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Globus pallidus deep brain stimulation for adult-onset axial dystonia

Aasef G. Shaikh*, Klaus Mewes, H.A. Jinnah, Mahlon R. DeLong, Robert E. Gross, Shirley Triche, Alan Freeman, and Stewart A. Factor

Department of Neurology, Emory University, Atlanta, GA, USA

Abstract

Introduction—Generalized dystonia, both primary and secondary forms, and axial dystonias such as tardive dystonia, and idiopathic cervical dystonia are responsive to globus pallidus interna (GPi) DBS. There is a paucity of investigations probing the impact of DBS on adult-onset axial dystonia. We assessed the efficacy of GPi DBS in four patients with rare adult-onset axial dystonia.

Methods—Primary outcome measure was improvement in the motor component of the Burke-Fahn-Marsden (BFM) rating scale. Secondary outcome measures were quality of life as determined by the SF-36 questionnaire, time to achieve best possible benefit and DBS parameters that accounted for the best response. In patients with prominent concomitant cervical dystonia we also used the Toronto Western Spasmodic Torticollis Rating Scale (TWSTRS).

Results—GPi DBS improved BFM scores by $87.63 \pm 11.46\%$. Improvement in total severity scale of TWSTRS was $71.5 \pm 12.7\%$. Quality of life also remarkably improved as evidenced by 109.38 ± 82.97 and $7.05 \pm 21.48\%$ percent change in psychometrically-based physical component summary (PCS), and a mental component summary (MCS) score respectively.

Conclusions—GPi DBS is a very effective treatment for adult-onset axial dystonia. Considering its refractoriness to medical therapy and significant impact on quality of life DBS should be considered for this disorder.

Keywords

Basal ganglia; Movement disorders; Functional neurosurgery

1. Introduction

Adult-onset axial dystonia (AAD) predominantly involves trunk, although sometimes it spreads contiguously to the cranio-cervical region but the arms and legs are usually spared or only mildly impaired [1–3]. This rare form of dystonia, accounting for less than 10% of segmental dystonias [2,4], is poorly responsive to medical therapy, and has a limited response to botulinum toxin injections [2,3]. The largest cohort, summarizing 18 cases,

*Corresponding author. 1841 Clifton Road, NE, Suite 350, Atlanta, GA 30329-4021, USA. Tel.: +1 313 850 8604; fax: +1 404 728 4892. ; Email: aasefshaikh@gmail.com (A.G. Shaikh)

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demonstrated a mean age of onset of 41 years with predominant forward bending or flexor-type [2]. The extensor-type was described in 20% of cases, while lateral bending was distinctly rare [2]. Many AAD patients develop a negative personal image, depression, and social isolation due to the debilitating nature of this disease [2].

It is known that deep brain stimulation (DBS) of globus pallidus pars interna (GPi) in patients with primary and secondary generalized dystonias, tardive axial dystonia, and idiopathic cervical dystonia leads to remarkable improvement [5–11]. Generalized and cervical dystonia improves up to 60% at six months [7,8]; while tardive dystonia can improve up to more than 90% with GPi DBS [9–11]. However, there is paucity of literature describing the effects of DBS in AAD. Here we describe outcomes of GPi DBS surgery in four patients with AAD.

2. Material and methods

2.1. Patients

The Emory Institutional Review Board approved the retrospective study of a patient database and medical record review in the movement disorder clinic. Our clinic maintains a list of patients who have undergone DBS, categorized according to the diagnosis. We reviewed all ($n = 140$) dystonia patients who have had DBS since 1998, and found four (two men and two women) with the rare form of adult onset axial dystonia. We assessed the impact of GPi DBS on these four AAD patients. The average age of onset was 55.5 ± 6.2 years. The average duration of the disease prior to surgery was 5.8 ± 6.2 years.

2.2. Clinical assessment

The AAD response to DBS was quantitatively measured prospectively at each visit by motor components of the Burke-Fahn-Marsden (BFM) dystonia rating scale. For patients with cervical dystonia, we also performed the Toronto Western Spasmodic Torticollis Rating Scale (TWSTRS). As part of the standard assessment we also used the Short Form-36 (SF-36) questionnaire to objectively assess quality of life. The SF-36 questionnaire provides scores for eight health domains, a psychometrically-based physical component summary (PCS), and a mental component summary (MCS) score. We scored responses to the SF-36 questionnaire using a norm-based scoring system.

