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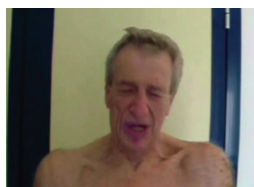
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Low-Voltage Bilateral Pallidal Stimulation for Severe Meige Syndrome in a Patient With Primary Segmental Dystonia: Case Report

BACKGROUND AND IMPORTANCE: Meige syndrome (MS) is an adult-onset segmental dystonia characterized by the combination of upper and lower cranial involvement. Its treatment is challenging and the use of oral medication or of botulinum neurotoxin treatment is not decisive. Deep brain stimulation of the globus pallidus internum (GPi DBS) has been used occasionally in severe cases.

CLINICAL PRESENTATION: We report the long-term efficacy of low-voltage chronic bilateral GPi DBS in a patient with segmental dystonia featuring severe MS and cervical brachial involvement. The patient received a bilateral ventroposterolateral GPi implant. Postoperative 3-dimensional reconstruction allowed checking of the definitive position of the electrode and contacts within the targeted nucleus. Following implant, the patient received bilateral low-voltage stimulation, consisting in amplitude of 1.3 V with a pulse width of 90 microseconds and a frequency of 130 Hz, yielding a current of 23 μ A. Clinical follow-up for 38 months showed a progressive and sustained improvement of dystonia with unchanged electrical settings throughout the observation period. The patient again undertook normal life activities.

CONCLUSION: Bilateral low-voltage GPi stimulation allowed efficient control of MS symptoms and the associated brachial cervical dystonia.

KEY WORDS: Deep brain stimulation, Dystonia, Globus pallidum stimulation, Meige syndrome, Movement disorders, Neurostimulation, Stimulation.

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Meige syndrome (MS) is a primary adult-onset segmental dystonia characterized by upper and lower cranial involvement.¹ Not uncommonly, dystonia spreads beyond cranial muscle groups to involve, in particular, the neck and the upper limbs.² The treatment of MS is challenging, because oral medications^{3,4} and botulinum neurotoxin (BoNT)^{5,6} often lead to partial or incomplete remissions. It has been recently shown that some patients with MS can benefit from deep brain stimulation of the globus pallidus internum (GPi DBS).⁷⁻¹² We describe

here the long-term efficacy of low-voltage chronic high-frequency bilateral GPi DBS in a patient who experienced segmental dystonia consisting of severe MS that had spread to involve the neck and the upper limbs. The value of this case is placed in the context of the available data on GPi DBS treatment of MS.

CLINICAL PRESENTATION

A right-handed attorney-at-law with no remarkable personal or family history and no exposure to neuroleptic drugs or other recognizable cause of dyskinesias developed a progressive bilateral blepharospasm in 1993, at the age of 56. By 1994, he developed involuntary lower face contractions and severe tongue spasms associated with difficulties in speech articulation and swallowing. A diagnosis of MS¹ was then formulated. There was no evidence of a somatoform or psychogenic disorder. Brain magnetic resonance imaging (MRI) was unremarkable. By 2001, dystonia gradually spread to further involve the cervical district.

ABBREVIATIONS: BoNT, botulinum neurotoxin; DBS, deep brain stimulation; GPi, globus pallidus internum; MS, Meige syndrome

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Upon examination in 2005, the patient presented with cranial and cervical dystonia, encompassing severe blepharospasm, oromandibular dystonia with prominent tongue protrusion, cervical dystonia with left head tilt and rotation to the left, proximal and distal upper limb dystonia (see Video 1, Supplemental Digital Content 1, <http://links.lww.com/NEU/A331>, which demonstrates dystonic features before surgical treatments. Note severe lower and upper face (with evident tongue protrusion) and cervical district involvement). He also reported temporomandibular pain, dysarthria, and dysphagia. *Gestes antagonistes* consisted in touching his chin with the right hand index and thumb and in chewing gum to facilitate speaking and swallowing (see Video 1, Supplemental Digital Content 1, <http://links.lww.com/NEU/A331>).

