Bilateral subthalamic stimulation improves aspects of non-motor symptoms in Parkinson’s disease

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Aims
To study the effects of bilateral subthalamic nucleus (STN) deep brain stimulation (DBS) on motor, non-motor symptoms (NMS), and Quality of Life (QoL) in patients with Parkinson’s disease (PD) using validated composite measures.

Background
• STN-DBS well established for the treatment of motor symptoms and QoL in patients with PD
• No systematic study of effects of DBS on NMS (apart from neuropsychiatric)
• Methodological limitations of available studies (lack of objective clinician-based assessment and small cohort sizes of 10 subjects)
• We hypothesized: STN-DBS associated with a reduction of a range of NMS in patients with PD

Methods
• Design:
  – Multicenter, open, prospective, European registry study (Cologne, London, Manchester)
  – Longitudinal 6 months follow-up (6MFU)
• Subjects:
  – Diagnosis: British Brain Bank criteria
  – Screening for DBS treatment: MDS criteria
  – L-dopa response: > 30% (MedOFF/MedON)
• Clinical assessment:
  – Motor symptoms and NMS assessed preoperatively (clinical MedON) and postoperatively on 6MFU (clinical MedON/StimON)
  – LEDD calculation
• Scales:
  – Motor symptoms (UPDRS-III) and complications (UPDRS-IV)
  – Non-motor symptoms scale (NMSS, clinician-administered scale which tests for 9 domains of NMS and questionnaire (NMSQ, patient-based self-assessment scale)
• Quality of Life: PD Questionnaire-8 Summary Index (PDQ-8 SI)
• Statistics:
  – Wilcoxon-signed-rank-tests or Student’s paired t-test (when parametric test criteria were fulfilled), Bonferroni correction
  – Relative change (RC), effect size (ES) = Cohen’s d, number needed to treat (NNT) = [1 / % of patients who improved ≥ 1 SD]

Table 1 – Significant improvement of all outcomes

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>Mean</th>
<th>SD</th>
<th>Follow-Up</th>
<th>Mean</th>
<th>SD</th>
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<tbody>
<tr>
<td>NMSS-T</td>
<td>65.86</td>
<td>39.35</td>
<td>44.28</td>
<td>25.20</td>
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<tr>
<td>NMSSQ-T</td>
<td>10.67</td>
<td>8.83</td>
<td>7.71</td>
<td>4.07</td>
<td>0.0002</td>
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<tr>
<td>UPDRS-III</td>
<td>29.50</td>
<td>9.56</td>
<td>20.88</td>
<td>9.44</td>
<td>0.0000</td>
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<tr>
<td>UPDRS-IV</td>
<td>6.80</td>
<td>3.59</td>
<td>3.59</td>
<td>3.11</td>
<td>0.0000</td>
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<tr>
<td>PDQ-8 SI</td>
<td>33.84</td>
<td>17.87</td>
<td>25.11</td>
<td>16.15</td>
<td>0.0003</td>
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Table 2 – RC, ES and NNT

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<th>Baseline</th>
<th>Mean</th>
<th>SD</th>
<th>Follow-Up</th>
<th>Mean</th>
<th>SD</th>
<th>RC (%)</th>
<th>ES</th>
<th>NNT</th>
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<tr>
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<td>2.32</td>
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<td>UPDRS-III</td>
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<td>0.9</td>
<td>1.6</td>
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<tr>
<td>UPDRS-IV</td>
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<td>0.9</td>
<td>1.58</td>
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<tr>
<td>PDQ-8 SI</td>
<td>-25.8</td>
<td>0.49</td>
<td>2.15</td>
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Results
• Thus far: inclusion of 58 patients (34 male) aged 61.87 years (+/-7.97) with long histories of PD (10.59 ±4.36 yrs.) and moderate to high LEDD (1163.75 ±526.79) at baseline (significant improvement on 6MFU: 624.88 ±1345.15)
• Significant improvement of all outcomes (s. tab. 1) and some NMSS domains: sleep/fatigue, perceptual problems/hallucinations, urinary and miscellaneous (s. fig. 1 and 2)
• Medium ES: NMSS-T & NMSQ-T, large ES: UPDRS-III & -IV, small ES: PDQ-8 SI (s. tab. 2)

Discussion/Conclusion
• Bilateral STN-DBS improves NMS burden
• At least two ways of action possible:
  – Direct modulation of basal ganglia-thalamocortical loops (activation of, e.g., autonomic centers of the thalamus, lateral frontal, and anterior cingulated cortex)
  – Spreading of electric current to regions in proximity of the STN (modulation of, e.g., the pedunculopontine nucleus)
• Influence of LEDD reduction being investigated
• Further studies needed to compare patient-related outcomes (PDO) to amorphine and intrajejunal l-dopa infusional therapies

References

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Figure 1 – Radar chart of NMSS domains. NMSS domain scores normalized with respect to baseline values per subject. Blue area: baseline, copper area: 6MFU data. A bigger copper area reflects an improvement of the NMSS domain (computation: 2 - 6MFU/baseline).

Figure 2 – Box plots of NMSS domains. Significantly improved domains are marked with a black star.