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Neuropsychological Impairment in Obsessive-Compulsive Disorder—Improvement Over the Course of Cognitive Behavioral Treatment

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A large body of studies demonstrates mild cognitive dysfunction in patients with Obsessive Compulsive Disorder (OCD). Few trials have investigated whether this dysfunction can be improved by treatment. Thirty unmedicated inpatients with OCD were administered a comprehensive neuropsychological test battery before and after 12 weeks of cognitive behavioral therapy (CBT). Thirty-nine carefully matched healthy controls were tested twice within the same interval. At baseline, patients exhibited significant impairments on several tests which normalized at follow-up. A significant group ×time interaction was found for tests of nonverbal memory, set shifting and flexible, self guided behavior. Major responders improved significantly more than minor responders on the Rey-Osterrieth Figure immediate and delayed recall. Results suggest that cognitive dysfunction in OCD can improve in the course of treatment. We hypothesize that particularly cognitive behavioral treatment enables OCD patients to think and act in a more flexible way that helps them to develop more effective cognitive strategies.

Introduction

Obsessive-compulsive (OCD) disorder is among the most common psychiatric disorders, with a 12 month prevalence of 0.6% and lifetime prevalence rates estimated at 2%–3% (Crino, Slade & Andrews, 2005; Karno, Golding, Sorenson & Burnam, 1988). OCD is characterized by recurrent intrusive thoughts, images or impulses and ritualized stereotyped behaviors or mental acts. Symptoms cause significant personal distress and interfere with daily activities. Both cognitive-behavior therapy (CBT) and pharmacological treatment with serotonin reuptake inhibitors (SRI) have been proven to be effective (Hohagen et al., 1998; McDonough & Kennedy, 2002). However, CBT seems to be most effective (Foa et al., 2005).

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There is a growing body of evidence indicating that OCD is associated with distinct patterns of dysfunction involving the orbitofrontal-subcortical circuitry (Baxter et al., 1988; Saxena, Brody, Schwartz & Baxter, 1998; Saxena, Bota & Brody, 2001). In most of the studies a hypermetabolism in the fronto-striatal loop was observed that was found to be decreased after both successful pharmacological and behavioural treatment (Baxter et al., 1992; Nakatani et al., 2003; Saxena et al., 1999; Schwarz, Stoessel, Baxter, Martin & Phelps, 1996).

Results of investigations into neuropsychological functioning have been inconsistent so far. Several studies in subjects with OCD suggest impairment on tests of set shifting ability (Abbruzzese, Bellodi, Ferri & Scarone, 1995; Abbruzzese, Ferri & Scarone, 1997; Purcell, Maruff, Kyrios & Pantelis, 1998), fluency (Harris & Dinn, 2003; Schmidtke, Schorb, Winkelman & Hohagen, 1998), planning and problem solving (van den Heuven et al., 2005) and visuospatial memory (Deckersbach, Otto, Savage, Baer & Jenike, 2000; Kim et al., 2003; Savage et al., 1999). In contrast, in some studies, results of OCD patients did not differ from those of healthy controls, or cognitive impairment was partially shown to be secondary to concomitant depression (Aycicegi, Dinn, Harris & Erkman, 2003; Basso, Bornstein, Carona & Morton, 2001; Moritz et al., 2001; Bohne et al., 2005). However, the majority of studies suggests that OCD is commonly associated with mild cognitive dysfunction on tasks involving executive functioning and nonverbal memory (for reviews see Greisberg and McKay, 2003; Kuelz, Hohagen & Voderholzer, 2004a).

Based on recent results of an underlying metabolic dysfunction that can be ameliorated by successful behavioral or pharmacological therapy, one can assume that neuropsychological deficits associated with OCD are reversible during the course of treatment as well. However, though postulated some years ago (Head, Bolton & Hymas, 1989), only a few studies have systematically examined the effects of behavioural or pharmacological treatment on cognitive functioning in OCD.

In several studies using a within-subject-design across time, no comparison group was included (Bolton, Raven, Madronal-Luque & Marks, 2000; Kang et al., 2003; Thienemann Koran, 1995). Thus, the interpretation of these results has therefore been somewhat limited due to possible practice effects as a confound.

In a study by Kim and colleagues (2002), OCD patients were significantly impaired on speed of information processing, visuospatial memory and verbal fluency at baseline. After 4 months of SSRI treatment, performance had significantly improved compared to that of healthy controls, but patients still displayed deficits on verbal fluency and visuospatial memory. However, almost half of the patients had already been medicated at baseline and patients were still symptomatic at follow up.

