Quality of life of patients with Parkinson’s disease: a comparison between preoperative and postoperative states among those who were treated with deep brain stimulation

Quality de vida de pacientes com doença de Parkinson: uma comparação dos estados pré-operatório e pós-operatório daqueles tratados com estimulação cerebral profunda

Maria Eduarda Turczyn DE LUCCA¹, Jhulia Farinha MAFFINI¹, Mariana Guerrini GRASSI¹, Amanda Elias ABDALA¹, Renato Mitsunori NISIHARA¹, Alexandre Novicki FRANCISCO², Marina FARAH², Tatiana von Hertwig Fernandes de Oliveira KUMER²

ABSTRACT

Background: Deep brain stimulation (DBS) is a well-established procedure for treating Parkinson’s disease (PD). Although its mechanisms of action are still unclear, improvements in motor symptoms and reductions in medication side effects can be achieved for a significant proportion of patients, with consequent enhancement of quality of life. Objective: To investigate the impact of DBS on the quality of life of PD patients. Methods: This was a retrospective longitudinal study with collection of historical data in a neurosurgery center, from June 2019 to December 2020. The sample was obtained according to convenience, and the Parkinson’s Disease Questionnaire (PDQ-39), Unified Parkinson’s Disease Rating Scale (UPDRS) III and IV, Trail-Making Test and Verbal Fluency Test were used. Results: Data were collected from 17 patients (13 with subthalamic nucleus DBS and 4 with globus pallidus pars interna DBS). Significant improvement (p=0.008) on the UPDRS III was observed in comparing the preoperative without DBS with the postoperative with DBS. About 47.0% of the patients showed post-surgical improvement in QoL (p=0.29). Thirteen patients were able to complete part A of the Trail-Making Test and four of these also completed part B. Almost 60% of the patients scored sufficiently on the semantic test, whereas only 11.8% scored sufficiently on the orthographic evaluation. No association between implant site and test performance could be traced. Conclusions: Improvements in quality of life and motor function were observed in the majority of the patients enrolled. Despite the limitations of this study, DBS strongly benefits a significant proportion of PD patients when well indicated. Keywords: Parkinson Disease; Deep Brain Stimulation; Quality of Life.

RESUMO

Antecedentes: A estimulação cerebral profunda (ECP) é um procedimento bem estabelecido para o tratamento da doença de Parkinson (DP). Embora seus mecanismos de ação não sejam claros, a melhora dos sintomas motores e a redução dos efeitos colaterais dos medicamentos são contempladas em uma proporção significativa de pacientes, com melhora da qualidade de vida. Objetivo: Investigar o impacto da ECP na qualidade de vida de pacientes em DP. Métodos: Trata-se de um estudo longitudinal retrospectivo, com coleta de dados históricos em um centro de neurocirurgia, de junho de 2019 a dezembro de 2020. A amostra foi feita por conveniência, e os questionários Parkinson’s Disease Questionnaire (PDQ-39), Unified Parkinson’s Disease Rating Scale (UPDRS) III e IV, Trail-Making Test e Teste de Fluência Verbal foram utilizados. Resultados: Dos dados coletados de 17 pacientes (13 ECP no núcleo subtalâmico e 4 ECP no globus pallidus pars interna) notou-se melhora significativa (p=0.008) no UPDRS III ao se comparar o pré-operatório sem ECP com o pós-operatório com ECP, e cerca de 47,0% deles apresentaram melhora pós-cirúrgica na qualidade de vida (p=0.29). Treze pacientes conseguiram completar a parte A do Trail Making Test e quatro também completaram a parte B. Quase 60,0% dos pacientes obtiveram pontuação suficiente no teste semântico, enquanto apenas 11,8% obtiveram pontuação suficiente no teste ortográfico. Não foi possível rastrear a associação entre local do implante e desempenho. Conclusões: Melhora na qualidade de vida e na função motora foi observada na maioria dos pacientes. Apesar das limitações do estudo, a ECP beneficia fortemente uma proporção significativa de pacientes em DP quando bem indicada. Palavras-chave: Doença de Parkinson; Estimulação Encefálica Profunda; Qualidade de Vida.

