Parkinsonism and Related Disorders 20 (2014) 514–519

Contents lists available at ScienceDirect

Parkinsonism and Related Disorders

journal homepage: www.elsevier.com/locate/parkreldis

Parkinson's disease patients with subthalamic stimulation and carers judge quality of life differently

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ARTICLE INFO

Article history:
Received 30 September 2013
Received in revised form
3 February 2014
Accepted 10 February 2014

Keywords:
Parkinson's disease
Subthalamic stimulation
Quality of life
Social functioning
Caregivers

ABSTRACT

Background: Quality of life (QoL) improves under subthalamic deep brain stimulation (STN-DBS) in Parkinson's disease (PD), whereas social functioning may be disrupted. This disruption could negatively influence the family dynamic, leading to different perceptions of the STN-DBS outcome by patients and caregivers.

Methods: We recruited 34 PD patients for this prospective, controlled trial, 28 of whom were examined preoperatively, three months and one year after STN-DBS surgery. The primary outcome was QoL. We compared the patients' ratings and caregivers' proxy QoL ratings. The secondary outcome was social functioning. Additionally, neurological, neuropsychiatric and cognitive domains were analyzed. Changes were analyzed with repeated-measures ANOVA. Regression analysis was used to determine the association between QoL and social functioning.

Results: Patients' QoL improved significantly under STN-DBS ($p = .003$). At baseline, patients' and caregivers' QoL ratings were similar. However, one year postoperatively, QoL ratings differed significantly ($p = .010$), whereby QoL was rated worse by caregivers. Social functioning was positively influenced during the first months postoperatively, but did not improve longitudinally. One year postoperatively, social functioning was significantly associated with QoL ratings (patients: $p = .004$, caregivers: $p = .002$). Motor scores significantly improved, whereas verbal fluency and apathy worsened.

Conclusions: Unequal perception of QoL between patients and caregivers exists under STN-DBS. The fact that social functioning does not improve longitudinally is perhaps due to patient's higher levels of apathy and reduced motivation following surgery. Our findings stress the importance of considering caregiver's input in DBS patients' outcomes and the need for pre-operative preparation.

1. Introduction

Bilateral deep brain stimulation of the subthalamic nucleus (STN-DBS) significantly improves motor symptoms in Parkinson's disease (PD), but its effect on cognitive and neuropsychiatric symptoms is still unclear [1,2]. Quality of life (QoL) also shows significant improvement under STN-DBS [3]. However, mainly in the motor subscales of QoL [4]. After one year under STN-DBS, reports show that QoL is still positively rated by patients, whereas social functioning, such as familial/socio-professional functioning might be disrupted [5]. This might negatively influence family dynamics [5], revealing differences in the perception of STN-DBS outcome between patients and caregivers. These findings are in accord with our clinical impression. However, it remains uncertain how and when this possible discrepancy between patients' and caregivers' perception develops. Moreover, as PD patients may

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http://dx.doi.org/10.1016/j.parkreldis.2014.02.009
1353-8020/

suffer from impaired decision making [6] and impaired self-awareness [7], the validity of self-reports might be compromised. These features could lead to discrepancies between caregivers' proxy ratings and patients' self-ratings of QoL.

Therefore, we conducted a prospective study in which the primary outcome parameter was the QoL of PD patients under STN-DBS, as rated by both patients and caregivers. We hypothesized a development of a discrepancy between the patients' QoL under STN-DBS, and the QoL proxy rating of their caregivers who, we further hypothesized, would rate their patient's QoL as worse than the patients themselves. As secondary goal, we hypothesized that there would be a decline in social functioning under STN-DBS [5]. Hence, we analyzed the association between QoL ratings and social functioning. Furthermore, the course of motor, neuropsychiatric and cognitive parameters was investigated.

2. Methods

This prospective study was conducted at the department of Neurology, University of Cologne (Germany), as part of the international and interdisciplinary project ELSA-DBS: "Ethical, Legal, and Social Aspects of Deep Brain Stimulation" [8].

2.1. Standard protocol, approvals, registrations, and patient consent

All participants gave written informed consent. The study was approved by the local ethics committee (09-064) and is registered in the German Clinical Trials Register (DRKS-ID: DRKS00003221). The center for clinical trials Cologne, ZKS Cologne, monitored the primary outcome parameter (PDQ-39) of all patients, as well as 20% of the remaining data, thereby ensuring high data quality.

2.2. Participants

A series of 34 advanced PD patients, receiving STN-DBS during the course of this study, was recruited together with 34 caregivers. Patients' inclusion criteria were equivalent to the inclusion criteria for STN-DBS surgery from the German Neurological Society [9]: We included patients between 40 and 75 years with motor symptoms refractory to medication and a good levodopa (L-dopa) response. Patients with dementia [10] (Mini Mental Status Examination (MMSE) score < 25) and severe psychiatric or additional neurological disorders were excluded. Caregivers with dementia (MMSE-score < 25) or psychiatric or neurological disorders influencing cognition and mood were also excluded.

