




Quality of Life after Deep Brain Stimulation in Parkinson's Disease: Does the Target Matter?

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Abstract: Background: Deep brain stimulation (DBS) of the subthalamic nucleus (STN) and globus pallidus internus (GPI) is an accepted therapy for Parkinson's disease (PD) with disabling motor complications. For elderly patients with poorer cognition and postural instability, GPI has been proposed as the preferable DBS target based on expert opinion, arguing GPI-DBS may be less complicated by depression, apathy, worsened verbal fluency, and executive dysfunction, resulting in greater improvement in quality of life (QoL). However, data supporting such patient-tailored approach are lacking.

Objectives: The aims were to analyze whether the DBS target influences QoL in a PD cohort and a matched subgroup of frail patients with poor cognitive status and reduced postural stability, and whether other factors affect the QoL outcomes.

Methods: In this retrospective study, we analyzed a single-center cohort of 138 PD patients who received bilateral STN-DBS (117) or GPI-DBS (21) using the mentioned approach for target selection. All patients underwent standardized clinical evaluations of motor- and nonmotor signs as well as QoL before and 1 year after surgery.

Results: DBS of both targets improved motor signs, dyskinesias, and pain. QoL improved without significant difference between the targets, but with a trend for greater improvement across all QoL domains in favor of the STN, even in an STN subgroup matched to the GPI group.

Conclusion: Our results contradict the prevailing belief that GPI-DBS is superior in frail PD patients with cognitive decline and postural instability, questioning the proposed patient-tailored approach of DBS target selection. Further studies are needed for a data-driven approach.

Parkinson's disease (PD) is a neurodegenerative disorder characterized by motor and nonmotor signs with a profound impact on quality of life (QoL).^{1,2} Deep brain stimulation (DBS) of the subthalamic nucleus (STN) or the globus pallidus internus (GPI) is a well-established therapy for levodopa (L-dopa)-responsive PD with disabling motor complications and is able to improve motor³ and nonmotor symptoms⁴ as well as QoL.^{5,6}

Although STN may be the first choice as a DBS target in many centers, as reflected by the striking numerical predominance of

STN-DBS studies over GPI-DBS studies⁷ and the belief that STN target leads to better motor outcomes,^{3,8,9} there is an ongoing debate about the optimal DBS target for PD.³ The results of the only 2 randomized controlled trials (RCT) directly comparing these 2 targets did not provide conclusive evidence to support the superiority of either GPI-DBS or STN-DBS,^{10,11} although 1 of these trials¹¹ demonstrated greater improvement in motor signs and activities of daily living (ADL) in *off*-medication phase with STN-DBS than with GPI-DBS. As a result, there is still a

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transatlantic divide on this issue, which can be explained in particular by differences between the European and North American health-care systems.¹² However, the interpretation of the secondary outcomes of the U.S. Veterans Administration study¹⁰ led to the promotion of a patient-tailored DBS target selection favoring the GPi in case of cognitive or behavioral issues.^{13,14}

In the following years, many experts chose the STN target in younger PD patients, whereas the GPi target became the preferred DBS target for elderly PD patients who were frailer with poorer cognitive function, higher neuropsychiatric burden, or prominent gait and axial impairment.¹⁵

Nevertheless, studies confirming the superiority of GPi-DBS applying such target selection criteria are lacking.³ Therefore, the current retrospective single-center study aimed to determine STN-DBS and GPi-DBS outcomes with a particular focus on the QoL in a real-world PD cohort that received target selection according to the proposed patient-tailored approach.

Patients and Methods

Standard protocol approvals, registrations, and patient consent were obtained. The Swiss Ethics approved the study (KEK no.: 2020-02392).

Study Population

We retrospectively identified patients diagnosed with Parkinson's disease who underwent bilateral STN-DBS or GPi-DBS implantation at the University Hospital of Bern between 2009 and 2018. The time window was defined based on the period in which the target selection was performed according to the patient-tailored approach similar to that proposed by Williams et al.¹⁵ General selection criteria for DBS included advanced PD, good response to L-dopa, disabling motor fluctuations refractory to medication and/or L-dopa-induced dyskinesia despite the best medical treatment, and the absence of surgical or medical contraindications, including major depression with suicidal thoughts, dementia, or acute psychosis. Advanced age, impaired postural stability, and mild cognitive impairment were individual features favoring the GPi target selection over STN. The choice of target was made during a multidisciplinary DBS board, taking into account the patient's motor, cognitive, and mood profiles, as well as the patients' own expectations.¹⁵

All patients underwent bilateral DBS surgery, which was performed as previously reported.¹⁶ The correct position of the electrodes was verified during awake surgery using electrophysiology. Microelectrode recording was used to identify the well-known electrophysiological target signatures, and macrostimulation was used to assess intraoperative improvement in rigidity and absence of pyramidal diffusion.

