Clinical Study

Stereotactic ^{and} Functional Neurosurgery

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Use of Pallidal Deep Brain Stimulation in Postinfarct Hemidystonia

Jennifer Witt^a Phillip A. Starr^b Jill L. Ostrem^a

Departments of ^aNeurology and ^bNeurological Surgery, University of California, San Francisco and Center for Movement Disorders, San Francisco, Calif., USA

Key Words

Deep brain stimulation • Globus pallidus • Dystonia • Movement disorders

Abstract

Background/Aims: Reports of outcomes in treating dystonia secondary to stroke with deep brain stimulation (DBS) are limited. We report our experience with 3 patients, all with infarcts involving the striatum, who developed hemidystonia and were treated with unilateral globus pallidus interna DBS. Methods: Case series describing characteristics and outcomes based on the Burke-Fahn-Marsden Dystonia Rating Scale (BFMDRS) scores before and after DBS at 3, 6 and at least 12 months. Results: All patients reported subjective improvements after surgery. At 1 year or more after surgery, none of the 3 patients displayed a measureable improvement in the BFMDRS movement score. Conclusion: Our findings are consistent with previous reports of limited benefits from pallidal DBS in secondary dystonia. Future work should focus on predictive factors for DBS outcomes and the development of more sensitive assessment tools specifically for secondary dystonias as well as the exploration of alternative brain targets for stimulation. Copyright © 2013 S. Karger AG, Basel

Introduction

Cerebral infarction is a well-described cause of secondary dystonia and is the most common etiology of symptomatic hemidystonia. Treatment with botulinum toxin injections and pharmacotherapy is frequently inadequate and is limited by dose-related side effects [1–3].

The use of deep brain stimulation (DBS) for secondary dystonias has been described in a few case reports and case series that included patients with a variety of etiologies, dystonia distribution and surgical targets. Overall, secondary dystonia responds less favorably to DBS than primary dystonia [4–9]. Treatment with DBS specifically for dystonia secondary to ischemic stroke has been previously reported in 3 cases [5, 8, 10]. Here, we report our experience using pallidal DBS to treat 3 patients with putaminal infarctions and resultant hemidystonia.

Methods

Three patients with medically refractory hemidystonia due to infarctions involving the putamen underwent unilateral pallidal DBS implantation with Medtronic 3389 leads ipsilateral to the infarction. The surgical technique for cases 1 and 2 followed previously reported stereotactic procedures using monitored anesthesia for scalp incision, and burr hole creation and awake microelectrode recording and test stimulation for side-effect thresholds [11]. In case 1, three microelectrode recording passes were made.

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Swedish Neuroscience Institute 550 17th Ave, Suite 540 Seattle, WA 98122 (USA) E-Mail je.landes@gmail.com

Jennifer Witt, MD

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Case	at at	Unset	Age at	Baseline medications	Stroke location	BFMU	KS MS (%)	mproveme	nt)	BFMI	%) SU SN(umprove	sment)	Distance from	UBS narameters
	stroke years	dys- tonia	years	(ma Am		base- line	3 months	6 months	≥12 months	base- line	3 months	6 months	≥12 months	porder ¹ at level of AC-PC axial plane, mm	at 12 months
-		6 months	29	metaxalone 3200, baclofen 80, tizanidine 32, zolpidem 10 PRN, clonzepam 1 PRN, simvastatin 20 and botulinum toxin injec- tions (left arm)	right putamen and frontal periventricular white matter extending to the anterior limb of the internal capsule	28	16 (42.8)	16 (42.8)	28 ²	4	ε	3 (25)	$4(0)^{2}$	4.5	Case+, 1–, 3.5 V, 90 μs, 160 Hz ²
5	4		16	trihexyphenidyl 24 and botulinum toxin (right leg)	left putamen, caudate and anterior limb internal capsule	32	32 (0)	32 (0)	28 (12.5)	~	7 (12.5)	7 (12.5)	6 (25)	2.2	Case+, 0- 1-, 5.0 V, 60 μs, 140 Hz
ŝ	peri- natal	8 years	10	levitiracetam 1000, baclofen 40 and trihexyphenidyl 2	left putamen and subinsular white matter and cortex	21	24 (-14.2)	22 (-4.8)	20 (4.7)	~	10 (-25)	7 (12.5)	6 (25)	2.6	Case+, 2-, 3.5 V, 90 μs, 135 Hz
and	Distanc adult cas Data ob	ce from p ses and di tained at	allidocaps ifferences 3 years at	ular border was used to report le in anatomy due to the infarcts. fter DBS surgery.	ad location rather than th	le AC-F	^o C x, y and	z coordinat	es to accou	nt for d	ifferences	in the siz	es of brain s	structures betwee	on the pediatric

