

SHORT REPORT

Pallidal and thalamic neurostimulation in severe tardive dystonia

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Abstract

A 70 year old woman presented with a 6 year history of medically refractory severe tardive dystonia. After informed consent, a bilateral stereotactic electrode placement targeting the ventral intermediate thalamic nucleus (VIM) and the globus pallidus internus (GPi) was performed. After bilateral stimulation of the GPi, the patient showed a clear and stable improvement of the painful dystonic syndrome within hours. Stimulation of the VIM did not improve the hyperkinetic movements and simultaneous stimulation of both the GPi and the VIM did not result in any additional benefit. The possible pathophysiological mechanisms are discussed.

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Tardive dyskinesia as a consequence of exposure to neuroleptic drugs has an average prevalence of 15%-20%¹ and may coexist with persistent tardive dystonia in 1%-4% of patients.² Tardive dystonia differs from tardive dyskinesia in epidemiology, clinical features, risk factors, pathophysiology, course, prognosis, and treatment outcome.³ The medical treatment of both tardive dyskinesia and especially tardive dystonia is notoriously difficult and often unsuccessful.³ For only 14% of tardive dystonic patients a remission over a mean follow up period of 8.5 years has been described, which occurred within a mean of 2.6 years after discontinuation of neuroleptic drugs.⁴

This is the first case report on the effects of high frequency deep brain stimulation of the posteroventrolateral part of the globus pallidus internus (GPi) and the ventral intermediate thalamic nucleus (VIM) on medically refractory tardive dystonia.

Case report

A 70 year old woman had a 6 year history of progressive involuntary movements, which worsened at the beginning of the movement disorder and consisted of orobuccolingual dyskinesia, blepharospasm, painful phasic opisthotonic posturing of the neck, and retropulsive

twisting movements of both arms. There was no involvement of the legs and only minimal of the trunk. Especially, the left sternocleidomastoid muscle was clearly hypertrophic. The remaining neurological status was normal.

Six to 12 months before the onset of the involuntary movements, the patient had been treated with weekly intramuscular injections of 2 mg fluspirilene, a diphenylbutylpiperidinic depot neuroleptic drug with a tranquillising action in neurotic syndromes and anxiety disorders. She received no other neuroleptic agents. There was no family history of psychiatric or neurological disorders and no relevant personal medical or psychiatric history. Paraclinical investigations had been insignificant. Extensive pharmacological treatment trials including baclofen, botulinum toxin, bromocriptine, clonazepam, clozapine, diltiazem, DL- α -tocopherolacetate, gabapentin, pimozide, tetrabenazine, tiapride, trihexyphenidyl, and verapamil had no lasting effect.

Methods

In November 1999, after informed consent, a bilateral stereotactic electrode (Medtronic Model 3387 DBS) placement targeting the VIM and the posteroventrolateral part of the GPi was performed without complications. The correct placement was verified intraoperatively by teleradiography using ventriculography (Guiot's landmarks) and a long distance bioorthogonal x ray system, as well as by electrical stimulation avoiding side effects resulting from stimulation of fibres in the internal capsule, of the optic tract, or of somatosensory thalamic nuclei. The coordinates of contact 1 of the quadripolar left and right electrodes were: VIM 13.8 and 14.0 mm lateral to the intercommissural line (ICL), 6.5 and 6 mm anterior to the posterior commissure, and 1 mm dorsal to the ICL; GPi 19 and 20 mm lateral of the ICL, 2 mm anterior to the midcommissural point, and 3 and 5 mm below the ICL. Postoperatively, the correct electrode placement and surrounding tissue was verified by MRI. To evaluate the clinical outcome, our patient was examined before and 6 months after the procedure by an independent neurologist and in a double blinded on and off stimulation condition using the Burke-Marsden-Fahn dystonia rating scale (BMFS) and the abnormal involuntary movement scale

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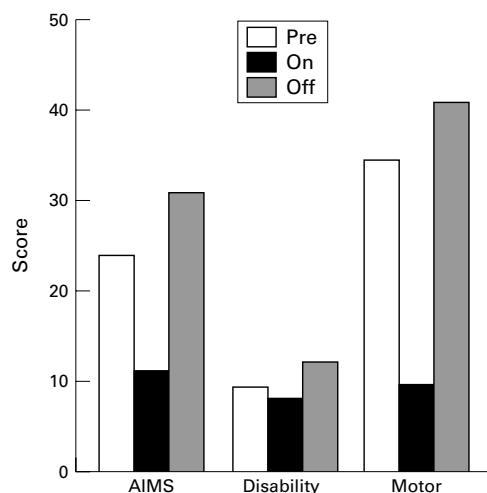


Figure 1 AIMS scores, disability, and motor scores of the BMFS scale of the preoperative (pre) and 6 month postoperative evaluation in the on and off GPi stimulation condition.

