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Short-Term Outcomes of Deep Brain Stimulation of the Subthalamic Nucleus in Patients with Parkinson's Disease - Pilot Study

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Abstract

Background: Deep brain stimulation (DBS) of the subthalamic nucleus (STN) provides efficient treatment for the alleviation of motor signs in patients with Parkinson's disease (PD), but more studies about gait and functionality are needed. We aimed to understand whether short-term DBS treatment will can relieve the symptoms of PD patients, specifically we examined its effect on motor-cognitive-complication parameters, fine motor skills and daily living activity (DLA) of these patients.

Method: Ten patients from Mustafa Kemal University Neurosurgery Department were recruited. The assessments were made twice, first time preoperatively, which was within one week prior to the surgery, second time postoperatively, which was 55-65 days post treatment. The motor scores, DLA scores, mental scores and complication scores were measured with Unified Parkinson's Disease Rating Scale (UPDRS), fine motor skills measured with The nine-hole peg test (9-HPT), balance measured with Berg Balance Scale (BBS) and falling risk measured with Timed Up and Go Test (TUG).

Results: 10 patients (5 female, 5 male) aged between 40-60 (mean=49.44±6.69 years) were included in the study. Duration of the disease's mean was 5.60 years. We found significant difference between pre-op and post-op results in UPDRS DLA, UPDRS motor, UPDRS complication, UPDRS total score and TUG tests (Table 2).

There was no significant difference between preop-postop assessment in UPDRS mental, BBS and 9-HPT results ($p>0.05$).

Discussion: Balance, walk and fine motor impairment occurs almost always in Parkinson's disease and resulting in difficulties with daily living activities. We found that DBS has positive effect on PD complications, balance and walking abilities. PD patients that have falling risk and multiple motor symptoms may have benefit from DBS.

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Introduction

Technological developments increase the effectiveness of the surgeries in Parkinson's disease (PD) treatment [1]. Deep brain stimulation (DBS) is a highly efficient treatment approach for movement disorders as PD [2]. Subthalamic nucleus (STN) has been a primer area of DBS for PD patients and influence of this region causes decreasing in motor bradykinesia and fluctuations, in tremor and a decline in dopaminergic drug requirements and dyskinesia [2,3]. Despite technological advances, there are different opinions about the motor and non-motor results of DBS. This situation causes problems about appropriate patient selection for surgery and becomes a paradox because of its possible complications [4].

STN DBS procedures affect balance, postural stability, gait, daily living activities and functionality. Previous studies have found conflicting results about them. Some of them reports positive results of functional balance tests, including TUG. But there is discrepancy regarding the effects of STN-DBS on other balance measures including BBS Scores conversely, surgery may worsen postural stability, degrade gait and increased fall risk [5,6,7,8,9].

Though there are some researches about effect of DBS on walking and balance abilities, fine motor skills have been ignored. It is unclear how STN-DBS affects fine motor skill in PD. Further, little is known about STN-DBS and medication effects on more complex fine motor skill, and functional balance, despite the fact that complex and fine motor skill tasks are encountered daily [9,10]. Also for short term studies, lesion effect is not discussed very much. We used the BBS, which is a functional and performance-based assessment of balance than UPDRS [6].

DBS of the STN provides efficient treatment for the alleviation of motor signs in patients with PD, but more studies about gait and functionality are needed. We aimed to understand whether short-term DSB treatment will can relieve the symptoms of PD patients, specifically we examined its effect on motor-cognitive-complication parameters, fine motor skills and DLA of these patients.

Material-Methods

Study Group

Ten patients (5 male, 5 female) from Mustafa Kemal University Neurosurgery Department were recruited. The assessments were made twice, first time preoperatively, which was within one week prior to the surgery, second time postoperatively, which was 55-65 days post treatment. Our inclusion criteria were: (1) clinically diagnosed PD with STN targeted, (2) neither dementia nor major ongoing psychiatric illness and nor other neurological disorder, (3) no surgical contraindications. Ten subjects (age range: 40 to 60 years, mean=49.44±6.69 years) were evaluated preoperatively and second months after surgery. The ethics committee of Mustafa Kemal University in Turkey approved our study, and all patients gave their written informed consent.

