

## Clinical Article

# Outcome of Pallidal Deep Brain Stimulation in Meige Syndrome

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**Objective :** Meige syndrome is the combination of blepharospasm and oromandibular dystonia. We assessed the surgical results of bilateral globus pallidus internus (GPI) deep brain stimulation (DBS) in patients with medically refractory Meige syndrome.

**Methods :** Eleven patients were retrospectively analyzed with follow-ups of more than 12 months. The mean follow-up period was  $23.1 \pm 6.4$  months. The mean age at time of surgery was  $58.0 \pm 7.8$  years. The mean duration of symptoms was  $8.7 \pm 7.6$  years. DBS electrodes were placed under local anesthesia using microelectrode recording and stimulation. After  $2.4 \pm 1.3$  days of trial tests, the stimulation device was implanted under general anesthesia. Patients were evaluated using the Burke-Fahn-Marsden Dystonia Rating Scale (BFMDRS).

**Results :** BFMDRS total movement scores improved by 59.8%, 63.5%, 74.1%, 74.5%, and 85.5% during the immediate postoperative period of test stimulation, 3, 6, 12, and 24 months ( $n = 5$ ) after surgery, respectively. The BFMDRS total movement scores were reduced gradually and the results reached statistical significance in the postoperative period (test period,  $p < 0.001$ ; 3 months,  $p < 0.001$ ; 6 months,  $p = 0.003$ ; 12 months,  $p < 0.001$ ; 24 months,  $p = 0.042$ ). There was no statistical difference between 12 months and 24 months. BFM subscores improved by 63.3% for the eyes, 80.9% for the mouth, 68.4% for speech/swallowing, and 87.9% for the neck at 12 months after surgery. The adverse effects were insignificant.

**Conclusion :** The bilateral GPI-DBS can be effective for the treatment of intractable Meige syndrome without significant side effects.

**KEY WORDS :** Globus pallidus · Meige syndrome · Deep brain stimulation.

## INTRODUCTION

In 1910, Henry Meige, a French neurologist, coined the term spasme facial median to describe a form of spasmodic torticollis consisting of spontaneous adult-onset dystonic movements of facial muscles causing blepharospasm and a variety of dystonic spasms of the lower face, jaw, and neck<sup>6</sup>. Meige syndrome typically begins in the fifth or sixth decade of life<sup>2</sup>. Frequently, symptoms do not support the benefits of medication or botulinum toxin injections<sup>3,5,10</sup>. There is a growing interest in the use of deep brain stimulation (DBS) in medically refractory forms of dystonia. DBS of the globus pallidus internus (GPI) has been shown to be effective in the

treatment of juvenile and adult onset primary generalized dystonia and segmental dystonia<sup>3,6</sup>. However, the experience of GPI-DBS in the treatment of segmental cranial dystonia, such as Meige syndrome, is still limited.

In this report, we retrospectively assessed the experiences of 11 patients with medically refractory Meige syndrome. The purpose of this study was to analyze the effect of GPI-DBS in the patients.

## MATERIALS AND METHODS

Between August 2006 and July 2008, 11 patients (9 females and 2 males) met the following criteria : 1) idiopathic cranial-cervical dystonia (blepharospasm, lower facial and oromandibular dystonia, with or without the involvement of cervical muscles), 2) severe functional impairment despite medical management, including failed botulinum toxin therapy, 3) absence of secondary causes of dystonia, 4) no history of exposure to neuroleptics, 5) normal neurological exam except for

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dystonia, and 6) normal magnetic resonance imaging (MRI) of the brain. None of the patients had major dementia, a familial history of dystonia, or psychiatric disorders except for one female patient. This patient presented with symptoms of Meige syndrome six years before she was diagnosed as schizophrenia. A MRI of the brain and a medical laboratory evaluation did not reveal abnormal findings, and the neurological examination was normal with the exception of symptoms of Meige syndrome.