1Universidade Positivo, Curitiba PR, Brazil. 
2Hospital Universitário Cajuru, Curitiba PR, Brazil.

METL https://orcid.org/0000-0002-7625-8193; JFM https://orcid.org/0000-0003-0980-7087; MGG https://orcid.org/0000-0002-4462-9084; AEA https://orcid.org/0000-0002-4723-1629; RMN https://orcid.org/0000-0002-1234-8093; ANF https://orcid.org/0000-0003-2039-6834; MF https://orcid.org/0000-0002-1211-1440; THFOK https://orcid.org/0000-0002-7242-7551

Correspondence: Maria Eduarda Turczyn De Lucca; Email: mariatdelucca@gmail.com.

Conflict of interest: There is no conflict of interest to declare.

Authors' contributions: The authors contributed equally to all stages of the work, and all authors approved the version submitted for publication.

Received on January 29, 2021; Received in its final form on April 11, 2021; Accepted on April 16, 2021.
INTRODUCTION

Parkinson’s disease (PD) is a common neurodegenerative disorder characterized by motor and nonmotor symptoms that is caused by progressive degeneration of dopaminergic neurons of the substantia nigra. Lewy bodies, in which the main component is alpha-synuclein protein, form in the substantia nigra in PD.

Deep brain stimulation (DBS) is a well-established treatment for the motor fluctuations and symptoms of PD. Although its mechanism of action is still unclear, satisfactory results are achieved when patients are properly selected. The targets most used are the subthalamic nucleus (STN), the globus pallidus pars interna (GPI) and the intermediate ventral nucleus of the thalamus (Vim).

Several issues need to be carefully evaluated when considering a surgical procedure. Currently, studies recommend implementation in patients over 5 years of age and under 70 years of age who have reached the maximum tolerable dose of the main drug (800 mg per day for 3 months), with motor symptoms that at some point were responsive to it. The objectives of stimulation are to alleviate the motor symptoms of the disease and reduce the adverse effects of drugs. The procedure is well indicated if an improvement of at least 30% is observed, in comparing scores from UPDRS III ON and OFF medication.

The symptoms most responsive to stimulation are tremor, bradykinesia, stiffness and dyskinesia, but the degree of individual response is variable. The adverse effects of DBS include axial symptoms, speech dysfunctions, cognitive or behavioral changes, dyskinesia, spontaneous muscle contractions and paresthesia, each at different degrees of intensity and incidence.

Use of DBS is associated with an improvement in quality of life (QoL), compared with pharmacological treatment alone. However, the degree of improvement varies according to prior drug responsiveness, the predominant symptom and presence of comorbidities.

Therefore, the objective of this study was to investigate the quality of life of PD patients who underwent DBS, comparing preoperative and postoperative conditions, and to assess postoperative motor and nonmotor symptoms in those patients.

METHODS

This was a retrospective uncontrolled analytical observational longitudinal cohort study that was approved by our institution’s research ethics committee. All participants signed an informed consent statement. It was conducted at the Hospital Universitário Cajuru (HUC), Curitiba, Paraná, Brazil, from June 2019 to December 2020.

Patients

The sample was obtained according to convenience and consisted of adult patients diagnosed with PD, without cognitive problems, who were able to answer the questionnaires. All the patients underwent DBS targeted at the STN or GPI and had at least three months of follow-up after the surgical procedure. PD had been diagnosed clinically, in accordance with the presence of at least three of the following: resting tremor, bradykinesia, rigidity and postural instability.

Patients with other movement disorders and/or severe cognitive and psychiatric problems that had previously been diagnosed, those who underwent DBS targeted at the Vim and those who underwent ablative surgeries were excluded.

Questionnaires

Preoperative questionnaires were applied during the preoperative examination, to confirm the indication for the surgery. The criterion for the postoperative evaluation was that it should be applied at least three months after the first regulation of the device, which led to variable periods after the surgery. This was due to the availability of the clinical care, as determined by the demand from patients within the public system in Brazil (Sistema Único de Saúde, SUS). In general, the examiners for the PDQ-39 and UPDRS questionnaires that were applied preoperatively were specialist doctors (neurologists and neurosurgeons). The questionnaires that were applied postoperatively were administered by the same examiners, watched by medical students who were undergoing training.

