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Spottke, Annika; Volkmann, Jens; Lorenz, Delia; Krack, Paul; Slama, Antje; Sturm, Volker; Gerstner, Anja; Berger, Karin; Hellwig, Dieter; Deuschl, Gunther; Freund, Hans-Joachim; Oertel, Wolfgang; Dodel, R. C.

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ORIGINAL COMMUNICATION

E. A. Spottke
J. Volkmann
D. Lorenz
P. Krack
A. M. Smala
V. Sturm
A. Gerstner
K. Berger
D. Hellwig
G. Deuschl
H. J. Freund
W. H. Oertel
R. C. Dodel

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E. A. Spottke · A. Gerstner · W. H. Oertel · R. C. Dodel, M. D. (✉)
Dept. of Neurology
Philipps-University Marburg
Rudolf-Bultmannstr. 8
35039 Marburg, Germany
Tel.: +49-64 21/2 86 54 80
Fax: +49-64 21/61 79 27
E-Mail: dodel@mailer.uni-marburg.de

J. Volkmann · H. J. Freund
Department of Neurology
Heinrich-Heine-University
Düsseldorf, Germany

D. Lorenz · P. Krack · G. Deuschl
Department of Neurology
Albrechts-Universität
Kiel, Germany

A. M. Smala
MERG
Medical Economics Research Group
Munich, Germany

V.Sturm
Department of Functional
and Stereotactic Neurosurgery
University of Cologne
Cologne, Germany

K. Berger
Department of Transfusion Medicine
and Haemostasis (Clinical Economics)
Ludwig-Maximilian-University
Munich, Germany

D. Hellwig
Department of Neurosurgery
Philipps-University
Marburg, Germany

Abstract *Objective* To assess the effects on motor functioning, health status and direct medical costs of high-frequency stimulation of the subthalamic nucleus (DBS-STN) in patients with idiopathic Parkinson's disease (PD). In addition, the cost-effectiveness of DBS-STN vs. drug treatment was investigated. *Methods* 16 consecutive patients with PD from two centers (Düsseldorf/Cologne; Kiel) treated by DBS-STN were prospectively evaluated. Clinical evaluations were done at baseline and 1, 3, 6, 12 months following surgery by means of the Unified Parkinson's disease Rating Scale (UPDRS). Health status of PD patients was assessed using the Sickness Impact Profile (SIP) at baseline and 6 months following surgery. Relevant economic data were taken from the medical records and costs (1999) were derived from different German medical economic resources. Costs were determined from the perspective of the health care provider. *Results* Following DBS-STN UPDRS scores (subscores and sum score) as well as health status improved considerably in PD patients. The overall SIP score and the physical dimension score ($p < 0.009$) were significantly different ($p < 0.01$) six month after surgery compared with baseline values. Mean costs of DM 40,020 (US$ 20,810, EUR€ 20,410, GB£ 12,810) per patient were spent during the 12 month observation period for in-patient and out-patient care. These expenses included already the costs for the electronic device for bilateral stimulation. Following DBS-STN medication was considerably reduced. Mean daily drug costs at baseline were DM 46.7±21.8 (US$ 24, EUR€ 24, GB£ 15) and DM 18.3±17.7 (US$ 10, EUR€ 9, GB£ 6) at 12 months following DBS-STN. Accounting for the decreased drug consumption, total annual costs amounted to DM 31,400 (US$ 16,330, EUR€ 16,010, GB£ 10,050). Further, we estimated the incremental cost effectiveness as DBS-STN had higher costs but was more effective than baseline treatment. The incremental total cost-effectiveness ratio for DBS-STN was DM 1.800 (US$ 940, EUR€ 920, GB£ 580) for one point decrease of the UPDRS. *Conclusion* DBS-STN is an effective treatment that considerably alleviates the severity of signs and symptoms and improves the health status of patients with PD. Compared with drug treatment, however, the expenditures associated with DBS-STN are increased when only direct medical costs are considered in a one year horizon. However, on a

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long-term basis costs will decrease considerably because of the reduction of the drug expenditure and improved functioning in all activities of daily living. To adequately evaluate the cost-effectiveness of DBS-STN compared with standard drug regimen for PD it is necessary to include direct, indirect and intangible costs on a long-term basis and under standardized circumstances.

