Long-Term Outcome of Idiopathic and Acquired Dystonia After Pallidal Deep Brain Stimulation: A Case Series

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Abstract

BACKGROUND

Among dystonia patients receiving globus pallidus internus (GPi) deep brain stimulation (DBS), long-term outcomes remain to be established.

OBJECTIVE

To report the long-term outcome of GPi DBS in a patient cohort with idiopathic and acquired dystonia.

METHODS

In this long-term follow-up cohort, there were 4 patients with idiopathic dystonia and 2 patients with acquired dystonia. The Burk-Fahn-Marsden Dystonia Rating Scale (BFMDRS) was used to evaluate 6 consecutive patients preoperatively and at 6 months, 12 months, and the last follow-up. The relationship between etiology and clinical improvement was analyzed. Stimulation parameters were evaluated for similarities and differences among these patients.

RESULTS

The mean follow-up of our cohort was 65.3 months (median 40.5 months). The average improvement in BFMDRS (mean ± SEM) was 56% ± 7.6, 67% ± 6.8 and 66% ± 9.7 at 6 months, 12 months, and last follow-up, respectively. There was greater improvement during long-term follow-up in the 4 patients with idiopathic dystonia than in the 2 patients with acquired dystonia. The 2 most ventral electrodes (contact 0 and 1) were activated in all 11 leads in this cohort. The average stimulation intensity, pulse width and frequency were 2.0 ± 0.24 mA, 252 ± 43 μs, and 99 ± 6.0 Hz, respectively.

CONCLUSION

Isolated dystonia, either monogenetic or idiopathic, usually responds better to GPi DBS than does acquired dystonia. Selection of patients by dystonia etiology, accurate placement of DBS leads in GPi targets, and proper stimulation programming are crucial to achieve better long-term outcomes.

Introduction

Dystonia is a movement disorder characterized by sustained or intermittent involuntary muscle contractions that cause abnormal movement or postures of the patient.[1] The symptoms of these patients may present as isolated dystonia or can be combined with other neurological symptoms.[1] The etiology of dystonia can be primary, either genetic or idiopathic, or secondary to a wide variety of neurological and systemic disorders.[2,3] The pathophysiology of dystonia is not yet clear. Studies suggest that dystonia is a network disorder, and the symptoms of dystonia often occur with pathophysiological conditions that disrupt the cortico-basal ganglia

circuit. Abnormal corticobasal ganglia circuit output signals can further cause cortical excitability alterations and aberrant synaptic plasticity.[4] In addition to phenomenology and classification, recent advances in genetic testing (e.g., next-generation sequencing) have made great progress in the diagnosis of primary dystonia. Many isolated dystonia and some combined dystonia are often caused by genetic disorders, and several candidate genes have been identified in different regions of the world, such as torsin family 1 member A (TOR1A, DYT1), thanatos-associated [THAP] domain-containing apoptosis-associated protein 1 (THAP1, DYT6) and lysine methyltransferase 2B (KMT2B, DYT28) mutations, in recent years.[2,5,6] This advancement in diagnosis has led to a more comprehensive evaluation of phenomenology and more appropriate selection of treatment strategies for primary dystonia patients, including deep brain stimulation (DBS).[2,5,6]

Currently, there is no cure for dystonia. In addition to pharmacological, physical, and botulinum toxin therapies, globus pallidus internus (GPi) DBS has become a major treatment for primary and secondary dystonia when the previously described methods fail to improve patient symptoms.[2,7] GPi DBS improves dystonic symptoms by electrical modulation of the abnormal neuronal signals in the basal ganglia output structure, i.e., GPi. This modulation may re-establish better signal transmission in the corticobasal ganglia circuit, which in turn reduces abnormal cortical excitability and normalizes aberrant synaptic plasticity in the motor cortex.[4] The fact that GPi DBS is effective in treating primary or secondary dystonia of various etiologies suggests that GPi DBS targets a common pathophysiological node point of dystonia. In addition, the aberrant synaptic plasticity of the motor cortex can be normalized by DBS treatment over time. This explains why it takes weeks or months of continuous pallidal stimulation for some dystonic symptoms to resolve.[8] It is noteworthy that the effect of DBS on dystonia may be variable when the pathology of the disease resides in the GPi or extends outside the cortico-basal ganglia circuit, which is often seen in secondary dystonia.[9] Furthermore, because of the different mechanisms underlying various primary genetic dystonias, the long-term outcome of GPi DBS was reported to vary among different patients.[6] In general, patients with primary dystonia responded better and more consistently to GPi DBS than patients with secondary dystonia.[3]

