

SHORT REPORT

Pallidal stimulation relieves myoclonus–dystonia syndrome

C M Magariños-Ascone, I Regidor, J C Martínez-Castrillo, M Gómez-Galán, R Figueiras-Méndez

See Editorial Commentary, p 904

J Neurol Neurosurg Psychiatry 2005;76:989–991. doi: 10.1136/jnnp.2004.039248

A patient with myoclonus–dystonia syndrome was treated by implanting electrodes in the internal segment of the globus pallidus (GPI) and applying deep brain stimulation. Surgery was done in two sessions. The most affected limb was treated first and the other limb one year later. Neuronal recordings showed that most pallidal neurones discharged in bursts at a relatively low firing rate (mean (SD), 46 (18) Hz) compared with cells in the GPI in patients with Parkinson's disease. Neurones modified the rate and mode of discharge with dystonic postures and rapid involuntary contractions of limb muscles. Neurological examination at 24 months after surgery showed a decline of 47.8% and 78.5% in the Burke–Fahn–Marsden and disability rating scales, respectively.

Myoclonus–dystonia syndrome is a combination of dystonia and rapid, jerky movements resembling myoclonus.¹ The movements comprise involuntary electromyographic bursts lasting 50 to 300 ms.¹ Treatment with anticholinergic drugs may help in about a third of the cases, and diazepam relieves the jerks to some extent, but relief of dystonia remains a difficult issue to resolve. However, pallidotomy² and pallidal stimulation³ have resulted in successful clinical improvement in patients with generalised dystonia. Furthermore, L-dopa-induced myoclonus and dystonia in Parkinson's disease are relieved by pallidal surgery, raising the interesting possibility that the same method may be useful for treating some manifestations of dystonia.

We present a successful result of bilateral pallidal stimulation along with the main neurophysiological characteristics recorded intraoperatively in a patient with myoclonus–dystonia syndrome.

CASE REPORT

A 26 year old man presented with a 23 year history of movement disorder. At two years of age he developed stuttering and one year later action tremor. He had to learn to write with his left hand at the age of 10 because of the pronounced jerking of his right hand. He had no family history of movement disorders. Pregnancy and delivery were normal. Treatment with benzodiazepines, levodopa/carbidopa, piracetam, or alcohol was unsuccessful.

On physical examination before surgery the patient had stuttering, neck hyperextension with slight rotation of the head to the right, and small amplitude jerks. He showed dystonia of the superior limbs, more pronounced on the right, with rapid proximal myoclonic movements exacerbated by action and posture and occasionally acquiring ballistic characteristics. EEG, somatosensory evoked potentials, and magnetic resonance imaging (MRI) were normal. Blood tests including amino acids, organic acids, copper, caeruloplasmin, vitamin E, lactic acid, and ammonium were within the normal ranges, and no acanthocytes or DYT1 mutations were

detected. Genetic tests for DYT5 and DYT11 mutations were not done, and tyrosine metabolic studies were normal.

Treatment was in two sessions. First we implanted one electrode in the left hemisphere to treat the right side, which was the worst affected. On obtaining unilateral clinical improvement, the neurological condition of the left arm became more obvious, so another electrode was implanted in the other hemisphere one year later.

The surgical procedure was similar to that done in patients with Parkinson's disease.⁴ The surgery was carried out under local anaesthesia. The globus pallidus target was determined by MRI, ventriculography, and unit cell recordings. The pallidal target in both procedures was 3 mm anterior to the mid-commissural plane, 20 mm lateral to the midline, and 4 mm below the intercommissural line. The optic tract determined the lower boundary of the globus pallidus. It was identified by phosphenes seen by the patient during stimulation. Pallidal firing was reduced compared with that recorded in Parkinson's disease⁵ or dystonia.⁶ The implanted electrode was a DBS model 3387 (Medtronic, Minneapolis, Minnesota, USA). DBS parameters were: 2.5 V, 120 μ s, 160 Hz. GPI single units were recorded for one to two minutes. Subsequently, cells were tested for their responses to passive and voluntary movements. Surface EMG activity was recorded before surgery, and in the operating theatre at the same time as neuronal recording. The same neurophysiological and clinical tests were done in both sessions. The position of the implanted electrodes was confirmed by ventriculography at the end of the operation.

