Psychoneuroendocrinology (2013) xxx, xxx—xxx

Available online at www.sciencedirect.com

SciVerse ScienceDirect

journal homepage: www.elsevier.com/locate/psyneuen

SHORT COMMUNICATION

Deep brain stimulation for obsessive—compulsive disorder is associated with cortisol changes

Pelle P. de Koning [a,*], Martijn Figee [a], Erik Endert [b], Jitschak G. Storosum [a], Eric Fliers [b], Damiaan Denys [a,c,**]

[a] *Department of Psychiatry, Academic Medical Center, University of Amsterdam, Amsterdam, The Netherlands*
[b] *Academic Medical Center, University of Amsterdam, Department of Endocrinology and Metabolism, Amsterdam, The Netherlands*
[c] *The Netherlands Institute for Neuroscience, An Institute of the Royal Netherlands Academy of Arts and Sciences, Amsterdam, The Netherlands*

Received 9 August 2012; received in revised form 9 December 2012; accepted 11 December 2012

KEYWORDS
Cortisol;
Adrenaline;
Noradrenaline;
Obsessive—compulsive disorder (OCD);
Hypothalamic—pituitary—adrenal (HPA) axis;
Deep brain stimulation (DBS)

Summary Deep brain stimulation (DBS) is an effective treatment for obsessive—compulsive disorder (OCD), but its mechanism of action is largely unknown. Since DBS may induce rapid symptomatic changes and the pathophysiology of OCD has been linked to the hypothalamic—pituitary—adrenal (HPA) axis, we set out to study whether DBS affects the HPA axis in OCD patients. We compared a stimulation ON and OFF condition with a one-week interval in 16 therapy-refractory OCD patients, treated with DBS for at least one year, targeted at the nucleus accumbens (NAc). We measured changes in 24-h urinary excretion of free cortisol (UFC), adrenaline and noradrenaline and changes in obsessive—compulsive (Y-BOCS), depressive (HAM-D) and anxiety (HAM-A) symptom scores. Median UFC levels increased with 53% in the OFF condition (from 93 to 143 nmol/24 h, $p = 0.12$). There were no changes in urinary adrenaline or noradrenaline excretion. The increase in Y-BOCS (39%), and HAM-D (78%) scores correlated strongly with increased UFC levels in the OFF condition. Our findings indicate that symptom changes following DBS for OCD patients are associated with changes in UFC levels.

1. Introduction

Obsessive—compulsive disorder (OCD) is a chronic disabling disorder characterized by recurrent intrusive thoughts and repetitive compulsory behaviors. Recently, deep brain stimulation (DBS) has become a successful treatment strategy for treatment refractory OCD (Denys et al., 2010). DBS is a neurosurgical treatment involving the implantation of electrodes that send electrical impulses to specific locations in

* Corresponding author. Tel.: +31 208913600; fax: +31 20 89136701.
** Corresponding author at: Academic Medical Center, University of Amsterdam, PA.2-179, PO Box 22660, 1100 DD Amsterdam, The Netherlands. Tel.: +31 20 8913899; fax: +31 20 89136701.
E-mail addresses: p.p.dekoning@amc.uva.nl (P.P. de Koning), ddenys@gmail.com (D. Denys).

0306-4530/$ — see front matter © 2013 Elsevier Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.psyneuen.2012.12.006

the brain selected according to the type of symptoms to be addressed. However, its underlying mechanism remains largely unclear. One of the most striking observations when OCD patients are treated with DBS is that symptoms decline dramatically within minutes or hours following DBS activation, and may immediately reoccur after DBS cessation (De Koning et al., 2011). These extreme changes include fluctuations in mood and anxiety (Denys et al., 2010).

The hypothalamic–pituitary–adrenal (HPA) axis and the sympathetic nervous system regulate peripheral concentrations of the main stress hormones cortisol, adrenaline and noradrenaline (De Kloet et al., 2005). Although the literature on the function of the HPA system in OCD is inconsistent, several recent papers report an increase in HPA axis activity (Fluitman et al., 2010; Kluge et al., 2007; Lord et al., 2011).

On this basis, we set out to study whether DBS affects the HPA axis in OCD patients. Determining concurrent changes in stress hormones and OCD symptoms induced by DBS is likely to enhance our understanding of the underlying mechanism of DBS for therapy-refractory OCD patients.

