Research paper

Cognitive effects of deep brain stimulation in patients with obsessive–compulsive disorder

Mariska Mantione, Msc; Dorien Nieman, PhD; Martijn Figee, MD, PhD; Pepijn van den Munckhof, MD, PhD; Rick Schuurman, MD, PhD; Damiaan Denys, MD, PhD

Background: Deep brain stimulation (DBS) is a promising treatment for treatment-refractory obsessive–compulsive disorder (OCD). However, the effects of DBS on cognitive functioning remain unclear. Therefore, we aimed to assess cognitive safety of DBS for treatment-refractory OCD and the association between clinical changes and cognitive functioning. **Methods:** Patients with treatment-refractory OCD treated with DBS targeted at the nucleus accumbens (NAcc) were compared with a control group of 14 patients with treatment-refractory OCD treated with care as usual. We assessed cognitive functioning at baseline, 3 weeks postoperatively and following 8 months of DBS. We compared change in clinical symptoms with cognitive changes. **Results:** There were 16 patients in the DBS group and 14 patients in the control group. Three weeks postoperatively, the DBS group showed a significantly reduced performance on measures of visual organization and verbal fluency and a trend toward reduced performance on measures of visual memory and abstract reasoning. Cognitive functioning was found to be stable on all other measures. After 8 months of DBS, reduced performances persisted, except for a significant improvement in verbal fluency. Cognitive functioning in all other domains remained unaffected. We found no correlation between improvement of clinical symptoms and cognitive changes. **Limitations:** A limitation of this study was its relatively small sample size. **Conclusion:** Deep brain stimulation targeted at the NAcc may be considered a safe method in terms of cognition because cognitive functioning was unaffected on most neuropsychological measures. Nevertheless, we observed some minor reduced performance on specific measures of executive functioning that were possibly associated with surgical intervention. Our results suggest that severity of OCD symptoms is independent of cognitive functioning.

Introduction

Recently, several studies have shown that deep brain stimulation (DBS) targeting the anterior limbs of the internal capsule, the ventral striatum, the nucleus accumbens (NAcc), the inferior thalamic peduncle and the subthalamic nucleus is effective in patients with treatment-refractory obsessive–compulsive disorder (OCD).[1–9] To date, the results of 7 controlled studies have been published worldwide and have reported that 34 of 63 patients experienced a reduction of at least 35% of OCD symptoms. Consequently, half of the treated patients can be considered responders, indicating that DBS is a promising technique.[10]

Neuropsychological evaluation in DBS treatment plays a vital role in preoperative neuropsychological screening of potential DBS candidates, in evaluation of outcome and in research.[11] The contribution of neuropsychological assessment in research is 2-fold: it may establish the cognitive safety of DBS treatment and it may demonstrate whether DBS alters the underlying cognitive deficits in individuals with OCD. Presently, there is evidence that the clinical effectiveness of DBS in patients with OCD is achieved with stable[3–8,12,13] and even improved[14] cognitive functioning. However, since small sample sizes, lack of a control group and the use of a limited range of tests hinder the interpretation of the results, the effect of DBS on cognitive functioning in patients with OCD is still unknown.

We conducted a prospective, controlled study investigating the cognitive effects of bilateral DBS targeted at the NAcc 3 weeks and 8 months postoperatively to examine its short- and long-term effects. In addition we investigated whether clinical changes after DBS treatment were associated with changes in cognitive functioning. Changes were compared at 3 time points with a matched control group of patients with treatment-refractory OCD who received conventional therapy.

Correspondence to: M. Mantione, Academic Medical Center, University of Amsterdam, PA.0-162, PO Box 22660 — 1100 DD Amsterdam; m.h.mantione@amc.uva.nl

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Methods

Patients

We recruited patients with OCD from the outpatient clinic for anxiety disorders at the Academic Medical Center (AMC), Amsterdam, the Netherlands. The study population consisted of patients with treatment-refractory OCD who participated in a trial in which the effectiveness and safety of DBS for treatment-refractory OCD was assessed.[9] Alongside the DBS group, we recruited a control group comprising patients with treatment-refractory OCD who received conventional therapy and who were on a waiting list for the DBS study. The groups were matched for mean age, premorbid intelligence and Yale–Brown Obsessive Compulsive Scale (Y-BOCS) score. The investigation was carried out in accordance with the latest version of the Declaration of Helsinki. The study was part of a registered clinical trial (trial number ISRCTN23255677) and approved by the Medical Ethical Committee of the AMC. We obtained the informed consent of all participants after the nature of the procedures had been fully explained.

