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Deep Brain Stimulation of Subthalamic Nucleus Improves Quality of Life in General and Mental Health Domains in Parkinson's Disease to the Level of the General Population

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ABSTRACT

Objectives: Parkinson's disease (PD) leads to significant impairment in quality of life (QoL) across various domains. Deep brain stimulation of the subthalamic nucleus (STN-DBS) is known to improve motor and nonmotor symptoms in PD. The aim was to study whether STN-DBS could improve the QoL of patients with PD to the level of the general population, and to determine factors predicting better motor outcomes.

Materials and Methods: The retrospective analysis included 43 patients who underwent either primary or revision STN-DBS. Patients filled out a general QoL questionnaire (RAND 36-item health survey) before and 12 months after surgery, and scores were compared with age- and sex-adjusted national population values. In addition, motor scores were calculated using Unified Parkinson Disease Rating Scale part 3 (UPDRS 3) with the best PD medication. Levodopa equivalent daily dose (LEDD) was also collected. Changes in the QoL were compared with operation age, disease duration, and preoperative QoL.

Results: Preoperatively, patients had significantly impaired QoL in all subsections compared with that of the general population. The mean postoperative UPDRS 3 improvement was 50.0%, and reduction in LEDD was 69.0%. Statistically significant QoL improvements were found in Physical Function, Mental Health, Social Function, Vitality, and Role Physical 12 months postoperatively compared with baseline. The mean differences compared with a healthy population were not statistically significant in General Health, Mental Health, Vitality, and Role Emotional. Furthermore, disease duration was found to be negatively correlated with improvements in UPDRS 3 score, and worse preoperative QoL positively correlated with changes in Physical Function.

Conclusions: Patients experienced significant QoL improvements after STN-DBS. The General Health and Mental Health of patients were postoperatively most comparable with age- and sex-adjusted population values. Moreover, earlier stimulation predicted better motor improvements, which emphasizes the importance of earlier timing of STN-DBS surgery and minimizing loss of function at a critical disease stage.

Keywords: Deep brain stimulation, nonmotor symptoms, Parkinson's disease, quality of life, subthalamic nucleus

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INTRODUCTION

Parkinson's disease (PD) is a progressive neurogenerative disease that results in a variety of motor and nonmotor symptoms. These symptoms are known to cause significant reduction in patients' quality of life (QoL), especially in physical function and mental health domains.[1] These changes in the QoL can be detected early in the disease progression, often in the first visit to a neurological center.[2]

Although the motor symptoms, for example, tremor and rigidity, may lead to the most visible impairments in PD, the most detrimental effect on the QoL may be due to nonmotor symptoms.[3,4] Interestingly, depression has been found to be the most frequently identified determinant of QoL in PD.[5] This emphasizes the widespread impact that PD can have on perceived health, and the need for holistic treatment approaches.

Deep brain stimulation (DBS) is a well-established treatment for advanced PD. The subthalamic nucleus (STN) is the most often used stimulation target in PD.[6] Current literature states that both motor symptoms and QoL can be improved with STN-DBS, and that it is superior to medical treatment alone in an advanced disease state.[7,8]

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Furthermore, STN-DBS is beneficial for early motor complications[9] and could reduce the need for medication in the future.[10]

Factors that predict better improvement in QoL after STN-DBS remain controversial.[11] Some studies have stated that younger age[12] and shorter duration of PD[13] could lead to better QoL outcomes, but others have contradicted these results.[14,15] Even the traditional contraindications, such as cognitive impairment and psychiatric dysfunction, have been questioned because evidence of worse postoperative QoL is deficient.[11] Worse baseline motor score[14] and QoL[15] have been considered to predict greater postoperative QoL improvement. Interestingly, it was recently proposed that patients with predominantly left-sided motor symptoms could experience less beneficial nonmotor outcomes from STN-DBS.[16]

Various methods have been used to evaluate the QoL of patients with PD, including generic and PD-targeted measures. Disease-specific questionnaires include more PD-related content, but those results are not comparable with the general population. The use of generic measures, such as the Short-Form Health Survey (SF-36), have been studied in patients with PD and found to be generally reliable.[17] Moreover, the SF-36 has been found to be more responsive than are PD-targeted measures.[18]

The QoL of patients with PD after STN-DBS has been compared with that of the general population in a previous study.[19] The study indicated that patients with PD had preoperatively significantly impaired QoL in every subsection studied, and similar results were seen postoperatively, except for Vitality and Bodily Pain, in which differences compared with general population values were not significant. Furthermore, significant postoperative improvement was seen only in Physical Functioning. General Health of patients with PD fell significantly short of the control population levels.

In this study, the first aim was to determine QoL of patients with PD preoperatively and 12 months after STN-DBS using the RAND-36 questionnaire, which has identical questions to those of the SF-36. The QoL was compared with age- and sex-adjusted control population values, with special interest in the subsections of General Health, Physical Function, and Mental Health, which are the most relevant domains for PD. We hypothesized that STN-DBS would significantly increase the QoL of the patients and that the postoperative QoL of some areas could be similar to that of the general population. Thus, STN-DBS could normalize QoL of patients with PD in some aspects. The second aim was to study whether age, disease duration, or preoperative QoL were correlated with postoperative changes in motor outcomes or QoL.

