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Research report

Long-term follow-up of patients with obsessive–compulsive disorder treated by anterior capsulotomy: A neuropsychological study

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ABSTRACT

Background: For treatment-refractory Obsessive–Compulsive-Disorder (OCD) patients, anterior capsulotomy is a potential therapy. We investigated what kinds of cognitive deficits treatment-refractory patients have and how anterior capsulotomy modifies their clinical and cognitive profiles.
Methods: Ten treatment-refractory OCD patients were examined in two groups (operated and non-operated) with 5 participants in each group, matched for symptom severity, gender, age and education. The operated group was treated with anterior capsulotomy; the non-operated group was treated only with pharmaco- and psychotherapy. The Yale–Brown Obsessive–Compulsive Rating Scale (Y-BOCS) was used to measure OCD symptoms, and ten neuropsychological tests were used to measure cognitive functioning.
Results: In the operated group, the score of Y-BOCS score significantly decreased during the two-year follow-up period. Additionally, we found a significant increase in neuropsychological test scores on the Wechsler Intelligence Test (MAWI), California Sorting Test Part A (CST-A), Stroop Test Interference Score (STR-I), Verbal Fluency Test and Iowa Gambling Test. As a negative result, we observed intrusion errors in the Category Fluency Test. In the non-operated group significant improvement was found in Y-BOCS scores. At follow-up, we found significant differences between the operated and non-operated groups on three neuropsychological tests: Trail Making Test Part B, Repeatable Battery for the Assessment of Neuropsychological Status (RBANS) Attention Index and RBANS Language Index, with better performance in the non-operated group.
Conclusions: Both treatment methods (i.e. anterior capsulotomy and pharmaco- and psychotherapy) seem effective in reducing OCD symptoms and cognitive deficits, but, importantly, to different degrees. The clinical and neuropsychological improvements were more impressive in the operated group.

1. Introduction

Over the last 30 years, remarkable developments have been made in the understanding of the underlying mechanism of obsessive–compulsive disorder (OCD). Despite the growing number of treatment options available, nearly 40% of OCD patients do not respond well to adequate therapeutic methods (Lopez et al., 2004). These patients are considered treatment-refractory patients. We define treatment-refractory OCD patients as those who undergo adequate trials of selective serotonin re-uptake inhibitors (SSRIs) (minimum 3 types of SSRI at maximum dosage for at least 12 weeks), standard augmentation strategies (two atypical antipsychotics) and behavior therapy (minimum 30 h) without satisfactory response (Husted and Shapira, 2004). Treatment-refractoriness

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might be considered one subtype of OCD. There is some evidence of treatment consequence resulting from the subtyping of OCD (Mataix-Cols et al., 1999) but relatively few studies have observed the features, cognitive profile and potential treatments of treatment-refractory OCD.

The appearance of neurosurgical methods was a breakthrough in managing treatment-refractory OCD patients (Jenike and Rauch, 1994). These neurosurgical methods cannot be understood without the most recent biological theories in OCD development, namely the loop theories. The loop theories (Modell et al., 1989; Baxter, 1999; Mashour et al., 2005; Cummings, 1993) describe the connections and interactions between neuro-anatomical structures involved in OCD and have been developed on the basis of neuro-imaging findings like structural (regional CT or MRI volume) (Szeszko et al., 1999; Kang et al., 2004) and functional (fMRI) (Whiteside et al., 2004) abnormalities in brain regions. These theories link the structural and functional results. In addition, an increasing amount of data is available on cognitive deficits in OCD patients from the late 1990s (Schmidtke et al., 1998; Miller and Cohen, 2001; Purcell et al., 1998; Cavallero et al., 2003). The most recent studies (Pujol et al., 1999; Kwon et al., 2003; Nakao et al., 2005; Rauch et al., 2007; Van der Wee et al., 2003) combine functional neuroimaging techniques with neuropsychological tasks by imaging brain functions during cognitive testing in order to objectify the activity of given brain areas. In our opinion, alongside functional imaging and cognitive tests, neurosurgical methods can also provide insight into the function of loops.

Most neurosurgical techniques try to find a way to influence the connections between cortical areas (e.g., orbitofrontal cortex and cingulum), basal ganglia (mainly the caudate nucleus) and the medial dorsal thalamic nucleus.

Surgical interventions are used at certain locations of neuronal pathways, with a consequent effect on the whole network, thereby improving symptoms. Irreversible (e.g., cingulotomy, subcaudate tractotomy, limbic leucotomy, and anterior capsulotomy) and reversible (e.g., deep brain stimulation) surgical techniques can also be used for the treatment of patients with OCD. In the present study, we focus on anterior capsulotomy.

