Sustained improvement of obsessive–compulsive disorder by deep brain stimulation in a woman with residual schizophrenia

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Co-occurrence of obsessive–compulsive disorder (OCD) and schizophrenia is not rare (Eisen et al., 1997). Given that the obsessional content is not related to psychotic subject matter, both disorders can be regarded as delimitable diagnostic entities (Bottas et al., 2005). Recently, a number of case reports and small case series have demonstrated that deep brain stimulation (DBS) targeting the fronto-striato-thalamic circuit can have beneficial effects on OCD (Abelson et al., 2005; Greenberg et al., 2006; Sturm et al., 2003). DBS treatment of patients with current or past psychotic disorders has not yet been reported. Here, we present a comprehensive clinical evaluation of a woman with intractable OCD and residual symptoms of schizophrenia that were treated with unilateral DBS of the right nucleus accumbens (NAc), including neuropsychological long-term follow-up, neurophysiological measurements and functional brain imaging.

Case report

This 51-yr-old right-handed woman suffered from a severely disabling, chronic and intractable form of OCD with excessive hand washing, cleaning, re-arrangement of objects and compulsive praying [Yale–Brown Obsessive Compulsive Scale (YBOCS) score 32/40, 1 month prior to treatment]. Psychosocial functioning as measured by the GAF (Global Assessment of Functioning) scale was severely impaired (31/100). The symptoms started during childhood and accumulated during her early twenties. Obsession consisted of preoccupation with thoughts about guilt and purgation. Later in the course of the disease, psychotic symptoms (delusions, hallucinations, disorganized behaviour) meeting DSM-IV criteria for schizophrenia occurred transiently. The remaining presence of a few odd beliefs, minor paranoid ideation and disorganized behaviour in an attenuated form that were unrelated to the obsessions and compulsions led to the diagnosis of residual schizophrenia according to DSM-IV using SCID (Structured Clinical Interview for DSM-IV). With regard to the severely disabling symptoms of OCD, long-term treatment with clomipramine, sertraline and cipramil, augmentation with olanzapine, quetiapine, risperidone and aripiprazole as well as cognitive-behavioural treatments (CBT) including exposure and response prevention (ERP) did not exert any persistent beneficial effect.

Following the guidelines on DBS for psychiatric disorders (Nuttin et al., 2002), the local DBS assessment committee ensured that the patient met the required medical, neurological and psychiatric criteria, particularly in respect of severity, chronicity, disability, and treatment refractoriness. After approval from the ethics committee of the University of Tuebingen, determination of the patient’s capacity to consent by a psychiatrist not involved in the treatment, and subsequent written informed consent, the patient was admitted to neurosurgery. Under stereotactic conditions a quadripolar DBS electrode was placed in the right anterior limb of the internal capsule with the tip into the approximate centre of the NAc. Electrode implantation was performed without complications. The stereotactic coordinates were 2.7 mm anterior, 6.8 mm lateral and 4.2 mm inferior to the anterior commissure. Due to safety considerations and previous data regarding effectiveness, we opted for this unilateral right-sided implantation (Sturm et al., 2003). An inter-current wound infection above the pulse-generator pouch was effectively treated with clindamycin. There were no other perioperative complications. Medication (60 mg citalopram, 300 mg quetiapine) remained unchanged during DBS treatment.

Within 4 wk of stimulation onset (most distal contact, 4.5 V, 60 µs, 130 Hz), the patient reported a
substantial reduction of obsessions and a moderate decrease of compulsions (YBOCS score reduced to 24/40). No further beneficial effects were achieved by modifying amplitude (up to 9 V), frequency (50–130 Hz) impulse duration (60–150 ms), and recruitment of additional electrodes. However, stimulation intensities above 6 V induced nausea, agitation and a transient worsening of OCD symptoms. The reduction of symptoms and improvement of psychosocial functioning under DBS was maintained at 6 months follow-up (YBOCS 23/40, GAF 40/100), 1 yr (Y-BOCS 24/40, GAF 44/100) and 2 yr (YBOCS 25/40, GAF 49/100) after implantation. The patient appraised the effect of stimulation as satisfying and never requested a cessation of treatment. Aggravation of psychotic symptoms was not observed at any time of the DBS treatment.

**Imaging study**

Effects of stimulation on brain metabolism were measured by [18F]FDG-PET (Figure 1a). Compared with findings obtained before electrode implantation, a second PET scan 3 months after starting stimulation revealed reduced brain metabolism (normalized FDG uptake 40–52 min reduced by >5%) in the right (ipsilateral) orbitofrontal and dorsolateral prefrontal cortex. These findings indicate a functionally relevant reduction of brain activity in areas involved in OCD pathophysiology (Aouizerate et al., 2004). Further, smaller clusters with reduced FDG uptake were found in the right caudate, right insula, posterior cingulate and in parts of the left prefrontal cortex and the left thalamus.

**Neuropsychology**

Neuropsychological assessments (Wisconsin Card Sorting Test, Continuous Performance Test, Stroop Test, Trail-Making Test A/B) at baseline and 3 and 10 months after DBS surgery did not indicate any decline in cognitive and executive functioning.

**Neurophysiology**

One day after implantation, local field potentials (LFP) were recorded from each electrode contact (nos. 0, 1, 2, 3). Frequency analysis (Figure 1b) indicated a peak in spectral power at 25.4 Hz (beta band) specific for the most distal electrode presumably located in the NAc. No clear-cut peak was present in electrode no. 1 but corresponding power peaks were identified in electrode no. 2 at 12.7 Hz and no. 3 at 12.7 Hz (alpha band) probably located in the anterior part of the inner capsule.

**Discussion**

This case study in a patient with treatment-resistant OCD demonstrates a decrease of symptoms (25% YBOCS) and a gain of psychosocial functioning (58% GAF) after unilateral DBS in the right NAc. Our results are in line with previous reports on the effects of DBS in the anterior part of the internal capsule and the NAc in OCD (Abelson et al., 2005; Greenberg et al., 2006; Sturm et al., 2003). Furthermore, it exemplifies that unilateral stimulation of the NAc can exert lasting, albeit moderate, beneficial effects on OCD even if the disorder is associated with residual symptoms of schizophrenia. The clinical relevance of a 25% reduction of symptoms may be questioned. Nevertheless, the reduction of the individual disease burden was perceived as essential by the patient and reflected by an enhancement of social integration and level of functioning in everyday life.

The additional imaging data demonstrate that unilateral stimulation of the NAc actually interferes with a neuronal network involved in the pathophysiology of OCD.
of OCD on the targeted side and agree with previous findings on the effects of DBS of the anterior limb of the internal capsule (Abelson et al., 2005). The neurophysiological findings provide first evidence in humans that beta power might be of localizing value in identifying the NAc. The observed LFP power peak at 25.4 Hz is consistent with single-unit activity of the NAc in rats with a mean at 25 Hz (Mulder et al., 1996).

In this case in particular, where a new and invasive technique is used in a patient with a history of psychotic symptoms, the ethical framework is of major relevance. Comprehensive and thorough judgement of indication (diagnosis, treatment resistance, chronicity and impairment) is indispensable. This involves a detailed clinical assessment by an interdisciplinary network including experienced psychiatrists, neurologists, neurosurgeons and an independent psychiatric specialist not involved in the treatment of the patient as well as the local ethics committee. It is mandatory to verify that the patient has the capacity to consent and adhere to the treatment. This and the reassurance of a close and continuous follow-up of the patient provided the essential prerequisites for a responsible shared decision and the safe and effective treatment of psychiatric disorders such as OCD with DBS.

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Statement of Interest

None.

References


