

# Effect of Deep Brain Stimulation on Quality of Life in Patients with Parkinson's Disease

## *Parkinsonlu Hastalarda Derin Beyin Stimülasyonunun Yaşam Kalitesine Etkisi*

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### Summary

**Objective:** The study aimed to investigate the effect of deep brain stimulation (DBS) on the quality of life (QOL) in patients with Parkinson's Disease (PD).

**Materials and Methods:** The study included 19 patients with idiopathic PD who underwent DBS surgery at Mustafa Kemal University Medicine Faculty Neurosurgery Department. Patient characteristics, duration of disease, and the dominant hand of each patient were noted from the clinical records of the patients. The QOL of the patients was assessed using the RAND 36-Item Health Survey 1.0 (RAND-36) and the symptoms of PD were evaluated using the Unified Parkinson's Disease Rating Scale (UPDRS), which was administered preoperatively when the medication was on (within one week prior to surgery) and postoperatively when the medication and stimulation were on (2 months after the surgery; range, 55-65 days).

**Results:** The study included 19 patients with PD, comprising 12 (63.2%) men and 7 (36.8%) females with a mean age of 52.07±9.89 (range, 38-72) years. Mean duration of disease was 6.60±5.92 years. A gender-based analysis on the RAND-36 scores indicated that there was a significant difference between the pre- and post-operative scores of the female patients for bodily pain (p=0.028) and between the pre- and post-operative scores of the male patients for emotional well-being (p=0.032). However, no significant difference was found between the pre- and post-operative scores of other subcategories in both genders (p>0.05). On the other hand, postoperative UPDRS scores decreased compared to preoperative scores in all the patients.

**Conclusion:** This study is the first region-wide prospective study to investigate the effects of STN-DBS in PD patients for our region. The results indicated that the STN-DBS surgery has a positive effect on the quality of life in PD patients.

**Keywords:** Deep brain stimulation, quality of life, Parkinson's disease

### Özet

**Amaç:** Çalışma, Derin Beyin Stimülasyonunun (DBS) Parkinson Hastalığı (PH) tanımlı bireylerde yaşam kalitesine etkisini bulmayı amaçlamaktadır.

**Gereç ve Yöntem:** Çalışmaya Mustafa Kemal Üniversitesi Tıp Fakültesi Beyin ve Sinir Cerrahisi Bölümünde ilaca dirençli idiopatik PH tanısıyla Subthalamic Nucleus bölgesine DBS cerrahisi uygulanmış 19 birey dâhil edildi. Demografik bilgiler hasta kayıtlarından toplandı. Değerlendirme cerrahi öncesi (cerrahi öncesi 1 hafta içinde) ve cerrahiden 2 ay sonra (55-65 gün arası) olmak üzere iki kez yapıldı. Değerlendirmede, yaşam kalitesi "RAND 36-Item Health Survey 1,0" ile Parkinson hastalığına özgü semptomlar ise Birleşik Parkinson hastalığı Derecelendirme Ölçeği ile değerlendirildi.

**Bulgular:** Çalışmaya dâhil edilen 12'si erkek 7'si kadın 19 hastanın yaş ortalaması 52.07 yıl (38 - 72 yıl arasında) ortalama hastalık süresi ise 6,60 yıldır. Kadın olguların RAND 36-Item Health Survey 1.0 değerlendirmesinin vücut ağrısı parametresinin median sonuçları cerrahi öncesi 33 (minimum-maksimum=0-80), cerrahi sonrası ise 90 (minimum-maksimum=23-100) olduğu ve aradaki farkın anlamlı olduğu (p=0.028). Erkek olguların duyu durum iyilik hali parametrelerinin median sonuçlarının ise cerrahi öncesi 72 iken (minimum-maksimum=48-96), cerrahi sonrası 64 (minimum-maksimum=48-88) olduğu ve aradaki farkın gene anlamlı olduğu tespit edildi (p=0.032). Her iki cinsiyet grubunun ameliyat öncesi ve sonrası diğer değerlendirme parametrelerinin sonuçlarının arasında ise anlamlı bir fark olmadığı tespit edildi (p>0.05). Bununla birlikte Birleşik Parkinson Hastalığı Derecelendirme Ölçeği motor parametreleri ortalamasında cerrahi sonrası düşüş saptanmıştır.