Studies using anterior capsulotomy can be divided into two groups: in the first, clinical condition is assessed prior to and after the surgical intervention, and changes in Yale–Brown Obsessive–Compulsive Scale (Y-BOCS) scores serve as indicators of the effectiveness of the operation (Oliver et al., 2003; Christiensen et al., 2002; Mindus et al., 1994; Liu et al., 2008). Mindus et al. (1994) analyzed how the scores improved as a function of time elapsed after the surgery. They found that the biggest improvement occurred within the first two months after the operation and observed no significant change during later follow-up. That is, patients' symptoms did not improve after two months.

In the other group of studies, in addition to using the Y-BOCS severity scales, neuropsychological tests are also part of the pre- and post-operative examinations. This serves the measurement of cognitive functions of patients with OCD, not only as an indicator of the effectiveness of the operation. See details in Table 1.

Studies related to anterior capsulotomy and additional neuropsychological tasks are difficult to compare given the small number of patients involved and due to the diversity of used test batteries. Additionally, the results of such studies are inconsistent. The results of Fodstad et al.'s (1982) case study of two patients imply that the post-operative scores on intelligence and memory tests did not change significantly compared to pre-operative scores. In Nyman and Mindus's study (1995), the scores of neuropsychological tests fell into the normal range before capsulotomy and remained within the normal range after the operation. They found similar results for the same sample in 2001 (Nyman et al., 2001), when they compared the test results of patients who underwent operations with patients who did not: findings revealed no significant difference between the two groups.

In a review of two studies of capsulotomy and neuropsychology, Mindus and Meyerson (1995) concluded that intellectual functioning did not decrease after capsulotomy and that surgical intervention did not affect frontal lobe functions. Moreover, the authors state that certain cognitive functions even improved after the operation. These findings indicate possible significant improvement in the third and seventh post-operative years.

Rück et al. (2008) observed 25 OCD patients, who underwent anterior capsulotomy between 1988 and 2000 at the Karolinska Institut, Stockholm, Sweden. Although, the mean follow-up was ten years, only seven patients had pre- and post-operative neuropsychological test results. The investigators found that clinical and cognitive improvement stagnated after one post-operative year and concluded that there were no significant differences from the 1-year to the long-term follow-up ratings, implying that improvement was generally stable. Rück emphasized the importance of adverse effects in his follow-up. Rück et al. measured severe side effects (suicide, neurosurgical complications, weight gain, and executive dysfunctions) and concluded that capsulotomy is effective in treating OCD but carries a substantial risk of adverse effects.

To date, five anterior capsulotomies have been performed in Hungary. In our present study, we describe the pre-operative and post-operative follow-up conditions of five treatment-refractory OCD patients treated by anterior capsulotomy and combined pharmaco- and psychotherapy and five treatment-refractory OCD patients treated only with pharmaco- and psychotherapy. We also present detailed neuropsychological test results.

The aim of our study was two-fold. We wanted to characterize the underlying cognitive deficits in treatment-refractory patients. Second, we aimed to determine how the irreversible method of anterior capsulotomy modifies (by cutting through neural pathways and therefore influencing the function of loops) the cognitive profiles of patients during the course of the long-term follow-up, by comparing them to those of the non-operated matched clinical control group. In the present study, we did not use a healthy control group, as our aim was to determine the effect of surgery on cognitive profiles as a function of elapsed time since treatment.

2. Methods

2.1. Participants

In total, ten treatment-refractory OCD patients were included in the present study. Treatment-refractory status was defined by the following criteria: (i) a score of more than 32 on the Y-BOCS test, (ii) obsessive–compulsive symptoms did

Table 1
An overview of studies using anterior capsulotomy for the treatment of OCD.

Author(s)	N	Diagnosis	Follow-up	Test(s)	Results
Oliver et al. (2003)	15	OCD	–	Y-BOCS	Clinical improvement
Christiensen et al. (2002)	2	OCD	2 years	Y-BOCS	Clinical improvement
Mindus et al. (1994)	22	OCD	8 years	Y-BOCS	Clinical improvement
Liu et al. (2008)	35	OCD	3 years	Y-BOCS	Clinical improvement
Fodstad et al. (1982)	2	OCD	1 year	Y-BOCS and cognitive tests (SRB Test and BVRT)	No change in IQ and memory function
Nyman and Mindus (1995)	10	Anxiety disorder (5 OCD and 5 anxiety disorder)	1 year	Y-BOCS and cognitive tests (VBI, VFT, BVRT, CDLR, TMT, WCST, and Halstead–Reitan Test)	Clinical improvement, perseveration, code error
Nyman et al. (2001)	21	OCD	7 years	Y-BOCS and cognitive tests (WBI, TMT Test, WCST, and Rey Complex)	No cognitive deficit
Rück et al. (2008)	26	OCD	10 years	Y-BOCS and cognitive tests (WFT, WCST, and Digit Span Test)	Clinical, cognitive improvement