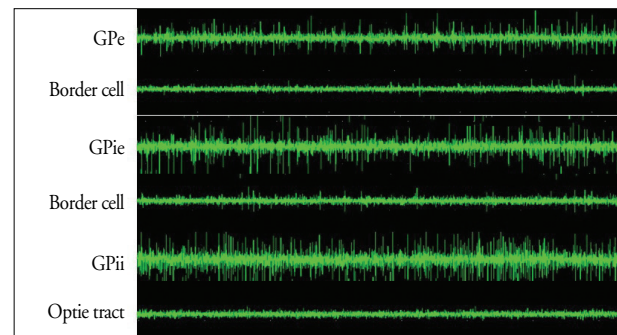
The clinical characteristics of the patients are summarized in Table 1. The ages of the patients ranged from 45 to 70 years (mean  $58.0 \pm 7.8$  years). The mean duration of symptoms was  $8.7 \pm 7.6$  years (range 1-20). The dystonia syndrome began with blepharospasm in nine patients and oromandibular dystonia in two patients. Nine patients had cervical dystonia. Three patients had slight pulling cervical dystonia, three patients had mild torticollis, two patients had moderate pulling cervical dystonia, and one patient had extreme pulling cervical dystonia. All of them had mobile or phasic type of the cervical dystonia. Patient 4 had a history of bilateral full-extended myectomy around the upper eyelashes for the treatment of blepharospasm. Patient 5 had a history of double eyelid operation for the treatment of blepharospasm. All patients had received botulinum toxins and medications with no remarkable improvement.

All evaluations were performed by one neurosurgeon and one neurologist using the Burke-Fahn-Marsden Dystonia Scale (BFMDRS) before and every three months after surgery<sup>1)</sup>. The mean follow-up period was  $23.1 \pm 6.4$  months (range 12-35) with bilateral GPi-DBS, and 5 (45.4%) of 11 patients were available for follow-up at 24 months after surgery.

The 11 patients underwent simultaneous bilateral implantation of quadripolar DBS leads (DBS Model 3387, Medtronic) into the GPi under local anesthesia. Electrode implan-

tation was based on indirect and direct targeting using a 1.5-tesla MRI (General Electric, USA) and a Neurosurgery Simulator (Dimos, Seoul, Korea) as surgical planning tools refined using microelectrode recording and stimulation (Fig. 1). The initially planned mean target was  $3.0 \pm 0.6$  mm the anterior to the mid-commissural point,  $22.2 \pm 1.3$  mm lateral to the midline, and  $4.0 \pm 0.0$  mm below the anterior commissure-posterior commissure plane. The mean distance between the anterior and posterior commissure was  $22.5 \pm 1.4$  mm. The mean arc and sliding angles were  $61.9 \pm 3.5$  and  $5.6 \pm 3.1$  degrees, respectively. Intraoperative test stimulation using a microelectrode was performed at 1.0 to 5.0 V, 200  $\mu$ s and 130 Hz to check motor, sensory and visual responses. All patients underwent a postoperative MRI or computed tomography to assess the electrode's position and surgical conditions.

The mean locations of the final 22 electrodes were  $21.6 \pm 1.3$  mm lateral to the midline,  $2.8 \pm 0.7$  mm anterior to the mid-commissural point, and  $4.0 \pm 0.0$  mm below the mid-commissure plane. Fig. 2 shows the final lead location in the axial plane passing through the anterior and posterior commissures. After  $2.4 \pm 1.3$  days (range 1-5) of trial testing



**Fig. 1.** Microelectrode recordings in the globus pallidus of patient 11. GPe : globus pallidus externa, GPie : external segment of globus pallidus internus, GPii : internal segment of globus pallidus internus.

