Moving the brain: Neuroimaging motivational changes of deep brain stimulation in obsessive-compulsive disorder

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Obsessive-compulsive disorder (OCD) is a chronic psychiatric disorder related to dysfunctional dopaminergic neurotransmission. Deep brain stimulation (DBS) targeted at the nucleus accumbens (NAc) has recently become an effective treatment for therapy-refractory OCD, but its effect on dopaminergic transmission is unknown. We measured the effects of NAc DBS in 15 patients on the dopamine D$_{2/3}$ receptor binding potential (D$_{2/3}$R BP) in the striatum with $^{[123]I}$iodobenzamide single photon emission computed tomography ($^{[123]I}$IBZM SPECT). We correlated changes in D2/3R BP with plasma levels of homovanillic acid (HVA) and clinical symptoms. Acute (1 hour) and chronic (1 year) DBS decreased striatal D$_2$R BP compared to the non-stimulated condition in the putamen. D$_{2/3}$R BP decreases were observed already following one hour of stimulation and were related to increased HVA plasma levels, implying DBS-induced dopamine release. D$_{2/3}$R BP decreases in the area directly surrounding the electrodes were significantly correlated with changes in clinical symptoms (45% symptom decrease).
DBS-induced striatal dopamine release, in association with increased HVA plasma levels and improved clinical symptoms, suggest that DBS may compensate for a defective dopaminergic system. DBS-induced striatal dopamine release, in association with increased HVA plasma levels and improved clinical symptoms, suggest that DBS may compensate for a defective dopaminergic system.

**Introduction**

Deep brain stimulation (DBS) has become an effective treatment for therapy-refractory obsessive-compulsive disorder (OCD) (chapter 10). The effects of DBS are substantial with on average almost 50% improvement of obsessive-compulsive symptoms (chapter 10). Despite these promising clinical observations, remarkably little is known about the underlying mechanism of action. OCD has been related to abnormalities in dopaminergic neurotransmission, predominantly on the basis of clinical evidence and molecular imaging studies. For example, dopamine receptor antagonists are effective as an adjunct to selective serotonin reuptake inhibitors (SSRIs) in reducing symptoms in OCD (Vulink *et al.*, 2009) and dopamine agonists may induce obsessive-compulsive behavior (Borcherding *et al.*, 1990). Molecular imaging studies consistently showed decreased dopamine D_{2/3} receptor binding in OCD (chapter 8), most prominently in the ventral striatum (Perani *et al.*, 2008). Most effective DBS targets for OCD are in or around the ventral striatum (chapter 10), and animal studies suggest that DBS in this area increases dopamine levels in the stimulated area or prefrontal cortex (Sesia *et al.*, 2010; van Dijk *et al.*, 2011). We therefore hypothesized that striatal dopamine release may be one of the key mechanisms of action behind DBS for OCD. We analyzed dopaminergic changes of DBS targeted at the border of the nucleus accumbens (NAc) core and anterior limb of the internal capsule in OCD patients, using [^{123}I]iodobenzamide single photon emission computed tomography ([^{123}I]IBZM SPECT) and plasma measurements of the dopamine metabolite homovanillic acid (HVA), which is thought to partially reflect central dopaminergic and noradrenergic changes.
Materials and methods

Study participants
We included 15 DBS-implanted patients with OCD and 18 age- and gender matched healthy controls (Table 1). Patients were recruited from the outpatient clinic for DBS at the Academic Medical Center (AMC), Amsterdam, The Netherlands. Healthy control subjects were only included if they were free of any mental disorder, had no family history of any psychiatric disorder and reported no history of head trauma, neurological or other medical disorders, alcohol or substance abuse. Participants provided written informed consent prior to participation and the local Ethics Committee approved this study.