(AIMS). A video recording of the clinical assessments was made.

Results

After bilateral neurostimulation of the GPi (voltage 3.0 V monopolar, pulse width 210 μ s, frequency 150 Hz, Kinetra model 7428, Medtronic Inc), the patient showed and reported a clear and stable improvement of the painful dystonic syndrome within a few hours. The BMFS score decreased from 34.5/120 points to 9.5/120 (-73%) with bilateral Gpi stimulation. The AIMS score improved from 24/40 points to 11/40 (-54%, fig 1). Six months postoperatively she still had slight orofacial dyskinesias and mild dystonic movements resulting in retrocollis, but the pain had subsided completely. Turning off stimulation clearly aggravated the syndrome within 1 to 2 hours with an obvious rebound phenomenon. Electrical stimulation of the VIM using different stimulus parameters did not improve the hyperkinetic movements; furthermore, simultaneous stimulation of both the GPi and the VIM did not result in any additional benefit. Stimulus related side effects such as paraesthesia and a shuffling gait were mild and reversible.

Discussion

This patient presented with tardive dyskinesia which rapidly progressed to severe tardive dystonia (type II according to Adityanjee *et al*⁷). The clinical picture was consistent with suggested characteristic features of patients with tardive dystonia.⁵ The development of tardive dystonia with orobuccolingual dyskinesia, severe phasic retrotorticollis, and torticollis as well as asymmetric choreiform involuntary movements of the arms has been reported even after short term use of low dose fluspirilene, a dopamine D₂ receptor antagonist.^{6,7} There is no recognised specific treatment for tardive dystonia, and treatment trials and strategies reported to be helpful in other cases were without lasting benefit in our patient.

To date there are only a few case reports of effective destructive stereotactic procedures in medically refractory tardive dystonia lesioning different targets. Weetman *et al*⁸ reported on a 31 year old schizophrenic man, who first noted 1 year after starting antipsychotic medication dyskinetic movements of his mouth and tongue, rapidly progressing to severe choreiform dyskinesias involving his limbs and trunk, combined with severe dystonia involving his neck and upper limb girdle, who was effectively treated with bilateral posteroventral pallidotomy. Hillier *et al*⁹ performed a two staged ventral thalamotomy on the right side in a 66 year old man with orofacial dyskinesia, torticollis and twisting of the trunk, induced by neuroleptic drugs, who was refractory to pharmacological treatment. Twelve months postoperatively there were only minimal dystonic neck movements, and the patient was off all medication. The lesions were mainly in the VIM and in the ventroposterior medial thalamic nucleus (VPM) extending to the centromedianum-parafascicular (CM-PF) complex. Other authors used thalamotomy in the treatment of tardive dyskinesia and dystonia without exactly specifying the region.^{10,11} Tardive dyskinesia that included facial grimacing, humming, grunting, tongue protrusion, and choreiform limb movements predominantly on the left side had been reduced in a 66 year old man by pallidotomy targeting the ventroposterior globus pallidus on the right side.¹² As no single target for deep brain stimulation has been shown to be superior, we decided to target both the VIM nucleus and the GPi. As a result, we could clearly ameliorate the involuntary movements using pallidal stimulation, whereas there was no benefit from stimulating the thalamic VIM nucleus.

The hypothesis of dopamine receptor hypersensitivity used to explain the development of tardive dyskinesia¹³ may also be applied to tardive dystonia. Trugman *et al*¹⁴ proposed that repetitive stimulation of the D₁ receptor by endogenous dopamine resulting in sensitisation of the D₁ mediated striatal output in the presence of D₂ receptor blockage is a fundamental mechanism that mediates tardive dyskinesia and dystonia. The hypothesis that sensitisation of the D₁ mediated striatal output is involved in the pathogenesis is consistent with both the delayed onset of dyskinesias after neuroleptic initiation and the persistence of symptoms after neuroleptic withdrawal. The model predicts that D₁ antagonists combined with stimulation of the D₂ receptor will be beneficial in the treatment of both tardive dyskinesia and tardive dystonia, which is in accordance with the observed moderate amelioration of these dyskinesias using bromocriptine, a partial D₁ antagonist and D₂ agonist.¹⁵⁻¹⁷ Furthermore, the hypothesis is based on a relative segregation of striatal outputs, whereby D₁ mediated striatal output is preferentially directed to the GPi and the substantia nigra, pars reticulata, and D₂ mediated output is preferentially directed to the external segment of the globus pallidus.¹⁴ By selectively reducing the overactivity of the D₁ mediated direct path of

the striatal motor circuits to the GPi, inhibitory neurostimulation of this site might have an effect on tardive dyskinesia and dystonia.

