



The effect of deep brain stimulation on motor functions and quality of life in the treatment of dystonia

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Abstract

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Aim: The present research aims to investigate the levels of depression and health-related quality of life (HRQoL) after surgical globus pallidus internus deep brain stimulation (Gpi-DBS) treatment in patients with generalized dystonia and segmental dystonia refractory to medical treatment.

Materials and Methods: Seventeen patients diagnosed with primary and secondary dystonia who were selected for GPi-DBS by the neurology, neurosurgery, and psychiatry council were included in the study. The patients were studied in two groups: primary dystonia and secondary dystonia. The Burke-Fahn-Marsden Dystonia Rating Scale (BFMDRS) was used to assess dystonia-related loss of function and disability, the Short Form 36 (SF-36) to assess HRQoL levels, and the Beck Depression Inventory (BDI) to assess depression levels in all patients before Gpi-DBS and 1 year after Gpi-DBS, retrospectively.

Results: In this study, significant improvement in BFMDRS scores and significant improvement in HRQoL levels were observed after 1 year of Gpi-DBS treatment in all dystonia types. Moreover, significant improvement was found in dystonia severity and disability levels, and HRQoL levels in the primary and secondary dystonia subgroups.

Conclusion: The study suggests that Gpi-DBS improves dystonia symptoms, and increases HRQoL levels in dystonia. In addition, this study is the first in Turkey to investigate the effect of Gpi-DBS on HRQoL levels in dystonia. However, we believe that further research with more participants is also needed in Turkey in this regard.



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Introduction

As a movement disorder, dystonia is identified by often repetitive, irregular movements, postures, or both, caused by sustained or intermittent muscle contractions [1].

A growing body of research focuses on the health-related quality of life (HRQoL) in dystonia, and the consensus is that individuals with dystonia tend to have lower HRQoL compared to their healthy counterparts [1].

The severity of low HRQoL due to dystonia depends on also non-motor symptoms such as anxiety, depression, sleep disturbances, and pain. Dystonia treatments aim to correct these non-motor symptoms and low HRQoL levels as well as to correct physical disability [2].

Deep brain stimulation (DBS) is a well-established surgical option for patients with dystonia who do not respond to medical treatments, such as botulinum toxin injections.

Research has revealed that deep brain stimulation is an

effective treatment in improving motor symptoms, particularly those linked to idiopathic and hereditary isolated dystonia. The globus pallidus internus (GPi) has been used more often than the thalamic targets and subthalamic nucleus in general and is still the most preferred target [3].

Previous research has indicated that deep brain stimulation of the Globus Pallidus interna improves HRQoL for those experiencing dystonia [4-6].

To date, there has been no research conducted in Turkey to evaluate the impact of surgical Gpi-DBS treatment on the HRQoL and levels of depression in patients with generalized and segmentary dystonia who have not responded to medical treatment. Therefore, the objective of this study is to assess the levels of depression and HRQoL in such patients after undergoing surgical Gpi-DBS treatment.

Materials and Methods

Approval of the research was granted by the local ethics committee (Memorial Bahçelievler Hospital Ethics Committee, Date: 05.01.2023, Decision Number: 71) and con-

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ducted by principles of the Helsinki Declaration 2013. Patients were informed and approved consent forms were obtained.

Participants

Patients who were admitted to Kocaeli Acibadem Hospital and Memorial Şişli Hospital neurosurgery clinic between June 2017 and March 2021 with the diagnoses of segmental dystonia (cervical dystonia, oromandibular dystonia, tardive dystonia) and generalized dystonia (cerebral palsy, PKAN), who were deemed candidates for surgical intervention by a council comprising psychiatrists, neurologists, and neurosurgeons, were retrospectively evaluated. Seventeen patients aged 18-50 years with dystonia resistant to medical treatment were included in the study.

Four out of twenty-one patients were excluded according to the exclusion criteria. Patients with a previous diagnosis of any psychiatric disease other than depression or with an active psychiatric disease receiving medical treatment, patients under 18 years of age, patients with impaired consciousness and cognitive impairment, and patients with speech problems were excluded from the study.

Data collection and research design

All participants admitted to the clinic for Gpi-DBS operation had their socio-demographic characteristics, such as gender, age, level of education, marital status, duration of dystonia disease, history of chronic systemic disease, and history of psychiatric illness recorded.

Patients were interviewed by the same clinician. To evaluate the dystonia-related loss of function and disability, the Burke-Fahn-Marsden Dystonia Rating Scale (BFMDRS) was utilized. To assess the levels of HRQoL, the Short

Table 1. Sociodemographic data, treatment status, and dystonia types of the patients.

Age	37.3 ± 8.7
Gender, n (%)	
Female	8 (47.1)
Male	9 (52.9)
Educational Status, n (%)	
Primary education	6 (35.3)
High School	8 (47.1)
University	3 (17.6)
Marital Status, n (%)	
Married	9 (52.9)
Single	8 (47.1)
Type Of Dystonia, n (%)	
Primary	11 (64.7)
Secondary	6 (35.3)
Treatment Status, n (%)	
Medical and Gpi-DBS	9 (52.9)
GPI-DBS only	8 (47.1)

Gpi-DBS: Globus Pallidus Internus- Deep Brain Stimulation.

