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Short communication

Stimulation challenge test after STN DBS improves satisfaction in Parkinson's disease patients

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ABSTRACT

Objective: Although subthalamic Deep Brain Stimulation (STN DBS) is proven effective in improving symptoms of Parkinson's Disease (PD), previous literature demonstrates a discrepancy between objective improvement and patients' perception thereof. We aimed to examine whether postoperative stimulation challenge tests (SCT) alters patients' satisfaction after STN DBS for PD.

Methods: Fifty-four PD patients underwent preoperative levodopa challenge tests and were routinely invited for SCT 1-2 years postoperatively. SEverity of predominantly Nondopaminergic Symptoms in PD (SENS-PD) scores quantified non-dopaminergic disease severity. Motor functioning was quantified using Movement Disorders Society Unified Parkinson's Disease Rating Scale (MDS-UPDRS) III scores; a ratio between conditions ON and OFF (preoperative Med-ON vs. Med-OFF, and postoperative Med-ON/Stim-ON vs. Med-OFF/Stim-OFF) reflected treatment benefit. 'Global Impression of Change' (GIC) and 'Global Satisfaction with Surgery' (GSS) Likert scales were filled out before and immediately after SCT.

Results: Postoperative Med-ON/Stim-ON severity was lower than preoperative ON severity. Disease severity scores were not different between assessments. GIC and GSS scores were higher after SCT versus before (GIC: Z = -3.80, r = 0.37, subjects indicating maximum scores before SCT: 32.1%, after SCT: 57.1%; GSS: Z = -3.69, r = 0.35, maximum scores before SCT: 25.0%, after SCT: 46.4%). Higher non-dopaminergic disease severity was associated with lower GIC and GSS scores (GIC: OR 1.2 (95%CI 1.0–1.3); GSS: OR 1.2 (95%CI 1.1–1.3), while motor-scores and magnitude of DBS-effects were not.

Conclusion: SCT improves patients' satisfaction and is recommended especially in case of suboptimal subjective valuations. This information should be considered in clinical practice and in the context of clinical trials.

1. Introduction

Subthalamic Deep Brain Stimulation (STN DBS) is an effective treatment for patients with Parkinson's Disease (PD) with motor complications refractory to medication. STN DBS yields an average motor improvement of approximately 40%, and reduces medication requirements by approximately 50% [1]. However, previous literature demonstrates a discrepancy between objective improvement and patients' perception thereof [2], with several patients reporting mixed or negative valuations in terms of postoperative satisfaction [2,3].

Many centres perform a stimulation challenge test (SCT) during DBS follow-up to evaluate the benefit of either STN DBS alone or combined with medication, compared to the benefit provided by medication alone. This procedure is considered a standard quality check to verify efficacy of STN DBS against the benchmark of levodopa response, and identify poor responders [4,5]. However, this test is time-consuming and bothersome for some patients. Hence, SCTs are sometimes performed only when clinically indicated, in case of suboptimal responses or complex side-effects.

We hypothesized that, in addition to the above-mentioned benefits, switching the stimulator OFF after overnight withdrawal from dopaminergic medication makes patients more aware of the severity of their motor symptoms in a practically defined OFF-state and allows them to compare this directly to their motor functioning during the ON-state

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Table 1
Clinical characteristics.

	Preoperative	Postoperative	95%CI of difference [c]
N		54	
Female sex (% (n))		32 (18)	
Age (years) [a]		62.7 (7.8)	
Follow-up (months) [a]		16.7 (5.5) (range 11–28)	
MDS-UPDRS-III Med-ON [a] (Med-ON/Stim-ON) [b]	20.5 (9.3)	17.5 (7.8)	0.2–5.7
MDS-UPDRS-III Med-OFF [a] (Med-OFF/Stim-OFF)	45.1 (12.7)	47.9 (9.6)	−6.6–0.9
MDS-UPDRS-III Med-OFF/Stim-ON [a]		25.7 (9.1)	15.5–23.2 [d]
Ratio MDS-UPDRS-III ON over OFF (Med-ON/Stim-ON over Med-OFF/Stim-OFF) [a, b]	0.45 (0.15)	0.37 (0.15)	0.04–0.14
SENS-PD [a]	11.4 (4.6)	12.1 (5.6)	−2.3–0.7

SENS-PD: SEverity of predominantly Nondopaminergic Symptoms in PD; MDS-UPDRS: Movement Disorders Society Unified Parkinson's Disease Rating Scale.
[a] Mean (SD).
[b] Three patients used no medication after DBS, MDS-UPDRS-III scores in the Med-OFF/Stim-ON condition were then used.
[c] Computed using generalized linear models (repeated measures).
[d] Relative to preoperative MDS-UPDRS III Med-ON.

afterwards.