**Sonuç:** Çalışmamız; bölgemizde STN – DBS cerrahisinin PH üzerindeki etkisinin araştırıldığı ilk kapsamlı çalışma olup, elde ettiğimiz sonuçlara göre STN-DBS cerrahisinin özellikle kadın olgularda yaşam kalitesi üzerinde istatistiksel olarak anlamlı pozitif etkiye sebep olduğu tespit edilmiştir.

**Anahtar Kelimeler:** Derin beyin stimülasyonu, yaşam kalitesi, Parkinson hastalığı

## Introduction

Deep brain stimulation (DBS) surgery is a neurosurgical procedure commonly used in the treatment of Parkinson's disease (PD). However, DBS was not considered a treatment method until early 1990s but was considered an experimental method (1). To date, a large number of patients have been treated with DBS since the administration of the first procedure. Moreover, numerous studies have shown that DBS has clinical effects on motor symptoms. DBS is primarily used for the treatment of neurological and psychiatric disorders and is mostly preferred for patients with PD who experience troublesome levodopa-related complications and patients with severe essential tremor and dystonia (2,3).

Patients with PD typically experience shaking, rigidity, slowness of movement, difficulty walking, and gait problems in early stage of the disease as opposed to cognitive and behavioral problems such as sleep and emotional problems, depression, severe fatigue and pain in the late stage. Moreover, these late-stage conditions mainly arise from the motor problems occurring in the early stage. On the other hand, these motor and psychological problems decrease the quality of life (QOL) of the patients (4,5), which is a important concern in the treatment of PD.

Oyama et al. retrospectively evaluated the effect of DBS on QOL and found that QOL was higher in the DBS group compared to the non-DBS group although this finding was considered to be speculative in the absence of pre-surgical data for comparison (6). Volkmann et al. examined the long-term effects of DBS using a QOL scale known as Sickness Impact Profile (SIP). The study revealed that DBS significantly improved the sub-categories of SIP including total, physical, and psychosocial parameters from baseline to 6 months. Moreover, although significant improvements occurred in some categories including body care/movement, eating, recreation/pastimes, social interaction, and mobility, the total, physical, and psychosocial SIP scores decreased significantly and also most of the SIP sub-category scores dropped to their baseline values after 3 years (7). However, as indicated by these studies, the effect of DBS on QOL remains inconclusive. Moreover, to our knowledge, there have been no studies in the literature investigating the effect of DBS on each gender separately. Accordingly, the present study aimed to investigate the effect of DBS on QOL in PD patients and to examine the gender-based effects of DBS.

## Materials and Methods

The study included 24 patients with idiopathic PD who underwent DBS surgery for movement disorders caused by PD at Mustafa Kemal University Medical Faculty Neurosurgery Department between 2015 and 2017. Of these, 3 patients were excluded due to communication problems and 2 others due to psychiatric problems. As a result, 19 patients were eligible to be included in the study.

Inclusion criteria were idiopathic PD responsive to L-Dopa treatment, aged between 35–75 years, having received bilateral

Subthalamic Nucleus (STN) DBS surgery for at least two months to ensure stable stimulation parameters, and mentally normal patients that could understand and fill in the questionnaire.

Exclusion criteria were aged >75 years, presence of secondary Parkinsonism, abnormal brain MRI findings, severe dementia, and history of a serious disease. Patient characteristics, duration of disease, and the dominant hand of each patient were noted from the clinical records of the patients. An ethical approval was obtained from Mustafa Kemal University Ethics Committee and a written informed consent was received from each participant. The study protocol was performed in accordance with the Declaration of Helsinki.