Benzodiazepines and trihexyphenidyl produced no benefit. Repeated local BoNT injections did not relieve dystonia. The patient was then scheduled for GPi DBS and provided written informed consent. Clinometric assessments were performed using the blepharospasm/oromandibular scale,¹³ the Toronto Western Spasmodic Torticollis Rating Scale,¹⁴ and the motor section of the Fahn-Marsden Dystonia Rating Scale.¹⁵

INTERVENTION

The patient was 68 years of age when stimulators were implanted bilaterally in the ventroposterolateral portion of the GPi, according to standard procedures.¹⁶ Preoperative MRI examination was performed to determine the intercommissural line, the intercommissural plane, and the midcommissural point. Under general anesthesia, a head frame (Leksell G; Elekta Instruments AB, Stockholm, Sweden) was tilted in the sagittal plane to the approximate AC-PC plane. A preoperative computed tomography (CT) examination was obtained in stereotactic conditions using a volumetric technique with a slice thickness of 1 mm and a gantry angle of 0°. Magnetic resonance images were fused with CT scans obtained under stereotactic conditions through an ad hoc workstation and software (Sofamor Danek Stealth Station, Frame-link 4.0; Medtronic, Inc., Memphis, TN) that provided stereotactic coordinates of the three-dimensional virtually built space.

The following coordinates were used for GPi targeting: 2 mm anterior to the midpoint of the AC-PC line, 20 mm lateral to the midline, and 6 mm below the intercommissural plane. These coordinates were used to identify a point that appeared to be in the GPi on the fused MRI images. A rigid cannula was inserted through a precoronal paramedian burr hole. A quadripolar DBS electrode (DBS-3389; Medtronic, Inc., Minneapolis, MN) was then inserted into the ventroposterolateral portion of each GPi. Intraoperative microelectrode recording was not performed. To verify the occurrence of possible unacceptable postoperative side effects during chronic stimulation, intraoperative test stimulation was performed in bipolar mode using contacts 0-3+, 130 Hz, and a 90-microsecond pulse width (3625 external tester; Medtronic, Inc., Minneapolis, MN). Voltage threshold for tonic facial contraction was 7.8 V for the left side GPi and 8.1 V for the right side GPi; tonic hand contraction was elicited only by stimulating left side GPi over 8.4 V. DBS electrode was then fixed and secured in the burr hole by using a flange (Ethicon Bioplate Co., J&J, Raynham, MA).

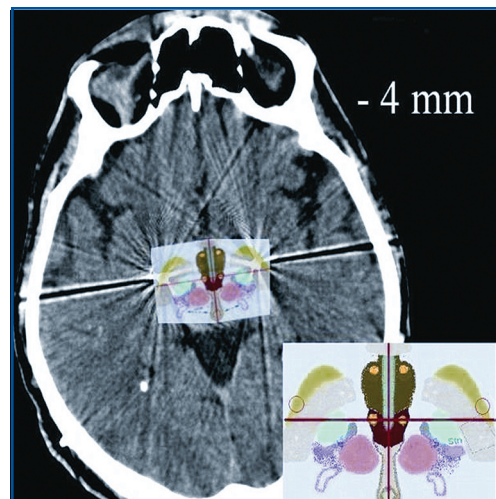


FIGURE. Postoperative CT slice merged with Franzini's stereotactic atlas, 4 mm below the commissural plane. The artifacts of active contacts are present on both brain sides and are represented by red circles on the corresponding atlas slice (lower right). Green = globus pallidus internum, pale blue = subthalamic nucleus, gray = internal capsule (Snapshot from the virtual ventriculography program by Wandor software, Dolgo, PC, Italy).

