RESEARCH PAPER

Patients' expectations of deep brain stimulation, and subjective perceived outcome related to clinical measures in Parkinson's disease: a mixed-method approach

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ABSTRACT

Objective To study patients' expectations of subthalamic deep brain stimulation (STN-DBS) and their subjective perceived outcome, by using qualitative and quantitative methods in Parkinson's disease (PD).

Methods PD patients were prospectively examined before and 3 months after surgery. Semistructured interviews regarding preoperative expectations and postsurgical subjective perceived outcome were conducted. These were analysed using content analysis. For statistical analyses, patients were classified according to their subjective perceived outcome, resulting in three different subjective outcome groups (negative, mixed, positive outcome). The groups were used for multiple comparisons between and within each group regarding motor impairment, quality of life (QoL), neuropsychiatric status and cognitive functioning, using standard instruments. A logistic regression analysis was conducted to find predictors of subjective negative outcome. Receiver operating characteristic curves were used to analyse cut-off scores for predictive tests.

Results Of the 30 PD patients participating, 8 had a subjective negative outcome, 8 a mixed and 14 a positive outcome. All groups significantly improved in motor functioning. Patients with subjective negative outcome were characterised by preoperative unrealistic expectations, no postsurgical improvement in QoL, and significantly higher presurgical and postsurgical apathy and depression scores. Higher preoperative apathy and depression scores were significant predictors of negative subjective outcome. Cut-off scores for apathy and depression were identified.

Conclusions The mixed-method approach proved useful in examining a patient's subjective perception of STN-DBS outcome. Our results show that significant motor improvement does not necessarily lead to a positive subjective outcome. Moreover, PD patients should be screened carefully before surgery regarding apathy and depression. (DRKS-ID: DRKS00003221).

INTRODUCTION

Parkinson's disease (PD) is a neurodegenerative disorder characterised by a variety of typical motor and non-motor impairments. While bilateral subthalamic deep brain stimulation (STN-DBS) significantly improves the motor difficulties,[1] there is an ongoing discussion on how STN-DBS influences behavioural and cognitive symptoms.[2 3] PD-specific quality of life (QoL), measured with the Parkinson's Disease Questionnaire-39 (PDQ-39),[4] is an often used outcome parameter for STN-DBS. By using this scale, a significant improvement of QoL under STN-DBS has been demonstrated.[1 5] This finding stands in contrast with reports on patients who perceive their outcome as disappointing, even though they had experienced significant motor benefits and improvement in QoL.[6] More in-depth examinations of QoL following STN-DBS have revealed a predominant improvement of physical domains, while mental subscales remain stable or even worsen.[7] The clinical need of identifying patients who are at higher risk of perceiving their postoperative outcome as unsatisfactory has attracted more attention lately.[6 8 9] By focussing on the patient, individual realistic and unrealistic expectations can be considered. To gain information about this, the combination of qualitative patient interviews with standard measures for a better understanding of subjective outcome might be a successful approach.[10 11] Concerning research on STN-DBS in PD patients, only a few studies used well-appreciated standard instruments (eg, the PDQ-39), as well as supplementary semistructured or open in-depth interviews to explore patient's subjective perception of DBS therapy.[6 12]

Predictors or influencing factors of psychosocial outcome and improved QoL after STN-DBS have been tried to be identified by using standard scales[13–16] or modified standard scales.[9] Postsurgical improved QoL has been linked to preoperative cumulative daily off time,[13] high l-dopa response,[14] changes in depression and anxiety,[13] and better cognitive functioning.[16] Furthermore, neuropsychiatric symptoms, such as depression and apathy, have a major impact on QoL in PD.[17 18]

In this study, we used a mixed-method approach of qualitative and quantitative methods to examine the patient's expectations of STN-DBS and perceived outcome at 3 months after surgery. As primary goal, we intended to analyse the number of patients who perceived their subjective outcome as negative, mixed, or positive. Secondarily, we sought to characterise differences between these patients by using standard clinical measures. Finally, we aimed to examine the predictive value

of preoperative scores for patients with subjective negative outcome.

METHODS

Patients

We prospectively examined patients with idiopathic PD, recruited from the Department of Neurology, University Hospital Cologne, before surgery (baseline) and 3 months after STN-DBS (3 mFU). All patients met the criteria for STN-DBS treatment according to the guidelines of the German Neurological Society.[19] Included were patients between 40 and 75 years of age who had medication refractory motor symptoms despite an unequivocal response to l-dopa in the off-state.

Patients with dementia (DemTect-score <9[20] and MMSE-score <25[21]), severe psychiatric or additional neurological disorders were excluded. The study was approved by the ethics commission of the University Hospital of Cologne, and all patients gave written informed consent. Furthermore, the study was registered at the German Clinical Trials Register (DRKS-ID: DRKS00003221).

Procedure

As part of the preoperative DBS screening routine in Cologne, all patients were examined by a movement disorder neurologist, a neurosurgeon, a psychiatrist and a neuropsychologist. These experts mutually approved DBS surgery for all patients. For the purpose of this study, patients were additionally interviewed, examined and cognitively tested 6 weeks to 3 days prior to surgery, and 3 months after implantation of the electrodes, by two trained clinical neuropsychologists (F.M. & C.L.).