The questionnaires applied postoperatively were examined by medical students who were undergoing training and were under the supervision of specialists in the field.

An identification questionnaire was applied, which asked for the subjects’ medical record number, age, date of birth, gender, date of data collection, age at the time of diagnosis, date of implementation of the DBS, date of completion of the electrode threshold, target site, disease pattern, smoking, harmful use of alcohol, comorbidities, medications with continuous use, education, income and marital status.

To evaluate quality of life, the PDQ-39 questionnaire was applied both before and after use of DBS. This had been adapted for use in Portuguese by Health Services Research Unit (Department of Public Health and Primary Care, University of Oxford) in 2005. It consists of eight dimensions: mobility, activities of daily living, emotional wellbeing, stigma, social support, cognition, communication and body discomfort. In total, there are 39 questions with scores ranging from 0 (never) to 4 (always) that are summed for each dimension before the final score is calculated. The final score ranges from 0 (indicating no problem) to 100 (maximum problem level).

For this study, the UPDRS parts III and IV were also applied. The score for each item ranges from 0 (normality) to 4. Data for the preoperative UPDRS III scale were collected from the medical records and the scale was divided into ON and OFF medication. This is also known as the
levodopa challenge test, in which 50 to 100% of the levodopa dose is provided in addition to the one usually taken by the patient, in order to identify the best response. An improvement of 30–50% is generally considered necessary for the surgical procedure to be indicated. The OFF preoperative score refers to the patient's baseline state. The postoperative score, applied by the same examiner, was obtained in a state of ON stimulation and ON medication.

The Trail-Making Test has two parts: part A evaluates motor function, while part B requires mental flexibility. Thus, this test accesses the combined performance of motor and cognitive function. The time taken for application of each part of the test needs to be counted. At the end, the times are added, resulting in a final score. Patients who were unable to perform the test within 300 seconds were given a score of 300.13,14 This test was applied only after implementation of DBS.

Lastly, an adapted verbal fluency test was applied based on a previous study. This was done only after implementation of DBS. In the first evaluation, patients were asked to say as many words as possible starting with a certain letter (e.g. B) within 60 seconds. They were then asked to say as many words as possible within a single category (e.g. animals), within 60 seconds. The score was given by the sum of the number of words (repeated words were counted only once and words that did not fit were deleted). A result consisting of 13 words or more was considered sufficient (or 9 words, in the case of illiterate patients).13,14

**Statistical analysis**

Frequency tables and contingency tables were created. The data distribution was determined through the Shapiro-Wilk test. Chi-square and Fisher tests were used to compare nominal and categorical data. Mann-Whitney U and unpaired t tests were used to compare numerical data. A regression analysis was performed as well, to verify the significance of the findings through a parametric test. Both tests resulted in the same conclusion. P values < 0.05 were considered significant. All tests were calculated using the GraphPad Prism 6.0 software.

**RESULTS**

Between January 2009 and January 2020, 98 patients underwent DBS at our neurosurgery center. The flow diagram for patient selection can be seen in Figure 1.

From the 17-patient sample, fourteen (82.3%) were male and three (17.6%), female. The median age was 57 years, with a range from 46 to 76 years. The patients' sociodemographic data and initial symptoms are described in Table 1. All the patients were using Levodopa and most were using one or more potentiating drugs.

The patients had, on average, been diagnosed approximately 12.1±4.2 years earlier when they underwent the first DBS procedure and 14.6 years had passed since receiving the diagnosis, at the time of data collection. The median age at

---

**Figure 1.** Distribution of patients during research data collection.
the first surgery was 55 years. The STN was the implementation site for 13 patients (76.5%), while GPI was chosen for four patients (23.5%). Twelve patients (70.6%) underwent operations bilaterally. Among the five patients with unilateral implementation, three (60.0%) received DBS in the STN and two (40.0%) in the GPI.