Inclusion criteria for patients were age 18–65 years, primary OCD according to the DSM-IV criteria,[15] severe illness with a total score of at least 28 on the Y-BOCS[16,17] and at least a 5-year history of OCD. All patients must have had insufficient response to 1) a minimum of 2 different selective serotonin reuptake inhibitors (SSRIs), 2) clomipramine and 3) an SSRI augmented with an atypical antipsychotic or clomipramine augmented with an atypical antipsychotic, and 4) a minimum of 16 sessions of cognitive behavioural therapy (CBT).

Exclusion criteria were comorbid DSM-IV diagnosis (except major depressive disorder and mild anxiety disorders), severe personality disorders and substance abuse within the past 6 months. We administered the Structured Clinical Interview for DSM-IV axis I disorders[18] and the Structured Clinical Interview for DSM-IV axis II disorders[19] to validate the diagnosis.

Procedure

A neuropsychological test battery was administered 1–3 months preoperatively, 3 weeks postoperatively and after an open 8-month treatment phase. To minimize the risk of hemorrhage during surgery for the DBS group, SSRIs were tapered off preoperatively. Immediately after surgery medication use resumed at a low dosage and was gradually increased to presurgery levels. Medication was kept constant for both the DBS and control groups. Before postoperative testing occurred, medication levels were similar as before surgery.

The surgical procedure has been described previously[9] and involved electrodes (model 3389, Medtronic Inc.) targeted to the NAcc, with the deepest contact at the original NAcc target reported by Sturm and colleagues.[2] After electrode implantation, monopolar stimulation was started using ventral contact points 0 and 1. Consistently, no changes in symptoms were observed on these parameters.

Three weeks postoperatively the neuropsychological test battery was repeated to investigate possible effects of surgery. After this assessment, patients entered an open phase of 8 months. Since no improvement was observed in any of the patients when stimulating the ventral contacts, the active contacts were switched to dorsal contacts 2 and 3, delivering active stimulation in the ventral part of the anterior limb of the internal capsule. After this switch in contacts clinical improvement on OCD symptoms was apparent in all patients. Stimulation parameters were then standardized to dorsal contacts 2 and 3, a frequency of 130 Hz and pulse width of 90 μs. Voltage ranged from 3.5 to 5.0 V. At the end of the open phase the same neuropsychological test battery was repeated to investigate the effects of stimulation. Where available, we used alternate forms of the neuropsychological tests in a balanced order across patients to minimize practice effects. Patients in the control group were assessed at similar time points as the DBS group.

Neuropsychological tests

Measures of intelligence

The Dutch version of the National Adult Reading Test (DART)[20,21] assesses premorbid intelligence and was used to match the DBS group and control group. The variable we used in the statistical analysis was IQ.

We used the short 12-problem version (set I) of the Raven Advanced Progressive Matrices (RAPM)[22] to assess abstract reasoning. The number of correct items was scored.

Memory

The Dutch version of the California Verbal Learning Test (CVLT)[23,24] is a verbal memory task that yields information on several aspects of verbal learning, organization and memory. The variable used in the analysis was the total recall in 5 trials. To prevent practice effects due to multiple assessments, we used the parallel version of the test in a counterbalanced design.

The digit span is a subtest of the Wechsler Adult Intelligence Scale (WAIS-III)[25] and was used as a measure of short-term verbal learning and working memory. We analyzed the total number of correct items.

Visuoconstructional function and memory

The Rey Complex Figure Task (RCFT)[26] is a test measuring visual memory and organization. We quantified accuracy for the copy and the immediate recall condition using a scoring system, with possible scores ranging from 0 to 36.[27,28]

Executive functions and inhibition

The Stroop Colour Word Test[29] consists of 3 trials measuring selective attention, perceptual interference and response inhibition. The outcome measure used in the analysis was the time needed for the third trial minus time needed for the second trial.

Verbal fluency[30,31] has been used to investigate a wide variety of cognitive functions, such as long-term verbal memory, attention, vocabulary size and executive functioning.[32] We used the number of words generated in 1 minute for phonemic ("N" and "A") and semantic cues (animals and occupations) as dependent variables.

The Trail Making Test (TMT)[33] consists of 2 trials; the first is considered a measure of mental speed and the second a measure of alternating attention. As performance in both parts exhibits a linear association, time B ÷ time A was used as an outcome variable for set-shifting.[34]

The Wisconsin Card Sorting Test (WCST)[35] is one of the most widely used tasks in the assessment of neurocognitive function. It assesses, among other things, set-shifting, category formation and set maintenance. The outcome variables we used in our analysis were the number of categories completed and the percentage of perseverative errors.