Form 36 (SF-36) scale was used, while the Beck Depression Inventory (BDI) scale was used to assess depression levels. Additionally, the same scales were applied to the same patients one year after the operation to assess motor and non-motor components of treatment response. The patients were categorized into two groups based on the type of dystonia: primary dystonia and secondary dystonia. Furthermore, patients were also classified into two groups based on the treatment type they received: those who received Gpi-DBS treatment in conjunction with medical treatment (benzodiazepines, anticholinergics, and botulinum toxin) and those who received only surgical treatment.

Scales used

Burke-Fahn-Marsden dystonia rating scale (BFMDRS)

This scale is a universal biomarker that indicates the severity of dystonia. The scale consists of 2 subscales (the Burke-Fahn-Marsden Movement Scale [BFMMS] and the Burke-Fahn-Marsden Disability Scale [BFMDS], respectively).

The BFMMS assesses dystonia in nine different regions of the body with scores ranging from 0 (minimum) to 120 (maximum). The BFMDS assesses self-reported or parent-reported daily activities with scores in the range of 0 to 30 (completely dependent) [7].

Short Form 36 (SF-36)

The scale consists of 36 items that assess the health-related quality of life over the past year, categorized into eight subdomains: social functioning, physical functioning, role limitations due to emotional problems, role limitations due to physical problems, energy and vitality, bodily pain, mental health, and general health perception. Each QoL subscale is assessed separately and scored from 0 (worst) to 100 (best) [8,9].

Koçyiğit et al. conducted a validity and reliability study of the scale in Turkish [10].

Beck depression inventory (BDI)

The scale, which was developed by Beck et al., consists of 21 items. Each item is scored between 0 and 3. It is a scale with a minimum of 0 and a maximum of 60 points, and the severity of depression increases as the score increases [11]. A Turkish validity and reliability study has also been conducted for this scale [12].

Statistical analysis

Parametric quantitative values were presented as mean values and standard deviation, while nonparametric values were presented as median, minimum, and maximum values. Qualitative values were reported as numbers and percentages. The normality test was performed using the Shapiro-Wilk test. For the comparison of qualitative values, the Chi-square test was used. The Mann-Whitney U test and t-test were used for quantitative values depending on normality distribution. The significance level was set at $p < 0.05$. Statistical analysis was conducted using the SPSS software, version 22 (IBM Corp, Armonk, NY).

Table 2. Comparison of BDA, SF-36, BFMMS, and BFMDs scale scores of the patients before Gpi-DBS and 1 year after Gpi-DBS procedure.

Scales	Before Gpi-DBS	1 st Year After Gpi-DBS	p value
BDI S	32.4 ± 8.0	17.7 ± 6.6	<0.001*
F-36	54.1 ± 15.2	25.9 ± 8.3	<0.001*
BFMMS	39.5 ± 18.7	19.6 ± 12.3	<0.001*
BFMDs	12.9 ± 4.9	6.9 ± 2.6	<0.001*

P <0.05*: statistically significant.

Gpi-DBS: Globus Pallidus Internus- Deep Brain Stimulation; BDI: Beck Depression Inventory; SF-36: Short Form-36; BFMMS: Burke-Fahn-Marsden Movement Scale; BFMDs: Burke-Fahn-Marsden Disability Scale.

Table 3. Comparison of BDA, SF-36, BFMMS, and BFMDs scale scores between primary dystonia and secondary dystonia subgroups before Gpi-DBS and 1 year after Gpi-DBS procedure.

Scales	Primary Dystonia n=11			Secondary Dystonia n=6		
	Before Gpi-DBS	1 st Year After Gpi-DBS	p value	Before Gpi-DBS	1 st Year After Gpi-DBS	p value
BDI S	33.1 ± 10.2	18.5 ± 7.1	<0.001*	32.0 ± 7.1	17.3 ± 6.7	<0.001*
F-36	62.6 ± 9.2	30.1 ± 6.7	<0.001*	49.4 ± 16.1	23.5 ± 8.4	<0.001*
BFMMS	60.7 ± 11.4	32.3 ± 11.1	<0.001*	27.9 ± 8.9	12.6 ± 5.3	0.035*
BFMDs	15.7 ± 4.2	7.5 ± 2.6	<0.001*	11.4 ± 4.7	6.6 ± 2.6	0.041*

P <0.05*: statistically significant.

Gpi-DBS: Globus Pallidus Internus- Deep Brain Stimulation; BDI: Beck Depression Inventory; SF-36: Short Form-36; BFMMS: Burke-Fahn-Marsden Movement Scale; BFMDs: Burke-Fahn-Marsden Disability Scale.

Results

In addition to Gpi-DBS treatment, nine patients continued to receive medical treatment, and 8 patients were followed up with Gpi-DBS surgical treatment only. Table 1 presents the sociodemographic characteristics of 17 patients. Significant improvements were observed in the BFMMS, BFMDs, SF-36, and BDA scores of the patients in the first year after the procedure compared to their scores before the Gpi-DBS procedure ($p < 0.001$, $p < 0.001$, $p < 0.001$, $p < 0.001$, respectively) (Table 2).