Nine patients (52.9%) had the tremor-dominant subtype. Among these, five (44.4%) showed improvements in motor function and quality of life, three (33.3%) had an improvement only in motor function and one (11.1%) improved only on the QoL scale. The most prominent symptoms before surgery are described in Table 2.

Comparing the results from the preoperative UPDRS III scale (OFF medication) and from the postoperative scale (ON medication and ON DBS), thirteen patients (76.5%) had improved scores. The mean improvement in this comparison was 49.6% (±20.4%). Among these 13 patients with improvements in relation to the preoperative OFF score, ten (76.9%) also improved in relation to the levodopa challenge test (ON medication), performed preoperatively. The mean improvement in this case was 29.3% (±15.6%). For nine (69.2%) of the 13 patients with motor improvement, the evaluation was made one year or more after the last surgical procedure. Two (50.0%) of the four patients without improvement on the UPDRS III scale had been diagnosed with PD more than 15 years earlier. Eight (61.5%) of the 13 patients with motor improvement were under 60 years of age. The distribution of scores can be observed in Figure 2a, 2b and 2c.

Regarding the assessment of quality of life through the PDQ-39, eight patients (47%) reported having improvements in quality of life after surgery, by an average of 48.3% (±30.3%), although this change was not statistically significant (p=0.29). Six (75%) of the eight patients with improved quality of life were less than 60 years of age. Three patients (37.5%) with unilateral electrode implantation had an average improvement in the PDQ-39 of 47.2% (±40.8%).

The individual evaluation of the domains in the PDQ-39 revealed that the domain that benefited the most was wellbeing, in which 68.75% of the patients showed improvements in relation to the presurgical scale. Furthermore, 31.25% showed improvement in mobility, and all of these patients also showed improvement in wellbeing and were under 60 years old. Out of the total number of patients under 60 years old, 55.56% showed improvements in both mobility and wellbeing. There were eight patients with worsening cognition, among whom 62.5% were over 60 years old, while 71.43% of the seven patients with improved cognition were under 60 years old. However, these results were not statistically significant. It is important to note that one of the patients included in the present study did not have presurgical data relating to each domain separately and was excluded from the individual analyses on the PDQ-39 domains. The distribution of scores on the PDQ-39 scale can be seen in Graph 1C. Most patients, when subjectively questioned, reported having substantial improvements in quality of life and motor function.

Among the 17 patients, five (29.4%) had had less than one year of follow-up after undergoing DBS, at the time of data collection. There was no relationship between a length of follow-up of less than one year and more promising results regarding motor function and quality of life.

Among the 13 patients with STN stimulation, twelve (92.3%) had improvements in UPDRS III score in relation to the preoperative OFF score, and six (46.1%) also showed improvements in the PDQ-39 score. Three (75.0%) of the four patients with GPI stimulation did not have any improvement in motor function and two (50.0%) reported having an improvement in quality of life. All the patients with postoperative improvement in relation to the preoperative UPDRS III ON had bilateral electrode implantation.

Part IV of the UPDRS was evaluated only in the postoperative period. The distribution of patients in different states of disease according to age and time since diagnosis can be seen in Table 3.
Regarding the Trail-Making Test, thirteen patients (76.5%) completed part A, and four of these (30.8%) completed part B. Four patients (23.5%) did not complete part A and did not proceed to the second part of the test. Two patients (50.0%) who completed both parts of the test had undergone GPi stimulation and two (50.0%) had undergone STN stimulation. The four patients (10.8%) who completed the test had a subtype of disease other than dominant tremor.

The distribution of the patients in the parts of the verbal fluency test according to the stimulation site is shown in Table 4.

**DISCUSSION**

Although DBS is a surgical procedure with a great impact on QoL, it is not clearly demonstrated in the literature how much it interferes in the most diverse areas of life of patients with PD. The sample obtained in our study was equivalent to more than a third of the population with potential for analysis. Our research reiterated some results already reported by others, but it also came up with other data, thus raising questions for possible future investigation.

In this study, a significant improvement in general motor function compared with the presurgical OFF period could be seen. Nevertheless, this cannot indicate any definitive conclusion regarding the efficacy of the method, considering that the comparison was with patients who were ON DBS and ON medication. Among the patients without any improvement in motor function, half presented disease at a more advanced stage.