MATERIALS AND METHODS

A total of 43 patients with PD who underwent bilateral STN-DBS were analyzed. Patients were operated on in the neurosurgical unit of Oulu University Hospital (OUH) from 2016 to 2021. The data included mainly primary operations, although six were revision surgeries. The most common reason for revision was lead fracture (three of six patients). The information on revision surgeries is provided in Supplementary Data Table S1. STN was used as a target for all the patients. Inclusion criteria for the operation were idiopathic PD diagnosed at least four years previously, medically refractory motor fluctuations, no substantial decline in cognitive functions or major psychiatric problems, and a good response to levodopa test.

The clinical symptoms and QoL were documented preoperatively and 12 months postoperatively. Unified Parkinson's Disease Rating Scale, part 3, motor score (UPDRS 3) was used for clinical evaluation of motor symptoms during the best medical response. The daily use of levodopa-including medication was converted[20] to levodopa-equivalent daily dose (LEDD). UPDRS 3 scores were available only from primary operations, but LEDD scores were analyzed for both primary surgeries and revisions. All data were collected retrospectively. The administration of OUH (number: 7/2013) approved the register study, and the local Ethics Committee was notified.

RAND-36

QoL was evaluated with the general QoL questionnaire RAND-36 1.0 (RAND Corporation), which is a widely used profile-based questionnaire that comprises eight different subsections addressing General Health, Physical Function, Mental Health, Social Function, Vitality, Bodily Pain, physical role functioning (Role Physical), and emotional role functioning (Role Emotional). The subsections received scores ranging from 0 to 100, with higher scores indicating better function. RAND-36 has identical questions to those of the SF-36, which is the most widely used health-related QoL measure. There are minor variations in the scoring of two subsegments (Bodily Pain and General Health) between the questionnaires. However, the correlation with both subsegments in RAND-36 and SF-36 is 0.99.[21]

For this study, general QoL meter was chosen to compare patients with age- and sex-adjusted population values. Therefore, PD specific questionnaires such as the Parkinson's Disease Questionnaire-39 (PDQ-39) were inadequate.

Pre- and postoperative RAND-36 scores of the patients with PD were compared with the sex- and age-adjusted values based on the Finnish population. Five-year age group values were used. For those patients whose relative population values changed in the 12-month follow-up (eg, shift from 55–59 to 60–64 years age group), the new values were used in the postoperative analysis.

Surgery

Bilateral DBS surgery was performed in all patients. Before the operation, the target nucleus was segmented manually from 3T-magnetic resonance imaging (MRI) scans. The surgery was performed in two phases. In the first phase, electrodes were implanted under local anesthesia using a stereotactic frame (Leksell G-frame or Vantage, Elekta, Stockholm, Sweden). Intraoperative stereotactic head computed tomography (CT) scans (Toshiba Aquilion One Vision Edition CT-scanner, Canon Medical Systems, Otawara, Tochigi, Japan) were performed using a CT coordination indicator box (Leksell, Elekta). Images were then fused with preoperative 3T-MRI scans. During surgery, microelectrode recording was used to verify the borders of the STN, and test stimulation was performed to evaluate motor improvements and side-effect thresholds. Permanent leads (Model 3389, Medtronic, Minneapolis, MN or Vercise Cartesia, Boston Scientific, Marlborough, MA) were placed. CT scan and fluoroscopic imaging were performed to confirm lead locations. During the second phase, double extension wires (Model 37086–40 cm, Medtronic; 55 cm, Boston Scientific) and pulse generator (Activa RC/PC, Medtronic; Vercise Gevia, Boston Scientific) were placed under general anesthesia. The surgical technique has been described in depth in our previous publication.[22]

Follow-up visits were arranged one, three, six, and 12 months postoperatively to adjust stimulation parameters and antiparkinsonian medication, if needed. Postoperative stereotactic head CT scan was performed during the one-month follow-up visit.

Table 1. Demographic Data of the Patients.

Variable	Value	Minimum	Maximum
Number of patients	43		
Sex, female:male	8:35		
Mean age, y	62.0 (SD = 5.5)	46	70
Surgery, primary:revision	37:6		
Mean disease duration before operation, y	11.4 (SD = 5.1)	4	26
Preoperative LEDD, mg	948 (SD = 381)	200	1895
Postoperative LEDD, mg	298 (SD = 227)	0	798
Preoperative UPDRS 3	36.2 (SD = 12.7)	10	64
Postoperative UPDRS 3	15.6 (SD = 6.9)	6	37

Statistical Methods

Statistical analysis was performed using SPSS (version 27.0, IBM, New York, NY) and Excel 2016 (Microsoft, Redmond, WA). R Foundation for Statistical Computing (version 4.2, Vienna, Austria) was also used for data visualization. Data analysis was performed on a per-patient basis to compare the QoL pre- and postoperatively but also with the adjusted population values. Mean differences, SDs, 95% CIs, and two-tailed *p* values of the differences were calculated using the paired samples *t*-test. *p* Value corrections for multiple comparisons of pre- with postoperative change were performed for RAND-36, and for comparison with population values individually using Benjamini-Hochberg procedure with a false discovery rate of 0.05.[23] *p* Value corrections are presented in Supplementary Data Table S2.