Key words deep brain stimulation · parkinson's disease · cost · cost-effectiveness · quality of life

Introduction

In the early stage of Parkinson's disease patients' symptoms are markedly alleviated by dopaminergic therapy. However, at later stages of the disease motor fluctuations and/or dyskinesias may develop which result in a major disability and a considerable decrease in the quality of life of parkinsonian patients [28, 31]. To avoid these long-term side-effects of levodopa therapy and to delay disease progression, various medical treatment options have been investigated in animal models of PD and in humans [16]. The failure of current medical regimes to prevent disease progression and to prevent long-term side effects has led to a resurgence of interest in surgical procedures such as pallidotomy [2]. More recently, interest has focused on high frequency intracerebral stimulation and the subthalamic nucleus (STN) as a target for intervention [4]. The rationale for targeting the STN lies in its unique position to affect the neuronal activity of both outputs of the basal ganglia as depicted by current models of basal ganglia circuit and pathophysiology [1]. Bilateral deep brain stimulation (DBS) of the subthalamic nucleus produces a dramatic reversal in all cardinal motor signs in PD patients, who are off their medications [30], but also provide improvements in the on-medication state [22]. In addition, subthalamic nucleus stimulation reduces medication requirements for PD patients [27].

Despite the rewarding results of DBS-STN for the treatment of PD, new and complex healthcare interventions need to be assessed medically as well as economically from different perspectives [13]. Once efficacy, safety and effectiveness of an intervention is established the question of its efficiency must be examined: "Does this therapy make the best use of available resources?" This is essential especially for those who are likely to have complex consequences, including long-term implications, and which entail large expenditure of public funds often diverted from other public schemes. Therefore, it is essential to take economic issues also into medical consideration.

The aim of this study was to assess the charges of treating PD patients with DBS-STN in Germany within a one year time horizon and to relate the charges to symptomatic relief as measured by the UPDRS. In addition, we evaluated the effects on the patients' health status.

Methods

Clinical evaluation

Patients were recruited from two German centers: Düsseldorf/Cologne and Kiel. In Düsseldorf/Cologne (D/C) nine consecutive patients and in Kiel seven consecutive patients with advanced PD were selected for implantation (1998). Each patient underwent a complete medical and neurological examination including a uniform, structured assessment of parkinsonian signs and symptoms (UPDRS) [17]. Selection and exclusion criteria of PD patients have been described previously [24, 33, 34].

Drug therapy for PD followed the guidelines proposed by Quinn and Oertel [29]. All patients were under a stable drug therapy before considering DBS-STN. The neurosurgical procedure used by the two centers has been previously described in detail [24, 33, 34]. One patient (Düsseldorf) was initially hospitalized for a final attempt of a high-dose dopamine agonist treatment and underwent surgery during the same stay after this treatment attempt had failed and his original medication had to be restituted. The study protocol was approved by the local ethics committee and all patients gave informed consent.

Health Status – Sickness Impact Profile

The Sickness Impact Profile (SIP) was used at baseline and at six months after surgery at medication on/DBS on-state. The SIP consists of 136 items which are subdivided in twelve categories and is scored as a percentage from 0 to 100 (0 percent represents no dysfunction and 100 percent represents maximal dysfunction) [11]. Each item represents a sickness-related change in behavior and the extent of the change. The 12 health-status categories of the SIP are: Sleep and Rest (7 items), Body Care and Movement (23 items), Home Management (10 items), Mobility (10 items), Ambulation (12 items), Work (9 items), Alertness/Intellectual Behavior (10 items), Communication (9 items), Recreation and Pastimes (8 items), Eating (9 items), Emotional Behavior (9 items), and Social Interaction (20 items). Sum scores were calculated for each category based on the weight values for each statement and presented as a percentage of the total possible dysfunction in that category. In addition, separate scores were calculated for Physical Dimension (sum score of Ambulation, Mobility, and Body Care and Movement) and Psychosocial Dimension (sum score of Emotional Behavior, Social Interaction, Alertness/Intellectual Behavior, and Communication).

