<td>0.6±0.8</td>
<td>0.4±0.8</td>
<td>0.1±0.5</td>
<td>0.3±0.6</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Rigidity</td>
<td>0–20</td>
<td>3.6±2.7</td>
<td>2.1±2.9</td>
<td>2.2±2.9</td>
<td>2.8±2.7</td>
<td>0.27</td>
</tr>
<tr>
<td>Akinesia</td>
<td>0–32</td>
<td>4.4±3.6</td>
<td>3.7±4.4</td>
<td>6.3±5.4</td>
<td>8.4±6.7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Speech</td>
<td>0–4</td>
<td>0.8±0.6</td>
<td>0.9±0.7</td>
<td>1.4±0.9</td>
<td>1.8±0.7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Postural stability</td>
<td>0–4</td>
<td>1.0±0.7</td>
<td>0.7±0.7</td>
<td>1.0±0.8</td>
<td>1.3±0.9</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Gait</td>
<td>0–4</td>
<td>0.5±0.6</td>
<td>0.6±0.8</td>
<td>0.8±1.0</td>
<td>1.0±0.9</td>
<td>0.02</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>7.3±4.2</td>
<td>7.4±4.8</td>
<td>10.7±6.4</td>
<td>14.0±7.0</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Writing</td>
<td>0–4</td>
<td>1.7±1.1</td>
<td>2.0±1.2</td>
<td>2.2±1.2</td>
<td>2.4±1.4</td>
<td>0.008</td>
</tr>
<tr>
<td>Freezing of gait</td>
<td>0–4</td>
<td>0.3±0.7</td>
<td>0.3±0.6</td>
<td>0.7±1.0</td>
<td>1.2±1.2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Motor complications</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Duration of dyskinesia</td>
<td>0–4</td>
<td>2.1±1.1</td>
<td>0.6±0.9</td>
<td>0.6±0.9</td>
<td>0.6±0.9</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Dyskinesia disability</td>
<td>0–4</td>
<td>1.9±0.8</td>
<td>0.7±0.8</td>
<td>0.6±0.6</td>
<td>0.8±0.8</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>
Behavioral disturbances in PD treated by STN stimulation
STN stimulation, Quality of life and behaviour

- Prospective study
- Quality of life
  - Psychopathology
  - Personnality
    - Unchanged
  - Impulsivity
- Social adaptation
  - Unchanged

**Table 3:** Effects of continuous bilateral stimulation of the STN on the PDQ-39 scores in 20 successive patients 6 and 24 months after surgery

<table>
<thead>
<tr>
<th>Dimension</th>
<th>Before stimulation</th>
<th>After stimulation</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>6 months</td>
<td>24 months</td>
</tr>
<tr>
<td>Mobility</td>
<td>65.7±17.4</td>
<td>50.9±22.7*</td>
</tr>
<tr>
<td>Activities of daily living</td>
<td>48.7±23.4</td>
<td>29±30.8*</td>
</tr>
<tr>
<td>Emotional well-being</td>
<td>43.5±18.4</td>
<td>33.8±22.7</td>
</tr>
<tr>
<td>Stigma</td>
<td>48.7±28.9</td>
<td>28.4±21.4*</td>
</tr>
<tr>
<td>Social support</td>
<td>22.5±23.3</td>
<td>22.5±27.7</td>
</tr>
<tr>
<td>Cognitions</td>
<td>28.1±17.5</td>
<td>25.9±17.4</td>
</tr>
<tr>
<td>Communication</td>
<td>30±18.8</td>
<td>20.4±19</td>
</tr>
<tr>
<td>Bodily discomfort</td>
<td>57.5±25.9</td>
<td>40.4±24.8*</td>
</tr>
<tr>
<td>PDQ-39 summary index</td>
<td>43.1±13.1</td>
<td>31.4±15.1*</td>
</tr>
</tbody>
</table>

Values expressed as mean (standard deviation); * = p<.02

**Table 2:** Number of patients with psychiatric disorders according to the DSM IV criteria assessed with the M.I.N.I. 5.0.0. (ref)

<table>
<thead>
<tr>
<th>Disorder</th>
<th>Before neurosurgery</th>
<th>After neurosurgery</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>At any point</td>
<td>one month</td>
</tr>
<tr>
<td>Major depressive episode</td>
<td>9</td>
<td>1</td>
</tr>
<tr>
<td>Hypomania</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Agoraphobia</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Panic Disorder</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Social Phobia</td>
<td>4</td>
<td>3</td>
</tr>
<tr>
<td>General Anxiety Disorder</td>
<td>12</td>
<td>10</td>
</tr>
<tr>
<td>Obsessive-Compulsive Disorder</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Post-Traumatic Stress Disorder</td>
<td>3</td>
<td>1</td>
</tr>
</tbody>
</table>

() observed only after surgery

Adapted from Houeto et al., 2006
Effects of STN-DBS on mood and anxiety in 20 PD patients

- Improvement
  - anxiety disorders
  - mood disorders (mild to moderate depression)
Effect of STN-Stimulation

- Modulation of cortico-subcortical neuronal circuits
  - sensori-motor
    - Improves
      - Motor symptoms
  - Limbic
    - Anxiety and obsessive compulsive disorders
Limitations of the current selection criteria

- Current patients selection criteria
  - Advanced form of PD (> 10-15 years of disease duration) …

- Patients have already developed a psychological and social disability
  - interruption of social and professional activities,
  - familial and affective maladjustment,
  - and economic problems

- Poor Postoperative socio familial adjustment

Houeto et al., 2002; Schupbach et al., 2007)
REMAINING ISSUE TO ADDRESS EARLIER STN-STIMULATION

• To improve
  – motor symptoms
  – QoL
• Effect on axial symptoms?
• Prevent patients from
  – Socio-familial
  – Professional
  – Personal, disabilities (?)

A randomized, prospective, multi-centre, parallel-group study in France & Germany “EARLYSTIM” → on-going
Conclusion

- DBS for ET and PD
- Improves motor symptoms, QoL, overall psychiatric morbidity
- As soon as motor complications impact QoL
  - in candidates carefully selected, operated, managed
- Will early-STN stimulation, have favourable risk-benefit ratio?
- Effect on axial symptoms remain matter of concern