All included patients had a primary diagnosis of OCD according to DSM-IV criteria, established by a psychiatrist and confirmed by the Mini International Neuropsychiatric Interview (Sheenan et al., 1998; van Vliet et al., 2007). Eight patients had predominantly OCD symptoms of the subtype contamination fear, four patients had predominantly high-risk assessment and checking symptoms, two patients mainly suffered from perfectionism and one patient had somatic obsessions. Mean duration of illness was 25.9 years (range 8-48 years). Four patients were diagnosed with comorbid major depressive disorder, one patient was diagnosed with comorbid panic disorder, and three patients were diagnosed with comorbid obsessive-compulsive personality disorder. Nine patients were medication-free for at least one year at the time of this investigation. Six patients had been using medication before the study for 11 to 63 months (mean 23 months). Because of potential interference with $[^{123}]$IBZM binding to dopamine D$_{2/3}$ receptors, medication was discontinued according to its pharmacological half-life: 16 days before the first scan for clomipramine (3 patients), 12 days for paroxetine (1 patient), 24 days for fluoxetine (1 patient), and one week for fluvoxamine (1 patient). At the day of the imaging session and within 24 hours before each scanning session, participants were not allowed to consume coffee, alcohol or nicotine as these substances have been associated with increased striatal dopamine release. Four patients and two controls smoked. Patients were chosen from a larger clinical DBS sample when they had finished the treatment optimization phase and remained clinically stable after at least one year of stimulation. At this stage, 12 patients
had Y-BOCS decreases of more than 25%, corresponding to responder-status, and 3 patients experienced less than 25% decrease (12% in 1 patient and 17% in 2 patients).

<table>
<thead>
<tr>
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<th>Patients (n=15)</th>
<th>Controls (n=18)</th>
<th>Statistic</th>
</tr>
</thead>
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<td>Age, mean (SD), years</td>
<td>43.8 (10.1)</td>
<td>38.3 (17.9)</td>
<td>t = 1.048</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>P = 0.303</td>
</tr>
<tr>
<td>Gender, Male: Female, Number</td>
<td>7:8</td>
<td>9:9</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>$\chi^2 = 0.133$</td>
</tr>
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<td></td>
<td></td>
<td></td>
<td>P = 0.716</td>
</tr>
</tbody>
</table>

**Table 1.** Demographics of the study sample

**DBS settings**

All patients had electrode implantation in the same target area (for details see Denys et al., 2010), i.e. two quadripolar electrodes (Model 3389, Medtronics Inc., Minneapolis, MN) with contact points 1.5-mm long and separated from adjacent contacts by 0.5 mm were implanted bilaterally following the anterior limb of the internal capsule into the target nucleus, with an anterior angle of approximately 75° to the intercommissural line. Target coordinates for the electrode tip were 7 mm lateral to the midline, 3 mm anterior to the anterior border of the anterior commissure, and 4 mm inferior to the intercommissural line. We included only patients that had completed the optimization phase of one to two years during which they were evaluated every 2 weeks for severity of symptoms and optimal stimulation parameters. For all 15 patients, receiving monopolar stimulation on the two dorsal contact points, the most effective stimulation area was located at the border of the NAc core and anterior limb of the internal capsule. At time of entrance of the study, patients were stimulated with an average of 4.8 Volt (range 3.5-6.2V), a frequency of 130 Hertz (11 patients) or 185 Hertz (4 patients), and a pulse-width of 90 microseconds (12 patients), 130 microseconds (2 patients), or 150 microseconds (1 patient).

**Symptom measures**

We assessed symptom severity in patients during chronic stimulation (session 1: clinically stable after at least one year of stimulation), during DBS OFF (session 2: after eight days of DBS discontinuation), and during acute stimu-
lation (session 3: one hour after turning the stimulator back on). Symptom severity was assessed using the Yale-Brown Obsessive-Compulsive Scale (Y-BOCS) (Goodman et al., 1989 I and II), the Hamilton Depression Rating Scale (HAM-D) (Hamilton, 1960), and the Hamilton Anxiety Rating Scale (HAM-A) (Hamilton, 1959).