We administered the Tower of London (ToL) test[36] to assess planning ability. The outcome variable was the total number of steps needed to complete problem-solving tasks.

Attention

The Continuous Performance Test — identical pairs[37,38] assesses sustained visual attention. We used response style (log-B) and the ability to discriminate between target and nontarget (d′) as outcome variables.

Digit Symbol Substitution[25] is a subtest of the WAIS measuring attention. The outcome variable used was the number of digits correctly filled out.

Motor system

The Purdue Pegboard[39] measures upper-extremity fine motor dexterity as well as gross motor coordination. We used the number of pegs in the dominant hand and nondominant hand subtests as outcome measures.

Clinical symptoms

We assessed obsessive–compulsive, anxiety and depressive symptoms in the DBS and control groups using the Y-BOCS,[16,17] the Hamilton Anxiety Scale (HAM-A)[40] and the Hamilton Rating Scale for Depression (HAM-D),[41] respectively.

Adverse events

Information about adverse events was collected in the open phase of the study as part of the original clinical trial.[9] At each visit (every 2 weeks), patients were asked, "Have you experienced a change in behaviour in the last 2 weeks?" Any change in behaviour that a patient reported was rated as an adverse event. Patients regularly reported changes is cognitive functioning when they answered question 5 of the HAM-A: "Have you experienced difficulties in concentration or memory?" Patients were always asked to rate the adverse events they mentioned as mild, moderate or severe.

Statistical analysis

All data were analyzed using the SPSS statistical package for Windows version 20.0 (IBM). At baseline, differences between the DBS and control groups in age and clinical symptoms were examined using independent 2-tailed *t* tests. Sex differences were analyzed using a χ^2 test. We conducted a linear mixed model analysis to assess changes in cognitive test parameters over 3 different time points (baseline, 3 weeks postoperatively and 8 months postoperatively). Considering the small sample sizes in both groups, we corrected for baseline differences in our analysis. We conducted a mixed model analysis with change scores as dependent variables and baseline scores as covariates. The change score at 3 weeks postoperative was defined as the score at 3 weeks – baseline score, and the change score at 8 months postoperative was defined as the score at 8 months – baseline score. We used raw test scores for all measures. To account for multiple comparisons, we used a more stringent threshold of $p < 0.01$ to assess statistical significance. Results between $p < 0.01$ and $p < 0.05$ are reported as trends.

We computed effect sizes according to Cohen *d*. Effect size is defined as the difference between the mean change scores of both groups ÷ the pooled standard deviation of the change scores. An effect size of 0.2 reflects a small effect, 0.5 a medium effect and 0.8 or higher a large effect. We used Spearman Rho coefficients to calculate correlations between change in clinical characteristics (Y-BOCS, HAM-A and HAM-D) and change in neuropsychological performance.

Results

Participants

Sixteen patients were included in the DBS group. Two patients of the DBS group were lost to follow-up at 8 months of stimulation because they refused further participation in the study. Their results were included in the baseline to 3 week analyses. The control group consisted of 14 patients with treatment-refractory OCD. Six of 16 patients in the DBS group and 5 of 14 patients in the control group fulfilled the criteria for comorbid major depressive disorder (MDD). A χ^2 test did not reveal a statistical significance in distribution of comorbid MDD between the groups ($\chi^2_1 = 0.01$; $p = 0.92$). There were no significant differences between the groups with respect to mean age; education; IQ; age at onset of illness; duration of illness or baseline Y-BOCS, HAM-A and HAM-D scores (Table 1).

Clinical symptoms

Three weeks postoperatively, the DBS and control groups showed no significant difference in OCD, anxiety or depressive symptoms. The mean scores of the DBS group compared with the control group were 32.6 ± 4.5 versus 31.1 ± 4.8 points on the Y-BOCS, 15.5 ± 5.4 versus 18.9 ± 8.2 points on the HAM-A and 16.3 ± 5.8 versus 16.4 ± 6.5 points on the HAM-D. In the DBS group, OCD, anxiety and depressive symptoms improved significantly during the open phase of the trial (8 months postoperative). They experienced mean decreases of 15.7 ± 10.8 points on the Y-BOCS, 10.7 ± 8.1 points on the HAM-A and 9.0 ± 6.2 points on the HAM-D.[9] In the control group, OCD, anxiety and depressive symptoms remained unchanged. At the third neuropsychological assessment they had experienced mean decreases of 0.4 ±

3.6 points on the Y-BOCS and 2.7 ± 5.6 points on the HAM-A and a mean increase of 0.7 ± 4.9 points on the HAM-D.

