Where emotion meets cognition
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Neuropsychological performance of OCD patients before and after treatment with fluoxetine: evidence for persistent cognitive deficits

Abstract

There is an ongoing debate about the nature of executive dysfunction that accompanies Obsessive-Compulsive Disorder (OCD). One reason for this may be that state-related factors, such as use of medication or comorbid symptoms, confound with task performance. This study tried to isolate trait from state dependent cognitive impairments by examining variability of cognition following treatment.

Nineteen OCD patients were tested on the Cambridge Neuropsychological Test Automated Battery (CANTAB) before and after treatment with fluoxetine. Their pattern of performance was compared to the one observed in healthy volunteers (n = 24). OCD patients displayed impairments in planning ability, spatial memory and motor speed that persisted after clinical improvement. With treatment, OCD performance diverged from that of controls on measures of focused attention and strategic ability. However, these effects were rather mild as they did not entail a significant deterioration of performance within the OCD sample. Our data suggest that cognitive impairments in OCD are not secondary to symptoms and therefore form a trait feature of the disorder. The nature of the deficits refers to a chronic dysfunction of the dorsolateral-striatal circuit. The minor effects of treatment on task performance is in line with recent evidence that serotonin mediates cognitive functions of orbitofrontal cortex to a greater extent than those associated with dorsolateral prefrontal regions.
Patients with Obsessive-Compulsive Disorder (OCD) suffer from recurrent, anxiety-provoking thoughts that are usually neutralized by performing ritualised, time-consuming behaviours (APA, 1994). Neuropsychological theories propose that behavioural problems of OCD follow from disruptive executive function, which is supported by neuro-imaging studies demonstrating abnormal activity within prefrontal regions (Baxter et al., 1988; Swedo et al., 1989; Saxena et al., 1998).

Unfortunately, studies investigating the nature of executive function in OCD have produced discordant results. For instance, impairments have been found in the domain of set shifting (Head et al., 1989; Veale et al., 1996), spatial working memory (Purcell et al., 1998ab), verbal fluency (Christensen et al., 1992; Smidtke et al., 1998) and focused attention (Martinot et al., 1990; Schmidtke et al., 1998) but these results were not replicated in other studies using the same cognitive measures. One possible explanation for this lack of convergence is that other factors, such as the use of antidepressants or the level of comorbid anxiety and depressive symptoms, have confounded with task performance. In order to gain insight in the specific neuropsychological dysfunctions of OCD, it seems important to separate them from state-dependent fluctuations in cognition.

One way to identify trait-related impairments is to study the variability of cognition with treatment. However, most studies on the relation between cognition and successful treatment in OCD were done in the context of response prediction. This means that neuropsychological performance was measured only at baseline in order to differentiate future responders from nonresponders. As far as we know, only two recent studies tested cognitive function with a repeated-measures design. Sanz et al. (2001) found (trend-like) evidence that pharmacological treatment enhanced the ability of OCD patients to discriminate relevant stimuli from distractors. In another study, OCD patients improved on set-shifting and verbal fluency tasks after cognitive-behavioural therapy (Bolton et al., 2000). However, it was difficult to determine the significance of these cognitive changes, as they may reflect improvement due to repeated task administration alone (Bolton et al., 2000).

The aim of the present study was to get insight in the stability of cognitive impairments in OCD. In order to estimate the size of practice effects on neuropsychological performance, a control group of healthy volunteers was tested twice as well. During the 12 weeks separating the assessments OCD patients were treated with the SSRI fluoxetine while there was no intervention for the normal
controls. Executive function was measured with tasks for planning, spatial working memory, attentional set shifting, and focused attention. In order to relate our results to the neuropsychological literature on OCD, we also added two visual memory tasks to the test battery.

**Method**

**Subjects**

The sample comprised of 21 patients with Obsessive-Compulsive Disorder diagnosed according to DSM-IV criteria (APA, 1994). Their age ranged between 19–52 years. All patients completed the Yale-Brown Obsessive Compulsive Scale (Y-BOCS, Goodman et al., 1989) to assess the severity of obsessive-compulsive symptoms. Comorbid depressive and anxiety symptoms were measured with the 17-item Hamilton Depression Rating Scale (HDRS) and the 14-item Hamilton Anxiety Rating Scale (HARS) (Hamilton, 1960). Exclusion criteria were the presence of major medical illness, head injury, alcohol or substance abuse. In addition, subjects with a major depressive disorder or having a HDRS score > 16 were excluded from the study. Clinical ratings were taken on the same day as the neuropsychological assessment. Three OCD patients had been treated with fluoxetine before, but in a daily dose that is considered to be ineffective for treating the disorder (i.e. 20 mg) (Tollefson et al., 1994). Of the 21 patients included, two dropped out from the study (one for unwanted side effects, one for unknown reasons) leaving the final number of patients that completed the study on 19. Statistical analyses were performed on a total of 19 OCD patients.