DBS surgery

All patients underwent STN-DBS surgery at the department for Stereotaxy and Functional Neurosurgery, University Hospital Cologne. Preoperative stereotactic CTs and 1.5T MRIs determined the coordinates of the target structure. Electrodes (standard model 3389; Medtronic, Minneapolis, Minnesota, USA) were implanted bilaterally in the STN under local anaesthesia. Microelectrode recordings and macroelectrode test stimulation determined the optimal implantation area in all patients. To monitor the final location of the electrodes, intraoperative and postoperative stereotactic x-rays were projected on the preoperative stereotactic MRI scans. The electrodes were connected to a pulse generator (Kinetra or Activa RC/PC; Medtronic, Minneapolis, Minnesota, USA) and implanted in the subclavicular area under general anaesthesia. Postoperatively, patients were hospitalised for up to 10 days, according to the standards of care of our centre. STN-stimulation was turned on 3–5 days after surgery on very low amplitudes (0.3–0.5 V, 60 µs, 130 Hz), allowing for immediate microlesion effects to wear off. The main microlesion effect decreased around day 6–10 after surgery. Stimulation amplitude was slowly increased accompanied by a stepwise reduction of antiparkinsonian medication.

Semistructured interviews

In addition to the quantitative data collection, we intended to gain knowledge about the patient's subjective perspective on their disease and DBS. We developed an interview guideline including various different domains that may have an impact on a patient's life with PD and DBS. Preoperatively, the interview focus was set on the following topics: subjective expectations from DBS, presurgical motor, emotional, social, behavioural and cognitive functioning, activities of daily living and QoL. At 3 mFU, the interview contained questions about the impact of DBS on the same domains. The interviews were pretested with five patients to prove understanding and mental resilience. All 60 interviews (30 baseline and 30 3 mFU) were recorded, transcribed and categorised by two independent trained coders (N. H. & C.L.). Categorisation was conducted according to Mayring's theory-based content analysis,[22 23] which is a widely used method in health research. For the purpose of this study, categories were analysed with respect to the patient's expectations from DBS before surgery, and the patient's perception of their personal outcome at 3 mFU. At baseline, all expectations that were stated by each patient throughout the interview were collected. At 3 mFU, all statements regarding the impact of DBS on the patient's life, such as improved or worsened symptoms or unexpected changes, were collected for each patient. Thereafter, the number of positive and negative statements related to DBS at 3 mFU was separately summed up, and a quotient was calculated by dividing the number of positive statements by the number of negative statements for each patient (eg, 12 positive divided by 3 negative statements is 4). Neutral responses, such as 'no change' answers, were not considered. Finally, patients were grouped according to their subjective outcome quotient: group 1 included patients with a quotient of ≤ 0.5, representing patients who had at least twice as many negative statements than positive statements. Therefore, the first group contained patients who perceived their subjective outcome as mainly negative (group-neg). The second group included patients with a quotient between >0.5 and <2.0, representing patients who considered their outcome as mixed positive and negative (group-mix). The third group contained patients with a quotient of ≥ 2, representing patients who had at least twice as many positive statements than negative statements and, thus, perceived their subjective outcome as mainly positive (group-pos).

Clinical rating scales

Motor performance was evaluated using the Unified Parkinson's Disease Rating Scale part III (UPDRS-III)[24] while on and off l-dopa. Off-state was defined as motor impairment following at least 12 h absence of antiparkinsonian medication, while on-state was the patient's best motor response to first l-dopa dose (at least 200 mg or 1.5 times the individual morning dose) after the off-state. Long-acting dopamine agonists were stopped 72 h prior to off-examination. Also, the l-dopa equivalent daily dose (LEDD)[25] was determined. At 3 mFU, patients were tested on the UPDRS-III with stimulation on and medication off.

Regarding neuropsychological testing, all patients were examined on the digit span forwards and backwards of the Wechsler memory scale,[26] phonemic verbal fluency task (letter B, M, S),[27] and the brief test of attention (BTA).[28]

To determine patient's QoL, the Parkinson's disease questionnaire-39 (PDQ-39)[4] was given to all patients at baseline (PDQ-base) and at 3 mFU (PDQ-3 mFU).

With respect to mood examination, the following tests were conducted: apathy evaluation scale (AES, range: 18–72),[29] Beck depression inventory-2 (BDI-2, range: 0–63),[30] self-report manic inventory (SRMI, range: 0–48),[31] and the state subscale of the State trait anxiety inventory (STAI-state, range: 20–80).[32] For all four scales, higher scores represent more severe symptoms.

Monitoring

All data was transferred into a SPSS database and independently controlled by the PI. To ensure data quality, the Cologne Centre for Clinical Studies (ZKS Cologne), an independent clinical

research organisation, monitored 20% of the data. The data quality was rated as very high by the ZKS Cologne.

Statistical analysis

All statistical analyses were conducted using IBM SPSS V.20.0 (SPSS, Chicago, Illinois, USA). Level of significance was set at 0.05. To ensure standard treatment outcome, the whole sample was compared regarding baseline and 3 mFU UPDRS-III-scores and PDQ-scores using paired samples t tests (assumptions for parametric distribution were fulfilled).