Abbreviation: Y-BOCS, Yale–Brown Obsessive–Compulsive Scale; SRB, Synonyms, Reasoning and Block Test; BVRT, Benton Visual Retention Test; WBI, Wechlser–Bellevue Intelligence Scales; WFT, Word Fluency Test; CDLR, Claeson–Dahl Learning and Retention Test; TMT, Trail Making Test; WCST, Wisconsin Card Sorting Test; Halstead–Reitan Test, Halstead–Reitan Neuropsychological Battery; Rey Complex, Rey Complex Figure Test.

not respond to three different, adequately performed SSRI treatments; and (iii) psychotherapy (CBT) was ineffective (we used Husted and Shapira's guidelines, as mentioned above). Five patients were treated with anterior capsulotomy combined with pharmaco- and psychotherapy, and five were treated only with pharmaco- and psychotherapy. In the case of anterior capsulotomy, the scientific-ethical guidelines do not make randomized selection possible: Hungarian regulations require that the patients apply for psychosurgery and give their consent to participate. As a result the selection of the operated group was not randomized. These five patients were the first ones to request psychosurgery. Patients were randomly selected for the non-operated group. The two groups were matched one-to-one for age (mean ± SD, 32.2 ± 6.3 years in the operated group and 31.8 ± 7.1 years in the control group), gender, education, symptom severity and cognitive profile. All ten patients — irrespective of group — participated in a special long-term rehabilitation program for patients with obsessive–compulsive disorder, which was carried out in the Department of Psychiatry of Gyula Nyírő Hospital, Budapest, Hungary. This rehabilitation program, developed by our team, included appropriate, novel medication (SSRI therapy) as well as individual (cognitive–behavior therapy) and group psychotherapy. The characteristics of this rehabilitation program include the new combination of classic psychotherapeutic and pharmacotherapeutic methods, which means that we combined different methods (cognitive–behavior therapy, psychodrama, family therapy, individual behavior training, group behavior therapy, art therapy, and relaxation) in an intensive program. Both groups (i.e. operated and non-operated) participated in the same rehabilitation program.

The clinical and demographic characteristics of the patients are outlined in Table 2.

For the operated group, the criteria for surgical intervention for patients with OCD have been elaborated by the Hungarian Board of Psychiatrists, based on international guidelines (Mindus and Meyerson, 1995) and have been approved by the Committee of Ethics and Science of Hungarian Psychiatric Association (Németh et al., 2002). All anterior capsulotomy procedures were performed in the Hungarian National Institute of Neurosurgery in 2001. The study protocol was approved by the ethics committee of Gyula Nyírő Hospital, and signed informed consent was obtained from all participants.

2.2. Measures

Pre-operative/pre-treatment examinations included structural (MRI) and functional (SPECT and PET) imaging only for operated patients, and detailed neuropsychological tests for all patients: the latter included the Hungarian version of the Wechsler Intelligence Test [MAWI], Verbal Fluency Test [VFT], Category Fluency Test [CFT], Trail Making Test [TMT], Stroop Test, Pieron Test, Corsi Test, California Sorting Test [CST], Iowa Gambling Test [IGT], and Repeatable Battery for the Assessment of Neuropsychological Status [RBANS]. To eliminate any learning effects, we used different versions of the tests at different time points, if that was possible (e.g. RBANS and Iowa Gambling Test). In the case that no other version of the test was available, we had to be satisfied with a 3-month period between two measurement times. Additionally, we used the Yale–Brown Obsessive–Compulsive Scale (Y-BOCS) to assess obsessive–compulsive symptoms and the Hamilton Depression (HAM-D) and Hamilton Anxiety Scales (HAM-A) to identify depression and anxiety symptoms, respectively. Pre-operative examination (for the operated group) was carried out one month before the operation. Post-operative follow-up examinations were performed in the first, sixth, twelfth and twenty-fourth months after the operation.

Table 2
Clinical and demographic characteristics of patients.

	Operated $N = 5$	Matched sample $N = 5$
	Mean (SD)	Mean (SD)
Male/female	3/2	3/2
Age at the time of operation/treatment	32.2 (6.3)	31.8 (7.1)
Education (years)	11.2 (1.3)	11.6 (0.54)
Onset of symptoms (age)	9 (6.74)	9 (5.09)
Y-BOCS score before operation/treatment	38.2(1.78)	36.2 (1.09)

Abbreviation: Y-BOCS, Yale–Brown Obsessive–Compulsive Scale.