The preoperative levodopa challenge test requires at least 30–50% improvement of motor symptoms in relation to the OFF phase, without medication. Furthermore, the indication should be individualized and should include assessment of nonmotor symptoms. The presence of comorbidities such as frank dementia or severe cognitive dysfunction formally contraindicate stimulation, as there will be no benefit from treatment. If the criteria are met, there is a higher likelihood of favorable results from stimulation.
The clinical worsening that was noticed in a few patients after DBS may be attributed to the disease progression itself. However, it is usually possible to adjust the stimulation patterns, with at least partial improvement of the condition\(^\text{19,24,25}\).

In the present study, no statistically significant improvement in QoL was observed through the PDQ-39, and bilateral stimulation did not reveal any greater impact, as had been reported by two other studies\(^\text{26,27}\). Despite the objective results, there was a substantial improvement in QoL according to the subjective perception of most patients. These assessments were made based on the patient’s report of perceived improvement or worsening of the clinical condition.

Objective scales for quality-of-life assessment are widely used, but some studies have also found no correlation between the scores obtained through the objective questionnaire and the overall satisfaction subjectively reported by patients\(^\text{16,17}\). Frizon et al. proposed three variables capable of predicting improvement in up to 81.4% of the cases: PDQ-39 preoperatively, percentage of improvement of UPDRS-III after levodopa use and years since the onset of symptoms. According to the literature, worse preoperative PDQ-39 scores and high percentage of medication response are predictors of greater chance of improvement in quality of life\(^\text{18,23,24,28}\).

Moreover, in large meta-analyses, an average improvement of 34.5% in the quality of life of patients with bilateral stimulation assessed through the PDQ-39 was reported, with a range from 14 to 62%. The average improvement through bilateral stimulation in the present study was slightly higher (41%; SD 27.5%). Few studies have been conducted regarding unilateral stimulation. The study by Słomiński et al., 2007, showed a mean improvement of 15% among patients with a unilateral electrode, while the study by Frizon et al. showed a median improvement of 34.6% among patients with unilateral stimulation, compared with an improvement of 44.1% among those with bilateral stimulation\(^\text{19,20}\).

It was not possible to observe any influence from more recent surgeries (less than one year) on motor function and quality of life in most of the patients. This was contrary to what most studies have shown, i.e. that the greatest benefit of therapy was within the first 6 to 12 months after surgery. Some other studies have indicated differences in motor outcomes, with worsening as the time elapsed after the procedure increased. However, those studies used longer intervals (five years) as the cutoff because it was believed that the main effects of STN-DBS could last for up to five years. The effects of GPI-DBS would last for a slightly shorter time, independently of the onset of PD. Motor fluctuations, dyskinesia and activities of daily living should also be improved through stimulation, although a decline in the benefit over the years has been identified\(^\text{19,25}\).

One group reported rates of improvement in UPDRS III score of 45% over five years and 42% over 29 years, which were similar to the rates observed in the present study. In addition, there is evidence that some patients can expect improvement even after 10 years of stimulation, but with reductions in the UPDRS-III score of 25.3%\(^\text{19}\).

Compared with STN, GPI stimulation does not allow significant reductions in medication intake. However, it has a direct effect on inhibition of drug-related dyskinesias, with a reduction in incidence of up to 80%. Thus, GPI-DBS enables increases in daily dosage with fewer concomitant side effects, and also improvement of nonmotor symptoms that are responsive to dopaminergic medication. According to Chao et al., the main advantage of DBS, regardless of the implementation site, is the potential for adjusting the stimulator at any time after surgery in order to maximize benefits and minimize adverse effects\(^\text{14,22,29}\).

Studies have indicated there is no significant difference in UPDRS results between implementation sites, except for the slight improvement of stiffness and axial symptoms seen with GPI-DBS\(^\text{15,23,24,26}\). However, we observed that STN-DBS produced a more significant improvement of symptoms during the OFF medication period. A previous study showed that there was an improvement in UPDRS-III of around 41% under these circumstances\(^\text{26}\). Thus, STN-DBS would be better indicated for patients with low levodopa tolerance, in order to enable greater postoperative dose reduction\(^\text{17,21,24}\).