After that and during the same surgical session, both electrodes were connected to a pulse generator (Soletra; Medtronic, Inc.). A postoperative CT scan was used to control the electrode positioning and to check for potential surgical complications before starting stimulation. Finally, 3-dimensional reconstruction based on postoperative CT was performed to check the definitive position of the electrodes and contacts within the targeted nuclei (Figure).

Twelve hours after the implant, the patient presented a right-sided faciobrachial paresis: a further CT scan revealed a little hemorrhage along the left lead track, contiguous to the genu of the internal capsule. A gradual recovery occurred during the next 24 hours, with the only sequela of a mild lower right facial paresis. The surgical procedure was otherwise uneventful.

Stimulation parameters were checked to identify the acute effects on dystonic movements and postures and to determine the threshold for side effects. Chronic stimulation started 4 days after surgery; amplitude and pulse width were gradually increased over a period of a week to reach the following final electrical settings on either side: amplitude, 1.3 V; pulse width, 90 microseconds; frequency, 130 Hz; contacts, 0 and 1 were cathodes with positive case. A total current of 23 μ A was delivered through the electrodes. Stimulation settings remained unchanged from the first week on, because we noted an acute effect of stimulation on dystonic signs, with gradual recovery of blepharospasm and oromandibular dystonia within days; the effect on neck and upper limb dystonia occurred later. Because of the clearly progressive clinical improvement, we were encouraged to further fix these

TABLE 1. Patient's Dystonia Scores Before and After Bilateral Globus Pallidus Internum Deep Brain Stimulation^a

	Before Implant	6 Mo	12 Mo	38 Mo
BS/OMD-RS				
<i>BS score</i>	4	1	0	0
<i>OMD score</i>	4	0	0	0
FMDRS-motor score				
<i>FMDRS eyes</i>	8	0.5	0	0
<i>FMDRS mouth</i>	8	0.5	0	0
<i>FMDRS speech and swallowing</i>	12	4	0	0
TWSTRS-total				
<i>TWSTRS-severity score</i>	31	3	4	4
<i>TWSTRS-disability score</i>	26	0	0	0
<i>TWSTRS-pain score</i>	6	0	0	0

^a BS/OMD-RS, Blepharospasm and Oromandibular Rating Scale; FMDRS, Fahn-Marsden Dystonia Rating Scale; TWSTRS, Toronto Western Spasmodic Torticollis Rating Scale; mo, months.

initial stimulation settings and observe their medium and long-term benefits.

At 6 months, clinical examination showed an almost complete recovery of dystonia with a complete relief of pain; blepharospasm, speech, and swallowing difficulties had almost completely resolved. Twelve months after implant, a further clinical improvement was evident. The marked improvement was still appreciable 38 months after the implant without the occurrence of fluctuations of motor conditions. Table 1 and supplemental videos (see Video 1, Supplemental Digital Content 1, <http://lww.links.com/NEU/A331> and Video 2, Supplemental Digital Content 2, <http://lww.links.com/NEU/A332>, which demonstrates dystonic features, at different follow-ups after GPi stimulation with evidence of residual postoperative lower right face paresis) show the patient's preoperative and postoperative clinical conditions.

The patient returned to a normal life and started a new job as a theater manager.

DISCUSSION

MS is a segmental adult-onset dystonia.^{1,17} The clinical course is variable and often complicated by dystonia spread to extracranial sites. Local BoNT injections are a first-line treatment option for blepharospasm,^{18,19} but no recommendations are available for the oromandibular component of MS. In cases, such as this patient, where medical options are of limited efficacy, DBS stands a viable alternative. Uncontrolled and controlled studies have yielded promising results^{16,20,21} in keeping with the observation that axial signs of dystonia may respond to DBS.^{16,21}

Table 2 compares stimulation settings and outcomes in 14 MS patients treated with GPi DBS. Earlier follow-up reached 24 months⁸ compared with 38 months in the present case. Furthermore, previous reports have applied a wide range of stimulation settings, with amplitude ranging from 2.5 to 5.2 V, frequency from 60 to 185 Hz, and duration of impulse from 90 to 500 microseconds. In this patient, voltage and pulse width were lower than previously reported. According to the postoperative reconstruction performed in most cases, pallidal stimulation site also differed among reported MS cases: it was posterior in 7, posteroventral in 4, and undetermined in the remaining 3 cases.