In contrast to Parkinson's disease (PD), which has a clearer pathophysiological mechanism and well-established treatment protocols, DBS for primary and secondary dystonia is still under investigation and development. This delay in progress is due to both heterogeneity in the etiology and the unclear pathophysiology of dystonia. The heterogeneous etiology of dystonia causes a major issue in patient selection for DBS.[10] There were few patients with each specific etiology receiving DBS treatment. With the increasing availability of newly developed genetic studies for primary dystonia and a better understanding of some secondary dystonias, an increasing number of cases receiving GPi DBS have recently been reported. These reports are helpful for improving the evaluation of the effects of DBS on different etiologies of dystonia. On the other hand, the unclear pathophysiology of dystonia also makes post-DBS programming in these dystonia patients challenging. There is great variability in the DBS parameter settings used within each dystonia subtype, and there are different approaches to DBS programming among different DBS centers. These settings were often based on heuristic evidence and personal experiences (mostly from DBS treatment for PD) rather than on the underlying pathophysiology of dystonia.[11] Unlike the programming for PD, which can be guided by its acute effect on tremor and rigidity, the delayed-onset DBS effect in dystonic patients makes programming even more difficult, and the protocol for setting optimal stimulation parameters is still not well established.[8] In addition, few reports have focused on the long-term outcomes of GPi DBS for dystonia.[12,13] Gaining experience with the

long-term outcomes of patients with highly heterogeneous etiologies can be helpful for the future development of DBS protocols for primary and secondary dystonia patients.

In this article, we report on a consecutive case series of six dystonia patients who received DBS therapy at our center. The etiologies, stimulation parameters and clinical outcomes are presented. The benefits of DBS therapy for primary and secondary dystonia with different etiologies and the findings pertaining to DBS programming in our cohort are also discussed.

Methods

Patients

We reviewed the medical records of 6 consecutive dystonia patients receiving DBS implantation surgery with the same neurosurgical team at National Taiwan University Hospital between 2009 and 2019. For all patients, the diagnosis of dystonia was made by an experienced movement disorder specialist. Next-generation sequencing was performed in patients with generalized isolated dystonia. The severity and disability of dystonic symptoms in each patient were recorded by a digital video recorder and were evaluated by a movement disorder specialist, a neurosurgeon, and a physician assistant using the Burke-Fahn-Marsden Dystonia Scale. The evaluation was performed before surgery and during regular follow-up visits after DBS. During the postoperative stage, all patients were followed and programmed by the same neurologist. The mean length of follow-up duration was 65.3 months (median 40.5 months, range 13-198 months). This study was approved by the institutional review board of National Taiwan University Hospital. Informed consent and permission to publish was provided by the patients. All methods have been performed in accordance with Declaration of Helsinki.

Neurosurgical procedure

All patients received complete presurgical evaluation by a neurosurgeon before DBS implantation. One day before surgery, we applied 5-6 fiducial markers on the skull for stereotaxic images and performed DBS trajectory planning on Stealth Station S7 (Medtronic, Minneapolis) with MRI-CT fusion images. On the day of surgery, each patient underwent bilateral frameless stereotactic implantation surgery targeting the GPi. All patients were sedated with intravenous anesthetics at the initial period of surgery followed by either awake (local anesthesia) or monitored anesthesia care (MAC) in the subsequent surgical procedures including micro-electrode recording (MER). The NexFrame (Medtronic, Minneapolis) stereotaxic apparatus was set up on a ring structure fixed to the burr hole under MRI image guidance on the Stealth Station S7. The trajectory was explored by microelectrode and Lead Point 4.0 (Medtronic, Minneapolis). The location of the GPi for implantation of the DBS electrodes was guided by electrophysiological information. A span of more than 4-6 mm in the GPi and optic tract signals induced by photic stimulation in a dark environment were required to confirm the proper implantation trajectory. Quadripolar electrodes (Model 3387 or 3389, Medtronic, Minneapolis) were placed after documentation of microelectrode position by intraoperative O-arm images (Medtronic, Minneapolis). The tips of the quadripolar electrodes were aligned with the lower border of the GPi. Each patient underwent MRI imaging to verify the correct lead position in the GPi and to exclude potential complications. Implantable pulse generators (IPGs, Medtronic, Minneapolis) were placed under general anesthesia 2-3 days after the DBS lead implantation surgery.