Surgery Procedure

STN-DBS procedures were performed by one expert surgeon in 2 stages: (1) insertion of bilateral electrodes under local anesthesia using microelectrode recording and macrostimulation, and (2) connection of the pulse generators with electrodes and subcutaneous placement to the pectoral region under general anesthesia, the second stage performed approximately five or seven days after the lead placement. The microelectrode recordings were used to define the most effective STN part and the macrostimulation was made to evaluate the possible side effects. The surgery technique was explained and detailed in other studies [11]. Electrodes were (Medtronic 37601 Activa PC or Boston Scientific DB-110-C Vercise) bilaterally implanted in all patients. After the surgery all patients underwent to CT for determine of the surgical complications and electrode placements.

Clinical Assessment

Patients were assessed preoperatively (within one week prior to surgery), and 2 months postoperatively (range: 55–65 days). A neurologist planned the medication after the DBS surgery and patients were on medication during that 2 months follow up. When patients had taken no medication for 8 to 12 h (off medication), unblinded assessments were performed both clinical performance tests had evaluated by an experienced physical therapist in all tests situations. Assessments were performed when patients had taken their medication (ON), in second assessment the stimulation was ON.

Unified Parkinson's Disease Rating Scale

Patients were clinically assessed with UPDRS. Different scores were extracted from this scale: the non-motor experiences of daily living score (items 1 and 4 of the UPDRS I), the motor experiences of daily living score (items 5 and 17 of the UPDRS II), the motor examination score (items 18-31 of the UPDRS III, including gait and postural stability parameters), and the motor complications score (items 32–35 of the UPDRS IV). The total UPDRS score was between 0 and 108; maximal worst value = 108 [12].

Nine-Hole Peg Test

9-HPT is used in clinical settings to assess dominant hand dexterity. Participants were asked to take 9 pegs from a container placing them into 9 holes on a board and vice versa as quickly as possible. Scoring was the average time taken to complete the test for four trials [13].

Berg Balance Scale

The Berg Balance Scale was used to test balance performance. Test includes 14 items common in everyday life and all items are graded on a 5-point ordinal scale from 0 to 4 and with the maximum total score is 56 points, and a higher score reflects better performance. [14].

The timed up and go Test

The subject sits in an armchair (seat height of 46 cm) with arms resting on the chair's arms and the back against the chair. With the instruction 'Go' initiates the subject walks 3 m away and turns back for sit again. Time period is measured between 'Go' and when the subject's back leaves the back of the chair and stops when the buttocks reach the seat of the chair. Average time used to complete the TUG test is reported [15].

Statistical Analysis

Statistical analysis were performed with using the Statistical Package for the Social Sciences (SPSS version 20.0). The Shapiro Wilk test was used to test normality of distribution and all data were non-parametric. The Wilcoxon Signed Rank Test was applied to compare the mean scores of two assessments (preoperative, postoperative 60th day). A level of $p < 0.05$ was considered significant.

Results

Patients' demographic characteristics are shown in Table 1.

We found significant difference between pre-op and post-op results in UPDRS DLA, UPDRS motor, UPDRS complication, UPDRS total score and TUG tests Table 2.

There was no significant difference between preop-postop assessment in UPDRS mental, BBS and 9-HPT results ($p>0.05$).

Discussion

The present study aimed to understand whether DBS is effective in motor-cognitive-complication parameters, fine motor skills, balance and DLA of PD patients. We found that DBS has positive effects on motor, complication, daily living activities and falling risk of PD patients while has no significant effect on static balance and fine motor skills.