Pre- and postoperative differences were also compared with minimal clinically important differences (MCID), a threshold value of change in QoL score thought to have clinical importance. Specific MCID value for RAND-36 was found to be 3 to 5.[24] Changes < 3 were considered clinically unimportant differences, whereas changes ≥ 5 were considered clearly clinically important differences.

Spearman correlation analysis was performed to calculate correlation coefficients (r) between operation age, disease duration, changes in Physical Function, and changes in UPDRS 3 score. UPDRS 3 analysis included only primary operations because scores were not available for revision surgeries. Correlation analysis was also performed between preoperative QoL and changes in QoL.

RESULTS

A total of 43 patients with PD were analyzed. There were 35 male and eight female patients. The mean patient age was 62.0 years, and the mean duration of PD was 11.4 years. Preoperatively, 88.4% of the patients answered the QoL questionnaire, whereas postoperatively, 86.0% of the patients answered. In total, 74.4% of the patients answered both pre- and postoperative questionnaires. The mean UPDRS 3 improvement was 50.0%, and the mean reduction in LEDD was 69.0%. Nine of the 43 patients were completely without levodopa medication 12 months after the surgery. Demographic data and clinical results are shown in Table 1.

Patients' QoL was improved 12 months after the operation. Statistically significant improvements were found in Physical Function, Mental Health, Social Function, Vitality, and Role Physical. The mean differences were equal to or larger than RAND-36 specific MCID (≥ 5) in every subsection. Overall, QoL improvements were equal to or larger than MCID for 50.0% of patients in General Health, 56.2% of patients in Physical Function, and 59.4% of

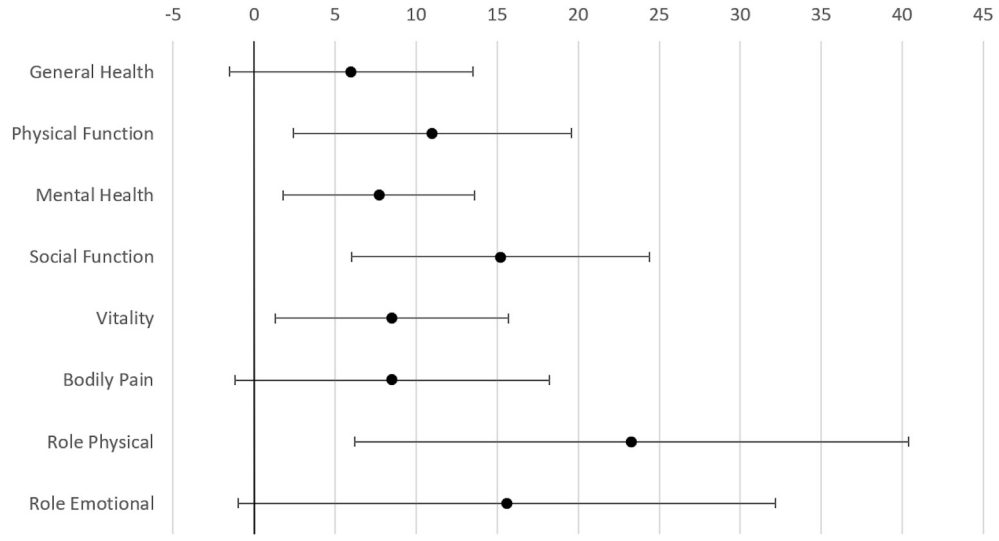

Figure 1. The mean improvements and 95% CIs of RAND-36 subsections 12 months postoperatively compared with baseline. Statistically significant improvements were achieved in Physical Function, Mental Health, Social Function, Vitality, and Role Physical domains.

