Case Report

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Effectiveness of Unilateral Pallidotomy for Meige Syndrome Confirmed by Motion Analysis

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Key Words
Meige syndrome · Orofacial dystonia · Blepharospasm · Globus pallidus internus · Stereotactic brain surgery · Pallidotomy · Motion analysis

Abstract
Background: We report the case of a 64-year-old woman with bilateral manifestation of Meige syndrome (MS) successfully treated with left-side unilateral ventroposterolateral pallidotomy. ***Methods:*** Symptoms were evaluated according to the Burke-Fahn-Marsden dystonia rating scale. Head tremor, blepharospasm and orofacial dyskinesia were measured with an infrared, video-based, computerized, real-time passive marker-based analyzer of motions (RTPAM). ***Results:*** The Burke-Fahn-Marsden score showed a 90.2% reduction (from 25.5 to 2.5) at 6 months, and an 88.2% long-lasting benefit (to 3.0) at the 3-year follow-up with good bilateral control of the blepharospasm and orofacial movements. The RTPAM showed a substantial regression of acceleration for all markers, and abolishment of the 4.8-Hz head tremor. The correlation between symmetrical markers, and between markers within the right and left sides, was significantly decreased. ***Conclusions:*** Pallidotomy with staged procedure is recommended for the treatment of MS in patients on whom deep brain stimulation could not be performed. In case of good bilateral benefits from the unilateral procedure, contralateral surgery is not needed. The RTPAM is a useful tool for the mapping of facial involuntary movements.

Introduction

In 1904, Henri Meige described a rare neurological movement disorder characterized by spasms of the muscles of the eyelids and associated loss of tone in these eyelid muscles [1]. Meige syndrome (MS) is an idiopathic, focal, adult-onset orofacial dystonia with a male-to-female ratio of 3:1 [2] which usually develops in middle age or beyond, and can be induced by neuroleptic drugs, varicella infection, head trauma, nasopharyngeal radiotherapy, calcification or ischemic lesions of the basal ganglia [3, 4]. The clinical course may include blepharospasm or lip pursing, but the mouth movements, as against parkinsonian or tardive dyskinesia, can be associated with tongue movements. Sometimes the chin is thrusting forward, movements may spread to the neck and shoulders, and interaction between oral and eye movements can be observed. MS is present at rest and with activity; it disappears in sleep and can be inhibited voluntarily to a certain degree, but it worsens with stress. Electromyography shows the disturbances of motor control of the facial

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muscles, burst discharges and a failure of reciprocal muscular activity [5].

A wide variety of medications have demonstrated limited efficacy. Some patients benefit from anticholinergics, muscle relaxants, anticonvulsants, and L-dopa, all of which have been employed with sporadic benefit [6]. The therapy of choice is local botulinum toxin injections, although secondary resistance to this kind of therapy has been increasing over the years. In such cases a treatment option can be stereotactic surgical ablation or deep brain stimulation (DBS) of the globus pallidus internus (GPi). A beneficial effect of GPi-DBS has been reported on the forms of MS associated with anterocollis and segmental axial dystonia [7], with multifocal dystonia [8], with segmental axial dystonia after ineffective bilateral thalamotomy [9], with spasmodic torticollis [10, 11] and with dystonic tremor [12]. There are only few reports on successful surgical treatment of isolated MS [13, 14].

Case Report

A 64-year-old woman was referred with bilateral blepharospasm and involuntary contractions of her lower facial muscles with occasional excessive blinking and sustained forceful eye closure with mild photophobia which had started 3 years before the referral. One year later, she developed facial grimacing, twitching of perioral muscles without dystonic movement of masticatory muscles, cervical dystonia involving the platysma, spasmodic dysphonia and dysphagia with consequent loss of weight (18 kg), and mild depression without hysterical traits. Blood chemistry was normal, including parathyroid and copper metabolism functions. The dystonia slightly improved after local injections of botulinum toxin A and B, which were repeated over 1 year. Then, a gradual loss of efficacy was noted. Sequential pharmacological trials did not yield a satisfactory improvement.

Her medical history shows recurrent herpes labialis, partial strumectomy and removal of left breast fibroadenoma. She has had no significant exposure to toxins and no psychiatric diseases, and her family history is negative for movement disorders. Bilaterally, in the pallidal regions, MRI showed several ischemic hyperintense spots by T_2-weighted imaging, and hypointense spots by T_1-weighted imaging. No neurovascular conflict was observed. Electromyography showed spontaneous myokymic and neuromyotonic discharges bilaterally in the orbicularis oculi and orbicularis oris muscles.