All patients underwent postoperative axial computed tomography or magnetic resonance imaging (MRI) within 1 week after surgery to exclude surgical complications. To determine the correct electrode position, the postoperative imaging was systematically fused with the preoperative T2-weighted MRI.

Postoperatively, stimulation settings and antiparkinsonian medication were gradually adapted based on the patient's need and clinical response. We included all patients who had completed the 39-item Parkinson's Disease Questionnaire (PDQ-39) to assess self-reported QoL at both preoperative and postoperative assessments 1 year after surgery.

Clinical Measures

All patients underwent standardized clinical evaluations before and 1 year after surgery. These assessments included the PDQ-39^{17,18} as the main outcome parameter as well as Part III of the Movement Disorder Society Unified Parkinson's Disease Rating Scale (MDS-UPDRS-III) or the Unified Parkinson's Disease Rating Scale (UPDRS-III),^{19,20} Schwab and England Activities of Daily Living,²¹ Marconi Dyskinesia Rating Scale,²² Mini-Mental State Examination (MMSE),²³ Hamilton Rating Scale for Depression (HAM-D),²⁴ Starkstein Apathy Scale,²⁵ and Visual Analog Scale for Pain (VAS worst pain).²⁶ Insomnia and postural stability subscores were extracted from the sum of items 4, 5, and 6 of the HAM-D, and item 30 of the UPDRS-III or 3.12 of the MDS-UPDRS-III, respectively. When only UPDRS-III total scores were available, these were transformed into MDS-UPDRS-III scores, as described by Goetz et al.²⁷ All scales were performed in "on-medication" condition except MDS-UPDRS-III, which was performed in "on- and off-medication" conditions before surgery and in "off-medication/ON-stimulation" and "on-medication/ON-stimulation" conditions 1 year postoperatively. The "off-medication" condition was assessed after 48 h of withdrawal of dopamine agonists and an overnight withdrawal of L-dopa medication. The best "on-medication" condition was assessed after the administration of a rapid-release L-dopa formulation. Levodopa equivalent daily dose (LEDD) was calculated according to Tomlinson et al.²⁸ and Schade et al.²⁹

Statistical Analysis

All statistical analyses were performed using R, version 4.2.2 (2022-10-31).³⁰ The code is accessible on GitHub (https://github.com/kilyth/qol_dbs).

Missing variables except PDQ-39 were imputed using a random forest algorithm provided in the R package *missForest*, version 1.5.³¹ This algorithm uses random forest trained on the observed clinical measures to predict the missing values. It can be used to impute continuous and categorical data simultaneously, including complex interactions and nonlinear relations between the variables.

Linear models were used to assess the relationship between different clinical factors and QoL. The signs of the differences between pre- and postoperative values were chosen such that a positive change indicates an improvement on the respective scale. Thus, positive coefficients resulting from the linear models for change variables indicate an improvement in QoL.

To quantify the relative contributions of the regressors to the linear model's total explanatory value, we calculated the relative importance metric *pmvd* (proportional marginal variance decomposition as proposed in Feldman³²) using the R package *relaimpo*, version 2.2-6.³³

For a direct comparison of QoL outcome between targets, STN and GPi groups were matched based on preoperative clinical factors (Table 2), thereby minimizing the selection bias due to the clinical choice of the stimulation target. Propensity score matching was calculated using the *R* package *Matching*, version 4.10-8,³⁴ and the resulting difference in QoL was compared to 10⁴ permutations to estimate the significance of the result.

Percentile bootstrap confidence intervals (CI) for the percentage change values were calculated using 10,000 samples and 0.025 and 0.975 quantiles of the resulting distribution. All results are given with their 95% CI or \pm standard deviation.