Deep brain stimulation programming

DBS with initial programming was usually performed 2-4 weeks after the lead implantation surgery, except in one patient (Patient F) who experienced a dystonic storm, and for whom DBS was initiated immediately, 1 day after implantation. Each electrode contact was tested in a monopolar configuration by steps of 0.5 mA to a maximum of 5.0 mA to determine the tolerance threshold by increasing the stimulation intensity. After the maximum tolerable intensity was detected, the maximum tolerable pulse width was also tested during this initial programming stage. We usually chose the most ventral electrode contacts for stimulation intensity just below the tolerance threshold of the patient in the first 2 weeks of DBS. If the patient's condition was not improved or remained uncertain during this period, we shifted to the contact dorsal to the previous one and applied a similar simulation intensity, which we then sustained for another 2 weeks to explore the best location for stimulation to relieve the dystonic symptoms. Furthermore, if no adequate effect was found during unipolar stimulation of each single electrode, we tried double monopolar or interleaving stimulation in the following programming sessions.

Statistical analysis

The Wilcoxon signed-rank test for matched pairs was used to compare BFMDRS scores at baseline, 6 months, and the last follow-up evaluation. A p value <0.05 was considered statistically significant.

Results

Clinical characteristics

The clinical and demographic characteristics of the six dystonia patients in this cohort, including two males and four females, are summarized in Table 1. The average age at dystonia onset was 25± 9.4 years (mean± sem), and the average age on receiving DBS was 32± 9.2 years. The average duration from symptom onset to receiving DBS surgery was 92± 27 months. All six patients had received oral medications, botulinum toxin injections, physical therapy and some form of alternative medicine treatments (such as acupuncture or chiropractic procedures) before DBS. Four of the six patients (Patients C, D, E, F) had generalized dystonia, one had hemidystonia (Patient B), and one (Patient A) had segmental dystonia. Two patients suffered from secondary dystonia, including one with cerebral palsy with a left basal ganglia lesion (Patient B) and one with genetically confirmed pantothenate kinase-associated neurodegeneration (PKAN) (Patient C). Four patients suffered from primary dystonia caused by different etiologies, including Meige's syndrome (Patient A), DYT-6 mutation (Patient D), and KMT-2B mutation (Patient E). No etiology was found in Patient F, who suffered from primary generalized dystonia, despite the extensive work-up for his diagnosis, including whole-exon sequencing. This patient also presented with pending dystonic storm, showing signs of fever, tachycardia, tachypnea, sweating and elevated CK levels, in addition to progressive severe generalized dystonia, before DBS surgery.

Table 1
Summary of patient clinical and demographic characteristics

Patient	Sex	Age at onset (yrs)	Age at DBS† surgery (yrs)	Symptom duration before DBS (months)	Dystonia distribution (Body regions involved)	Primary or Secondary	Etiology
Patient A	F	63	65	24	Focal (eyes, mouth, speech/swallow, neck)	Primary (Idiopathic)	Meige's syndrome (Crnio-facial dystonia)
Patient B	F	0	10	120	Hemi-body (neck, L arm, L leg, trunk)	Secondary	Cerebral palsy (Right putamen lesion)
Patient C	F	25	40	180	General (mouth, speech/swallow, arms, legs, trunk)	Secondary	NBIA† (PKAN†)
Patient D	M	7	12	60	General (neck, arms, trunk)	Primary (Genetic)	THAP1 (DYT-6)
Patient E	F	37	49	144	General (neck, back, fingers, arms, legs)	Primary (Genetic)	KMT2B (DYT-28)
Patient F	M	15	17	24	General (eyes, mouth, speech/swallow, neck, arms, legs, trunk)	Primary (Idiopathic)	Unknown

†Abbreviations: DBS, deep brain stimulation; NBIA, Neurodenegeration with Brain Iron Accumulation; PKAN, pantothenate kinase-associated neurodegeneration