The 34 PD patients were operated on between July 2009 and April 2011 at the Department of Stereotaxy and Functional Neurosurgery of the University of Cologne (M.M.). Six patients dropped-out during the course of the study (see Fig. 1). One caregiver refused to participate, thus excluding one patient and one patient refused to participate further at the 1-year FU. Following surgery, one patient was lost to follow-up as a result of infection resulting in the removal of the leads. In two patients follow up was not possible due to postoperative cognitive decline, as questionnaires could no longer be filled out, although careful screening before surgery was conducted and the criteria for STN-DBS surgery from the German Neurological Society were fulfilled. One patient died following an accident (unrelated to the DBS-procedure).

Also, one caregiver refused to participate further at the 1-year FU. However the baseline and 3-months FU data of this caregiver were included in the analysis.

	Patients	Caregivers
Baseline	N = 34	N = 34
	drop-outs n = 1 - refusal	
3-months FU	N = 33	N = 33
	drop-outs n = 5 - explantation - cog. impairment - refusal - deceased	drop-outs n = 2 - refusal
1- year FU	N = 28	N = 27

Fig. 1. Flow-chart of the study cohort naming reasons for drop-outs. FU = follow-up.

2.3. Study design

The 28 remaining patients (11 female/17 male) and caregivers (19 female/9 male) were assessed before surgery (between six weeks and three days preoperatively), and three months (3-months FU) and one year postoperatively (1-year FU), by clinical neuropsychologists and neurologists. All tests for all subjects took place at the department of Neurology, University Hospital Cologne. At baseline, patients were assessed in their best medication on and postoperatively under best stimulation- and medication-settings. At all three assessment points, the test battery for the PD patients included QoL, neurological, neuropsychiatric and cognitive evaluations, whereas the caregivers' test battery included neuropsychiatric and cognitive evaluations, as well as the rating of PD patients' QoL.

2.4. Outcome parameters

The Parkinson's disease Questionnaire-39 (PDQ-39) [11] total, the primary outcome, was used to measure disease-related QoL (range 0–100, with 100 stating the worst QoL). Standardized scores of the PDQ-39 total and eight subscales were analyzed.

Social functioning, the secondary outcome parameter, was evaluated with the Social and Occupational Functioning Assessment Scale (SOFAS) [12], an expert-rating scale (range 0–100, with 100 representing better social functioning).

2.5. Neurological assessment

Motor performance was measured with the Unified Parkinson's Disease Rating Scale part III (UPDRS-III) [13]. Pre-operatively, movement was measured with and without medication. The medication off-state was defined as at least 12-hours absence of anti-parkinsonian medication, whereas the on-state was defined as the patient's best response to 1.5 times their morning dose or at least 200 mg L-dopa after the med off-state. Dopamine agonists were stopped 72 h prior to the off-state evaluation. Postoperatively, the UPDRS-III was measured in the medication off-state, with stimulation on optimized stimulation parameters. Additionally the levodopa equivalent daily dose (LEDD) [14] was calculated.

2.6. Neuropsychiatric and cognitive assessment

Mood was assessed with the Beck's-Depression Inventory-2 (BDI-2; range 0–63) [15], the Apathy Evaluation Scale (AES, range 18–72) [16], the state subtest of the State-Trait Anxiety Inventory (STAI-state, range 20–80) [17] and the Self-Report Manic Inventory (SRMI, range 0–48) [18]. Higher scores on all scales correspond to higher depression/apathy/anxiety/mania.

Phonetic (letter B, M, S) and semantic (category animals) verbal fluency was also measured [19]. Working memory was evaluated with the digit span test backwards (DS backwards) [20]. Attention was analyzed with the forward condition of the digit span test (DS forward). Standardized scores were used, with higher scores indicating better performance. Global cognition was tested at baseline with the Mattis Dementia Rating Scale (MDRS) [21] and at baseline and the 1-year FU with the MMSE.

2.7. Assessment of caregivers

Caregivers' mood was measured with the BDI-2 at all three assessment points. Cognition was measured at baseline and the 1-year FU with the MMSE. Additionally, caregivers completed PDQ-39 proxy forms estimating the patients' QoL at all assessment points, where the layout as well as the wording of the questions was identical to the patient's questionnaire, except that questions were not in the first-person.

2.8. Surgical procedure

For the DBS surgery, stereotactic CTs and 1.5T MRIs were used to determine the coordinates of the target structure. After microelectrode recordings and macro-electrode test stimulation to determine the optimal area for implantation, electrodes were implanted in the STN bilaterally. Intraoperative and postoperative 2 planar stereotactic X-rays with markers were carried out in the stereotactic frame to verify the exact location of the electrodes. Subsequently, the electrodes were connected to a pulse generator. STN-stimulation was first activated 3–5 days after surgery, accompanied by a stepwise reduction of anti-parkinsonian medication.

2.9. Statistical analysis

Data were analyzed with IBM SPSS version 20.0 (SPSS Corp, Chicago, Ill, USA). Repeated-measures ANOVAs were used to analyze QoL, neurological, neuropsychiatric and cognitive measurements over the course of one year (baseline, 3-months FU and 1-year FU), in the on-state. In the case of non-parametric distribution, the Friedman test was administered. Additionally, paired-samples *T*-tests (or Wilcoxon test for non-parametric samples) were used to specify significant differences between two points in time (baseline versus 3-months FU and baseline versus 1-year FU). Additionally, we compared patients' QoL ratings to their caregivers' QoL ratings,