Deep Brain Stimulation in Parkinson’s Disease – Impact on Quality of Life

Mathias Toft

Physician and Researcher, Department of Neurology, Oslo University Hospital, Oslo, Norway

DOI: 10.17925/ENR.2012.07.51.27

Abstract
Health-related quality of life (HRQoL) is reduced in Parkinson’s disease patients. Deep brain stimulation (DBS) is an established treatment for motor problems and motor fluctuations in advanced Parkinson’s disease. Three randomised trials were recently conducted to assess the effects of DBS on HRQoL. All studies found improvements in HRQoL after surgery. DBS of the subthalamic nucleus and the globus pallidus interna improved HRQoL to a similar degree. However, in the long-term, such improvements may not be maintained, perhaps because HRQoL is a subjective measure and subjective perceptions of disability may change over time. DBS has proven long-term efficacy on motor symptoms, and the decline in benefit over time may also be explained by progression in the non-motor symptoms of the disease. Several predictors of HRQoL improvements after DBS have been identified, including good levodopa response, young age and good cognitive function.

Keywords
Parkinson’s disease, continuous dopaminergic stimulation, deep brain stimulation, health-related quality of life, motor fluctuations

Disclosure: Mathias Toft has received consulting and lecturing fees from Medtronic, Inc. and lecturing fees/travel support from Abbott, Lundbeck, Sanofi-Aventis, GlaxoSmithKline, Destin, Orion and UCB.

Acknowledgements: The V International Forum on Parkinson’s Disease (Helsinki, Finland, 6–7 May 2011) was funded by an unrestricted educational grant from Abbott. Abbott funded the development of this supplement by ESP Bioscience (Crowthorne, UK). Emily Chu and Nicole Meinel of ESP Bioscience provided medical writing and editorial support to the author in the development of this publication. Abbott had the opportunity to review and comment on the publication’s content; however, all decisions regarding content were made by the author.

Received: 22 June 2012 Accepted: 23 July 2012 Citation: European Neurological Review, 2012;7(Suppl. 1):27–30

Correspondence: Mathias Toft, Department of Neurology, Oslo University Hospital - Rikshospitalet, P.O. Box 4952 Nydalen, N-0424 Oslo, Norway. E: mathias.toft@ous-hf.no

Health-related Quality of Life in Parkinson’s Disease

In general, measures of Parkinson’s disease (PD) symptoms, biomedical markers or survival do not cover every aspect of the disease relevant or important to the patient. Health-related quality of life (HRQoL) is defined as the perception and evaluation by the patient of the impact that the illness and its consequences has had on their life. Therefore, it is a subjective measurement, but one that helps in providing a more rounded picture of the effects of a disease on the patient. Several forms and questionnaires have been developed to measure HRQoL, including generic forms such as the Short-Form 36 Health Survey (SF-36), and disease-specific forms such as the 39-item Parkinson’s Disease Questionnaire (PDQ-39).

HRQoL is reduced in PD patients. In a study that measured HRQoL using the Nottingham Health Profile in 233 PD patients and 100 healthy elderly people, PD patients had lower HRQoL in all measured dimensions (emotional reactions, energy, pain, physical mobility, sleep, social isolation and total score of the Nottingham Health Profile) compared with the healthy elderly people.1

Many factors in PD could impact on HRQoL, such as motor symptoms, non-motor symptoms (NMS), disability, social functioning limitations and drug side-effects. A study showed that a decline in physical mobility was the most important single factor contributing to worsening HRQoL in people with PD during long-term follow-up.2 It also showed that a deterioration in NMS, when taken together, had a greater impact on overall HRQoL than a decrease in physical mobility. In addition, poor HRQoL was predicted by more advanced disease, greater severity of depressive symptoms and presence of insomnia.