Adverse events

Five patients reported forgetfulness. Specifically, patients mentioned short-term memory deficits that were possibly related to difficulty following a conversation. Three patients reported word-finding problems, which were described as a "tip of the tongue" phenomenon. All symptoms were rated as mild adverse events.

Neuropsychological tests

The outcomes on neuropsychological tests for both groups at baseline, 3 weeks postoperatively and 8 months postoperatively are shown in Table 2. At baseline, the DBS and control groups did not differ significantly in cognition except that the DBS group scored lower on the Digit Symbol Substitution Test. Three weeks postoperatively the DBS group had significantly reduced performance compared with the control group on the RCFT copy and verbal fluency tests (category occupations). There was a trend toward reduced performance on RCFT recall and RAPM in the DBS group compared with the control group; these effects on RCFT copy score, RCFT recall score and RAPM were still present at the 8-month follow-up. Verbal fluency, on the other hand, had improved.

Correlations

To assess whether clinical changes after DBS were associated with changes in cognitive functioning, we performed exploratory correlational analyses to examine associations after 8 months of stimulation between change in clinical measures and change in neuropsychological performance in the DBS group. We found no significant correlations between change in symptoms and change in cognitive functioning. Reduced performance on the RCFT copy test did not significantly correlate with decrease of OCD (r = –0.42, p = 0.14), anxiety (r = –0.30, p = 0.29) or depression symptoms (r = –0.15, p = 0.61). We found no significant correlation between reduced performance on the RCFT recall test and decrease of OCD (r = –0.28, p = 0.34), anxiety (r = 0.42, p = 0.14) or depression symptoms (r = 0.40, p = 0.15). Reduced performance on the semantic verbal fluency task did not significantly correlate with decrease of OCD (r = 0.10, p = 0.75), anxiety (r = 0.25, p = 0.40) or depression symptoms (r = 0.27, p = 0.35). Reduced performance on the RAPM did not correlate significantly with decrease of OCD (r = –0.20, p = 0.52), anxiety (r = 0.070, p = 0.82) or depression symptoms (r = 0.37, p = 0.20).

Discussion

We investigated cognitive functioning of patients with OCD treated with DBS targeted at the NAcc preoperatively, 3 weeks postoperatively and at 8-month follow-up. To our knowledge, this is the first longitudinal study on cognitive functioning in patients who have received DBS that included a matched control group and thus controlled for test–retest effects and natural fluctuations in cognitive functioning. The goals of the present study were to establish the cognitive safety of DBS and to investigate whether clinical changes after DBS are associated with changes in cognitive functioning.

With respect to the first goal, our results show that 3 weeks after surgery, performance was reduced in the DBS group compared with the control group on measures of visual organization and semantic verbal fluency. We found a trend toward reduced performance in the DBS group on visual memory and abstract reasoning tasks. Cognitive functioning was unaffected on measures of cognitive flexibility, planning and cognitive inhibition and the domains of verbal memory, attention and motor system functioning. Despite substantial improvement in clinical symptoms following 8 months of stimulation, the DBS group continued to show a reduced performance on a measure of visual organization and a trend toward reduced performance on measures of visual memory and abstract reasoning compared with the control group. Semantic verbal fluency, on the other hand, improved from 3 weeks postoperative to 8-month follow-up. Cognitive functioning was stable on measures of cognitive flexibility, planning and cognitive inhibition and in the domains of verbal memory, attention and motor system functioning.

Our findings are consistent with those of an earlier study of unilateral DBS of the NAcc in patients with treatment-

Table 1: Baseline demographic and clinical characteristics of participants

	Group, mean ± SD*			
Characteristic	DBS, n = 16	Control, n = 14	Statistic	p value
Age, yr	42.56 ± 11.4	38.00 ± 9.8	t = 1.18	0.25
Sex, male:female	9:7	5:9	χ^2 = 1.27	0.26
DART-IQ	92.4 ± 9.2	94.4 ± 9.0	t = –0.62	0.54
Age at onset, yr	14.2 ± 7.4	16.3 ± 6.8	t = –0.81	0.43
Duration of illness, yr	29.0 ± 12.5	23.7 ± 8.4	t = 1.37	0.18
Y-BOCS score	33.7 ± 3.6	32.4 ± 4.6	t = 0.87	0.40
HAM-A score	20.9 ± 5.9	20.21 ± 8.3	t = 0.25	0.80
HAM-D score	19.5 ± 6.7	17.6 ± 8.3	t = 0.70	0.49

