Impact of STN-DBS on life and health satisfaction in patients with Parkinson’s disease

Joseph Ferrara, Alan Diamond, Christine Hunter, Anthony Davidson, Michael Almaguer, Joseph Jankovic

ABSTRACT

Objective Advanced Parkinson’s disease (PD) is associated with various motor and non-motor symptoms which adversely impact health-related quality of life (HRQoL). Subthalamic nucleus (STN) deep brain stimulation (DBS) has been reported to improve some dimensions of HRQoL in appropriately selected candidates. Prior studies of HRQoL following DBS have used instruments comprising a predetermined list of questions which assess issues that are generally relevant in PD, but that may not be of equal or consistent importance to all individuals. In this study, we evaluate the effect of STN DBS on quality of life using the QLSM, a modular questionnaire in which satisfaction scores for each item are weighted in light of patient-rated importance.

Methods We prospectively analysed QLSM scores in 21 patients with PD (11 men, mean age 61.5 ± 8.6 years) before STN DBS surgery and at a mean 7.4 ± 1.5, and again at a mean 16.6 ± 6.8 months postoperatively.

Results Following STN DBS, patients experienced an improvement in HRQoL as measured by various items of the movement disorder and health modules of the QLSM. Specifically, QLSM items pertaining to energy level/enjoyment of life, independence from help, controllability/fluidity of movement and steadiness when standing and walking showed significant improvements, although items concerning general life issues (eg, occupational function, interpersonal relationships, leisure activities) did not improve.

Conclusion Following STN DBS, symptomatic and functional improvements translate into higher HRQoL, with high satisfaction in domains related to movement disorders and general health.

INTRODUCTION

Parkinson’s disease (PD) is a progressive neurodegenerative disorder characterised by motor, sensory, autonomic, cognitive-behavioural and sleep-related symptoms. Dopaminergic medications, the cornerstone of PD treatment, alleviate a subset of these symptoms, but drug efficacy may wane over time. Furthermore, dopamine replacement therapy, especially levodopa, often produces complications which have a negative impact on patient function, including motor fluctuations and dyskinesias. In a subset of PD patients with levodopa-induced motor complications, high-frequency DBS is uniquely suited to improve both PD motor deficits as well as medication-related complications, and the efficacy of DBS in this setting is now well established. STN DBS, however, fails to address numerous symptoms that are disabling in advanced PD, such as levodopa-refractory axial motor disturbances. Also, DBS is itself associated with potential side effects including postoperative complications, 2 cognitive dysfunction, 4 depression, 7 social maladjustment and impaired articulation—all of which may impact patient satisfaction.11–15

Given these complexities, clinicians have increasingly utilised patient-based outcome measures, such as health status (HS) and health-related quality of life (HRQoL), to characterise and quantify the benefits of PD treatments. There is not yet a universally accepted definition of either HS or HRQoL, but there is growing opinion that, though inter-related, HS and HRQoL are distinct constructs. HS refers to an individual’s assessment of his/her physical, mental and social condition and function.11,16 The WHO defines quality of life as ‘an individual’s perception of his/her position in life in the context of the culture and value systems in which he/she lives and in relation to his/her goals, expectations, standards and concerns’.11 HRQoL is conceptually similar to quality of life but targeted to matters of medical well-being. Accordingly, HS questionnaires focus on the presence of symptoms (eg, motor dysfunction, fatigue, pain, embarrassment or loneliness) and their impact on one’s ability to perform various life activities (eg, housework, bathing, communicating or leisure activities), while HRQoL instruments measure a patient’s subjective experience of symptoms and satisfaction with health conditions. HRQoL differs from HS in that it gauges not only the presence and severity of functional limitations, but also to what extent such restrictions actually disturb the individual.11,16 The distinction between HS and HRQoL is of consequence because differences in lifestyle, social support, coping mechanisms and personality traits may influence how HS variables affect HRQoL.13,19 and available data indicate that patients themselves view HS and HRQoL as distinct constructs.11,15,16,20

The division is not meant to invalidate the utility of HS instruments, rather to emphasise that a modest problem in an area of great personal importance may impact an individual’s quality of life more so than a severe problem that is of lesser personal importance.