**Table 1.** Clinical characteristics of patients with Meige syndrome

No.	Sex	Age at onset (yr)	Duration of illness (yr)	Site of onset	Preoperative BFMDRS	BFMDRS at 12 months after surgery	Postoperative follow-up(mo)	Cervical involvement
1	F	41	20	E	17	8	35	Yes
2	F	62	4	M	34	10	29	Yes
3	F	43	20	E	24	0	28	Yes
4	M	51	6	E	17	5.5	25	No
5	F	53	2	E	22	0	24	No
6	F	56	4	E	30	4.5	23	Yes
7	F	37	8	M	20	0	23	Yes
8	F	69	1	E	32	18	20	Yes
9	M	44	3	E	20	3	19	Yes
10	F	45	8	E	26	10	16	Yes
11	F	43	20	E	28	10	12	Yes

BFMDRS : Burk-Fahn-Marsden dystonia rating scale, E : eye, M : mouth

(Model 3625 external tester, Medtronic Inc.) in the hospital ward, the stimulation device (Solettra, Medtronic Inc.) was implanted subcutaneously in the subclavicular area while the patient was under general anesthesia. The stimulation parameters of the test stimulation were : frequency, 130 Hz; pulse width, 60 (in two patients) or 210 (in nine patients)  $\mu$ s; and amplitude, 2.0 to 3.5 V. The pulse generator was programmed on the first postoperative day. The frequency was set at 60, 130, and 185 Hz, the pulse width was set at 60, 90, 120, 180 and 210  $\mu$ s, and the voltage was set 2.6 to 5.0 V at the last follow-up (Table 2).

The statistical significance of the changes in clinical rating scales at 3, 6, 12, and 24 months after surgery compared with the baseline were assessed using the Wilcoxin signed rank test (paired). A significance threshold of 0.05 was used. We also analyzed preoperative factors to determine which correlated with outcomes in each patient.

**Table 2.** Summary of patients' data

No. of patients	11
Age at onset (yr)	49.4 $\pm$ 9.7 (range 37-69)
Sex-no. (%)	
Male	2 (18)
Female	9 (82)
Duration of illness (yr)	8.7 $\pm$ 7.5 (range 1-20)
Site of onset-no. (%)	
Eye	9 (82)
Mouth	2 (18)
Stimulation measurements at latest follow-up	
Amplitude (V)	3.4 $\pm$ 0.6 (range 2.6-5.0)
Pulse width ( $\mu$ s)	133.6 $\pm$ 57.4 (range 60-210)
Frequency (Hz)	143.1 $\pm$ 38.1 (range 60-185)
Follow-up (mo)	23.0 $\pm$ 6.3
Preoperative BFMDRS	24.5 $\pm$ 5.9
Postoperative BFMDRS	
During test period	9.9 $\pm$ 5.3
At 3 months after surgery	8.9 $\pm$ 7.7
At 6 months after surgery	6.4 $\pm$ 6.8
At 12 months after surgery	6.3 $\pm$ 5.6
At 24 months after surgery	3.3 $\pm$ 1.8
12 Mo % improvement from baseline (%)	74.5 $\pm$ 19.8