DART-IQ = Dutch Adult Reading Test Intelligence Quotient; DBS = deep brain stimulation; HAM-A = Hamilton Anxiety Rating Scale; HAM-D = Hamilton Rating Scale for Depression; SD = standard deviation; Y-BOCS = Yale–Brown Obsessive Compulsive Scale.
*Unless otherwise indicated.

refractory OCD[7] in which stable cognitive functioning was found 1 year after implantation on measures of planning, verbal fluency and sustained attention. However, a recent study of DBS in the anterior limb of the internal capsule/ventral striatum for OCD and MDD reported a significant improvement in verbal memory.[14] In addition, a study of DBS of the NAcc in MDD found significant improvements in sustained attention, visual organization, verbal and visual memory and visual perception.[42] Differences in outcomes between these studies and ours might be related to differences in patient groups and the resulting differences in neuropsychological profiles at baseline. For example, OCD, contrary to MDD, is not associated with deficits in verbal memory. The lack of a control group and resulting practice effects (4 neuropsychological assessments in 1 year) in the second study[42] may also have contributed to differences in outcomes.

Although the magnitude of the changes on measures of visual organization, visual memory, verbal fluency and abstract reasoning is relatively small compared with total baseline scores, the effect sizes were large on all measures. Reduced visual memory, as assessed with the recall performance on the RCFT has been related to failures in the use of appropriate organizational strategies, suggesting that failures on recall performance are secondary to impaired executive functioning.[43,44] In addition, the reduced performance in visual organization and verbal fluency and the trend toward decline in abstract reasoning hints at reduced executive functioning. Since all reduced performance was already present at the neuropsychological assessment 3 weeks postsurgery, it may result directly from surgical intervention (i.e., the insertion of electrodes through the frontal lobe). On the other hand, we cannot exclude the possibility that the reduced performances are stimulation-related since ventral contact points were directly activated after surgery. The first hypothesis seems more likely because it is supported by the extensive literature on the effects of DBS on cognition in patients with Parkinson disease. Deep brain stimulation for Parkinson disease seems to result in mild deficits in executive functioning, particularly in verbal fluency, that seem to occur immediately after surgery. Comparison of "on" and "off" conditions of stimulation suggest that these deficits could be partly due to electrode implantation through the frontal lobe, resulting in disruption of frontal–striatal–thalamic circuitry.[45] The lack of recovery in visual organization, visual memory and abstract reasoning after 8 months of stimulation in our study may indicate a persistent effect of surgery. The improvement in semantic verbal fluency and stabilization of abstract reasoning, however, could be due to several factors: a transient effect of surgical intervention, a positive effect of stimulation and/or an effect related to improvement in clinical symptoms. As changes in cognition did not correlate with changes in clinical symptoms, our results do not support the latter hypothesis.

What can be stated about the neuropsychological safety of DBS targeted at the NAcc? Cognitive functioning was unaffected on the majority of neuropsychological measures, and the magnitude of the changes on measures of visual organization, visual memory and abstract reasoning was relatively small. A recent study in this same group of patients showed that DBS had a positive impact on patients' perception of their quality of life.[46] In the present study, patients rated their cognitive problems as mild side effects, and none requested that stimulation be discontinued. This supports our assumption that the advantages in daily life resulting from the clinical effects of DBS outweigh the reduced cognitive performances. For these reasons we conclude that DBS targeted at the NAcc is a safe treatment in terms of cognition. Nevertheless, we observed some reduced performance on specific measures of executive functioning and found large effect sizes on these measures. This underlines the clinical relevance of our findings. It is likely that these effects result from the surgical intervention, while there seems to be no effect of stimulation. Because of the potential mildly reduced performance on cognitive functioning associated with the surgical intervention, it is important to fully inform patients before surgery about possible side effects so they can make a deliberate decision for DBS treatment.

The second goal of our study was to investigate whether clinical changes after DBS treatment were associated with changes in cognitive functioning. Various cognitive deficits across several domains have been identified in patients with OCD, including impaired performance on memory tasks as a consequence of strategy failures, deficits in reversal learning and impaired response inhibition.[47] It has been proposed that these impairments arise from inhibitory deficits consistent with lateral orbitofrontal loop dysfunction, particularly in the orbitofrontal cortex.[47] Impaired reversal learning has been identified as a neurocognitive endophenotype of OCD in a study comparing patients with OCD and their unaffected siblings.[48] Conversely, a prospective study indicates that the neuropsychological deficits in patients with OCD might be state-dependent: effective CBT in patients with OCD improved performance on a memory task requiring organizational strategy (RCFT).[49] Our study provides the opportunity to investigate the association between large and rapid changes in symptoms and changes in cognitive functioning. Despite substantial clinical improvement after DBS treatment, patients' performance on the RCFT deteriorated. Furthermore, changes in clinical symptoms and changes in cognitive functioning were unrelated. Therefore, our results do not support the hypothesis that neuropsychological deficits in patients with OCD are state-dependent and suggest that OCD symptoms and cognitive functioning may have a distinct neurobiological substrate.