Healthcare utilization

The study estimated the direct healthcare costs from the perspective of the "Gesetzliche Krankenversicherungen" (statutory health insurance) in Germany. The costs were determined before and after implantation of deep brain stimulators and the cost evaluation focused on the charges for drug treatment, in-patient hospital care and outpatient hospital care ("direct costs").

The drug prices were attained from the official German price lists of drugs [8] withdrawing 5 % deduction according to the guidelines of the "Gesetzliche Krankenversicherung" (statutory health insur-

ance). If available, "Festbeträge" (fixed prices) were used for the calculation. In addition, the prices were adjusted for the smallest available package. Patients fee for drugs were not considered because chronic ill patients can be exempted from fees. There was no reimbursement for the electronic device (Itrel® II, Medtronic; Düsseldorf; according to the manufacturer's information, the costs of the device for bilateral stimulation amounts to DM 27,800 (US$ 14,460, EUR€ 14,180, GB£ 8,900, price as of July 1999). The costs for the electronic device were compensated through the inpatient charge, that means no further costs due to surgery and medical devices were additional to the inpatients charge per day (see below).

The expenditure for hospital care included the costs of clinical care and additional costs of treatment, examination, drugs, and paramedical care (e. g. physiotherapy). The inpatient costs were calculated by multiplying the total number of days of hospital stay by the mean costs of one day of inpatient care. The costs were estimated by adding the basic daily hospital costs (DM 175, US$ 91, EUR€ 89, GB£ 56) to the costs for the inpatient stay on the neurological (Düsseldorf/Cologne (D/C): DM 555, US$ 289, EUR€ 284, GB£ 180; Kiel (K): DM 580, US$ 302, EUR€ 302, GB£ 186) or neurosurgical ward (D/C: DM 1,013, US$ 530, EUR€ 518, GB£ 327; K: DM 915, US$ 476, EUR€ 467, GB£ 293). The outpatient hospital care was calculated by the number of visits multiplied by a fixed quarterly charge of DM 75 (US$ 39, EUR€ 38, GB£ 24) (Universitätsklinik Düsseldorf, Verwaltung, 1999).

All currency was converted at the rates in November 1999: DM 1=US$ 0.52, DM 1=EUR€ 0.51, DM 1=GB£ 0.32.

Evaluation of cost-effectiveness

The cost and effectiveness for patients treated by drug therapy alone and following DBS-STN was calculated after twelve months. We used UPDRS scores at baseline and one year following surgery as outcome measurement.

A strategy is cost-effective if it results in better effectiveness at a similar or lower cost, or if it results in lower cost at a similar or better effectiveness than the alternative strategy [18]. When one of the strategies is more effective, but also more costly than the alternative strategy, it is necessary to calculate the incremental cost-effectiveness ratio. Incremental cost-effectiveness was calculated using the formula:

$$\text{Incremental cost-effective ratio} = \frac{\text{Cost (A)} - \text{Cost (B)}}{\text{Effect (A)} - \text{Effect (B)}}$$

The incremental cost-effectiveness ratio expresses the extra cost per additional unit of effectiveness when choosing strategy A instead of strategy B [18]. The cost that it is reasonable to pay for an extra unit of effectiveness is a matter for the relevant decision maker [20].

Statistical analysis

We calculated means ± standard deviation and range. To evaluate statistical difference between the different observations, we used the Wilcoxon signed rank test. A p-value ≤0.05 was chosen for significance.

Results

Clinical evaluation

Table 1 displays the clinical characteristics of the study patients in the two centers. Surgery and subsequent chronic high-frequency stimulation resulted in no chronic morbidity. Transient and usually mild adverse events were attributed to changes in medication or stimulation parameters and subsided after therapy adjustments including anhedonia or depression, confusion, double vision, dyskinesias and dysarthria.

