Neuropsychological Deficits in Obsessive-compulsive Disorder

A Comparison With Unipolar Depression, Panic Disorder, and Normal Controls

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Background: The neuropsychological dysfunction associated with obsessive-compulsive disorder (OCD) has similarities to the deficits reported in other affective or anxiety disorders. We directly compared cognitive function in patients with OCD with that in matched patients with unipolar depression and panic disorder and healthy control subjects to establish the specific nature of neuropsychological deficits in OCD.

Methods: Thirty patients with OCD, 30 patients with panic disorder, 20 patients with unipolar depression, and 30 controls completed a computerized neuropsychological battery that assessed the accuracy and latency of executive, visual memory, and attentional functions.

Results: The groups did not differ according to age, years of education, or estimated IQ. However, we found group differences in cognitive performance. The patients with OCD were impaired on measures of spatial working memory, spatial recognition, and motor initiation and execution. In contrast, performance of these tasks by patients with panic disorder or depression did not differ from that of controls. There were no group differences for performance on the measures of planning, cognitive speed, pattern recognition, and delayed matching to sample, although patients with depression were impaired for attentional set shifting.

Conclusions: Neuropsychological deficits were observed in patients with OCD that were not observed in matched patients with panic disorder or unipolar depression. As such, the cognitive dysfunction in OCD appears to be related to the specific illness processes associated with the disorder.

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SUBJECTS AND METHODS

SUBJECTS

Patients with OCD, panic disorder, and unipolar depression were recruited consecutively to the Depression and Anxiety Research and Treatment Clinic of the University of Melbourne, Royal Melbourne Hospital, Parkville, Victoria. Patients aged 18 to 65 years who met the criteria of the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV)42 for 1 of the relevant diagnoses underwent screening for inclusion. Patients who presented with a comorbid Axis 1 diagnosis, a neurological disorder or head injury, a serious medical condition, or a history of alcohol or other substance abuse were excluded. Of 45 patients meeting the criteria for OCD, 15 were excluded for comorbid major depression (n=5), comorbid generalized anxiety disorder (n=1), alcohol abuse (n=1), stroke (n=1), withdrawal before cognitive testing (n=1), and refusal to participate (n=6). Of the 43 patients meeting the criteria for panic disorder, 13 were excluded for comorbid medical illnesses (n=2), comorbid major depression (n=5), specific phobias (n=2), and refusal to participate (n=4). Of 36 patients meeting the criteria for unipolar depression, 16 were excluded for comorbid anxiety disorder (n=5), comorbid eating disorder (n=1), bipolar disorder (n=2), abuse of drugs other than alcohol (n=2), history of electroconvulsive therapy (n=4), and refusal to participate (n=2). The presence of comorbid depression or anxiety symptoms in each group did not constitute exclusion criteria. These symptoms were assessed using the 24-item Hamilton Depression Rating Scale (HAM-D) and 17-item Hamilton Anxiety Rating Scale (HARS). The Anxiety Disorders Interview Schedule for DSM-IV (ADIS-IV)43 was used to confirm diagnosis and to assess the presence of comorbid Axis I disorders. Each subject completed the Yale Brown Obsessive Compulsive Scale (YBOCS)44 to assess the presence and severity of obsessions and compulsions. Twenty-three patients with OCD were receiving medication at the time of testing, as were 19 patients with panic disorder and 12 patients with depression. Table 1 provides a summary of the subjects' demographic and clinical characteristics. Controls were recruited from advertisements and matched to the patient groups according to sex, age, handedness,45 education, and premorbid intellectual functioning as assessed by the National Adult Reading Test46 (Table 1). Controls underwent screening using the ADIS-IV to exclude any history of psychiatric illness, significant family history of mental illness, or history of alcohol or other substance abuse and were administered the HAM-D, HARS, and YBOCS. Each patient and control provided written informed consent to participate in the study, which was approved by the Royal Melbourne Hospital Ethics Committee.

PROCEDURE AND TASKS

The interview and neuropsychological assessments were completed on separate days. The cognitive tasks were selected from the Cambridge Neuropsychological Test Automated Battery (CANTAB).33,34 Seven subtests were presented in a random order on a high-resolution color monitor with a touch-sensitive screen (AccuTouch touchscreen; Redflex Touchscreens Pty Ltd, Melbourne, Victoria). Subjects were seated 0.5 m from the monitor and were instructed to respond to stimuli in each task by touching the screen. None of the patients with OCD reported distress related to the response method. The testing session lasted 70 to 90 minutes, with the duration of each task approximately 10 minutes. The tasks were administered according to standard protocols.36,37,41 Descriptions of the tasks follow.

Executive Function Tasks

Spatial Span. This computerized version of the Corsi Block Tapping Task47 assessed the subject's spatial short-term memory capacity. The spatial span was the highest level (minimum, 2; maximum, 9 boxes) at which the subject successfully remembered at least 1 sequence of stimuli (Figure 1, A).

Spatial Working Memory. This self-ordered task required subjects to locate tokens that were hidden in boxes. The accuracy of working memory was measured by the number of between-search errors committed (ie, returning to search a box in which a token had already been found during a previous searching sequence). A strategy score was calculated to reflect how often a searching sequence was initiated from the same box during the trial, indicating the ability to adopt a systematic searching approach (Figure 1, B).

