Original Article

Subjective Assessments of Voice in Parkinson's Disease Subjects with and without STN-DBS Therapy

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Abstract

Introduction: The causal relation between STN-DBS and speech problems and the associated clinical features are in the incipient stages of being investigated. **Methods:** All the Parkinson's disease (PD) subjects with and without STN-DBS who applied to our movement disorders outpatient clinics between January 2022 and June 2022 and agreed to participate in the study were enrolled. The demographic data and clinical features were noted. Besides, the MDS-UPDRS was administered during the medication off-state in all subjects. All the participants completed the voice handicap index (VHI). Besides, the Freezing of Gait Questionnaire (FOGQ) and the quality of life (QoL) scales including the Parkinson's Disease Questionnaire (PDQ-39) and the Schwab and England Activities of Daily Living (ADL) scale were also administered to all the individuals. **Results:** We have included 66 patients with PD (F/M = 23/43). Thirty-five patients were those with DBS therapy whereas 31 patients were without. The results of the comparative analyses between the patients with and without DBS therapy revealed that the DBS group had a higher disease duration ($P = 0.006$) and FOGQ scores ($P = 0.008$). The VHI scores did not differ between groups ($P = 0.577$), and the correlation analyses did not reveal an association between the VHI scores and the duration of DBS therapy. However, the VHI scores correlated with the disease duration as well as the FOG scores. **Conclusion:** We did not find convincing evidence supporting the increased risk of speech disturbance with STN-DBS therapy. We suggest that the frequent existence of speech disturbance in this patient subgroup with STN-DBS is associated with the classical nature of PD.

Keywords: Parkinson's disease, speech, STN-DBS, voice handicap index

Introduction

Various randomized controlled trials on STN-DBS therapy have demonstrated that this procedure can improve the motor condition of patients substantially both in the short-term and in the long-term after surgery.[1-3] The STN-DBS therapy is particularly effective on the dopaminergic-responsive motor symptoms, including bradykinesia, rigidity, and severe medication "off" periods and marked reduction of dopaminergic medication can be achieved after the implant.[2-4] However, with the progression of Parkinson's disease (PD), particularly, the involvement of non-dopaminergic motor circuits leads to the appearance of axial motor features and of non-motor symptoms[5] which do not respond to DBS therapy. Such that the long-term follow-up studies of patients with DBS revealed that functionality and QoL indexes of patients worsen over time albeit sustained motor benefit of the stimulation[2,4] which is explained by the progression of PD and particularly the emerging stimulation-resistant symptoms in the following course of the disease. Among these treatment-resistant symptoms, speech problem is an intriguing one that can be commonly seen in all stages of the disease and associated with significant challenges in social interactions that may lead to functional problems, social isolation, and reduced QoL.[6] Remarkably, speech disturbance is one of the axial symptoms in PD, and strong correlations are reported between speech disturbance and axial motor symptoms, particularly FOG.[7] Similar to the other axial symptoms, the response of speech disturbance to DBS therapy is unclear. Several studies using distinct methods investigated the association between the DBS therapy and speech problems in PD patients. In a large cohort, Wertheimer *et al*.[6] demonstrated that speech problems in patients under STN-DBS therapy are more common and severe in comparison to those without DBS. Some other authors published their prospective study results, including a smaller number of patients which revealed inconsistent results, including both deteriorations (phonatory control, syllable repetition capacity, perceptual ratings)[3,8,9] and improvement in the speech indexes (that varied between the studies[10,11] following STN-DBS. Furthermore, considering that speech disturbances are more common in the advanced stage of PD, and patients undergoing STN-DBS surgery are those in the advanced stage of disease, excluding several confounding factors is strictly critical while interpreting the results of these

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studies reliably.[3,6,12] Besides, the causal relation between STN-DBS and speech problems and the clinical features associated with speech problems constitute topics which are in the incipient stages of being investigated.

In this context, we planned not only to investigate the association between STN-DBS therapy and speech problems but also to evaluate various other clinical parameters in the analyses. Voice handicap index (VHI) is a validated method to measure the subjective impact of voice disorders on patients' QoL,[13] and it is acknowledged to correlate with objective acoustic voice parameters.[14] The utility of VHI for the clinical management of PD subjects and also for academic purposes has been shown by several authors.[15] Taken together, we investigated the link between speech problems and DBS using this subjective method of VHI. First, we aimed to compare the speech disturbance indexes in our PD patients with and without DBS. We sought to evaluate the possible impact of DBS on speech performance through multiple analyses. Finally, in addition to DBS therapy, we aimed to examine the associations between speech performance and several clinical features.