Surgical Procedure

Bilateral pallidal DBS has been proposed to the patient, but she was against implant surgery. As the right side of the face was more affected, we decided to start with surgery to the left side. On the frameless MR, the ventroposterolateral GPi target was determined to be 2 mm anterior, 20 mm lateral and 5 mm ventral to the midcommissural point. After CT-guided planning with 3D coordinate transformation (home-developed Vister 3.6 software) and microelectrode recording, the patient underwent left-side unilateral pallidotomy with 3 contiguous lesions (MHT stereotactic device, Freiburg, Germany; Neuro N-50 Lesion generator, Striker; electrode diameter: 1.8 mm; tip: 3.0 mm).

Video Recording

After having given written informed consent, the patient was video recorded. In a second session, 17 passive markers (7.0-mm-diameter adhesive retroreflective disks, 0.1 g each) were attached to the most representative anatomical landmark points of her face (8 on each side). One of them (marker 0) was positioned on the nose for detection and subtraction of head movements. Trajectories of the marker movements were determined with a passive marker-based analyzer of motions (PAM) [15]. The system consists of a Sony TR8100E digital video camera, with synchronized flashing infrared LED around the lens, an IEEE1394 interface and PC-based real-time recording software (RTPAM). Horizontal and vertical coordinates of the marker positions are determined at a sampling rate of 50 frames per second. Recordings were taken prior to and 6 months after surgery.

Data Analysis

Calibrated displacement time series were analyzed by MATLAB 7.1 (Mathworks, Sherborn, Mass., USA). The data were filtered by a 5th-order Butterworth filter (pass band: 0.4–20 Hz). The matrix of correlation coefficients (R) was calculated together with the level of significance (p). Frequency domain analysis was done by computing the power spectral density with 0.05-Hz frequency bins.

Results

Postoperative T_1- and T_2-weighted MRI sequences showed a circumscribed 5.4 × 5.4 × 8.0 mm lesion above the optic tract 20 mm laterally, 2.4 mm anterior and 5 mm ventral to the midcommissural point, corresponding to the ventroposterolateral part of the left GPi, and extending slightly to the ventral external pallidum (fig. 1). There were no adverse postoperative reactions. Blepharospasm, oromandibular dystonia and dystonia-dyskinesia in the neck improved bilaterally within days. The Burke-Fahn-Marsden dystonia rating scale [16] score 6 months postoperatively showed a 90.2% reduction, and at the 3-year follow-up a 88.2% reduction in symptoms (table 1). Postoperative RTPAM showed excellent bilateral control of blepharospasm, and a significant reduction in orofacial involuntary movements (online suppl. video 1, www.karger.com/doi/10.1159/000323341). Analysis of the marker movements showed a substantial regression of acceleration for all markers (fig. 2). As one can see from power spectral density, the head tremor with a 4.8-Hz dominant frequency was abolished. The correlations between the displacement of symmetrical right and left markers, and between the markers on the right and left sides were significantly decreased (fig. 3). Thus, surgery to the second side was abandoned.

Discussion

It was suggested that the overactivated GPi played a key role in the pathogenesis of MS. Capelle et al. [13] described good results after bilateral GPi-DBS for eye and mouth movements with a lesser effect on speech and swallowing after a 2-year follow-up. However, after alternate switching of the sides, unilateral stimulation in MS had bilateral effects, but with predominant improvement in contralateral symptoms. It is well known that unilateral pallidal surgery in Parkinson's disease may have a bilateral effect. After pallidotomy there often is some improvement in bradykinesia, rigidity and L-dopa-induced dyskinesias on the ipsilateral side [17].

Foote et al. [18] reported excellent temporary intraoperative bilateral effects of right GPi-DBS in a 47-year-old patient with a 5-year history of craniofacial dystonia with blepharospasm, but over the 6-month follow-up, only a 40–50% reduction in symptoms was noted; 1 year later, however, a left-side electrode was also implanted, and a 75% improvement was achieved. They raised the issue of staged implantation surgery. A bilateral beneficial effect of unilateral pallidotomy on MS has not previously been reported. The decreases in correlation between the displacement of symmetrical markers and between the markers on the right and left sides are likely related to a common central oscillator that has a bilateral influence on at least some parts of the face.

