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Mood improvement after deep brain stimulation of the internal globus pallidus for tardive dyskinesia in a patient suffering from major depression

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Abstract

Deep brain stimulation (DBS) has the unique characteristic to very precisely target brain structures being part of functional brain circuits in order to reversibly modulate their function. It is an established adjunctive treatment of advanced Parkinson's disease and has virtually replaced ablative techniques in this indication. Several cases have been published relating effectiveness in neuroleptics-induced tardive dyskinesia. It is also investigated as a potential treatment of mood disorders. We report on the case of a 62 years old female suffering from a treatment refractory major depressive episode with comorbid neuroleptic-induced tardive dyskinesia. She was implanted a deep brain stimulation treatment system bilaterally in the globus pallidus internus and stimulated for 18 months. As well the dyskinesia as also the symptoms of depression improved substantially as measured by the Hamilton Rating Scale of Depression (HRSD) score and the Burke–Fahn–Marsden-Dystonia-Rating-Scale (BFMDRS) score. Scores dropped for HRSD from 26 at baseline preoperatively to 13 after 18 months; and for BFMDRS from 27 to 17.5. This case illustrates the potential of deep brain stimulation as a technique to be investigated in the treatment of severe and disabling psychiatric and movement disorders. DBS at different intracerebral targets being actually investigated for major depression might have similar antidepressant properties because they interact with the same cortico-basal ganglia-thalamocortical network found to be dysfunctional in major depression.

Keywords: Deep brain stimulation (DBS); Treatment refractory major depression; Tardive dyskinesia; Neuroleptics; Globus pallidus internus (GPI)

1. Introduction

Bilateral deep brain stimulation (DBS) of the globus pallidus internus (GPI) and the subthalamic nucleus is a recognized treatment of refractory tremor and motor fluctuations in Parkinson's disease and has a sustained therapeutic effectiveness (Deuschl and Bain, 2002; Eskandar et al., 2003; Krack et al., 2003).

DBS to the GPI is effective in primary dystonia after 12 months in a retrospective analysis of 22 patients. Mood did not change (Vidailhet et al., 2005). In a case series of 15 patients suffering from dystonia (two from tardive dystonia) DBS improved dystonic symptoms and a mild improvement on depression scales was noted after 3–12 months (Halbig et al., 2005). In several reported cases DBS to the GPI was successful to treat drug induced tardive dyskinesia and dystonia. (Franzini et al., 2005; Schrader et al., 2004; Trottenberg et al., 2001, 2005).

Antidepressant activity of bilateral DBS to the white matter underlying the cingulate area Cg 25 was investigated in 6 treatment refractory patients (Mayberg et al., 2005).

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Four showed significant improvement after three months of stimulation. DBS of brain areas such as Brodmann area 25 can therefore be associated with mood modulating properties.

We report a case of a patient suffering of treatment resistant depression with comorbid neuroleptic induced tardive dyskinesia, who was treated during 18 months with bilateral DBS to the GPI.

2. Case

Ms. A., a 62-year-old, married housewife suffered from recurrent depression (current diagnosis: major depressive episode with melancholic features, DSM IV R 296.32, according to SCID-I (Wittchen et al., 1997)) for 15 years prior to consultation at our clinic. She was treated 10 times in psychiatric hospitals for a total of 60 weeks. In total, she was prescribed about 60 different psychotropic drugs. The current episode lasted for eight years. Due to a persistent feeling of tension, inner unrest and sleep problems, she was treated with typical and atypical neuroleptics and severe tardive dyskinesia (TD) developed during the last ten years involving primarily orofacial muscles but also distal parts of the extremities. There was no family history of dystonia or other causes of secondary dystonia/dyskinesia. The TD did not improve after withdrawal of typical neuroleptics, administration of atypical neuroleptics and benzodiazepines. Other diagnosis included diabetes mellitus type IIb. Due to treatment resistance and the disabling character of the TD, Ms. A. was offered DBS of the GPI.

The severity of depression was assessed before, and one and two weeks and 1, 2, 3, 5, 7, 10, 15 and 18 months after implantation using the Hamilton Depression Rating Scale (HRSD) and the Beck Depression Inventory (BDI) (Hamilton, 1967; Beck and Beamesderfer, 1974). The dystonia was assessed using the Burke–Fahn–Marsden-Dystonia-Rating-Scale (BFMDRS), before and 18 months after implantation (Burke et al., 1985). The psychotropic and neurological drugs (Mirtazapine 30 mg/d, Trimipramine 175 mg/d, Lorazepame up to 5 mg/d, Zolpidem 10 mg/d and Trihexyphenidyl 8 mg/d) remained unchanged during the two months prior to implantation.

DBS electrodes (3387 DBS lead, Kinetra 7428 Neurostimulator, Medtronic Inc, Minneapolis, USA) were implanted without complications to target the ventral part of the GPI, 1-2 mm above (dorsal to the ventral border of the postero-lateral GPI), 1.5 mm rostral and 2 mm medial of the target used in Parkinson's disease and generalized dystonia to more selectively stimulate the facial area within the ventral GPI. The trajectories were calculated by using stereotactical MR- and CT-imaging. The position of the electrodes was verified with intraoperative X-ray. Final postoperative X-rays were performed and matched with the planning MRI to control for correct positioning of the electrodes. After six weeks of testing for optimal parameters, the left GPI was stimulated with contact 1 negative, case positive, at 3.5 V, 90 μs pulse width and 130 Hz; at the right GPI contact 4 negative, case positive, at 3.8 V, 90 μs pulse width and 130 Hz. As indicated by the constant impedance, the function of the system was maintained.