DBS surgery

A total of 11 leads were implanted during the image-guided frameless stereotaxic procedures. There were no intracranial hemorrhages or infections during surgery in any of the six patients. One patient (Patient B) received unilateral right GPi lead implantation for treating her left hemidystonia, while all the other patients were implanted with bilateral GPi DBS. Three patients (Patients B, E, F) underwent the surgical procedure under general anesthesia, and the other three (Patients A, C, D) underwent the procedure under local anesthesia. Microelectrode recording (MER) was performed in all cases to clearly delineate the anatomical structures traversed, the dorsal and ventral borders of the GPi, and the optic tract and to determine the final implantation location. We considered performing all DBS implantation surgeries with local anesthesia to improve the quality of MER but chose general anesthesia if the patient had severe dystonia or could not tolerate the long surgical procedure well. DBS leads with wider span stimulation electrodes (10.5 mm, Model 3397) were implanted in the earlier three patients and electrodes with a shorter span (7.5 mm Model 3387) were chosen for the later three patients for better programming in GPi. Only one patient (Patient A) received nonrechargeable battery implantation due to economic reasons, while the other five patients underwent implantation with rechargeable IPGs (Table 2). Electrode locations were confirmed by post-operative imaging and the average distance between

electrode tip and optic tract (OT) was 2.67 ±0.18 mm (mean± sem) in the eleven DBS leas of the six patients. The mean distance between active electrode and OT was 5.19 ± 0.22 mm, which was later caulculated after DBS programming task finished. (Table 3)

Table 2
Surgical implants and targets in this cohort

Patient	Lead	Target	Battery
Patient A	3387	Bilateral GPi[†]	Kinetra
Patient B	3387	Right GPi	Activa RC
Patient C	3387	Bilateral GPi	Activa RC
Patient D	3389	Bilateral GPi	Activa RC
Patient E	3389	Bilateral GPi	Activa RC
Patient F	3389	Bilateral GPi	Activa RC

[†]Abbreviation: GPi, globus pallidus internus

Table 3

Locations of electrode tip and active electrodes in this GPi† DBS† cohort.

		DBS electrode tip			Electrode tip-to-Optic tract	DBS active contact			Active contact-to-Optic tract
		X	Y	Z	(mm)	X	Y	Z	(mm)
Patient A	L	-21.35	2.77	-2.32	3.125	-21.72	3.27	0.21	6.103
	R	20.21	1.98	-3.11	3.514	20.89	2.71	-0.43	5.325
Patient B	R	18.47	3.17	-6.33	2.669	17.34	6.13	-3.78	5.530
Patient C	L	-19.96	0.36	-2.38	3.432	-20.63	0.67	0.22	6.080
	R	19.98	4.12	-3.35	2.811	20.33	4.80	-0.69	5.497
Patient D	L	-22.38	2.90	-3.92	3.046	-22.77	3.70	-1.27	5.562
	R	21.83	3.46	-5.33	2.333	21.89	4.26	-2.71	3.990
Patient E	L	-19.59	2.81	-4.59	2.470	-20.06	3.85	-2.07	5.101
	R	19.78	3.22	-3.96	1.825	20.42	4.36	-0.40	5.089
Patient F	L	-20.18	2.91	-2.76	1.724	-20.88	3.98	-0.35	3.907
	R	21.72	4.87	-3.04	2.463	22.08	5.94	-0.54	4.900

*Abbreviation: GPi, globus pallidus internus; DBS, deep brain stimulation

DBS programming

MRI was performed after DBS surgery, and the location of the electrodes in the GPi was confirmed in each patient. (Figure 1) Unipolar configurations were tested in all patients initially, followed by bipolar or interleaving configurations. After 2-3 months of testing different combinations of stimulation configurations, one of the configurations was selected for the next mid- to long-term treatment. Programming parameters at the last follow-up were variable among our patients and are summarized in Table 4. In two patients (Patients A and B), single or multiple unipolar configurations were used. Interleaving configurations were selected in the other 4 patients according to the best benefit or the lowest number of side effects in the individual patient. In all 11 implanted leads, the most ventral electrode (contact 0) was activated in 10 leads (91%), and the next electrode (contact 1) was activated in all 11 leads (100%). More dorsal contact (contact 2) was only used in 2 leads 18%), while the most dorsal contact (contact 3) was not used in all patients. The average stimulation intensity (mean± sem) was 2.0± 0.24 mA among the six DBS patients. The average pulse width was 252± 43 μs, and the average stimulation frequency was 99± 6.0 Hz.

