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Rebound of Affective Symptoms Following Acute Cessation of Deep Brain Stimulation in Obsessive-compulsive Disorder

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ABSTRACT

Background: Deep brain stimulation (DBS) is regarded as an effective way to treat refractory obsessive-compulsive disorder (OCD). Little is known about the effects of DBS cessation following a longer period of stimulation.
Objective: To determine the relapse and rebound effects of psychiatric symptoms, and their impact on Quality of Life (QoL) following acute cessation of DBS in OCD patients.
Methods: We included 16 out of 32 patients who were treated with DBS between April 2005 and January 2011 at the Academic Medical Center, Amsterdam. After treatment for at least one year, patients entered a 1-week phase in which DBS was switched off. We evaluated psychiatric symptoms and QoL at three time points: before DBS surgery (pre-DBS), following at least one year of DBS treatment (DBS-on) and following 1 week of DBS off (DBS-off). Psychiatric symptoms were assessed with the Yale-Brown obsessive-compulsive disorder scale (Y-BOCS), the Hamilton anxiety rating scale (HAM-A) and the Hamilton depression rating scale (HAM-D). QoL was assessed using the World Health Organization QOL scale (WHOQOL-Bref).
Results: Switching from DBS-on to DBS-off, Y-BOCS scores increased with 50%, HAM-A scores with 80% and HAM-D scores with 83%. In the DBS-off period, HAM-A and HAM-D scores exceeded pre-surgery levels with approximately 40%, suggesting a rebound phenomenon. Furthermore, a deterioration of physical and psychological QoL to levels comparable with pre-surgery was found during DBS-off.
Conclusion: Acute DBS cessation causes a relapse of obsessions and compulsions and a rebound of anxiety and depression. Additionally, improvements on QoL disappear.

Introduction

Deep brain stimulation (DBS) is a safe and effective treatment strategy for therapy-refractory obsessive-compulsive disorder (OCD). Studies report overall responder rates of approximately 50%, limited side effects, and a positive influence on functioning and quality of life (QoL) [1]. However, maintaining these positive effects most likely requires chronic and likely life-long application of DBS. Given this permanent reliance on DBS, it is important to consider that unintended cessation occurs on a regular base. Videnovic and Metman reported a hardware complication rates of 8.4%–10.3% per electrode year [2], which often causes unintended temporary cessation of DBS. Moreover, especially in OCD treatment, high currents are used, which causes battery depletion every 1–2 years. The advent of rechargeable batteries has reduced this problem considerably. However, to function properly these batteries have to be recharged often, on average ranging from once a day to once in five days, dependent on stimulation setting. Therefore unintended cessation of DBS is nowadays often related to recharging issues.

Despite the frequent interruption of active stimulation, little is known about its impact on clinical symptoms and general wellbeing of the patients. Case-series [3–5] and efficacy studies with DBS on-off design [6,7] generally report an acute worsening of psychiatric

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Table 1
Demographic and clinical characteristics.

	Patients ($n = 16$)	
	Mean (range)	SD
Gender (Males/females)	9/7	
Age (years)	45 (27–59)	9.73
Age at onset (year)	16.12 (5–35)	8.15
Age at DBS surgery (year)	42 (22–55)	9.75
Y-BOCS before DBS surgery	33.88 (28–40)	3.32
HAM-A before DBS surgery	21.89 (12–42)	7.66
HAM-D before DBS surgery	19.75 (5–30)	6.97
Duration of DBS treatment (months)	33.19 (12–56)	18.05
Percentage decrease on Y-BOCS	41% (0–84)	19.72

symptoms when batteries are depleted or stimulation is abruptly stopped. Typically, though individually highly variable, a worsening of mood and anxiety is observed immediate after DBS cessation, followed by a more gradual and less marked relapse of OCD symptoms [3,8]. In a previous DBS efficacy study of our group [6], we found indications for worsening of symptoms even exceeding baseline levels, so called rebound phenomena. Recently, Vora et al., described such a rebound in one patient consisting of increased severity of OCD symptoms compared to pre-surgery levels following battery depletion [9]. In none of these studies however, anxiety or depressive symptoms were systematically compared between pre-surgery and DBS-off, making it uncertain whether depressive and anxiety symptoms also rebound after DBS cessation. Furthermore, none of these studies assessed the patient perspective, leaving it unclear how patients experience DBS cessation, and whether cessation influences their QoL. This information is important to obtain a more complete understanding of the clinical impact of DBS cessation.