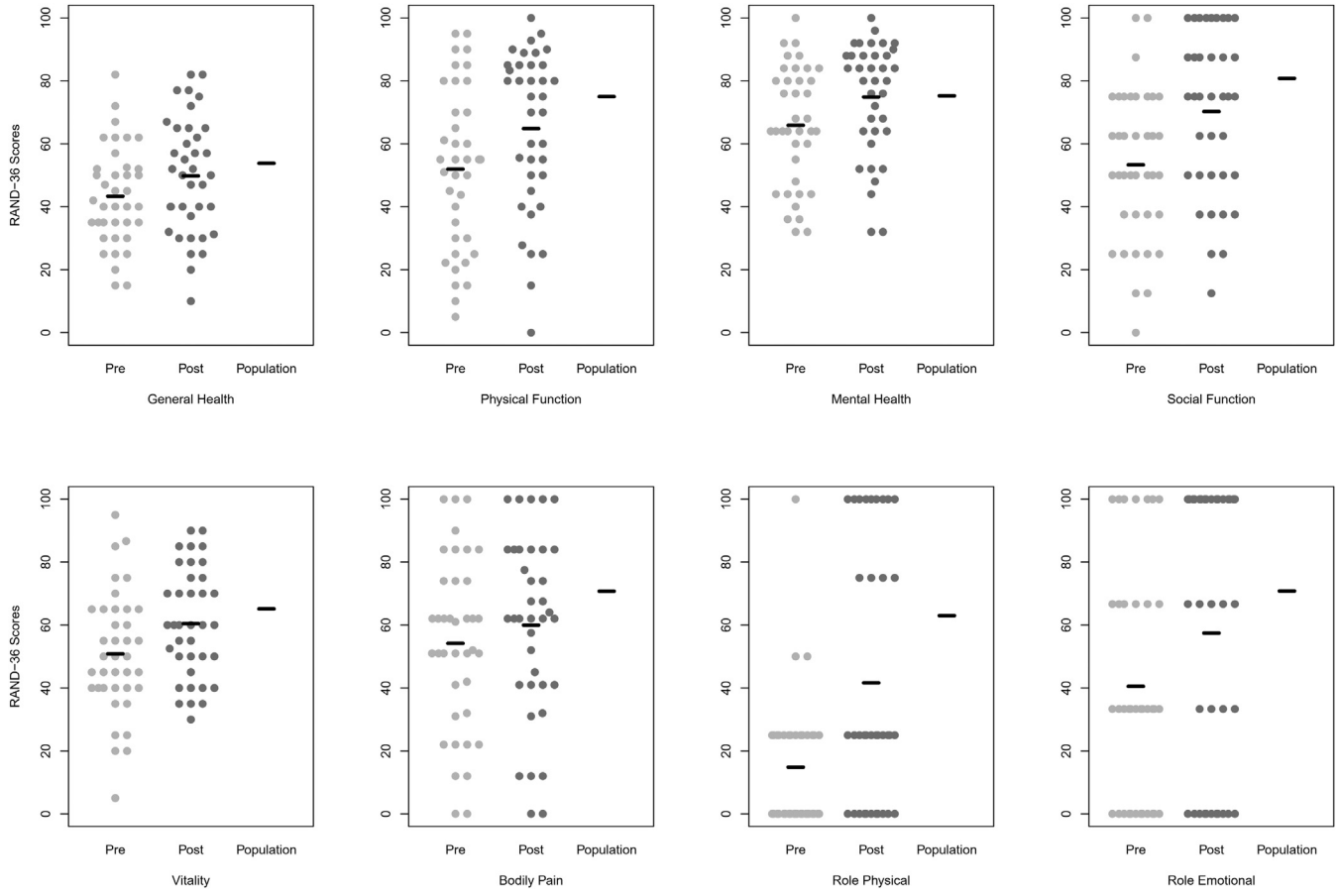

Figure 2. QoL of patients with STN-DBS compared with that of general population. The mean values (horizontal line) for preoperative, postoperative, and population QoL scores are presented for each RAND-36 subsection. The mean differences between preoperative values and general population values were statistically significant in all subsections, whereas postoperative values and the general population values were not statistically significant in General Health, Mental Health, Vitality, and Role Emotional subsections.

patients in Mental Health. The postoperative improvements are presented in Figure 1.

Preoperatively, patients had significantly lower mean QoL scores in all subsections than the adjusted general population values. Differences in Physical Function, Social Function, and Role Physical were especially substantial. *p* Values were significant for all subsections analyzed. Preoperatively, only a minority of the patients had a QoL score that was comparable with that of the general population, meaning that the difference was smaller than MCID (< 3), or patient QoL was better than QoL in the general population

Table 2. Pre- and Postoperative Quality of Life Scores.

RAND-36 subsections	Pre-DBS	Post-DBS	Mean difference	95% CI*		Significance (2-tailed) *p* value**	Change ≥ MCID*** (%)
	Mean (SD)	Mean (SD)		Lower	Upper		
General Health	43.0 (15.4)	49.0 (19.2)	6.0	−1.6	13.5	0.116	50.0
Physical Function	52.8 (25.5)	63.8 (26.2)	11.0	2.4	19.6	0.014†	56.2
Mental Health	66.2 (19.2)	73.9 (18.9)	7.7	1.8	13.6	0.012†	59.4
Social Function	53.1 (24.4)	68.4 (26.2)	15.2	6.0	24.4	0.002†	56.2
Vitality	51.6 (20.3)	60.1 (17.7)	8.5	1.3	15.6	0.022†	56.2
Bodily Pain	51.0 (27.8)	59.6 (30.5)	8.5	−1.2	18.4	0.083	56.2
Role Physical	14.2 (21.5)	37.5 (38.1)	23.3	6.2	40.5	0.009†	53.3
Role Emotional	43.3 (39.3)	58.9 (42.6)	15.6	−1.0	32.1	0.065	50.0

*CI of the difference.
**Postoperative (12 months) *p* value between before and after DBS operation (paired samples *t*-test).
***Percentage of patients with change equal to or larger than MCID (5).
†Statistically significant after controlling for multiple comparisons (Benjamini-Hochberg procedure).

Table 3. Patient QoL Scores Compared With Age- and Sex-Matched Population Values.