Table 4

Setting of DBS[†] parameters at last follow-up

Patient	Lt Hemisphere				Rt Hemisphere			
	Contact	Amp[†] (mA)	Pulse width (μs)	Frequency (Hz)	Contact	Amp (mA)	Pulse width (μs)	Frequency (Hz)
Patient A	0-1-2-C+	2.2	450	100	8-9-10-C+	2.6	450	100
Patient B	-	-	-	-	0-1-C+	1.0	450	60
Patient C	0-2+	2.6	80	90	8-10+	2.2	60	90
	1-3+	2.2	70	90	9-10+	2.3	60	90
Patient D	0-C+	1.9	450	125	8-C+	1.8	450	125
	1-C+	0.9	90	125	9-C+	0.8	90	125
Patient E	1-C+	2.2	450	60	9-C+	2.3	450	60
	0-3+	1.0	450	60				
Patient F	1-3+	2.2	120	120	9-11+	2.8	120	120
	0-3+	1.8	120	120	8-11+	2.0	120	120

[*]Abbreviation: DBS, deep brain stimulation; Amp, amplitude

Clinical outcomes

The BFMDRS motor subscores of the six patients at the preoperative stage and at 6 months, 12 months, and the last follow-up after DBS are summarized in Table 5. After DBS, the average improvement in the BFMDRS motor subscore was 56%± 7.6, 67%± 6.8 and 66% ± 9.7 (mean± sem) at 6 months, 12 months, and the last follow-up, respectively (Figure 2). Due to variable etiologies in our cohort, the treatment effects were not the same, and the clinical courses also differed after DBS. In the two patients with secondary dystonia (Patient B, C), the BFMDRS was stable in the first 12 months of DBS treatment, but the effect declined at the last follow-up visit (average follow-up: 68 months). In the four patients with primary dystonia (Patients A, D, E, F), there was a clear trend of persistent improvement after long-term DBS treatment at the last visit (average follow-up: 66 months). Among these 4 patients, more than 6 months were required to reach a plateau in the treatment effect for two of the patients (Patient E, F) after DBS. There was no correlation of disease duration and clinical outcome among these patients.

Table 5

BFMDRS† motor subscores before and after DBS†

Patient	Preop† BFMDRS	Postop† 6-months BFMDRS	%Change from preop	Postop 12-months BFMDRS	%Change from preop	At last follow-up BFMDRS	%Change from preop	Time to last follow-up (months)
Patient A	32	7.5	77%	9	72%	8	75%	198
Patient B	26.5	16.5	35%	17.5	34%	21.5	19%	77
Patient C	48	13.5	72%	14.5	70%	16.5	66%	50
Patient D	22	7.5	66%	5	77%	4	82%	31
Patient E	33	21.5	35%	10	70%	8.5	74%	23
Patient F	104	53	49%	21	80%	19.5	81%	13

*Abbreviations: BFMDRS, Burk-Fahn-Marsden Dystonia Rating Scale; DBS, deep brain stimulation; Preop, preoperation; Postop, postoperation

Discussion

In our series of 6 consecutive patients with medically refractory dystonia treated by GPi DBS, we observed significant improvement in dystonic symptoms, with 56%± 7.6 and 67%± 6.8 improvement in BFMDRS at the 6- and 12-month follow-ups in all patients. There was a persistent reduction in BFMDRS motor subscores in four of the six patients during the last follow-up visit. These four patients had idiopathic or genetically isolated dystonia, which included Meige's syndrome (Patient A), KMT-2b dystonia (Patient D), DYT6 dystonia (Patient E) and primary generalized dystonia of unknown etiology (Patient F). The improvements in patients A, D, E and F were 75%, 82%, 74% and 81%, respectively (mean± sem: 78%± 2.0), at the last follow-up visit. The two patients with acquired dystonia, one with cerebral palsy (Patient B) and the other with PKAN (Patient C), both showed some degree of deterioration in symptoms, as shown by the increase in BFMDRS motor subscore during the last follow-up visit. This discrepancy in results may be related to the influence of the underlying pathology of the secondary dystonia patients. Similar to the observations from previous studies, patients with idiopathic or genetic dystonia respond better and more consistently to GPi DBS than patients with acquired dystonia.[3,9,14]

Primary dystonia patients with different genetic etiologies, such as DYT-TOR1A (DYT1), DYT-THAP (DYT6), and DYT-KMT2B (DYT28) mutations, may show different responses to DBS treatment.[5,6,15] Although variable outcomes were reported in previous studies, Patient D, who had the DYT-THAP mutation and presented with dystonia involving the trunk rather than the orofacial region, showed excellent improvement after a 31-month follow-up.[16] DYT-KMT-2B was reported to have good improvement after GPi DBS, and a similar improvement was also observed in Patient E during the 23-month follow-up.[17] For Patient F in our cohort, who presented with

progressive generalized dystonia that rapidly developed into a dystonic storm, we could find no definite cause even after serial diagnostic work-up and whole-exon sequencing. This patient also responded well after GPi DBS, similar to other patients with primary dystonia. Our results suggest that primary dystonia patients with identifiable genetic causes or idiopathic etiologies should always be evaluated for DBS therapy when other treatments fail and before skeletal deformity develops. In patients with acquired dystonia, more careful evaluation of their underlying pathology and possible benefits of DBS should be performed before DBS because of the heterogeneous pathology and variable long-term outcomes after DBS in this population.[9]