In all but one²² of the earlier patients, the clinical benefit on dystonia prevailed in the upper face compared with the lower cranial muscles. The article reporting lower cranial improvement used low-voltage stimulation with long pulse duration.²² We found that low-amplitude stimulation (1.3 V) is appropriate to attain a sustained clinical and functional control of both upper and lower facial dystonia in MS. This is confirmed by a 3-year follow-up showing progressive and stable benefit over time. It has been previously reported that clinical habituation to stimulation may occur 1 week⁹ to 6 months²² after continuous stimulation. In the present patient, there was no habituation and no need to vary electrical setting after the first postoperative week.

We decided not to withdraw stimulation in the postoperative period. This would have allowed verifying the possible recurrence of dystonia features, but may have exposed the patient to unnecessary distress. Accidental arrest of stimulation is associated with recurrence of mobile (phasic) dystonia features within few minutes and of tonic features with a longer delay.²³

The present observation further emphasizes the role played by the GPi in the pathophysiology of MS. In patients with generalized dystonia it has been shown that posteroventral GPi locations provide better control of axial dystonia features (in particular, trunk and neck).²⁴ Furthermore, reports on MS cases secondary to GPi lesions indicate that this basal ganglia component is particularly involved in this type of dystonia.^{25,26}

Clinical outcome after DBS implant most likely depends on contact location: in the near future, more standardized protocols will provide a somatotopically oriented implant procedure aimed to give the maximal clinical improvement on dystonia.

CONCLUSION

Low-voltage stimulation of the ventroposterolateral component of the globus pallidus internum is efficacious in controlling MS and the associated spread of dystonia to the cervical and upper-limb segments. The efficacy and safety profiles of GPi DBS treatment for severe MS is favorable. With low-voltage stimulation, there was no evidence for habituation even in the long term. Further studies are necessary to better elucidate the pathophysiology of dystonia and the ways by which electrical modulation of corticobasal ganglia-thalamic-cortical circuitry counteracts this movement disorder.

TABLE 2. Clinical Features and Improvement in Meige Syndrome Patients After Globus Pallidus Internum Stimulation^a

References	Patient/ Sex	Age at Implant, y	Disease Duration, y	Last FU, mo	Extracranic Involvement	Site of DBS Implant	Best Stimulation Parameters	Dystonia Score Improvement at Last FU
Muta et al, 2001 ¹⁰	1/F	61	18	NA	Neck, trunk, R hand	Bil GPI	3.6 V, 500 μ s, 60 Hz.	FMDRS 80%
Capelle et al, 2003 ⁸	1/F	60	5	24	None	Bil GPI	4.3 V, 210 μ s, 130 Hz.	FMDRS eyes 92%, FMDRS mouth 75%, FMDRS speech/swallowing 30%
Footte et al, 2005 ²²	1/M	47	5	15	None	PV GPI	R: 2.5 V, 450 μ s, 185 Hz; L: 3.3 V, 450 μ s, 185 Hz.	UDRS eyes 57%, UDRS lower face 83%
Houser and Waltz, 2005 ⁹	1/F	46	2	6	None	PV GPI	R: 3.8 V, 210 μ s, 160 Hz; L: 2.6 V, 210 μ s, 160 Hz.	FMDRS 75%, UDRS 85%
Opherk et al, 2006 ¹¹	1/M	65	NA	4	Torticollis	Bil GPI	NA	NA
Ostrem et al, 2007 ¹²	6/M 1/F	62.2 (range 52–70)	8.2 (range 2–20)	6	Mild arm or trunk dystonia in two pts	P GPI	Range: 2.9–5.0 V, 90–210 μ s, 145–185 Hz.	FMDRS eyes 78.5%, FMDRS mouth 73.3%, FMDRS speech/ swallowing 48%; TWSTRS 54%
Blomstedt et al, 2008 ⁷	1/M	44	18	18	R hand tremor	PV GPI	R: 5.2 V, 120 μ s, 145 Hz; L: 4.9 V, 120 μ s, 145 Hz.	FMDRS 71.5%
Present patient	1/M	67	11	38	Neck, upper limbs	PV GPI	1.3 V, 90 μ s, 130 Hz.	BS/OMD-RS 100%, FMDRS eyes 100%, FMDRS mouth 100%, FMDRS speech/swallowing 100%; TWSTRS 93%