Materials and Methods

All the PD subjects with and without STN-DBS who applied to our movement disorders outpatient clinics at Diskapi Yildirim Beyazit Training and Research Hospital between January 2022 and June 2022 and accepted to participate in the study were enrolled. In addition to the demographic data, the clinical features, including the disease year, symptom onset side, and disease subtypes were noted. Besides, to evaluate the disease severity, the Movement Disorder Society-sponsored revision of the Unified Parkinson›s Disease Rating Scale (MDS-UPDRS) was performed during the medication off-state in all subjects. In patients with STN-DBS, the evaluations were performed during the medication "off"-stimulation-on period. All four subscale scores of MDS-UPDRS were calculated. All the participants completed the VHI which is the standardized and validated measure designed to assess the psychosocial consequences of a voice disorder.[13] The total score and the sub-scores of the functional, physical, and emotional domains of VHI for all individuals were calculated. The Freezing of Gait Questionnaire (FOGQ)[16] was used to evaluate freezing of gait (FOG) which is also another axial component of PD. The Parkinson's Disease Questionnaire (PDQ-39)[17] was administered to all participants to assess the PD-specific health-related QoL. Finally, the Schwab and England Activities of Daily Living (ADL)[18] scale was also performed to assess the patient's ability to function in activities of daily living. The informed consent form has been obtained from every participant. The ethics committee approval for the study has been obtained from the clinical research ethics committee unit of Diskapi Yildirim Beyazit Training and Research Hospital.

Statistical Analyses

Univariate descriptive analyses were used for reporting sample-level demographic and clinical characteristics, including the clinical scales. The independent samples' two-tailed *t*-test for normal distribution data or Mann–Whitney U-test for non-normal data were used to compare the demographic data, clinical features, and clinical scales between the subgroups of patients (with and without DBS). The correlation analyses were performed to investigate the association between the VHI scores and clinical parameters (Pearson's for parametric distributions and Spearman's for nonparametric distributions). The correlation analyses between other clinical parameters were also performed. Finally, partial correlation analyses were performed to exclude the effect of disease duration which was found to differ between groups. The statistical analyses were performed using IBM SPSS, version 26.

Results

We have included 66 patients with PD (F/M = 23/43). Thirty-five patients were those with DBS therapy whereas 31 patients were without. Side of symptom onset was left in 35 patients whereas 31 patients were those with right-side symptom onset [Table 1]. The results of the comparative analysis between the patients with and without DBS are listed in Table 2. These comparisons revealed that there was no difference in the age, gender, symptom onset-side, and MDS-UPDRS scores between groups. However, the DBS group had a higher disease duration (12.9 ± 5.5y, 8.8 ± 5.9y; $P = 0.006$) and FOGQ scores (12 (20), 5 (21); $P = 0.008$). The rate of patients with voice handicaps (VHI score >11) was higher in the DBS group; however, it did not reach the significance level [17 patients with DBS (49%), 12 patients without DBS (39%), $P = 0.289$]. Besides, the VHI scores did not differ between groups ($P = 0.577$) and the correlation analyses did not reveal an association between the VHI scores and DBS year [Table 3]. The physical and emotional domains of VHI differed between groups [Table 2]; however, the results of the correlation analyses between the DBS year and these sub-scores were nonsignificant. On the other hand, the VHI scores correlated with the disease duration, FOG scores, MDS-UPDRS-1 scores, and QoL scores [Tables 4 and 5]. Of note, there were positive correlations between the disease year and the sub-scores of all the VHI domains (functional, CC: 0.292, $P = 0.017$; physical, CC: 0.291, $P = 0.018$; emotional, CC: 0.316, $P = 0.010$). The partial correlation analyses after controlling the effect of disease year also showed that VHI scores correlated significantly with the PDQ-30 scores and

Table 1: The demographic features and clinical characteristics of the overall patients (*n*=66)

Demographic and clinical features	
Age, mean ±SD	61.4±8.9
Gender, F/M	23/43
Tremor-dominant/AR	39/27
Lateralization, Right-symptom onset/Left-symptom onset	31/35
Duration of PD in years, mean ±SD	11.0±0.6.0
Average duration since DBS, median (R)	4 (10)

Table 2: The results of the comparative analyses between patients with and without DBS therapy