Several prior studies have demonstrated improvements in HS following DBS,11,21–23 yet all have employed questionnaires (such as the PDQ-39 and PDQ-L) that evaluate HS in PD, thus providing only an approximation of HRQoL. Furthermore, studies have arrived at conflicting results regarding the effect of DBS on certain HS parameters,24–26 such as communication.23–26 Most studies have
shown that cognitive and social HS remains static following DBS,25 27–30 but results in these domains are also mixed.31–33 Accordingly, we sought to provide pilot data regarding outcome following STN DBS using the Questions on Life Satisfaction (QLSM) modular questionnaire, a recently validated movement disorder and DBS-specific HRQoL instrument in which satisfaction scores for each item are weighted in light of patient-rated importance.34

METHODS

Participants

We enrolled 23 consecutive patients with PD, defined according to the UK Parkinson’s Disease Brain Bank criteria,32 who underwent DBS at the Baylor College of Medicine Movement Disorders Clinic in Houston, Texas. All had an excellent response to levodopa but developed motor complications refractory to medical management and met inclusion criteria for STN DBS, as per the recommendations of the CAPSIT-PD panel.36 Exclusion criteria were as follows: age <30 or >75 years, Mini-Mental Status Examination (MMSE) score <24 or other evidence of dementia on a comprehensive neuropsychological evaluation, medically uncontrolled psychiatric comorbidity and medical contraindications to surgery. The final decision for implantation was made in a multidisciplinary meeting attended by a neurosurgeon, movement disorder specialists, clinical nurses and a neuropsychologist. One hundred per cent of eligible patients consented to participate in the study, but two were lost to follow-up after their baseline (preoperative) assessment due to geographical limitations and were not included in our analysis. An additional two patients completed their first but not second follow-up assessment. All patients signed an informed consent before entering the study, and the study protocol was approved by the Baylor College of Medicine Internal Review Board for Human Research.

Surgical procedure

All STN DBS procedures were performed by one neurosurgeon in two stages: (1) insertion of bilateral electrodes (Medtronic 3389, Minneapolis, Minnesota) under local anaesthesia, and (2) connection of the electrodes to pulse generators under general anaesthesia, performed approximately 1 week after lead placement. For electrode implantation, stereotactic guidance, microelectrode recording and macroelectrode stimulation with neurological monitoring were used to determine the optimal site for placement. During the follow-up period, medication and DBS parameters were individually optimised in repeated programming sessions.

Evaluation procedures

HRQoL was prospectively measured via an expanded version of the Questions on Life Satisfaction (QLSM), a modular questionnaire that has been designed specifically to evaluate quality of life in the DBS population.34 The QLSM contains modules which address general life satisfaction (QLSM-A), general health satisfaction (QLSM-G), movement disorder-specific health satisfaction (QLSM-MD) and satisfaction with DBS (QLSM-DBS). The QLSM-MD comprises 12 items, the QLSM-DBS comprises five items, and the QLSM-A and QLSM-G each have eight. QLSM-MD includes questions concerning fluidity of movement, balance, hand dexterity, speech, swallowing, sensory phenomena, bladder and intestinal function, sexual function, sleep, memory and clarity of thinking, independence from help, and conspicuousness of illness. QLSM-DBS includes questions concerning reliability, visibility, independent handling, physician care and side effects of the neurostimulator. Questions on the QLSM-A concern friendships, leisure activities, overall health, financial security, occupational function, living conditions, family life and partner (spousal) relationships. The QLSM-G comprises questions regarding physical condition, relaxation and inner peace, energy level, discomfort and pain, mobility, hearing and vision, anxiety and independence. Each QLSM module is divided into two sections: one section rates the importance of various items and the other, the satisfaction associated with each item. Importance and satisfaction scores for each item are combined to provide information about weighted satisfaction; accordingly, scores reflect one’s satisfaction with items that one considers to be important. Weighted satisfaction scores may range between −12 and +20 for each item, with higher scores indicating an increase in quality of life. Weighted satisfaction is calculated by the following formula: weighted satisfaction = (importance rating −1) × [(2 × satisfaction rating) − 5]. Patient scores reflect HRQoL over the preceding 4 weeks. Floor and ceiling effects of the scale are negligible. Content validity of the QLSM was obtained through exploratory interviews with patients. Construct validity was established by means of correlations with established instruments: Medical Outcomes Study 36-Item Short-Form Health Survey (SF-36) and the EuroQol (EQ-5D).37–39 The Cronbach α values of the module summary-scores are as follows: 0.70 for the QLSM-A, 0.75 for the QLSM-G, 0.87 for the QLSM-MD and 0.73 for the QLSM-DBS.34–39

Supplemental assessments included the Geriatric Depression Scale (GDS),40 Unified Parkinson’s Disease Rating Scale (UPDRS),41 Lang–Fahn activities of daily living dyskinesia scale (LABFADLDS),42 Modified Hoehn and Yahr score,43 Folstein Mini-mental status examination44 and EQ-5D.37–39 The EQ-5D is a standardised instrument for valuing HS across five domains (mobility, self-care, usual activity, pain/discomfort and anxiety/depression). Data were collected and scored as per the published guidelines for each instrument.