The UPDRS scores I-IV following surgical implantation after 6 and 12 months are shown in Table 2. In every subscore an improvement due to the DBS-STN-stimulation could be observed. After surgery all patients experienced a major improvement of "OFF"-symptoms during DBS-STN stimulation and a reduction of dyskinesias and motor fluctuations (Table 2). The Schwab and England activities of daily living score (D/C) increased

Table 1 Demographics of patients at study entry (HY stage: Hoehn & Yahr stage; D/C: Düsseldorf/Cologne; K: Kiel)

Gender	Age (years)	Duration of Disease (years)	HY-stage		Professional Status before Surgery	Professional Status 12 M after Surgery
			On	off		
F	56	8	2.5	5.0	Never worked	No change
F	62	12	1.0	5.0	Early retirement	No change
F	63	23	3.0	4.0	Early retirement	No change
M	73	15	2.0	4.5	Unemployed	No change
F	35	6	4.0	5.0	Early retirement	No change
M	55	11	1.5	5.0	Early retirement	No change
F	61	10	2.5	5.0	Never worked	No change
F	47	8	1.0	3.5	Never worked	No change
M	58	10	2.5	4.0	Unemployed	Full time employment
F	48	14	2.0	5.0	Never worked	No change
M	59	12	2.0	4.0	Early retirement	No change
F	61	10	2.0	3.0	Never worked	No change
M	55	10	2.0	5.0	Early retirement	No change
F	58	8	2.0	3.0	Early retirement	No change
F	61	9	2.0	4.0	Never worked	No change
M	46	7	3.0	5.0	Early retirement	No change
MEAN	56.1±8.5	10.8±3.9	2.2±0.7	4.4±0.7		
D/C	56.7±10.1	11.4±4.8	2.2±0.9	4.6±0.6		
K	55.4±5.7	10.0±2.2	2.1±0.3	4.1±0.8		

Table 2 UPDRS I-IV scores baseline. 6 months. and 12 months after surgery at Düsseldorf / Cologne (n=9).

	Baseline	6 Months	12 Months
UPDRS I			
Medication On	3.4±2.1	2.1±1.2	2.1±2.1
UPDRS II			
Medication Off	23.6±9.7	–	–
Medication On	15.7±9.7	–	–
Medication Off/ DBS On	–	13.9±9.6	12.8±7.6
Medication On/ DBS On	–	12.2±6.7	10.9±6.1
UPDRS III			
Medication Off/ DBS Off	57.9±21.7	60.3±16.7	63.1±17.4
Medication Off/ DBS On	–	19.3±17.8	19.6±18.0
Medication On/ DBS Off	18.8±16.5	46.6±21.6	22.1±16.5
Medication On/ DBS On	–	18.8±15.4	12.9±11.0
UPDRS IV			
Medication On	13.4±3.1	–	–
Medication On/DBS On	–	2.7±1.7	1.9±2.0

significantly from baseline medication on-state 71.3±18.3 % (n=9) to 88.6±14.6 % (p=0.005; n=7) in the medication on/DBS on-state at one month, to 86.7±12.2 % at three months (p=0.03; n=9), to 85.7±12.7 % at six months (p=0.01; n=7) and at twelve months to 90±8.7 % (p=0.03; n=9).

Health status – Sickness Impact Profile

A major reduction of the scores (i. e. improvement) of all categories of the SIP was observed from baseline to six months (Fig. 1). The physical dimension score (mean reduction = 67 %) as well as the overall SIP score were significantly different (mean reduction = 58 %) six month after surgery compared with baseline values. Although there was a considerable difference in the psychosocial dimension score compared with baseline (mean reduction = 51 %), the results did not reach statistical significance.

Resource Consumption and Direct Medical Costs

In the preoperative observation period, all patients in the study received levodopa (in combination with a dopamine decarboxylase inhibitor) with a mean dose of 550±150 mg. Additionally, eight patients (K: 5 patients) were treated with dopamine agonists (pergolide, pramipexole, dihydroergocryptine, lisuride), four patients (K: 2 patients) with selegiline, six patients (K: 2 patients) with tolcapone, one patient (K:0 none) with entacapone and one patient (K: 3 patients) with amantadine and anticholinergics (Table 3).

At twelve months following surgery seven patients received levodopa with a mean dosage of 270±85 mg.