Two weeks after implantation, Trimipramine was reduced to 150 mg/d. After 15 months, Trimipramine and Mirtazapine were discontinued and replaced by Reboxetine 2 mg/d and Pipamperone 80 mg/d by the treating psychiatrist. At the same time, Trihexyphenidyl could be reduced to 2 mg/d and Lorazepame was reduced to 1.25 mg/d, Zolpidem was stopped and Lormetazepame 2 mg was introduced.

3. Results

The BFMDS score was 27 two days before implantation and 17.5 18 months later, a reduction of 35%. Trihexyphenidyl could be substantially reduced. The improvement concerned essentially the distal parts of the lower extremity and also the neck as well as a slight improvement of uncoordinated repetitive action of swallowing. The depression improved significantly (Fig. 1). Compared to 1 week before implantation, the HRSD-score dropped from 26 to 13, 15 months later (improvement of 50%, considered as a clinically significant response). The BDI score dropped from 22 one month before implantation to 16 at 15 and to 17, 18 months later. The patient improved substantially: six weeks after the start of stimulation, she began to read magazines again, 2.5 months later, she was increasingly able to do work at home. One month later, she took up driving her car again and she went abroad on holidays for two weeks with her husband. She had been unable to do these activities for 6 years. The last 3 months of our observation period were the longest time during the last years during which the patient enjoyed such a sustained improvement of her depression.

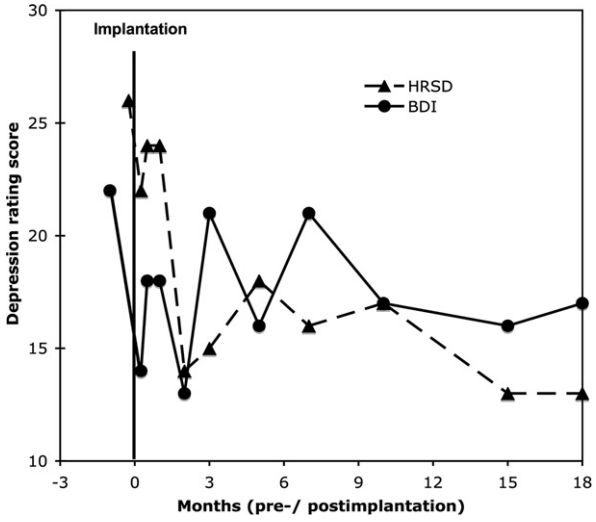

Fig. 1. Evolution of the severity of measures of depression before and after deep brain stimulation. Time 0 indicates the implantation of the DBS-system. HRSD : Hamilton Rating Scale of Depression 21-item version; BDI: Beck depression inventory.

4. Discussion

Our patient is one of only a few suffering from treatment resistant depression improving after DBS. Besides the study by Mayberg et al. (2005), in which the stimulation of Brodmann area 25 had antidepressant effects, the bilateral stimulation of the thalamic peduncle led to a remission of depressive symptoms in a single case study (Jimenez et al., 2005). In another case study of a patient suffering from obsessive compulsive disorder and major depression, DBS of the ventral caudate nucleus induced remission of both disorders (Aouizerate et al., 2005). The primary indication to treat Ms. A. with bilateral DBS of the GPI was her neuroleptic-induced TD. The GPI is the major output nucleus of the basal ganglia-system with GABA-ergic function. It is driven by the excitatory, glutamatergic activity of the subthalamic nucleus and inhibits thalamo-prefrontal circuits. Both ventral pallidum and the GPI per se have descending projections to the substantia nigra converging on individual neurons (Bevan et al., 1996). Thus, not only the ventral pallidum, but also the GPI area stimulated in the reported case, can potentially modulate mesolimbic dopaminergic circuits similar to the antidepressant effects of Levodopa (Schneider et al., 2003). The relation of the GPI with limbic circuits are reviewed elsewhere (Temel et al., 2005).

DBS is known to be particularly effective on trunk and limb dystonic and less on oromandibular symptoms. Diskinetic symptoms in our case improved, especially at the limbs, whereas the subjectively most disabling symptom, the oromandibular dyskinesia, improved only slightly. However, the depression improved significantly after 15 and 18 months of stimulation. We therefore believe that DBS to the GPI exerts antidepressant effects independent of effects on movement disorders. Several targets are under investigation to treat refractory depression, such as Cg25, the anterior limb of the internal capsule and the nucleus accumbens. In depression, a dysfunction of a limbic–cortical–striatal–pallidal–thalamic network has been proposed (Sheline, 2003; Mayberg, 2003). DBS at different targets located within this network, including the GPI, could therefore lead to a modulation of mood.

5. Competing interests

Dr. Schlaepfer and Dr. Sturm are principal investigators on investigator-initiated research grants funded partly by Medtronic Inc., Minneapolis, a manufacturer of DBS stimulators.

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