All patients were classified according to their individual outcome quotient into three subjective outcome groups (group-neg/-mix/-pos).

Group differences

First, the three groups were compared concerning presurgical expectations, and postoperative positive and negative statements using the χ^2 test or the Fisher's exact test when one value was not available. Thereafter, for clinical tests, differences between the subjective outcome groups were analysed separately at baseline and at 3 mFU with one-way ANOVAs for parametric variables and with the Kruskall–Wallis H test for nonparametric variables. Significant p values were α-corrected by dividing 0.05 by the number of tests for each analysis. Posthoc Bonferroni test was used to further specify significant group differences. To compare baseline and 3 mFU data within each group, paired samples t tests were computed. Neurological data, neuropsychological measurements, QoL, and mood scales were analysed separately.

Predictors of subjective negative outcome

A binary logistic regression model was used (forward; LR method), to analyse predictors for group-neg. For this analysis, we only included test scores which showed significant group differences between group-neg and group-mix or/and group-pos at baseline. Because we mainly focussed on patients of group-neg, the dichotomised dependent variable comprised group-neg versus a cluster of group-mix and group-pos.

Exploratively, to determine possible clinically relevant cut-off scores for significant predictors, receiver operating characteristic (ROC) curves were conducted and the area under the curve (AUC) was calculated. Also, sensitivity and specificity were examined for each cut-off score.

RESULTS

Sample

Thirty patients with PD were enrolled in this study. Mean age of all patients (18 men/12 women) was 61.20±8.65 with an average disease duration of 11.97±6.79 years. Standard treatment outcome was classified as good, as patient's baseline UPDRS-III off-score (42.48±13.07) significantly improved under stimulation at 3 mFU (UPDRS-III stimulation on and medication off: 26.76±13.86; p<0.001, paired samples t test). Similarly, the PDQ-base improved from 37.01±16.54 for all patients to PDQ-3 mFU 26.47±14.94 (p<0.001, paired samples t test).

According to the subjective outcome quotient, 8 patients (26.67%) were assigned to group-neg, 8 patients (26.67%) were classified as group-mix, and 14 patients (46.66%) were assigned to group-pos (see table 1). Regarding the three subjective outcome groups, no significant differences were found for demographic data and global cognitive state.

Expectations from DBS and subjective outcome reports

All patients expected an improvement of motor symptoms (see figure 1) while all other expectations varied between the subjective outcome groups. Group-neg patients significantly more often expected 'improvement of mental state' compared with the other two groups (p=0.028). Moreover, although not significant, group-neg more often expected 'more socialising' or 'improvement of partnership', which can usually not be directly improved by STN-DBS (for details see online supplementary). With respect to patient's subjective outcome at 3 mFU (see figures 2 and 3), all patients of group-mix and group-pos experienced 'improved motor symptoms' which was significantly more often compared with group-neg (p=0.010). Also, all patients of group-pos, and 87.5% of group-mix named QoL as being improved, which was significantly more often compared with group-neg (p<0.001). Regarding negative statements, group-neg significantly more often reported a worse mental state than the other two groups (p=0.002) (see online supplementary data).

Subjective outcome group differences at baseline and 3 mFU

Results of the outcome group differences are depicted in tables 2 and 3.

Neurological data

Corrected levels of significance were determined for baseline (p=0.017; 0.05 divided by 3) and 3 mFU (p=0.025; 0.05

Table 1 Group classification, demographic data, and global cognitive functioning of the three outcome groups

	Group-neg	Group-mix	Group-pos	F/χ^2	p Value
N (%)	8 (26.67)	8 (26.67)	14 (46.66)		
Number of positive statements	1.88±1.25	5.75±1.67	8.71±1.86	42.971[a]	<0.001
Number of negative statements	7.25±1.91	5.13±2.23	1.29±1.49	29.875[a]	<0.001
Subjective outcome quotient	0.26±0.14	1.23±0.37	6.45±3.48	21.009[a]	<0.001
Age (yr)	60.50±7.19	58.88±9.33	62.93±9.24	0.577[a]	0.568
Sex (m/f)	5/3	3/5	10/4	2.470[b]	0.291
Education (yr)	11.75±4.71	11.38±4.44	11.29±4.20	0.006[b]	0.997
Disease duration (yr)	11.00±4.78	14.38±8.14	11.14±7.07	0.672[a]	0.519
Mini mental state exam	28.88±0.64	29.50±1.07	28.36±1.98	3.178[b]	0.204
DemTect	13.38±2.92	14.75±3.65	15.57±2.41	1.449[a]	0.252

Values are means (±SD) unless stated otherwise. p Values by [a] ANOVA (F) or [b] Kruskall–Wallis H-test (χ^2).
N, number of patients; group-neg, subjective outcome negative; group-mix, subjective outcome mixed; group-pos, subjective outcome positive.

