The effect of deep brain stimulation on quality of life in movement disorders

A Diamond, J Jankovic

Deep brain stimulation (DBS) is a viable treatment alternative for patients with Parkinson’s disease (PD), essential tremor (ET), dystonia, and cerebellar outflow tremors. When poorly controlled, these disorders have detrimental effects on the patient’s health related quality of life (HRQoL). Instruments that measure HRQoL are useful tools to assess burden of disease and the impact of therapeutic interventions on activities of daily living, employment, and other functions. We systematically and critically reviewed the literature on the effects of DBS on HRQoL in PD, ET, dystonia, and cerebellar outflow tremor related to multiple sclerosis.

METHODS

We reviewed the literature in English from 1965 to 2005 using the following sources to identify clinical studies: Medline, Pre-medline, Sociofile, Psych Info, Health and Psychosocial instruments, Healthstar, the Cochrane Library, and reference lists of included publications. We used the following search terms: Parkinson’s disease, ET, dystonia, and MS combined with surgery, DBS, treatment, subthalamic nucleus (STN), globus pallidus (GPi), thalamus (Vim) AND quality of life, patient reported, satisfaction, preference, and health status. The identified articles were then reviewed to verify that they included patient reported outcomes; those that did not were excluded. The review was restricted to articles assessing HRQoL instruments in PD treated with STN-DBS, Vim-DBS, or GPi-DBS; ET and MS treated with Vim-DBS; and dystonia treated with GPi-DBS. The level of evidence was rated using criteria adapted from the Oxford Centre for Evidence-Based Medicine (table 1).

RESULTS

Parkinson’s disease

Parkinson’s disease is a chronic, progressive neurological disorder characterised by tremor, bradykinesia, postural instability, and rigidity. Features that strongly influence HRQoL in PD are progressive motor impairments, depression, anxiety, and mobility. In PD, there is a strong association between motor complications with deterioration of HRQoL and advancing stages of Parkinson’s disease.

Abbreviations:

ADL, activities of daily living; BAI, Beck’s Anxiety Index; BDI, Beck Depression Index; BFMD, Burke-Fahn-Marsden dystonia scale; DBS, deep brain stimulation; ET, essential tremor; GPi, globus pallidus; HRQoL, health related quality of life; MS, multiple sclerosis; NHP, Nottingham Health Profile; PD, Parkinson’s disease; PMS, Profile of Mood State; QUEST, Quality of Life in Essential Tremor Questionnaire; SF-36, Medical Outcomes Study 36-item Short-Form General Health Survey; SIP, Sickness Impact Profile; STN, subthalamic nucleus; TWSTR Scale, Toronto Western Spasmodic Torticollis Rating Scale; Vim, ventral intermediate nucleus of the thalamus.
the disease.10–11 In addition to their detrimental impact on HRQoL, motor impairments disrupt mobility and ADL,14 which restricts patients’ independence leading to an increased reliance on caregivers.

We identified 13 prospective studies that assessed HRQoL as an outcome in patients with STN-DBS. We excluded five of these as two were not available in English15 16 and three lacked sufficient detail to be included.17–19 Of the remaining eight articles, there were various levels of evidence; only one study provided class 1b evidence20 and the remaining seven were categorised as class 221–26 (table 2). In the class 1b study, 34 patients were randomised to unilateral pallidotomy or bilateral STN-DBS.25 The Parkinson’s Disease Quality of Life questionnaire (PDQL) was a secondary outcome. Both groups showed similar improvements in mean PDQL total scores at 12 months.25 Furthermore, all dimensions of the PDQL improved: social function (63%; p = 0.001), PD related symptoms (48%; p < 0.001), systemic symptoms (34%; p < 0.001), and emotional functioning (29%; p = 0.001). There was a significant improvement in depression after surgery.

A total of 84 patients in five class 2 studies with STN-DBS were evaluated with the Parkinson’s Disease Questionnaire 39 (PDQ-39) instrument.10–12 13 25 27 Mobility, ADL, stigma, emotional wellbeing, and bodily discomfort showed consistently greater improvements, whereas social support, cognition, and communication were less improved. Tröster et al found the improvements in PDQ-39SI correlated with improvements in depression rather than in motor function.25 In contrast, others have found improvements in levodopa induced motor complications and UPDRS scores correlated with improvements in the PDQ-39SI whereas depression and anxiety did not.23 27

