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ORIGINAL COMMUNICATION

Deep brain stimulation for dystonia: outcome at long-term follow-up

T. J. Loher
H.-H. Capelle
A. Kaelin-Lang
S. Weber
R. Weigel
J. M. Burgunder
J. K. Krauss

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T. J. Loher · A. Kaelin-Lang · S. Weber · J. M. Burgunder
Dept. of Neurology
University of Berne, Inselspital
Berne, Switzerland

H.-H. Capelle · Prof. Dr. J. K. Krauss (✉)
Dept. of Neurosurgery
Medical University, MHH
Carl-Neuberg-Str. 1
30625 Hannover, Germany
Tel.: +49-511/532-6650
Fax: +49-511/532-5864
E-Mail: krauss.joachim@mh-hannover.de

R. Weigel
Dept. of Neurosurgery
University Hospital
Mannheim, Germany

Abstract *Objective* Deep brain stimulation (DBS) has emerged as a useful therapeutic option for patients with insufficient benefit from conservative treatment. *Methods* Nine patients with chronic DBS who suffered from cervical dystonia (4), generalized dystonia (2), hemidystonia (1), paroxysmal dystonia (1) and Meige syndrome (1) were available for formal follow-up at three years postoperatively, and beyond up to 10 years. All patients had undergone pallidal stimulation except one patient with paroxysmal dystonia who underwent thalamic stimulation. *Results* Maintained improvement was seen in all patients with pallidal stimulation up to 10 years after surgery except in one patient who had a relative loss of benefit in dystonia ratings but continued to have improved disability scores. After nine years of chronic thalamic stimulation there was a mild loss of efficacy which was regained when the target was changed to the pallidum in the patient with paroxysmal dystonia. There were no major complications related to surgery or to chronic stimulation. Pacemakers had to be replaced within 1.5 to 2 years, in general. *Conclusion* DBS maintains marked long-term symptomatic and functional improvement in the majority of patients with dystonia.

Key words deep brain stimulation · dystonia · long-term follow-up

Introduction

Chronic deep brain stimulation (DBS) has widened the spectrum of therapeutic options for patients with disabling and medically-refractory dystonia. It has been introduced only after DBS became an accepted treatment for advanced Parkinson's disease (PD). The posteroventral lateral globus pallidus internus (GPi) is considered the main target for primary dystonia, whereas the optimal target for secondary dystonia remains unclear [1, 6, 11]. We have demonstrated previously its usefulness in patients with complex cervical dystonia [8, 9]. Pallidal DBS has been confirmed to be effective in primary generalized dystonia in a multicenter 1-year follow-up study with a partially blinded study design [19]. Furthermore, pallidal DBS was more effective than sham stimulation in a recent randomized controlled clinical trial [12]. Beneficial effects of pallidal DBS have also been reported for patients with segmental or focal dystonia [11]. Very little, however, is known about its long-term effects [20]. We therefore present outcome data of our early patients with follow-up of three years and beyond.

Methods

From 1995 until 2000, a total of 14 dystonia patients with insufficient benefit from medical treatment underwent DBS surgery at the Department of Neurosurgery in Berne, Switzerland, or in Mannheim, Germany. All patients except the first two were enrolled in a prospective study protocol. Short-term follow-up results were published else-

where [3, 8–10, 13, 14]. Exclusion criteria for surgery were major psychiatric disorders, dementia and cerebral atrophy. Nine patients were available for follow-up of three years or longer. Patient characteristics are shown in Table 1. There were five men and four women with a mean age at surgery of 43.9 years (range, 24–60 years). Four patients had complex cervical dystonia (CD), two had generalized dystonia (GD), one hemidystonia (HD), one paroxysmal nonkinesigenic dystonia (PNKD), and one Meige syndrome. The etiology of dystonia was idiopathic in six patients. One patient had a positive family history for dystonia. In patient 6, dystonia developed after severe closed head injury [13]. Patient 7 suffered from severe brachial plexus neuropathy prior to the onset of dystonic attacks [14]. All patients, except the one with posttraumatic HD, had unremarkable MR imaging studies. Anticholinergics were given in all patients prior to surgery, but the response was either insufficient or higher doses were not tolerated.

Patients were assessed preoperatively and at defined follow-up examinations postoperatively, at 3 months, at 1 year and on an annual basis thereafter. The assessments included the Burke-Fahn-Marsden dystonia scale (BFM), the Unified Dystonia Rating Scale (UDRS), a modified Toronto Western Spasmodic Torticollis Rating Scale (TWSTRS), and standardized videotaping. No formal ratings were obtained after the 3-year follow-up. Assessments were performed by the neurological team members.