the external and internal segments, but included 2 cells with strong contralateral arm and leg movement-related activity. Test stimulation using 0 negative and 3 positive, 185 Hz and 90 µs elicited contralateral arm contraction at 7 V and hypophonia at 9 V. For case 2, the single microelectrode recording pass demonstrated an 8-mm segment of pallidal discharges. The first 4 mm were followed by a 1-mm gap and then 3 more millimeters of dense activity ranging from 40 to 80 Hz. There was no strong contralateral movement-related activity. Test stimulation was performed using 0 negative and 3 positive, 180 Hz and 200 µs. Hypophonia and facial contraction occurred at 8 V. The third case was performed under general anesthesia using an interventional MRI technique [12]. Lead location was measured with postoperative Stealth Station[®]-reformatted MRI images. To account for interindividual variations in the spatial coordinates of the pallidum, the lead locations are reported as the distance from the pallidocapsular border at the level of the anterior commissure-posterior commissure (AC-PC) plane instead of the AC-PC coordinates. Burke-Fahn-Marsden Dystonia Rating Scale (BFMDRS) movement score (MS) and disability score (DS) were performed

The final pass, 2-mm posterior to the initial target, had the longest run of pallidal cells (7 mm) without clear differentiation between

at baseline and at 3, 6 and at least 12 months postoperatively. Contacts were surveyed for stimulation-induced side effects, and the initial contact was chosen based on either the lead placement or symptom benefit during the initial survey. Voltage and active contact configurations were adjusted at each visit to maximize clinical benefit. The highest amplitude settings were used that did not induce stimulation-related side effects, and if greater benefit was not achieved with high amplitudes, patients were returned to the lowest settings that achieved maximum benefit.

Cases

Refer to table 1 and figure 1. Patient 1 is a 29-year-old male who developed painful left hemidystonia 6 months after a lenticulostriate territory infarction at the age of 7 years. Despite left-arm botulinum toxin injections, pharmacotherapy and ankle-to-knee tendon transfer, he remained impaired. On examination, the fingers were flexed but able to be reduced passively and there was flexor posturing in the proximal arm with activation. His left foot was plantar-flexed and inverted with toe curling and a limited range of motion.

Patient 2 is a 16-year-old female with right-arm and leg dystonia since the age of 4 years following lenticulostriate territory infarction. Medication trials, botulinum toxin injections and surgical correction of right-hip displacement and a tendon transfer at the right ankle were inadequate. She had no functional use of her right upper limb. On examination, there was increased tone, mild weakness and atrophy in the right arm and leg. Without an anklefoot orthotic, she was unable to bear weight on the right foot due to severe ankle inversion and toe curling. The dystonia relaxed with sensory tricks, but worsened with action or ambulation.

Patient 3 is a 10-year-old female with a history of left-middle cerebral artery perinatal infarction presenting with transient right hemiparesis which resolved to allow unaided ambulation as a toddler. At the age of 8 years, she developed choreiform and dystonic movements in her right arm and leg. She had no functional use of her arm and her walking was impaired despite pharmacotherapy. Constant phasic movements in the upper limb were so severe that writing with the unaffected hand was impaired, result-

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 Table 1. Patient baseline characteristics and outcomes after globus pallidus interna DBS



Fig. 1. a MRI: T2-weighted axial images showing stroke locations at the level of the putamen. **b** MRI: T1-weighted axial images showing lead artifact at the level of the AC-PC plane. L = Left; R = right.

ing in placement in special education classes. On examination, she had mild weakness in the ankle and wrist. The foot was inverted with toe curling except for the extended big toe. She had tonic shoulder elevation, elbow flexion, wrist extension with ulnar deviation, finger flexion and large-amplitude jerky irregular abduction/adduction of the upper arm at the shoulder joint, especially with activity of the limb or other body regions. Dystonic posturing of the wrist and fingers could be corrected by brushing the dorsum of the hand.

Results

Refer to table 1. Patient 1 experienced microlesioning benefit for 4 days with relaxation of his hand, toe curling, foot eversion and pain reduction. Contact 1 was initially chosen based on intraoperative microelectrode recordings and postoperative imaging. Contact 0 was temporarily stimulated at 3 months, but resulted in subjective tightness in his hip. At 3 and 6 months after surgery, a 42.8% improvement in the BFMDRS MS was noted. He reported less pain and analgesic requirement, improved ambulation and the ability to run for exercise, resolution of the skin breakdown on his hand and toes from severe flexion into the palm and shoe, respectively, and botulinum toxin injections in the arm being required less often. The patient was lost to follow-up until 3 years after DBS, at which time no clear benefit was noted in his dystonia compared to his baseline status. Historically, the initial benefit he had gained at 3 and 6 months after surgery had waned overtime.

