Subthalamic Deep Brain Stimulation in Patients with a Previous Pallidotomy

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Abstract

OBJECTIVE: To evaluate the safety and efficacy of subthalamic nucleus deep brain stimulation (STN DBS) in PD patients who previously had a unilateral pallidotomy. **BACKGROUND:** STN DBS has gradually replaced ablation of the globus pallidus internus (pallidotomy) as a surgical treatment of choice in patients with PD and troublesome levodopa-induced motor complications. **METHODS:** We identified 10 patients, 9 male, at the Baylor College of Medicine Parkinson's Disease Center who underwent STN DBS after prior unilateral pallidotomy. Demographics, efficacy as determined by "off" UPDRS part II scores, and adverse events (AE) were analyzed. We then compared these to an age and sex matched group of 25 DBS patients that had no prior pallidotomy. **RESULTS:** The age at the time of pallidotomy was 53.3±11.2 years. After their initial pallidotomy, the mean UPDRS motor "off" medicine scores improved from 51.3±14.3 to 34.9±12.8, and the UPDRS dyskinesia score improved from 1.8±1.0 to 0.8±0.7. Age at the time of their STN DBS was 56.0±10.2 years [range: 41-73 years]. Their pre-DBS "off" UPDRS motor scores improved by 16.6% from 53.1±9.7 [range: 42-68] to 44.5±12.6 [range: 25-67]. In contrast, the UPDRS "off" motor scores in a control group of 25 DBS patients improved by 40.2%, from 49.7±11.1 to 29.7±13.8. The DBS improvement (16.6%) in the post-pallidotomy group was significantly less robust than that (40.2%) in the control group ($p<0.005$). The UPDRS dyskinesia score improved was similar in both groups. AE thought to be related to the STN DBS following pallidotomy included worse dysarthria (3) and worse balance (2). **CONCLUSIONS:** STN DBS patients with prior pallidotomy had less improvement in "off" motor UPDRS score compared to other STN DBS patients, despite relatively good outcomes immediately after their pallidotomy. This may be partially due to a selection bias with the post-pallidotomy group representing more severe symptoms or atypical features, but it may also indicate that prior pallidotomy is a negative predictor of outcome of STN DBS and should be considered in patient selection.

Introduction

Deep brain stimulation (DBS) of the subthalamic nucleus (STN), and other targets is increasingly employed in Parkinson's disease (PD) and other movement disorders. Ablation of the globus pallidus internus (pallidotomy) has been used extensively in the past, and continues to be used, especially when cost or logistics prohibit the use of DBS. Although pallidotomy usually improved motor features of PD and levodopa-related complications (1), many patients progressed and later required STN DBS. There is paucity of data on efficacy and safety outcomes of STN DBS following pallidotomy.

Methods

Patients were included if they underwent both their pallidotomy and STN DBS at the Baylor College of Medicine. Inclusion criteria for either surgery usually consisted of levodopa-responsive PD in which levodopa-related motor complications could not be adequately controlled with medications. The surgical methodologies used in our center were previously described (2, 3) We performed motor Unified Parkinson's Disease Rating Scale (UPDRS) scores as part of the complete assessment before and at 3 months after pallidotomy, and again before and after STN DBS while both "on" and "off" medications. We used the latest post-operative DBS examination where patients underwent examinations both "on" and "off" of their medications. Only "off" motor scores (UPDRS #18-31) and dyskinesia duration scores (UPDRS #32) are reported here. We then compared the change in UPDRS motor scores following STN DBS to a control group of 25 age, sex, and target matched STN DBS patients who did not have a prior pallidotomy.