The aim of this study was to examine whether postoperative ON-OFF testing alters patients' perceived impression of DBS effects and improves satisfaction after surgery.

2. Methods

2.1. Study participants

Seventy-four consecutive patients who underwent STN DBS surgery between September 2015 and April 2019 at the Leiden University Medical Centre/HAGA Teaching Hospital received routine preoperative levodopa challenge tests and were invited for a SCT 1-2 years postoperatively in the context of routine follow-up examinations. A formal ethical evaluation was waived by the local medical ethics committee as all data originated from standard clinical procedures.

2.2. Outcome measures

PD patients were examined after overnight withdrawal from dopaminergic medication in the following sequence [1]: Stimulation 'ON' (Stim-ON)/Medication 'OFF' (Med-OFF) [2], Stim-OFF/Med-OFF [3], Stim-ON/Med-ON [4], Stim-OFF/Med-ON. After the Med-OFF conditions, patients were given a supra-threshold dosage (dispersible Levodopa/Benserazide) of 120% of the morning levodopa equivalent dose. Between conditions [1,2], and between [3,4], 15 min were provided to adjust to the altered settings; 60 min were required between conditions [2,3] to ensure maximum medication benefit.

The Movement Disorders Society Unified Parkinson's Disease Rating Scale (MDS-UPDRS) III scores were used to quantify motor functioning [6]. A ratio between conditions ON and OFF (i.e. preoperative Med-ON vs. Med-OFF, and postoperative Med-ON/Stim-ON vs. Med-OFF/Stim-OFF) was used to reflect treatment benefit. The SEverity of predominantly Nondopaminergic Symptoms in PD (SENS-PD) scale [7] was used to assess nondopaminergic disease severity during Stim-ON/Med-ON. The SENS-PD scale is a composite score comprising six predominantly non-dopaminergic domains: postural instability and gait difficulty (PIGD), psychotic symptoms, excessive daytime sleepiness, autonomic dysfunction, cognitive impairment, and depressive symptoms. This scale, validated for PD patients, includes symptoms typically unresponsive to dopaminergic medication and may more accurately reflect progression of an underlying disease-mechanism than dopamine-sensitive measures [8], particularly in PD patients sensitive to motor-fluctuations such as the DBS population. Higher scores on all scales indicate greater impairment.

Four weeks prior to testing, patients filled out two 7-point Likert scales at home: 'Global impression of change' (GIC) ranging from 'symptoms worsened a lot' to 'symptoms improved a lot', and 'Global satisfaction with surgery' (GSS) ranging from 'very dissatisfied' to 'very satisfied'. Both Likert scales were filled out again immediately after the SCT.

2.3. Statistical analysis

Symptom severity scores before and after DBS were compared using Repeated Measures General Linear Models. Responses in GIC and GSS were compared before and after SCT using Wilcoxon signed rank tests. Wilcoxon test statistics were approximated towards a standard normal distribution to give a standardized Z statistic, which was subsequently divided by the square root of the sample size to provide an effect size. The critical cut-off for Z statistics for $\alpha = 0.05$ is 1.96, and for $\alpha = 0.01$ is 2.58. The effect of symptom severity (either MDS-UPDRS III or SENS-PD scores) on GIC and GSS response was assessed using ordinal regression (Polytomous Universal Models); responses were pooled on three levels for analytic purposes (0 = very satisfied/a lot improved (i.e. optimal responses), 1 = satisfied/improved, 2 = slightly satisfied/slightly improved or lower scores). The assumption of proportional odds was confirmed by checking the individual multinomial logistic regression coefficients. All analyses were performed using IBM SPSS 25 Software (SPSS Inc., Chicago, Illinois, USA). De-identified data may be shared upon request.