The Burke–Fahn–Marsden (BFM) dystonic scale and the disability rating subscale (DRS; the disability scale of the BFM) were applied pre- and postoperatively.

RESULTS

With a limb posture, the patient showed co-contraction of antagonistic muscles (fig. 1A). The jerks occurred irregularly and were superimposed on a sustained dystonic contraction (fig 1B). The bursts were of short duration (200–300 ms; fig 1C) and were distinct from the episodic sustained dystonic spasms.

Immediate benefit of myoclonia and dystonia was observed in the operating theatre on stimulating the pallidal target, as reported previously.⁷ The GPI firing rate ($n = 18$) was of lower frequency (mean (SD), 46 (18) Hz) than that recorded in the GPI of patients with Parkinson's disease⁵ or dystonia.⁶ Major differences in the neuronal recording could result from our patient having a syndrome not considered by those investigators. Several cells discharged spontaneously in bursts (6/18; 33%). Passive and voluntary contralateral upper limb movements modulated the firing activity in five of 18 cells tested (23%). Rapid involuntary muscular contractions of a limb placed in a postural position were of long duration (300 to 400 ms), low frequency (1 to 3 Hz), and induced

Abbreviations: BFM, Burke–Fahn–Marsden scale; DBS, deep brain stimulation; DRS, disability rating subscale; Gpi, internal segment of the globus pallidus

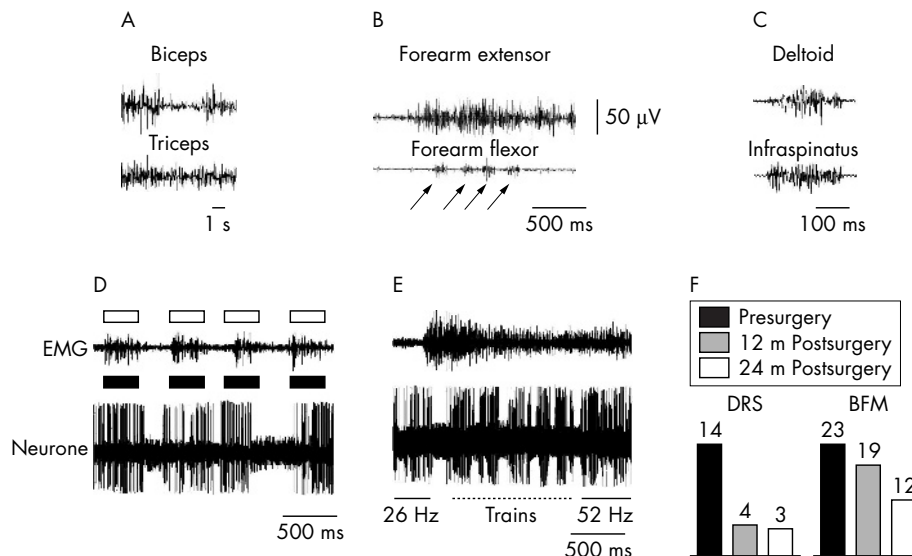


Figure 1 EMG activity. (A) Co-contraction of antagonistic proximal muscles. (B) Sustained contraction (above) and jerks (arrows) of antagonistic distal muscles. (C) Short duration jerks in antagonistic proximal muscles. Panels D to E: intraoperative recordings (two different cells; EMG (upper) and GPI neurone activity (lower)). (D) The cell discharges in correlation with jerks (forearm flexor). (E) The patient makes an involuntary sustained muscle contraction (biceps). (F) Disability rating subscale (DRS) and Burke-Fahn-Marsden (BFM) scale.

cyclical neuronal firing (black bars in fig 1D; 42 Hz; $n = 2$) correlated with the EMG bursts (white bars). Figure 1E shows a neurone that modifies the rate and mode of firing during a dystonic posture. The unit displays a regular discharge (that is, no burst firing) before EMG activity (left side of the recording). The initial rapid muscular contraction correlates with neuronal inhibition, while the decay of this phase imposes a rhythmical discharge with trains of decreasing duration. Afterwards, with the maintenance of the posture (right side of the recording), the neurone regains the original regular firing pattern but at a higher rate.