Tests of the patients in the matched sample group were carried out at the time of entering the hospital, and one and six months after finishing the special rehabilitation program.

2.3. Surgical technique of anterior capsulotomy

Bilateral, CT- and MRI-guided anterior capsulotomy was performed in February, 2001. A stereotaxic surgical frame (CRW, Radionics, Burlington, USA) was fixed to the skull with screws with local anesthesia to provide accurate targeting. A localization box was temporarily fixed to the frame and from all of these a cranial CT scan was performed. Data were fed into a special high-performance computer and CT images were merged with MRI images obtained earlier from the patients. Target points were selected in bilateral anterior capsular radiation with the aid of special computer software (from Target, BrainLAB, Munich, Germany). Subsequently, monopolar electrodes (Radionics, Burlington, USA) were led into the target brain points, the position of which was determined in the aforementioned way through a drilled skull hole. The position of the electrode was set by a micromanipulator placed on the frame. Brain lesions were made by radiofrequency-stimulation below and right at the target points, first on the right side, then on the left side. Prior to each radio-frequency-stimulation, the position of the electrode was checked by macro-stimulation.

2.4. Rehabilitation program for treatment-refractory OCD patients

The rehabilitation program included pharmaco-therapy and individual and group psychotherapy. We carried out daily individual behavior therapy and weekly group behavior therapy. The patients also participated in two sessions of cognitive psychotherapy a week, in free-interaction group therapy once per week, and assertiveness training once per week. Additionally, we organized psycho-education programs for participants' relatives once per month. The patients who were operated on were transferred back to the Department of Psychiatry within three to six days after the surgery to participate in the rehabilitation program.

2.5. Data analysis

We examined how the cognitive profile of treatment-refractory OCD patients changed during the follow-up. The neuropsychological test scores were statistically analyzed by SPSS software (SPSS 13.0 for Windows). Considering the small sample size and the particularly non-normal distribution of the data, we used non-parametric tests. In the case of the operated group, Friedman's ANOVA was performed using "time" (before and 1, 6, 12, and 24 months after the surgery) as within-subjects factor. In the case of the non-operated group, Friedman's ANOVA was also performed using "time" (before, and 1 and 6 months after treatment) as within-subjects factor. Level of significance was defined using the Bonferroni correction method. Wilcoxon signed-rank tests were used as post hoc tests to identify the time points at which test scores were significantly different from those measured prior to the operation. Subsequently, we compared the scores of the operated group with that of the non-operated group using Mann–Whitney tests.

3. Results

3.1. Results for the operated group

Changes in the patients' clinical conditions were measured using three scales: the Y-BOCS, the HAM-A and the HAM-D during the course of the follow-up. Results are outlined in Table 3. Each of the patients who underwent surgery showed post-operative improvement. A significant decrease was found in Y-BOCS ($\chi^2(4) = 12.93$, $p = < 0.01$) and HAM-A ($\chi^2(4) = 14.16$, $p < 0.01$) scores, whereas there was a decrease in the scores of the HAM-D, but the overall result here showed only a tendency ($\chi^2(4) = 7.46$, ns). Wilcoxon signed-rank tests were used to follow-up this finding. Y-BOCS scores showed significant improvement ($z = -2.03$, $p < 0.05$, $r = -0.41$) from as early as one month after operation, whereas HAM-A ($z = -2.02$, $p < 0.05$, $r = -0.41$) and Hamilton-D ($z = -2.02$, $p < 0.05$, $r = -0.41$) scores showed significant improvement 3 months after the operation. The Hamilton-D score changes also showed a strong tendency after 6 months, one year and two years ($p = 0.063$). Two of five patients became medication-free after the anterior capsulotomy.

Changes in the patients' neuropsychological profiles were measured by the neuropsychological test battery mentioned above. Five tests out of ten showed significant improvement, while only one showed deterioration.

We found a significant increase in the operated group's IQ test scores ($\chi^2(4) = 13.3$, $p < 0.01$). IQ scores of the operated patients significantly increased during the two-year follow-up period, with higher scores after the operation. The operated patients found significantly more categories in the California A Sorting Test ($\chi^2(4) = 9.52$, $p < 0.05$), significantly more words in the Verbal Fluency Test ($\chi^2(4) = 10.38$; $p < 0.05$), and were significantly faster in the Stroop Test Interference Scale ($\chi^2(4) = 10.08$, $p < 0.05$) at follow-up.