Changes in Health-related Quality of Life after Deep Brain Stimulation

Thousands of patients have been treated with deep brain stimulation (DBS) since the first procedure in 1993, and clinical results on motor symptoms and motor complications have been reported in a large number of publications.3 In the last few years, there have been three randomised studies that used measurements of HRQoL as important endpoints.4

One of these trials conducted pairwise comparison of subthalamic nucleus DBS (STN-DBS) plus medication (n=78) and medication alone (n=78).5 The primary endpoints were the changes from baseline to six months in HRQoL, as assessed by PDQ-39, and the severity of symptoms without medication, as assessed by the Unified Parkinson’s Disease Rating Scale Part III (UPDRS-III). Only the STN-DBS group showed significant improvements, which were in five of the eight PDQ-39 domains (see Figure 1). The domains that did not improve significantly with STN-DBS were social support, cognition and communication.

Another randomised controlled trial compared DBS (STN-DBS, n=60); globus pallidus interna DBS (GPI-DBS), n=61) and best medical therapy
improvement in the PDQ-39 summary index score at one year (n=134). Patients were monitored for six months and HRQoL was assessed by PDQ-39. Compared with baseline, the surgery group demonstrated a higher change from baseline to six months for PDQ-39 summary index (28.2 ± 25.3 points) than in the medical therapy group (20.1 ± 19.3 points) (p<0.001). The social support subscore did not change significantly between the two surgical therapies for any of the items. Table 1 demonstrates that DBS has a stable long-term effect on motor function, which may have a positive impact on patients’ HRQoL in the long-term.

Figure 1: Changes in 39-item Parkinson’s Disease Questionnaire Subscores from Baseline to Six Months in Patients Treated with Subthalamic Nucleus Deep Brain Stimulation plus Medical Therapies or Medical Therapies Alone

Table 1: Change in Quality of Life from Baseline to 24 Months, as Assessed by the 39-item Parkinson’s Disease Questionnaire, in Patients Treated with Pallidal Deep Brain Stimulation or Subthalamic Deep Brain Stimulation

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Pallidal Stimulation (n=152)</th>
<th>Subthalamic Stimulation (n=147)</th>
<th>Pallidal versus Subthalamic Stimulation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Quality of Life</td>
<td>Baseline 24 Months</td>
<td>Baseline 24 Months</td>
<td>Difference (95 % CI) p value†</td>
</tr>
<tr>
<td>Mobility</td>
<td>57.0 ± 22.3 46.6 ± 25.3</td>
<td>61.6 ± 20.6 54.0 ± 24.5</td>
<td>-2.3 (-7.6 to 3.1) 0.40</td>
</tr>
<tr>
<td>Activities of daily living</td>
<td>55.0 ± 18.6 41.4 ± 20.7</td>
<td>55.7 ± 18.1 46.6 ± 23.7</td>
<td>-4.4 (-9.3 to 0.5) 0.08</td>
</tr>
<tr>
<td>Emotional wellbeing</td>
<td>36.5 ± 18.9 33.4 ± 19.1</td>
<td>41.1 ± 18.6 39.1 ± 21.1</td>
<td>-1.2 (-5.6 to 3.2) 0.58</td>
</tr>
<tr>
<td>Stigma</td>
<td>38.7 ± 25.3 28.2 ± 22.4</td>
<td>42.1 ± 24.6 30.7 ± 25.3</td>
<td>1.0 (±4.5 to 6.4) 0.73</td>
</tr>
<tr>
<td>Social support</td>
<td>23.8 ± 17.2 26.0 ± 18.6</td>
<td>30.1 ± 19.3 29.4 ± 20.1</td>
<td>3.1 (±12.7 to 7.4) 0.16</td>
</tr>
<tr>
<td>Cognition</td>
<td>39.8 ± 16.7 38.9 ± 18.4</td>
<td>44.1 ± 17.0 43.5 ± 19.3</td>
<td>-0.4 (-4.2 to 3.5) 0.85</td>
</tr>
<tr>
<td>Communication</td>
<td>44.7 ± 19.5 48.5 ± 20.5</td>
<td>47.8 ± 18.6 53.1 ± 22.1</td>
<td>-1.5 (-6.3 to 3.3) 0.54</td>
</tr>
<tr>
<td>Bodily discomfort</td>
<td>48.1 ± 21.1 40.5 ± 21.8</td>
<td>52.8 ± 23.4 46.3 ± 24.0</td>
<td>-1.0 (±5.6 to 3.5) 0.65</td>
</tr>
<tr>
<td>Single index</td>
<td>42.8 ± 13.6 38.0 ± 15.3</td>
<td>46.9 ± 12.6 42.7 ± 15.6</td>
<td>-0.6 (±3.6 to 2.4) 0.69</td>
</tr>
</tbody>
</table>