3. Results

Fifty-four patients (32% female, mean ± SD age 62.7 ± 7.8 years) were included. Reasons for exclusion were: refusal of the SCT (n = 15), forgotten to withdraw dopaminergic medication (n = 1), patient moved (n = 1), previous SCT elsewhere (n = 1), severe comorbidity unrelated to this study (n = 1, malignancy, not invited to participate), and language barrier (n = 1). Excluded patients were not demographically different.

Postoperative (mean (SD)) Med-ON/Stim-ON scores (17.5 (7.8)) were lower than preoperative ON-scores (20.5 (9.3)). DBS markedly reduced MDS-UPDRS-III scores postoperatively (mean (SD) Med-OFF/Stim-ON 25.7 (9.1), Med-OFF/Stim-OFF 47.9 (9.6)). MDS-UPDRS-III OFF-severity was not different before and after surgery, neither was non-dopaminergic disease severity (Table 1). Both GIC (optimal response (i.e. 'my symptoms improved a lot') before SCT: 32%, after SCT: 57%) and GSS scores (optimal response (i.e. 'very satisfied with surgery) before SCT: 25%, after SCT: 46%) were higher after SCT (GIC: $Z = 3.80$, $r = 0.37$; GSS: $Z = 3.69$, $r = 0.35$) (Fig. 1), demonstrating a medium-to-large effect according to Cohen's Criteria.

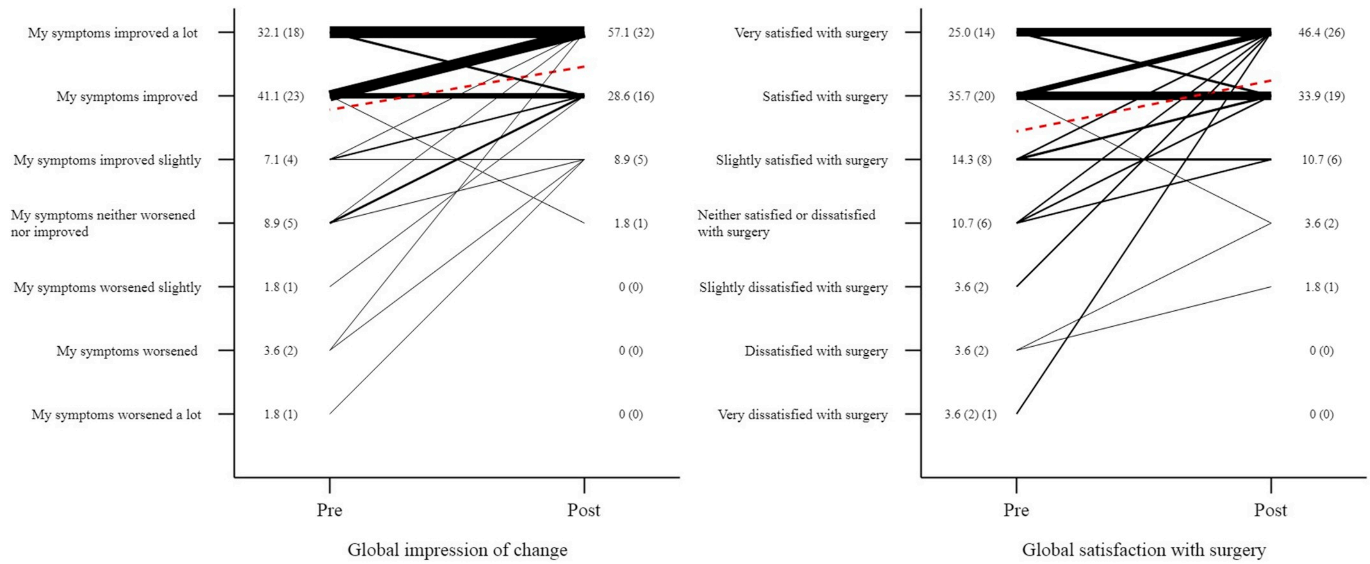

Fig. 1. Global Impression of Change and Global Satisfaction with Surgery before and after stimulation challenge tests Seven-point Likert-scales shown on the Y-axes, before and after stimulation challenge tests. The thickness of the lines reflects the number of patients. The red dashed lines reflect the pre- and postoperative averages (Global Impression of change: Z = -3.800, Global Satisfaction with Surgery: Z = = -3.685). The proportions per response option are denoted next to the lines, responses are shown as % (n).". (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