All patients underwent pallidal DBS except patient 7 with PNKD who had DBS of the ventrointermediate (Vim) thalamic nucleus. Seven patients had bilateral surgery, whereas patients 6 and 7 underwent unilateral procedures. Standard quadripolar electrodes (model 3387, Medtronic Inc., Minneapolis, MN) were implanted with the aid of CT-stereotactic surgery and microelectrode recording [9, 10]. All patients were operated on under local anesthesia without sedatives. The target was the posteroventral lateral globus pallidus internus. The target was approached using the following stereotactic coordinates: $x = 20, y = +3$, and $z = -4$. The final target was refined considering both the results of microelectrode recording and macrostimulation.

Implantable pulse generators (IPG; Itrel II, Medtronic Inc., Minneapolis, MN) were placed in an infraclavicular subcutaneous pouch. Programming of the IPGs was started on the first postoperative day and the amplitudes were gradually increased up to 2–3 V on the following days. Stimulation settings were further adjusted on subsequent visits. The usual set-up started with bipolar stimulation as it had been routine for years in our departments. When voltage increased above 3.6 V monopolar stimulation of single contacts was also tested, and that combination which was thought to provide the best benefit was programmed.

Results

Formal follow-up assessments at 3 years were available in all 9 patients, while long-term follow-up ranged between 5 years and 10 years. There were no intraoperative or postoperative complications related to surgery. Postoperative imaging studies confirmed appropriate location of the electrodes. As described earlier, improvement of dystonia was noted within days after surgery, but it took up to 6 months until full benefit was achieved upon adjustment of the stimulation voltage. Patient 4 had three episodes of sudden clinical deterioration due to lead fractures necessitating repeat surgery. Three patients with CD had sustained benefit, whereas the motor scores of patient 2 returned almost to baseline, despite continuous improvement of disability scores. Overall, the mean TWSTRS scores of the four CD patients were improved by 61 % at 1 year postoperatively and by 49 % at the last available assessment. Patients 5 and 8 with GD benefited markedly as was reflected in a 82 % and a 70 % postoperative improvement of the BFM dystonia score at 1 year and 76 % and 57 % at 3 years, respectively, accompanied by similar improvement for the UDRS dystonia scores (Patient 5). Dystonia scores were not significantly different when compared for the different follow-up examinations. In patient 8 there was continued improvement of all components of dystonia except for blepharospasm beyond 3 years follow-up, which has been well controlled since then, however, with botulinum toxin injections.

Patient 6 with posttraumatic hemidystonia benefited from both sustained symptomatic and functional improvement. In patient 7, Vim DBS resulted in a marked decrease of frequency, duration, and intensity of the paroxysmal dystonic attacks. After nine years of chronic thalamic stimulation there was an increase of the frequency of the attacks from 3 times per week to about 10 per week. It was decided then to change to pallidal stimulation. Thereafter, there was a decrease of the frequency

Table 1 Demographic and clinical characteristics of 9 patients with dystonia

Pat	Sex	Age at surgery	History of dystonia (years)	Etiology	Phenomenology
1	M	47	4	Idiopathic	Cervical dystonia (sagittal shift + retrocollis)
2	F	41	5	Idiopathic	Cervical dystonia (lateral shift + lateral tilt)
3	M	28	6	Idiopathic	Cervical dystonia (antecollis)
4	F	53	6	Idiopathic	Cervical dystonia (retrocollis/torticollis)
5	M	51	39	Primary genetic	Generalized dystonia
6	M	24	9	Posttraumatic	Hemidystonia (right arm > leg)
7	M	33	4	Plexus neuropathy	Paroxysmal nonkinesigenic dystonia (right arm)
8	F	58	12	Idiopathic	Generalized dystonia
9	F	60	5	Idiopathic	Meige syndrome