Limitations

A limitation of our study is that patients were not randomized to either the DBS group or the control group. We did not include a third group consisting of healthy controls; therefore it is unclear whether the cognitive deficits at baseline in the DBS group were OCD-specific or how these deficits were possibly influenced by DBS. Another limitation of this study is the immediate activation of stimulation at the ventral contact points after surgery, whereby discrimination between surgical effects and stimulation effects is hindered. Therefore, we recommend postsurgery neuropsychological assessment with inactive stimulation parameters for future

Table 2. Raw cognitive test scores at baseline and change scores at 3 weeks and 8 month follow-up for the DBS and control group (part 1 of 2)

Test score*	Group, mean ± SD		Statistic	*p* value†	Cohen *d*‡
	DBS	Control			
Memory					
California Verbal Learning Test					
Total recall in 5 trials	52.9 ± 10.8	57.8 ± 11.9			
Change score 3 weeks	–1.9 ± 6.9	0.5 ± 5.5	$t_{28} = –1.08$	0.28	–0.4
Change score 8 months	2.5 ± 6.6	4.6 ± 8.9	$t_{28} = –0.58$	0.57	–0.3
Stability of time			$t_{27} = 0.10$	0.92	
Digit span					
Forward	9.3 ± 1.9	9.5 ± 2.0			
Change score 3 weeks	0.2 ± 1.7	0 ± 2.1	$t_{27} = 0.17$	0.87	0.1
Change score 8 months	–0.3 ± 1.8	–0.2 ± 2.4	$t_{27} = –0.14$	0.89	–0.1
Stability of time			$t_{27} = –0.30$	0.77	
Backward	5.7 ± 1.5	6.6 ± 2.1			
Change score 3 weeks	1.4 ± 1.6	0.4 ± 1.4	$t_{27} = 1.14$	0.26	0.7
Change score 8 months	1.0 ± 1.9	0.9 ± 2.0	$t_{29} = –0.19$	0.85	0.1
Stability of time			$t_{28} = –1.17$	0.25	
Rey Complex Figure Test					
Copy score	31.6 ± 2.7	30.9 ± 4.1			
Change score 3 weeks	–1.7 ± 1.9	1.7 ± 3.7	$t_{27} = –3.64$	0.001	–1.2
Change score 8 months	–2.3 ± 3.1	2.6 ± 4.3	$t_{28} = –3.92$	0.001	–1.3
Stability of time			$t_{28} = –1.59$	0.11	
Immediate recall score	21.6 ± 7.6	19.9 ± 6.3			
Change score 3 weeks	–1.8 ± 5.9	3.1 ± 5.0	$t_{28} = –2.2$	0.030	–0.9
Change score 8 months	0.4 ± 4.4	6.4 ± 4.7	$t_{27} = –3.75$	0.001	–1.3
Stability of time			$t_{28} = –0.52$	0.60	
Executive functioning					
Stroop Colour Word Test					
Time card 3 – time card 2 seconds	44.0 ± 22.4	32.9 ± 11.8			
Change score 3 weeks	–6.5 ± 14.1	–3.6 ± 7.9	$t_{27} = 0.43$	0.67	–0.3
Change score 8 months	–7.6 ± 15.8	–3.2 ± 11.6	$t_{28} = 0$	> 0.99	–0.3
Stability of time			$t_{28} = –0.39$	0.70	
Verbal fluency					
Phonemic (A)	11.8 ± 3.8	11.0 ± 4.9			
Change score 3 weeks	–1.8 ± 2.4	–0.2 ± 4.8	$t_{27} = –1.10$	0.27	–0.4
Change score 8 months	–0.6 ± 3.0	1.9 ± 4.5	$t_{28} = –1.61$	0.11	–0.7
Stability of time			$t_{28} = –0.75$	0.46	
Phonemic (N)	11.9 ± 4.2	13.4 ± 3.5			
Change score 3 weeks	–2.0 ± 4.4	–1.6 ± 3.5	$t_{28} = –0.87$	0.38	–0.1
Change score 8 months	–0.1 ± 3.8	–0.1 ± 4.5	$t_{28} = –0.48$	0.63	0
Stability of time			$t_{28} = 0.25$	0.80	
Semantic (animals)	22.3 ± 5.6	23.3 ± 5.5			
Change score 3 weeks	–1.5 ± 5.2	0.5 ± 3.8	$t_{27} = –1.66$	0.10	–0.4
Change score 8 months	–0.7 ± 4.5	0.2 ± 4.2	$t_{27} = –0.68$	0.50	–0.2
Stability of time			$t_{28} = 0.58$	0.56	
Semantic (occupations)	15.6 ± 2.9	14.8 ± 3.5			
Change score 3 weeks	–0.9 ± 3.9	2.9 ± 2.5	$t_{27} = –3.04$	0.002	–1.2
Change score 8 months	3.1 ± 3.5	–0.5 ± 4.0	$t_{27} = –0.03$	0.98	1.0
Stability of time			$t_{28} = 2.28$	0.025	
Trail Making Test					
Time B ÷ time A	2.0 ± 0.4	2.2 ± 0.7			
Change score 3 weeks	0.6 ± 0.8	0.1 ± 0.7	$t_{28} = 1.31$	0.19	0.7
Change score 8 months	0.8 ± 1.6	–0.2 ± 0.6	$t_{29} = 1.91$	0.06	0.8
Stability of time			$t_{28} = 1.08$	0.28	