Nielen and Den Boer (2003) examined cognitive performance of 19 OCD patients before and after 12 weeks of treatment with fluoxetine. Compared with healthy controls, patients were impaired on planning ability, spatial memory and motor speed before and after treatment. The authors conclude that neuropsychological deficits in OCD are trait-related features that persist after pharmacological treatment. However, they also point out that their test battery may have not been sensitive enough for evaluation of cognitive functions involving the orbitofrontal loop.

To our knowledge, there are only two studies so far examining changes of cognitive functioning before and after *behavioral* treatment compared with healthy controls (Moritz, Kloss, Katenkamp, Birkner & Hand, 1999; Sieg, Leplow & Hand, 1999).

Moritz and colleagues (1999) compared neuropsychological performance of OCD responders (n = 14) and nonresponders (n = 7) before and after behavioral treatment. They found that the whole sample of OCD patients performed worse than healthy controls on

tasks of set shifting and selective attention at baseline, but that after therapy only nonresponders were still impaired on these tasks, whereas responders reached normal scores.

Sieg and colleagues (1999) compared neurocognitive performance of 24 initially unmedicated OCD patients before and after 9 weeks of behavioral therapy with performance of 13 healthy controls tested within the same time interval. Minor responders, who showed less improvement of OC symptoms, obtained significantly lower scores on verbal fluency tasks as well as on a visual learning test compared to controls. These cognitive impairments were found before and after therapy. However, the potential effects of additional medication during behavioural treatment were not considered.

The aim of the following study was to systematically evaluate the impact of cognitive behavioral therapy on neuropsychological functioning of initially unmedicated OCD patients. Thirty patients with OCD were tested before and after three months of cognitive behavioral therapy with stimulus exposure and response management in comparison with a group of healthy controls. To consider possible confounding factors, the potential impact of depressive symptoms, severity and duration of illness as well as additional medication during behavioral therapy were taken into account.

Method

Subjects

Thirty-five inpatients diagnosed with OCD by an experienced clinician according to the DSM-IV criteria were recruited from the Department of Psychiatry and Psychotherapy, University Hospital of Freiburg. Four patients were lost to follow-up and one patient was prescribed neuroleptic medication during the course of treatment, giving a final number of 30 patients that were included. All patients were unmedicated for at least two weeks prior to baseline testing. Exclusion criteria included the presence of substantial neurological impairment, head injury, substance abuse, current or previous psychotic episodes, Major Depression and age above 65 years. Comorbid Axis-I disorders were systematically assessed via clinical interview. One patient was additionally diagnosed with a panic disorder and one patient had a history of alcohol abuse but was abstinent at the time of testing.

Forty healthy volunteers were recruited through newspaper advertisements that did not specify the disorder under investigation. A total of 39 healthy control subjects completed both sessions. Additional exclusion criteria for the normal subjects were evidence for personal or family lifetime history of Axis I disorder as assessed by a clinical interview.

The study protocols were approved by the Ethical Commitee of the Albert Ludwig University Freiburg. Informed written consent was obtained from each subject before testing.

Study Design and Experimental Procedure

Neuropsychological and questionnaire data were collected before and after 12 weeks of manualized inpatient CBT with stimulus exposure and response management, a procedure that has been proven to be strongly effective (Hohagen et al., 1998). There were two individual therapeutic sessions per week, each lasting about 50–60 min. In the initial phase, the treating clinician, experienced in therapy of OCD, explored OCD symptomatology, pre-disposing, precipitating and maintaining factors. Based on this information, a working model was introduced to guide the treatment procedure. In the following, an exposure hierarchy was developed and the patient exposed himself to the individually triggering stimuli. Furthermore, cognitive appraisals of feared situations or intrusive thoughts were

challenged and alternate, more adequate appraisals were developed. Individual treatment was supplemented by physiotherapeutic and ergotherapeutic groups.

Healthy controls were tested within the same interval without undergoing any behavioral treatment. At baseline, all patients were unmedicated. After baseline testing, seven patients were given citalopram with a mean daily dose of 40 mg additionally to CBT. All other patients were drug-free during CBT. Groups were matched for age, sex and education as well as for intelligence as assessed by a verbal IQ test (Mehrfachwahl-Wortschatztest B, MWT-B; Lehrl 1992) and the Standard Progressive Matrices (Raven 1991).