Twenty-four healthy adults (age range 18–59 years) participated as control subjects. They were recruited from advertisements and matched to the OCD group according to age and intelligence as estimated with the Raven Standard Progressive Matrices (Raven, 1960). None of the volunteers reported the presence of a medical or psychiatric diagnosis in the past. All subjects provided written informed consent after the study procedure had been explained to them.

**Study design**

The design of the study was a 12-week open trial. It is suggested that 12 weeks is sufficiently long enough to register clinically significant changes in OCD. All OCD patients had been medication-free at least 4 weeks prior to treatment. Patients
were treated with oral fluoxetine hydrochloride in a daily dose of 60 mg, which is the recommended quantity for the treatment of OCD (Tollefson et al., 1994). Controlled studies have repeatedly shown its efficacy in the treatment of OCD (Tollefson et al., 1994; Romano et al., 2001). Immediately after baseline neuropsychological testing, fluoxetine administration started from 20 mg in week 1 to 60 mg in week 6–12. Treatment compliance and physical health were checked at regular visits during the treatment period. In order to measure the ‘pure’ effect of treatment on cognitive variables, we requested patients to remain abstinent from other therapies during the period of treatment. Two patients reported the use of benzodiazepines during treatment. All other patients could accomplish to the requirement.

**Neuropsychological assessment**

At baseline, before entering the treatment phase, all subjects were administered a series of cognitive tasks, selected from cantab (Cambridge Neuropsychological Test Automated Battery). This battery is sensitive to cognitive changes due to pharmacological challenges (e.g. Elliott et al., 1997; Mehta et al., 2001). cantab has been able to detect cognitive impairments in OCD before (Veale et al., 1996; Purcell et al., 1998; Barnett et al., 1999). Tests from cantab have been extensively described elsewhere (Robbins et al., 1994) and their administration was according to standard protocols. Subjects were seated approximately 0.5 m from a high-resolution colour monitor with a touch-sensitive screen (Nijkerk Display Systems, Amsterdam, the Netherlands) and were instructed to respond to stimuli by touching the screen. None of the OCD patients reported distress related to this response method. Description of the six cantab tasks follows below. The Stroop colour word task was added as a measure of focused attention.

**Tower of London planning task** – TOL (Sahakian et al., 1988)

This test was originally derived from the ‘Tower of London’ task and measures spatial planning and behavioural inhibition. Planning accuracy was measured by the number of trials solved in the minimum number of moves and the total number of excess moves. The program also recorded the selection (initial thinking) and execution (subsequent thinking) latencies during the problems to provide estimates of cognitive speed. For each problem, a control condition was used to provide baseline measures of motor initiation and execution times that were independent from thinking times.
**Spatial working memory task** – *SWMT* (Owen et al., 1990)
This self-ordered searching task requires subjects to locate tokens that are hidden in boxes. Accuracy of spatial working memory is measured by the number of between-search errors (returning to an ‘empty’ box in which already a token has been found). In addition, a strategy score is calculated for the most difficult six- and eight-move problems. This score reflects how often a searching sequence was initiated from the same box during the trial, thus, how efficient the searching is performed.

**Attentional set shifting task** – *ID/ED* (Downes et al., 1989)
This task assesses the ability to maintain attention to different examples within a reinforced stimulus dimension (*ID* shift) and then shift attention to the previously irrelevant stimulus dimension (*ED* shift). Task performance was measured as total trials needed to reach criterion at the *ID* and *ED* stage.

**Stroop Colour Word task** (Stroop, 1935)
This test measures the ability to perform a task in the face of a powerful distracting stimulus. The test involves the reading aloud of three subsequently presented cards. In the first task subjects read colour names printed in black ink. The second task requires the reading of the ink colour of coloured rectangles. In the third task the colour names are printed in a non-matching colour; for example, ‘red’ is printed in green ink. Subjects are required to name the colour of the ink. The interference score reflects the individual’s vulnerability to interference by the colour name of the word.

