Case Report

A manic episode after bilateral subthalamic stimulation in a patient with advanced Parkinson's disease

Claeys I, Santens P, Van den Abbeele D, Van Roost D, Lemmens GMD.
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Deep brain stimulation (DBS) has proven to be an effective treatment for patients with refractory symptoms in the advanced stages of Parkinson's disease. However, different psychiatric and cognitive problems may occur after DBS. We report a case of a manic episode after DBS of the subthalamic nucleus in a patient with advanced Parkinson's disease. After slow and gradually restart of the neurostimulation using the lowest effective intensity, the motor symptoms remained sufficiently under control without causing any psychiatric problems.

Isabel Claeys¹, Patrick Santens², Dirk Van den Abbeele¹, Dirk Van Roost³, Gilbert MD Lemmens¹

¹Department of Psychiatry, Ghent University Hospital, Ghent, Belgium; ²Department of Neurology, Ghent University Hospital, Ghent, Belgium; and ³Department of Neurosurgery, Ghent University Hospital, Ghent, Belgium

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Isabel Claeys, Department of Psychiatry, University Hospital Ghent, Ghent, Belgium
Tel: 0032-(0)9/332.71.58;
Fax: 0032-(0)9/260.35.00;
E-mail: Isabel.Claeys@azghm.be

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Parkinson's disease (PD) is a common progressive neurodegenerative disorder leading to increasing motor disability (1,2). The main clinical features include asymmetric resting tremor, rigidity, bradykinesia, postural instability and gait abnormalities. In addition, in later stages of the disorder, cognitive and behavioural problems may become a serious burden (e.g. depression, bradyphrenia and psychotic symptoms). Multiple neurotransmitter systems degenerate in PD, but the loss of dopaminergic neurons in the substantia nigra is considered as a major cause of the symptomatology, especially the motor symptoms (3).

Long-term pharmacological treatment is often associated with the development of several side effects such as motor fluctuations and abnormal movements (e.g. dyskinesia). More recently, deep brain stimulation (DBS) has proven to be an effective treatment, in particular, for patients with such refractory symptoms in advanced stages of the disease. DBS has targeted different brain areas including the ventro intermediate nucleus of the thalamus, the globus pallidus internus and

the subthalamic nucleus (STN). Nowadays, the STN is generally accepted to be the target of choice, because of its beneficial effects on all cardinal motor symptoms and its potential to reduce medication dosage (4).

Despite the promising results several complications of DBS have been reported. They vary from surgery-related (e.g. intracerebral hemorrhage, infection), to hardware-related (e.g. lead breaking, stimulator malfunction) and stimulation-related (e.g. dyskinesia, blepharospasm and speech disturbances) problems (4,5). Furthermore, a number of different psychiatric and cognitive problems have been reported with DBS: depression (8%), transient hypomania (8%), manic episodes (4%) and, to a lesser extent, anxiety disorders, personality changes, apathy and aggressive behaviours (3,5).

Case report

A 68-year-old man with a 12-year history of Parkinson's disease (PD) was treated with

subthalamic DBS because of motor fluctuations and increasing off episodes characterised by severe rigidity. Additionally, he had camptocormia during both on and off phases. In the early stages of the illness he showed more prominent motor symptoms in the right hemisoma but over the years he developed bilateral and especially axial symptoms. He has consecutively been treated with different combinations of pergolide, amantadine, levodopa, entacapone and rasagiline. Although he had prominent axial symptomatology with camptocormia, he was considered for DBS in view of the increasing and debilitating off episodes.

The pre-operative Unified Parkinson's Disease Rating Scale (UPDRS) motor scores were 48 and 74 in the on and off phase, respectively. The high motor score was mainly due to the axial symptomatology. Extensive neuropsychological testing displayed only minor executive dysfunction as can be seen with PD. No signs indicative of more widespread cognitive deficits were found. The pre-operative score of the first part of the UPDRS, mentation, behaviour and mood, was 3. The patient was daily treated with a combination of levodopa (6×150 mg), carbidopa (6×37.5 mg), entacapone (6×200 mg), pergolide (6×1 mg), rasagiline (1×1 mg) and amantadine (1×100 mg).

His past medical history showed a benign prostate hypertrophy, low back pain and one episode of transient global amnesia. He had never demonstrated any psychiatric disorder, nor did the family members reported any neurological or psychiatric disorders. The pre-operative MRI of the brain showed no abnormalities.

Deep brain electrodes were stereotactically implanted in both subthalamic nuclei, using a conventional planning based on MRI and Schaltenbrandt coordinates. In addition, a microelectrode recording with five microelectrodes was used to determine the optimal target. Finally, intra-operative stimulation and clinical testing was used to verify the optimal location, based on clinical effects on the cardinal symptoms and the large threshold for evoking stimulation-induced side effects. Indirect targeting with the mid-commissural point as the origin of stereotactic space was used. The final electrode location was defined after verification by means of microrecordings and macrostimulation. The left electrode was placed in the calculated trajectory, while macrostimulation 2 mm more laterally elicited a speech disturbance (corresponding with the internal capsule). The right electrode was placed 2 mm anterior to the calculated trajectory, because macrostimulation in the central trajectory elicited paresthesiae and macrostimulation 2 mm lateral from the latter elicited a speech disturbance. The implantation procedure was uneventful. In a second intervention, one week later, the

pulse generator was implanted and the extensions were internalised. A gradual increase of the current output was clinically tested and finally the patient was stimulated with a voltage of 2 V bilaterally. Motor symptoms, including the camptocormia, significantly improved. The post-operative UPDRS motor score was 28 without medication. The patient was able to walk without walking aid.