In a class 3 study, 39 patients with PD were treated with unilateral pallidotomy (n = 23), unilateral GPi-DBS (n = 9), or unilateral Vim-DBS (n = 7; see below).28 The surgical option was selected based on the patient’s symptoms (that is, tremor dominant PD was treated with Vim-DBS). In the unilateral GPi-DBS treated group, the mean SIP total score (improved from 21.6 to 10.9; p = 0.021) and SIP physical impairment score (improved from 23.3 to 9.4; p = 0.008) showed significant improvements, while the SIP psychosocial impairment score showed only a trend towards improvement (from 21.2 to 12.4; p = 0.086). In addition, depression and anxiety as measured by Beck’s Anxiety Index (BAI) (from 18.2 to 11.9; p = 0.007) and the Beck Depression Index (BDI) (from 9.9 to 7.0; p = 0.067) also improved, although the latter did not reach statistical significance.

Two studies have assessed the effects of Vim-DBS on the HRQoL in patients with PD (table 2).

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### Table 1 Evidence-Based Medicine criteria

<table>
<thead>
<tr>
<th>Level</th>
<th>Description</th>
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<tbody>
<tr>
<td>1a</td>
<td>Systematic review of randomised controlled trials</td>
</tr>
<tr>
<td>1b</td>
<td>Randomised controlled trial</td>
</tr>
<tr>
<td>2</td>
<td>Cohort study (consecutive patients) or low quality randomised controlled trial (for example, &lt;80% follow up)</td>
</tr>
<tr>
<td>3</td>
<td>Open label, non-randomised study with historical or other control group or open label study using convenience (that is, non-consecutive) or unspecified sample; cohort studies with five or fewer patients</td>
</tr>
<tr>
<td>4</td>
<td>Case series (that is, not designed as a clinical study; typically including five or fewer patients)</td>
</tr>
</tbody>
</table>

Adapted from the Oxford Centre for Evidence-Based Medicine criteria.8

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### Table 2 Quality of Life in Parkinson’s disease

<table>
<thead>
<tr>
<th>Reference</th>
<th>Class</th>
<th>Target</th>
<th>n</th>
<th>Age, mean (years)</th>
<th>Mean duration of disease (years)</th>
<th>HRQoL tool</th>
<th>Follow up (months)</th>
<th>HRQoL improvements</th>
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<tbody>
<tr>
<td>Esselink et al.20</td>
<td>1b STN</td>
<td>S = 20</td>
<td>S: 61 (55–66)</td>
<td>P: 14</td>
<td>P: 62 (57–68)</td>
<td>S: 12 (9–17)</td>
<td>PDQL</td>
<td>6</td>
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<tr>
<td>Lagrange et al.25</td>
<td>2 STN</td>
<td>60</td>
<td>S: 56 (SD 10)</td>
<td>P: 14</td>
<td>P: 62 (57–68)</td>
<td>14 (SD 8)</td>
<td>PDQL</td>
<td>12</td>
</tr>
<tr>
<td>Spotteke et al.27</td>
<td>3 STN</td>
<td>16</td>
<td>S: 56 (SD 8.5)</td>
<td>P: 10</td>
<td>P: 62 (57–68)</td>
<td>10.8 (SD 3.9)</td>
<td>SIP</td>
<td>6</td>
</tr>
<tr>
<td>Martinez-Martin et al.26</td>
<td>2 STN 17</td>
<td>60.9 (43–74)</td>
<td>16.4 (7–38)</td>
<td>PDQ-39</td>
<td>6</td>
<td>Total score improved 49%</td>
<td></td>
<td></td>
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<tr>
<td>Patel et al.22</td>
<td>2 STN</td>
<td>16</td>
<td>S: 56 (SD 11)</td>
<td>P: 10</td>
<td>P: 62 (57–68)</td>
<td>10 (SD 2.9)</td>
<td>PDQ-39</td>
<td>12</td>
</tr>
<tr>
<td>Just and Ostergaard21</td>
<td>2 STN</td>
<td>S = 11</td>
<td>M = 13</td>
<td>59.8 (51–80.9)</td>
<td>M: 61.4 (53.8–69.2)</td>
<td>14 (9–17)</td>
<td>PDQ-39</td>
<td>6</td>
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<tr>
<td>Tröster et al.27</td>
<td>2 STN</td>
<td>26</td>
<td>S: 56.6 (SD 11)</td>
<td>P: 13</td>
<td>P: 62 (57–68)</td>
<td>9.5 (SD 4.9)</td>
<td>PDQ-39</td>
<td>3</td>
</tr>
<tr>
<td>Lezzoni et al.29</td>
<td>2 STN</td>
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<td>S: 63 (SD 8.6)</td>
<td>P: 13</td>
<td>P: 62 (57–68)</td>
<td>14.3 (SD 5)</td>
<td>PDQ-39</td>
<td>12, 24</td>
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<td>Woods et al.30</td>
<td>3 Vim</td>
<td>7</td>
<td>S: 65.1 (SD 12.0)</td>
<td>P: 3</td>
<td>P: 62 (57–68)</td>
<td>7.33 (SD 2.66)</td>
<td>PDQ-39</td>
<td>12</td>
</tr>
<tr>
<td>Straits-Troster et al.31</td>
<td>3 Vim</td>
<td>7</td>
<td>S: 65.1 (SD 12.0)</td>
<td>P: 3</td>
<td>P: 62 (57–68)</td>
<td>8 (SD 3.8)</td>
<td>SIP</td>
<td>3</td>
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<tr>
<td>Straits-Troster et al.31</td>
<td>3 GPi</td>
<td>9</td>
<td>S: 65.1 (SD 12.0)</td>
<td>P: 3</td>
<td>P: 62 (57–68)</td>
<td>10.3 (SD 4.9)</td>
<td>SIP</td>
<td>3</td>
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</tbody>
</table>