For quantitative assessment of obsessive-compulsive and depressive symptoms the following scales were used: Yale-Brown Obsessive-Compulsive Scale (Y-BOCS; Goodman et al. 1989), Beck Depression Inventory (BDI, Beck, Ward, Mendelson, Mock & Erbaugh, 1961) and the Hamilton Rating Scale for Depression (HDRS; Hamilton, 1960). Item 21 of the HDRS, assessing obsessive-compulsive symptoms, was not included in the overall score.

Tasks were administered at the beginning of treatment (max. 14 days after assignment) and immediately before discharge. Baseline results of a part of the sample and a part of the test battery have been published elsewhere (Kuelz, Riemann, Zahn & Voderholzer, 2004b). The rationale for the selection of measures is based on previous neuropsychological studies in OCD. Since the aim was to evaluate the impact of CBT on cognitive functioning, predominantly those tests were chosen, which have been shown to discriminate between OCD patients and healthy controls.

All subjects were tested at the University Clinic Freiburg by an experienced clinical psychologist. Neuropsychological tests were administered in one session that lasted about two and a half hours. To avoid positional effects, tests were presented in a randomized order that was alternated between subjects.

Neuropsychological Assessment

Speed of Information Processing

Trail Making Test A. Trail Making Test A (TMT A; Reitan, 1958) requires connecting digits from 1–25, which are arranged on a sheet, with a continuous line. The measure of performance is the time needed to complete the trial.

Fluency Tests

Verbal Fluency. The verbal fluency task is derived from the performance-test-system ("Leistungsprüfsystem", Horn, 1962), subtest 6. The subject has to write down as many words as possible, beginning with a certain letter, within one minute. The test consists of three trials, covering the letters F, P and K.

Nonverbal Fluency. The Five-Points Test (Regard, Strauss & Knapp, 1985), a task similar to the design fluency test, was applied to assess nonverbal fluency. The test involves a sheet with 35 squares, each containing five black dots. The subject's task is to connect any number of dots with any number of straight lines. In each square a different pattern of connection has to be produced. The number of correct solutions produced by the subject within 3 minutes is taken as the measure of performance.

Verbal Creativity. The subject's task is to write down as many different and unusual uses for a can and for a piece of string as possible (e.g., use a can as a flower-pot). The measure of performance is the number of ideas produced within 4 minutes (Schoppe, 1975). At second testing, a parallel version covering different items was used.

Test of Planning and Problem Solving

Tower of London—planning version. A computerized version of the Tower of London (ToL; Shallice 1982) similar to the Tower of London paradigm of the CANTAB (Robbins et al., 1994) was performed. On the problem solving condition, the subject's task is to rearrange a set of balls presented on the lower half of the screen to reach a goal state presented on the upper half of the screen. The minimum number of moves needed to solve the problem is specified before each trial on the screen. The number of moves needed to complete the trial varied between two and six moves. Planning accuracy was measured by the number of trials solved in the minimum number of moves. Initial thinking times (time between presentation of the problem and the first move) and subsequent movement times (time needed to complete the move) were also recorded.

Test of Visuoconstructive Functioning and Nonverbal Memory

Rey-Osterrieth Complex Figure Test (RCFT). The subject is instructed to draw a complex figure and to subsequently draw what he or she remembers immediately as well as after a delay of 30 minutes. Construction accuracy was quantified using the system of Meyers and Meyers (1995). In this approach, 18 segments of the complex figure are identified and evaluated according to accuracy and correct placement irrespective of the order of drawing. Organizational strategy was evaluated according to Savage et al. (2000). The figure is divided in five configural elements defined by Binder (1982). To underline the importance of the large rectangle for organization, it is assigned two points. The measure of performance is the number of configural elements drawn as unfragmented units.

Tower of London—memory version. On the memory condition of the Tower of London, the subject has to repeat a combination of moves of the balls that was presented on the screen immediately before. The number of moves needed to complete the trial varies between two and six moves. Thinking times and subsequent movement times were also considered.

Tests of Set Shifting Ability

Object Alternation Test (OAT). The OAT (Freedman & Oscar-Berman 1986) was administered in a computerized version. The investigator instructs the participant to detect a virtual coin that is hidden under one of two objects presented on the computer screen (a blue triangle and a red square). Every time the objects appear on the screen, the participant has four seconds to choose one of the objects by pressing one of two corresponding keys, respectively. A detailed description of the procedure can be found elsewhere (Kuelz et al., 2004b).