	Patients with DBS (*n*=35)	Patients without DBS (*n*=31)	*P*
Age	59.8±8.6	63.2±9.1	0.120
Gender, F/M	11/24	12/19	0.359
Tremor-dominant/AR	17/18	22/9	0.055
Right-symptom onset/Left-symptom onset	18/17	13/18	0.300
Duration of PD in years	12.9±5.5	8.8±5.9	0.006
Average duration since DBS, median (R)	4 (10)		
PDQ-39	46.1±29.3	45.3±23.9	0.903
Schwab-England ADL			
Independent (70%–100%)	25	24	0.394
Dependent (0%–60%)	10	7	
VHI			
Voice handicap-present	17 (49%)	12 (39%)	0.289
Absent	18	19	
FOGQ score	12 (20)	5 (21)	0.008
VHI-total score	10 (32)	4 (30)	0.577
VHI-functional	3 (11)	1 (10)	0.071
VHI-physical	4 (11)	1 (10)	0.039*
VHI-emotional	3 (12)	2 (10)	0.05*
Schwab-England ADL, median (R)	80 (80)	80 (60)	0.817
MDS-UPDRS-1, median (R)	14 (31)	14 (29)	0.884
MDS-UPDRS-2	16 (11)	16 (11)	0.817
MDS-UPDRS-3	22 (15)	32 (54)	0.139
MDS-UPDRS-4	4 (14)	5 (11)	1.000
MDS-UPDRS-Total	57 (114)	75 (116)	0.087

DBS=Deep brain stimulation, PDQ-39=The Parkinson's Disease Questionnaire, VHI=Voice handicap index, FOGQ=Freezing of Gait Questionnaire, ADL=Activities of Daily Living, MDS-UPDRS=The Movement Disorder Society-Sponsored Revision of the Unified Parkinson's Disease Rating Scale

Table 3: The correlation analyses revealed that the disease year was correlated with freezing of gait (FOG) score and VHI scores. However, no correlation between the DBS year and VHI was found, whereas the FOGQ score and Schwab and England ADL scale correlated with the DBS year

	VHI	FOGQ	Schwab and England ADL scale
Duration of PD in years (*n*=66)			
Correlation Coefficient	,279*	,415	-,395
Sig. (2-tailed)	,023*	,001*	,001*
N	66	66	66
Average duration since DBS, y (*n*=35)			
Correlation Coefficient	,306	,043*	-,180
Sig. (2-tailed)	,074	,807	,300
N	35	35	35

Voice handicap index, FOGQ=Freezing of Gait Questionnaire, ADL=Activities of Daily Living

MDS-UPDRS1-2 scores [Table 6]. Of note, the analyses after controlling the effect of the FOGQ score also did not reveal a correlation.

Discussion

In this study, we did not find a difference in the VHI total scores between the patients with and without DBS. The correlation analyses also did not reveal a link between VHI and the duration of DBS therapy. Besides, considering that there were differences in the disease duration and FOG scores between the groups, the partial correlations after controlling the effects of disease year and FOG scores were also performed which did not reveal a correlation between the VHI and DBS year. Taken together, our conclusions did not suggest an impact of chronic DBS therapy on voice problems that we measured with VHI. On the other hand, higher VHI scores were found to be associated with a longer duration of the disease and higher FOG scores. However, no correlation was found between the VHI and MDS-UPDRS scores (evaluated during the stimulation-on period). In this regard, our results suggest that speech problems may rather be associated with the natural course of PD and this problem may be correlated with axial symptoms such as FOG which is more commonly seen in the advanced phase of the disease and does not respond significantly to therapy (including DBS). Considering that we have evaluated the possible associations between the speech problems and multiple clinical parameters that we evaluated by comprehensive assessments, our results provide substantial perspectives.

The effect of STN-DBS on speech performance is controversial in the literature. Some studies have found that STN-DBS provides benefits in speech-related subsystems, improving "motor systems" involved in speech production, helping individuals increase the motor force needed to produce speech and increase acoustic components of speech.[19,20] However,

Table 4: The VHI was also correlated with the scores of QoL indexes

	Schwab England ADL	PDQ-39	UPDRS-1	UPDRS-2	UPDRS-3	UPDRS-4	UPDRS-Total
VHI							
CC	-,563	,592	,321	,171	,039	,107	,158
Sig.	,000*	,000*	,009	,169	,756	,390	,204

PDQ-39=The Parkinson's Disease Questionnaire, VHI=Voice handicap index, ADL=Activities of Daily Living, MDS-UPDRS=The Movement Disorder Society-Sponsored Revision of the Unified Parkinson's Disease Rating Scale

Table 5: The correlation analyses between FOGQ scores and VHI, QoL indexes scores