GPi, globus pallidus; M, medically treated; NA, not available; P, unilateral pallidotomy; PDQ-39SI, Parkinson’s Disease Questionnaire Summary Index; PDQL, Parkinson’s Disease Quality of Life questionnaire; S, STN-DBS; SF-36, Medical Outcomes Study 36-item Short-Form General Health Survey; SIP, Sickness Impact Profile; STN, subthalamic nucleus; v, Spanish version; Vim, thalamus.

* p < 0.05.

† Mean score improvement.
In a class 3 study, six of 11 patients with unilateral Vim-DBS were assessed at 1 year with the PDQ-39. At follow up, only mean ADL (improved from 52 to 28.67; \( p < 0.05 \)) and emotional wellbeing (improved from 40.8 to 17.5; \( p < 0.05 \)) dimensions were significantly improved. In addition, anxiety and depression as measured by BAI (improved from 17.2 to 12.7; \( p < 0.05 \)) and the BDI (improved from 10.0 to 7.3; \( p < 0.05 \)) were also improved.

In a class 3 study, seven patients were treated with unilateral Vim-DBS (see above) and at 3 months there were non-significant improvements in mean SIP total score (from 14.1 to 13; \( p = 0.735 \)), physical dysfunction (from 10.8 to 9.1; \( p = 0.735 \)), and psychosocial dysfunction (from 13.8 to 12.7; \( p = 0.612 \)). In addition, there was no improvement in depression as measured by the BDI (from 7.7 to 10.0; \( p = 0.655 \)). This was in contrast to the pallidotomy and GPI-DBS treated groups where there were improvements in the physical dysfunction dimension and total SIP score. The authors concluded that the lack of improvement in the SIP in the Vim-DBS patients was due to the fact that tremor does not affect HRQoL as much as bradykinnesia or postural instability, symptoms usually not improved with Vim-DBS.

Pooled analysis of the three treatment groups revealed that improvements in mean SIP total score (from 8.59 to 6.37; \( p < 0.05 \)) and the SIP overall score worsened, suggesting a lack of sensitivity of the SIP in items important to patients with tremor. Although the BAI showed improvement in tension and anxiety (\( p < 0.05 \)) at 1 and 12 months, this was not verified with the BDI. Regarding a disease specific questionnaire, the authors used a modified PDQ-39, where they replaced the words “Parkinson disease” with “essential tremor”. At 12 months, there were improvements in ADL (from 48.55 to 27.38; \( p < 0.05 \)), emotional wellbeing (from 23.9 to 14.38; \( p < 0.05 \)), and stigma (from 35.69 to 16.28; \( p < 0.05 \)). Although improvements in communication were present at 3 months (from 21.03 to 10.90; \( p < 0.05 \)), they were no longer present at 12 months. In addition, emotional wellbeing, stigma, and ADL showed subtle declines between 3 and 12 months, but these were not significant. They authors attributed the declines to a possible honeymoon effect. A significant limitation of this study is that the PDQ-39 is not designed or validated for ET. The recently validated Quality of Life in Essential Tremor Questionnaire (QUEST) is the only disease specific questionnaire for ET and should provide valuable information regarding Vim-DBS effects on HRQoL in patients with ET. In addition to improving ADL, improvements in functional disability impact HRQoL.

