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The impact of deep brain stimulation on health related quality of life and disease-specific disability in Meige Syndrome (MS)

Ana Aires[a,b,*], Tiago Gomes[c,d], Paulo Linhares[b,e,f], Filipe Cunha[e,f], Maria José Rosas[a,f], Rui Vaz[b,e,f]

[a] Department of Neurology, Centro Hospitalar São João, Porto, Portugal
[b] Department of Clinical Neuroscience and Mental Health, Faculty of Medicine, University of Porto, Portugal
[c] Northern Genetics Service, The Newcastle upon Tyne Hospitals NHS Foundation Trust, Newcastle upon Tyne, NE1 3BZ, UK
[d] John Walton Muscular Dystrophy Research Centre, Institute of Genetic Medicine, Newcastle University, Newcastle upon Tyne, NE1 3BZ, UK
[e] Department of Neurosurgery, Centro Hospitalar São João, Porto, Portugal
[f] Movement Disorders and Functional Surgery Unit, Centro Hospitalar São João, Porto, Portugal

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ABSTRACT

Meige Syndrome (MS) is a disabling movement disorder which impairs daily routines such as eating and speaking and, when not responsive to best medical treatment, deep brain stimulation (DBS) of the globus pallidus interna (GPi) has been considered. Previous evidence has shown a significant improvement in motor dysfunction with DBS, however its benefit on disease-specific disability and quality of life has not been thoroughly studied. We describe two patients with severe MS submitted to GPi-DBS. Patient improvement was assessed preoperatively and 24 months after the surgery by applying the movement subscore of the Burke-Fahn-Marsden Dystonia Rating Scale (BFMRS) and Jankovic Rating Scale (JRS) for motor function and the BFMRS disability subscore and Blepharospasm Disability Scale (BDS) for disability. At 24-month follow-up, dystonia improved 68% in Patient 1 and 96% in Patient 2, while disability improved 77%–92% respectively. No major adverse effects were observed. Improvement in motor function is in agreement with previous findings, but we emphasise the important improvement in disability and consequently in quality of life. Therefore, we suggest that DBS should be a therapeutic tool in refractory cases of MS.

1. Introduction

Meige syndrome (MS) is a segmental craniofacial dystonia comprehending a preponderant blepharospasm and a variable involvement of other muscles supplied by the cranial nerves, both synchronous and symmetric [1–5]. Most commonly mild episodes of blepharospasm start around the fifth or sixth decade of life, with a female to male ratio ranging from 3:2 to 2:1 [6], and are usually triggered by certain actions [4,5]. As the disease worsens, the blepharospasm tends to assume the form of episodes of visually incapacitating blepharotonus lasting seconds to minutes [4]. The dystonia spreads caudally in a contiguous fashion to affect other facial muscles around the mouth and nose, but also the jaw, the soft palate and tongue [4–6]. As the condition progresses, other muscle groups may get involved, such as pharyngeal and laryngeal muscles, and the dystonic spasms become even more intense and persisting [6]. MS can severely impair ingestion and provoke dangerous malnourishment, and may also cause communication difficulties and vision disturbance with functional blindness. Most patients complain of significant psychosocial distress, despite best medical treatment [4,5].

Since MS was described by Meige [5], its pathophysiology remains mainly unknown and treatment is still only symptomatic and mostly disappointing, especially when considering the non-ocular component [7]. Botulin toxin injections are the standard treatment, however, the response diminishes with time and patients can develop antibodies that render the treatment ineffective. Uncontrolled MS can have a dramatic negative impact on the patients' health and quality of life [8]. Deep brain stimulation (DBS) of the globus pallidus internus (GPi) is indicated in medically refractory generalized dystonias and there is growing evidence of its potential benefits in segmental dystonia, including MS [8–30]. However, few reports assess the impact of DBS on disease-specific disability and health-related quality of life (HRQoL) [16,17,25–27,29,31]. Therefore, our main aim is to report our experience with bilateral GPi-DBS in two cases of medically refractory MS with emphasis on the effects on disability and HRQoL. We also compared our findings with cases previously reported.

* Corresponding author at: Department of Neurology, Centro Hospitalar São João, Alameda Prof. Hernâni Monteiro, Porto, 4200-319, Portugal.
E-mail addresses: u010302@hsjoao.min-saude.pt, u010302@chsj.min-saude.pt (A. Aires), tiago.gomes@newcastle.ac.uk (T. Gomes), paulo.linhares@chsj.min-saude.pt (P. Linhares), filipe.ricardo.cunha@chsj.min-saude.pt (F. Cunha), maria.rosas@chsj.min-saude.pt (M.J. Rosas), rui.vaz@chsj.min-saude.pt (R. Vaz).

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Table 1
Demographic and clinical data, including BFMRDS subscores for each of our patients with Meige Syndrome.

Pt	Gender	Age at surgery	Disease duration at surgery, years	BFMRDS Movement scale			BFMRDS Disability scale			CAB		JRS	
				M0	M24	M0 to M24 improvement	M0	M24	M0 to M24 improvement	M0	M24	M0	M24
1	F	73	5	11	3.5	68%	12	1	92%	9	0	8	2
2	F	67	17	54	2	96%	13	3	77%	–	–	–	–

Pt = patient; BFMRS = Burke-Fahn-Masden Dystonia rating scale, CAB = Clinical assessment Blepharospasm, JRS = Jankovic Rating Scale; M0 = preoperative assessment; M24 = follow-up assessment at 24 months.