Figures were created using the *R* package *ggplot2*, version 3.4.1.³⁵

Results

Study Population

In total, the cohort included 202 PD patients who received bilateral STN-DBS or GPi-DBS at the University Hospital of Bern

between 2009 and 2018. From these, 21 withdrew consent, 35 were lost to follow-up, and 8 did not complete the PDQ-39 at both visits. Finally, 138 patients were included in the analysis, of whom 117 received STN-DBS and 21 GPi-DBS. No serious intra- or postoperative complications with disabling long-term side effects occurred.

As shown in Table 1, the 2 groups had different baseline characteristics, with patients in the GPi group being older and having a longer disease duration, worse QoL, less improvement in MDS-UPDRS-III in the L-dopa challenge, higher dyskinesia scores, and worse postural stability. For the MMSE there was a statistically significant difference of <1 point. There were no significant differences regarding LEED, MDS-UPDRS-III in the “off-medication” condition, ADL (Schwab and England Scale), insomnia, pain, or neuropsychiatric symptoms (Hamilton, Starkstein scales).

In a subanalysis to compare the QoL between the GPi and STN groups, we used a propensity score-matched cohort to minimize selection bias. The matched cohort included 42 patients, 21 patients in the STN subgroup and 21 in the GPi group, who differed only by the target (Table 2).

TABLE 1 Demographics and baseline characteristics (N = 138)

		STN	GPi	P-value
N		117	21	
Gender (%)	Male	76 (65.0)	9 (42.9)	0.094
	Female	41 (35.0)	12 (57.1)	
Age at surgery		63.19 (8.90)	70.11 (6.77)	0.001
Disease duration (yr)		11.88 (4.32)	14.51 (4.75)	0.013
Time from surgery to assessment (weeks)		58.55 (13.47)	61.72 (21.56)	0.373
PDQ-39 SI		28.51 (12.90)	34.52 (10.25)	0.045
LEDD		1246.15 (608.42)	1149.05 (483.28)	0.490
MDS-UPDRS-III (off medication)		41.83 (14.43)	41.76 (12.95)	0.984
MDS-UPDRS-III (% improvement)		60.62 (14.19)	54.67 (10.21)	0.069
Schwab and England		64.36 (17.86)	62.86 (13.09)	0.714
MMSE		28.62 (1.32)	27.38 (1.72)	<0.001
Hamilton		7.52 (5.32)	6.38 (4.68)	0.360
Starkstein		11.57 (5.35)	12.90 (5.26)	0.294
Pain		4.48 (3.22)	4.53 (2.89)	0.945
Marconi		6.44 (5.82)	9.00 (5.07)	0.061
Insomnia		1.85 (1.52)	1.76 (1.30)	0.793
Postural stability		0.74 (0.79)	1.14 (0.96)	0.041
Stimulator type (%)	Medtronic	67 (57.3)	16 (76.2)	0.165
	Boston	50 (42.7)	5 (23.8)	

Note: Continuous variables are summarized by mean and standard deviation (in parentheses), whereas the categorical variables are listed in counts and percentage (in parentheses).

Abbreviations: STN, subthalamic nucleus; GPi, globus pallidus internus; PDQ-39 SI, Parkinson's Disease Questionnaire Summary Index; LEED, levodopa equivalent daily dose; MDS-UPDRS-III, Movement Disorder Society Unified Parkinson's Disease Rating Scale, Part III; MMSE, Mini-Mental State Examination.

TABLE 2 Baseline characteristics of the matched cohort

		STN subgroup	GPI	P-value
N		21	21	
Gender (%)	Male	10 (47.6)	9 (42.9)	1.000
	Female	11 (52.4)	12 (57.1)	
Age at surgery		68.83 (5.25)	70.11 (6.77)	0.497
Disease duration (yr)		13.60 (3.86)	14.51 (4.75)	0.504
Time from surgery to assessment (weeks)		59.35 (16.77)	61.72 (21.56)	0.693
PDQ-39 SI		34.19 (11.80)	34.52 (10.25)	0.923
LEDD		1096.67 (456.85)	1149.05 (483.28)	0.720
MDS-UPDRS-III (<i>off</i> medication)		42.90 (11.16)	41.76 (12.95)	0.761
MDS-UPDRS-III (% improvement)		56.19 (10.76)	54.67 (10.21)	0.640
Schwab and England		58.90 (17.38)	62.86 (13.09)	0.410
MMSE		27.86 (1.20)	27.38 (1.72)	0.303
Hamilton		8.24 (7.78)	6.38 (4.68)	0.354
Starkstein		14.38 (5.71)	12.90 (5.26)	0.389
Pain		4.77 (3.34)	4.53 (2.89)	0.802
Marconi		7.76 (5.73)	9.00 (5.07)	0.463
Insomnia		1.52 (1.50)	1.76 (1.30)	0.586
Postural stability		0.81 (0.60)	1.14 (0.96)	0.186
Stimulator type (%)	Medtronic	15 (71.4)	16 (76.2)	1.000
	Boston	6 (28.6)	5 (23.8)	