Prospective clinical assessments were performed at baseline (within 30 days prior to surgery), and at approximately 6 (7.4±1.5) and 12 (16.6±6.8) months postoperatively. All three assessments were identical, with two exceptions. First, prior to DBS, the UPDRS was performed in the medically ‘off’ and ‘on’ states. The medical ‘off’ state was achieved by having patients hold anti-PD medications for >12 h prior to their examination; subsequently the medical ‘on’ state was achieved by having patients take 1–1.5 times their usual morning levodopa dose, followed by an examination 1–2 h later. After DBS surgery, the UPDRS was assessed off dopaminergic medications following optimisation of stimulation parameters. Second, the QLSM-DBS satisfaction scores could not be assessed preoperatively, but the importance subsection of the QLSM-DBS was completed at baseline. Adverse events were prospectively recorded at each clinic visit.

Data analysis

The primary outcome measure was the change from baseline in the QLSM-MD summary weighted score following DBS. Secondary outcome measures included change from baseline in other QLSM modules, UPDRS, LABFADLDS and the additional instruments cited above. Change from baseline was analysed by repeated-measures analysis of variance (ANOVA). Huyhn–Feldt epsilon correction was used to compensate for lack of independence. The Pearson product-moment correlation (ρ) was used to identify associations between HRQoL (change in QLSM-MD summary score from assessment 1 to 3) and clinical variables. The criterion for statistical significance was set at a two-sided
RESULTS
Sociodemographic and baseline clinical characteristics are listed in tables 1, 2. STN DBS produced significant improvements in LFAQLDS and UPDRS part II, III and IV scores as well as general health (QLSM-M-G) and movement disorder health (QLSM-MD) satisfaction (table 2). The following HRQoL domains significantly improved following surgery: QLSM-G items pertaining to energy level/enjoyment of life and independence from help; and QLSM-M-D items pertaining to controllability/fluidity of movement, steadiness when standing and walking, hand dexterity (eg, when eating and writing), absence of false bodily sensations, undisturbed sleep, independence from help and inconspicuousness of illness. QLSM-M-D items concerning swallowing, bladder/intestinal function and cognition insignificantly improved following surgery, while items related to articulation and sexual excitability insignificantly worsened. No items on the general life satisfaction module (QLSM-A) changed significantly following surgery. On the QLSM-DBS, patients rated neurostimulator reliability, doctoral care and the absence of bodily symptoms as more important than inconspicuousness or independent handling of the stimulator. Weighted scores on the DBS module of the QLSM showed high satisfaction (table 2), which remained stable between the two postoperative assessments (Student t test, p=0.45).

The difference in preoperative Hoehn and Yahr scores between the medically ‘off’ and ‘on’ states correlated with improvement in the QLSM-M-D summary score (r=0.72, p=0.0005). No other baseline variable predicted long-term improvement in HRQoL. We also assessed the relationship between HRQoL and changes in clinical parameters following surgery. HRQoL benefits correlated with the postoperative improvements in the off-state UPDRS part II (r=−0.59, p=0.046) and the GDS (r=−0.47, p=0.007). HRQoL benefits did not correlate with changes in other variables, including a reduction in dopaminergic therapy.

Following DBS, patients reduced dopaminergic therapy by an average of 499±881 LEU mg/day. There was no change in postoperative MMSE (27.4±6.8 at baseline, 26.7±7.6 at assessment 2, and 28.5±1.7 at assessment 3, p=0.7) or Geriatric Depression Scale scores (5.1±2.9 at baseline, 4.4±2.7 at assessment 2, 5.1±3.3 at assessment 3, p=0.8). No patient experienced serious or persistent complications related to DBS, and none has required DBS revision.