Table 2. Raw cognitive test scores at baseline and change scores at 3 weeks and 8 month follow-up for the DBS and control group (part 2 of 2)

Test score*	Group, mean ± SD		Statistic	*p* value†	Cohen *d*‡
	DBS	Control			
Wisconsin Card Sorting Test					
No. of categories	4.4 ± 2.1	5.1 ± 1.9			
Change score 3 weeks	–0.6 ± 2.1	–0.5 ± 1.6	$t_{28} = –0.24$	0.65	–0.1
Change score 8 months	0.1 ± 1.7	0.1 ± 1.2	$t_{28} = –0.34$	0.74	0
Stability of time			$t_{28} = 0.12$	0.90	
% of perseverative errors	19.9 ± 17.8	13.6 ± 11.1			
Change score 3 weeks	–1.8 ± 12.5	2.4 ± 12.5	$t_{28} = –0.18$	0.86	–0.3
Change score 8 months	–4.0 ± 8.4	–2.7 ± 12.0	$t_{27} = 0.54$	0.59	–0.1
Stability of time			$t_{28} = 0.78$	0.44	
Tower of London Test					
Total no. of steps	32.6 ± 5.5	32.2 ± 5.1			
Change score 3 weeks	–2.1 ± 5.6	0.7 ± 8.0	$t_{27} = –1.01$	0.31	–0.4
Change score 8 months	–2.0 ± 7.2	3.9 ± 7.7	$t_{27} = –1.89$	0.07	–0.8
Stability of time			$t_{28} = –0.90$	0.38	
Raven Advanced Progressive Matrices	9.2 ± 1.7	8.4 ± 3.0			
Change score 3 weeks	–0.8 ± 1.9	0.6 ± 1.7	$t_{27} = –1.97$	0.05	–0.8
Change score 8 months	–0.4 ± 2.5	0.5 ± 2.4	$t_{28} = –0.74$	0.46	–0.4
Stability of time			$t_{28} = 0.53$	0.60	
Attention					
Continuous Performance Test					
Figures d-prime	1.7 ± 0.7	1.6 ± 0.7			
Change score 3 weeks	–0.1 ± 0.7	0.5 ± 0.9	$t_{26} = –1.84$	0.07	–0.7
Change score 8 months	0 ± 0.5	0.4 ± 0.7	$t_{26} = –1.16$	0.26	–0.7
Stability of time			$t_{28} = 0.58$	0.57	
Figures Log-B	0.4 ± 0.8	–0.2 ± 0.9			
Change score 3 weeks	–0.1 ± 0.9	0.1 ± 1.0	$t_{28} = 1.24$	0.22	–0.2
Change score 8 months	–0.2 ± 1.0	0 ± 1.1	$t_{27} = 1.05$	0.30	–0.2
Stability of time			$t_{28} = –0.14$	0.89	
Digit Symbol Substitution Test					
No. of digits	63.5 ± 11.1	68.7 ± 16.4			
Change score 3 weeks	2.9 ± 5.6	1.1 ± 10.1	$t_{27} = 1.04$	0.30	0.2
Change score 8 months	6.5 ± 7.4	2.7 ± 10.0	$t_{28} = 1.33$	0.19	0.4
Stability of time			$t_{28} = 0.67$	0.52	
Motor system					
Purdue Pegboard					
Dominant hand	14.1 ± 1.7	13.5 ± 2.3			
Change score 3 weeks	–0.2 ± 1.9	0.7 ± 1.9	$t_{27} = –1.2$	0.23	–0.5
Change score 8 months	–0.3 ± 1.4	0.3 ± 1.4	$t_{27} = –0.63$	0.54	–0.4
Stability of time			$t_{28} = 0.50$	0.62	
Nondominant hand	13.2 ± 2.6	12.8 ± 1.7			
Change score 3 weeks	0.4 ± 1.6	0.2 ± 1.6	$t_{27} = 0.62$	0.54	0.1
Change score 8 months	0.5 ± 2.4	1.4 ± 1.9	$t_{28} = –0.94$	0.35	–0.4
Stability of time			$t_{28} = –1.30$	0.20	