The QOL of the patients was assessed using the RAND 36-Item Health Survey 1.0 (RAND-36). This survey was preferred since it is frequently used in clinical practice. This survey embodies eight subcategories including physical functioning, bodily pain, role limitations due to physical health problems, role limitations due to personal or emotional problems, emotional well-being, social functioning, energy/fatigue, and general health perceptions. A high score defines a more favorable health state and each item is scored on a 0-100 scale. The survey includes the same items as those in the SF-36 but the recommended scoring algorithm is different from that of the SF-36. Moreover, the RAND-36 survey is an exact replica of the SF-36, which is a valid and reliable scale commonly used in Turkey (8,9,10).

The symptoms of PD were evaluated using the Unified Parkinson's Disease Rating Scale (UPDRS), which was administered preoperatively when the medication was on (within one week prior to surgery) and postoperatively when the medication and stimulation were on (2 months after the surgery; range, 55-65 days). UPDRS is a golden standard reference scale which was developed to examine the typical PD symptoms. In addition, the UPDRS has been the most widely used scale to assess impairment and disability in PD, in which a higher score indicates a poor health status for the patient. The scale itself has four components: Part I, Mentation, Behavior and Mood; Part II, Activities of Daily Living; Part III, Motor; Part IV, Complications (11,12). Of these parts, we examined only Part III in our patients.

### Surgical Procedure

Firstly high-resolution T1 and T2 weighted Magnetic Resonance Images (MRI) was obtained within 1 week prior to the procedure using a 1.5 Tesla MRI scanner (Philips, Ingenia). On the day of the surgery, a stereotactic frame (Radionics® CRW™) was mounted under local anesthesia and then the patients were sent to the Computerized Tomography (CT) scan and the obtained CT images were fused with the previously obtained MRI by the aim of the preoperative stereotactic planning software (NeuroSight™ Arc). After identifying the anterior and posterior commissures, the dorsolateral part of the STN was targeted, which was confirmed by stereotactic atlases. Subsequently, the X, Y, and Z coordinates were calculated and then the surgical procedure was initiated.

The surgical procedure was conducted in two parts. In the first part, eight contact leads (Vercise™ Boston Scientific) were

implanted in both sides of the targeted area under local anesthesia. Before the placement, micro electro recording (NeuroNav™ Alpha-Omega) was performed using a maximum of three electrodes in each patient in order to select the best effective area. After the implantation of the eight contact leads, macrostimulation was performed to evaluate the effect of the stimulation and to exclude the adverse effects. Subsequently, after securing the leads and the wound closure, the second part of the procedure was proceeded. In this part, a neurostimulator (Vercise™ Boston Scientific) was placed in the subclavicular region under general anesthesia and was connected to the electrodes by the extension cables. The second part of the surgery was performed either immediately or within a maximum period of 1 week after the first part, depending on the clinical condition of the patients or the preference of the surgical team. After the second part of the procedure, a repeat CT scan was performed and the CT images were fused with preoperative MRI images using GUIDE™ DBS software in order to evaluate the exact position of the electrodes.

Stimulation was initiated at least two weeks after the procedure and thresholds were determined for any stimulation-induced side effects in all contacts. The final stimulation parameters were determined based on the results of the side effects and on the optimal antiparkinsonian effects. The adjustments of the stimulation and the medication were made depending on the long-term effects of the procedure.

#### Statistical Analysis

Statistical analyses were performed using IBM SPSS Statistics for Windows, Version 22.0. (Armonk, NY: IBM Corp.). Descriptive statistics were expressed as mean±standard deviation (SD) for continuous variables and as minimum-maximum for categorical variables. Normal distribution of the data was tested by using the Shapiro-Wilk test. Comparison of pre- and post-operative differences was achieved by using the Wilcoxon Signed Rank Test. A p value of <0.05 was considered significant.

## Results

The study included 19 patients with PD, comprising 12 (63.2%) men and 7 (36.8%) females with a mean age of 52.07±9.89 (range, 38-72) years. Mean duration of disease mean was 6.60±5.92 years. Postoperative UPDRS scores decreased compared to preoperative scores in all the patients (Table 1).

Table 2 presents the pre- and post-operative median scores for each subcategory in the RAND-36 survey. Although the postoperative scores increased compared to preoperative scores, no significant difference was found between the pre- and post-operative scores (Table 2).