TAP—Change of Reaction. This test is a computerized task of the Test Battery for the Assessment of Attentional Dysfunction (TAP; Zimmermann and Fimm, 1994). The tests consists of 70 trials; on each trial a letter and a digit appear on the left and on the right side of the monitor. The subject's task is to alternatively press the left or the right button corresponding to the position of the letter or to the position of the digit, respectively. The program records the average reaction time as well as the number of errors.

Trail Making Test B. Trail Making Test B (TMT B; Reitan, 1958) involves alternately connecting digits (1–13) and letters (A–L) that are arranged on a sheet. The time needed to complete the trial and the number of errors are registered.

Test of Self-guided, Flexible Behaviour. The *Weight-Sorting Test* (WST) involves 28 identical looking plastic cylinders that should be arranged according to their varying

weights on a double-S shaped chain of circles within a time limit of 9 minutes. The sum of the deviations in grams between the chosen and the correct serial positions was the measure of performance. This test requires coordinated, goal directed and flexible behavior and persistency and is described to be sensitive to cerebral dysfunction (Bäumler, 1995).

Statistical Analysis

Data were analyzed using the SPSS-PC package, version 11.5. To evaluate an overall group-difference, the neuropsychological measures were entered into a multivariate analysis of variance (MANOVA). Subsequently, repeated measures of the analysis of variance (ANOVA) with the time of testing as the within-subject factor and the group as between-subject factor were calculated. To minimize type I errors, only for those domains subsequent univariate comparisons at baseline and follow-up were conducted, where a significant group x time interaction was observed. The relationship between neuropsychological test scores and the results of the questionnaires in OC patients was explored by use of Pearson's product moment correlations

The strict criterion of $p < 0.01$ was chosen for all separate group comparisons and correlational analyses to indicate statistical significance. To get a clear grasp of the magnitude of differences between groups at both baseline and at follow-up, effect sizes were additionally calculated for all neurocognitive parameters.

Results

Demographic Measures and Clinical Results

Table 1 summarizes the demographic and clinical characteristics of both groups at baseline and at follow-up. There were no significant differences between groups regarding age, sex, educational level and general intelligence (for intelligence, see Table 2).

Table 1
Demographic and clinical characteristics of the samples

Variable	OCD patients, n = 30		Healthy Controls, n = 39	T/χ^2-Score	p
	Baseline	Follow-up	Baseline		
Demographic characteristics					
Age	29.5 ± 8.4		28.2 ± 7.6	t = 0.67	ns
Sex (male/female)	9/21		17/22	χ^2 = 1.33	ns
Years of school education	11.3 ± 1.7		11.8 ± 1.8	t = –1.11	ns
Clinical data					
Y-BOCS total score	24.1 ± 6.0	13.7 ± 7.0	0.5 ± 1.2		
Y-BOCS obsessions	12.3 ± 3.1	7.5 ± 4.2	0.3 ± 1.0		
Y-BOCS compulsions	11.9 ± 4.0	7.0 ± 3.9	0.2 ± 0.7		
HDRS	8.2 ± 5.7	8.5 ± 6.2	1.9 ± 2.2		
BDI	13.9 ± 7.4	10.3 ± 8.2	3.4 ± 3.1		