Greater postoperative non-dopaminergic severity was associated with lower GIC and GSS scores (GIC: OR (95%CI) 1.2 (1.0–1.3); GSS: OR (95%CI) 1.2 (1.1–1.3)). Motor severity, either Med-OFF/Stim-OFF, Med-ON/Stim-ON, or a ratio reflecting motor improvement produced by combined stimulation and medication with respect to postoperative OFF, were not associated with GIC and GSS responses after SCT (supplementary table e-1).

4. Discussion

In this study we show that patients are generally satisfied after STN DBS and that satisfaction and subjective perception of benefit after surgery increase after a postoperative SCT. These results could be driven by a tendency to forget the experienced preoperative motor severity, since patients generally no longer experience motor fluctuations to the same degree as before surgery. In a previous study, where PD patients were asked to recall their preoperative QoL scores six months after surgery, they substantially overestimated their preoperative functioning [9], indicating impaired perception of the postoperative improvement due to recall bias. Experiencing the OFF condition during the SCT confronts patients with their actual motor severity and provides a more accurate perception of their disease severity and the relief that DBS has brought. These results may have clinical utility to improve patient awareness and thus satisfaction, particularly for patients who consider themselves dissatisfied with the results of DBS. Our analyses included patients who reported optimal satisfaction and could by definition either remain optimally satisfied after SCT, or regress towards a lower level of satisfaction, whereas including only suboptimally satisfied patients would have provided even larger effect sizes.

In the Netherlands, performing SCTs at least once postoperatively (typically around 1-year follow-up) is considered routine clinical practice to estimate the magnitude of stimulation-induced motor benefits and accordingly optimize treatment when needed [10]. Our study demonstrates clear patient benefits in terms of improved postoperative satisfaction as well, and provides further arguments in favour of postoperative SCTs.

Strikingly, the magnitude of motor improvement due to DBS was not correlated to either GIC or GSS, indicating that the exact amount of improvement does not influence perception of change or satisfaction. This is in line with previous studies [2,3] that demonstrated no correlation between subjective perception of outcome and objective motor improvement. We speculate that patients may have different, possibly unrealistic, expectations of DBS surgery, which may contribute to perceiving the overall post-operative situation as less satisfactory [3,11]. On the opposite, we found that greater non-dopaminergic disease severity correlated with lower GSS and GIC scores. Previous literature indicated that non-dopaminergic disease severity is mostly unaffected by DBS [12], which is confirmed by our results, and that non-motor symptoms are important determinants of quality of life in PD [13]. We speculate that the stimulation-induced relief of severe motor fluctuations shifts patients' focus to those aspects of the disease that are unresponsive to STN DBS. Although this was not systematically investigated, several patients indeed reported non-dopaminergic symptoms such as cognitive impairment and balance impairments to be more prominent post-surgery.

In this study we show, for the first time, that use of a SCT can improve postoperative satisfaction in a cohort of consecutive patients. A four-week interval was considered sufficient to ensure that patients would not exactly recall their initial responses to GIC and GSS questionnaires. Limitations include the substantial number of patients that refused participation (20%, n = 15). Reasons for refusal were not systematically documented, but included unavailability, difficulty to reach the centre, and anxiety at the idea of switching the stimulator off. Another consideration is the possibility of 'participant reactivity' - where patients may be prone to please the investigator by providing more favourable responses after personal contact compared to the situation prior to the SCT, especially after prolonged patient-caregiver relationships. This factor was likely limited in our study, as the treating neurologist was not involved in the ON-OFF testing.

A SCT provides a reliable method to quantify motor improvement after DBS, but is also useful to increase patients' postoperative satisfaction. In addition, this information should be taken into account when designing clinical trials with patients' satisfaction as outcome. We recommend to use the SCT as part of the routine follow-up after DBS, especially in case of suboptimal postoperative satisfaction. Future research should identify whether increases in GIC and GSS after a SCT are sustained or whether this fades over time.

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Declaration of competing interest

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.parkreldis.2019.10.014.

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