**Pattern / Spatial Recognition** (Sahakian et al., 1988)
Pattern recognition tests the ability to recognize a previously presented abstract coloured pattern from two stimuli. For spatial recognition, the task is to recognize the spatial location of white boxes on the screen. Performance on both tasks was defined as the percentage of correct responses and mean latency of total correct responses.
Statistical Analysis

Data were analysed using the Statistical Package for the Social Sciences (SPSS) version 9.0 (Nie et al., 1970). Response latencies received a log transformation in order to reduce skewness. The Stroop interference score was computed using the following formula:

\[
\frac{(\text{time card 3})}{\left(\frac{(\text{time card 1} + \text{time card 2})}{2}\right)} \times 100\%
\]

(Houx et al., 1993). Performance on pattern and spatial memory, Stroop interference score, spatial working memory accuracy and strategy score, attentional set shifting ID and ED trials, and TOL accuracy were analysed with repeated measures ANOVA. Measures of cognitive and motor speed on the Tower of London were compared between groups with a multivariate ANOVA design using level of difficulty as within-subject variable. In case of significant interaction effects, separate t-tests were carried out to examine the nature of the interaction effects. Pearson’s product moment correlations were computed between clinical symptoms and neuropsychological performance.

Results

Clinical effects of treatment in OCD

A treatment effect was found on all clinical outcome measures. First, OCD patients showed an average reduction of 56% in total Y-BOCS scores. When we defined clinical recovery as a reduction of > 40% in total Y-BOCS score, we found that 63% of the patients could be classified as responding to fluoxetine, which is in line with the literature. Significant reductions were also observed in depressive (46.6% reduction of total HDRS) and anxiety symptoms (57.9% reduction of total HARS) of the OCD group (see table 1).

Pre- and post treatment neuropsychological performance

Table 2 summarizes mean performance on baseline and follow-up of OCD patients and healthy volunteers.
Neuropsychology and treatment effects

Tower of London

On both sessions, OCD patients produced significantly fewer minimum move solutions ($F_{1,41} = 4.61, p < 0.05$) than controls. In addition, patients needed more moves in excess of the minimum to solve a problem ($F_{1,41} = 9.98, p < 0.01$). However, there were no significant interactions between group and session. Using the ‘yoked control’ condition, we could analyse thinking time and motor speed separately. With respect to thinking times, exploratory analysis revealed that two OCD patients displayed extremely long (> 2×SD) initial thinking times on the most easy levels of the task (level 2 & 3). When we compared planning speed for problems on level 4 & 5, there was a significant effect of group only for subsequent thinking times ($F_{1,41} = 6.77, p < 0.05$), which was due to OCD patients needing more time to complete a problem after the first move had been made. Finally, OCD patients needed more time than controls for the initiation ($F_{1,39} = 10.0, p < 0.01$) and completion ($F_{1,39} = 10.6, p < 0.01$) of a sequence of single moves.

Table 1 — Demographic and clinical characteristics of OCD patients and healthy volunteers. The severity of OCD, depressive and anxiety symptoms is given before (‘pre’) and after (‘post’) treatment. Y-BOCS = Yale Brown Obsessive Compulsive Scale; HDRS = Hamilton Depression Rating Scale; HARS = Hamilton Anxiety Rating Scale.

<table>
<thead>
<tr>
<th></th>
<th>OCD [n = 19, mean (SD)]</th>
<th>Controls [n = 24, mean (SD)]</th>
<th>F</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>37.2 (2.4)</td>
<td>31.3 (2.1)</td>
<td>3.51</td>
<td>0.07</td>
</tr>
<tr>
<td>Male : female</td>
<td>8 : 11</td>
<td>7 : 17</td>
<td></td>
<td></td>
</tr>
<tr>
<td>IQ</td>
<td>114.1 (2.2)</td>
<td>117.3 (2.7)</td>
<td>0.77</td>
<td>0.38</td>
</tr>
<tr>
<td>Length of illness (years)</td>
<td>16.5 (2.3)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Y-BOCS obsessions pre – post</td>
<td>11.4 (5.1) – 6.0 (4.1)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Y-BOCS compulsions pre – post</td>
<td>12.7 (3.7) – 7.6 (4.5)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Y-BOCS total pre – post</td>
<td>24.1 (5.8) – 13.6 (7.4)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HDRS pre – post</td>
<td>10.1 (3.27) – 4.6 (3.0)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HARS pre – post</td>
<td>13.5 (4.6) – 7.8 (4.0)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Previous medication (no. of subjects)

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>9</td>
</tr>
<tr>
<td>Fluoxetine (dd. 20 mg)</td>
<td>3</td>
</tr>
<tr>
<td>Other antidepressants</td>
<td>5</td>
</tr>
<tr>
<td>Benzodiazepines</td>
<td>2</td>
</tr>
</tbody>
</table>

Neuropsychology and treatment effects | 37
Table 2 — Group means of baseline and follow-up neuropsychological assessment for OCD patients and healthy volunteers.