**SPECT data acquisition**

All patients were scanned on three separate occasions: during chronic stimulation, DBS OFF and acute stimulation (sessions 1-3). All healthy controls were scanned once. Subjects received a potassium iodide solution to block thyroid uptake of free radioactive iodide. For administration of the radiotracer, we used a sustained equilibrium/constant infusion technique to achieve stable regional brain activity levels during scanning (Boot et al., 2008; Booij et al., 1997). In session 1, dopamine D$_{2/3}$ receptors (D$_{2/3}$R) were measured with the well-validated radiotracer $[^{123}\text{I}]$IBZM while the patients were on chronic DBS stimulation. In this session, approximately 80 MBq $[^{123}\text{I}]$IBZM (specific activity>200 MBq/nmol and radiochemical purity>95%) was administered intravenously as bolus, followed by 3 hours of continuous infusion of 20 MBq/h $[^{123}\text{I}]$IBZM. Acquisition of the images started 2 hours after the bolus injection when a state of sustained binding equilibrium can be expected (Booij et al., 1997). Also the healthy controls were scanned using this paradigm. In session 2, patients were scanned after eight days DBS discontinuation (DBS OFF). In session 3, one hour after session 2, patients were scanned after 1 h acute stimulation. For sessions 2 and 3, approximately 80 MBq $[^{123}\text{I}]$IBZM was administered intravenously as bolus, followed by 5 h of continuous infusion of 20 MBq/h $[^{123}\text{I}]$IBZM. In the interval 2 to 3 h after $[^{123}\text{I}]$IBZM bolus injection patients were scanned to measure D$_{2/3}$R in the DBS OFF situation. Then, the stimulation was reactivated and one hour later (i.e., the interval between 4 and 5 h after $[^{123}\text{I}]$IBZM bolus injection) the patients were scanned again to assess the effects of acute stimulation, since previous $[^{123}\text{I}]$IBZM SPECT studies showed that one hour after the induction of dopamine release, a new steady state was established (Booij et al., 1997). SPECT scans were acquired on a 12-detector single slice brain-dedicated scanner (Neurofocus 810, which is an upgrade of the Strichmann Medical Equipment), with a full-width at half maximum resolution of approximately
6.5 mm, throughout the 20 cm field-of-view (http://www.neurophysics.com). After positioning of the subjects with the head parallel to the orbitomeatal line, axial slices parallel and upward from the orbitomeatal line to the vertex were acquired in 5 mm steps. Each acquisition consisted of approximately 10-12 slices with 5 min scanning time per slice, acquired in a 64×64 matrix. The energy window was set at 135-190 keV.

**MRI data acquisition**

Co-registered T1-weighted structural images of all implanted patients were acquired on a 1.5 Tesla Siemens MAGNETOM Avanto Scanner. To minimize exposure of the DBS device to the pulsed radio-frequency field, we scanned all subjects using a transmit/receive (Tx/Rx CP) head coil. Two minutes before patients entered the scanner, the DBS system was turned off and programmed at 0 V in bipolar mode. Specific absorption rate (SAR) levels were limited to 0.1 W/kg. For T1-weighted structural images the following parameters were used: field of view 256 mm, voxel size 1 x 1 x 1 mm³, slice thickness = 1 mm.

**SPECT data analysis**

SPECT data were reconstructed and analyzed blind to clinical data. Our primary outcome parameter was non-displaceable binding potential (BP_{ND}) of \[^{123}\text{I}]\text{IBZM}, as a measure of D_{2/3}R availability. BP_{ND} was calculated as \[^{123}\text{I}]\text{IBZM} binding in the target tissue minus activity in the reference tissue divided by activity in the reference tissue. We used binding in the occipital cortex, which is devoid of D_{2/3}R, as reference tissue. We first performed attenuation correction of all SPECT images and then reconstructed them in 3D mode (http://www.neurophysics.com) (Boot et al., 2008; Booij et al, 1997). With these 3D images we performed two different region-of-interest (ROI) analyses:

1. For quantification of BP_{ND} in the striatum and its subdivisions in patients and controls we used standard templates with fixed ROIs on the 3D SPECT images (Fig. 1a). Striatal BP_{ND} was calculated by first selecting three consecutive SPECT slices, representing the most intense striatal binding. Next, standard templates with fixed ROIs were manually placed on the striatum and occipital cortex, which we used for the calculation of the ratio of specific striatal (caudate nucleus and putamen) to occipital binding (BP_{ND}).
For quantification of $BP_{ND}$ in the stimulated area of the patients we defined ROIs based on the individual co-registered MRI scans (Fig. 1b). We manually re-aligned each individual SPECT scan to the MR data in all three dimensions followed by an automated registration based on a mutual information algorithm with in-house software (van Herk et al., 2000). We calculated the radius of the electrode activation centers for each patient using the individual DBS voltage settings in the following formula: $R \text{ (mm)} = \sqrt{(\text{Voltage/3})} \times 3$ (Butson et al., 2006). Next, ROIs were manually delineated on the MR image by drawing a 3D sphere of radius $R$ around the centers of the active electrode points. We also manually delineated ROIs around the occipital cortex on each MRI slice and then calculated the ratio of specific binding in the ROI to occipital binding ($BP_{ND}$).