Gpi-DBS procedure was performed in 11 patients with primary dystonia (9 patients with cervical and 2 patients with oromandibular dystonia), 6 patients with secondary dystonia (3 patients with cerebral palsy, 1 patient with Wilson's disease, 1 patient with PKAN, 1 patient with tardive dystonia). In the primary dystonia subgroup, improvements were statistically significant in the BFMMS, BFMDs, SF-36, and BDA scores of the patients in the 1st year after the procedure compared to their scores before the Gpi-DBS procedure ($p < 0.001$, $p < 0.001$, $p < 0.001$, $p < 0.001$, respectively) (Table 3). In the secondary dystonia subgroup, there were also statistically significant improvements in the BFMMS, BFMDs, SF-36, and BDA scores of the patients in the 1st year after the procedure compared to their scores before the Gpi-DBS procedure ($p < 0.001$, $p < 0.001$, $p = 0.035$, $p = 0.041$, respectively) (Table 3).

Discussion

A significant improvement in dystonia severity and disability levels, a significant decrease in depression levels of patients, and a significant improvement in HRQoL levels

were found 1 year after the Gpi-DBS treatment in all types of dystonia in this study. Moreover, significant improvement was found in dystonia severity and disability levels, and HRQoL levels in primary dystonia and secondary dystonia subgroups.

Dystonia significantly impairs HRQoL in patients due to movement limitation, pain, depression, anxiety, and disability [13]. Anticholinergics, benzodiazepines, and botulinum toxin applications have been used in its treatment for many years. However, in cases refractory to medical treatments, Gpi-DBS treatment, which has been applied in Turkey in recent years, significantly improves symptom severity in the treatment of dystonia [14]. The BFMDs scale is widely used to assess dystonia severity and disability. In many studies and meta-analyses, it has been reported that Gpi-DBS treatment improves BFMDs scale scores. Previous studies investigating the effectiveness of DBS in treating isolated dystonia have reported that an improvement of 25% or more in BFMDs scores is the threshold for improvement, 25% to 50% improvement is a partial response, and more than 50% improvement is a good response [13,15-19].

In primary dystonias, cervical dystonia, blepharospasm, oromandibulolingual dystonia, and writer's cramp are the most frequently observed types of dystonia in that order. Primary dystonias that start in childhood often begin in the legs and later generalize, whereas the adult form starts in craniocervical or segmental form and does not generalize. Secondary dystonias can occur due to many causes, and in some cases, the etiologic factor must be eliminated (drug-induced dystonia) or the cause must be treated, such as trauma, metabolic disorders, and other movement disorders [13].

However, it has been reported that Gpi-DBS treatment was more successful in primary dystonia than in secondary dystonia and showed better improvement in BFM-DRS scale scores [20].

In our study, BFM-DRS scale scores were found to be significantly lower in primary dystonia patients who underwent Gpi-DBS treatment compared to patients with secondary dystonia.

Meta-analysis studies in the literature indicate that Gpi-DBS has been shown to improve the severity and disability associated with dystonia and, as a result, indirectly enhance HRQoL [19,21].

A prospective multicenter study carried out in France evaluated the effects of Gpi-DBS on 22 patients with primary generalized dystonia, revealing a 51% reduction in BFM-DRS scale scores after 1 year and a 58% reduction after 3 years. Additionally, the study reported a significant improvement in patients' HRQoL after 1 year [3,22].

In a prospective multicenter study conducted in Spain, it was reported that after 1 year of Gpi-DBS, BFM-DRS scale scores decreased by 50% and HRQoL of the patients improved significantly in 24 dystonia patients. Moreover, 16 generalized and segmentary dystonia patients were observed 1 year after Gpi-DBS treatment, and HRQoL was reported to improve significantly [4].

After performing DBS operation on 10 dystonia patients in Greece, the patients were evaluated with the SF-36 scale, and a 32.42% improvement in physical components and 29.46% improvement in mental components was achieved. However, no satisfying improvement was observed in the depression and anxiety levels of the patients [24].

Our study had a limitation in terms of sample size as we included only a small number of patients. Secondly, the duration of the evaluation of the HRQoL level of the patients after surgery was short, and the early HRQoL level could not be evaluated. However, since the effects of Gpi-DBS treatment on dystonia symptoms take time to become apparent, an early assessment was not conducted.

Moreover, the average evaluation period of the HRQoL level in the studies conducted is 1 year.

Conclusion

As a result, we conclude that Gpi-DBS improves dystonia symptoms and improves HRQoL levels due to dystonia. Furthermore, this is the first study in Turkey to assess the impact of Gpi-DBS on the HRQoL levels of patients with dystonia. However, we believe that further research with more participants is also needed in Turkey in this regard.

Ethical approval

Ethical approval was obtained for the research from the Ethics Committee of Memorial Bahçelievler Hospital (Date: 05.01.2023, Decision No: 71).

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