Table 1: Summary of Pallidotomy and STN DBS Results in Off Motor Scores

	Initial Pallidotomy				Subsequent STN DBS			
Sex	Age	Location	Pre-Op	Post-Op	Age	Location	Pre-Op	Post-Op
M	41	L	73	30	48	B	58	43
M	51	L	70	46	58	B	56	56
F	70	L	43	27	73	B	46	50
M	37	R	62	31	41	B	68	48
M	55	R	34	36	56	B	49	33
M	59	L	43	25	66	B	43	36
M	66	L	56	61	67	B	61	52
M	42	L	41	23	46	L	65	67
M	49	L	44	41	53	B	43	39
M	48	R	ND	ND	52	B	42	31
	53.3		51.3	34.9	57.7		53.1	45.5

Results

Ten patients are included in this study; 3 additional patients had either their pallidotomy or STN DBS done elsewhere and were, therefore, excluded. Also, we excluded one patient with bilateral pallidotomies followed by bilateral STN DBS.

The mean age of the 10 patients at the time of pallidotomy was 51.8±10.8 years. After the initial pallidotomy, their mean UPDRS motor off scores improved from 51.3±14.3 to 34.9±12.8 (n=9), and the UPDRS dyskinesia score improved from 1.8±1.0 to 0.8±0.7 [Table 1].

The mean age at the time of the final STN DBS implantation (9 bilateral and one ipsilateral to their pallidotomy) was 56.0±10.2 years [range: 41-73 years]. In five patients, both hemispheres were operated on simultaneously and in four they were staged. The mean pre-DBS "off" UPDRS motor score was 53.1±9.7, [range: 42-68]. The "off" UPDRS motor scores determined 15.7±11.1 months [range 5-42 months] after DBS implantation improved only by 16.6% to 44.5±12.6 [range: 33-67]. Only 2/10 (20%) of subjects had at least a 33% improvement in their motor "off" examination. The dyskinesia scores improved from 1.7±1.5 to 0.4±0.5.

The mean UPDRS "off" scores in the control group of 25 DBS patients improved 40.2%, from 49.7±11.1 to 29.7±13.8, with 16/25 (64%) demonstrating a greater than 33% improvement [Table 2]. The 40.2% improvement with STN DBS was significantly greater than the 16.6% improvement in patients with prior pallidotomy ($p<0.005$, 2-tailed, unpaired t-test). The improvement in dyskinesia scores, from 1.7±1.1 to 0.6±0.6, in the control group was similar to that in the post-pallidotomy group. AEs thought to be related to the STN following pallidotomy included worse dysarthria (3) and worse balance (2)

Table 2: Comparison of Post-Pallidotomy DBS vs. DBS Controls

	Post-Pallidotomy DBS (N=10)	DBS Controls (N=25)	
Age	56.0±10.2	56.3±10.8	NS
Sex	9 male (90%)	21 male (84%)	NS
STN: unilateral vs. bilateral	9 bilateral (90%)	23 bilateral (92%)	NS
UPDRS "off" motor (#18-31)	53.1 to 44.5 (16.6%)	49.7 to 29.7 (40.2%)	P<0.005
UPDRS Dyskinesia (#32)	1.7 to 0.4	1.7 to 0.6	NS

Discussion

We found less robust off-drug motor improvement in STN DBS patients who had previously undergone pallidotomy compared to those who had not had prior ablative surgery. Improvement in dyskinesia was similar in both groups. Although we did not perform statistical analysis, the frequency of AEs appeared to be higher than in the general STN DBS population.(4)

Several case reports have highlighted problems with unilateral pallidotomy on one side and STN DBS on the other side. (5, 6) However, two previous small series of bilateral STN DBS following unilateral pallidotomy generally found no loss on motor efficacy (7, 8). Kleiner-Fisman et al reported similar motor outcomes in post-pallidotomy STN DBS patients but less improvement in activities of daily living and dyskinesia compared to a control group of STN DBS. In contrast, one series, reported only in as an abstract (9), demonstrated less improvement following pallidotomy. Also, a single case of a levodopa non-responsive PD patient who failed to improve after pallidotomy also failed to improve after DBS STN (10). Our patients were all levodopa responsive and improved after their pallidotomy.

