Patient selection for surgery: Parkinson’s disease

Dr. María C. Rodríguez-Oroz
Neurology and Neuroscience.
University Hospital Donostia, Research Institute BioDonostia, Ikerbasque Senior Researcher
San Sebastian, Spain
Criteria for DBS

- PD
- motor complications:
  - fluctuations
  - severe dyskinesias
- tremor
- refractory to optimal medical treatment
- important enough (severity/duration) to justify surgical risk
- Intolerance to dopaminergic drugs
Factors assessed before surgery

- diagnosis, disease duration,
- age
- levodopa responsiveness: type and severity of levodopa-unresponsive symptoms
- cognitive and psychiatric issues
- comorbid disorders
- brain magnetic resonance imaging (MRI)
CAPSIT-PD protocol

• PD: duration of at least 5 years
• Age: no specific age cutoff
  – 70 y.o.
  – Older: individual evaluation of risk-benefit ratio (comorbidities, cognitive state, prevalence levodopa-resistant symptoms and severity, overall risk of surgical complications)
    • Unilateral
    • GPi
Pre-operative L-dopa responsiveness:

- L-dopa challenge (150%) of the first dose in the morning, in the defined Off state (12 h without dopaminergic treatment)
- At least a 33% decrease in the UPDRS- III score
- L-dopa-resistant features: gait and balance, dysarthria, dysphagia, usually do not improve or may even worsen after DBS. Careful evaluation at the peak of optimal L-dopa benefit.
- Careful weighing of residual disability, and risks
- Tremor is an exception.
Cognitive evaluation

• Dementia is an absolute contraindication for surgery.
• There are no clear recommendations regarding mild cognitive impairment.
Motor outcome of PD patients with and without MCI

No differences between the two groups

Merola et al, J Neurol 2014
Cognitive outcome of PD patients with and without MCI

Comparing PD-MCI and normal cognition groups, no different neuropsychological outcomes were observed after the first year of surgery apart from Phonemic Verbal Fluency, which showed a more marked worsening in normal cognition subjects. This finding could be probably explained by the significant differences already evident at the baseline evaluation between the two groups: Phonemic

Survival curves for the risk of developing dementia: MCI versus normal patients

No patient became demented after 1 year

Merola et al, J Neurol 2014
Predictors of dementia and mortality

The baseline UPDRS-I score was found to be directly associated to the risk of developing dementia (HR: 1.466; \(p\): 0.043), while a trend was observed for older age at DBS surgery (HR: 1.1; \(p\): 0.093) and higher UPDRS-III score in ON condition (HR: 1.09; \(p\): 0.065). Gender, age at disease onset, other UPDRS subscores did not reveal a relevant predictive value.

The mortality rate was associated with older age at disease onset (HR: 1.17; \(p\): 0.016) and higher pre-surgical UPDRS-I and -II scores in OFF condition (HR: 1.43; \(p\): 0.049 and HR:1.13; \(p\): 0.033 respectively); higher score of UPDRS-III in ON condition showed a trend, not reaching the significance threshold (\(p\): 0.062).
Results: We identified 130 patients [71% male, mean age: 63 ± 9.1, mean PD duration: 10.7 ± 5.1]. At preoperative assessment, 60% of patients had multiple-domain MCI, 21% had single-domain MCI, and 19% had normal cognition. MCI presence and type as well as DRS performance did not affect immediate outcomes. Attention impairment predicted longer postoperative hospitalization (P = 0.0015) and showed a trend towards occurrence of postoperative confusion (P = 0.089).

For intermediate and long-term outcomes we identified 56 patients [73.2% male, mean age: 61.3 ± 9.6, mean PD duration: 10.6 ± 4.7]. Visuospatial impairment showed a trend towards less improvement in 6-month functional score (P = 0.0652), and 1-year QOL score (P = 0.0517).
Psychiatric evaluation

• Unstable psychiatric conditions (depression and psychosis): deferred surgery until they improve.
• Severe depression with suicidal ideation is an absolute contraindication
• GPi may be safer than STN for patients with either mild cognitive or behavioural issues
Physical condition

- Serious comorbidities: contraindication to DBS (bad risk-benefit ratio)

- Preoperative MRI:
  - Aside from obvious structural lesions, imaging findings alone should not be considered absolute contraindications to DBS
  - Severe cortical atrophy increases the risk of postoperative subdural hematomas.
  - Extensive atrophy and cerebral vasculopathy: conclusive data are lacking.
Expectations and social support

• Careful weighing of expected benefits

Change in PDQ-39 domain scores and satisfaction

Hasegawa et al, World Neurosurg 2014
Relationship between expected change and actual change in PDQ-39 scores

Relationship between expectations and satisfaction

Hasegawa et al, World Neurosurg 2014
Expectations and social support

• Careful weighing of expected benefits

• Careful evaluation of personal, professional, and social issues is fundamental. A great amount of cooperation and motivation from patients and caregivers is needed before, during and after surgery.