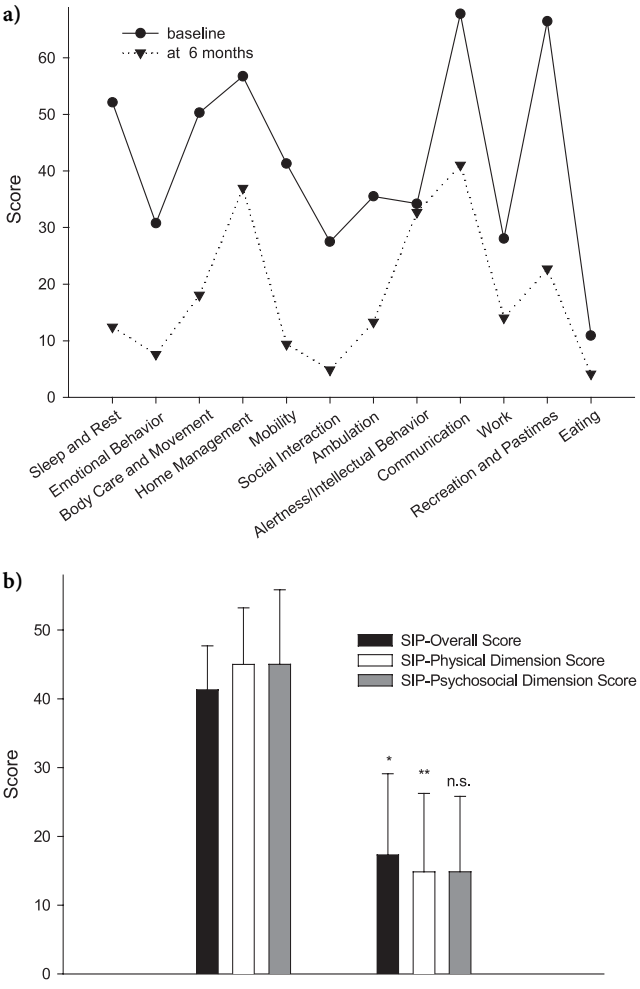

Fig. 1 **A**: Sickness Impact Profile at baseline and at six months following DBS-STN surgery in Düsseldorf/Cologne (n=5). **A**: Subscores of the sickness impact profile. **B**: The SIP-overall score, the SIP-psychosocial dimension score as well as the SIP-physical dimension score were plotted. (* $p < 0.01$; n. s. not significant)

Four patients were off levodopa. Following DBS-STN six patients (K: 2 patients) were treated with dopamine agonists. Three patients were treated with amantadine (K: 3 patients; Table 3).

We calculated mean daily drug costs of DM 46.7±21.8 (US$ 24, EUR€ 24, GB£ 15) in Düsseldorf and in Kiel of DM 42.6±25.8 (US$ 22, EUR€ 22, GB£ 14) before surgical treatment. With the reduction of drug consumption following surgery, a decrease of drug costs between 14 % and 100 % was achieved in the first postoperative month. At 6 and 12 months following DBS-STN, costs in Düsseldorf/Cologne were DM 15.4±18.8 (K: DM 15.2±14.0), DM 18.3±17.7 (K: DM 23.9±15.4) respectively.

The preoperative mean in-patient stay in the neurological ward was 9.6±12.0 days (range: 1–40) in D/C and 7.9±4.0 days (range: 4–16) in Kiel. The mean inpatient stay in Düsseldorf/Cologne for the first operation was 8.1±4.0 days (range: 5–18) in the neurosurgical ward

Table 3 Reduction of daily drug costs at twelve months compared to baseline.

	Daily drug costs at baseline (DM)		Daily drug costs at twelve months (DM)	
Drug	Düsseldorf/Cologne	Kiel	Düsseldorf/Cologne	Kiel
Levodopa	6.0±1.7 (n=9)	3.5±2.3 (n=7)	2.8±1.2 (n=7)	40.6±3.3 (n=5)
Dopamine agonists	29.8±15.1 (n=8)	41.6±12.1 (n=5)	24.5±19.2 (n=6)	36.4±3.4 (n=2)
Selegiline	5.4±4.0 (n=4)	7.7±4.1 (n=2)	–	–
COMT-inhibitors	18.1±8.0 (n=6)	10.9 (n=2)	–	24.8 (n=1)
Amantadine	0.9 (n=1)	2.7±1.1 (n=5)	2.0±0.3 (n=3)	2.4±0.7 (n=2)
Anticholinergics	2.1 (n=1)	0.6±0.1(n=2)	–	1.4 (n=1)
Total	46.7±21.8 (n=9)	42.6±25.8 (n=7)	18.3±17.7 (n=9)	23.9±15.4 (n=7)