Note: Continuous variables are summarized by mean and standard deviation (in parentheses), whereas the categorical variables are listed in counts and percentage (in parentheses).

Abbreviations: STN, subthalamic nucleus; GPI, globus pallidus internus; PDQ-39 SI, Parkinson's Disease Questionnaire Summary Index; LEDD, levodopa equivalent daily dose; MDS-UPDRS-III, Movement Disorder Society Unified Parkinson's Disease Rating Scale, Part III; MMSE, Mini-Mental State Examination.

QoL Outcome for the DBS Cohort: 1-Year Follow-Up

Overall, Parkinson's Disease Questionnaire Summary Index (PDQ-39 SI) improved by 19.4% (CI: [9.68, 28.18]) 1 year post-operatively. Except for communication in both groups and emotional well-being in the GPI group, all subscores improved, especially ADL, stigma, and bodily discomfort (Fig. 1). Although not statistically significant, we observed a trend toward higher improvement in both PDQ-39 SI and all its respective subscores in the STN group compared to the GPI group. All other clinical outcome variables as well as stimulation parameters are shown in the Data S1 and in Figure S1, shown separately by target.

Pre- and Postoperative Predictors of Improvement in QoL after DBS

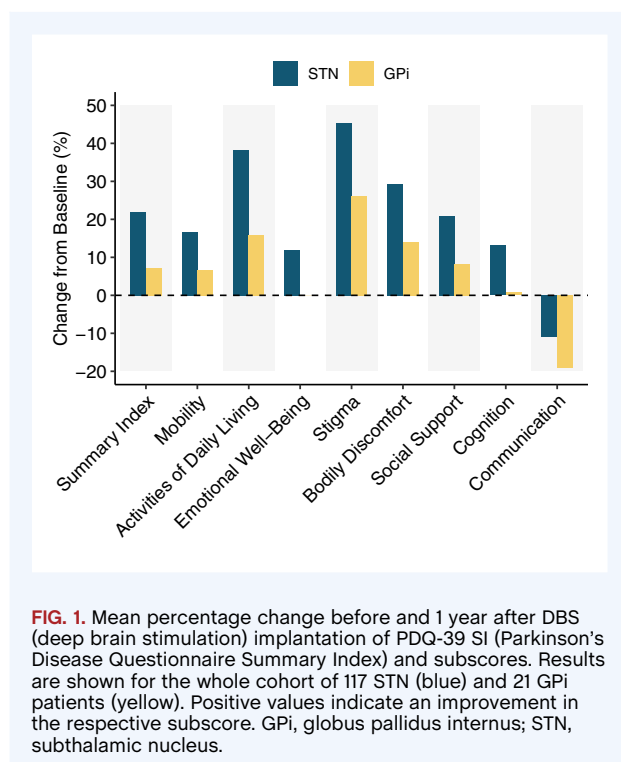
Using multiple linear regression, age was the only preoperative predictor of QoL improvement at 1-year follow-up, showing on

average a lower improvement in QoL at older ages (-0.27 , CI: $[-0.52, -0.01]$, P -value = 0.039; Table S1).

To identify variables whose change after DBS influenced QoL, we performed a multivariable linear regression (Fig. 2) entering all factors modifiable by surgery as dependent variables. Improvement in motor outcome (MDS-UPDRS-III "*off* medication") (0.23, CI: [0.09, 0.37], P = 0.001), reduction in pain (0.94, CI: [0.40, 1.47], P = 0.0007), and improvement in apathy (0.58, CI: [0.20, 0.97], P = 0.003) were factors that significantly contributed to improvement in QoL. Postural stability, dyskinesia, LEDD, ADL (Schwab and England), insomnia, cognition (MMSE), depression (Hamilton scale), and the target were not significantly related to change in PDQ-39 SI.