Although most studies have suggested that GPI is the most appropriate site, considering cognitive and neuropsychiatric symptoms, discrepancies in the results still exist among different centers. Authors who obtained more favorable outcomes with GPI-DBS used higher doses of dopaminergic medication, and this factor may explain this finding\(^\text{23,24,28}\).

The results found in the current study emphasized the deterioration of executive function. This was characterized by increased time taken to perform the Trail-Making Test, part B. Therefore, as noticed in previous studies, a possible relationship with older age and the natural progression of the disease was identified. Nonetheless, despite the hypotheses, the impact of DBS on executive function is not yet well established, and existing studies have demonstrated discordant results. Some cognitive changes observed after brain stimulation can be evaluated through the Trail-Making Test. In the study by Sáez-Zea et al. there was an increase in the time taken to perform part B of the test, both among patients with STN-DBS and among those treated only with pharmacotherapy. However, it is noteworthy that there was a statistically significant relationship between older age and longer time taken to perform this part of the test. Both the neuropsychological and the motor changes observed after surgery vary according to disease subtype, lead position, distribution of electric current and changes in drug therapy\(^\text{28,30}\).

Semantic and phonemic verbal fluency were found to have become impaired after surgery in our patients. Phonemics were worsened regardless of implantation site, while semantics became more impaired in patients with
STN-DBS. This was possibly due to decreased activation of the lower prefrontal and temporal cortex of the left cerebral hemisphere. Longer follow-up (more than one year), education level and age did not interfere with the outcomes, which differed from the results obtained in the study by Olchik et al., where these factors were associated with worse cognitive performance.

Speech disorders occur in up to 89% of individuals with PD, regardless of age and length of time with the disease. Although some studies have shown that DBS helps to improve speech mechanisms, most have demonstrated that patients with STN-DBS present deteriorated speech intelligibility, and this procedure has also been associated with negative impacts on intonation, rhythm and articulation, and hypophony has been found to be the most frequent effect. In patients who underwent GPi-DBS, speech deterioration has not been so commonly reported. However, its effects on speech have been less studied than those of STN-DBS. Although phonemic verbal fluency was more affected, semantics were also impaired.

The limitations of this study were its small sample size and cross-sectional design; strict inclusion criteria; and the impossibility of expanding the face-to-face evaluation due to paralysis of outpatient activities caused by the Covid-19 pandemic. Further research to understand QoL after DBS to treat PD is still required.

In conclusion, both quality of life and motor function presented improvements through DBS, although quality-of-life improvements were not statistically significant. Nonmotor symptoms did not present a favorable outcome in most patients. Despite the favorable results achieved through DBS for treating PD, further research is still required.