### Multiple sclerosis
MS can be associated with action tremor in 50–75% of patients. Medical treatment usually does not provide adequate long term tremor suppression. Brice and McLellan reported 100% improvement in tremor suppression in two patients with MS. Vim-DBS has been reported to result in suppression of tremor in 88% of patients and 76% experience improvement in ADL. Even though Vim-DBS is associated with tremor improvement and less social embarrassment, this is not necessarily associated with improved overall disability. MS is associated with poor HRQoL and patients with MS are most concerned with mental health, emotional problems, and vitality, whereas clinicians are more concerned with physical problems. In MS, non-tremor related disabilities that affect HRQoL are gait abnormalities, pain, depression, loss of ability to work or engage in hobbies, incontinence, and stigma. Tremor can further decrease HRQoL by interfering with ADL, feeding, drinking, and hygiene. Although depression, fatigue, and disability level are independent predictors of HRQoL in MS, the effects of Vim-DBS have not been studied. In addition, declining cognition is associated with poorer HRQoL.

We identified two studies assessing Vim-DBS effects on HRQoL in patients with MS. One was excluded because...
results were presented as combined thalamotomy and Vim-DBS. There was one class 3 study assessing a general HRQoL instrument in MS. In this study, 12 patients with MS were treated with Vim-DBS and followed for 12 months (table 5). At 2 months, there were significant improvements in resting tremor (58%, p = 0.02), postural tremor (57%, p < 0.001), action tremor (70%, p < 0.001), and overall tremor severity (63%, p < 0.001) as measured by blinded videotape assessment. These improvements were maintained for 12 months. At 2 months, there were improvements in ability to feed oneself (p = 0.01) and a trend for improvement in dressing (p = 0.08), but changes in hygiene (p = 0.16) and writing (p = 0.34) were not significant, and at 1 year, the improvement in feeding was no longer significant (p = 0.17). At 12 months, there were negligible improvements in the Medical Outcomes Study 36-item Short-Form General Health Survey (SF-36) summary index and eight subscales. The authors concluded that although tremor was improved at 1 year, this did not correlate with improved HRQoL or patient satisfaction, possibly due to patient expectations or ataxia being uncovered. These results are in line with previous reports of a lack of improved disability or function in the setting of improved tremor. This is likely due to progression of MS or lack of appropriate tremor sensitive outcome measures, or because MS tremor does not make an important independent contribution to disability.

**Dystonia**

Treatment with GPI-DBS has been effective in patients with primary generalised dystonia, segmental dystonia, cervical dystonia (CD), blepharospasm-oromandibular cranial dystonia, myoclonus dystonia, and tardive dystonia. Patients with CD have poor HRQoL and predictors for HRQoL include self esteem, self deprivation, retired status, and disease severity. In addition, depression and anxiety worsen HRQoL. Longer disease duration and educational status are associated with better HRQoL, probably due to coping strategies.

We identified three articles that assessed HRQoL in patients with dystonia and GPI-DBS; one was class 2, while the others were class 3 and 4 (table 5). All studies used general HRQoL questionnaires and one used a modified PD specific questionnaire. In the class 2 study, 22 consecutive patients with primary generalised dystonia who underwent bilateral GPI-DBS were assessed at 3, 6, and 12 months with the Burke-Fahn-Mardsen dystonia scale (BFMD) and the SF-36. There were significant improvements in mean BFMD and disability score at 12 months. The SF-36 showed significant improvements at 12 months in measures of general health (16%), physical function (21%), and vitality (10%). There were no changes in mood or cognition. In a class 3 study, four patients with generalised dystonia and one with segmental dystonia were treated with bilateral and unilateral GPI-DBS, respectively. Four patients were DYT-1 negative, while one patient with generalised dystonia was DYT-1 positive. The SFMD, EuroQol 1, EuroQol 2, and PDQ-39 were assessed at 3–12 months. There was a 43% (p < 0.02) improvement in BFMD at follow up. The EuroQol 1 and EuroQol 2 improved by 56% (p < 0.05) and 400% (p < 0.02), respectively. Using a modified PDQ-39 (the words “Parkinson disease” were replaced with “disease”), there was a 65% improvement (p < 0.05) in PDQ-39SI. Dimension subscores were not available. One class 4 study, a preliminary report of two of 10 patients with CD treated with bilateral GPI-DBS, was published. The first patient, a 63 year old man, had improved Toronto Western Spasmodic Torticollis Rating (TWSTR) severity (from 15 to 4), pain (from 29 to 0), and disability (from 19 to 6) scores at 1 year. The SF-36 total score improved from 82.5 to 124.4 (146 represents perfect health). The second patient, a 48 year old man, had improved

