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

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Endorsed by International Parkinson and Movement Disorder Society

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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[1,2]
- No systematic study of effects of DBS on NMS (apart from neuropsychiatric)
- Methodological limitations of available studies (lack of objective clinician-based assessment[3] / small cohort sizes of 10 subjects[4,5]).
- 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[6]
- 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)
  - QoL: 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 ≥½ SD])[7]

Table 1 – Significant improvement of all outcomes

	Baseline		Follow-Up		
	Mean	SD	Mean	SD	p
NMSS-T	65,86	39,35	44,28	25,20	0,0000
NMSQ-T	10,67	4,83	7,71	4,07	0,0002
UPDRS-III	29,50	9,56	20,88	9,44	0,0000
UPDRS-IV	6,80	3,59	3,59	3,11	0,0000
PDQ-8 SI	33,84	17,87	25,11	16,15	0,0003

Table 2 – RC, ES and NNT

	RC (%)	ES	NNT
NMSS-T	-32,77	0,55	2,32
NMSQ-T	-27,68	0,61	2,1
UPDRS-III	-29	0,9	1,6
UPDRS-IV	-47,31	0,9	1,58
PDQ-8 SI	-25,8	0,49	2,15

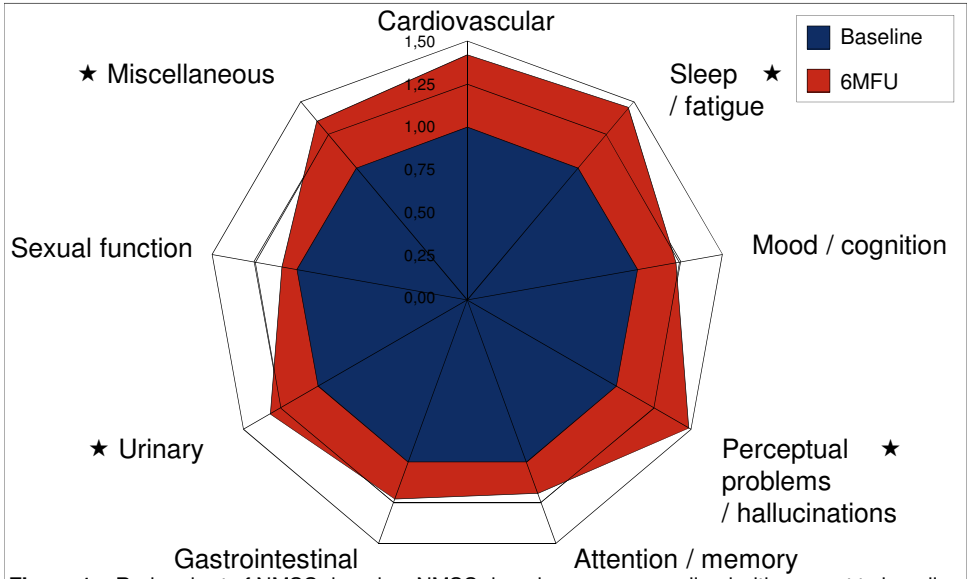

Figure 1 – Radar chart of NMSS domains. NMSS domain scores normalized with respect to baseline values per subject. Blue area: baseline, copper area: 6MFU data. A bigger copper area reflects an improvement of the NMSS domain (computation: 2 - 6MFU/baseline).

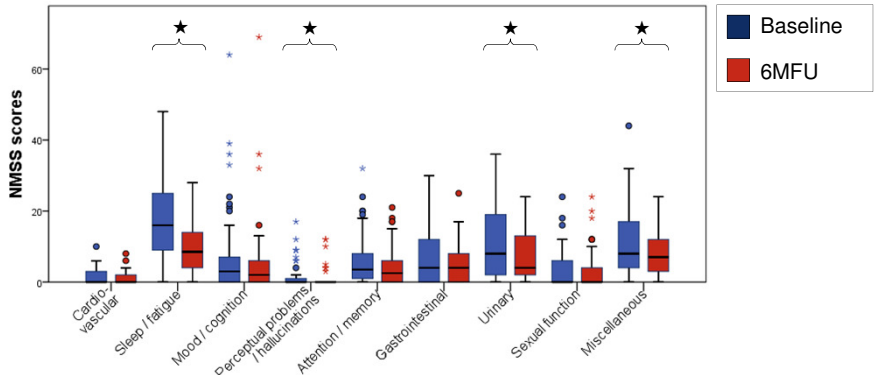

Figure 2 – Box plots of NMSS domains. Significantly improved domains are marked with a black star.

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 (1103.75 ±526.79) at baseline (significant improvement on 6MFU: 624.88 ±345.15)
- 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)[7]

Discussion/Conclusion

- Bilateral STN-DBS improves NMS burden
- At least two ways of action possible:
  - Direct modulation of basal ganglia-thalamo-cortical 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 (PRO) of DBS to apomorphine and intrajejunal l-dopa infusional therapies

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