Wilcoxon signed-rank tests were used to follow-up this finding. Interestingly, significant improvement appears as early as one month after the operation in the Stroop Test ($z = -2.03$, $p < 0.05$, $r = -0.41$) and IQ test ($z = -2.04$, $p < 0.05$, $r = -0.41$), whereas such an increase is first seen one year after the operation in Verbal Fluency ($z = -2.02$, $p < 0.05$, $r = -0.41$) and two years after the surgery in the California A Sorting Test ($z = -2.04$, $p < 0.05$, $r = -0.41$). The operated

Table 3
Changes in clinical condition of patients in the operated group during the course of the follow-up.

Test name	Pre	Post1	Post6	Post12	Post24	χ^2	p
	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)		
Y-BOCS	38.2 (1.78)	26.4 (5.12)	20 (9.13)	19.6 (8.56)	18.2 (9.95)	12.93	0.003
HAM-D	22.6 (13.72)	10.6 (5.85)	7.2 (4.32)	8.6 (5.54)	7.2 (4.65)	7.46	ns
HAM-A	21.2 (7.15)	11 (6.67)	7.2 (4.6)	9.2 (4.65)	11 (7.87)	14.16	0.001

Abbreviations: Y-BOCS, Yale–Brown Obsessive–Compulsive Scale; HAM-D, Hamilton Depression Scale; HAM-A, Hamilton Anxiety Scale; Pre, prior to operation; Post1, 1 month after the operation; Post6, 6 months after the operation; Post12, 12 months after the operation; Post24, 24 months after the operation; ns not significant. For statistical analysis Friedman's ANOVA was used.

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patients in the Gambling Task selected significantly more cards from the advantageous decks than from the disadvantageous decks after one ($z = -2.02$, $p < 0.05$, $r = -0.41$) and two years ($z = -2.02$, $p < 0.05$, $r = -0.41$).

Table 4 summarizes the pre- and post-operative neuropsychological test improvements in the operated group.

We observed decreased performance in the operated group on the Category Fluency Test after the operation. The intrusion errors increased significantly on this test two years after operation ($z = -2.06$, $p < 0.05$, $r = -0.41$). The performance of the patients in the Trail Making Test Parts A ($\chi^2(4) = 5.57$, ns) and B ($\chi^2(4) = 1.12$, ns) was quite poor and speed did not improve after the surgery. Moreover, the performance of spatial working memory was also poor in the Corsi task, with low spatial working memory capacity at the initial measurement point (pre-operation). This capacity did not increase significantly after the operation ($\chi^2(4) = 4.93$, ns). The results are summarized in Table 5.

3.2. Side effects in the operated group

The patients tolerated anterior capsulotomy well, with the exception of one patient, who became anxious. After the anterior capsulotomy, we registered temporary incontinency in two patients, periorbital tumescence in two patients, and fever for several days in four patients. One patient became sleepy for four days following the operation. Three to six days after the operation, patients were taken back to the psychiatric department. We observed increased appetite and weight gain (5 and 7 kg) in two patients, which proved to be permanent. Two patients developed a temporary — 10-day long — moderate depressive status. After the anterior capsulotomy, the condition of all patients was adequate for participation in the rehabilitation program.

Table 4
Neuropsychological test results showing significant pre-to post-operation improvement in the operated group.

Test name	Pre	Post1	Post6	Post12	Post24	χ^2	p
	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)		
IQ	91.8 (10.94)	102 (7.38)	107.4 (4.39)	107.8 (7.04)	107.2 (7.19)	10.3	0.002
CST-A	3 (1.22)	4.2 (1.3)	4.4 (1.51)	4.4 (1.14)	5 (1)	9.52	0.036
STR-I	39.6 (12.97)	26.4 (13.72)	33.4 (17.86)	33.2 (21.76)	35 (19.44)	10.08	0.026
VFT	32.4 (3.78)	34.8 (5.71)	36.8 (7.15)	43.6 (6.14)	46.4 (10.73)	10.38	0.021
IGTDA	57.4 (20.32)	50.6 (13.81)	56 (9.05)	34.6 (6.34)	34.4 (9.39)	7.04	0.13
IGT-A	42.6 (20.32)	49.2 (13.71)	44 (9.05)	65.4 (6.34)	66.4 (10.31)	7.04	0.13

Abbreviations: IQ, Wechsler Intelligence Quotient; CST-A, California Sorting Test Part A: right concept; STR-I, Stroop Test Interference Scale: time; VFT, Verbal Fluency Test: number of words; IGTDA, Gambling Test: selection from disadvantageous desks; IGT-A, Gambling Test: selection from advantageous desks; Pre, prior to operation; Post1, 1 month after the operation; Post6, 6 months after the operation; Post12, 12 months after the operation; Post24, 24 months after the operation; ns not significant.
For statistical analysis Friedman's ANOVA was used.