**Figure 1A**: example of transverse SPECT slice with fixed regions-of-interest (ROI) placed on the striatum, caudate nucleus, putamen and occipital cortex.

**Figure 1B**: example of two corresponding coronal MRI and SPECT slices with ROI of stimulated area (red) based on a manually delineated sphere around the active contact points (white asterisk).

**HVA data acquisition and analysis**

Ten ml blood was collected for assessment of peripheral HVA levels during the three sessions (chronic stimulation, DBS OFF, acute stimulation), right after each SPECT scan acquisition. Timing of HVA samples was standardized to limit diurnal variation. The blood samples were collected in ice-chilled polypropylene tubes containing EDTA. Tubes were centrifuged at 3000 rpm for 15 min...
at 4°C and plasma was stored at −20°C until analysis. Plasma levels of HVA were determined by liquid chromatography (HPLC, Shimadzu, Eindhoven, the Netherlands) and electrochemical detection (DECADE 1 equipped with a VT-03 cell at a potential setting of 700 mV vs. Ag/AgCl reference electrode at 40°C. (ANTEC Leyden, Zoeterwoude, the Netherlands). The sensitivity of the method for HVA was 2ng/mL plasma and the coefficient of variation was less then 6% (Westenberg and Verhoeven, 1988).

Statistics
We used repeated measures ANOVA to analyze symptomatic and dopaminergic changes between the three sessions and a two-sample t test for comparing patients and healthy controls. We included hemisphere in our analyses of DBS-induced [¹²³I]IBZM binding because the stimulation was applied in the left and right hemisphere and based on previous studies we expected that this would result in different effects on either side (Kuhn et al., 2012). Correlation analyses were performed applying Pearson’s correlation. All statistical tests were computed with SPSS for Windows 18.0 (SPSS Inc. Chicago, IL, USA).

Results

Symptom changes
Figure 2 summarizes clinical changes related to DBS. Active stimulation (acute or chronic stimulation) compared to DBS OFF was related to an average 35% improvement of obsessive-compulsive symptoms, 49% improvement of depressive symptoms and 46% improvement of anxiety symptoms. All symptom scores changed significantly over the three sessions, with increases from chronic stimulation to DBS OFF, and decreases from DBS OFF to acute stimulation (YBOCS $F(2, 13)=10.42, P=0.002$; HAMD $F(2, 13)=13.08, P=0.001$; HAMA $F(2, 13)=9.16, P=0.003$).
Changes in dopamine $D_{2/3}$ receptor binding

Table 2 and Figure 3 summarize striatal $[^{123}\text{I}]$IBZM $BP_{ND}$ changes related to DBS. Irrespective of DBS condition, OCD patients had significantly lower striatal $[^{123}\text{I}]$IBZM $BP_{ND}$ than healthy controls (Table 2), also when including age as a covariate. Active stimulation (acute or chronic) compared to DBS OFF was related to an average 10.2% decrease of striatal $BP_{ND}$ and an average 20.1% decrease of $BP_{ND}$ in the stimulated area. Repeated measures ANOVA for the three scanning sessions showed a significant time by hemisphere interaction in the putamen ($F(2, 13)=6.34$, $P=0.012$). Contrasts showed an increase of $BP_{ND}$ in the putamen from chronic stimulation to DBS OFF in both hemispheres ($P=0.044$), which reversed more rapidly in the left than right putamen after acute stimulation ($P=0.002$). Although we found a similar pattern of results in the caudate and in the stimulation area, that is $BP_{ND}$ increases from chronic stimulation to DBS OFF followed by a reversal from DBS OFF to acute stimulation, these changes were not significant. Nevertheless, we found a positive correlation between $[^{123}\text{I}]$IBZM $BP_{ND}$ changes and YBOCS-changes in the stimulation area between chronic stimulation and DBS OFF ($r=0.536$, $P = 0.039$). $BP_{ND}$ changes in putamen and caudate were not correlated to...
changes in YBOCS-scores. BP_{ND} changes in the putamen remained statistically significant when including medication, OCD subtype, treatment response, age or duration of illness as covariates.