RAND-36	Post-DBS					Post-DBS				
	Mean difference (SD)	95% CI*		*p* Value (2-tailed)**	Difference < MCID*** (%)	Mean difference (SD)	95% CI*		*p* Value (2-tailed)**	Difference < MCID*** (%)
		Lower	Upper				Lower	Upper		
General Health	10.5 (15.9)	5.3	15.7	< 0.001†	28.9	3.7 (18.8)	−2.6	9.9	0.240	51.4
Physical Function	23.1 (26.1)	14.5	31.7	< 0.001†	23.7	8.8 (23.7)	0.9	16.7	0.030†	51.4
Mental Health	9.4 (18.9)	3.2	15.6	0.004†	42.1	0.4 (17.5)	−5.5	6.2	0.901	64.9
Social Function	27.5 (24.6)	19.4	35.6	< 0.001†	15.8	10.8 (25.7)	2.2	19.3	0.015†	48.6
Vitality	14.3 (19.8)	7.8	20.8	< 0.001†	28.9	4.6 (17.3)	−1.1	10.4	0.111	48.6
Bodily Pain	16.6 (27.5)	7.6	25.7	< 0.001†	23.7	10.9 (27.8)	1.6	20.1	0.023†	37.8
Role Physical	47.9 (23.8)	40.0	55.9	< 0.001†	8.1	19.5 (39.0)	6.3	32.7	0.005†	36.1
Role Emotional	30.0 (37.7)	17.5	42.6	< 0.001†	24.3	11.9 (43.8)	−2.9	26.7	0.111	50

*CI of the difference.
***p* Value of the difference between pre-/post-DBS and general population values (paired samples *t*-test).
***Percentage of patients with difference <MCID (3) compared with population values.
†Statistically significant after controlling for multiple comparisons (Benjamini-Hochberg procedure).

(28.9% in General Health, 23.7% in Physical Function, and 42.1% in Mental Health) (Fig. 2).

Although patients with PD experienced significant QoL improvements after the surgery, there were still differences to the adjusted general population values. However, the mean differences to the general population were not statistically significant in General Health, Mental Health, Vitality, and Role Emotional (Fig. 2). Notably, 51.4% of patients had a postoperative General Health score that was comparable with that of the general population. Similar results were found for 51.4% and 64.9% of patients in Physical Function and Mental Health subsections, respectively. The QoL scores are presented in Tables 2 and 3.

Factors Associated With QoL Improvement

The impact of disease duration, operation age, and baseline QoL were studied using Spearman correlation coefficient (r). Disease duration was negatively correlated with the improvement in UPDRS 3 score ($r = -0.48$, $p = 0.004$), but no statistical significance was achieved with the improvements in Physical Function ($r = -0.33$, $p = 0.068$). These results indicate that patients with longer disease duration experience less motor benefit from DBS. Statistically significant correlation was not found between operation age and UPDRS 3 ($r = -0.11$, $p = 0.558$) or Physical Function ($r = -0.28$, $p = 0.124$), which would conversely suggest motor outcome was not associated with patient age. There were no similar correlations when analyzing changes in General Health and Mental Health (Fig. 3).

In analyzed subsections, the lower preoperative QoL was associated with greater improvements in the domains of General Health ($r = -0.42$, $p = 0.016$), Physical Function ($r = -0.41$, $p = 0.021$), and Mental Health ($r = -0.44$, $p = 0.012$).

DISCUSSION

These results indicate that the QoL of patients receiving STN-DBS can become closer to the general population in many domains, and the differences between postoperative and population values were not statistically significant for General Health and Mental Health 12 months after surgery. For over half of patients, postoperative QoL was comparable with that of the general population at least in General Health, Mental Health, and Physical Function subsections. We also showed that STN-DBS improves the QoL not only in motor but in nonmotor subsections, which have a major impact on total QoL. Moreover, PD duration was found to be negatively correlated with motor improvements, which emphasizes the importance of earlier timing of STN-DBS surgery.

This study underlines the variety of motor and nonmotor symptoms in PD and ways they affect QoL. Patients had preoperatively substantially lower QoL in various domains, which is concordant with previous studies.[3,4,19] Moreover, it was indicated that STN-DBS can improve the QoL in most subsections compared with the preoperative state with the best medical treatment already in use.

Earlier timing of STN-DBS surgery appears to be beneficial. In this study, disease duration was an even more important factor than age at the time of operation for predicting motor improvement. Previous studies have stated that older patients, especially with shorter disease duration, can benefit from STN-DBS.[25] The literature on the risk of complications with older patients is controversial[26] because there is also some evidence of complication rates with