<table>
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<tr>
<th>Citation</th>
<th>Class</th>
<th>n</th>
<th>Age, mean (years)</th>
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<th>HRQoL tool</th>
<th>Follow up (months)</th>
<th>HRQoL improvements</th>
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<td>Vidalhiet et al</td>
<td>2</td>
<td>22</td>
<td>30 (14–54)</td>
<td>18 (4–37)</td>
<td>SF-36</td>
<td>12</td>
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<td>Physical function 21%*</td>
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<td></td>
<td></td>
<td></td>
<td>Vitality 10%*</td>
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<td>Kiss et al</td>
<td>4</td>
<td>2</td>
<td>63</td>
<td>14</td>
<td>SF-36</td>
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<td>SF-36 total score 41.9</td>
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<td>SF-36 total score 30.3</td>
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<td>EuroQol 1</td>
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<td>34.5 (28–42)</td>
<td>NA</td>
<td>SF-36</td>
<td>12</td>
<td>No change in SF-36 total score or subscores</td>
</tr>
</tbody>
</table>

*p < 0.05.

NA, not available; PDQ39SI, Parkinson’s Disease Questionnaire Summary Index; SF-36, Medical Outcomes Study 36-item Short-Form General Health Survey.
Summary and comments

Most studies have focused on DBS and HRQoL in PD. In PD, most effects on global HRQoL appear to correlate with improved motor complications, although psychological aspects such as improved depression and anxiety play a role as well. To date, there has been only one randomised controlled trial evaluating the HRQoL in patients with DBS. Another drawback is that the PDQ-39 and PDQol questionnaires are not designed to address specific issues directly relevant to DBS, such as device inconspicuousness, controllability, reliability, the availability of qualified medical care, and safety and tolerability. Furthermore, more studies are required to adequately assess the impact of anxiety and depression on patient derived outcomes. There is a paucity of studies assessing HRQoL in ET, MS, and dystonia. It is apparent that there is little consensus on which HRQoL tool to utilise as outcome measures. Even though ET is more common than PD, studies on the effects of DBS on HRQoL in patients with ET are lacking. Previous studies have used modified PD questionnaires which were not designed or validated for ET and have questions that are not pertinent to patients with ET. However, the recently designed QUEST, an ET specific questionnaire, should provide valuable information regarding HRQoL in ET patients. Concerning MS and dystonia, further work is needed to better delineate the effects of DBS on HRQoL in these disorders. A recently published disease specific HRQoL instrument designed and validated for ET, PD, and dystonia (QLS-sm-MD), combined with a DBS specific questionnaire (QLS-sm-DBS) and generic questionnaires in a modular format (QLS-sm-A, and QLS-sm-G) should be utilised in future assessments of the impact of DBS on HRQoL. Despite the limitations of the published studies, there is growing evidence that DBS has a favourable impact on HRQoL in patients with PD and other movement disorders.

ACKNOWLEDGEMENTS

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Competing interests: none declared

REFERENCES

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ADDENDUM

After submission of the revised manuscript, two additional papers (class 2 evidence) assessing HRQoL in PD patients treated with bilateral STN-DBS were published. Draper et al evaluated 27 consecutive patients with the PDQ-39 and SF-36. At 12 months follow up there were significant improvements in the PDQ-39SI (21.1%) and mobility (25.6%), ADL (34.5%), and stigma (40.1%) subscores. In addition, the SF-36 global score improved by 22.5%; however, only physical function (28.4%) and physical role (76.6%) subscores were significantly improved. In another study, 29 consecutive patients were evaluated with the PDQ-39 and NHP. At follow up intervals of 1 and 12 months, there were significant improvements in the PDQ-39SI. Furthermore, four PDQ-39 subscores showed significant improvements: ADL, emotional well being, stigma, and bodily discomfort. There were significant improvements in NHP subscores assessing sleep, energy, emotional reaction, and social isolation. Interestingly, there was a negative correlation between the patient’s age and improvements in the PDQ-39 ADL subscore (r = 0.417; p = 0.031).
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