STN- versus GPI-Matched Groups: 1-Year Follow-Up

Because the DBS target was chosen following a patient-tailored approach, the lack of influence of the target on QoL could be due to selection bias. Using propensity score matching, we formed an STN subgroup, whose average baseline variables did



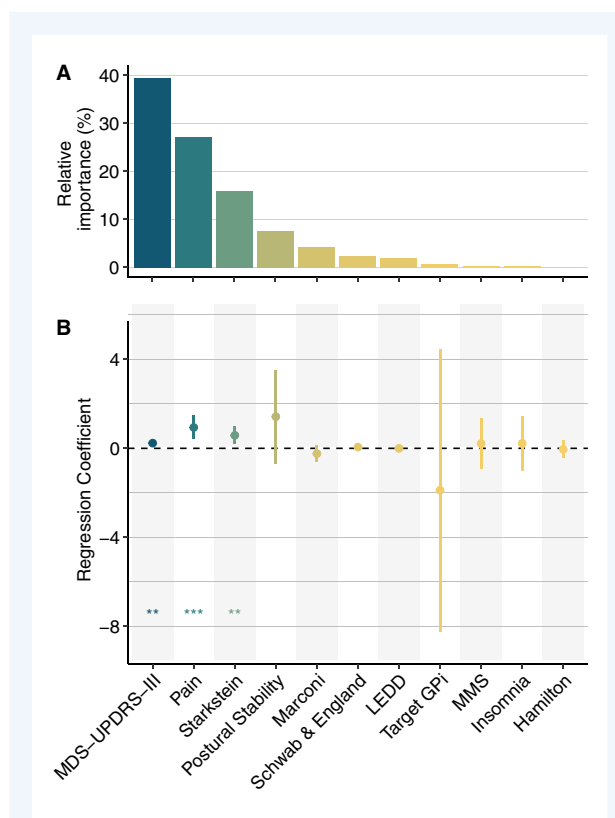
not differ from the GPI cohort (Table 2). Comparing these 2 groups, we observed no significant differences on the postoperative PDQ-39 SI but a tendency for STN patients to have a better QoL 1 year after surgery (4.3 ± 4.4 points on the PDQ-39 SI, $P = 0.17$).

Postural stability and MMSE outcomes were important criteria for target selection. In the matched group, postural stability improved in the “off-medication” condition in the STN subgroup (mean improvement: 0.19 ± 0.98), whereas in the GPI group it slightly worsened (mean change: -0.52 ± 1.12 , P -value = 0.03). There was no difference at 1 year postoperative in MMSE outcome between the 2 targets (Fig. 3).

Discussion

In our retrospective analysis of a single-center PD cohort with STN-DBS or GPI-DBS, we observed an average improvement in QoL of 19.4% measured by the PDQ-39 (CI: [9.68, 28.18]) 1 year after DBS surgery, which is in line with previously reported findings from RCTs.^{10,11,36,37} Notably, the improvement in QoL was not different between the STN and GPI cohorts, even after the clinical baseline profile of both target groups was matched. The findings of the present work therefore challenge the commonly proposed DBS target selection criteria preaching the noble art of patient-tailored target selection by favoring the GPI in a frail population of PD patients with older age, poorer cognition, and postural instability.^{14,15}

Recently, Boogers and Fasano¹² emphasized that the GPI should be more often reconsidered as a DBS target in PD and should be prioritized in elderly frail patients with poorer



cognitive function, higher neuropsychiatric burden, or prominent gait and axial impairment. However, this recommendation is primarily based on individual experiences and the interpretation of the secondary outcomes from the U.S. Veterans Administration study,¹⁰ which demonstrated in a large neuropsychological assessment battery a significant but only slight decrease in processing speed and a minimal increase of 2/63 points on the Beck Depression Inventory-II in the STN group compared to the GPI group, with no correction for multiple assessments. Studies justifying such a patient-profile-oriented DBS target selection are currently lacking. With overall heterogeneous and contradictory results in the literature, the question of the influence of the DBS target on QoL also remains unanswered. In contrast to our study, the few available comparative studies do not focus on frail PD patients and moreover provide contradictory results on QoL.^{38,39} In addition, the short follow-up period of 6 months⁴ could bias the results in favor of GPI-DBS. Furthermore, studies with unilateral stimulation^{38,39} do not provide any information that allows conclusions about the effect of bilateral DBS. Noteworthy, our analysis revealed a tendency