<table>
<thead>
<tr>
<th>Measure</th>
<th>OCD (n = 19)</th>
<th>Controls (n = 24)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>baseline</td>
<td>follow-up</td>
</tr>
<tr>
<td></td>
<td>mean (SD)</td>
<td>mean (SD)</td>
</tr>
<tr>
<td><strong>Tower of London</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total number of perfect solutions</td>
<td>8.68 (1.56)</td>
<td>9.00 (1.82)</td>
</tr>
<tr>
<td>Total number of excess moves</td>
<td>10.68 (5.31)</td>
<td>11.52 (8.30)</td>
</tr>
<tr>
<td>Initial thinking time, log</td>
<td>4.86 (1.18)</td>
<td>4.71 (1.14)</td>
</tr>
<tr>
<td>Subsequent thinking time, log</td>
<td>4.37 (0.40)</td>
<td>4.21 (0.49)</td>
</tr>
<tr>
<td>Initial movement time, log</td>
<td>3.76 (0.19)</td>
<td>3.77 (0.11)</td>
</tr>
<tr>
<td>Subsequent movement time, log</td>
<td>3.92 (0.09)</td>
<td>3.95 (0.07)</td>
</tr>
<tr>
<td><strong>Spatial Working Memory</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total number of between-search errors</td>
<td>23.63 (20.57)</td>
<td>25.00 (18.46)</td>
</tr>
<tr>
<td><strong>Attentional set shifting</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>EDS trial score</td>
<td>6.78 (1.87)</td>
<td>7.31 (1.66)</td>
</tr>
<tr>
<td>EDS trial score</td>
<td>12.25 (4.90)</td>
<td>11.75 (9.74)</td>
</tr>
<tr>
<td><strong>Stroop</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Time card 1, seconds</td>
<td>43.55 (9.05)</td>
<td>39.22 (5.19)</td>
</tr>
<tr>
<td>Time card 2, seconds</td>
<td>56.11 (14.42)</td>
<td>51.67 (7.62)</td>
</tr>
<tr>
<td>Time card 3, seconds</td>
<td>85.51 (22.50)</td>
<td>81.72 (16.17)</td>
</tr>
<tr>
<td><strong>Spatial recognition</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total % correct</td>
<td>76.58 (10.42)</td>
<td>69.47 (15.97)</td>
</tr>
<tr>
<td>Latency, log</td>
<td>3.39 (0.15)</td>
<td>3.35 (0.14)</td>
</tr>
<tr>
<td><strong>Pattern recognition</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total % correct</td>
<td>83.33 (15.09)</td>
<td>88.29 (9.30)</td>
</tr>
<tr>
<td>Latency, log</td>
<td>3.40 (0.11)</td>
<td>3.32 (0.09)</td>
</tr>
</tbody>
</table>

*) One OCD patient did not complete the Stroop task on follow-up.
**Spatial Working Memory**

With respect to strategy score, we found a significant group \times session interaction (F\(_{1,41} = 4.81, p < 0.05\)) but no significant effect of group (F\(_{1,41} = 0.17, ns\)). Apparently, OCD patients and controls displayed a different strategic ability over time (see figure 1). However, post-hoc t-tests demonstrated that the interaction effect was not due to a significant deterioration in OCD patients (t\(_{18} = 1.87, ns\)) or to significant practice effects of controls (t\(_{23} = 0.84, ns\)). This suggests that this effect emerged because of concurrent changes in both groups. With regard to the number of between-search errors for the most difficult six and eight box problems, there was a trend towards a group \times session interaction (F\(_{1,41} = 3.81, p = 0.058\)) but no main effect of group (F\(_{1,41} = 1.11, ns\)).