(electrode implantation) and 7.5±3.8 days (range: 4–15) in the neurological ward (testing period with externalized leads). For the second operation (the implantation of the pulse generators) the mean inpatient stay in the neurosurgical ward was 5.1±1.3 days (range: 4–7). In Kiel the mean inpatient stay at the department of neurosurgery was 6.9±1.8 days (range: 5–9) and 3.2±1.8 days (range: 1–5) in the department of neurology.

The follow-up care for the patients in the neurological department (adjustment of medication and stimulation parameters) amounted to a mean inpatient stay per year of 8.3±4.1 days (range: 4–16) in Düsseldorf/Cologne and 18.1±11 days (range:5–37) in Kiel.

Including the quarterly outpatient or inpatient follow-up DM 32,500±10,020 (US$ 16,930, EUR€ 16,620, GB£ 10,480) were spent in Düsseldorf/Cologne for care at the department of neurology, while DM 15,930±4,320 (US$ 8,300, EUR€ 8,150, GB£ 5,140) were spent for in-patient care in the department of neurosurgery (Table 4). The costs in Kiel were DM 24,140±11,380 (US$ 12,500, EUR€ 12,260, GB£ 7,690) in the department of neurology and DM 7,460±1,480 (US$ 3,880, EUR€ 3,810, GB£ 2,390) in the department of neurosurgery.

Calculation of Cost-Effectiveness

We calculated the incremental costs for each unit decrease of the subscore and the total UPDRS after 12 months following DBS-STN compared with drug therapy at baseline (Table 5). The highest amount had to be spent for a one unit improvement of the UPDRS-I (DM 28,580, US$ 14,860, EUR€ 14,580, GB£ 9,150) and the lowest for an improvement of the UPDRS-IV (DM 4,170, US$ 2,170, EUR€ 2,130, GB£ 1,330). Based on the UPDRS total score, the incremental cost per unit improvement was DM1,800 (US$ 940, EUR€ 920, GB£ 580).

Table 5 Incremental costs calculated per one point decrease of the UPDRS-score 12 months after DBS-STN (in German Marks). For the description of the calculation procedure please see the methods section.

	Baseline Medication On (mean)	12 Months Medication On/ DBS-STN On (mean)	Score Difference	Incremental Costs
UPDRS I	3.44	2.11	1.33	28.580
UPDRS II	15.67	10.88	40.79	7.935
UPDRS III	18.78	12.88	5.90	6.440
UPDRS IV	10.78	1.67	9.11	40.170
UPDRS Total score	48.67	27.54	21.13	1.800

Discussion

The direct medical costs of performing DBS-STN in patients with PD amounted to DM 48,430 in Düsseldorf/Cologne and DM 31,600 in Kiel during the twelve months observation period. In contrast to the expenditure due to in- and out-patient treatment, the costs for drug treatment following DBS-STN were reduced. Previous studies have shown that the mean dosage of levodopa as well as the mean dosage of dopamine agonists could be reduced following DBS-STN [22, 27]. Furthermore, one study reported that in nine out of ten patients the expensive treatment with apomorphine could be discontinued 12 months following continuous high-frequency stimulation [24]. Similar results were observed in our group of patients. The mean levodopa dose six

Table 4 Hospital costs during the study period of patients with PD treated with DBS in Düsseldorf/Cologne and Kiel (in German Marks).