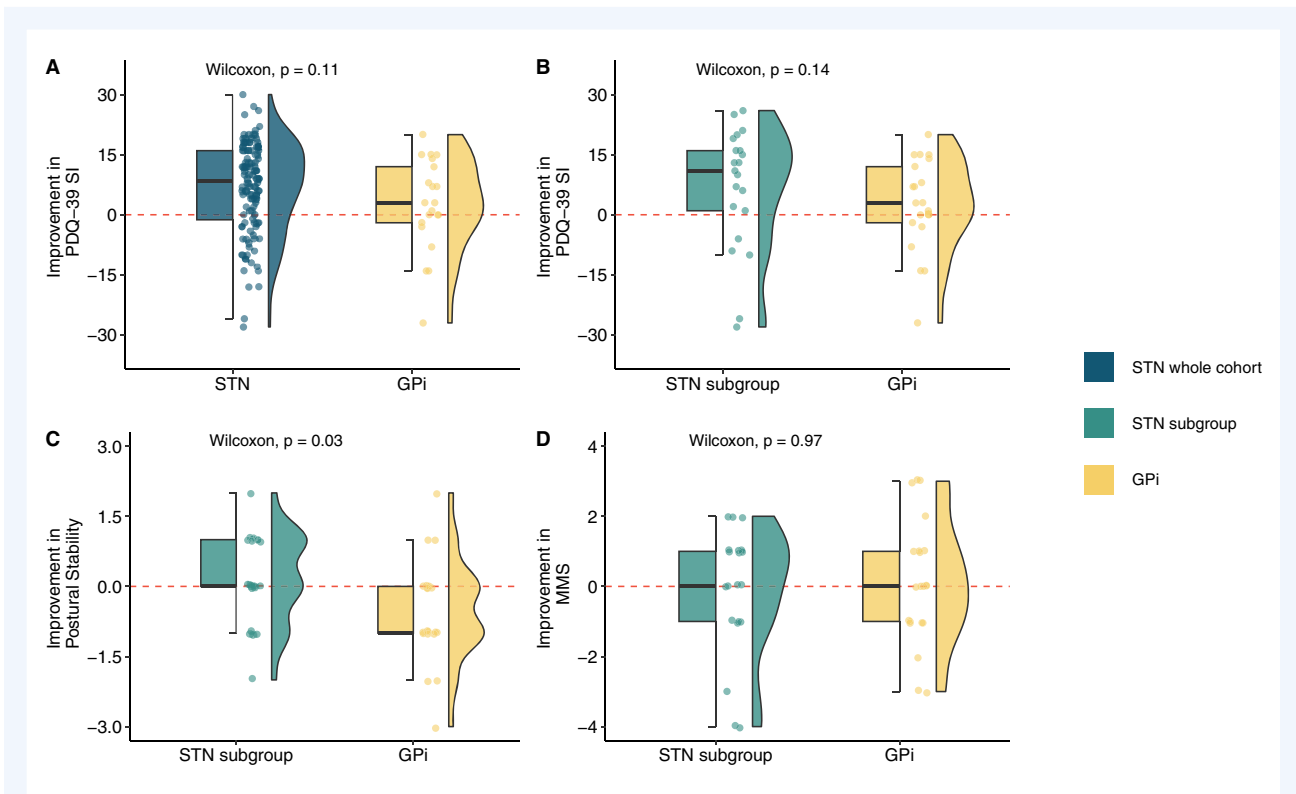


FIG. 3. Absolute improvement in (A, B) PDQ-39 SI, (C) postural stability, and (D) MMSE after DBS (deep brain stimulation). (A) Results for the whole cohort of 117 STN and 21 GPi patients. (B–D) Results of the 21 matched patients. GPi, globus pallidus internus; MMSE, Mini-Mental State Examination; PDQ-39 SI, Parkinson's Disease Questionnaire Summary Index; STN, subthalamic nucleus.

for the STN-DBS group to show a greater improvement after DBS in the overall PDQ-39 and all its dimensions compared to the GPi-DBS group. Nevertheless, the influence of the surgical target on QoL was not statistically significant, which might be explained by group differences due to our patient-tailored approach with choosing the GPi as the DBS target for patients with older age, worse cognitive status, and poorer postural stability. However, since in our cohort the target selection was based on individual clinical judgment with many variables rather than using a strict selection algorithm, we identified a matched subgroup of older patients with worse cognitive scores and postural stability in the STN group that differed from the GPi-DBS group only by target. Contrary to the expectation that the GPi target would be more beneficial in this subgroup of patients, there was no statistically significant difference in QoL improvement depending on the target. Instead, the trend of greater improvement persisted in the STN-DBS subgroup. Whereas cognitive screening scores remained stable with no differences between the targets, postural stability in the “off-medication” condition improved slightly in the STN subgroup and significantly worsened in the GPi group.