Table 5
Perseverative tendencies, spatial working memory and attention deficit of patients in the operated group.

Test name	Pre	Post1	Post6	Post12	Post24	χ^2	p
	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)		
CFT-IE	0.6 (0.89)	0.6 (0.54)	0.8 (0.83)	1.4 (2.07)	2.6 (2.51)	10.36	0.022
CST-BPE	3.6 (1.67)	3.2 (0.83)	3.4 (0.54)	3.2 (0.83)	2.8 (1.3)	0.63	ns
VFT-P	1 (1)	2.8 (3.42)	3.8 (3.76)	3.8 (4.26)	1.8 (4.02)	7.22	ns
Corsi	3.4 (0.74)	3.2 (1.03)	3.5 (0.5)	3.9 (0.89)	3.9 (1.19)	4.93	ns
TMTA	76.4 (45.08)	64.8 (26.22)	69 (40.1)	64 (37.8)	70.8 (72.42)	5.57	ns
TMTB	229.4 (137.89)	201.6 (100.33)	192.6 (116.1)	170 (79.9)	203.6 (204.01)	1.12	ns

Abbreviations: CFT-IE, intrusion errors in Category Fluency Test; CST-B-PE, perseverative errors in California Sorting Test Part B; VFT-P, perseverative errors in Verbal Fluency Test; Corsi, Corsi spatial working memory Test; TMTA, Trail Making Test Part A; TMTB, Trail Making Test Part B; Pre, prior to operation; Post1, 1 month after the operation; Post6, 6 months after the operation; Post12, 12 months after the operation; Post24, 24 months after the operation; ns not significant.
For statistical analysis repeated measure ANOVA was used.

3.3. Results for the non-operated group

Patients in the non-operated group show significant improvement on clinical tests during the course of the follow-up. Significant decrease was found in Y-BOCS ($\chi^2(2) = 8.4$, $p < 0.01$) and HAM-A ($\chi^2(2) = 10$, $p < 0.01$) scores. Y-BOCS scales showed significant improvement from as early as one month after the beginning of the treatment ($z = -2.06$, $p < 0.05$, $r = -0.53$), and this improvement continued. HAM-A scores also showed significant improvement after the beginning of the treatment ($z = -2.04$, $p < 0.05$, $r = -0.53$).

We did not find significant improvement or decreased neuropsychological performance during the course of the follow-up.

3.4. Comparison between operated and non-operated groups

All patients were of the same symptom severity, and there were no significant differences in Y-BOCS scores between the

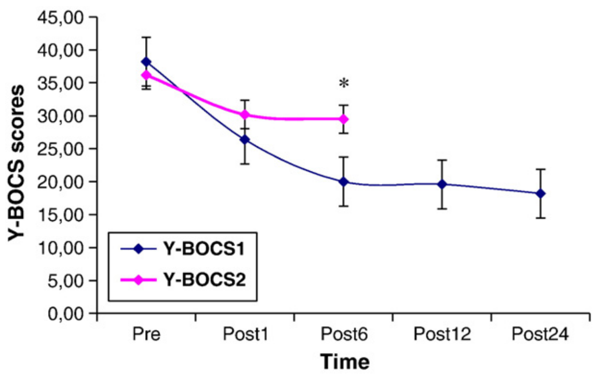

Fig. 1. Changes in Y-BOCS scores at follow-up. Abbreviations: Y-BOCS1, Yale–Brown Obsessive–Compulsive Scale in the operated group. Y-BOCS2, Yale–Brown Obsessive–Compulsive Scale in the non-operated group.

Table 6
Neuropsychological test results of patients in the operated and non-operated groups.

Variable	Test of independence	Significance
	Mann–Whitney *U* test	
RBANSLIPre	$U=4$, $z=-1.8$	0.04
RBANSLIPost 1	$U=12$, $z=-.10$	ns
RBANSLIPost 6	$U=1$, $z=-2.49$	0.008
RBANSAIPre	$U=5.5$, $z=-1.49$	ns
RBANSAIPost1	$U=7$, $z=-1.16$	ns
RBANSAIPost6	$U=3.5$, $z=-3.89$	0.032
TMTBPre	$U=4$, $z=-1.44$	0.048
TMTBPost1	$U=1$, $z=-2.4$	0.008
TMTBPost6	$U=3$, $z=-2$	0.028