2. Clinical cases

2.1. Methods

Our report includes two women diagnosed with medically refractory Meige syndrome (MS) and submitted to bilateral GPi-DBS at the Centro Hospitalar São João, Portugal, in 2012 and 2014, respectively. All medical assessments were performed by two specialists in movement disorders. Indication for surgery was based on clinically diagnosed MS unresponsive to available pharmacotherapy (i.e. anticholinergic agents, benzodiazepines, tetrabenazine) and poorly responsive to botulinum toxin injections. Brain MRI revealed no structural causes. Details on patients' characteristics and surgical procedure are summarized in Table 1. Dystonia was assessed using the movement subscore of the Burke-Fahn-Marsden Dystonia Rating Scale (BFMRDS-M) [32]. More specifically, blepharospasm was evaluated with Jankovic Rating Scale (JRS) [33]. The functional subscore of the BFMRDS (BFMRDS-D) and Blepharospasm Disability Scale (BDS) were used to determine disability [32,34]. Scales were scored in absolute values and the effect of the intervention is reported in percentage of variation between values collected at pre-operative and 24 months follow-up assessments. Patients or their legal representatives gave written informed consent.

2.1.1. Patient 1

Woman, 76-year-old, who suffered from insidious onset of blepharospasm at 68 years of age and progressive oromandibular dystonia since the age of 70. Thereafter, she complained of difficulties with communication and eating that caused a significant impact on her health and social life and were due to functional blindness secondary to blepharospasm and severe oromandibular dystonia affecting her ability to speak, chew and swallow. At the age of 72, she scored 8/8 on the JRS, 11/120 on the BFMRDS-M, 9/19 on the BDS and 12/30 on the BFMRDS-D. Her neuropsychological assessment (including the Montreal Cognitive Assessment, the Frontal Assessment Battery, the Dementia Rating Scale – 2 and other tests assessing memory, constructive capacity and executive functions) was performed by specialized neuropsychologists and was normal. Brain MRI, complete blood count, biochemistries (including renal and liver function, detailed ionogram, vitamin b12 and folate), serum ceruloplasmin, serum and urine copper levels and thyroid function tests showed no relevant alterations. She had been treated with tetrabenazine and botulinum toxin injections unsuccessfully for 5 years. Because of her disabling and medically refractory MS without contraindications for surgery, she was submitted to bilateral GPi-DBS in November 2012 to attempt symptomatic control. Two days after the surgery there was a significant clinical improvement (video 1). A month after surgery, it was observed a prompt reduction on BFMRDS-M from 11 to 3.5, but unchanged BDS and JRS. No clinically relevant adverse effects, including emotional instability, were observed and she was discharged 4 days after surgery. She kept improving and soon noticed progressively less disability and better quality of life and at 24 months follow-up was scoring 0/19 on the BDS, 2/8 on the JRS and 1/30 on the BFMRDS-D. This was achieved with adjuvant botulin toxin for optimal blepharospasm control, but no other treatments were needed.

2.1.2. Patient 2

Woman, 68-year-old, with progressive oromandibular dystonia since her 50's and first seen at age 62 for difficulties to speak and eat. On examination she scored 54 on the BFMRDS-M and 13 on the BFMRDS-D (BDS and JRS not applicable). Her neuropsychological assessment (including the Montreal Cognitive Assessment, the Frontal Assessment Battery, the Dementia Rating Scale – 2 and other tests assessing memory, constructive capacity and executive functions) was performed by specialized neuropsychologists and was normal. Brain MRI, complete blood count, biochemistries (including renal and liver function, detailed ionogram, vitamin b12 and folate), serum ceruloplasmin, serum and urine copper levels and thyroid function tests showed no relevant alterations. Genetic testing for Huntington disease revealed no mutations. She had been treated with clobazam, trihexyphenidyl hydrochloride, amantadine hydrochloride unsuccessfully for 4 years. Because of her disabling and medically refractory MS without contraindications for surgery, she was submitted to bilateral GPi-DBS in January 2014 to attempt symptomatic control. After surgery, no clinically relevant adverse effects were recorded. She improved over time (video 2) and 6 months after surgery she maintained slight dyskinesia without incapacity to feed herself. At 24 months follow-up was scoring 2 on the BFMRDS-M and 3 on the BFMRDS-D, without any other treatments.

2.2. Surgery and stimulation settings

Bilateral DBS electrodes were implanted in the GPi with support from stereotactic planning and intraoperative live microelectrode recording, as described by Sobstyl, Zabek [27]. In patient 1, monopolar settings were used initially with a pulse width of 60 μsec, frequency of 130 Hz and amplitude of 4 V on the right side, and a pulse width of 60 μsec, frequency of 130 Hz and amplitude of 3 V on the left side. In patient 2, the parameters initially used were monopolar stimulation with a pulse width of 60 μsec, frequency of 125 Hz and amplitude of 3.4 V on the right side, and a bipolar stimulation with a pulse width of 60 μsec, frequencies of 125 and 135 Hz and amplitudes of 3.3 and 2 V on the left side. During the follow-up period stimulation parameters were appropriately adjusted according to clinical response assessed during follow up appointments, as shown in Table 2.

2.3. Literature search

In June 2017, we searched for articles about the use of DBS in MS patients in the PubMed database and used the terms "deep brain stimulation" and "dystonia". After reading abstracts, we only included articles written in English, with complete patient descriptions and using BFMRDS as an outcome measure.

3. Results

Demographic and clinical data of our two patients are listed in Tables 1 and 2 describes the evolution of the BFMRDS subscores after