2.3. Surgery and DBS programming

The DBS electrodes were stereotactically placed in the GPi using a CRW head frame (Integra, Plainsboro, New Jersey), a frame attached microdrive system (Axon Guideline System 3000, FHC, Inc, Bowdoin, ME) and MRI-guided targeting (Framelink software, Medtronic). Micro-electrode recording (Axon Guideline System 3000, FHC, Inc.) and electrophysiological mapping (Onetrack software, developed at Emory University) were utilized to confirm and refine the MRI-based target selection. The Onetrack software makes use of a three-dimensional anatomical model of the basal ganglia, which is adjusted to fit the anatomy based on MRI scans for each patient. Each recording track and the microelectrode advancement was monitored with the screen image presented by the Onetrack software. At the conclusion of the mapping procedure the DBS lead placement was chosen and the lead

was plotted on-screen in a size-proportional manner. This technique is critical to facilitate electrophysiological mapping and to increase the accuracy of DBS placement with a minimal number of penetrations. We also used Onetrack and the anatomical model postoperatively to produce reconstructions of the DBS lead placement based on postoperative MRI scans. This allowed us to optimize DBS programming, since it displays the actual electrode contact positions within the target and facilitates the selection of the optimal contact(s) for stimulation. Programming was initiated approximately four weeks after surgery. Patients were initially assessed after the first month and then every three months for up to 30 months.

3. Results

Table 1 summarizes the clinical features, prior pharmacotherapy, motor measures and stimulation parameters from four patients. Patient #1 developed extension of the neck and back associated with sitting. She also experienced episodic pain in right chest wall related to dystonia. Dystonia and associated pain significantly impaired her quality of life and activities of daily living. Patient #2 manifested dystonia as difficulty in standing upright, with a tendency to bend forward in a tonic fashion with phasic contractions; prominent when sitting, standing or walking and disappeared when lying down. In the patient #3 dystonia interfered with her ability to stand up straight. While standing she felt tightening of her abdomen and her trunk was pulled downward and forward. She also described being unable to breathe normally because of chest constriction. Patient #4 had trunk dystonia that pulled him into a severely extended position with some additional twisting character. None of these patients had a history of exposure to neuroleptics.

The average motor component of the Burke-Fahn-Marsden (BFM) dystonia rating scale prior to DBS surgery was 24.9 ± 18.1 . The average TWSTRS motor score for three patients with cervical involvement was 21.3 ± 5.9 before DBS surgery. Dystonia significantly impaired quality of life: average PCS and MCS scores from SF-36 prior to DBS surgery were 27.6 ± 12.9 and 51.5 ± 10.3 , respectively. Fig. 1A illustrates average values of eight health domain scales for each patient. In all domains except vitality (VT) and role-emotional (RE) the scales were below average. These scales increased to above average in all domains after DBS surgery (Fig. 1B). The improvement was evidenced by 109.38 ± 82.97 and $7.05 \pm 21.48\%$ percent increase in PCS and MCS respectively.

Fig. 2 illustrates the course of improvement in dystonia as measured with the BFM rating scale after DBS in three of four patients. BFM scores were not available during initial post-operative visits for patient #4, but he gradually improved over the course of two years. The inset of Fig. 2 depicts BFM score before DBS and about two years after the surgery in this patient. The responses for patients #1–3 were variable after first programming visit, improvement in total BFM ranged from 0 to 75% ($29.63 \pm 39.9\%$, mean $\pm$ SD, Fig. 2). The BFM continuously improved over time. The improvement in average motor BFM from all four patients was $87.6 \pm 11.5\%$ at 24-months. We assessed total severity scale of TWSTRS before and during at least the 24 month period after DBS surgery in three patients who also had neck involvement: the average improvement in the TWSTRS severity score was $71.5 \pm 12.7\%$.

3.1. Electrode locations and DBS parameters for optimum outcome

Average values and standard deviation for the distance of the active electrode contact from the mid-commissural point for best achieved BFM outcome was 20.2 ± 1.6 mm in the axial plane, 2.7 ± 1.4 mm in the sagittal plane, and -0.5 ± 1.6 mm in coronal plane. The average stimulation frequency was 82.5 ± 30.6 Hz, amplitude was 3.9 ± 0.4 V, and pulse-width was 157.5 ± 47.4 μ s at the time of best outcome assessed by BFM score in all four patients (Table 1).

4. Discussion

Patients with AAD demonstrated an excellent response to GPi DBS. Motor function rapidly improved after DBS surgery with nearly 30% change in the first month and over 80% change after two years. One patient became almost completely normal. Two of four patients had the common trunk flexion-type of AAD, while two had the relatively rare extension-type. Both subtypes had comparable benefit. Two previous case reports showed successful treatment of adult-onset axial dystonia with DBS, comprising three patients in total, but one patient had generalized dystonia with prominent trunk involvement [12,13]. Our study included four patients; all with phenomenology typical of AAD [2].