Table 2
Neuropsychological test results at baseline and at follow-up

	Baseline		Follow-up		ANOVA Effect of group		ANOVA Effect of time		ANOVA Interaction effect		Effect size[+]	
Test	OCD patients	Controls	OCD patients	Controls	F (1,67)	p	F (1,67)	p	F (1,67)	p	Base line	Follow up
MWT-B	111.2 ± 14.3	116.8 ± 13.3	—	—	2.92	.093						
SPM	97. 2 ± 14.0	103.7 ± 16.6	—	—	2.93	.093						
Speed of information processing			—	—								
Trail Making Test A (time)	31.3 ± 9.5	24.0 ± 7.0	26.6 ± 8.6	22.8 ± 7.0	10.9	.002**	9.97	.002**	3.19	.079	1.04	.54
Fluency												
Verbal Fluency	35.3 ± 11.2	40.3 ± 8.1	39.1 ± 12.6	41.4 ± 8.4	2.99	.088	12.62	.001**	2.36	.132	.62	.27
Five-Points-Test	29.7 ± 7.7	39.2 ± 9.2	35.2 ± 8.7	42.2 ± 8.8	18.93	<.001***	18.18	<.001***	2.33	.133	1.03	.79
Verbal Creativity	12.4 ± 5.5	13.7 ± 5.2	13.3 ± 6.2	12.8 ± 5.1	.11	.75	.00	.994	2.12	.151	.25	.09
Visuoconstructive abilities and nonverbal memory												
Rey Figure: copy	32.4 ± 2.1	33.7 ± 2.7	32.9 ± 3.2	33.2 ± 2.3	2.26	.14	.07	.799	1.72	.191	.48	.13
Rey Figure: 3 min	19.8 ± 6.9	25.3 ± 5.3	24.4 ± 7.4	26.8 ± 5.5	10.26	.002**	19.65	<.001***	3.75	.057	1.04	.43
Rey Figure: 30 min	19.8 ± 6.5	24.7 ± 6.1	24.2 ± 6.4	26.2 ± 5.6	5.53	.013*	23.80	<.001***	6.83	.011*	.80	.36
Rey Figure strategy	3.9 ± 2.2	5.3 ± 1.2	5.2 ± 1.5	5.1 ± 1.5	16.13	.039*	5.94	.017	13.49	<.001***	1.17	.06
Tower of London – memory task	9.5 ± 3.8	11.5 ± 2.8	10.8 ± 3.6	12.4 ± 2.5	5.42	.023*	14.73	<.001***	2.41	.125	.71	.64
Flexible, self-guided behaviour and set-shifting												
Trail Making Test B (time)	76.2 ± 40.4	53.2 ± 19.1	62.4 ± 24.6	50.5 ± 23.4	8.68	.004**	9.46	.003**	3.84	.054	1.20	.49
TAP, Change of Reaction	830.3 ± 327.4	674.5 ± 141.3	697.1 ± 194.7	631.5 ± 129.0	5.83	.019*	32.36	<.001***	7.94	.006**	1.10	.51
Weight Sorting Test	97.9 ± 61.5	52.9 ± 34.7	66.0 ± 44.1	49.4 ± 31.4	11.97	.001**	10.80	.002**	7.71	.007**	1.29	.53
Object Alternation Test	3.5 ± 1.8	3.2 ± 2.3	2.8 ± 1.5	2.6 ± 2.1	.04	.851	7.03	.010*	.081	.776	0.11	.09
Planning and problem solving												
Tower of London-Planning task	13.1 ± 2.7	13.8 ± 1.7	13.4 ± 2.0	14.5 ± 1.5	4.91	.030*	5.87	.018*	.644	.425	0.41	.60

Note: [+]effect sizes, i.e., differences in group means divided by standard deviation of control group.

Table 3
Demographic characteristics of major responders and minor responders

Variable	Major responders n = 15	Minor responders n = 15	T/χ^2-Score	p
Age	31.3 ± 9.1	27.6 ± 7.6	t = 1.20	ns
Sex (male/female)	4/11	5/10	χ^2 = 0.69	ns
Years of school education	11.3 ± 1.6	11.3 ± 1.8	t = 0.00	ns