References

1. Coriolano M, Balbino J, Silva B, Cabral E, Asano A, Lins O, et al. Pain characterization in patients with Parkinson’s disease. Rev Dor. 2014 Apr-Jun;15(2):79-82. https://doi.org/10.5935/1806-0013.20140019
2. Olchik M, Ayres A, Ghisi M, Schuh A, Rieder C. The impact of cognitive performance on quality of life in individuals with Parkinson’s disease. Dement Neuropsychol. 2016 Oct-Dec;10(4):303-9. https://doi.org/10.1590/s1980-5764-201611004008
3. Chao Y, Gang L, Na Z, Ming W, Zhong W, Mian W. Surgical management of Parkinson’s disease: update and review. Interv Neuroradiol. 2007 Dec;13(4):359-68. https://doi.org/10.1017/S11701990701300407
4. Dostrovsky J, Hutchison W, Lozano A. The globus pallidus, deep brain stimulation, and Parkinson’s disease. Neuroscientist. 2002 Jun;8(3):284-90. https://doi.org/10.1177/107385842008003014
5. Negida A, Elminawy M, El Ashal G, Essam A, Eysa A, Abd Elalem Aziz M. Subthalamic and pallidal deep brain stimulation for Parkinson’s disease. Curr. 2018 Feb 16:e2232. https://doi.org/10.7769/cureus.2232
6. Pollak P. Deep brain stimulation for Parkinson’s disease – patient selection. Handb Clín Neurol. 2019;116:97-105. https://doi.org/10.1016/B978-0-444-53497-2.00009-7
7. Sprenger F, Poewe W. Management of motor and non-motor symptoms in Parkinson’s disease. CNS Drugs. 2013 Apr;27(4):259-72. https://doi.org/10.1007/s40263-013-0053-2
8. Dafarsi H, Reker P, Stalinski L, Silverdale M, Rizos A, Ashkan K, et al. Quality of life outcome after subthalamic stimulation in Parkinson’s disease depends on age. Mov Disord. 2018 Jan;33(1):99-107. https://doi.org/10.1002/mds.27222.
9. Deuschl G, Paschen S, Witt K. Clinical outcome of deep brain stimulation for Parkinson’s disease, Handb Clin Neurol. 2013 (S).107-28. https://doi.org/10.1016/B978-0-444-53497-2.00010-3
10. Mansouri A, Taslimi S, Badhiwala J, Turmaz G, Nasciutti-Prudente C, Goulart F, Teixeira-Salmela L, Cardoso F. Percepción da qualidade de vida de indivíduos com doença de parkinson através do PDQ-39. Rev Bras Fisioter. 2007 Sep-Oct;11(5):397-402. https://doi.org/10.1590/S1413-35552007000500011
11. Goetz C, Tilley B, Shaftman S, Stebbins G, Fahn S, Martinez-Martin P, et al. Movement Disorder Society-sponsored revision of the Unified Parkinson’s Disease Rating Scale (MDS-UPDRS): scale presentation and clinimetric testing results. Mov. Disord. 2008 Nov;23(15):2129-70. https://doi.org/10.1002/mds.22340
12. Gurd J. Reward deficits in Parkinson’s disease: individual differences in underlying cognitive mechanisms. J Neurolinguist. 2000 Jan;13(1):47-65. https://doi.org/10.1016/S0911-6044(99)00011-1
13. Shapiro KA, Mottaghy F, Schiller N, Poeppel T, Fluß M, Müller H, et al. Dissociating neural correlates for nouns and verbs. Neuroimage. 2005 Feb;24(4):1058-67. https://doi.org/10.1016/j.neuroimage.2004.10.015
14. Frizon L, Hogue O, Achey R, Floden D, Nagel S, Machado A, et al. STN vs GPi deep brain stimulation for Parkinson disease: a meta-analysis. Medicine (Baltimore). 2018 Aug;97(35):e12153. https://doi.org/10.1097/MD.0000000000012153
15. Karl J, Ouyang B, Colletta K, Verhagen Metman L. Long-term satisfaction and patient-centered outcomes of deep brain stimulation in Parkinson’s disease. Brain Sci. 2018 Apr;8(4):60. https://doi.org/10.3390/brainsci8040060
16. Malva F, Lewis C, Horstkoetter N, Eggers C, Kalbe E, Maarouf M, et al. Patients’ expectations of deep brain stimulation, and subjective perceived outcome related to clinical measures in Parkinson’s disease: a mixed-method approach. J Neurol Neurosurg Psychiatry. 2013 Oct;84(1):1273-81. https://doi.org/10.1136/jnnp-2012-303670
17. Frizon L, Hogue O, Achey R, Floden D, Nagel S, Machado A, et al. Quality of life improvement following deep brain stimulation for Parkinson's disease: development of a prognostic model. Neurosurgery. 2019 Sep;85(3):343-9. https://doi.org/10.1093/neo/mny287
18. Castiello A. Ten-year outcome of subthalamic stimulation in Parkinson disease. Arch Neurol. 2011;68(12):1550-56. https://doi.org/10.1001/archneurol.2011.182
19. Slowinski J, Putzke J, Uitti R, Lucas J, Turk M, Kall B, et al. Unilateral deep brain stimulation of the subthalamic nucleus for Parkinson disease. J Neurosurg. 2007 Apr;106(4):626-32. https://doi.org/10.3171/jns.2007.106.4.826
20. De Lucca MET, et al. Quality of life in Parkinson’s disease with deep brain stimulation.
21. Dafsari H, Weiß L, Silverdale M, Rizos A, Reddy P, Ashkan K, et al. Short-term quality of life after subthalamic stimulation depends on non-motor symptoms in Parkinson’s disease. Brain Stimul. 2018 Jul-Aug;11(4):867-74. https://doi.org/10.1016/j.brs.2018.02.015