The reason for ineffective thalamic stimulation in this patient could be seen in the more lateral target site in the VIM. Caparros-Lefebvre *et al*¹⁸ showed that both tremor and drug induced choreiform dyskinesias in Parkinson's disease were abolished by a more posteromedial VIM target. However, only the tremor was relieved by the more anterolateral electrode position, which might point to an antichoreiform dyskinetic effect being secondary to involvement of the CM-PF complex. These results are consistent with neuroanatomical data showing that the CM-PF is included in the motor circuits of the basal ganglia system that receives important input from the GPi and are in accordance with thalamotomy lesions shown to be effective in tardive dyskinesia, which were mainly in the VPM extending to the CM-PF complex.⁹

The clinical importance of this case report lies in the demonstration that stimulation of a single ventroposterolateral GPi target can achieve a clear amelioration of medically refractory severe tardive dystonia, whereas deep brain stimulation targeting the VIM does not translate into a reduction in tardive dystonia.

- 1 Gerlach J, Casey DE. Tardive dyskinesia. *Acta Psychiatr Scand* 1988;77:369-78.
- 2 Raja M. Tardive dystonia. Prevalence, risk factors, and comparison with tardive dyskinesia in a population of 200 acute psychiatric inpatients. *Eur Arch Psychiatry Clin Neurosci* 1995;245:145-51.

- 3 Adityanjee, Aderibigbe YA, Jampala VC, *et al*. The current status of tardive dystonia. *Biol Psychiatry* 1999;45:715-30.
- 4 Kiriakakis V, Bhatia KP, Quinn NP, *et al*. The natural history of tardive dystonia. A long-term follow-up study of 107 cases. *Brain* 1998;121:2053-66.
- 5 Burke RE, Fahn S, Jankovic J, *et al*. Tardive dystonia: late-onset and persistent dystonia caused by antipsychotic drugs. *Neurology* 1982;32:1335-46.
- 6 Kappler J, Menges C, Ferbert A, *et al*. Severe late dystonia after neuroleptic anxiolysis with fluspirilene. *Nervenarzt* 1994;65:66-8.
- 7 Laux G, Gunreben G. Severe late-onset dystonia while on fluspirilene. *Dtsch Med Wochenschr* 1991;116:977-80.
- 8 Weetman J, Anderson IM, Gregory RP, *et al*. Bilateral posteroverentral pallidotomy for severe antipsychotic induced tardive dyskinesia and dystonia [letter]. *J Neurol Neurosurg Psychiatry* 1997;63:554-6.
- 9 Hillier CE, Wiles CM, Simpson BA. Thalamotomy for severe antipsychotic induced tardive dyskinesia and dystonia [letter]. *J Neurol Neurosurg Psychiatry* 1999;66:250-1.
- 10 Goldman HW, Cooper IS, Simpson GM, *et al*. Reversal of severe tardive dyskinesia and dystonia following bilateral CT-guided stereotactic thalamotomy. *The 4th World Congress of Biological Psychiatry*. Philadelphia (conference proceedings): 1985.
- 11 Yadalam KG, Korn ML, Simpson GM. Tardive dystonia: four case histories. *J Clin Psychiatry* 1990;51:17-20.
- 12 Wang Y, Turnbull I, Calne S, *et al*. Pallidotomy for tardive dyskinesia [letter]. *Lancet* 1997;349:777-8.
- 13 Klawans HL, Tanner CM, Goetz CG. Epidemiology and pathophysiology of tardive dyskinesias. *Adv Neurol* 1988;49:185-97.
- 14 Trugman JM, Leadbetter R, Zalis ME, *et al*. Treatment of severe axial tardive dystonia with clozapine: case report and hypothesis. *Mov Disord* 1994;9:441-6.
- 15 Lenox RH, Weaver LA, Saran BM. Tardive dyskinesia: clinical and neuroendocrine response to low dose bromocriptine. *J Clin Psychopharmacol* 1985;5:286-92.
- 16 Lieberman JA, Alvir J, Mukherjee S, *et al*. Treatment of tardive dyskinesia with bromocriptine. A test of the receptor modification strategy. *Arch Gen Psychiatry* 1989;46:908-13.
- 17 Luchins DJ, Goldman M. High-dose bromocriptine in a case of tardive dystonia. *Biol Psychiatry* 1985;20:179-81.
- 18 Caparros-Lefebvre D, Blond S, Feltin M-P, *et al*. Improvement of levodopa induced dyskinesias by thalamic deep brain stimulation is related to slight variation in electrode placement: possible involvement of the centre median and parafascicularis complex. *J Neurol Neurosurg Psychiatry* 1999;67:308-14.