The Safety of Deep Brain Stimulation in Patients with Parkinson's Disease, Essential Tremor, and Other Movement Disorders

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Abstract

OBJECTIVE: To evaluate short and long term safety of deep brain stimulation (DBS) in patients with Parkinson s disease (PD), essential tremor (ET), and other movement disorders. **BACKGROUND:** DBS has replaced ablative procedures in the treatment of PD and other movement disorders since the early 1990s; it has been used at Baylor College of Medicine and The Methodist Hospital since 1995. While the benefits of DBS are well recognized, there is a need for assessment of short- and long-term safety and tolerability of this procedure. **METHODS:** All patients operated at our institution since 1995 were assessed at baseline and at 3 to 6 month-intervals with rating scales and videos during off/on medication and off/on DBS. All adverse events (AE) were captured, categorized, and entered into a database. **RESULTS:** During the past decade, 300 patients (67% male, mean age 62.6 years at the time of surgery) with a variety of movement disorders were implanted with DBS and followed at our center. The surgical targets include subthalamic nucleus (STN) (124), ventral intermediate nucleus of the thalamus (VIM) (155), combination VIM/STN (7), and GPi (14). The most common intraoperative AEs were syncope, sinus tachycardia, soft palate laceration, intracranial hemorrhage, and hypotension. Post-operative AEs included hallucination, fever, nausea, headache, and pharyngitis. Stimulation-related AEs were coordination abnormality, dysarthria, paresthesia, gait abnormality, and hypophonia. Complications relating to DBS device were pain or discomfort near the surgical sites, malfunction of implantable pulse generator (IPG), lead or extension fractures, and lead migration. A subgroup of patients (8.7%) experienced 59 incidents of loss of effect (i.e., loss of initial benefit despite all attempts of DBS programming) due to system component malfunction, disease progression, suboptimal stimulation or other reasons. Overall, 10.7% of patients developed 54 hardware-related complications, 21 of which occurred either intraoperatively or immediately postoperatively. **CONCLUSION:** Our study, based on intra-, post-operative, and long-term follow-up, provides evidence that DBS is safe and well tolerated in patients with advanced PD, ET, and other movement disorders.

Introduction

Deep brain stimulation (DBS) has been used for the treatment of movement disorders for over a decade, but data on long-term safety and efficacy has been reported in relatively few studies. Although many reports briefly list complications resulting from the surgical procedure or the implanted hardware, only few provide details of the nature or time course of the safety and tolerability of DBS [Lyons et al, 2004]. Hardware-related problems have been reported to occur in up to 25% of cases [Oh et, al 2002]. Serious surgical complications, including infection over the implantable pulse generator (IPG) site and along the extracranial lead (6%), have been reported in up to 21% of patients, with 6% reported to have persistent neurological sequelae such as dysarthria, accessory nerve palsy, partial complex seizure, dysexecutive syndrome [Beric et al, 2001].

We have used DBS as a treatment strategy in patients with advanced Parkinson's disease (PD) and essential tremor (ET) since 1995. In order to assess the safety of this procedure we have analyzed intraoperative, post-operative, and long-term complications of DBS in these and other movement disorders associated with disabling symptoms despite optimal medical therapy.

Methods

All patients were evaluated according to a pre-specified protocol at baseline, within two weeks before surgery during true "off" state (at least 12 hours after last dose of levodopa) and optimal "on" state after taking morning dose of levodopa. The DBS was turned on about two weeks after surgery and the patients were evaluated every three to six months thereafter.

The intraoperative, hospital, and clinic records were carefully reviewed for demographics, clinical information and any adverse events. Data was categorized and entered into a database. Pre-existing medical conditions which worsened after surgery were only then included as an adverse event.

All adverse events were categorized as intraoperative, immediately post-operative (before discharge from the hospital), or long-term. Etiology was then determined based surgical procedure, stimulation or device components. Revisions (relocation of either the lead or IPG), IPG exchanges and explantations prior to 1 year were reported as hardware-related adverse events. Descriptive data was presented in tabular format.