**Attentional set shifting task**

OCD patients and controls needed an equal number of trials to complete the task (F\(_{1,40} = 0.073, ns\)). With respect to the critical shifting stages of the task, there were no significant interaction effects for either the ID (F\(_{1,39} = 2.74, ns\)) or the ED stage (F\(_{1,37} = 0.023, ns\)). We also found no significant group effects for the ID (F\(_{1,39} = 2.55, ns\)) and ED stage (F\(_{1,27} = 3.55, ns\)).

![Figure 1](image-url)

**Figure 1** — Ability of OCD patients and healthy controls to employ a systematic searching strategy on the Spatial Working Memory Test. Higher numbers correspond to a less efficient strategy. Session 1: before treatment. Session 2: after treatment. Bars represent standard errors of the mean (S.E.M.).
**Stroop Colour Word test**

There were no group or interaction effects for reading time on the individual cards. With respect to the measure of interference, there was a significant group × session interaction ($F_{1,40} = 4.97, p < 0.05$) (see figure 2). Again, post-hoc comparisons did not reveal a significant effect of session in either the OCD ($t_{17} = 1.41, ns$) or the control group ($t_{23} = 1.79, ns$). Furthermore, there were no significant between-group differences on either the first or the second testing session.

**Spatial Recognition**

With respect to accuracy, OCD patients recognized fewer spatial locations than controls ($F_{1,41} = 5.06, p < 0.05$). We also found a significant effect of session ($F_{1,41} = 6.04, p < 0.05$) indicating that both groups performed worse on follow-up. There was no significant group × session interaction ($F_{1,41} = 0.79, ns$).

**Pattern Recognition**

Accuracy data revealed no significant interaction or main effects. A significant ANOVA was found for response latency ($F_{1,41} = 16.24, p < 0.001$), showing that OCD patients overall needed more time than controls to recognize the correct pattern.

![Figure 2](image-url)

**Figure 2** — Level of interference of OCD patients and healthy controls on the Stroop Colour Word task. Session 1: before treatment. Session 2: after treatment. Bars represent standard errors of the mean (S.E.M.).
Correlation between clinical characteristics and task performance

Before treatment, severity of depressive symptoms was strongly related to colour naming time on card 2 and 3 of the Stroop test \((r = 0.598, p < 0.01\) and \(r = 0.607, p < 0.01\) respectively) but not to level of interference \((r = 0.222, ns)\). After treatment, only latency on card 3 was related to severity of depressive symptoms \((r = 0.625, p < 0.01)\). There were no significant correlations between neuropsychological performance over time and individual levels of clinical improvement.

Discussion

The main goal of this study was to examine the persistence of cognitive deficits of patients with OCD. To this end, we examined neuropsychological function of OCD patients before and after fluoxetine treatment with tests from the CANTAB battery. This battery has a recognized sensitivity for pharmacologically induced cognitive effects in healthy subjects (e.g. Elliott et al., 1997; Mehta et al., 1999), allowing us to differentiate state from trait dependent cognitive deficits.

Persistent cognitive deficits

Our results reveal that OCD performance on attentional shifting, SWMT accuracy and pattern recognition was normal and unchanging over time. However, OCD patients displayed clear and persistent impairments on the TOL planning task, in that they not only produced fewer perfect solutions but also needed more moves to solve a particular problem. Furthermore, after correction for their significantly slowed motor speed, OCD patients still showed a significant prolongation of the time taken to complete the most difficult problems, while initial thinking times were normal. A similar pattern of TOL performance has been reported in patients with frontal lobe damage (Owen et al., 1990), in schizophrenia (Pantelis et al., 1997) and recently in subjects with antisocial personality disorders (Dolan & Park, 2002). This pattern would reflect a tendency to initiate the solution before it has been fully planned (Owen et al., 1990), with the result that patients need extra moves and time to complete the problem. At first sight, this inefficient planning behaviour contrasts with earlier reports of normal TOL performance in OCD (Veale et al., 1996; Purcell et al., 1998ab). However, the latency data of the Veale et al., study show that their OCD patients needed more time to switch to an alternative strategy after having made a mistake (Veale et al., 1996) suggest-
ing that these patients also had some difficulties in selecting the most adequate solution to a problem. With respect to visual memory, OCD patients consistently recognized fewer spatial locations than controls, while memory for objects was intact. This supports the notion that the previously observed visual memory impairment in OCD (Zielinski et al., 1991; Boone et al., 1991; Christensen et al., 1992; Savage et al., 1999) is not general but limits itself to the spatial domain (Purcell et al., 1998b).