The distribution of human corticobulbar motor excitatory and inhibitory outputs is not fully understood. It is still unclear whether the pattern of innervation is the same for upper and lower facial muscles, and whether the motor cortical area is giving rise to such innervation. Our data suggest differences in representation for the upper and lower facial areas. Corticobulbar axons project bilaterally to upper and lower facial muscles via polysynaptic connections such as reticular neurons or corticotegmentonuclear loops [19]. The GPi outflow directly influences the brainstem motor centers such as the pedunculopontine nucleus relating to the mesencephalic tegmental field, which in turn controls axial and proximal appendicular musculature by descending the reticulospinal tract. Iacono et al. [20] observed this benefit after bilateral GPi-DBS had been carried out on a patient with segmental axial dystonia and MS refractory to bilateral thalamotomy. It has been suggested that, unlike thalamotomy, which interrupts the thalamocortical output that controls distal appendicular musculature via corticospinal and corticobulbar tracts, pallidal surgery may also influence control of otherwise inaccessible axial muscles. In monkeys, the 10–20% of fibers from the GPi lie across the midline at the rostral pole of the centromedian nucleus and in the supramammillary decussation, and reach the ventral anterior, ventral lateral and centromedian nuclei of the contralateral thalamus. Labeled fibers were also noted bilaterally to the thalamic reticular and pedunculopontine nuclei [21]. Output from the entopeduncular nucleus (the equivalent of the GPi in the cat) provides a modest direct input to the red nucleus as well as a more substantial indirect input via projections to the zona incerta and the fields of Forel. Regions of the red nucleus also receive input from the cerebellar dentate nucleus and project to the contralateral facial nucleus and upper segments of the cervical spinal cord [22]. Such contralateral projections play a major role in the subcortical organization of the bilateral aspect of normal basal ganglia function and may provide a substrate for a variety of

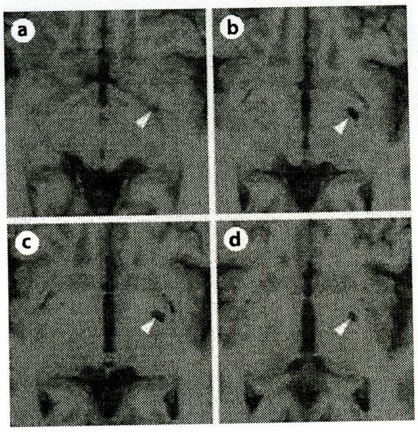

Fig. 1. Postoperative axial T_1-weighted MR images with slice thickness of 1.0 mm. Arrowheads: left-side pallidotomy lesion at the level (**a**), and 2.0 mm (**b**), 4.0 mm (**c**) and 6.0 mm (**d**) above the optic tract.

Table 1. Burke-Fahn-Marsden rating scores before and after surgery

Region	Baseline	Postoperatively	
		6 months	3 years
Eyes	6.0	0.5	0.5
Mouth	6.0	0.5	1.0
Speech and swallow	9.0	1.0	1.0
Neck	4.5	0.5	0.5
Product	25.5	2.5	3.0