GPi DBS has been considered one of the most effective treatments for status dystonicus (SD, or dystonic storm).[18–20] This is a life-threatening condition that can lead to respiratory, infectious, and metabolic complications and can even result in the need for intubation and ventilatory support. SD can occur in patients with rapidly progressing dystonia and is refractory to other medical treatments.[18,20,21] Patient F in our cohort presented with SD three months before surgery. After a brief diagnostic workup, emergent DBS implantation surgery was performed and GPi DBS was initiated urgently. After stimulating bilateral ventral GPi electrodes (contact 0 and 1) for 1 week, this patient showed some early symptomatic relief from SD, which prevented him from a life-threatening condition. This is also compatible with previous literature describing that SD usually responds to DBS sooner than does stable dystonic symptoms.[18–20] Although no genetic or other etiology was found in this patient, his dystonic symptoms continued to improve after GPi DBS until the last follow-up (13 months). This case clearly demonstrates that immediate action in performing GPi DBS for patients with SD has great value in relieving this emergent condition and that it can be life-saving.[19]

Programming of DBS in dystonic patients is still a challenging issue. In contrast to PD, in which the effect of DBS on tremor and rigidity can be observed within seconds to minutes, the DBS effect on dystonic symptoms usually has an onset of several days or weeks after stimulation is initiated, and the peak effect is often not reached until several months of GPi stimulation.[8,11] The phasic component of dystonia may respond to GPi DBS much earlier than the tonic component. This delayed effect was observed in our cohort with idiopathic isolated dystonia (Patients A, D, E, F). The BFMDRS motor subscore improved by an average of 56.6% at 6 months and reached 74.8% at 12 months and 78% at the last follow-up visit (average 66 months) after DBS therapy. There is considerable heterogeneity in stimulation settings among centers. Thus, the approach to GPi DBS programming is rather empirical.[8,11]

Checking whether the DBS electrodes are correctly placed in the posteroventral GPi by postoperative imaging is an important step in good DBS programming. Another step in assuring good DBS outcomes is selecting the best electrode location within GPi. This is usually done over a period of 6 to 8 weeks. The most ventral electrodes of the GPi, just above the optic tract (contact 0), are usually first selected in the first 2 weeks, followed by contacts 1, 2 and 3, each lasting for a 2-week period. Because the stimulation side effects are rather acute and the beneficial effects are often delayed in GPi DBS, the highest tolerable amplitude and pulse width in each electrode, just below the level that elicits adverse effects, are often used to maximize the stimulation effects while avoiding side effects. The side effects of GPi DBS often include paresthesia, muscle spasms, phosphenes, or nonspecific symptoms (malaise, nausea). After determining the location of the most effective electrode during this testing period, the best DBS electrode and its configurations are chosen for long-term treatment.[8] In a previous review study, data extraction from 192 publications and 1,505 patients, larger amplitude range (average 3.3 V), wider pulse width range (average 112~446 μs) and common frequency range

(average 131 Hz) were used with favorable outcomes.[11] In our cohort, the average stimulation parameters (2.0± 0.24 mA in intensity, 252± 43 μs in pulse width, and 99± 6.0 Hz in frequency) were similar to or lower than the average, but there was more common use of double unipolar or interleaving stimulation configurations. These findings may suggest that better stimulation location was more significant than higher stimulation settings for GPi DBS in this cohort.

Conclusion

Our case series provides added evidence that GPi DBS is an effective long-term treatment for dystonia patients whose symptoms are intractable to medical treatment. In this cohort, idiopathic isolated dystonia usually responded better to GPi DBS than did acquired dystonia. Dystonic storms in idiopathic isolated dystonia can be effectively treated by GPi DBS. There are great variations in programming parameters between patients, but the important step in programming, as shown in our cohort, is selecting the proper electrode location for stimulation. In conclusion, the three key steps, including selecting patients by dystonia etiology, accurate placement of DBS leads in GPi targets, and proper stimulation programming, are crucial in achieving better long-term outcomes. Larger prospective trials focusing on patient selection and programming protocols are needed to further improve patient outcomes and for future development.