Abbreviations: RBANSLIPre, RBANS Language Index before the operation/treatment; RBANSLIPost1, RBANS Language Index one month after the operation/treatment; RBANSLIPost6, RBANS Language Index six months after the operation/treatment; RBANSAIPre, RBANS Attention Index before the operation/treatment; RBANSAIPost1, RBANS Attention Index one month after the operation/treatment; RBANSAIPost6, RBANS Attention Index six months after the operation/treatment; TMTBPre, Trail Making Test Part B before the operation/treatment; TMTBPost1, Trail Making Test Part B one month after the operation/treatment; TMTBPost6, Trail Making Test Part B six months after the operation/treatment; ns, not significant.

operated and non-operated groups at the initial measurement point. After treatment (anterior capsulotomy and rehabilitation program in the operated group, and rehabilitation program in the non-operated group) the Y-BOCS scores decreased significantly for both groups. In the operated group the mean decrease in scores was 20 Y-BOCS units, whereas in the non-operated group the mean decrease in scores was 6.8 Y-BOCS units (see Fig. 1). In the non-operated group the symptoms remained in a serious range.

Table 6 shows the comparison of patients' neuropsychological test results in the operated and non-operated groups, respectively. The neuropsychological profiles of the two groups were also almost the same. Performance on the Trail Making Test Part B was extremely poor in the operated group, such that this test showed significantly different scores between the two groups at the pre-treatment/pre-operation time point ($U=4$, $p<0.05$, $r=-0.46$). At follow-up, we found significant differences between the operated and non-operated groups in three out of ten neuropsychological tests: Trail Making Test Part B (after one month's: $U=1$, $p<0.01$, $r=-0.62$; after six month's: $U=3$, $p<0.05$, $r=-0.52$), RBANS Attention Index (after six month's: $U=3{,}5$, $p<0.05$, $r=-0.49$) and RBANS Language Index (after six month's: $U=1$, $p<0.01$, $r=-0.64$). Performance on these three tests was significantly better in the non-operated group.

4. Discussion

Few studies focus on treatment-refractory OCD patients, with most investigating potential treatments, i.e. psychosurgery (Rasmussen and Eisen, 1997; Jenike and Rauch, 1994; Liu et al., 2008). In the literature to date only one study has identified the possibility of the treatment-refractoriness as a subtype of OCD, and investigated its neuropsychological features (O'Connor, 2005). In the present study, we focused on treatment-refractory patients and their cognitive profiles. We observed ten treatment-refractory OCD patients with similar symptom severity according to treatment-refractory criteria. Five patients underwent anterior capsulotomy and combined pharmaco- and psychotherapy, whereas the other five underwent only pharmaco- and psychotherapy. Both groups improved in clinical symptoms, implying that each treatment method was effective in the reduction of obsessive–compulsive symptoms. The clinical improvement was more impressive in the operated group than in the non-operated group, a point in favor of psychosurgery. In the operated group we observed side effects (temporary incontinency, fever, depressive mood, and permanent weight gain), but they were not as severe as those found in other studies (Rück et al., 2008). According to Rück et al. (2008) weight gain is a well-known adverse effect of capsulotomy. The sample used in the present study is relatively small, and this needs to be taken into account, for example it is not certain, that all possible side effects appeared.

In our limited experience, anterior capsulotomy is a relatively safe and effective method for reducing OCD symptoms.

In the extant literature, differing results can be found regarding the efficacy of anterior capsulotomy. Mindus et al. (1994) found that 61% of participants responded satisfactorily after anterior capsulotomy; Lopez et al. (2004) offered a review of anterior capsulotomy, reporting an efficacy level between 38 and 100%. According to Gabriels et al. (2003), 50% of treatment-refractory patients showed clinical improvement after anterior capsulotomy. The clinical improvement of the operated group was more impressive than that of the non-operated group. In both groups Y-BOCS and HAM-A scores showed significant improvement, but the decrease of the Y-BOCS scores was greater in the operated group then in the non-operated group. The most intensive improvement of OCD and anxiety symptoms in the operated group was observed at the first month after surgery. Depressive symptoms improved only later, i.e., 3-month after surgery. Our results showed an apparent improvement of OCD symptoms — very impressive in itself — that stabilizes six months after the surgery; however, anxiety symptoms declined. In our follow-up, we did not observe a relapse of OCD symptoms. When relapse occurs, other investigators (Mindus and Meyerson, 1995) report performing a second surgery. In a study of Mindus and Meyerson (1995), 7 out of 22 OCD patients underwent a second anterior capsulotomy due to relapse within 3 to 6 months after the first surgical intervention. The second intervention was performed one year after the first capsulotomy.

We found that in the non-operated group, clinical improvement also appears as soon as one month after the beginning of treatment, and improvement is continuous.