M male; *F* female

Table 2 Surgical procedures and individual outcome measures

Pat	DBS	Assessment	Preoperative	Outcome			Adverse effects/remarks
				1 year	3 years	Last FU	
1	Bilateral GPi	TWSTRS severity	20	10	12	9 years	Perioral tightness upon chronic DBS
		TWSTRS disability	46	21	30		
		TWSTRS pain	8	6	8		
2	Bilateral GPi	TWSTRS severity	19	7	20	8 years	Local infection 6 months postop, treated with antibiotics
		TWSTRS disability	35	15	22		
		TWSTRS pain	6	4	5		
3	Bilateral GPi	TWSTRS severity	21	6	10	9 years	–
		TWSTRS disability	37	3	0		
		TWSTRS pain	3	0	0		
4	Bilateral GPi	TWSTRS severity	22	14	17	6 years	Three reoperations for lead fractures (lost to follow-up after 6 years)
		TWSTRS disability	44	16	11		
		TWSTRS pain	7	3	2		
5	Bilateral GPi	BFM dystonia	71	13	17	5 years	Lethal accident 5 years after surgery
		BFM disability	17	5	4		
		UDRS	77	23	23		
6	Unilateral GPi	No formal assessment	About 50% improvement of pain, dystonia and tremor			10 years	–
7	Unilateral Vim	Frequency of attacks	10/day	2/week	3/week	10 years	Switch to pallidal DBS after 9 years
8	Bilateral GPi	BFM dystonia	91	28	39.5	6 years	–
		BFM disability	20	7	11		
9	Bilateral GPi	BFM	6/6/6 eyes/mouth/speech & swallowing	05./3/4	0.5/1.5/4	7 years	Perioral tightness upon chronic DBS

FU follow-up; *GPi* globus pallidus internus; *Vim* ventrointermediate thalamic nucleus; *TWSTRS* modified Toronto western spasmodic torticollis rating scale; *BFM* Burke-Fahn-Marsden scale; *UDRS* Unified Dystonia Rating Scale

of the attacks again to about three per week. Patient 9 with Meige syndrome achieved reduction of her oromandibular dyskinesias and blepharospasm, which was reflected by changes of the subscores for BFM eyes, mouth and speech.

At the last follow-up, stimulation settings were bipolar in six, and monopolar in two patients. In one patient (Patient 9) settings were bipolar for one side and monopolar for the other. All patients were stimulated with a pulse width of 210 μs and a frequency of 130 Hz on long-term. Voltage ranged between 2.0 and 5.0 V. Five of seven patients who were under anticholinergic medication at the time of surgery discontinued medication. In patient 2 a wound infection was treated successfully by antibiotic therapy 6 months postoperatively. Patient 5, who had marked and sustained benefit from surgery had a lethal accident 5 years after the procedure. Two patients had perioral tightness and mild dysarthria upon chronic bilateral GPi DBS. The IPGs were replaced within 1.5 – 2 year intervals, except in patients 6 and 7 who had unilateral stimulation. Upon depletion of the IPGs dystonia recurred in every instance [7].

Discussion

Our study demonstrates that DBS maintains marked symptomatic and functional improvement in the majority of patients with dystonia in the long term. While a gradual increase in benefit is observed over a period of several months after surgery, in general little changes in rating scores occur later. Nevertheless, in one patient with pallidal stimulation there was a loss of the initial benefit as expressed by deterioration of BFM motor scores and in one patient with thalamic stimulation switch to pallidal stimulation proved to be beneficial even after nine years. Consistent with the recent multicenter study we have seen some interpatient variability of the response to DBS [19].

It appears that patients both with cervical and generalized dystonia gain similar long-term improvement. This is in accordance with short-term follow-up data from other groups [2, 4–6, 17–19]. Overall, patients with idiopathic generalized dystonia may achieve improvement which is similar to those who test positive for DYT1 mutation [4]. Since patients with early onset of generalized dystonic movement disorders are at a high risk to develop degenerative spinal disorders, it is important to treat dystonia at an early stage before improvement is

limited by permanent neurologic deficits [9, 15]. The positive results seen in our patient with Meige syndrome have been confirmed meanwhile also by other groups [11, 16].

Long-term benefit may also be achieved in secondary dystonia, although to a more limited extent. Posttraumatic hemidystonia was improved up to 10 years with GPi DBS and peripherally-induced PNKD with thalamic DBS and later with pallidal DBS. Thought to be less useful for secondary dystonia in the past, pallidal stimulation has recently demonstrated benefit in several such patients [6, 18]. Nonetheless, thalamic DBS may still be considered an alternative treatment option for selected cases [11]. Thus far, however, comparative studies are lacking and no definite conclusions can be drawn.

The costs of chronic DBS for dystonia patients in general are higher than those for PD patients due to the younger age of dystonia patients and due to higher energy consumption and more frequent battery replacements. Future strategies to reduce costs for chronic stimulation should include the use of rechargeable IPG batteries, the use of batteries with a longer life span, and the exploration of other alternative stimulation modalities.

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