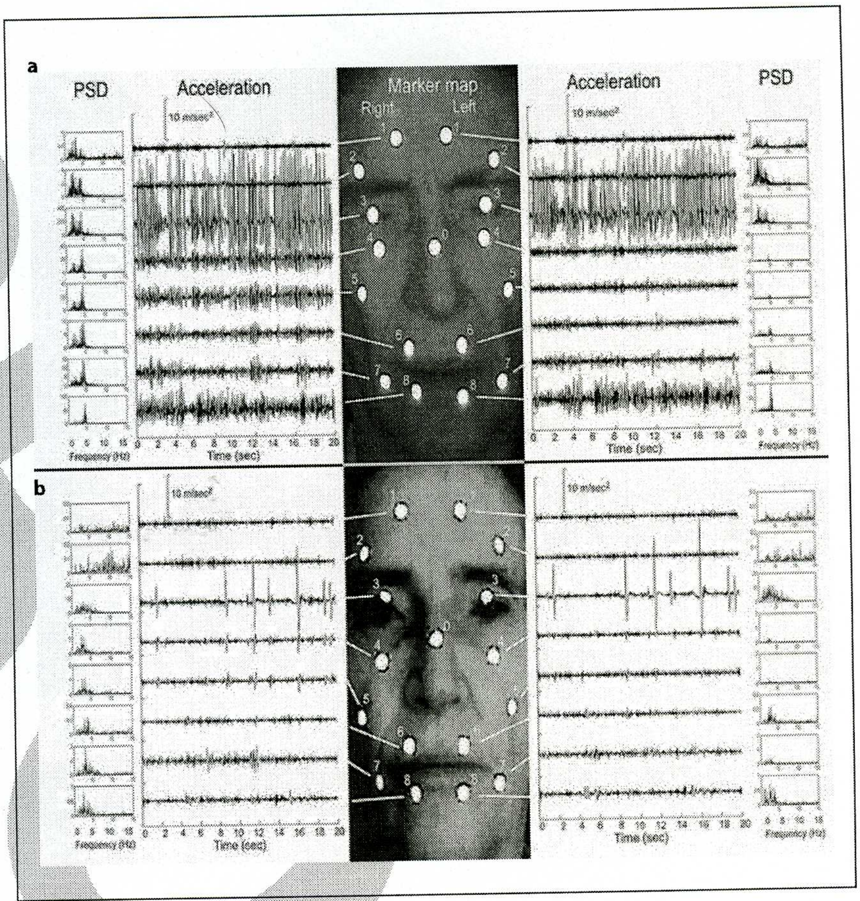

Fig. 2. Comparison of preoperative (**a**) with postoperative (**b**) facial movements of the patient by RTPAM. Acceleration-time functions clearly show the decrease in intensity. The power spectral density (PSD) diagrams on both sides have a peak at 4.8 Hz that disappears after unilateral pallidotomy.

a

CORRELATION BETWEEN MARKERS

Right-to-Left

1-1	0.83
2-2	0.89
3-3	0.99
4-4	0.67
5-5	0.76
6-6	0.57
7-7	
8-8	0.90

Right side

	2	3	4	5	6	7	8
1	0.73						
2		0.79	-0.74	-0.72	-0.60		
3			-0.84	-0.85	-0.70		
4				0.99	0.83	0.73	
5					0.87	0.77	
6						0.79	
7							0.54
8							

Left side

	2	3	4	5	6	7	8
1	0.58						
2		0.81					
3				-0.60			
4				0.77			
5						0.65	
6							
7							
8							

b

1-1	0.62
2-2	
3-3	0.98
4-4	0.81
5-5	0.79
6-6	
7-7	
8-8	0.80

	2	3	4	5	6	7	8
1	0.69						
2							
3			-0.85	-0.83			
4				0.95	0.52		
5					0.61		
6						0.53	
7							
8							

	2	3	4	5	6	7	8
1	0.63						
2							
3			-0.65	-0.69			
4				0.84			
5							
6							
7							
8							

Fig. 3. Correlations between marker trajectories before (**a**) and after (**b**) left ventroposterolateral pallidotomy. Correlation coefficients R are shown for paired marker trajectories. Only values for $R > 0.5$ are included with $p < 0.05$. The correlation between the two sides disappeared for markers 2 and 6, decreased for markers 1 and 8, remained almost the same for markers 3 and 5, and slightly increased only for marker 4. The correlation between markers on the right side was significantly decreased after surgery. The same holds for the left side, where the correlation between markers was much smaller even before the operation.

movement disorders including Parkinson's facies, impairment of blinking and dystonia of the face and neck.

The exact mechanism of pallidal surgery and the pathophysiological basis for dystonia are still poorly understood, and so far there is little experience in its use for MS. Although bilateral surgery is superior, in cases when for different reasons there is no possibility of performing bilateral GPi-DBS, staged pallidotomy may be an effective modality of treatment. The effectiveness of unilateral pallidotomy is an advantage as bilateral pallidotomy has a higher rate of adverse effects such as increased drooling, worsening of speech and cognitive impairment [23]. Because of the rapid replacement of pallidotomy with pallidal DBS, the published series contain small numbers of patients, and standardized measures were not always used. Pallidotomy remains a viable alternative in situations where DBS is not available because of expense, or is not feasible when a patient does not want implanted hardware, does not want to – or due to logistics cannot – participate in the device programming, or is medically unable to undergo general anesthesia [24]. The outcome assessment in secondary dystonia is complicated by the heterogeneity of this population, but some data suggest that phasic movements may improve more markedly than dystonic postures [11].

It was the first time that the RTPAM was used for mapping and analyzing the behavior of facial involuntary movements. It is a method easy to install and handle, with displacement data recording for immediate and eventual advanced time series analysis of marker movements. The advantage is that no wires are needed, and the markers cause no discomfort and do not alter the analyzed movement. Further studies with long-term follow-up are needed on this issue.

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