Regardless of the DBS target, our analysis further identified motor improvement in the “off-medication” state, reduction in pain, and improvement in apathy as factors positively affecting

QoL 1 year after DBS. Although numerous studies have already suggested a positive impact of motor improvement on QoL of PD patients after DBS,^{40,41} current knowledge of PD-related pain after DBS is limited. Nevertheless, and in line with our results, there is evidence for the overall efficacy of DBS in alleviating PD-related pain,^{42,43} with no significant differences observed between different DBS targets.⁴³ Apathy, which is frequently identified as a determinant of QoL in PD,² overall worsened after DBS in our cohort. Whereas for STN-DBS this can be explained by the relevant reduction in dopaminergic medication,⁴⁴ the increase in apathy among GPi-DBS is surprising and might possibly be explained by an overlap with the observed worsening of depression scores. Nevertheless, our results highlight the impact of apathy on QoL after DBS and the importance of its early detection, as it can be improved by reintroducing or increasing dopamine agonists^{45,46} provided that apathy is related to lack of motivation and not to dementia.⁴⁷ Surprisingly, although depression has been identified as a significant predictor of QoL in PD,^{1,2} it did not play a relevant role in the changes observed in our analysis. This discrepancy may be due to the fact that baseline depression scores and postoperative changes in depression were relatively low in both treatment groups, with no cases of severe depression as it is a contraindication for DBS in both targets. In the literature, postoperative changes in depression have been observed in both directions and

are overall inconclusive. Moreover, the clinical relevance of very small changes reported in the past¹⁰ has probably been overestimated, as substantial changes are needed to affect QoL, which is a very robust measure. Thus, our study was likely underpowered to investigate such a hypothetical benefit.

Because QoL is a very complex construct, many other factors besides motor and nonmotor PD signs are likely to have an important impact on QoL, such as social support and family environment, individual expectations and coping strategies, patients' cultural background, and distressing feelings such as shame. Tools and scales to measure these factors are needed to better understand and further improve the QoL of people with PD.

Our study has several limitations. As a retrospective study, data availability was limited; however, it is representative of real-life outcomes, albeit from a single center with a long track of experience in both targets.^{48,49} The small number of patients in the GPi group compared with the STN group may have an impact on our results. Furthermore, not all nonmotor signs were analyzed because of the lack of comparable scales in the assessments, parts I, II, and IV being hardly comparable between UPDRS and MDS-UPDRS. For a differentiated and comparative assessment of cognition as an influential factor for QoL, the MMSE has limitations because it is a screening tool and is not very sensitive to detection of mild dysexecutive syndrome, which is typical for PD. The 21 STN patients matched to the GPi group indicated a good balance of clinical variables at baseline (Table 2). However, although this method accounts for known outcome parameters/covariates of analyses, thus minimizing selection bias, an imbalance of unknown parameters cannot be ruled out.

In conclusion, the analysis of our real-life data confirms that both STN-DBS and GPi-DBS have a positive impact on QoL in PD. However, contrary to the prevailing belief that GPi should be the preferred target for older patients with worse cognitive status and poorer postural stability,^{14,15} our analysis indicates that the GPi target is not superior to the STN target in improving QoL in this specific patient cohort. Moreover, considering our findings that motor improvement in the “off-medication” condition is a factor that significantly affects QoL and that this improvement is even greater in STN-DBS than in GPi-DBS,^{3,11} the STN might be the preferable DBS target even for patients with older age, worse cognitive status, and poorer postural stability. Although there are 10 times less published data on outcomes of GPi-DBS compared to STN-DBS in the classical indications,³ practically none exists for patients with borderline selection criteria concerning age, cognition, and L-dopa-resistant axial signs in either target, and indeed such patients have been excluded in past trials for good reasons.^{50,51} Therefore, there is a need for prospective studies to explore the boundaries for indications, particularly because the current criteria for DBS target selection are based more on the interpretation of results and expert opinions^{13,14} than on definitive study outcomes. Although this need exists, conducting such RCTs may be impractical given the existing studies comparing both DBS targets. Instead, it would be of great importance for clinical practice to develop a DBS registry to analyze and publish more retrospective data, which are readily available given the widespread use of DBS in recent decades with