Patient 2 was initially programmed using contact 2 because of a subjective sense of relaxation in her lower limb. She had gradually increased the voltage from 3.0 to 5.7 V by her 3-month follow-up visit. Given the lack of objective improvement, a ventral contact was tried with home titration of voltage. By 6 months at 7.5 V, she reported that her toes and upper limb were looser. However, she still had no change in BFMDRS MS and only a 1-point improvement in DS. At 12 months she reported similar improvement in her leg and arm.

Patient 3 also reported microlesioning benefit prior to the initial programming. She was able to open the right

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hand and rest it on her leg. Contact 1 was first used and her voltage was increased from 2.5 to 3 V the following month. At her 3-month visit, she reported improved use of her hand to grasp objects (not observed in the clinic). Changing to contact 2 allowed her to hold her arm in front of her body instead of behind her back, and by 6 months she felt her walking was improved. The hyperkinesia in her right arm had decreased enough to allow her left-hand writing to become legible and she was moved to mainstream classes. Despite her positive subjective reports, performance on the BFMDRS MS and DS remained basically unchanged at 6 and 12 months.

Discussion

Patients in this series were similar in terms of dystonia type (hemidystonia), etiology and lesion location; however, the outcomes after unilateral pallidal DBS were variable. Patient 1 showed a measurable and subjective improvement initially for the first 6 months, but this effect waned. He differed from the 2 less responsive patients in that he was older at both the time of stroke and surgery, had more preoperative pain and his electrode placement was further from the pallidocapsular border, perhaps stimulating globus pallidus externa. His infarct also did not involve the caudate (as in patient 2) or the cortex (as in patient 3) (table 1; fig. 1). Although there was no measurable BFMDRS improvement in patient 3, she reported sustained meaningful benefit due to decreasing the amplitude of the dystonic tremor. She was the youngest of the series and was implanted only 2 years after onset of the dystonia. In primary generalized dystonia patients, shorter disease duration has been correlated with greater improvement from pallidal DBS [13]. Determining if these factors in postinfarct secondary hemidystonia are useful predictors is precluded by the small sample. We also recognize that the length of follow-up for this series may not be adequate to have fully explored programming options.

The discrepancy between the subjective reports supplied by patients 2 and 3 and their lack of improvement on the BFMDRS is notable. While a placebo effect cannot be excluded, this could be explained by an inadequate sensitivity of current rating scales for measuring subtle but meaningful change in secondary dystonia. The BFMDRS and other traditionally used dystonia rating scales were developed for primary dystonia, but patients with secondary dystonia often have additional phenomenology and may not follow the same patterns of provocation. For example, although the improvement in the amplitude of the dystonic upper limb movements of patient 3 allowed her to enter mainstream classes, she was still unable to grasp an object and dystonia was still present at rest, leading to continued maximal scoring for that limb.

The lack of measured improvement in this series is comparable with other reports on DBS for secondary dystonias. Response may be limited by atrophy of the DBS target, destruction or disturbance of connecting pathways and simultaneous occurrence with hypertonia of pyramidal origin. A subset of secondary dystonias having preserved basal ganglia architecture, including tardive dystonia and some postanoxic dystonias, may be an exception [8]. However, a series of 13 dystonia-choreoathetosis cerebral palsy cases with structural preservation of the basal ganglia treated with bilateral pallidal DBS reported a wide variation of outcomes ranging from 7.4% worsening to 55% improvement in BFMDRS [9].

Previously reported cases of postinfarct dystonia treated with DBS were mixed with respect to lesion location (if reported), brain target and outcomes. Following globus pallidus interna stimulation in 1 patient (stroke location within the basal ganglia not specified), there was no improvement [8]. A second case (pallidal stroke) was treated with ventrolateral thalamic DBS leading to a 31% improvement in BFMDRS MS at 36 months, but without improvement in DS [5]. Subthalamic nucleus DBS provided the highest improvement of 90.8% in the BFMDRS MS in a patient with a small thalamic infarct [10]. The optimal DBS target has still to be determined given the scarcity and heterogeneity of reported cases.

As the benefit of current DBS targets in the setting of structural and connective abnormalities is limited, cortical stimulation delivered to the primary motor cortex, supplementary motor and/or cingulate motor areas may be worthy of exploration. All of these areas receive output from the basal ganglia-thalamic circuit [14]. Both the supplementary motor area and cingulate motor area are metabolically overactive during movement of a dystonic limb in acquired-hemidystonia patients [15] and there are mixed reports of motor cortex stimulation improving movement disorders and pain that occur after stroke [16].

This series adds to the small body of literature describing DBS outcomes in postinfarct hemidystonia patients. Larger, prospective, controlled and blinded studies of more homogeneous groups of secondary dystonia, using assessments designed specifically for secondary dystonias are needed to better define and predict the utility of this therapy, and novel targets for stimulation should be explored.

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