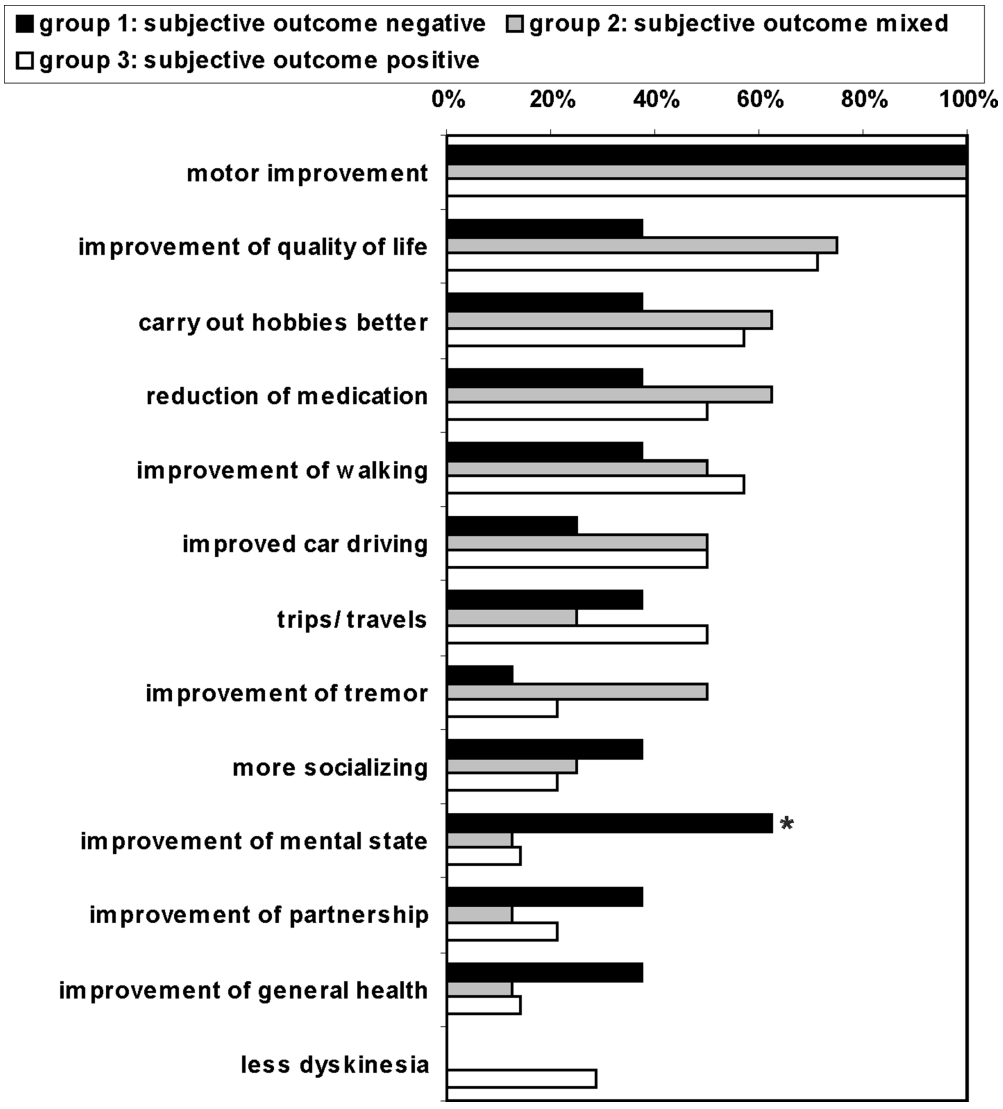

Figure 1 Patient's expectations concerning STN-DBS for the three groups. All patients were asked to name their expectations regarding STN-DBS in a semistructured interview. Expectations were sorted according to their frequency of being stated by all patients and then classified concerning the three subjective outcome groups. Included were only such statements which were named by >25% of patients within one of the three groups. * Significant difference between the subjective negative outcome group and the other two groups.

divided by 2). No significant group differences were found for UPDRS-III on-score and off-score, and LEDD at baseline and 3 mFU. Within the groups, paired samples t tests revealed significant improvement of UPDRS-III scores (baseline med off vs 3 mFU stim on/med off) and reduced LEDD for each group.

Neuropsychological measures

Applying corrected levels of significance (baseline and 3 mFU: p=0.0125) no group differences were found in any cognitive test results. Within the groups, verbal fluency significantly worsened in group-neg. All other within-group changes were not significant.

Quality of life

No significant group difference was found for the PDQ-base, although group-neg had the worst QoL. At 3 mFU, PDQ-scores were significantly higher in group-neg compared with group-mix and group-pos. Within-group changes revealed that QoL only significantly improved in group-mix and group-pos.

Mood scales

One-way ANOVAs (see table 3) showed significant group differences on the AES and BDI-2 at baseline and 3 mFU applying a corrected level of significance of 0.0125 (0.05 divided by 4 for both time points). Apathy scores were significantly worse in group-neg compared with group-mix and group-pos, verified by posthoc Bonferroni test, at baseline and 3 mFU. Depression scores were significantly higher in group-neg compared with group-mix at baseline, and significantly higher compared with group-mix and group-pos at 3 mFU. State anxiety of the STAI tended to be higher in group-neg compared with group-mix at baseline, and higher in group-neg compared with group-mix and group-pos at 3 mFU. No significant result was found for the SRMI at baseline and 3 mFU. Paired samples t tests showed that only in group-pos, depression significantly improved at 3 mFU.