• The absence of a solid support from a caregiver should be considered a reason to preclude DBS.
When PD with motor complications should be considered for DBS?

• PD with motor complications refractory to optimal medical treatment important enough (severity/duration) to justify surgical risk.

• When is this? At the beginning of motor complications or after having tried been all/most other pharmacological strategies?

• Considering surgery sooner in the course of the disease would prevent or delay motor, social, and psychological disability.
Neurostimulation for Parkinson’s Disease with Early Motor Complications

Schuepbach NEMJ 2013

Randomized
STN 124
BMT 127
2 years
Blinded assessment
Neurostimulation for Parkinson’s Disease with Early Motor Complications

Schuepbach NEMJ 2013

<table>
<thead>
<tr>
<th>Primary end point</th>
<th>Between-Group Difference in Change from Baseline (95% CI)</th>
<th>P Value</th>
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<tbody>
<tr>
<td>PDQ-39 summary index score, intention-to-treat population</td>
<td>8.0±1.6 (4.2 to 11.9)</td>
<td>0.002</td>
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<tr>
<td>PDQ-39 summary index score, per-protocol population</td>
<td>8.1±1.7 (2.8 to 13.4)</td>
<td>0.02</td>
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<tr>
<th>Major secondary end points</th>
<th>mean ±SE</th>
<th>P Value</th>
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<tbody>
<tr>
<td>UPDRS-III score, without medication</td>
<td>16.4±1.4 (13.7 to 19.1)</td>
<td>&lt;0.001‡</td>
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<tr>
<td>UPDRS-II score during worst condition</td>
<td>6.2±0.9 (4.5 to 8.0)</td>
<td>&lt;0.001‡</td>
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<tr>
<td>UPDRS-IV score</td>
<td>4.1±0.4 (3.2 to 4.9)</td>
<td>&lt;0.001‡</td>
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<td>Time with good mobility and no troublesome dyskinesia (hr)§</td>
<td>1.9±0.8 (0.4 to 3.4)</td>
<td>0.01‡</td>
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<th>Minor secondary end points</th>
<th>mean ±SE</th>
<th>P Value</th>
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<tr>
<td>SCOPA-PS score</td>
<td>2.1±0.7 (0.4 to 3.9)</td>
<td>0.02</td>
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Motor outcomes

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<th>mean ±SE</th>
<th>P Value</th>
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<tr>
<td>UPDRS-III score, without medication and without assessment of rigidity, on blinded review</td>
<td>8.6±1.1 (6.4 to 10.9)</td>
<td>&lt;0.001</td>
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<tr>
<td>UPDRS-III score, with medication and stimulation</td>
<td>4.5±0.9 (2.7 to 6.4)</td>
<td>&lt;0.001</td>
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Impulse control disorders
ICD, was suppressed in six patients, improved in three and unchanged in one. UPDRS-III reduction in off =69.8%
Impulse control behaviors and subthalamic deep brain stimulation in Parkinson disease. Merola et al. J Neurol. 2017

- Over an average follow-up of 4.3 ± 2.1 years of chronic STN-DBS there was an overall trend for reduction in ICBs (from 17.3 to 12.7 %; p = 0.095) with significant improvement in hypersexuality (12-8.0 %; p = 0.047), gambling (10.7-5.3 %; p = 0.033), and DDS (4.7-0 %; p < 0.001). ICB remitted in 18/26 patients (69 %) and persisted in 8/26 (31 %); the latter group was characterized by higher levodopa equivalent daily dose.
Multidisciplinary team experienced in DBS

- movement disorders specialist
- neurosurgeon
- neuropsychologist
- Psychiatrist
- neuroradiologist
- nurses
Conclusions

- Best results in patients with excellent L-Dopa response, younger age, no or few axial non-L-Dopa-responsive motor signs, no or very mild cognitive impairment.
- Psychiatric comorbidities have to be controlled before surgery.
- Adequacy of expectations to the real outcomes, personal features of the patient and social support favor a better outcome.
- A thorough and personalized evaluation of the risk-benefit by a specialized multidisciplinary team is mandatory in all cases.