Neuropsychological studies of obsessive–compulsive disorder have found major deficits related to OCD in the following domains (Greisberg and McKay, 2003):

1. attention deficit (Muller and Roberts, 2005; Schmidtke et al., 1998)
2. fluency (Martinot et al., 1990; Schmidtke et al., 1998; Kim et al., 2002)
3. set-shifting (Okasha et al. 2000; Moritz et al. 2001, 2002; Abbruzzese et al., 1995)
4. decision-making (Sachdev and Hay 1995; Cavallero et al., 2003; Lawrence et al., 2006).

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Results from the present study support several earlier findings and conflict with some others.

Our data regarding the pre-operative cognitive status of the patients are inconsistent with the findings of Nyman and Mindus (1995) who found that all neuropsychological test results were in the normal range before the operation. This raises the question of whether it is possible for treatment-refractory obsessive–compulsive disorder to exist without cognitive deficits.

In response to our first question (what kinds of cognitive deficits do treatment-refractory patients have?), we found that pre-surgery/treatment performance is similar, but that specific neuropsychological deficits are demonstrated in the group that later underwent psychosurgery. The patients who underwent anterior capsulotomy had extremely serious attention deficits and set-shifting deficits before surgery. Linguistic performance was better in the non-operated group than in the operated group upon entering treatment. In response to our second question (how does anterior capsulotomy modify the cognitive profile of patients with OCD?), results indicate that there are improvements in the majority of the measured cognitive functions after anterior capsulotomy and the rehabilitation program. In general, neuropsychological tests measuring fluency (VFT), inhibition function, set-shifting (Stroop, CST), and decision-making (IGT) showed pre-to post-operation improvement. Importantly, IQ scores increased after the operation, indicating that intervention in the loops affects both cognitive performance and IQ scores.

More importantly, the decision-making related Gambling Test results show that patients become more sensitive to feedback (i.e., reward and punishment) and improve their ability to create strategize. Furthermore, the Gambling Test can be of significance for psychotherapy and rehabilitation, because the test results also imply that, in the case of treatment-refractory patients, the purpose of the operation could be to make these patients suitable for psychotherapy and rehabilitation.

It is important to note that tests that showed improved results measure the function of dorsolateral prefrontal and ventromedial prefrontal cortical areas. As mentioned in the Introduction, neurosurgical interventions might provide an insight into the function of loops. Our data also emphasize the importance of long-term follow-up: improvement in certain cognitive functions appears later, at a minimum of one year after the surgery.

The perseverative tendencies that we observed are consistent with Nyman's earlier results (Nyman and Mindus, 1995). As stated above, the goal of the neurosurgical interventions can be to achieve better clinical condition of treatment-refractory patients with the consequence of greater sensitivity to pharmaco- and psychotherapy.

Our findings show that attention and spatial working memory deficits are characteristic of treatment-refractory patients. Both groups show improvement in cognitive performance, but the improvement is stronger and statistically significant only in the operated group. Comparison of the two groups showed that despite improvement, the operated group lagged behind in certain cognitive functions, such as attention and set-shifting, compared to the non-operated group.

As the cognitive performance of non-operated patients was mostly constant, we did not find significant test improvements in this domain: this indicates that (i) practice effect, and (ii) effects of other therapies (i.e., pharmaco- and psychotherapy) on cognitive functions are not likely to be responsible for the results found in the operated group.

In many countries, the application of neurosurgical techniques, alongside pharmaco- and psychotherapy, is taken into account in the treatment of treatment-refractory OCD patients. Overcoming the problem of treatment-refractory OCD is definitely an important and acute issue today. In our opinion, neurosurgery is a potential therapeutic approach. The data in the literature are conflicting regarding the efficacy of surgical techniques and neuropsychological test results. Thus, further comparative investigations are needed to clarify how neurosurgical techniques influence the cognitive functioning of patients. Investigations (Nyman and Mindus, 1995; Nyman et al., 2001; Mindus and Meyerson, 1995; Rück et al., 2003) have pointed out that surgical interventions and, moreover, the application of reversible techniques (deep brain stimulation) (Gabriels et al., 2003; Anderson and Ahmed, 2003; Rauch et al., 2006) can improve the clinical condition of patients who do not respond to other treatments. Our study confirms that thorough and long-term psychological and neuropsychological follow-up studies of patients, along with complex rehabilitation programs, are definitely necessary.

4.1. Limitations

The sample used in the present study is relatively small, and this needs to be taken into account. For example it is not certain, that all possible side effects appeared. We did not have a control group which was treated with anterior capsulotomy but not with the rehabilitation program. This is because our sample consisted of the only five patients in Hungary who have undergone psychosurgery to date. Finally, the neuropsychological tests may have produced learning effects; however when possible we used different version of tests at different time points.

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Conflict of interest

The authors do not have an affiliation with, or financial interest in any organization that might pose a conflict of interest.

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