Neurological examination was done at 12 and 24 months after implantation of the first electrode and at 12 months after implantation of the second electrode. Myoclonus was completely relieved. Rating scales (fig 1F) show the result of the neurological evaluation after the first operation (12 months) and after both operations (24 months). There was a decline of 17.3% and 47.8% in the BFM scale and 71.4% and 78.5% in the DRS scale, respectively. It should be noted that the patient had stuttered since childhood and this item accounts for 9 points on the BFM scale (speech/swallowing).

DISCUSSION

This report suggests that DBS in the GPI is an effective treatment for myoclonus-dystonia syndrome. The symptoms continued to improve until there was complete recovery one year after surgery on the most affected side and marked improvement on the other side. Our results are consistent with previous reports in patients with dystonia⁸ and focal myoclonic dystonia.⁹

Obviously, the result from one patient with few cells recorded is insufficient to draw any conclusions. Nevertheless, our data may be of interest because of the difficulty in recording neuronal activity in myoclonus-dystonia syndrome and the scarcity of patients with this disorder. The temporal correlation found with passive and voluntary limb movements, as demonstrated in parkinsonian patients,¹⁰ and the relation with the motor symptoms suggests that some GPI cells may play a regulatory role. For instance, cell firing was modulated during jerks. As both patterns were rhythmic, with some EMG bursts in advance and others lagging, the origin of the encoding cannot be

estimated with certainty. However, similar patterns of alternating activity between neuronal firing and EMG activity have been used to indicate the nature of a motor command genesis, a sensory feedback control, or a mixed activity.^{11, 12}

Neuronal firing was also related to dystonic postures. Interestingly, there was a pause in firing with the rapid rising phase of the contraction (dynamic phase) followed by cyclic discharges of decreasing duration with the decay of that phase until the limb attained a holding posture (static phase), which was correlated with a higher neuronal rate. A plausible explanation for this could be that the pause in firing releases GPI target neurones from the normal tonic inhibitory activity so that a motor strategy can be initiated,¹³ while the oscillatory pattern coordinates the neural activities responsible for the maintenance of a motor sequence.¹⁴ In this respect it is relevant that inactivation of the GPI in primates—by giving muscimol, an agonist of GABA (γ -aminobutyric acid)—promotes muscle co-contraction.¹⁵ This led to the proposal that pallidal outputs interfere with the postural holding mechanisms promoting the maintenance of co-contraction of agonist and antagonist muscles.^{15, 16}

With respect to the neuronal discharge of the GPI in dystonia, our results match the low firing rate obtained by Vitek's group,⁸ although their patients were operated on under general anaesthesia. In contrast, Hutchinson's dystonic patients⁶ showed a higher mean firing frequency, but neurone activity was recorded under local anaesthesia as we did, raising the possibility that our data may represent an isolated case. Nevertheless, low GPI firing rates were found during dystonic posturing in a parkinsonian patient operated on without sedation,¹⁷ suggesting that under certain circumstances there may be a group of hypoactive cells within the GPI.

Authors' affiliations

C M Magariños-Ascone, M Gómez-Galán, Neurología Experimental, Departamento de Investigación, Hospital Ramón y Cajal, Madrid, Spain
 C M Magariños-Ascone, I Regidor, R Figueiras-Méndez, Unidad de Cirugía Funcional, Hospital Ramón y Cajal
 J C Martínez-Castrillo, Neurología, Hospital Ramón y Cajal

Competing interests: none declared

Correspondence to: Dr Carlos Magariños-Ascone, Neurología Experimental, Departamento de Investigación, Hospital Ramón y Cajal, Madrid 28034, Spain; carlos.magariños@hrc.es

Received 26 March 2004
In revised form 8 November 2004
Accepted 25 November 2004

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