Declarations

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Author contributions

C.H. Tai, S.H. Tseng wrote the manuscript. C.H. Tai, C.H. Lin, W.T. Lee, R.M. Wu examined the patients. S.C. Chou, S.H. Tseng performed the DBS surgery on these patients.

C.H. Tai, S.H. Tseng analyzed the clinical data. C.H. Lin, W.T. Lee, R.M. Wu analyzed the genetic data. All authors reviewed the manuscript.

Competing Interests Statement

All authors declare no competing interests.

Data availability statement

The clinical and image data acquired and analyzed during the current study are available from the corresponding author on request.

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Figures

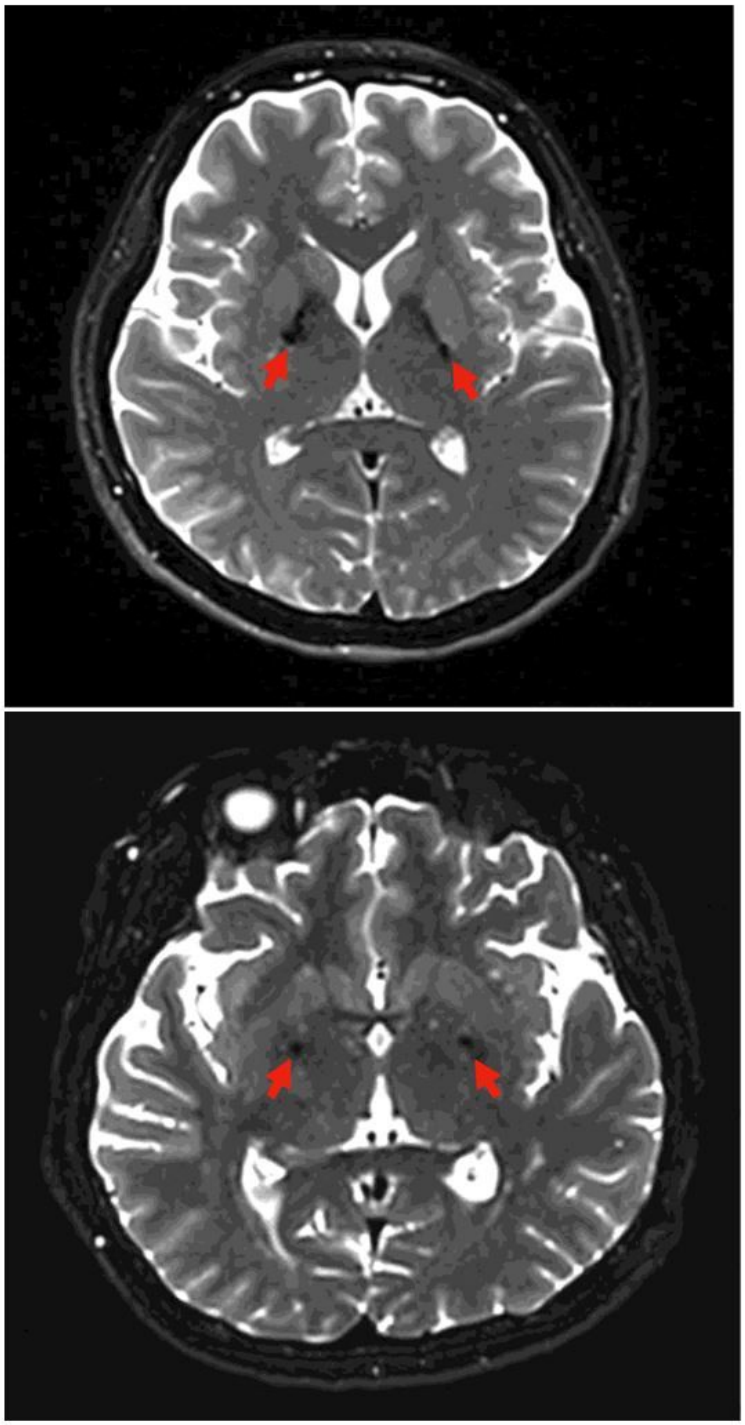

Figure 1

The location of bilateral GPi† DBS† leads as shown by post-operative MRI† in two patients in this cohort. (A) Secondary dystonia caused by PKAN† (B) Primary dystonia caused by DYT-KMT2B. The red arrows indicate the location of DBS electrodes in posteroventral palladium. †Abbreviations: GPi, globus pallidus internus; DBS, deep brain stimulation; MRI, magnetic resonance imaging; PKAN, pantothenate kinase-associated neurodegeneration