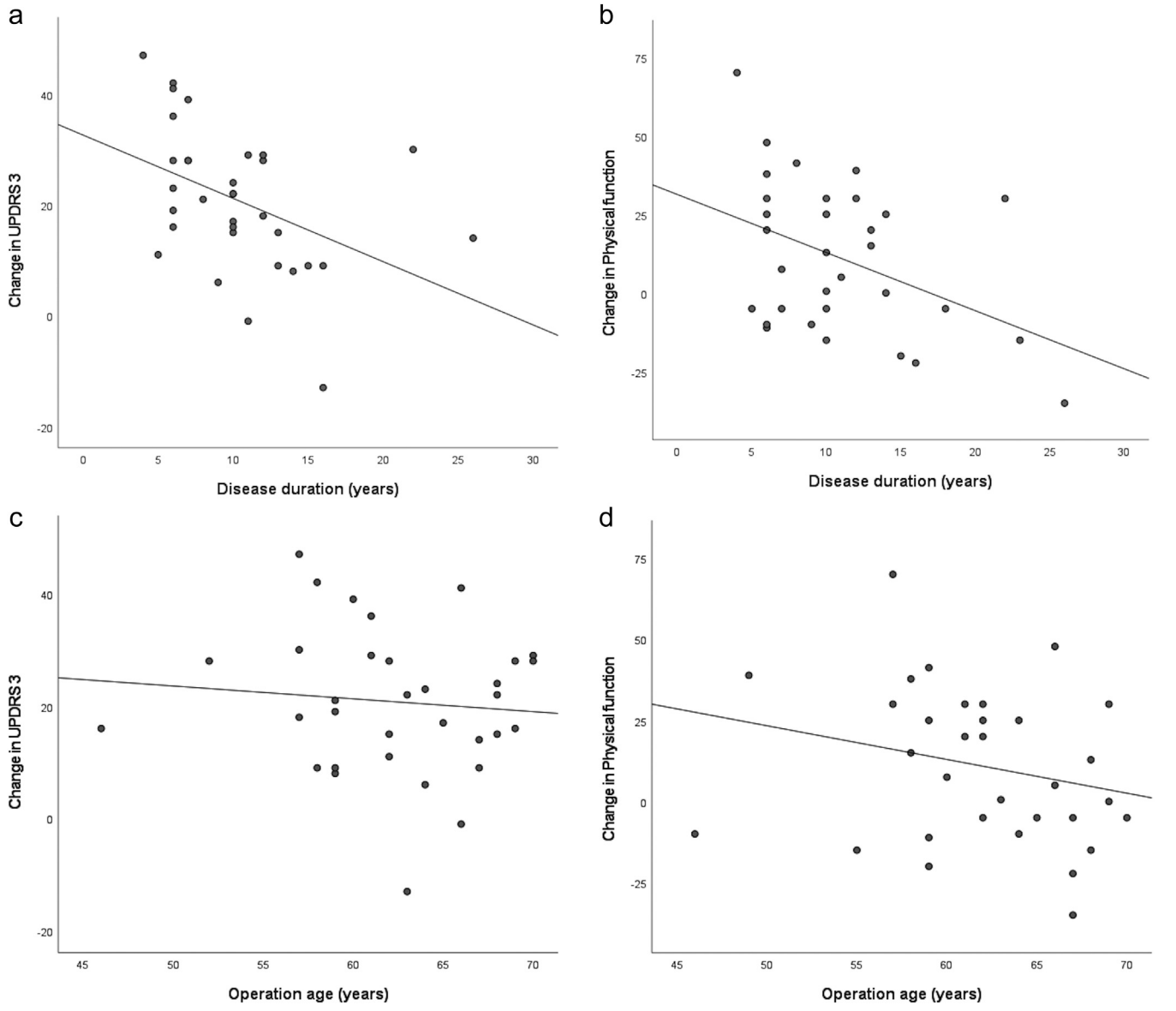

Figure 3. Physical function and UPDRS 3 score improvements compared with disease duration. Improvement in UPDRS 3 score was negatively correlated with disease duration ($r = -0.48$, $p = 0.004$) (panel a), but no statistical significance was achieved between the improvements in Physical Function and disease duration ($r = -0.33$, $p = 0.068$) (panel b). This implies that patients with longer disease duration experience less benefit. However, correlation was not found between operation age and UPDRS 3 ($r = -0.11$, $p = 0.558$) (panel c) or Physical Function ($r = -0.28$, $p = 0.124$) (panel d).

older patients being similar to those of younger patients.[27] Our results suggest that besides patient age, disease duration should be regarded in the patient selection for STN-DBS in the future. Importantly, this study followed the inclusion criteria of age < 70 years and disease duration ≥ four years, and therefore, these results should be interpreted with caution for patients outside these criteria.

The QoL of patients with PD may be impaired owing to a variety of reasons, some of which cannot be improved with DBS. Comorbidities, such as musculoskeletal disorders, are likely to persist after the surgery. Psychosocial environment and previous decline in motor skills may also affect the QoL. These impaired functions may be the reason for modest improvements in, for example, Bodily Pain. Furthermore, it is unlikely that QoL comparable with that of the general population can be achieved in all domains for patients with the most advanced disease states because they might have already developed these comorbidities.

Although the QoL of patients was significantly increased 12 months after the surgery, it remains unclear how long these benefits will last. In the previous studies, the QoL was improved after STN-DBS, but in three-year follow-up scores approached baseline in many domains, however motor improvements were sustained[28] and motor benefits seem to last for up to ten years.[29] The loss of benefits from STN-DBS is a consequence of the progressive nature of PD, but some of this effect might be preventable with, for example, stimulation adjustments.

Patients with longer disease duration were found to have worse motor improvements, and in some cases, QoL was decreased. These results differ from those of a previous study.[15] However, the

study comprised younger patients in early disease stage. Comparison, therefore, between different disease durations may not be possible. Notably, impaired baseline QoL predicted greater QoL improvements in both studies.

Further evidence on factors predicting stimulation outcome is still needed. The aim should be to identify patients who will experience the greatest benefits from stimulation, and then treat these patients early in their disease progression. However, these results suggest earlier stimulation to be independently predictive of better treatment results. Furthermore, if the QoL after subthalamic stimulation can be comparable with that of the general population, even in some domains, DBS could reduce loss of function for many patients in a critical stage of disease progression.