<table>
<thead>
<tr>
<th>ROI</th>
<th>controls</th>
<th>1.chronic stimulation</th>
<th>2.DBS OFF</th>
<th>3.acute stimulation</th>
<th>P¹</th>
<th>change 1 - 2</th>
<th>change 2 - 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Caudate</td>
<td>left</td>
<td>1.28 (0.06)</td>
<td>0.89 (0.10)</td>
<td>1.01 (0.16)</td>
<td>0.86 (0.10)</td>
<td>0.082</td>
<td>13.5%</td>
</tr>
<tr>
<td></td>
<td>right</td>
<td>1.16 (0.04)</td>
<td>0.78 (0.10)</td>
<td>0.87 (0.15)</td>
<td>0.85 (0.09)</td>
<td>0.001</td>
<td>11.5%</td>
</tr>
<tr>
<td>Putamen</td>
<td>left</td>
<td>1.43 (0.06)</td>
<td>0.91 (0.10)</td>
<td>1.03 (0.13)</td>
<td>0.90 (0.08)</td>
<td>0.015</td>
<td>13.2%</td>
</tr>
<tr>
<td></td>
<td>right</td>
<td>1.20 (0.06)</td>
<td>0.87 (0.10)</td>
<td>0.96 (0.11)</td>
<td>0.95 (0.07)</td>
<td>&lt;0.001</td>
<td>10.3%</td>
</tr>
<tr>
<td>Stimulated region</td>
<td></td>
<td>0.52 (0.15)</td>
<td>0.62 (0.17)</td>
<td>0.41 (0.13)</td>
<td></td>
<td></td>
<td>19.2%</td>
</tr>
</tbody>
</table>

Table 2. [¹²³I]IBZM binding potential in controls and patients

ROI: region of interest; BP_{ND}: non-displaceable binding potential; SEM: standard error of mean; DBS: deep brain stimulation. P¹ is for BP_{ND} difference between controls and the average of sessions 1-3 in patients (independent t-test).

Figure 3: D_{2/3} receptor binding potential in controls and patients; Error bars indicate SEM

Peripheral dopaminergic changes (HVA)

Patients with or without stimulation had higher plasma HVA levels than healthy controls (Fig. 4). Our results of lower [¹²³I]IBZM BP_{ND} during stimulation indicate increased dopamine. Therefore, we tested the hypothesis that stimulation would increase plasma HVA levels, as a peripheral indication of dopamine.
DBS induces dopamine release in OCD

release. Active stimulation (acute or chronic) compared to DBS OFF induced an average 17.8% increase in plasma HVA levels. HVA decreased significantly from chronic stimulation to DBS OFF ($t(13)=2.37, P = 0.034$), which correlated with increases in obsession scores ($r = -0.699, P = 0.013$). HVA did not change significantly from DBS OFF to acute stimulation.

![Figure 4: Plasma homovanillic acid levels in controls and patients; Error bars indicate SEM](image)

Discussion

This study shows that DBS targeted at the NAc for OCD induces a reduction in striatal $D_{2/3}R$ binding. Patients that had been stimulated for either one hour or one year had improved symptom scores along with lower availability of striatal $D_{2/3}$ receptors as measured by $[^{123}]$IBZM binding, compared to DBS OFF for one week.

To the best of our knowledge, no other study has investigated in vivo dopaminergic changes of acute and chronic DBS, using a combination of central and peripheral measures. Increased postmortem tissue concentrations of dopamine have been found in the NAc shell of rats after acute stimulation of that area (Sesia et al., 2010), and acute stimulation of the NAc core increased dopamine release in prefrontal areas but not in the stimulated area, as measured with in
vivo microdialysis (van Dijk et al., 2011). Comparable to our findings, chronic DBS decreased D_{2/3}R availability in the putamen of three patients with Parkinson’s disease with globus pallidus internus (GPi) electrodes (Nakajima et al., 2003) and of two patients with Tourette’s disorder with thalamic electrodes (Kuhn et al., 2012), although the latter study found opposite results in the thalamus. Decreased D_{2/3}R availability in these studies may reflect increased competition with the radiotracer caused by dopamine release, or alternatively, diminished D_{2/3}R affinity or a structural receptor decrease due to down-regulation. BP decreases in our study likely reflect dopamine release because they occurred already during the first hour of stimulation. Although concurrent HVA increases during stimulation also indicate dopamine release, results in the chronic stimulation condition may still be explained by D_{2/3}R down-regulation.