a substantial number of so-called “frail” patients who have already undergone and continue to undergo DBS surgery. In this context, differences in health-care systems and center experiences are also important to consider. Our results further suggest that in addition to the improvement in motor signs in the “off state,” change in pain and apathy are critical determinants of improvements in QoL after DBS and should be carefully and individually assessed. Identifying factors influencing QoL change after DBS may assist clinicians in focusing their assessments and treatment strategies to minimize PD-associated disability.

Author Roles

(1) Research project: A. Conception, B. Organization, C. Execution; (2) Statistical analysis: A. Design, B. Execution, C. Review and critique; (3) Manuscript preparation: A. Writing of the first draft, B. Review and critique.

S.M.C.: 1A, 1B, 1C, 2A, 2C, 3A

K.P.: 1A, 1B, 1C, 2A, 2B, 3B

I.D.: 1C, 2C, 3B

D.A.: 1B, 2C, 3B

M.S.: 1C, 2C, 3B

J.W.: 1C, 2C, 3B

A.-A.D.: 1C, 2C, 3B

G.T.: 1C, 2C, 3B

A.N.: 1C, 2C, 3B

C.P.: 1C, 2C, 3B

M.S.: 1C, 2C, 3B

P.K.: 1A, 2C, 3B

M.L.L.: 1A, 1B, 1C, 2A, 2C, 3B

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Disclosures

Ethical Compliance Statement: This study was approved by the Swiss Ethics (Bern Cantonal Ethics Committee, KEK no.: 2020-02392). Written informed consent for research was obtained from all individual participants involved in the study and documented in their electronic health records. We confirm that we have read the journal's position on issues involved in ethical publication and affirm that this work is consistent with those guidelines.

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Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request. ■

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Supporting Information

Supporting information may be found in the online version of this article.

Figure S1. Percentage change before and 1 year after DBS (deep brain stimulation). Results are shown for the whole cohort of 117 STN and 21 GPi patients. Positive values indicate an improvement in the respective score. Single dots, result for each patient; bars, mean percentage change. GPI, globus pallidus internus; LEDD, levodopa equivalent daily dose; MDS-UPDRS-III, Movement Disorder Society Unified Parkinson's Disease Rating Scale, Part III; MMSE, Mini-Mental State Examination; PDQ-39 SI, Parkinson's Disease Questionnaire Summary Index; STN, subthalamic nucleus.

Table S1. Results of the linear model showing the relationship between the improvement in PDQ-39 SI (Parkinson's Disease Questionnaire Summary Index) and the preoperative variables. Positive regression coefficients indicate that an increase in the respective variable leads to an improvement in QoL (quality of life). Residual standard error: 11.19 on 122 degrees of freedom (DF), adjusted R^2 : 0.051, F-statistic: 1.492 on 15 and 122 DF, P -value: 0.11822. GPI, globus pallidus internus; LEDD, levodopa equivalent daily dose; MDS-UPDRS-III, Movement Disorder Society Unified Parkinson's Disease Rating Scale, Part III; MMSE, Mini-Mental State Examination; STN, subthalamic nucleus; VAS, Visual Analog Scale for Pain.

Table S2. Results of the linear model showing the relationship between the improvement in PDQ-39 SI (Parkinson's Disease Questionnaire Summary Index) and the improvement (or change in the target) in the respective variables. Positive regression coefficients indicate that an improvement in the respective variable leads to an improvement in QoL (quality of life). Residual standard error: 10.46 on 126 degrees of freedom (DF), adjusted R^2 : 0.198, F-statistic: 4.075 on 11 and 126 DF, P -value <0.001. GPI, globus pallidus internus; LEDD, levodopa equivalent daily dose; MDS-UPDRS-III, Movement Disorder Society Unified Parkinson's Disease Rating Scale, Part III; MMSE, Mini-Mental State Examination; STN, subthalamic nucleus.

Data S1. Clinical outcome variables and average stimulation parameters for the Parkinson's disease (PD) cohort.