Predictors of subjective negative outcome

Baseline group comparisons revealed AES-scores and BDI-2-scores as showing significant differences between group-

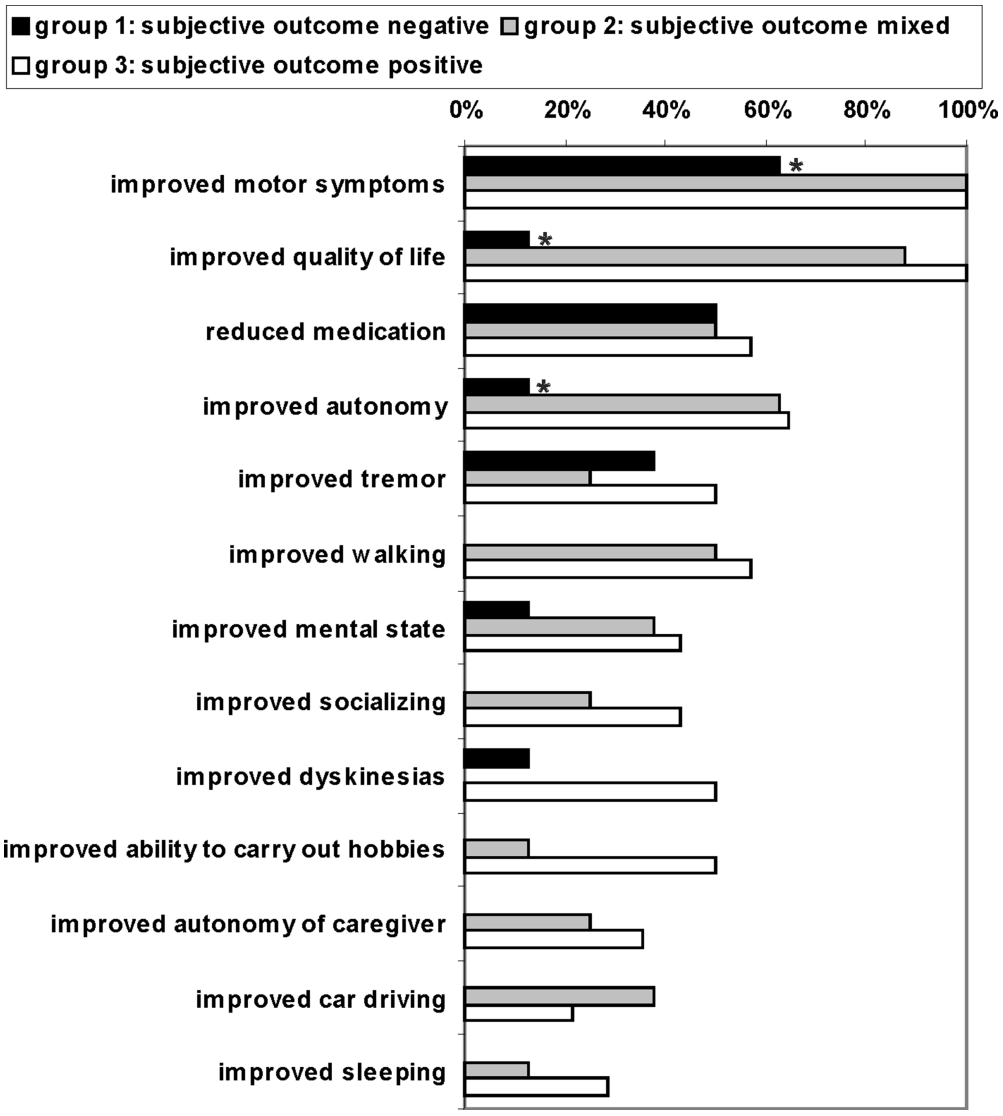

Figure 2 Positive statements at 3 months after STN-DBS for the three groups. All patients were asked to reflect their subjective outcome regarding STN-DBS in a semistructured interview. Positive statements were sorted according to their frequency of being stated by all patients, and were then classified concerning the three subjective outcome groups. Included were only such statements which were named by >25% of patients within one of the three groups. *Significant difference between the subjective negative outcome group and the other two groups.

neg (N=8) and the other groups (N=22). Therefore, AES and BDI-2 were included in the binary logistic regression analysis. Both tests remained as significant predictors and accounted for 65.8% of the variance (Nagelkerkes R^2). This model correctly classified 27 of 30 patients (90%), applying a criterion value of 0.5. The sensitivity to find patients with negative subjective outcome (true positive cases) was 87.5% (7 out of 8), while the specificity (true negative cases) was 90.9% (20 out of 22). The AUC was 0.86 for the AES (p=0.003, 95% CI 0.71 to 1.00) and 0.78 for the BDI-2 (p=0.022, 95% CI 0.55 to 1.00). The ROC curves are shown in figure 4. The optimal cut-off score (best trade-off between sensitivity and specificity) on the AES was 36/37 (sensitivity=0.75, specificity=0.73), and a score of 16/17 on the BDI-2 (sensitivity=0.75, specificity=0.86). To reduce the false positive rate (1-specificity), a higher cut-off score can be determined. For the AES, a score of 42/43 (sensitivity=0.63, specificity=0.91) and for the BDI-2 a score of 17/18 (sensitivity=0.63, specificity=0.91), reduces the probability of false positives.