On the other hand, a gender-based analysis on the RAND-36 scores indicated that there was a significant difference between the pre- and post-operative scores of the female patients for bodily pain (p=0.028) and between the pre- and post-operative scores of the male patients for emotional well-being (p=0.032). However, no significant difference was found between the pre- and post-operative scores of other subcategories in both genders (p>0.05) (Tables 3, 4).

## Discussion

This study aimed to evaluate the effect of DBS on QOL in PD patients. The results indicated that DBS has positive effects on QOL in both male and female patients.

In our study, preoperative UPDRS part III scores were lower in men (13.58) compared to female patients (23.71) and these scores decreased to 4.58 in men and to 9.86 points in women postoperatively. These findings indicated that the rate of motor recovery in women was greater than that of men, implicating that the probability of motor recovery is greater in patients that have a poor health status compared to patients that have a relatively better health status preoperatively.

The effect of DBS on QOL is associated with the motor scores of the patients. Accordingly, presence of postural instability, high body mass index, and worse baseline motor scores are key

**Table 1. Demographic characteristic of the patients**

Variable	
Mean age (year; X±SD)	52.07±9.89
Male (year; X±SD)	51.87±8.64
Female (year; X±SD)	48.40±8.44
Gender	12 Male / 7 Female
Duration of disease (year; X±SD)	6.60±5.92
Dominant hand	15 right / 4 left
Mean UPDRS score (mean±SD; pre-op/post-op)	17.31±12.18/11±10.33
UPDRS score - Female patients (mean±SD; pre-op [on medication]/post-op [on medication, on stimulation])	23.71±17.18/13.85±14.42
UPDRS score - Male patients (mean±SD; pre-op [on medication]/post-op [on medication, on stimulation])	13.58±6.38/9.0±6.34

Table 2. Pre- and post-operative median scores for the subcategories in the RAND-36 survey

Subcategories	Pre-op Median (min-max)	Post-op Median (min-max)	z	p
Physical functioning	35 (5-100)	60 (0-100)	-0.840	0.401
Bodily pain	58 (0-100)	65 (20-100)	-1.336	0.182
Role limitations due to physical health problems	0 (0-100)	25 (0-100)	-1.605	0.108
Role limitations due to personal or emotional problems	0 (0-100)	67 (0-100)	-1.582	0.114
Emotional well-being	68 (16-96)	68 (36-100)	-0.258	0.796
Social functioning	50 (13-100)	75 (13-100)	-1.536	0.125
Energy/fatigue	50 (5-90)	60 (10-100)	-1.856	0.063
General health perceptions	65 (10-90)	70 (10-95)	-1.312	0.190

Wilcoxon Signed Rank Test

Table 3. Pre- and post-operative RAND-36 scores for female patients

Subcategories	Pre-op Median (min-max)	Post-op Median (min-max)	z	p
Physical functioning	30 (5-60)	60 (0-95)	-1.577	0.115
Bodily pain	33 (0-80)	90 (23-100)	-2.201	0.028*
Role limitations due to physical health problems	0 (0-100)	25 (0-100)	-1.242	0.214
Role limitations due to personal or emotional problems	0 (0-25)	0 (0-100)	-1.089	0.276
Emotional well-being	68 (16-80)	76 (36-100)	-1.191	0.320
Social functioning	25 (13-38)	75 (13-88)	-1.897	0.058
Energy/fatigue	40 (15-80)	60 (10-100)	-1.581	0.114
General health perceptions	55 (10-80)	65 (10-90)	0.000	1.000

Wilcoxon Signed Rank Test, \*p<0.05

predictors of poorer functional and QOL outcomes after DBS (13). On the other hand, QOL is also related to functional independence (14). Floden et al. examined the disease, treatment, cognitive, and psychological factors associated with QOL before and after surgery by assessing the strength of these factors in the prediction of QOL outcomes. The study showed that 51% of their patients reported clinically significant improvements in QOL while 47%

reported stable QOL and 2% worsened (13,15). Appleman et al. reported that individuals with PD who experienced rigidity, gait and balance impairments at diagnosis reported a significantly worse QOL than individuals who experienced tremor as their initial symptom (16). Lyons et al. found that the significant improvements in QOL following DBS were strongly correlated with improvements in motor function, primarily with regards