DISCUSSION
The primary finding of our study was that various aspects of HRQoL improved following STN DBS, particularly satisfaction with motor function and independence. Improvements, however, did not extend to the QLSM-A, which addresses general life issues, such as occupational function, interpersonal relationships, leisure activities and living conditions. Importantly, in our population, no QLSM domains significantly worsened following DBS. Overall, the results of this study are consistent with those that have utilised HS questionnaires, such as the PDQ-39. As we did not directly compare the QLSM with the PDQ-39, we cannot establish how these instruments might correlate or diverge in clinical practice. A recent cross-sectional survey of PD patients compared the PDQ-39 to the SEIQoL, a generic quality-of-life instrument which, like the QLSM, allows each patient to factor in what elements he/she considers to be important at that time.3 The authors found that social, cognitive and emotional factors better predict overall quality of life compared with physical aspects of disease, but there was significant variability among individuals. As the PDQ-39 heavily emphasizes motor function, the findings of that study question its relevance as a quality of life measure in PD. Our study cannot comment on which life areas are most important in PD patients at large, but it does demonstrate that patients undergoing DBS place high importance on the motor aspects of their disease and that many important health domains improve following surgery. The fact that other relevant life domains (eg, financial security) do not improve is incontrovertible but should not diminish the benefits which are obtained.

The present study was not focused on cognitive parameters and did not include postoperative psychometric testing apart from the MMSE, which is insensitive to the spectrum of cognitive deficits that have increasingly been associated with STN DBS.4-7 The study does, however, provide some insight regarding how patients perceive their cognitive status following DBS. Despite evidence that even subtle cognitive problems which follow STN stimulation may restrict patient function,4 we found a trend towards improved satisfaction regarding memory and clarity of thinking after DBS (p=0.08). In contrast, there was a decline in satisfaction regarding articulation and fluency of speech which did not reach statistical significance (0.71±5.8 at baseline, 4.63±5.7 at assessment 2, and −1.58±2.8 at assessment 5, p=0.15). This is consistent with our findings of declines in verbal fluency and recall in our patients following STN DBS despite good motor outcome.5 A prior study found that some PD patients suffer from a negative alteration of body image, loss of vitality, and both social and professional maladaptation after DBS.9 The QLSM-DBS does not have content regarding alterations in self-perception, but satisfaction regarding stimulus side effects and conspicuousness (including the casing and scars) was high. Furthermore, the QLSM-G (general health module) showed a significant improvement in ‘energy level/enjoyment of life,’ and no trend towards diminished ‘inner peace’ following DBS. It is unknown whether a formal psychological assessment would have found evidence of personal or interpersonal maladjustment following DBS, and further work is needed to better define how the neuropsychiatric and cognitive changes which follow STN DBS impact patient function and HRQoL.

We found a moderate association between HRQoL and improvements in the GDS. This finding is congruent with prior work which has shown that depression is an important

<table>
<thead>
<tr>
<th>Table 1 Sociodemographic and clinical characteristics at baseline</th>
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<tbody>
<tr>
<td><strong>Sex, male/female</strong></td>
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<tr>
<td><strong>Age (years), mean±SD</strong></td>
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<tr>
<td><strong>Age (years) at onset, mean±SD</strong></td>
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<tr>
<td><strong>Level of education (years), mean±SD</strong></td>
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<tr>
<td><strong>Employment status</strong></td>
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</tr>
<tr>
<td>Retired (no)</td>
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<tr>
<td>Disabled (no)</td>
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<tr>
<td><strong>Marital status, number</strong></td>
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<tr>
<td>Married (no)</td>
</tr>
<tr>
<td>Divorced (no)</td>
</tr>
<tr>
<td>Single (no)</td>
</tr>
<tr>
<td><strong>Family history of Parkinson’s disease (no)</strong></td>
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<tr>
<td><strong>Lеводопа equivalent units dosage, mean mg/day±SD</strong></td>
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<tr>
<td><strong>Patients on dopamine agonist (no)</strong></td>
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<tr>
<td><strong>Hoehn and Yahr score, mean±SD</strong></td>
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<tr>
<td>On-state</td>
</tr>
<tr>
<td>Off-state</td>
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</tbody>
</table>

*Similar to prior studies, LEU was based on the following formula: regular levodopa dose + controlled-release levodopa × 0.75 + levodopa × 0.25 if on entacapone + pramipexole × 0.67 + ropinirole × 16.7 + apomorphine × 8 (all dosages in milligrams).15
indicator of HS.12–14 46 HRQoL was also associated with UPDRS part II scores, a measure of activities of daily living, as might be expected based upon shared content between these measures. Among baseline characteristics, HRQoL correlated best with the reduction in Hoehn and Yahr score between the medially ‘off’ and ‘on’ states. Because the Hoehn and Yahr score is heavily influenced by balance, we hypothesise that postural instability influences movement disorder-related quality of life to a greater extent than other motor features, such as tremor. Worsening Hoehn and Yahr scores have previously been shown to negatively impact HS.14 15 Our work shows that among DBS candidates, those who have the most robust reduction in Hoehn and Yahr score with dopaminergic therapy are the most likely to experience better HRQoL following surgery. Additional studies are needed to better define which clinical variables best predict enhanced HRQoL following DBS, as such data will guide refinements in patient selection criteria.