## RESULTS

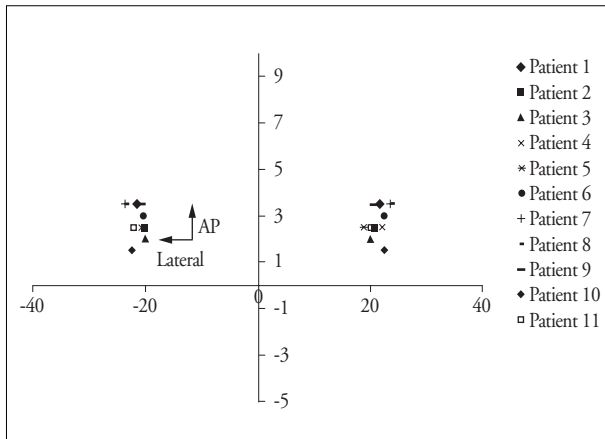
The mean BFMDRS total movement scores were the following : 24.5  $\pm$  5.9 at baseline; 9.9  $\pm$  5.3 during the immediate postoperative period of test stimulation; 8.9  $\pm$  7.7 at 3 months after surgery; 6.4  $\pm$  6.8 at 6 months after surgery; 6.3  $\pm$  5.6 at 12 months after surgery; and 3.3  $\pm$  1.8 at 24 months after surgery (Table 2). The mean BFMDRS total movement scores improved by 59.8  $\pm$  21.3% during the immediate postoperative period of test stimulation ( $p < 0.001$ , Wilcoxin signed rank test), 63.5  $\pm$  30.6% at 3 months after surgery ( $p < 0.001$ ), 74.1  $\pm$  22.3% at 6 months after surgery ( $p = 0.003$ ), 74.5  $\pm$  19.8% at 12 months after surgery ( $p < 0.001$ ), and 85.5  $\pm$  10.1% at 24 months after surgery ( $p = 0.042$ ) (Table 1, 2). The BFMDRS total movement scores were reduced gradually and the results reached statistical significance in the postoperative period (test period, 3, 6, 12, and 24 months after surgery). There was no statistical difference between 12 months and 24 months ( $p = 0.075$ ). The mean BFMDRS disability score also improved, from 6.7  $\pm$  2.7 before surgery to 1.4  $\pm$  1.2 at 12 months after surgery, reflecting a 79.1  $\pm$  20.1% improvement. The results reached statistical significance ( $p = 0.003$ ). At 12 months after surgery, the mean individual BFMDRS movement scores were as follows : for eyes 6.0  $\pm$  2.2 at baseline and 2.2  $\pm$  2.1 at 12 months after surgery, reflecting a 63.3  $\pm$  34.2% improvement ( $p = 0.005$ ); mouth at baseline 6.3  $\pm$  1.9, and 1.2  $\pm$  1.3 at 12 months after surgery, reflecting an 80.9  $\pm$  24.8% improvement ( $p < 0.001$ ); speech/swallowing at baseline 7.9  $\pm$  3.2, and 2.5  $\pm$  1.9 at 12 months after surgery, reflecting a 68.4  $\pm$  43.8% improvement ( $p = 0.006$ ); and neck 3.3  $\pm$  2.6 at baseline and 0.4  $\pm$  1.2 at 12 months after surgery, reflecting an 87.9  $\pm$  46.7% improvement ( $p = 0.011$ ) (Table 3). All the results reached statistical significance. The postoperative course in BFMDRS movement scores in each site is shown in Fig. 3.

In our study, five patients had severe blepharospasm (initial eyes BFM subscore 8) and six patients had mild to moderate blepharospasm (initial eyes BFM subscore < 8). The mean total BFMDRS scores in the first group were 24.6  $\pm$  6.1 at baseline and at 12 months after surgery 9.3  $\pm$  5.72, reflecting

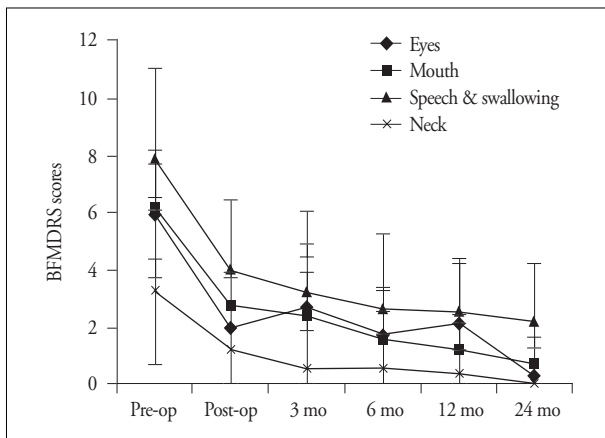
**Table 3.** Summary of BFMDRS in sites

Sites	Baseline	Test period	3 mo	6 mo	12 mo	24 mo	12 mo % improvement from baseline
Eyes	6.0	2.0	2.7	1.7	2.2	0.4	-63.3%
Mouth	6.3	2.7	2.4	1.6	1.2	0.7	-80.9%
Speech/Swallowing	7.9	4.0	3.2	2.6	2.5	2.2	-68.4%
Neck	3.3	1.2	0.6	0.6	0.4	0.0	-87.9%