Table 1. Demographics (N = 300, 67% male)

Demographics	Mean	SD	Min	Max
Age first implanted (yr)	62.6	13.6	13.9	88.4
Total number of follow-up visits (yr)	10.3	7.0	2.0	50.0
Duration of follow-up (yr)	2.4	1.8	< 0.1	7.8
Time between 1st & 2nd implant (mo)	4.4	10.0	0.0	62.1

Table 2. Primary Indication for DBS

Indication	Total	VIM	STN	GPi	VIM/STN
Essential tremor	94	93	1	0	0
Parkinson's disease	187	56	122	2	7
Dystonia	14	3	0	11	0
Multiple sclerosis	3	3	0	0	0
Hemiballism	1	0	1	0	0
Myoclonus	1	0	0	1	0
Total patients	300	155	124	14	7

Table 3. DBS Target Nuclei

Surgical procedure	Total	VIM	STN	GPi	VIM/STN
Staged					
Unilateral	127	102	22	3	—
Bilateral	75	39	26	3	7
Cancelled	13	8	4	1	0
Simultaneous					
Bilateral	98	14	76	8	—
Cancelled	25	8	16	1	0
Unknown					
Cancelled	4	0	3	1	0
Implanted, N	300	155	124	14	7

Table 4. Adverse Events During and Immediately Following DBS Surgery (N = 300)

Adverse effect	Intra-OP	Immediately Post-OP	Total
Hallucination	0	8	8
Fever	0	7	7
Nausea	0	6	6
Headache	0	5	5
Pharyngitis	0	4	4
Pain	0	3	3
Sinus tachycardia	2	1	3
Anxiety	0	2	2
Bronchospasms	0	2	2
Confusion	0	2	2
Depression	0	2	2
Diplopia	0	2	2
Hypertension	1	1	2
Seizure	0	2	2
Syncope	2	0	2
Agitation	0	1	1
Angina, pectoris	0	1	1
Apnea	0	1	1
Bradycardia	1	0	1
Discomfort, extension	1	0	1
Dizziness	0	1	1
Ecchymosis	0	1	1
Edema pulmonary	0	1	1
Finger nails slightly blue	0	1	1
Fluid collection around IPG area	0	1	1
Gout	0	1	1
Hemorrhage, intracranial	1	0	1
Hypotension	1	0	1
Infection, urinary tract	0	1	1
Injury, accidental	0	1	1
Lead migration	0	1	1
Paresthesia	0	1	1
Ptosis	0	1	1
Soft palate laceration	1	0	1
Somnolence	0	1	1
Thinking, abnormal	0	1	1
Total	10	63	73

Results

There were 300 patients operated in The Methodist Hospital and followed at our Parkinson's Disease Center and Movement Disorders Clinic since 1995 [Tables 1, 2 and 3]. There were 124 (41.3%) patients in whom subthalamic nucleus (STN) was the target (22 unilateral, 102 bilateral - 76 simultaneous and 26 staged), 155 (51.7%) patients were implanted into ventral intermediate nucleus of the thalamus (VIM) (102 unilateral, 53 bilateral VIM - 14 simultaneous and 39 staged); 7 had bilateral staged VIM/STN and 14 had GPi implants (3 unilateral, 11 bilateral - 8 simultaneous and 3 staged). The following most frequent adverse events were encountered: 1. Intra-operative: syncope (2), sinus tachycardia (2), soft palate laceration (1), intra-cranial hemorrhage (1), hypotension (1); 2. Post-operative: hallucination (8), fever (7), nausea (6), headache (5), pharyngitis (4); 3. Stimulation related: coordination abnormality (47), dysarthria (45), paresthesia (22), gait abnormality (18), hypophonia (12); 4. DBS device related: pain or discomfort (head, neck and IPG area) (11), malfunction of IPG (7), lead fracture (6), lead migration (3). A total of 26 (8.7%) patients (59 incidents) lost their initial benefit despite all attempts of DBS programming: in 16 patients due to system components, 10 due to disease progression, 6 due to stimulation, and 9 patients had a loss of benefit due to other reasons. Overall, 32 (10.7%) patients had 54 hardware related complications, 21 of those occurred either intraoperatively or immediately postoperatively [Tables 4, 5, and 6]. Death in 21 patients resulted from disease progression (5), patient-related comorbid conditions (5), unexpected circumstances (e.g., accidental fall (1), suicide (1), and other unspecified causes (9)).

Table 6. Long-term Adverse Events Related to DBS Device (N = 300)

Adverse event	n	%
Pain or discomfort (Head, neck and IPG area)	11	33.3
Malfunction, IPG	7	21.2
Malfunction, Lead Fracture	6	18.2
Malfunction, Lead Migration	3	9.1
Pressure Buildup	3	9.1
Hypertrophy Skin	1	3.0
Infection	1	3.0
Psychosis	1	3.0
Total	33	

Table 5. Long-term Adverse Events Related to Stimulation (N = 300)

Adverse event	n	%
Abnormal coordination	47	24.7
Dysarthria	45	23.7
Paresthesia	22	11.6
Abnormal gait	18	9.5
Hypophonia	12	6.3
Tremor	7	3.7
Diplopia	5	2.6
Myoclonus	4	2.1
Paresthesia	4	2.1
Dizziness	3	1.6
Dystonia	3	1.6
Speech disorder	3	1.6
Blurred vision	2	1.1
Depression	2	1.1
Dysphagia	2	1.1
Others ^	1	0.5
Total	190	