	Neurology				Neurosurgery		
	Baseline	Postsurgical period	Follow-up visits	Total	Surgery 1	Surgery 2	Total
Düsseldorf/Cologne	6,970±8,260	12,810±3,240	12,720±7,070	32,500±10,020	9,530±4,640	6,400±1,500	15,930±4,320
Kiel	4,230±2,820	11,850±2,940	8,060±6,400	24,140±11,380	7,460±1,480	–	7,460±1,480

months after implantation was reduced by 58 %. COMT-inhibitors were discontinued and the dose of dopamine agonists was markedly reduced. This reduction in drug requirement resulted in a drop of daily drug cost from DM 44.7 (US$ 23, EUR€ 23, GB£ 14) at baseline to DM 21.1 (US$ 11, EUR€ 11, GB£ 7) twelve months following DBS-STN (Fig. 4). Extrapolating these data, annual savings of DM 8,610 (US$ 4,480, EUR€ 4,390, GB£ 2,760) can be achieved following DBS-STN in our group of PD patients. The annual savings would be even higher if the subcutaneous administration of apomorphine could be discontinued thanks to the effects of DBS-STN [12, 24, 26]. No patients using s. c. apomorphine were included in this study.

The cost of therapy cannot be judged without also considering the outcome of therapy, and cost-effectiveness analysis links these two measures explicitly. As outcome measurement we used the UPDRS to evaluate the clinical endpoint as well as the sickness impact profile to evaluate the health status following DBS-STN. Bilateral stimulation of the subthalamic nucleus improved considerably the motor symptoms and the functional disability in our group of 16 PD patients during the observation period. Motor fluctuations were attenuated and patients with "on-off" fluctuations before DBS-STN had milder fluctuations or none thereafter (Table 2). The improvement of both the motor score (UPDRS III) and the activities of daily living score (UPDRS II), was paralleled by an increase of the Schwab and England score up to 50 % six months after the surgical procedure which reflected the higher level of independence. These data are in accordance with recently published results from clinical studies [7, 22, 24, 27].

To evaluate the influence of DBS-STN on patients' health status we used the Sickness Impact Profile [11]. The SIP is a multidimensional, reliable and well-validated measure of functional disability that has been used with a variety of medical conditions including Parkinson's disease [3, 25]. At baseline the results in SIP values were in accordance with published findings [25]. Following DBS-STN we observed a significant improvement in the SIP overall score as well as in the SIP physical dimension score compared with baseline values (Fig. 1). The improvement was due to decreased scores of the items *Body Care and Movement, Sleep and Rest, Ambulation, Social Interaction* as well as the *Recreation and Pastimes* (Fig. 1). Despite the limited number of patients included in this present study there is a considerable improvement in the perception of the health of PD patients following DBS-STN. Similar findings with a considerable improvement of the quality of life following DBS-STN have been reported in two studies using different quality of life scales [10, 14]. So far, these studies are available only in abstract form, therefore a detailed discussion and comparison is not yet feasible.

The cost-effectiveness of DBS-STN was evaluated by calculating the incremental costs of patients treated with DBS-STN against the drug costs at baseline using the UPDRS as an outcome measurement. Unfortunately, we were not able to evaluate quality adjusted life years (QALY) as the calculation of utilities was not feasible. Neither the SIP- nor the UPDRS-scale are easily transferable into utility scores (difference in scales (profile vs. index scales); requirement of cardinal data) [6].

For each unit amelioration in UPDRS (total score) additional costs of DM 1800 have to be spent in patients with DBS-STN compared with patients on drug treatment alone. Unfortunately, no cost-consequence or cost evaluation studies have been performed for drug treatment or DBS so far, which would allow a direct comparison. Recently, a French group evaluated the costs of DBS-STN from the perspective of the hospital [5]. Total costs were FF 192,814 (EUR€ 29,390) including FF 57,732 (EUR€ 8,800) for hospital stay, and FF 135,082 (EUR€ 20,590) for material and personel. Unfortunately, only immediate costs were included and costs due to long-term follow-up were not assessed. For another surgical treatment option of PD, pallidotomy, a preliminary report is available. Using a decision analytic model from a societal perspective with a one year time horizon, Siderowf et al. evaluated the incremental cost-effectiveness of stereotactic pallidotomy compared with add-on treatment with pramipexole [32]. In this study costs due to medical services were approximately US$ 22,000. The incremental cost-effective ratio for pallidotomy relative to pramipexole was US$53 718 per QALY (quality adjusted life years). The authors concluded that cost-effectiveness of pallidotomy reaches that of pramipexole when procedure costs are reduced by two-thirds or the utility after the procedure is equivalent to being restored to normal health. Pallidotomy produces a greater benefit but at a substantially higher cost. This may be also true for DBS-STN. However, the clinical improvement following DBS-STN seems to be more pronounced than in patients with pallidotomy. Despite the high initial costs in the first year, we would hypothesize that DBS-STN would have a more favorable cost-effectiveness ratio: 1) a longer time horizon would need to be evaluated. As far as studies are available for the long-term efficacy and long-term side-effects, major costs occur within the first 6–12 months following surgery. Thereafter, costs associated with the electronic device are considerably decreased (the generator exchange due to battery exhaustion after 4–5 years would generate additional costs and the adjustment of the stimulation parameters). 2) if all types of costs, including indirect and intangible costs [15, 21] are considered. Several studies, which evaluated the economic burden of PD have shown that these costs have a considerable impact on the total expenditure [9, 19, 23]. Although only one patient in this study returned to full-time employment following DBS-STN, we have several patients who were able to return to a regular