DBS = deep brain stimulation; SD = standard deviation.
*Change score at 3 weeks was defined as the score at 3 weeks postoperative – baseline score. Change score at 8 months was defined as the score at 8 months postoperative – baseline score. Negative change scores indicate decline in performance except for test variables assessing speed and error scores (Stroop Colour Word Test; Trail Making Test; Wisconsin Card Sorting Test, % perseverative errors).
†A significant *p* value at 3 weeks refers to an effect of the intervention at 3 weeks. A significant *p* value at stability of time refers to an effect of the intervention at 8 months. A nonsignificant *p* value at stability of time with a significant *p* value at 3 weeks refers to an effect from the intervention at 3 weeks that is still present at 8 months. The *p* values were corrected for differences at baseline.
‡The effect size (Cohen *d*) is negative if the DBS group shows more decline in performance on this variable than the control group, or positive if the DBS group shows more improvement, except for the test variables assessing speed and for error scores.

studies. The stimulation of the dorsal contacts at 8-month follow-up compared with the stimulation of the ventral contacts 3 weeks postoperatively could hinder the interpretation of our findings. However, it is unlikely that this was a confounding factor since previous literature showed that ventral stimulation compared with dorsal stimulation did not result in differences in cognitive functioning.[50] Although our DBS group was relatively large compared with those in previous neuropsychological DBS studies, the small sample size is still a limitation of the present study. The possible resulting lack of power might explain the discrepancy between the subjective reports of our DBS patients and the objective cognitive results. Mild forgetfulness was reported by 5 of 16 patients and word-finding problems were reported by 3 of 16 patients as permanent side effects of DBS treatment.[9] However, these subjective neuropsychological effects were not objectified in the present study. On the other hand, this discrepancy might reflect the difference between subjective experiences of side effects and objective cognitive functioning after DBS, emphasizing the importance of objective neuropsychological assessment in DBS research. Interestingly, a similar discrepancy was recently reported in a study of DBS of the subgenual cingulate gyrus in patients with treatment-resistant depression: short-term memory deficits, paraphasic errors of speech and word-finding difficulties were reported while neuropsychological testing revealed general stability of cognitive functioning over time.[51] It may be that patients with certain characteristics (e.g., older patients) are more prone to cognitive effects of DBS, which level out if group means are investigated. This should be investigated in future studies with larger samples.

Conclusion

Our results show an overall picture of preserved cognition following bilateral DBS targeted at the NAcc in patients with treatment-refractory OCD. Consequently, DBS could be considered a relatively safe treatment in terms of cognition. We observed reduced performance on specific tasks measuring executive functioning that were likely related to the surgical intervention. The lack of improvement in cognitive functioning with ongoing stimulation despite pronounced symptomatic changes may suggest an independent association between cognitive functioning and severity of OCD symptoms. Before firm conclusions can be drawn, replication studies should be performed, for which we recommend the inclusion of larger samples of patients undergoing DBS, inclusion of control groups and use of a comprehensive neuropsychological battery.

Affiliations: From the Department of Psychiatry, Academic Medical Center, University of Amsterdam, Amsterdam, the Netherlands (Mantione, Nieman, Figee, Denys); the Department of Neurosurgery, Academic Medical Center, University of Amsterdam, Amsterdam, The Netherlands (van den Munckhof, Schuurman); and the Netherlands Institute for Neuroscience, an institute of the Royal Netherlands Academy of Arts and Sciences, Amsterdam, The Netherlands (Denys).

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Contributors: All authors designed the study. M. Mantione and D. Denys acquired and analyzed the data and wrote the article, which all authors reviewed and approved for publication.

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Correction

Adolescence as a unique developmental period

In the September 2015 print issue, the affiliation listed for Natalia Jaworska, first author of the editorial "Adolescence as a unique developmental period," (DOI: 10.1503/jpn.150268) was incorrect. She is with the Department of Psychiatry, McGill University, Montreal, Canada. The affiliation was listed correctly in the online version.

We apologize for this error.