Our study objectively assessed an improvement in quality of life measured with SF-36 questionnaire using a norm-based scoring system. Such a scoring system is simple to interpret as there is no need to consider the norms of the eight health domain scales as the general population norm is built into the scoring algorithm. For all population scales, the means below 47 in all domains are considered as being below average for the range of the general population (User's Manual for the SF-36v2 Health Survey, Second Edition, Chapter 7, pages 81–84).

Analysis of electrical parameters revealed that higher pulse-width and amplitude of electrical stimulation (voltage) often correlated with the therapeutic success in AAD. Increase in voltage and pulse-width increase the electrical charge, hence stimulating neuronal soma and fibers with higher baseline stimulation thresholds. Increased amplitude (voltage) of electrical stimulation intuitively increases the volume of stimulated area around the electrode location. Hence an increase in pulse-width and/or voltage is not only capable for increasing the volume of stimulated neural substrate, but it also empirically stimulates neuronal soma and fibers with a wider spectrum of stimulation threshold. Stimulation frequency in three out of four patients was in the range of 60–70 Hz. Since low-frequency stimulation was associated with the clinical improvement in these patients, we did not make further attempts to increase stimulation frequencies. Therefore we cannot comment further on the influence of stimulation frequency on AAD.

In summary, our results provide further evidence for very good therapeutic outcome in patients with medically refractive AAD with bilateral GPi DBS. This represents an important treatment option for a very disabling disorder. We also observed that better outcome correlates with higher voltage and longer pulse-width DBS. Considering its generally poor response to medical therapy and significant impact on quality of life DBS should be considered early on in the course of this disorder.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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Appendix A. Supplementary data

Supplementary data related to this article can be found at <http://dx.doi.org/10.1016/j.parkreldis.2014.09.005>.

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Fig. 1.

Objective measurement of the quality of life before and after DBS is depicted. Panels A,B illustrate these measures before DBS and panels C,D are after DBS, when Burke-Fahn-Marsden rating scale was at the best. Each colored bar depicts one patient. Each patient is assigned the same color in each plot. PF: physical function; RP: role physical; BP: bodily pain; GH: general health; VT: vitality; SF: social functioning; RE: role-emotional; MH: mental health; PCS: physical health; MH: mental health. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

Fig. 2.

Trend of change in total motor component of Burke-Fahn-Marsden (BFM) dystonia rating scale. The value of BFM is plotted on y-axis. The x-axis depicts corresponding time in months. Each colored line illustrates individual subjects. Main figure depicts this analysis on three patients. Inset shows improvement in BFM motor scale for patient #4 two years after DBS surgery, immediate BFM scales were not available for this patient.

Table 1

Clinical profile, DBS stimulation parameters, and outcome in patients with adult-onset axial dystonia.

	Patient 1	Patient 2	Patient 3	Patient 4
Age at the time of surgery/gender	66/F	53/M	59/F	67/M
Age of onset	64	50	56	52
Anatomic involved	Lower face and jaw, neck, arms, trunk, leg	Neck, trunk	Trunk	Eyes, trunk, neck
Pharmacotherapy prior to DBS	Trihexyphenidyl, baclofen, cyclobenzaprine, botulinum toxin type A	Levodopa-carbidopa, trihexyphenidyl, baclofen, tetrabenazine, botulinum toxin type A	Trihexyphenidyl, levodopa-carbidopa	Baclofen, botulinum toxin type A
Pre-operative BFM score/percent improvement after DBS	36/87.5%	16/90.62%	4/100%	43.5/72.4%
Pre-operative TWSTRS severity scale/percent improvement after DBS	28/71.43%	19/84.21%	N/A (no cervical dystonia)	17/58.82%
Stimulus parameters for best outcome (volts, micro-seconds, Hertz)	Left: 3.5, 150, 60 Right: 3.8, 150, 60	Left: 3.4, 90, 130 Right: 3.6, 120, 130	Left: 4.0, 210, 60 Right: 4.0, 210, 60	Left: 4.5, 210, 80 Right: 4.0, 120, 80
Stimulation contact	Right 2 –ve, case +ve Left: 2 –ve, case +ve	Right 1 –ve, case +ve Left: 2 –ve, case +ve	Right 0 –ve, case +ve Left: 1 –ve, case +ve	Right 0 –ve, Case +ve Left: 1 –ve, case +ve