CI = confidence interval. †A higher score indicates worse functioning. ‡p values are for changes in scores from baseline to 24 months in the group undergoing pallidal stimulation compared with those undergoing subthalamic stimulation. Source: Adapted from The New England Journal of Medicine, 342, 2077–91. Copyright © 2010 Massachusetts Medical Society. Reprinted with permission from Massachusetts Medical Society.
Another predictor of HRQoL improvement is age. Derost et al.11 response) has a good chance of improvement in HRQoL after surgery. very limited symptoms in the ‘on’ state (i.e., a high levodopa Thus, a patient with severe motor symptoms in the ‘off’ state and HRQoL improvement correlated with levodopa challenge test results. patients showed a substantial improvement in HRQoL. Moreover, controls (Cohen’s d=0.9). At the individual level, 32 % of the STN-DBS showed that STN-DBS reduced motor complications to a similar degree in ‘young’ (mean age 57.4 ± 4.9 years, n=53) and ‘old’ patients (mean age 68.8 ± 2.8 years, n=34), but that HRQoL improved only in ‘young’ patients. This may be explained by differences between the two groups: the ‘old’ patients had more significant worsening in UPDRS motor score (p=0.001) and axial score (p=0.0001) under on-medication and on-stimulation conditions during the study.

Other factors may also be involved. One such factor is cognition, which is related to age in PD; cognitive deficits are not improved by DBS. While patients with cognitive decline may show motor improvements for a short period of time, the progressive deterioration of cognitive symptoms will greatly impair their HRQoL. The development of cognitive deficits in PD is not linear; there is a sharper decline with advancing disease. This has implications for the timing of DBS; if surgery is performed when the patient is on the verge of cognitive deterioration, the benefit in HRQoL is likely to be reduced.
Conclusions

HRQoL is markedly reduced in PD patients. Randomised studies have shown that DBS leads to significant improvement in HRQoL, although only one long-term study has been published. Furthermore, STN-DBS and Gpi-DBS appear to have similar effects on HRQoL. Important predictors of HRQoL improvement were found to include levodopa response, age and cognitive function; thus a young patient with well preserved cognitive function and motor symptoms that are highly responsive to levodopa has the best chance to see an improvement in HRQoL after DBS. Trials are needed to further investigate the long-term effects of DBS on HRQoL, and predictors of favourable outcome in terms of HRQoL, in order to optimise patient selection for this therapy.


Mean plus standard error of the mean shown. **p<0.01; *p<0.05; ns = not significant compared with baseline. Source: Adapted from J Volkmann, A Albanese, J Kulisevsky, et al., “Long-term effects of pallidal or subthalamic deep brain stimulation on quality of life in Parkinson’s disease,” Mov Disord, 2008;23:1400–7, copyright © 2008 Movement Disorders Society, with permission from John Wiley and Sons.

Figure 4: Change in Total Sickness Impact Profile (SIP), Physical SIP and Psychosocial SIP Scores from Baseline to Six and 36 Months after Deep Brain Stimulation of the Subthalamic Nucleus (A) or Globus Pallida Interna (B)