We addressed the following research questions. (1) Is DBS (ON vs OFF) associated with changes in urinary free cortisol, adrenaline and noradrenaline excretion? (2) Are these changes associated with alterations in obsessive–compulsive, depressive and anxiety symptoms?

2. Method

2.1. Participants

We included treatment-refractory OCD patients who were treated with deep brain stimulation (DBS) targeted at the border between the accumbens core and the ventral part of the internal capsule (Denys et al., 2010). Subjects were chosen from a larger clinical sample of DBS-treated OCD patients and were included if they had been treated with DBS for at least one year.

All patients consented to participate in this study and signed an informed consent form. All participants were diagnosed as having primary OCD according to DSM-IV criteria using the Structured Clinical Interview for DSM-IV Axis I disorders (First et al., 1997). In total we included 16 participants, 7 women and 9 men, aged between 32 and 56 years. Six had one or more comorbid disorders: major depressive disorder ($N = 4$), dysthymia ($N = 1$) and panic disorder ($N = 1$). Seven participants used psychotropic medication (6 selective serotonin reuptake inhibitors (SSRIs) and 1 atypical antipsychotic). Participants were asked to stop smoking during the investigation, as nicotine is a strong activator of the HPA axis (Rohleder and Kirschbaum, 2006) and to restrict coffee intake to one cup per day. Other substances influencing vigilance such as alcohol or excessive exercise were prohibited.

Five out of 16 participants were excluded because they showed more than 150% 24-h urine creatinine excretion difference (see Section 2.3) between two consecutive urine collections, and another 3 were excluded because they continued smoking excessively. As a result, we used data from 8 out of 16 participants for final analysis of UFC and urinary (nor)adrenaline. Participant characteristics and an overview of the DBS-induced changes in psychiatric symptoms, UFC and urinary catecholamines are presented in Table 1.

2.2. Procedure

While the DBS had been constantly activated for at least one year, participants collected 24-h urine samples (DBS ON) on two consecutive days. The following day the DBS was turned off. After one week of DBS cessation, two more consecutive 24-h urine samples were collected (DBS OFF) (Fig. 1). Although 24-h urine cortisol sampling is the gold standard for an integrative measure of total free cortisol, it is also a fairly blunt method for measuring HPA axis activity.

During the DBS ON and OFF 24-h urine sampling a psychiatrist assessed obsessive–compulsive, anxiety- and depressive symptoms with the Yale-Brown Obsessive–Compulsive Symptom Scale (Y-BOCS), the Hamilton Anxiety Rating Scale (HAM-A) and the Hamilton Depression Rating Scale (HAM-D) (Goodman et al., 1989a,b; Hamilton, 1960).

DBS parameters varied between participants in voltage (3.5–6.2 V), frequency (90–150 Hz) and pulse width (130–185 μs). Medication was continued during the DBS OFF condition.

Table 1 Baseline characteristics, and changes in psychiatric symptoms and endocrine parameters after one week of DBS cessation.

Subjects	Age (years)	Sex	Med.	Y-BOCS ON–OFF	HAM-A ON–OFF	HAM-D ON–OFF	Cortisol (nmol/24 h) ON–OFF	Adrenaline (nmol/24 h) ON–OFF	Noradrenaline (nmol/24 h) ON–OFF
1.	45	M	None	19–28	19–26	6–20	119–156	22–18	116–120
2.	50	F	None	22–28	22–34	16–18	73–76	4–0	149–168
3.	50	F	None	6–39	4–18	0–21	111–236	28–25	135–99
4.	41	M	SRI/AP	25–40	17–38	10–27	70–74	21–31	232–201
5.	56	M	None	32–28	25–23	30–33	219–130	53–50	326–345
6.	32	F	SRI	30–34	16–27	13–20	158–158	7–5	196–198
7.	41	F	None	19–32	31–51	23–40	76–192	4–37	389–196
8.	39	M	None	14–28	6–29	5–16	49–92	48–61	130–362

Δ: difference DBS ON → DBS OFF (1 week DBS cessation); SRI: serotonin reuptake inhibitor; AP: atypical antipsychotic medication; Med.: medication.

Please cite this article in press as: de Koning, P.P., et al., Deep brain stimulation for obsessive–compulsive disorder is associated with cortisol changes. Psychoneuroendocrinology (2013), http://dx.doi.org/10.1016/j.psyneuen.2012.12.006