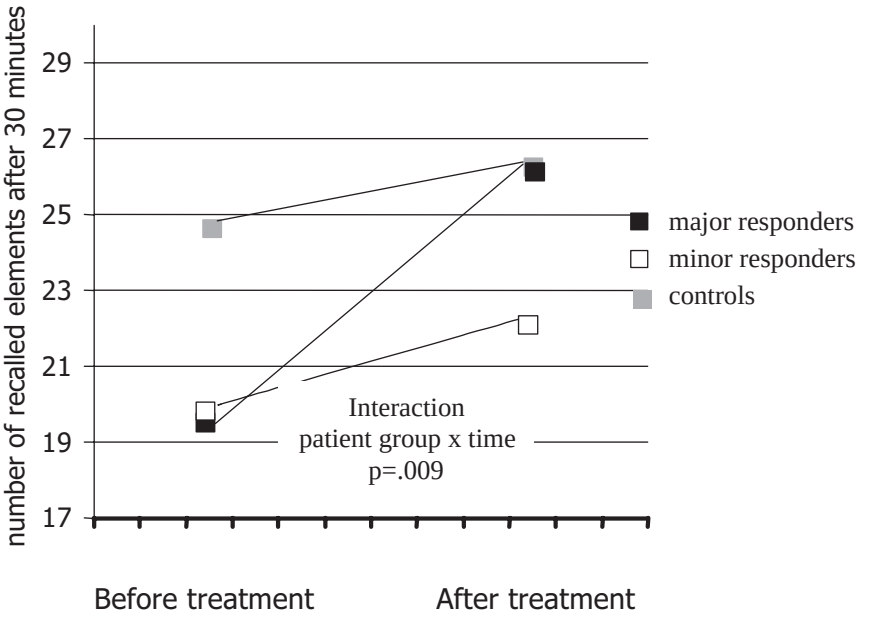

Figure 1. Delayed recall on the Rey-Osterrieth Complex Figure Test in major responders, minor responders and healthy controls. Effect of interaction between time and patient group (major responders vs. minor responders): p = .009.

At follow-up, OC symptoms as measured by the Y-BOCS were significantly reduced (–42.1% ± 26.3%, t(29) = 8.01, p < .001) compared with baseline.

Neuropsychological Test Results at Baseline and Follow-up

MANOVA including all of the baseline measures with exception of general intelligence yielded a highly significant difference between groups (F = 3.75, p < .001).

As can be derived from Table 2, there was a significant effect of group in 10 out of 14 measures with patients performing worse than healthy controls. As expected, there was also an effect of time on 11 parameters. With regard to effect sizes, there was a very large effect (>1.0) on 7 measures when comparing performance of patients and controls at baseline, but not at follow-up.

A significant effect of interaction (p < .05) was found for delayed recall on the Rey Figure. Univariate follow-up tests revealed that patients performed significantly worse

than controls at baseline ($t(67) = -3.39$, $p = .001$), but reached results comparable to those of controls at follow-up ($t(67) = -1.37$, $p = .176$). A highly significant interaction effect ($p < .001$) was also observed for the strategy score of the Rey Figure with patients drawing much fewer configural elements as unfragmented units compared with healthy controls at baseline ($t(67) = -3.0$, $p = .002$) but not at follow-up ($t(67) = .197$, $p = .845$). Furthermore, there was a tendency towards a significant interaction for RCFT immediate recall, which, however, became not significant at .05-level ($F(1,67) = 3.75$, $p = .057$).

Furthermore, the repeated measures ANOVA performed on the test "change of reaction" of the TAP showed a significant group × time interaction ($p < .01$) for time required to complete the task with patients performing more slowly than controls only at baseline ($t(67) = 2.67$, $p = .01$ and $t(67) = 1.67$, $p = .10$, resp.). There was also a significant ($p < .01$) group × time interaction with regard to the Weight Sorting Test, assessing flexible, self-guided behavior. OCD patients showed significantly more deviations than healthy controls at baseline ($t(67) = 3.38$, $p < .001$), but did no longer differ significantly from controls at follow-up ($t(67) = 1.82$, $p = .073$).

Secondary Analyses

Secondary analyses regarding total number of errors and response time on the OAT did not reveal any difference between groups. Even no effects of group or interaction for number of errors were found with respect to the TAP and the TMT B. Regarding the RCFT, there was no significant effect when testing for response time of drawing the figure. However, a significant effect of interaction was found for thinking times and movement times on the ToL problem solving condition ($F(1,67) = 5.24$, $p = .03$ and $F(1,67) = 4.93$, $p = .04$, resp.) and for thinking times on the ToL memory condition ($F(1,67) = 4.41$, $p = .04$). There were no significant differences between groups at baseline or follow up. OCD patients, however, tended to be more slowly than controls regarding all parameters of the ToL.

Impact of Depressive Symptoms on Neuropsychological Measurements

At baseline, depression as measured by the HDRS and by the BDI was not significantly correlated with any cognitive parameter. At follow-up, both the HDRS score and the BDI score were significantly correlated with delayed recall on the RCFT ($r = -.533$, $p = .002$ and $r = -.498$, $p = .005$, resp.).

Impact of Therapy Response on Neuropsychological Improvement

To evaluate the impact of therapy response, the OCD sample was divided into two groups according to the Median of symptom improvement (43.4%). Demographic characteristics of the groups can be derived from Table 3.