There are several reasons why post-pallidotomy STN DBS may result in less robust motor improvement. First, there is an obvious referral bias toward patients who were not satisfied after their pallidotomy, either for objective or subjective reasons. This may represent a more aggressive disease process or more atypical course. The pre- and post-pallidotomy "off" drug UPDRS scores; however, were similar in this group of pallidotomy-DBS patients compared to our pallidotomy population in general (N=89) (1). Dyskinesia scores were also similar. Second, electrophysiologic recordings, on which we greatly rely for placement, can be altered in the STN following GPi ablation, possibly resulting in suboptimal placement. (11). Third, there could be redundant physiological effects that would mitigate subsequent improvement after the second procedure. A single study that simultaneously implanted GPi and STN DBS found that combined stimulation was no more effective than STN stimulation alone. (12) Fourth, we present a relatively small number of patients and the results could be different with a larger sample.

Overall, the small corpus of literature on the efficacy and safety of post-pallidotomy STN DBS is mixed. We recommend prudence when considering DBS in this population.

References

1. Lai EC, Jankovic J, Krauss JK, Ondo WG, Grossman RG. Long-term efficacy of posteroventral pallidotomy in the treatment of Parkinson's disease. Neurology 2000;55(8):1218-1222.
2. Krauss JK, Simpson RK, Jr., Ondo WG, Pohle T, Burgunder JM, Jankovic J. Concepts and methods in chronic thalamic stimulation for treatment of tremor: technique and application. Neurosurgery 2001;48(3):535-541.
3. Ondo WG, Desaloms JM, Jankovic J, Grossman RG. Pallidotomy for generalized dystonia. Mov Disord 1998;13(4):693-698.
4. Silay Y, Jankovic J, Vuong K, et al. The safety of deep brain stimulation in patients with Parkinson's disese, essential tremor, and other movement disorders. Ann Neurol 2004;56(supple 8):S54-S55.
5. Su PC, Tseng HM. Gait freezing and falling related to subthalamic stimulation in patients with a previous pallidotomy. Mov Disord 2001;16(2):376-377.
6. Merello M, Nouzeilles MI, Cammarota A, Betti O, Leiguarda R. Comparison of 1-year follow-up evaluations of patients with indication for pallidotomy who did not undergo surgery versus patients with Parkinson's disease who did undergo pallidotomy: a case control study. Neurosurgery 1999;44(3):461-467.
7. Moro E, Esselink RA, Van Blercom N, et al. Bilateral subthalamic nucleus stimulation in a parkinsonian patient with previous unilateral pallidotomy and thalamotomy. Mov Disord 2000;15(4):753-755.
8. Kleiner-Fisman G, Fisman D, Zamir O, et al. Subthalamic nucleus deep brain stimulation for Parkinson's disease after successful pallidotomy: clinical and electrophysiological observations. Mov Disord 2004;19: 1209-1214.
9. Revilla F, Mink J, Rich K, Dowling J, Loepker A, Perlmutter J. Clinical outcome of bilateral subthalamic nucleus stimulation in patients with Parkinson's disease and previous pallidotomy. Mov Disord 2002;17:S189.
10. Samii A, Giroux ML, Slimp JC, Goodkin R. Bilateral subthalamic nucleus stimulation after bilateral pallidotomies in a patient with advanced Parkinson's disease. Park & Rel Disord 2003;9(3):159-162.
11. Mogilner AY, Sterio D, Rezai AR, Zonenshayn M, Kelly PJ, Beric A. Subthalamic nucleus stimulation in patients with a prior pallidotomy. J Neurosurg 2002;96(4):660-665.
12. Peppe A, Pierantozzi M, Bassi A, et al. Stimulation of the subthalamic nucleus compared with the globus pallidus internus in patients with Parkinson disease. J Neurosurg 2004;101(2):195-200.