	Average duration since DBS	VHI	Schwab England ADL scale	PDQ-39
FOGQ				
Correlation Coefficient	,043	,526	-,621	,555
Sig. (2-tailed)	,807	,000*	,000*	,000*
N	35	66	66	65

FOGQ=Freezing of Gait Questionnaire, PDQ-39=The Parkinson's Disease Questionnaire, VHI=Voice handicap index, ADL=Activities of Daily Living

Table 6: The results of the partial correlation analyses after controlling for the disease year did not reveal a correlation between the VHI and DBS year (CC=0.146, *P*=0.410), however, there were positive correlations with the QOL index scores

Control variable	PDQ-39	MDS-UPDRS_1	MDS-UPDRS_2
Duration of PD in years			
VHI			
CC	,605	,394	,459
Sig.	,000*	,021*	,006*
	32	32	32

PDQ-39=The Parkinson's Disease Questionnaire, MDS-UPDRS=The Movement Disorder Society-Sponsored Revision of the Unified Parkinson's Disease Rating Scale

a large number of studies have found no improvement in speech performance following STN-DBS.[10] Wertheimer *et al*.[6] conducted cross-sectional research in a large cohort, including 758 individuals (287 subjects with DBS and 471 subjects without DBS), and they focused on the differential speech profiles between PD subjects with and without DBS from the patient's perspective. In conclusion, they found that patients with DBS reported more severe symptoms related to speech disturbance as well as more significant symptom interference with social interaction and with daily experiences encountered relating to functional, physical, and emotional issues of a voice disorder.[6] The authors also noted that the difference between groups persisted independent of age and disease duration.[6] However, no additional clinical features or scales were evaluated in this study to investigate the other associations and possible other clinical confounder factors.[6] In a prospective follow-up study, Krack *et al*. examined the long-term outcome of bilateral DBS-STN in 49 PD patients and found that speech functioning had declined in these patients five years after the initiation of DBS therapy. Besides, they found worsening of akinesia, postural stability, FOG, and cognitive function between the first and the fifth year of DBS which they interpreted as compatible with the natural history of PD.[3] In the other study, including long-term follow-up of 26 patients undergoing bilateral STN-DBS, the general motor symptoms were found to improve significantly still at follow-up 11 years after.[2] However, the speech had slightly worsened as well as no change in the axial symptoms and postural instability was found.[2] Fasano *et al*.[4] reported similar results on 20 consecutive patients who had received continuous stimulation for eight years. The overall motor improvement reported at five years was 55.5% (at UPDRS-III) which was partly retained three years later (39%, $P < 0.001$, compared with baseline; -16.5%, $P < 0.01$, compared with five years). However, they found that speech performance had not improved, and postural stability had worsened within this period ($P < 0.05$). In accordance with these results, we also found an association between FOG and VHI both of which reflect axial symptoms. The axial symptoms and non-motor symptoms involve in the later phase of the disease and respond poorly to levodopa and DBS therapy.[4] Such that the long-term follow-up studies of patients with DBS revealed that functionality and QoL indexes of patients worsen over time albeit sustained motor benefit of the stimulation[2,4] which is explained by the progression of this medication- and stimulation-resistant symptoms due to the progression of PD. To support these conclusions, although we did not find correlations between the VHI and disease severity (evaluated with MDS-UPDRS), both VHI and FOGQ scores correlated consistently with the QoL indexes. Besides, the correlation between the VHI and the QoL indexes persisted after excluding the effect of disease year making the association, we found, more valuable.

In conclusion, we did not find reliable evidence supporting the increased risk of speech disturbance with STN-DBS therapy. In light of the literature data, our results may rather suggest that the frequent existence of speech disturbance is associated with the classical nature of PD where we expect the occurrence of therapy-resistant axial symptoms, including speech disturbance in the advancing phase of the disease. Besides, based on the

results of the correlation between the VHI and QoL indexes, we remark on the clinical significance of speech disturbance in patients with STN-DBS. Finally, future prospective studies also evaluating the dynamic alterations of the speech parameters with stimulation adjustments in patients with chronic DBS therapy may provide substantial contributions.

Compliance with ethical standards

The ethical approval has been obtained from the local committee of the Diskapi Yildirim Beyazit Training and Research Hospital.

Authors' contributions

Concept – H.O.; Design – H.O.; Supervision – S.C.; Materials – H.O, Z.T.B., S.C.; Data Collection and/or Processing – H.O., Z.T.B.; Analysis and/or Interpretation – HO., Z.T.B., S.C.; Literature Search – H.O; Writing Manuscript – H.O., S.C. Critical Review – S.C.

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Conflicts of interest

There are no conflicts of interest.

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