Pallidal and thalamic neurostimulation in severe tardive dystonia

T Trottenberg, G Paul, W Meissner, K Maier-Hauff, C Taschner, A Kupsch

Trottenberg, G Paul, W Meissner, K Maier-Hauff, C Taschner, A Kupsch

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.

Keywords: neurostimulation; tardive dystonia; globus pallidus

Tardive dyskinesia as a consequence of exposure to neuroleptic drugs has an average prevalence of 15%-20% and may coexist with persistent tardive dystonia in 1%-4% of patients. Tardive dystonia differs from tardive dyskinesia in epidemiology, clinical features, risk factors, pathophysiology, course, prognosis, and treatment outcome. The medical treatment of both tardive dyskinesia and especially tardive dystonia is notoriously difficult and often unsuccessful. 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.

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.

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 teleangiography 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.
Tardive dystonia that included orofacial dyskinesia, torporotics, 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. 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 dyskinesias may also be applied to tardive dystonia. Trugman et al proposed that repetitive stimulation of the D₂ receptor by endogenous dopamine resulting in sensitisation of the D₂ mediated striatal output in the presence of D₁ receptor blockade is a fundamental mechanism that mediates tardive dyskinesia and dystonia. The hypothesis that sensitisation of the D₂ 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 D₂ 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 D₂ antagonist and D₂ agonist. 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. By selectively reducing the overactivity of the D₂ mediated direct path of the thalamostriatal pathway, we could clearly ameliorate the involuntariness and the hyperkinetic movements of the GPi. 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 dyskinesias may also be applied to tardive dystonia. Trugman et al. proposed that repetitive stimulation of the D₂ receptor by endogenous dopamine resulting in sensitisation of the D₂ mediated striatal output in the presence of D₁ receptor blockade is a fundamental mechanism that mediates tardive dyskinesia and dystonia. The hypothesis that sensitisation of the D₂ 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 D₂ 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 D₂ antagonist and D₂ agonist. 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. By selectively reducing the overactivity of the D₂ mediated direct path of the thalamostriatal pathway, we could clearly ameliorate the involuntariness and the hyperkinetic movements of the GPi. 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 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. 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.

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.

Pallidal and thalamic neurostimulation in severe tardive dystonia

T Trottenberg, G Paul, W Meissner, K Maier-Hauff, C Taschner and A Kupsch

J Neurol Neurosurg Psychiatry 2001 70: 557-559
doi: 10.1136/jnnp.70.4.557

Updated information and services can be found at:
http://jnnp.bmj.com/content/70/4/557

These include:
References
This article cites 17 articles, 5 of which you can access for free at:
http://jnnp.bmj.com/content/70/4/557#BIBL

Email alerting service
Receive free email alerts when new articles cite this article. Sign up in the box at the top right corner of the online article.

Notes

To request permissions go to:
http://group.bmj.com/group/rights-licensing/permissions

To order reprints go to:
http://journals.bmj.com/cgi/reprintform

To subscribe to BMJ go to:
http://group.bmj.com/subscribe/