^a FMDRS, Fahn-Marsden dystonia rating scale; TWSTRS, Toronto Western Spasmodic Torticollis Rating Scale; UDRS, Unified Dystonia Rating Scale; FU, follow-up; mo, months; L, left; R, right; F, female; M, male; Bil, bilateral; NA, not available; DBS, deep brain stimulation; GPI, globus pallidus internum; PV GPI, posteroventral GPI; P GPI, posterior GPI.

Disclosure

A. Albanese and A. Franzini have received occasional honoraria from Medtronic Inc.

REFERENCES

- Tolosa E, Kulisevsky J, Fahn S. Meige syndrome: primary and secondary forms. *Adv Neurol*. 1988;50:509-515.
- Jankovic J, Ford J. Blepharospasm and orofacial-cervical dystonia: clinical and pharmacological findings in 100 patients. *Ann Neurol*. 1983;13(4):402-411.
- Paleacu D, Giladi N, Moore O, Stern A, Honigman S, Badarny S. Tetrabenazine treatment in movement disorders. *Clin Neuropharmacol*. 2004;27(5):230-233.
- Yardimci N, Karatas M, Kilinc M, Benli S. Levodopa treatment in Meige's syndrome. *Acta Neurol Scand*. 2006;114(1):63-66.
- Ceballos-Baumann AO, Gasser T, Dengler R, Oertel WH. [Local injection treatment with botulinum toxin A in blepharospasm, Meige syndrome and hemifacial spasm. Observations in 106 patients]. *Nervenarzt*. 1990;61(10):604-610.
- Costa J, Espirito-Santo C, Borges A, et al. Botulinum toxin type A therapy for blepharospasm. *Cochrane Database Syst Rev*. 2005;(1):CD004900.
- Blomstedt P, Tisch S, Hariz MI. Pallidal deep brain stimulation in the treatment of Meige syndrome. *Acta Neurol Scand*. 2008;118(3):198-202.
- Capelle HH, Weigel R, Krauss JK. Bilateral pallidal stimulation for blepharospasm-oromandibular dystonia (Meige syndrome). *Neurology*. 2003;60(12):2017-2018.
- Houser M, Waltz T. Meige syndrome and pallidal deep brain stimulation. *Mov Disord*. 2005;20(9):1203-1205.
- Muta D, Goto S, Nishikawa S, et al. Bilateral pallidal stimulation for idiopathic segmental axial dystonia advanced from Meige syndrome refractory to bilateral thalamotomy. *Mov Disord*. 2001;16(4):774-777.
- Opherk C, Gruber C, Steude U, Dichgans M, Botzel K. Successful bilateral pallidal stimulation for Meige syndrome and spasmodic torticollis. *Neurology*. 2006;66(4):E14.
- Ostrem JL, Marks WJ Jr, Volz MM, Heath SL, Starr PA. Pallidal deep brain stimulation in patients with cranial-cervical dystonia (Meige syndrome). *Mov Disord*. 2007;22(13):1885-1891.
- Berardelli A, Formica A, Mercuri B, et al. Botulinum toxin treatment in patients with focal dystonia and hemifacial spasm. A multicenter study of the Italian Movement Disorder Group. *Ital J Neurol Sci*. 1993;14(5):361-367.
- Kaji R, Osawa M, Yanagisawa N. [Inter-rater reliability while using the Toronto Western Spasmodic Torticollis Rating Scale (TWSTRS) in patients with cervical dystonia]. *Brain Nerve*. 2009;61(1):65-71.
- Burke RE, Fahn S, Marsden CD, Bressman SB, Moskowitz C, Friedman J. Validity and reliability of a rating scale for the primary torsion dystonias. *Neurology*. 1985;35(1):73-77.
- Zorzi G, Marras C, Nardocci N, et al. Stimulation of the globus pallidus internus for childhood-onset dystonia. *Mov Disord*. 2005;20(9):1194-1200.
- Elston JS. Blepharospasm and Meige syndrome: a review of diagnostic, aetiological and treatment approaches. *J Psychosom Res*. 1986;30(1):103.
- Albanese A, Barnes MP, Bhatia KP, et al. A systematic review on the diagnosis and treatment of primary (idiopathic) dystonia and dystonia plus syndromes: report of an EFNS/MDS-ES Task Force. *Eur J Neurol*. 2006;13(5):433-444.
- Simpson DM, Blitzer A, Brashear A, et al. Assessment: Botulinum neurotoxin for the treatment of movement disorders (an evidence-based review): report of the

Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology. *Neurology*. 2008;70(19):1699-1706.

20. Kupsch A, Benecke R, Muller J, et al. Pallidal deep-brain stimulation in primary generalized or segmental dystonia. *N Engl J Med*. 2006;355(19):1978-1990.
21. Vidailhet M, Vercueil L, Houeto JL, et al. Bilateral deep-brain stimulation of the globus pallidus in primary generalized dystonia. *N Engl J Med*. 2005;352(5):459-467.
22. Foote KD, Sanchez JC, Okun MS. Staged deep brain stimulation for refractory craniofacial dystonia with blepharospasm: case report and physiology. *Neurosurgery*. 2005;56(2):E415.
23. Grips E, Blahak C, Capelle HH, et al. Patterns of reoccurrence of segmental dystonia after discontinuation of deep brain stimulation. *J Neurol Neurosurg Psychiatry*. 2007;78(3):318-320.
24. Tisch S, Rothwell JC, Bhatia KP, et al. Pallidal stimulation modifies after-effects of paired associative stimulation on motor cortex excitability in primary generalised dystonia. *Exp Neurol*. 2007;206(1):80-85.
25. Herraiz J, Roquer J, Escudero D, Maso E. Meige's syndrome and bilateral pallidal calcification. *J Neurol*. 1988;235(6):384.
26. Yoshida M, Sakai T, Kimura S. Meige's syndrome with Bipallidal ischemic lesions. *Mov Disord*. 2005;20(9):1232-1234.

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COMMENT

This single report shows good effectiveness of bilateral deep brain stimulation (DBS) of the globus pallidus internum in a single patient with Meige syndrome (MS), replicating several other reports but distinct in showing effects at only 1.4 V. It is unclear why the low voltage is effective in this case compared with others, possibilities including (1) that others did not try this low voltage, (2) location of the DBS leads (which is not substantially different than other reports, individual variability notwithstanding), (3) difference in this individual patient, or (4) that low voltage is indeed different than higher voltages. Of course, the critical parameter is not the voltage per se, but the current density and the voltage gradient it induces in the surrounding tissue. Ranck discussed many years ago that there can be depolarization close to the current source and hyperpolarization beyond that: one wonders whether the latter is working at odds with the former, and by limiting the size of the field one is actually improving results. It will be interesting to see follow-up of low-voltage and smaller pulse width stimulation in a cohort of patients, both with MS and more generalized dystonias.

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