Dopamine release in the putamen suggests direct excitatory effects of DBS on this structure, which is situated adjacent to the stimulation site at the border of the NAc and internal capsule. Alternatively, stimulation may have spread from the ventral to the dorsal striatum through spiraling striatoni-grostriatal pathways (Haber et al., 2000), as there is evidence for functional hyperconnectivity between these regions in OCD (Harrison et al., 2009).

The finding of stimulation related D_{2/3} decreases, away from values in healthy controls, may seem paradoxical and warrant clarification. Similar to our finding, lower striatal D_{2/3}R BP in OCD patients relative to controls has been consistently reported in other studies (chapter 8) (Denys et al., 2004; Perani et al., 2008; Schneier et al., 2008), which is usually interpreted as D_{2/3}R down-regulation due to increased dopaminergic neurotransmission. However, recent acute dopamine depletion studies indicate that lower D_{2/3}R availability might actually be also related to decreased endogenous dopamine (Martinez et al., 2009). Pharmacological-induced dopamine depletion can induce obsessive-compulsive symptoms (de Haan et al, 2005), and habitual responding (de Wit et al., 2012), whereas dopamine agonists can improve compulsive behaviors in drug-addicted subjects (Ersche et al., 2011). These lines of evidence and the fact that our OCD patients were all non-responders to dopamine antagonizing agents, implies an underlying dopaminergic deficit in this refractory group which is compensated by stimulatory dopamine release. Lower D_{2/3}R availability in patients without stimulation (DBS OFF) may thus reflect increased receptor
occupancy or down-regulation related to intrinsic compensatory dopamine release, which is further aggravated by DBS. Finally, the presently observed dopamine release induced by DBS may compensate for serotonergic deficits, as OCD has been related to serotonergic deficits combined with dopaminergic hyperactivity (Perani et al., 2008). DBS-induced dopamine release might also explain why higher voltages can induce behaviors that have been linked to excessive striatal dopaminergic activity, such as impulsivity, pathological buying (Luigjes et al, 2011) and tics (unpublished observation).

The present study has a number of potential limitations. We have only scanned our healthy control subjects once, so we cannot rule out that changes over the three sessions in patients are not related to stimulation but rather to spontaneous fluctuations in time. However, we found $D_{2/3}$R BP changes in the range of 10 to 21%, which is highly unlikely in case of spontaneous fluctuations, since the reproducibility of the measurement of dopamine release with the bolus/constant infusion $[^{123}\text{I}]$IBZM SPECT technique is high in humans (Kegeles et al., 1999). Moreover, $D_{2/3}$R and HVA changed in the same direction during acute and chronic stimulation. Together, these characteristics strongly support an effect of stimulation. Variance in $B_{\text{ND}}$ values was larger in the stimulation area compared to putamen and caudate nucleus, which could be related to the lower $B_{\text{ND}}$ than in the in the putamen and caudate nucleus and may explain why $B_{\text{ND}}$ changes in the stimulation area failed to reach significance levels. In addition, our current non-stimulation condition of 8 days DBS discontinuation is not a true baseline pre-treatment measure for comparison with stimulation conditions. Other results may have been found when comparing patients before implantation with acute and continued stimulation. Nevertheless, symptom severity during DBS OFF in the present study was comparable to severity that patients reported before implantation (see Denys et al., 2010). Also, longer DBS discontinuation than 8 days may have yielded stronger dopaminergic changes, however we felt that the severity of symptom relapse had to be balanced against the scientific value. Notably, DBS discontinuation or acute activation was followed by changes in anxiety and mood within seconds or minutes, and changes in obsessions and compulsions occurred within the first minutes till hours. Thus, our measures appear to reflect clinical relevant changes. Another potential limitation is the fact that we cannot completely
rule out the possibility that the plasma HVA changes we found do not only reflect central dopaminergic changes but also noradrenergic changes. Finally, we could not accurately delineate striatal areas on co-registered MRI scans due to artifacts around the electrodes, and for safety reasons images were acquired on a 1.5T MRI scanner with low SAR-values resulting in relatively low grey to white matter contrast in the striatum.

In conclusion, DBS targeted at the NAc appears to release dopamine in the striatum, which is related to improved control over obsessive-compulsive behaviors. These changes hint at a causal role of dopamine in the therapeutic efficacy of DBS, but future research should clarify whether they co-occur with other mechanisms.