^ Apnea; Arrhythmia; Burning sensation; Confusion; Hearing loss; Emotional lability; Involuntary tongue movements; Paralysis, facial; Pulling sensation on top of head; Scotoma; Voice alteration

Discussion

In this largest reported long-term study of 300 patients treated with DBS for PD, ET and other movement disorders, followed for up to 7.8 years (mean 2.4 yrs), we found DBS procedure to be safe and the DBS device is well-tolerated. Although efficacy was not the primary focus of the study, essentially all patients were found to have some initial benefit and only 8.7% experienced loss of therapeutic effect, usually due to malfunction of system components or progression of the underlying disease.

Our intraoperative and post-operative complications as well as DBS-related adverse events appear to be less frequent than those reported from other centers [Table 7]. Appropriate patient and surgical target selection, as well as an experienced neurosurgeon and intra- and post-operative care, are essential elements to a successful short- and long-term outcome of DBS. For patients with PD, ET and other movement disorders who fail to obtain satisfactory benefits from conventional, medical management, DBS offers a safe and effective alternative.

Table 7. Reported Hardware-Related Complications of DBS (For reported complications, either the number of patients or rates given depending on the published literature and number of implanted electrodes is denominator for rate given in parentheses, unless stated otherwise)

First Author	Year	Patient (Procedure)	Mean FU in Months	Lead Fracture	Lead Migration	Short or Open Circuit	Malfunction	Infection / Erosion	Intracerebral Hemorrhage
Levy	1987	141 (304)	80	NR	14.2 (20x, 14 Pt)	0.9 (14x, 12 Pt)	7.8 (11 Pt)	23.4 (23 Inf, 10 Ero)	3.5 (5 Pt)
Kumar	1997	68 (74)	78	2.9 (2.7)	NR	1.5 (1.4)	2.9 (2.7)	5.9 (5.4)	1.5 (1.4)
Benabid	1998	197 (316)	NR	NR	NR	0.9 (3 Pt)	NR	2.5 (3 Inf, 5 Ero)	0.3 (1)
Limousin	1999	110 (135)	12	NR	NR	NR	NR	2.7 (2.2)	0.9 (0.7)
Shuurman	2000	34 (34)	6	NR	NR	NR	NR	2.9 (2.9)	2.9 (2.9)
Oh	2002	79 (124)	33	5.1 (3.2)	5.1 (3.2)	3.8 (2.4)	0 (0)	15.2 (9.7)	3.6 (2.3)
Koller	2001	49 (NR)	40	NR	NR	NR	NR	NR	6.1
Joint	2002	39 (NR)	36	20% HRP	20% HRP	20% HRP	20% HRP	20% HRP	20% HRP
Kondziolka	2002	66 (NR)	29	10 Pt	1 Pt	1 Pt	3.0 (1 Pt)	14 (7 Pt)	0 (0)
Beric	2001	86 (149)	NR	8 Peri-AE, 8 Post-AE, 9 Hw-AE, 4 Stim-AE	NR	NR	6.5 HF	6.5 Inf	NR
PSG	2001	134 (198)	NR	5.5 HF	NR	NR	5.5 HF	5.5 Inf	NR
Lyons	2001	9 (NR)	40	NR	1 Pt	NR	NR	1 Ero	2 Pt
Pahwa	2003	33 (NR)	28	9 LR, 7 LRV	NR	12 IR	6 ER	NR	NR
Lyons	2004	81 (160)	17 (1–54)	2 LF, 1 EF, 1 EE	5 LM, 14 LMP	5 IR	15 IMF	6 Inf (3 IPG, 3 Sys)	1 (no neurological sequelae)
Silay (present series)	2004	300 (727)	29 (1–94)	6 LF (5 Pt)	3 LM (2 Pt)	NR	7 IMF (4 Pt)	2 Inf (1 IPG, 1 Sys)	2 (no sequelae)

EE = Extension erosion; EF = Extension fracture; ER = Extension replacement; Ero = Erosion; FU = Follow-up; HF = Hardware failure; HRP = Hardware-related problem; Hw-AE = Hardware induced adverse effect; IMF = IPG malfunction; Inf = Infection; IR = IPG replacement; LF = Lead fracture; LM = Lead migration; LMP = Lead misplaced; LR = Lead replacement; LRV = Lead revision; NR = Nor reported; Peri-AE = Perioperative induced adverse effect; Post-AE = Postoperative induced adverse effect; PSG = Parkinson's disease Study Group; Pt = Patient; Stim-AE = Stimulation induced adverse effect; Sys = System