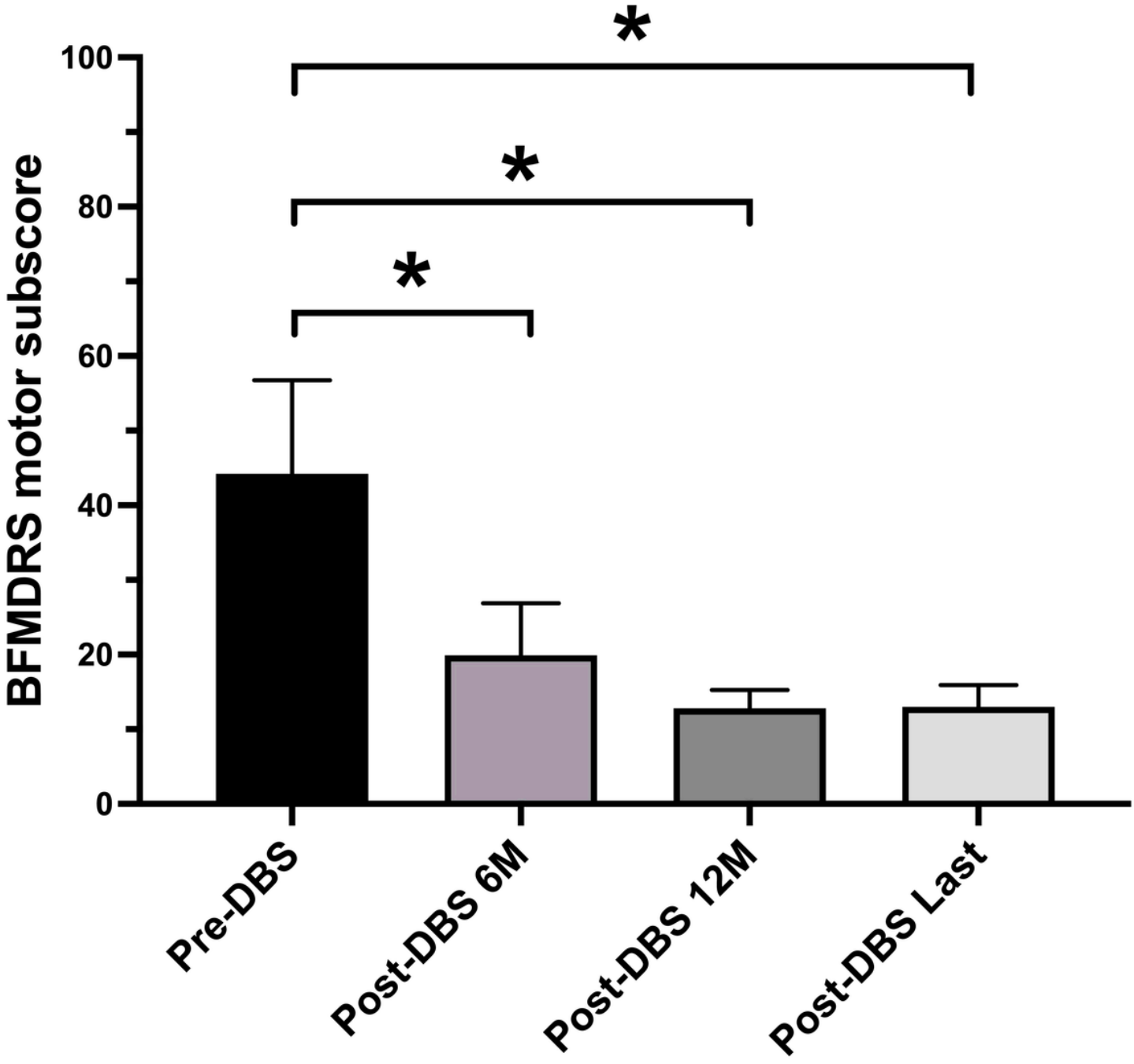

Figure 2

The columns showing average BFMDRS† motor subscore of entire cohort before, at 6-months, 12-months after DBS and at last follow-up. The columns indicate the mean value with SEM† of the six patients. (* indicate $p<0.05$) †Abbreviations: BFMDRS, Burk-Fahn-Marsden Dystonia Rating Scale; SEM, standard error of the mean