Limitations

The limitations of this study include the use of a generic QoL questionnaire and the known shortcomings of self-assessed health scores. The questionnaire used in this study has been found to be reliable in PD,[17] and it was chosen to allow comparison with the age- and sex-adjusted general population. However, PD-targeted measures could be more sensitive to changes in specific symptoms of PD. It is well known that in QoL questionnaires, patients may overestimate improvements in their health owing to the poor QoL that some patients experience before the operation. Conversely, some patients may have unrealistic expectations regarding the neurosurgical operation and thus be disappointed with the results. The data set was not exclusive to the primary DBS because it also included revision surgeries. Moreover, this study did not include patients aged > 70 years because of common exclusion criteria. Evidence of operation age is thereby limited. It should also be noted that although lower preoperative QoL was correlated with better improvements in QoL, there may be a ceiling effect in the higher QoL scores. Further studies could be conducted using the PD-specific questionnaire PDQ-39 alongside a general QoL survey.

CONCLUSIONS

Patients experienced significant QoL improvements after subthalamic stimulation. The General Health and Mental Health scores of patients were most comparable with age- and sex-adjusted population values after STN-DBS. Moreover, earlier stimulation predicted better motor improvements, which emphasizes the importance of earlier timing of STN-DBS surgery to minimize loss of function at a critical disease stage.

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Authorship Statements

Maija Lahtinen and Jani Katisko designed the study. Maija Lahtinen was responsible for patient recruitment and data collection. Maija Lahtinen and Jani Katisko were responsible for all the surgeries performed. Johannes Kähkölä and Maija Lahtinen analyzed the data. Johannes Kähkölä prepared the manuscript draft with crucial comments from Jani Katisko and Maija Lahtinen. All authors approved the final version of the manuscript.

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SUPPLEMENTARY DATA

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REFERENCES

1. Zhao N, Yang Y, Zhang L, et al. Quality of life in Parkinson's disease: a systematic review and meta-analysis of comparative studies. *CNS Neurosci Ther*. 2021;27:270–279. https://doi.org/10.1111/CNS.13549.
2. Hariz GM, Forsgren L. Activities of daily living and quality of life in persons with newly diagnosed Parkinson's disease according to subtype of disease, and in comparison to healthy controls. *Acta Neurol Scand*. 2011;123:20–27. https://doi.org/10.1111/J.1600-0404.2010.01344.X.
3. Martinez-Martin P, Rodriguez-Blazquez C, Kurtis MM, Chaudhuri KR, NMSS Validation Group. The impact of non-motor symptoms on health-related quality of life of patients with Parkinson's disease. *Mov Disord*. 2011;26:399–406. https://doi.org/10.1002/MDS.23462.
4. Fereshtehnejad SM, Shafieesabet M, Farhadi F, et al. Heterogeneous determinants of quality of life in different phenotypes of Parkinson's disease. *PLoS One*. 2015;10:e0137081. https://doi.org/10.1371/JOURNAL.PONE.0137081.
5. Soh SE, Morris ME, McGinley JL. Determinants of health-related quality of life in Parkinson's disease: a systematic review. *Parkinsonism Relat Disord*. 2011;17:1–9. https://doi.org/10.1016/J.PARKRELDIS.2010.08.012.
6. Lee DJ, Lozano CS, Dallapiazza RF, Lozano AM. Current and future directions of deep brain stimulation for neurological and psychiatric disorders. *J Neurosurg*. 2019;131:333–342. https://doi.org/10.3171/2019.4.JNS181761.
7. Williams A, Gill S, Varma T, et al. Deep brain stimulation plus best medical therapy versus best medical therapy alone for advanced Parkinson's disease (PD SURG trial): a randomised, open-label trial. *Lancet Neurol*. 2010;9:581–591. https://doi.org/10.1016/S1474-4422(10)70093-4.
8. Deuschl G, Schade-Brittinger C, Krack P, et al. A randomized trial of deep-brain stimulation for Parkinson's disease. *N Engl J Med*. 2006;355:896–908. https://doi.org/10.1056/NEJMOA060281.
9. Schuepbach WMM, Rau J, Knudsen K, et al. Neurostimulation for Parkinson's disease with early motor complications. *N Engl J Med*. 2013;368:610–622. https://doi.org/10.1056/NEJMOA1205158.
10. Hacker ML, Turchan M, Heusinkveld LE, et al. Deep brain stimulation in early-stage Parkinson disease: five-year outcomes. *Neurology*. 2020;95:e393–e401. https://doi.org/10.1212/WNL.0000000000009946.
11. Geraedts VJ, Feleus S, Marinus J, van Hilten JJ, Contarino MF. What predicts quality of life after subthalamic deep brain stimulation in Parkinson's disease? A systematic review. *Eur J Neurol*. 2020;27:419–428. https://doi.org/10.1111/ENE.14147.
12. Dafsari HS, Reker P, Stalinski L, et al. Quality of life outcome after subthalamic stimulation in Parkinson's disease depends on age. *Mov Disord*. 2018;33:99–107. https://doi.org/10.1002/MDS.27222.
13. Welter ML, Houeto JL, Tezenas Du Montcel S, et al. Clinical predictive factors of subthalamic stimulation in Parkinson's disease. *Brain*. 2002;125:575–583. https://doi.org/10.1093/BRAIN/AWF050.
14. Abboud H, Genc G, Thompson NR, et al. Predictors of functional and quality of life outcomes following deep brain stimulation surgery in Parkinson's disease patients: disease, patient, and surgical factors. *Parkinsons Dis*. 2017;2017:5609163. https://doi.org/10.1155/2017/5609163.
15. Schuepbach WMM, Tonder L, Schnitzler A, et al. Quality of life predicts outcome of deep brain stimulation in early Parkinson disease. *Neurology*. 2019;92:e1109–e1120. https://doi.org/10.1212/WNL.0000000000007037.
16. Voruz P, Pierce J, Ahrweiller K, et al. Motor symptom asymmetry predicts non-motor outcome and quality of life following STN DBS in Parkinson's disease. *Sci Rep*. 2022;12:3007. https://doi.org/10.1038/S41598-022-07026-5.
17. Hagell P, Törnqvist AL, Hobart J. Testing the SF-36 in Parkinson's disease. Implications for reporting rating scale data. *J Neurol*. 2008;255:246–254. https://doi.org/10.1007/S00415-008-0708-Y.