At baseline, both major responders ($n = 15$) and minor responders ($n = 15$) showed significant impairment on seven measures assessing nonverbal fluency and memory and flexible, self-guided behavior at .01 level (immediate and delayed recall as well as strategy score of the Rey Figure, Weight-Sorting Test, Change of Reaction of the TAP, Five-Points-Test and Trail Making B). Additionally, minor responders differed significantly from controls on Trail Making A ($t(42) = 4.03$, $p < .001$) indicating impaired speed of information processing. After cognitive behavioural treatment, major responders

performed comparable to controls on all tests, whereas minor responders still showed deficits on nonverbal fluency ($t(42) = -3.34$, $p = .002$).

An effect of group × time interaction regarding response to treatment was found for both immediate and delayed recall on the Rey Figure ($F(1,28) = 7.75$, $p = .010$ and $F(1,28) = 8.04$, $p = .009$, resp.) (see Figure 1) with major responders improving to a significantly larger extent. There were no significant differences with respect to depressive symptoms between major responders and minor responders at any time of testing.

Besides, there was a correlation at .05-level between symptom change, as measured by the Y-BOCS, and cognitive improvement on both immediate ($r = .410$, $p = .027$) and delayed ($r = .449$, $p = .015$) recall condition of the RCFT.

Impact of Severity and Duration of Illness and Effects of Medication

There was no significant correlation between severity or length of illness and any of the neuropsychological parameters at baseline. At follow-up, length of illness was significantly correlated with the number of correct solutions on the ToL memory condition ($r = .494$, $p = .006$).

Medicated ($n = 7$) and unmedicated patients ($n = 23$) did not differ with regard to cognitive improvement on any parameter. In addition, at baseline as well as at follow-up, there were no differences between treatment groups on any clinical or cognitive parameter.

Discussion

The major finding of our study is that some of the cognitive functions improve in the course of cognitive behavioral treatment of OCD. There was a significant group x time interaction for measures of delayed nonverbal memory, organizational strategies, flexible, self-guided behavior and speed related set shifting with patients performing significantly ($p < .01$) worse than controls at baseline but not at follow-up. These improvements cannot be explained by practice effects alone, which were controlled by a large sample of healthy subjects tested twice within the same time interval. With respect to therapy response, after CBT, performance of major responders was comparable to that of controls on all cognitive measures. Minor responders improved to a significantly smaller extent on immediate and delayed recall of the Rey Figure compared with major responders and were still impaired on nonverbal fluency at follow-up.

Our results are in contrast to the findings of Nielen and den Boer (2003) suggesting persistent cognitive deficits in OCD patients after treatment. Patients in the latter study, however, were solely treated with pharmacological therapy. In the study of Kim et al. (2002), patients showed significant improvements on nonverbal memory and verbal fluency, but were still impaired at follow up. However, only 8 out of 39 patients received cognitive behavioral therapy. We propose that particularly systematic cognitive behavioral treatment enables OCD patients to think and to act in a more flexible way that helps them to develop more effective cognitive strategies. Hence, patients might benefit from a more adaptive way of thinking at follow-up testing although they were not directly instructed how to act on the neuropsychological tasks, of course. This hypothesis is supported by the fact that our patients mainly improved on tasks requiring flexible, productive thinking (organizational strategies, flexible, self-guided behavior). Interestingly, improvement in cognitive performance of patients being additionally treated with SSRI did not differ significantly from the one in patients treated with CBT alone. These results suggest

that CBT might be similarly effective as combination therapy regarding cognitive functioning. Sub-samples, however, were too small to draw further conclusions.

In view of the low association between neuropsychological and psychometric scores it is unlikely that neuropsychological dysfunction at baseline resulted from a lowered mood. In addition, unlike severity of OC symptoms and neuropsychological performance, symptoms of depression, which were only mild, were not markedly reduced at follow-up (see Table 1).

Regarding the predictive value of neuropsychological functioning, only speed of information processing (Trail Making A) discriminated between major responders and minor responders at baseline. We have to bear in mind that response to treatment was solely assessed by the Y-BOCS-score. Thus, it can not be excluded that a more comprehensive assessment of OC symptoms would yield some association between cognitive dysfunction at baseline and clinical improvement. However, the lack of a consistent pattern of cognitive dysfunction as a predictor for nonresponse contradicts the findings of Sieg et al. (1999), but is in line with the results of several other studies (Bolton et al., 2000, Moritz et al., 2005; Thienemann and Koran, 1995).