We recognise limitations of this study including the small sample size and lack of a control population. To date, there have been few randomised controlled trials of DBS versus medical management, and both ethical and practical concerns preclude a double-blind, placebo-controlled study.29 47 Studies comparing surgical patients with those treated with optimal medical therapy have reported efficacy data favouring DBS, but the surgical patients generally experienced more severe adverse effects.31 48 Since our study only included patients with bilateral STN DBS, it cannot address whether unilateral stimulation or an alternate target, such as the globus pallidus, would be preferable.3 49–51 Like all questionnaires, the QLSM has limitations. It has not yet been extensively studied in the PD population, so its test–retest reliability, sensitivity to change and the minimum clinically relevant change have not been established. Because the QLSM is designed to assess a range of movement disorders (including essential tremor and dystonia), it is less targeted to PD than currently available HS instruments, such as the PDQ39 and PDQL. For example, the QLSM does not include questions regarding sleep attacks (like the PDQ39) or drooling (like the PDQL). However, QLSM does assess the core motor and non-motor features of PD including balance, dexterity, independence, fatigue, anxiety, pain and autonomic symptoms, and it is the only available movement disorder questionnaire to weight satisfaction in light of patient-rated importance. Our findings, therefore, extend the previously reported beneficial effects of STN DBS on various HS measures by demonstrating high personal satisfaction with DBS, particularly with respect to domains of the QLSM related to general health and disorders of movement.

Table 2 Clinical outcome following STN DBS

<table>
<thead>
<tr>
<th>Instrument</th>
<th>Assessment 1 (baseline)</th>
<th>Assessment 2 (7.4±1.5 months)</th>
<th>Assessment 3 (16.6±6.8 months)</th>
<th>Significance (p value)</th>
</tr>
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<tr>
<td>LFADLDS</td>
<td>12.4±5.9</td>
<td>3.7±4.7</td>
<td>4.1±6.0</td>
<td>0.001</td>
</tr>
<tr>
<td>UPDRS</td>
<td>Part I</td>
<td>2.6±1.7</td>
<td>1.8±1.4</td>
<td>2.0±2.4</td>
</tr>
<tr>
<td></td>
<td>Part II off-state (on-state)</td>
<td>20.7±7.4 (11.7±5.9)</td>
<td>14.0±7.6</td>
<td>15.3±6.3</td>
</tr>
<tr>
<td></td>
<td>Part III off-state (on-state)</td>
<td>36.9±19.4 (27.3±16.4)</td>
<td>25.1±11.9</td>
<td>23.2±11.9</td>
</tr>
<tr>
<td></td>
<td>Part IV</td>
<td>8.5±3.5</td>
<td>3.6±3.6</td>
<td>4.7±3.4</td>
</tr>
<tr>
<td>EQ-SD Preference-weighted Index Score</td>
<td>0.95±0.07</td>
<td>0.98±0.05</td>
<td>0.96±0.08</td>
<td>0.3</td>
</tr>
<tr>
<td>QLSM Summary Scores</td>
<td>General life (A)</td>
<td>58.2±32.6</td>
<td>56.1±39.5</td>
<td>53.6±32.0</td>
</tr>
<tr>
<td></td>
<td>General health (G)</td>
<td>11.6±50.3</td>
<td>37.5±43.6</td>
<td>28.4±48.4</td>
</tr>
<tr>
<td></td>
<td>Movement disorders (MD)</td>
<td>10.5±73.4</td>
<td>89.1±54.0</td>
<td>49.0±65.3</td>
</tr>
<tr>
<td></td>
<td>Deep brain stimulation (DBS)</td>
<td>not applicable</td>
<td>59.9±19.0</td>
<td>54.6±20.2</td>
</tr>
</tbody>
</table>

All results are listed as mean ± SD. Scores for the QLSM-A and QLSM-G modules may range between 96 and 160; scores for the QLSM-MD and QLSM-DBS modules may range from 144 to 240 and from 60 to 100, respectively.

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Competing interests None.

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