**State-related cognitive functions**

A second aim of this study was to explore which cognitive functions varied with the clinical status of OCD patients. Our results indicate that with treatment, performance of OCD patients moved away from that of normal controls on measures of strategic ability and focused attention. This deviant pattern of performance was (i) independent of the level of clinical improvement and (ii) present in both OCD responders and nonresponders, suggesting that these effects occurred in a cognitive system that does not directly mediate obsessive-compulsive symptoms. However, we should emphasize that although these effects were significant, they were not very strong. For instance, post-hoc testing revealed that OCD performance on the second session was still within the normal range, suggesting that treatment did not induce real cognitive decrements. Moreover, we found that the treatment effect did not consist of a significant change within the OCD group itself, but was instead composed of a joint effect in both patients and volunteers. Therefore, the abnormal pattern seen in the OCD group seems to reflect only a slight effect of treatment on cognition. This makes it very unlikely that state dependent fluctuations in cognition account for the conflicting results of previous studies on executive function in OCD.

**Implications of our findings for the neuropsychology of OCD**

Our OCD patients displayed impaired planning and spatial memory, while their set shifting ability, spatial working memory, focused attention and object memory were intact. Most importantly, we found that their deficits were not secondary to symptoms, but instead reflected chronic cognitive impairments that persisted after clinical recovery. These findings agree with recent work reporting similar neuropsychological performance of medicated and unmedicated OCD patients (Purcell et al., 1998b; Mataix-Cols et al., 2002).
The pattern of performance in our OCD sample, however, contrasts to some degree with previous CANTAB studies (Purcell et al., 1998ab; Barnett et al., 1999). One possible explanation for this is that some OCD patients are able to compensate sufficiently for their weak visuospatial skills by working very efficiently. However, if they adopt a somewhat less strategic approach (for instance, by taking not enough time to think about a problem on the TOL as was shown in this study), their level of performance will deteriorate rapidly, probably even falling outside the normal range. Although this explanation is tentative and awaits further testing, it could make clear why OCD patients perform so unpredictable on executive tasks even when these tasks engage the same neurocognitive (DLPFC) network (Owen et al., 1996).

We also aimed to get insight in the state-related investigation the effect of fluoxetine treatment on cognition. Our data show that treatment, despite its clinical efficacy, did not alter cognitive function of OCD patients to any significant degree. This suggests that fluoxetine produced its clinical effects by acting on a neural system whose cognitive functions were not measured directly in our study. The most likely candidate for this system seems to be the orbitofrontal circuit, as neural activity of this circuit specifically changes with successful treatment (Baxter et al., 1992; Saxena et al., 1999). In addition, there is growing evidence that cognitive functions of the orbitofrontal cortex (OFC) play a role in obsessive-compulsive symptomatology (Barnett et al., 1999; Hermesh et al., 1999; Cavedini et al., 2002; Nielen et al., 2002). Finally, studies on prefrontal function in healthy volunteers show that only cognitive functions associated with the OFC such as reversal learning (Rolls et al., 1994; O’Doherty et al., 2001) and decision making (Bechara et al., 1994; Rogers et al., 1999c) are selectively affected by manipulations of the central serotonergic system (Rogers et al., 1999ab). This explains the minor treatment effects in our study, as our executive tasks are all associated with prefrontal regions outside the orbitofrontal cortex. These data also suggest that examining the effects of serotonergic medication on tasks subserved by the OFC will contribute importantly to our understanding of the relation between cognition and OCD symptoms.

Study limitations
One limitation of this study is that OCD patients were treated while normal controls were not. Our analyses were based on the presumption that practice effects of OCD patients would not differ from those observed in controls, and that any deviation from normal performance would be indicative of a treatment-related effect. However, due to our design we do not have complete certainty about the
nature of the observed effects. Therefore, future work will greatly benefit from the use of a double-blind placebo-controlled design, which not only allows a more precise interpretation of the observed treatment effects but also a validation of our finding of treatment-persistent cognitive deficits in OCD.

Conclusions

OCD patients showed enduring cognitive impairments in the domain of spatial memory, planning, and motor speed. These impairments are reminiscent of a chronic dysfunction of a neural network involving dorsolateral prefrontal cortex and striatum. The deviant pattern of performance on tasks for focused attention and strategic ability seems to reflect only minor effects of treatment on cognition. This may be explained by the fact that our tasks were not specifically suited to assess cognitive functions of the orbitofrontal circuit.

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