18. Brown CA, Cheng EM, Hays RD, Vassar SD, Vickrey BG. SF-36 includes less Parkinson disease (PD)-targeted content but is more responsive to change than two PD-targeted health-related quality of life measures. *Qual Life Res*. 2009;18:1219–1237. https://doi.org/10.1007/S11136-009-9530-Y.
19. Daneault JF, Sadikot AF, Barbat-Artigas S, et al. Physical activity in advanced Parkinson's disease: impact of subthalamic deep brain stimulation. *J Parkinsons Dis*. 2015;5:85–93. https://doi.org/10.3233/JPD-140426.
20. Tomlinson CL, Stowe R, Patel S, Rick C, Gray R, Clarke CE. Systematic review of levodopa dose equivalency reporting in Parkinson's disease. *Mov Disord*. 2010;25:2649–2653. https://doi.org/10.1002/MDS.23429.
21. Hays RD, Sherbourne CD, Mazel RM. The RAND 36-item health survey 1.0. *Health Econ*. 1993;2:217–227. https://doi.org/10.1002/HEC.4730020305.
22. Kähkölä J, Lahtinen M, Keinänen T, Katisko J. Stimulation of the presupplementary motor area cluster of the subthalamic nucleus predicts more consistent clinical outcomes. *Neurosurgery*. Published online December 30, 2022. https://doi.org/10.1227/neu.0000000000002292
23. Benjamini Y, Hochberg Y. Controlling the false discovery rate: a practical and powerful approach to multiple testing. *J R Stat Soc B (Methodol)*. 1995;57:289–300. https://doi.org/10.1111/J.2517-6161.1995.TB02031.X.
24. Samsa G, Edelman D, Rothman ML, Williams GR, Lipscomb J, Matchar D. Determining clinically important differences in health status measures: a general approach with illustration to the Health Utilities Index Mark II. *Pharmacoeconomics*. 1999;15:141–155. https://doi.org/10.2165/00019053-199915020-00003.
25. Dafsari HS, Reker P, Silverdale M, et al. Subthalamic stimulation improves quality of life of patients aged 61 years or older with short duration of Parkinson's disease. *Neuromodulation*. 2018;21:532–540. https://doi.org/10.1111/NER.12740.
26. Zrinzo L, Foltynie T, Limousin P, Hariz MI. Reducing hemorrhagic complications in functional neurosurgery: a large case series and systematic literature review. *J Neurosurg*. 2012;116:84–94. https://doi.org/10.3171/2011.8.JNS101407.
27. DeLong MR, Huang KT, Gallis J, et al. Effect of advancing age on outcomes of deep brain stimulation for Parkinson disease. *JAMA Neurol*. 2014;71:1290–1295. https://doi.org/10.1001/JAMANEUROL.2014.1272.
28. Volkmann J, Albanese A, Kulisevsky J, et al. Long-term effects of pallidal or subthalamic deep brain stimulation on quality of life in Parkinson's disease. *Mov Disord*. 2009;24:1154–1161. https://doi.org/10.1002/MDS.22496.
29. Limousin P, Foltynie T. Long-term outcomes of deep brain stimulation in Parkinson disease. *Nat Rev Neurol*. 2019;15:234–242. https://doi.org/10.1038/S41582-019-0145-9.

COMMENTS

In this manuscript by Johannes Kahkola et al, the authors describe the change in multiple domains of QoL after STN-DBS in patients with PD and compare the postoperative QoL with that of the general population. The authors have a respectable cohort size and through their primary outcome can assess changes in QoL and compare QoL measures with those of the age-matched general population. Their major findings are that 1) STN-DBS improved QoL across multiple domains, 2) postoperative QoL was similar to that of age-matched people without PD, 3) shorter disease duration predicted greater QoL improvement, and 4) age did not predict QoL improvement. These findings are largely consistent with previous findings and add to the literature suggesting that earlier DBS may be beneficial. However, these findings are limited by the age of the study group (maximum age 70 years) and disease duration (minimum disease duration of four years). Furthermore, the cohort size of 43 patients is likely too small to identify risk factors for DBS complications. Nonetheless, they provide an important contribution to the literature describing predictors of DBS outcomes.

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This manuscript is an interesting addition on estimating QoL (using a common scale applicable to the population in general) after DBS for PD. The study is a retrospective review but clearly shows improved QoL in this population.

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