TUG test is used to determine fall risk and measure the progress of balance, sit to stand, and walking. We found that DBS has positive effect on PD complications, balance and walking abilities. PD patients that have falling risk and multiple motor symptoms may have benefit from DBS.

Both of BBS and TUG measure the falling risk in patients. We found significant difference only in TUG test. TUG test examines dynamic balance while the BBS examine both dynamic and static balance. We think DBS affect mostly dynamic balance than static balance so we could find significant difference only in TUG test.

In the present study, we used pulses of 90 µs duration and 2-4 V amplitude, delivered in the STN at 130 Hz frequency, which it refer to the most appropriate settings for the patients.

In the post-operative assessment, we found that DBS STN showed significant improvements in all Parkinsonian motor sign as expected in the literature. There are other studies that found positive results of STN-DBS on motor signs and total UPDRS score [9,16,17,18].

Non-significant and significant improvements in TUG and UPDRS DLA (which relates to severity of

Table 1. Demographic characteristic of Patients with PD.

Variable	**PD (n=10)**
Age (year), $\bar{X}$±SD	49.44±6.69
Sex	5 male/5 female
Duration of the disease (year) $\bar{X}$±SD	5.60±4.70
Dominant hand	8 right/2 left

Table 2. Pre-op, post-op results of UPDRS mental, UPDRS DLA, UPDRS motor, UPDRS complication, UPDRS total score, BBS, TUG and 9-HPT.

	Pre-op		**Post-op**			
	X ± SD	**Min-max**	**X ± SD**	**Min-max**	**z**	**p**
UPDRS Mental	2.10±2.46	0-8	1.40±1.57	0-4	-0.997	0.319
UPDRS DLA	14.70±9.73	5-34	5.60±3.68	0-13	-2.091	0.037
UPDRS Motor	17.40±13.16	3-47	6.30±4	0-13	-2.191	0.028
UPDRS Complication	7.5±5.94	0-17	1.6±2.27	0-6	-2.689	0.007
UPDRS Total Score	39.70±24.88	8-92	14.50±9.24	0-30	-2.191	0.028
BBS	46.30±16.10	3-56	53.20±2.97	47-56	-1.612	0.107
TUG	18.80±23.15	6-84	14.96±20.11	6-72	2.524	0.012
9-HPT	31.10±10.59	20-50.36	28.55±7.32	20-45.30	-1.067	0.286

Wilcoxon Signed Ranks Test

disease and fear of falling [5,6,19,20,21,22,23] have been reported. In the present study, TUG improved significantly (p=0,012) because of gained motor ability after surgery.

Fine motor and articulation impairment occurs almost always in Parkinson's disease and resulting in difficulty with daily living activities, such as griping different objects and speech disturbances [24,25]. STN DBS, had positive results on performance of the 9-HPT but it was not statistically significant (p=0.286). Altug et al. found that the Purdeu Pegboard test score and hand writing test score significantly improved after postoperative six months [21]. We think Purdue Pegboard Test is a more complicated and detailed test than 9-HPT and it examines the results better. That is why we did not find significant effect of DBS on fine motor skills.

The most common adverse effects of DBS are related with mood and behaviours but they seem very rarely especially when there isn't any target problem, and generally conceived to have a little impact on the quality of life.

Limitations of this study is that we did not follow long term outcomes of our parameters and we gave a preliminary result in this study and we do not have a control group. A weakness of this study includes the small number of subjects, the nonobjective outcome measures, and the nonrandomized order of the conditions and take the early stage could be matched with the PD control group with the DBS group. The fact that medication dose had not considered in the study.

However, the similar dose did allow the DBS effects to be better controlled in this study.

STN-DBS has positive effects on many parameters of PD patients. So, in the clinic it may be offered to the PD patients that have multiple motor problems. Also, patients that have dynamic balance problems have benefit more than patients that have static balance problems.

Conflict of Interest

Dr Yilmaz has disclosure with Medtronic and Boston Scientific in terms of proctorship.

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