No marked impairment was found in patients regarding the number of correct solutions on the ToL. Previous results on planning ability in OCD have been contradictory (Nielen and Den Boer, 2003; Purcell et al., 1998; Schmidtke et al., 1998; van den Heuvel et al., 2005). As suggested by neuroimagung studies (Rowe, Owen, Johnstrude & Passingham, 2001, Unterrainer et al., 2004) performance on the ToL is mainly associated with dorsolateral-prefrontal activation, which seems to go along with decreased responsiveness of dorsal prefrontal-striatal circuits during planning in OCD patients (van den Heuvel et al., 2005).

Previous studies on effects of treatment, however, suggest that neural activity in OCD changes predominantly within the orbitofrontal-striatal circuit (Baxter et al., 1992; Schwartz et al., 1996). Based on the assumption that the observed state-dependency of neuropsychological performance in OCD is secondary to the metabolic changes described in the literature (Baxter et al., 1992; Nakatani et al., 2003; Schwartz et al., 1996; Saxena et al., 1999), one might hypothesize that cognitive functions corresponding to the orbitofrontal feedback-loop are particularly susceptible to CBT. In a study by Kang et al. (2003), for example, there were metabolic decreases in the orbitofrontal cortex, the hippocampus, the cerebellum and the right putamen after treatment. Interestingly, the metabolic changes were significantly correlated with improvement on the immediate- and delayed recall of the Rey Figure, a task where improvement was significant in our OCD sample, too. Poor performance on this test is suggested to be based on ineffective encoding strategies that are hypothesized to result from dysfunction of the frontal-subcortical circuits (Deckersbach 2000; Savage, 1999, 2000). Our patients indeed showed poor organizational strategies when copying the Figure. These were related to accuracy of recall and improved significantly after behavioural therapy. In particular, major responders showed significantly larger improvement on immediate and delayed recall of the Rey Figure compared to minor responders. In addition, recent studies using positron emission tomography (PET) suggest that the orbitofrontal cortex, together with its bi-directional connections to the medial temporal cortex, is a critical frontal region underlying memory formation (Frey and Petrides, 2002). Interestingly, in a PET study of Savage and colleagues (2001) blood flow in the orbitofrontal cortex during the first spontaneously encoding of 24 words was correlated with semantic clustering scores during immediate free recall. The authors suggest that the orbitofrontal cortex is an important region to support the mobilization of strategies during novel and ambiguous tasks.

Taken together, these data confirm our hypothesis that neuropsychological impairment before therapy is based on metabolic dysfunction of the orbitofrontal feedback-loop that may return to normal during the course of treatment.

The OAT, however, a task that is also considered to be sensitive for orbitofrontal dysfunction, did not show any significant differences between patients and controls in our study. In face of recent results, it seems questionable whether the OAT is a valid instrument for measuring cognitive impairment in OCD (Kuelz et al., 2004b). This issue, however, requires further investigation.

In conclusion, results of our study hint at cognitive improvement in OCD patients after CBT on tasks of nonverbal memory, organizational strategies, flexible, self guided behavior and set-shifting. Especially, our results suggest that successful CBT may mainly influence performance on cognitive tasks involving the orbitofrontal-striatal feedback loop and/or involving skills that are improved by cognitive treatment in OCD in general (e.g., cognitive flexibility).

However, there are also some limitations of our study. First, we cannot rule out that unspecific effects of hospitalization may have contributed to improvement of cognitive symptoms in our patients. An additional comparison group consisting of inpatients suffering from a different disorder could help in identifying characteristic patterns of cognitive improvement in OCD by CBT.

Secondly, from a statistical point of view, cognitive improvement in OCD patients can only be attributed to treatment in those measures, where a significant interaction effect was found. This was the case for some measures of nonverbal memory (delayed recall) and organizational strategies, flexible, self guided behavior and set-shifting, but not for tasks assessing speed of information processing, fluency and planning ability. Improvement of other test results may be confounded by practice effects. With regard to healthy controls, we cannot exclude that ceiling effects may have contributed to lack of change in that group. Thus, for future studies a careful selection of sensitive tasks seems to be necessary to focus on those cognitive functions that are particularly susceptible to treatment-induced changes.

An interesting avenue to explore would be the inclusion of an additional sample of untreated OCD patients tested twice within the same time span without undergoing behavioral treatment. Finally, neuroimaging studies should be of value in revealing neuronal correlates of the described cognitive dysfunctions before and after CBT.

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