DISCUSSION

This is the first study reporting data on PD patients' expectations of STN-DBS, and on how patients subjectively perceive their outcome at 3 months after surgery. Clearly, all patients expected motor improvement from DBS, and the majority expected improvement in QoL. At 3 mFU, 14 patients reported a subjective positive outcome, 8 patients a mixed outcome, and 8 patients a subjective negative outcome. The latter had significantly higher apathy and depression scores at baseline and 3 mFU, even though motor scores significantly improved. Also, binary logistic regression analysis identified AES and BDI-2 baseline scores as significant predictors of a negative subjective outcome. Cut-off scores of 36/37 for the AES and of 16/17 for the BDI-2 are being suggested.

Considering our results, it has to be questionable whether group-neg patients should be considered as candidates for STN-DBS, even though they fulfilled the formal criteria for DBS surgery, according to leading expert's opinions.[19 33] Group-neg had the best preoperative motor on-state compared with the

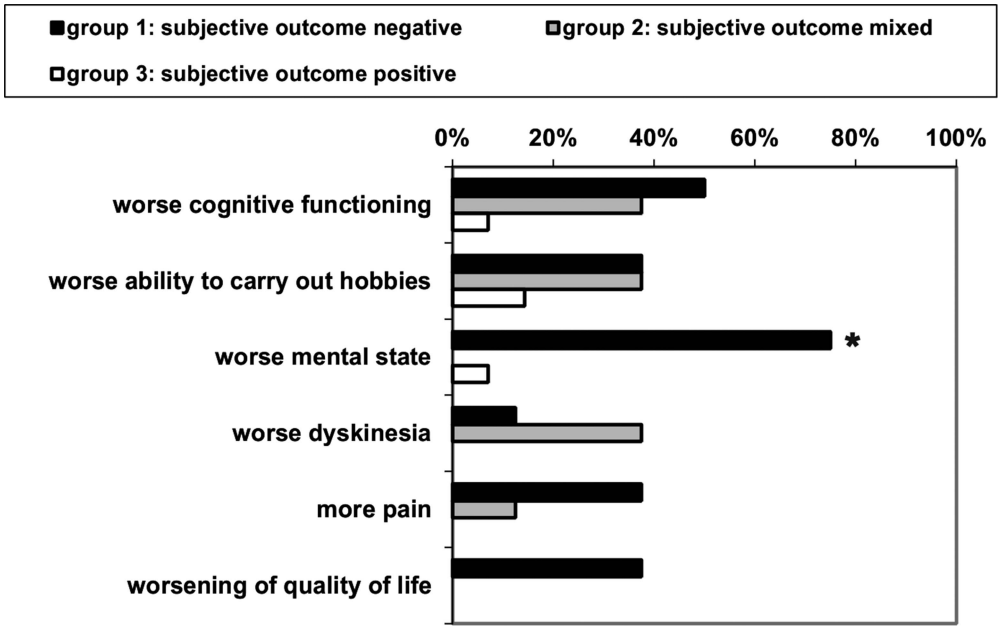

Figure 3 Negative statements at 3 months after STN-DBS for the three groups. All patients were asked to reflect their subjective outcome regarding STN-DBS in a semistructured interview. Negative statements were sorted according to their frequency of being stated by all patients and were then classified concerning the three subjective outcome groups. Included were only such statements which were named by >25% of patients within one of the three groups. *Significant difference between the subjective negative outcome group and the other two groups.

other groups. Therefore, it might have been better to continue treatment exclusively with antiparkinsonian medication. However, despite their subjective negative outcome, group-neg experienced significant motor improvements by STN-DBS as measured with the UPDRS-III. Also, their LEDD decreased significantly from baseline to 3 mFU. Therefore, these patients cannot be considered as 'motor non-responders'. Still, group-neg did not improve in QoL and even worsened in verbal fluency.

Table 2 Neurological and neuropsychological data, and quality of life for the three groups at baseline and 3 mFU