22. Rughani A, Schweib J, Sidiropoulos C, Pilitsis J, Ramirez-Zamora A, Sweet J, et al. Congress of neurological surgeons systematic review and evidence-based guideline on subthalamic nucleus and globus pallidus internus deep brain stimulation for the treatment of patients with Parkinson’s disease: Executive Summary. Neurosurgery. 2018 Jun;82(6):753-6. https://doi.org/10.1093/neuros/nyy037

23. Xie C, Shao B, Chen J, Zhou Y, Lin S, Wang W. Effects of neurostimulation for advanced Parkinson’s disease patients on motor symptoms: a multiple-treatments meta-analysis of randomized controlled trials. Sci Rep. 2016 May;6:25285. https://doi.org/10.1038/srep25285.

24. Xu H, Zheng F, Krischek B, Ding W, Xiong C, Wang X, et al. Subthalamic nucleus and globus pallidus internus stimulation for the treatment of Parkinson’s disease: a systematic review. J Int Med Res. 2017 Oct;45(5):1602-12. https://doi.org/10.1177/0300060517708102

25. Acera M, Molano A, Tijero B, Bilbao G, Lambarrí I, Villoria R, et al. Impacto de la estimulación subtalámica a largo plazo sobre la situación cognitiva de los pacientes con enfermedad de Parkinson avanzada. Neurología. 2019 Nov-Dec;34(9):573-81. https://doi.org/10.1016/j.neur.2017.05.009

26. Lee PS, Crammond DJ, Richardson RM. Deep brain stimulation of the subthalamic nucleus and globus pallidus for Parkinson’s disease. Prog Neurol Surg. 2018;33:207-21. https://doi.org/10.1159/000481105

27. Mao Z, Ling Z, Pan L, Xu X, Cui Z, Liang S, et al. Comparison of efficacy of deep brain stimulation of different targets in Parkinson’s disease: a network meta-analysis. Front Aging Neurosci. 2019 Feb;11:23. https://doi.org/10.3389/fnagi.2019.00023

28. Wu B, Han L, Sun B, Hu X, Wang X. Influence of deep brain stimulation of the subthalamic nucleus on cognitive function in patients with Parkinson’s disease. Neurosci Bull. 2014 Feb;30(1):153-61. https://doi.org/10.1007/s12264-013-1389-9

29. Tsuboi T, Lopes J, Patel B, Legacy J, Moore K, Eisinger RS, et al. Parkinson’s disease motor subtypes and bilateral GPi deep brain stimulation: one-year outcomes. Parkinsonism Relat Disord. 2020 Jun;75:7-13. https://doi.org/10.1016/j.parkreldis.2020.05.004

30. Sáez-Zea C, Escamilla-Sevilla F, Katati M, Mínguez-Castellanos A. Cognitive Effects of Subthalamic Nucleus Stimulation in Parkinson’s disease: a controlled study. Eur Neurol. 2012;68(6):361-6. https://doi.org/10.1159/000341380

31. Fasano A, Romito L, Daniele A, Piano C, Zinno M, Bentivoglio A, et al. Motor and cognitive outcome in patients with Parkinson’s disease 8 years after subthalamic implants. Brain. 2010 Sep;133(9):2664-76. https://doi.org/10.1093/brain/awq221.

32. Wertheimer J, Gottuso A, Nuno M, Walton C, Duboille A, Tuchman M, et al. The impact of STN deep brain stimulation on speech in individuals with Parkinson’s disease: The patient’s perspective. Parkinsonism Relat Disord. 2014;20(10):1065-70. https://doi.org/10.1016/j.parkreldis.2014.06.010