In the current study we determine the effects of acute DBS cessation with validated scales for OCD, anxiety, depressive symptoms and QoL. We aim to determine whether (1) patients experience a relapse (severity higher than with DBS-on, but at a lower or similar level than before surgery) or rebound (severity higher than with DBS-on and higher than before surgery) of symptoms following cessation of DBS and (2) if and to what extend QoL is affected during DBS cessation. These results will help us understand the impact of DBS cessation in OCD patients, which will be crucial for good patient education and follow-up care, especially considering the growing number of patients treated with this technique.

Methods

Subjects

From April 2005 until January 2011, 32 patients were treated with DBS at the Academic Medical Center (AMC) Amsterdam. Details of the surgical technique are described elsewhere [6,10]. Inclusion criteria for the current study were (1): Time since surgery had to be at least 1 year and (2) patients had to have a stable pattern of OCD, mood and anxiety symptoms for at least 5 months. Table 1 summarizes the clinical and demographic characteristics of 16 out of the 32 patients who met both inclusion criteria. Six of the 16 patients who were excluded from the study did not meet the first inclusion criterion, four were considered to have an instable pattern of psychiatric symptoms, and six others did not want to participate because of fear of turning DBS off.

Study design

The current study was part of a larger experiment investigating the neural mechanisms of DBS in a one week DBS-off design, of which parts have been published earlier [11]. At the beginning of the study, symptom severity and QoL were assessed while DBS was still on (DBS-on). The next day DBS was turned off and remained off for the next seven days. At the seventh day of the off-period, patients were again assessed (DBS-off). One day later DBS was turned back on. Patients and clinicians were aware of the DBS condition during the whole period. The responsible psychiatrist (MF) assessed all symptoms scales. The results where compared to pre-surgery data which were obtained one month before DBS surgery (pre-DBS). The study was approved by the medical ethics committee of the Academic Medical Center (AMC) Amsterdam.

Outcome measures

Severity of OCD symptoms was measured using the Yale–Brown Obsessive Compulsive Scale (Y-BOCS) [12], a 10-item semi-structured, clinician-administered scale. Each item is scored on a 5-point Likert scale ranging from 0 to 4. Depressive symptoms were rated with the 17-item Hamilton Depression Rating Scale (HAM-D) [13], scores ranging from 0 to 54. Anxiety was evaluated with the Hamilton Anxiety Scale (HAM-A) [14], a 14-item scale with a range of 0–56 points. All three scales are widely used and have well-established psychometrics [15–17]. For all three measures, higher scores indicate more severe symptoms.

Quality of life was assessed using the abbreviated version of the World Health Organization quality of life questionnaire (WHOQOL-BREF) [18]. This instrument measures the individuals' perceptions of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns. It compromises 26 questions summarized in four domain scores: physical, psychological, social and environmental. All questions are rated on a 5-point Likert scale. An example item is: *How satisfied are you with hour health? 1 = very dissatisfied, 5 = very satisfied*. The scores of the four domains range from 4 to 20. Higher scores indicate a higher perceived quality of life. The Dutch translation of the WHOQOL-bref displays a good content and construct validity and test-retest reliability in a psychiatric population [19]. The recall period was adjusted to one week for the purpose of this study (two weeks in the original version).

Statistical analysis

Repeated-measures analysis of variance (ANOVA) with the three time points (pre-DBS, DBS-on and DBS-off) as within-subject factors were used to examine if the mean scores on the different time points were statistically different. To control for the influence of baseline variables, age, gender and length of follow up were entered in the model as covariates. However, in none of the analysis they proofed to be significant, so only main effects were reported. Significant main effects were explored using post-hoc *t*-test between DBS-on and DBS-off, and pre-DBS and DBS-off. To adjust for multiple testing, Bonferroni correction ($\alpha = 0.05/2 = 0.025$) was used. Cohen's *d* effect sizes were calculated to estimate effect size. To identify relapse or rebound of symptoms, the scores of each subject at DBS-off were compared with their own scores at DBS-on and pre-surgery. Relapse was defined as an increase in score between DBS-on and DBS-off. Rebound as an increase in score between pre-surgery and DBS-off. All statistical analyses were performed using commercially available statistical software (SPSS, version 20.0; SPSS Inc, Chicago, Illinois).

Results

Clinical symptoms

Repeated measures ANOVA showed a significant effect of time between the three time points on the Y-BOCS ($F(2,15) = 33.074$,