			Group-neg (n=8)	Group-mix (n=8)	Group-pos (n=14)	F/χ^2	p Value
Neurological data							
UPDRS-III	Med on	Baseline	16.00±4.14	20.88±7.36	23.57±12.75	2.333[b]	0.312
UPDRS-III	Med off	Baseline	39.88±7.97	40.00±11.89	46.79±16.09	0.985[a]	0.386
	Stim on and med off	3 mFU	28.63±10.47**	28.13±9.13*	24.77±18.11***§	0.232[a]	0.795
LEDD (mg)		Baseline	900.75±576.63	806.25±371.63	709.86±340.60	0.534[a]	0.593
		3 mFU	479.58±299.94*	250.42±243.01**	326.36±116.41**	2.000[b]	0.368
Neuropsychological data							
Digit span forwards T-scores		Baseline	58.13±9.46	57.86±9.25§	53.86±11.26	0.581[a]	0.566
		3 mFU	52.50±13.31	53.25±5.87	49.79±12.59	0.280[a]	0.758
Digit span backward T-scores		Baseline	49.00±11.59	43.43±6.13§	47.14±9.35	0.677[a]	0.517
		3 mFU	49.13±12.68	41.88±19.78	45.15±7.16	0.866[b]	0.649
Verbal fluency (letters) T-scores		Baseline	54.58±8.75	47.67±9.06§	49.93±10.25	1.050[a]	0.364
		3 mFU	47.87±6.88*	46.63±9.95	50.02±10.95	0.333[a]	0.720
Brief test of attention raw scores		Baseline	11.88±4.12	9.86±3.53§	10.14±4.69	0.535[a]	0.592
		3 mFU	9.00±4.14	11.25±3.06	10.07±4.83	0.560[a]	0.578
Quality of life							
PDQ-39		Baseline	47.09±19.46	34.71±16.05	33.58±13.55	2.001[a]	0.155
		3 mFU	43.17±14.01†,‡,§	20.44±9.28†*	21.56±12.06‡**	9.143[a]	0.001

Values represent means±SD. p Values by [a] ANOVA (F) or [b] Kruskall–Wallis H-test (χ^2).
*Represent significant changes for paired samples t test for UPDRS-III (baseline med off vs 3 mFU stim on/med off), LEDD, PDQ-39 and verbal fluency data within a group, *<0.05, **<0.01, ***<0.001.
†Bonferroni posthoc test: significant difference between group-neg and group-mix.
‡Bonferroni posthoc test: significant difference between group-neg and group-pos.
§Missing data for one patient.
N, number of patients; group-neg, subjective outcome negative; group-mix, subjective outcome mixed; group-pos, subjective outcome positive; med off, medication off; stim on, stimulation on; 3 mFU, 3 months follow-up; UPDRS, Unified Parkinson's Disease Rating Scale-III; LEDD, l-dopa equivalent daily dose; PDQ-39, Parkinson's Disease Questionnaire-39.
Test score range: UPDRS-III, 0–108, higher scores equal more impairment; digit span forwards, 0–100, higher scores equal better performance; digit span backwards, 0–100, higher scores equal better performance; verbal fluency (letters), 0–100, higher scores equal better performance; brief test of attention, 0–20, higher scores equal better performance; PDQ-39, 0–100, higher scores equal more impaired quality of life.

Table 3 Group comparisons of mood scales at baseline and 3 months after surgery

	Group-neg (n=8)	Group-mix (n=8)	Group-pos (n=14)	F	p Value
Apathy evaluation scale					
Baseline	45.25±11.52†,‡	29.88±8.59†	31.64±7.85‡	7.251	0.003
3 mFU	44.50±7.15†,‡	27.00±6.63†	33.31±6.85‡	13.465	<0.001
Beck depression inventory-2					
Baseline	18.25±8.70†	6.63±6.28†	11.43±4.89	6.626	0.005
3 mFU	18.38±5.83†,‡	5.88±9.19†	7.36±6.86‡*	7.541	0.003
Self-report manic inventory					
Baseline	7.25±6.50	2.75±3.85	7.07±6.06	1.742	0.194
3 mFU	11.14±6.62§	3.75±3.28	10.14±7.36	3.328	0.052
State trait anxiety inventory state					
Baseline	49.63±14.44	34.63±9.40	40.14±8.99	4.009	0.030
3 mFU	47.00±7.64§	34.13±11.84	35.14±8.87	4.413	0.022

Values represent means±SD.
*Represents significant changes for paired samples t test for BDI-2 results within group-pos, *<0.01.
†Bonferroni posthoc test: significant difference between group-neg and group-mix.
‡Bonferroni posthoc test: significant difference between group-neg and group-pos.
§Missing data for one patient.
Group-neg, subjective outcome negative; group-mix, subjective outcome mixed; group-pos, subjective outcome positive; 3 mFU, 3 months follow-up.
Test score range: apathy evaluation scale, 18–72, higher values equal more apathy; Beck depression inventory-2, 0–63, higher values equal more depression; self-report manic inventory, 0–48, higher values equal more mania; state trait anxiety inventory, 20–80, higher values equal more state anxiety.

It may seem unexpected, that group-neg presented with best preoperative motor functioning and l-dopa response, but had the highest apathy and depression scores at the same time. Past studies have shown that apathy and overall motor impairment were not associated, implying an involvement of non-motor frontal-subcortical loops.[34 35] Similar results have been reported for depression and motor impairment,[36] although this relationship often depends on how depression and its severity was assessed, and what other psychiatric comorbidities existed.[37 38] Further research is needed to clarify the association between severity of apathy, depression and overall motor symptoms.

As a baseline expectation, group-neg patients significantly more often named 'improvement of mental state', which can usually not be directly improved by DBS, and which might therefore be considered as unrealistic. Too high and unrealistic expectations can lead to disappointment with DBS outcome, even though patients might have marked motor improvement.[39 40] Moreover, a patient with more complaints than beneficial changes after DBS is a high burden for the family, the society paying for the procedure, as well as for the involved medical team.