working role. Furthermore, a recent study described "that women reported a striking improvement in coping with domestic chores and social life [27]. Five housewives regained the ability to cook, wash, iron and take care of the family. In all patients the improvement in self-care reduced the need for helpers." Although the monetary evaluation of improved activities of daily living, the reduced amount of help by care-givers and increased quality of life is difficult, they are markedly affected following DBS-STN and should be considered.

There are several limitations to this study. First, the cost calculations as well as the duration of hospital stay presented in this study must be used with caution as they depend highly on the health care provider, the reimbursement of the electronic device and the daily hospital charges, which may influence the decision of the treating physicians of whether to provide the necessary care in an in- or outpatient setting (one patient in Düsseldorf required a preoperative in-patient stay of 40 days in the neurological ward because the decision for surgery was made after a final attempt of a high-dose agonist therapy had failed during the same hospitalization, which resulted in total hospital costs of DM 77,360 for this patient). As outlined in Material and Methods, the costs for the electronic device were reimbursed through the inpatient stay. In other settings, for example the costs for the device will be paid by the health care provider and only a short pre- and post-operative stay will be reimbursed.

A second factor which could confound this analysis is the long-term cost of follow-up and late complications. For our study the observation period was set at 12 months. At the moment no studies are available on the long term efficacy and the side-effects of DBS-STN. This complicates a statement on the expenses associated with DBS and makes a modeling of the costs of DBS in a 5- or 10-year horizon difficult. Third, only direct costs were included in this study. We have not attempted to place a value on the improved quality of life of PD patients and reduced social stress as well as the reduced dependency. The current analysis also did not assess the effect of DBS-STN on the indirect costs. One patient of this study returned to full employment. As this treatment option, given current evidence, is also helpful to younger PD patients, indirect costs may have a considerable impact and must be included in an economic evaluation of DBS.

In conclusion, DBS-STN is an effective treatment which considerably alleviates the severity of sign and symptoms and improves the patients' perceived health status as well as quality of life of patients with PD. When costs of DBS-STN are compared with best medical treatment, DBS-STN is considerably more expensive when only direct medical costs are considered in a one year follow up. We would assume, that a study, which would evaluate expenses over a long-term and which would also include other costs (direct and indirect) would have a more favorable outcome.

Is DBS-STN for the treatment of Parkinson's disease cost-effective? Currently, in most countries, including Germany, there is no consensus about levels of expenditure that are cost-effective. The cost that is reasonable to pay for an extra unit of effectiveness is a matter for the relevant decision maker [20]. Our analysis suggests that using DBS-STN will require more than DM 1800 per UPDRS-point gained compared with best drug treatment. Unfortunately, no cost-effective studies of treatment options in PD are available, which would allow for a comparison. Furthermore, we were not able to calculate QALYs in this study, therefore a comparison in "league tables" with other treatments is not feasible. More precise estimates of cost-effectiveness and cost-utility will be possible when ongoing clinical trials have measured the long-term effect of DBS-STN in large samples of patients. This study is underway in Germany within the "Medical Kompetenznetz Parkinson-Syndrome".

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