Table 4. Pre- and post-operative RAND-36 scores for male patients

Subcategories	Pre-op Median (min-max)	Post-op Median (min-max)	z	p
Physical functioning	55 (10-100)	60 (0-100)	-.0338	0.735
Bodily pain	60.5 (10-100)	61.5 (20-100)	-0.356	0.416
Role limitations due to physical health problems	0 (0-100)	37.5 (0-100)	-0.813	0.416
Role limitations due to personal or emotional problems	0 (0-25)	67 (0-100)	-1.179	0.238
Emotional well-being	72 (48-96)	64 (48-88)	-1.201	0.032*
Social functioning	56.5 (13-100)	69 (13-100)	-0.315	0.735
Energy/fatigue	60 (5-90)	62.5 (15-100)	-1.120	0.263
General health perceptions	67.5 (15-90)	75 (30-95)	-1.722	0.238

Wilcoxon Signed Rank Test , \*p<0.05

to bradykinesia (17). In our study, the average UPDRS score for female patients decreased from 23.71 to 9.86 only in 2 months, which indicates a remarkable improvement in the QOL of female patients. In contrast, no remarkable improvement was observed in the QOL of male patients since they had a relatively lower decrease rate between the pre- and post-operative UPDRS scores and their preoperative scores were already high compared to those of female patients. This finding could be ascribed to the fact that the male patients had higher expectations from the DBS surgery and thus were less satisfied by the surgery compared to the female patients.

Tamas et al. examined the effect of STN stimulation on distal and proximal upper limb movements in PD patients and found that the STN stimulation improved the speed, amplitude and rhythm of upper limb movements. However, the assessments were performed within an average period of 2.1 years after the surgery (18). We consider that this period is long enough to notice the effect of DBS on motor recovery. Accordingly, since we performed the assessments at postoperative month 2, we consider that this time period is not enough for evaluating the actual outcomes of the surgery and thus the evaluation should be repeated at later stages throughout the follow-up period.

Chan et al. also conducted a study to evaluate the effects of STN-DBS in patients with PD at post-operative first and second years and found that the patients had satisfactory outcomes. Moreover, the results showed that the reduction in the UPDRS motor scores as well as the awake "off"-time and the daily levodopa dosage were the major predictors of overall improvement in the 39-item PD questionnaire (19). In our patients, postoperative assessment was performed at a relatively earlier period compared to the time periods reported in the literature. Therefore, we are planning to re-examine our patients in the first year to better evaluate the outcomes in our patients.

Jiang et al. conducted a meta-analysis that reviewed 39 studies published between 1993 and 2014. The analysis indicated that DBS led to significant improvement in QOL as well as motor symptoms in patients with PD after surgery. Moreover, a significant improvement was achieved in QOL following DBS compared to no improvement after medical therapy (20). Similarly, Chou et al. examined the effect of DBS in both motor and non-motor symptoms after bilateral STN-DBS for PD. The authors compared preoperative (baseline) and postoperative scores (approximately six months following the initial programming visit) in 20 patients and revealed that both motor and non-motor symptoms improved with bilateral STN stimulation 6 months after the stimulation (21). However, it is worth noting that these studies mainly focused on the motor and non-motor symptoms of PD and most of them ignored the QOL of the patients. We consider that QOL is an important indicator of physical and mental wellbeing and thus should be considered by the clinicians during the assessment of PD patients.

The main limitation of our study was that there was no control group and the sample size was relatively small. Therefore, further studies with larger patient series are needed to investigate of STN-DBS surgery on QOL. Secondly, postoperative assessment was performed at an early stage compared to the literature. Finally, Patients' socioeconomic status, stage of the disease and family's support could affect the results too.

Our results indicated that the STN-DBS surgery has a positive effect on the quality of life in PD patients.

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