Wilcoxin signed rank test (paired). All the result reached statistical significance at 12 months in comparison to baseline scores (for eye,  $p = 0.005$ ; mouth,  $p < 0.001$ ; speech/swallowing,  $p = 0.006$ ; neck,  $p = 0.011$ ). Significant  $p$  value ( $< 0.05$ )



**Fig. 2.** Scatterplots of the final target (the lowest electrode position) at the axial plane. AC : anterior commissure, PC : posterior commissure.

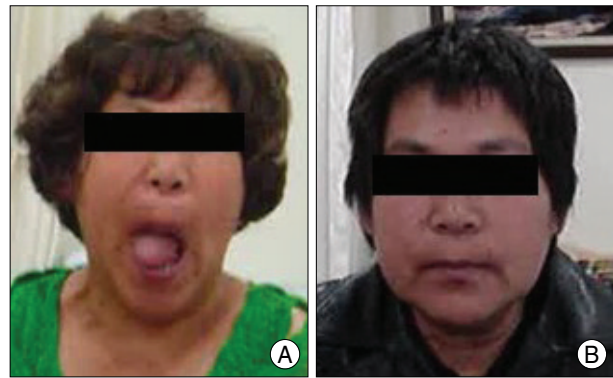


**Fig. 3.** Postoperative course showing gradual and sustained improvement in Burk-Fahn-Marsden dystonia rating scale (BFMDRS) movement scores in each site. Pre-op : preoperation, Post-op : postoperation.

a  $76.7 \pm 14.7\%$  improvement. The mean total BFMDRS scores in the second group were  $24.5 \pm 6.4$  at baseline and at 12 months after surgery  $3.8 \pm 4.5$ , reflecting an  $84.5 \pm 19.6\%$  improvement. However, the results between the two groups did not reach statistical significance ( $p = 0.079$ , Mann-Whitney test).

Five patients in the study had severe oromandibular dystonia (initial mouth BFM subscore 8) and six patients had mild to moderate oromandibular (initial mouth BFM subscore < 8). The mean BFMDRS total movement scores in the first group were  $26.4 \pm 6.2$  at baseline and at 12 months after surgery  $5.6 \pm 8.2$ , reflecting an  $78.8 \pm 25.3\%$  improvement. The mean BFMDRS total movement scores in the second group were  $23.0 \pm 5.7$  at baseline and  $6.9 \pm 2.9$  at 12 months after surgery, reflecting a  $70.0 \pm 13.0\%$  improvement. However, the results between the two groups did not reach statistical significance ( $p = 0.196$ , Mann-Whitney test).

Oromandibular dystonia presents as a jaw opening type, a jaw closing type, and as a mixed type. Most patients suffered



**Fig. 4.** Preoperative (A) and postoperative (B) photographs of patient 7 showing clinical feature of jaw opening type oromandibular dystonia.

from the jaw closing type<sup>8)</sup>. In our study, two patients had the jaw opening type with tongue protrusion and twisting (Fig. 4). The mean BFMDRS total movement scores in this group were  $24.0 \pm 5.7$  at baseline and  $5.0 \pm 7.1$  at 12 months after surgery, reflecting a  $79.2 \pm 24.9\%$  improvement. The mean BFMDRS total movement scores in the other group with jaw closing were  $24.7 \pm 6.3$  at baseline and  $6.6 \pm 5.7$  at 12 months after surgery, reflecting a  $73.3 \pm 19.9\%$  improvement. However, the results between the two groups did not reach statistical significance ( $p = 0.813$ , Mann-Whitney test).