Freezing, tremor, rigidity and even dysarthria markedly improved. The antiparkinson medication was discontinued. Two weeks after the electrode implantation the patient was discharged from the hospital.

Four weeks later, the patient was urgently admitted to the hospital with important behavioural changes. He was not able to sleep at night and slept only 1–2 h during the daytime. His mood was elevated. He had logorrhea. His behaviour was impulsive (buying lots of things) and disinhibited (making inappropriate sexual comments). Psychomotor activity was increased and the patient was agitated ('working in the garden at night', 'climbing on the roof of the house ...'). Furthermore, grandiose ideas (building a swimming pool on top of his flat) were present. The patient had no insight in his behavioural changes and felt fantastic. No hallucinations or suicidal ideas were present. The partner of the patient mentioned retrospectively that after the discharge from the hospital, the patient only slept for 4 h per night and that his mood was a bit elevated but not problematic. Initially, this was ascribed to his feelings of relief after the surgical procedure. The patient was diagnosed with a manic episode, probably elicited by DBS. Consequently, the DBS was turned off. Motor symptoms including rigidity and camptocormia rapidly re-appeared but all behavioural changes disappeared. Because of the motor symptoms, the DBS was again initiated and gradually but more slowly increased to 1.5 V bilaterally. This stimulation sufficiently controlled the motor symptoms without causing any behavioural problems and any need for further antiparkinson medication. Only trazodone 100 mg was daily given for sleep difficulties.

Discussion

Chronic bilateral DBS of the STN is an effective neurosurgical procedure for treatment of serious motor symptoms in patients with advanced PD, which cannot be sufficiently treated with pharmacological medication (5). However, several psychiatric complications have been reported after DBS. The most frequent problems are cognitive dysfunction and depression. Hypomanic or manic symptoms are relatively rare but may occur in about 4–8% of the

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patients undergoing DBS (1,2,5). They often start soon after the initiation of the stimulation and are mostly transient (2,5).

Several hypotheses have been put forward to explain the (hypo)manic symptoms after DBS. They may result from a pre-existing psychiatric illness, surgery-related stress or the neurostimulation (5). No pre-existing psychiatric illness was present in our patient. Any type of surgery may cause stress, but the surgical procedure went without any complications and resulted in significant motor improvements making it less likely the cause of the manic episode in our patient. Since all antiparkinson medication was discontinued after DBS, a drug-induced manic episode is highly unlikely. One would also expect rather depressive than manic symptoms after discontinuation of antiparkinson medication (5). The most likely hypothesis for the occurrence of the manic episode in our patient is the stimulation of the STN itself. It may be explained by the anatomical relation between the neural structures of the motor, the associative and limbic pathways within the STN (2,3). Cognitive and limbic information related to the basal ganglia is processed by the associative and limbic circuits, respectively. The STN has a central position within these circuits. Additionally, these circuits are represented within the STN by specific groups of neurons located medially (limbic) and ventromedially (associative). The STN probably has a regulatory function in the processing of associative and limbic information towards the cortical and subcortical regions (3).

Neurophysiological and neuroimaging studies suggest that emotional, cognitive and motor components of behaviour are integrated and distributed within the STN (2,3). Minor modifications in these circuits, such as those evoked by DBS, may result in behavioural changes like manic symptoms.

It may also be possible that a lower stimulation intensity, resulting in a smaller electrical field,

affects the cognitive and limbic pathways to a lesser extent compared to a larger electrical field. Yet another mechanism may be involved. In our patient the stimulation of the DBS was relatively rapidly increased over the course of seven days to 2 V. The manic symptoms did not return when the DBS stimulation was more gradually and more slowly increased to 1.5 V. This may further point to the importance of slow and gradual initiating the neurostimulation in order to avoid psychiatric symptoms.

Conclusion

Manic episodes may occur after STN stimulation in patients with PD. Although further research will be necessary, a manic episode may be prevented by a slow and gradual increase of the neurostimulation and using the lowest effective intensity to control the motor symptoms.

References

1. CONTARINO MF, DANIELE A, SIBILIA AH et al. Cognitive outcome 5 years after bilateral chronic stimulation of subthalamic nucleus in patients with Parkinson's disease. *J Neurol Neurosurg Psychiatry* 2007;**78**:248–252.
2. RAUCHER-CHÉNÉ D, CHARREL CL, DOE DE MAINDREVILLE A, LIMOSIN F. Manic episode with psychotic symptoms in a patient with Parkinson's disease treated by subthalamic nucleus stimulation: improvement on switching the target. *J Neurol Sci* 2008;**273**:116–117.
3. TEMEL Y, KESSELS A, TAN S, TOPDAG A, BOON P, VISSER-VANDEWALLE V. Behavioural changes after bilateral subthalamic stimulation in advanced Parkinson disease: a systematic review. *Parkinsonism Relat Disord* 2006;**12**: 265–272.
4. ROMITO LM, ALBANESE A. Dopaminergic therapy and subthalamic stimulation in Parkinson's disease: a review of 5 year reports. *J Neurol* 2010;**257**(Suppl. 2):S298–S304.
5. KRACK P, BATIR A, VAN BLERCOM N et al. Five-year follow-up of bilateral stimulation of the subthalamic nucleus in advanced Parkinson's disease. *N Engl J Med* 2003;**349**:1925–1934.