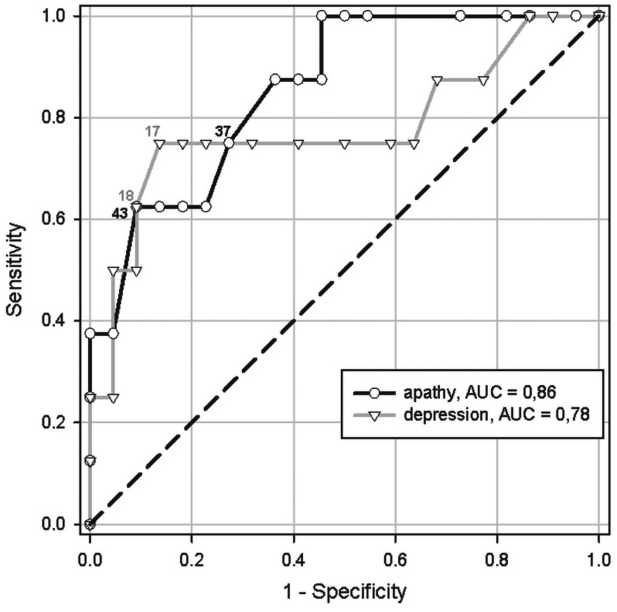

Figure 4 Receiver operating characteristic curves and cut-off scores for apathy (AES) and depression (BDI-2).

There is an ongoing debate on psychiatric symptoms as possible exclusion criteria for STN-DBS.[33] Large trials on the efficiency and side effects of STN-DBS usually do not define specific cut-off scores for exclusion but, instead, exclude patients with major or severe psychiatric disorders.[1 2] Also, severe medication-refractory depression is a recommended exclusion criterion for DBS, generally based on DSM-IV diagnosis.[41] In our study, patients with subjective negative outcome showed significantly more apathy and depression compared with the other groups at baseline and 3 mFU, although preoperative severe psychiatric diseases were not found by an experienced psychiatrist. An explanation for the high affective test scores might be l-dopa-induced mood swings or neurovegetative elevation of BDI-2-scores. Nevertheless, apathy and depression are frequent non-motor symptoms in PD.[3] The relationship between these mood impairments is still unclear. It has been suggested that apathy and depression are discrete components in PD,[42] while others emphasise an overlap between these two.[43] Regarding the use of the AES in PD, cut-off scores of 37/38, and for the BDI-2, cut-off scores of 14/15, have been shown to separate patients with apathy/depression from those without.[44 45] With respect to exclusion from DBS therapy, no specific cut-off scores have been defined for the use of these scales. We found cut-off scores of 36/37 on the AES, and of 16/17 on the BDI-2, to be the most sensitive and specific cut-offs, to predict possible subjective negative outcomes in our patient group. This finding suggests that patients should be screened carefully before surgery, and even milder or subclinical psychiatric difficulties should raise our attention with respect to subjective patient outcome and approval to have STN-DBS surgery. Furthermore, apathy and depression should be treated prior to surgery to improve subjective patient outcomes. Also, counselling or psychotherapy accompanying the DBS-procedure might be helpful to stabilise

patient's affective state and make sure that expectations can be fulfilled.[46]

Apathy and depression also decrease QoL in PD.[17 18] We assume that the preoperative affective state (ie, high apathy and depression scores) of patients with postoperative negative subjective outcome contributes to the unimproved QoL at 3 mFU. We speculate that preoperative apathy and depression prevents improvement of QoL after surgery. Regarding neuropsychological results, a worsening in verbal fluency, especially in the more depressed group-neg, is not surprising, since this is a frequent cognitive change after STN-DBS.[33]

Our study has several limitations. The small sample size may limit statistical results and power. However, the very time-consuming assessment, transcription and evaluation of semistructured interviews usually reduce the number of patients. The use of semistructured interviews makes a comparison between patients more difficult since each person answers questions according to their own perception. Therefore, the objectivity of our interview results is reduced. Moreover, neutral interview responses were not considered in the analysis, which could lead to loss of information. Another limitation is the early follow-up examination at 3 months after surgery. Until now, we were not able to make an assumption regarding the subjective outcome of groups beyond this time point. Further research is needed to examine patients' subjective perception in the long run.

CONCLUSIONS

PD patients who undergo STN-DBS have specific hopes and wishes regarding a successful outcome of surgery that does not simply depend on motor improvement. Like others,[40 41] we recommend to discuss expectations with the patient before surgery and highlight probable realistic benefits. It seems that a more careful examination of preoperative depression and apathy, as well as a more limited approval for surgery in the case of moderate psychiatric disorders, increases the patient's subjective positive outcome. Preoperative apathy and depression scores might be helpful tools to identify 'risk candidates' for STN-DBS, providing the opportunity of an accompanying psychosocial support and counselling. Future studies which analyse subjective patient outcomes longitudinally are crucial to get a better understanding of the long-term impact of STN-DBS on a patient's life.

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