Nine patients experienced their first symptom in the eyes and two patients in the mouth. The mean BFMDRS total movement scores in the first group were  $24.0 \pm 5.5$  at baseline and  $6.6 \pm 5.7$  at 12 months after surgery, reflecting a  $73 \pm 19.9\%$  improvement. The mean BFMDRS total movement scores in the other group were  $27 \pm 9.9$  at baseline and  $5 \pm 7.1$  at 12 months after surgery, reflecting a  $81.5 \pm 20.9\%$  improvement. The results between the two groups did not reach statistical significance ( $p = 0.288$ , Mann-Whitney test).

We also compared the prognosis of male patients with females, older onset age (> 50 years) with younger (< 50 years), and longer duration (> 7 years) with shorter (< 7 years); however, these factors did not affect the prognosis statistically ( $p = 0.345$ ,  $p = 0.508$ ,  $p = 0.608$ , Mann-Whitney test).

No significant peri-operative complications were noted. No patient had a permanent major complication due to a hardware-related problem or to chronic stimulation. Five patients reported with transient reversible side effects, such as slowness in their walking, heaviness in their legs, subtle difficulty in speaking and swallowing, fatigue, depression, and general weakness.

## DISCUSSION

The present retrospective analysis of the 11 patients with medically refractory Meige syndrome with a mean follow-up period of 23.1 months contributes to our understanding of

the outcome rates of treatment by bilateral GPi-DBS. In our study, the prognosis shows a 59.8% improvement in the BFMDRS total movement scores during the immediate postoperative period of test stimulation, 63.5% improvement at 3 months, 74.1% improvement at 6 months, 74.5% improvement at 12 months, and 85.5% improvement at 24 months postoperatively. The BFMDRS total movement scores were reduced gradually and the results reached statistical significance. The mean disability score was also statistically improved, from 6.7 before surgery to 1.4 at 12 months after surgery, reflecting a 79.1% improvement. Results of these findings are similar to those of earlier study<sup>9</sup>. Ostrem et al.<sup>7</sup> reported the results of bilateral pallidal DBS in six patients with cranial-cervical dystonia showing a 72% improvement in the BFMDRS total movement score at 6 months.

In the present study, the most pronounced improvement in symptoms was oromandibular dystonia (80.9%), followed by speech/swallowing (68.4%), and blepharospasm (63.3%) except for cervical dystonia (87.9%) at 12 months after surgery. However, the results of our findings are inconsistent with a study that reported that blepharospasm and facial dystonia responded to treatment better than speech and swallowing symptoms in six cases that were followed for more than 12 months<sup>4</sup>. This suggests to be either a clinical heterogenous condition of dystonia or a small case series. Nine patients (81.8%) had cervical dystonia. All of them had mobile or phasic type of the cervical dystonia. These results correspond with the results of earlier study which reported that GPi-DBS can improve mobile type cervical dystonia significantly<sup>3</sup>.

The prognostic factors of bilateral GPi-DBS in Meige syndrome have not been established. In the present study, the prognostic factors such as sex, onset age, duration of symptoms, onset site, type of jaw opening or closing, and severity of symptoms of blepharospasm and oromandibular dystonia did not affect the prognosis. More cases and studies will be required to confirm the prognostic factors of GPi-DBS in the treatment of Meige syndrome.

## CONCLUSION

We conclude that the bilateral GPi-DBS can be an effective and safe treatment option in refractory Meige syndrome despite the varied clinical expressions of this disease. Blepharospasm, oromandibular dystonia, and speech/swallowing all improved with GPi-DBS. The most pronounced improvement in symptoms was oromandibular dystonia, followed by speech/swallowing and blepharospasm. There is no significant difference in outcome according to age, sex, onset site, type, severity, or duration of symptoms.

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