Before likely neural substrates underlying the functional deficits of OCD can be postulated on the basis of neuropsychological performance, an examination of the specificity of cognitive impairment to OCD is warranted. Therefore, the aim of our study was to compare neuropsychological performance in patients with OCD directly with that of patients with unipolar depression or panic disorder and a group of healthy control subjects. To measure neuropsychological performance, we used a computerized test battery33 to assess the accuracy and latency of executive, visual memory, and attentional functions. This battery has been validated in the assessment of cognition in healthy subjects34 and patients with psychiatric disorders,26,27,35 focal neocortical lesions,36-38 and neurodegenerative diseases that preferentially involve subcortical brain areas.39-41 For each task, the group mean performance and statistical comparisons are summarized in Table 2. Analysis indicated that the groups differed by length of illness (Table 1). However, within each patient group, no correlations between length of illness and clinical characteristics (ie, illness severity) or neuropsychological performance were observed. Therefore, length of illness was not entered as a covariate in the planned group comparisons.

EXECUTIVE FUNCTION TASKS

For between-search errors on the spatial working memory task, there were significant main effects of group (Table 2) and task difficulty (F[4, 103] = 63.41; P<.001), but no
Tower of London Planning Task. This test required subjects to rearrange a set of balls in a specified minimum number of moves that increased in difficulty. The accuracy of planning was measured by the number of trials (of 12) completed within the minimum number of moves and the total number of moves in excess of the minimum (Figure 1, C). The program recorded initial and subsequent thinking latencies during these trials to provide estimates of cognitive speed. For each planning trial, a yoked control condition was employed. During these “following” trials, subjects were instructed to execute a sequence of single moves as quickly as possible (Figure 1, D). The following trials acted as a control condition to the test trials, as they were exact replications of the subject’s earlier planning moves. Initial and subsequent movement latencies in these following trials provided estimates of motor speed.

Visual Memory Tasks

Delayed Matching to Sample (DMTS). This task assessed the subject’s ability to remember a previously presented colored pattern target. Each target was presented with 3 similar distractor stimuli, after delays of 0, 4, or 12 seconds. Performance was defined as the percentage of correct responses for each delay level (Figure 2, A).

Pattern Recognition. This task measured the subject’s ability to recognize a previously presented abstract colored pattern from 2 stimuli (1 target and 1 distractor). Two blocks of 12 stimuli were presented. Performance was defined as the percentage of correct responses and the mean latency of total correct responses (Figure 2, B).

Spatial Recognition. This task assessed the subject’s ability to recognize the spatial location of white boxes previously presented at different positions on the screen. Two locations were shown in each trial (1 target and 1 distractor), and 4 blocks of 3 trials were given. Performance was defined as the percentage of correct responses and the mean latency of total correct responses (Figure 2, C).

Attentional Set-Shifting Task

Intradimensional-Extradimensional (ID-ED) Set Shift. This task assessed the subject’s ability to maintain attention to different examples within a reinforced stimulus dimension and then to shift attention to a previously irrelevant stimulus dimension. The task involved 9 stages, with subjects proceeding to the next stage only when a criterion of 6 consecutive correct responses had been attained. Performance was defined as the percentage of subjects successfully completing each stage of the task, the number of trials to reach the criterion for each stage, and the mean latency of correct responses for each stage (Figure 2, D).

STATISTICAL ANALYSIS

Analyses were conducted using SPSS (Version 7.5; SPSS Inc, Cary, NC). Performance on the spatial working memory and DMTS tasks and the Tower of London measures of cognitive and motor speed were compared between groups using a group-by-task difficulty repeated-measures analysis of variance (ANOVA) within a multivariate ANOVA design. Performance on the spatial span task, spatial working memory strategy measure, spatial and pattern recognition tasks, ID-ED trials to criterion, and the Tower of London accuracy measures were compared between groups using 1-way ANOVA. Significant group main effects were investigated using the Newman-Keuls test. The number of subjects succeeding at each level of the ID-ED task were compared between groups using the likelihood ratio method, with the statistic being distributed as $\chi^2$. Response latencies for the Tower of London measures of cognitive and motor speed, the ID-ED task, and the spatial and pattern recognition tasks were recorded as centiseconds and transformed into logarithms (base 10) to reduce skewness in the distribution.30,31 The Pearson product moment and Spearman correlation coefficients were calculated to examine the relationship between the patients’ clinical characteristics and the measures of impaired cognitive function. Previous research has found that performance on the CANTAB tests is highly correlated within the specific domains (executive, memory, and attention).32,33,34,35,36,37 and, as such, the Bonferroni correction was considered too conservative. Therefore, we adjusted type I error rate according to the number of domains compared (demographic, clinical, and the 3 cognitive domains). Subsequently, for the planned group comparisons, the error rate required to demonstrate significance was set at .01 (.05/5 domains). For post hoc correlational analyses examining the relationship between patient characteristics and impaired cognitive performance, the error rate was reduced to .001.

VISUAL MEMORY TASKS

Accuracy on the spatial recognition task differed between groups, although performance on the pattern recognition or the DMTS tasks did not (Table 2).

ATTENTIONAL SET-SHIFTING TASK

Analysis of the percentage of subjects reaching the criterion at each stage indicated that 25 of 30 controls (83%) completed all 9 stages successfully, compared with 21 of 30 patients with panic disorder (70%), 18 of 30 patients with OCD (60%), and 10 of 20 patients with
Table 1. Subject Demographic and Clinical Characteristics*

<table>
<thead>
<tr>
<th>Variable</th>
<th>With OCD (n = 30)</th>
<th>With Panic Disorder (n = 30)</th>
<th>With Depression (n = 20)</th>
<th>Controls (n = 30)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Demographic characteristics</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. of subjects, female: male</td>
<td>20:10</td>
<td>24:6</td>
<td>12:8</td>
<td>18:12</td>
<td>.32</td>
</tr>
<tr>
<td>Age, y</td>
<td>40.6 (13.6)</td>
<td>38.9 (9.1)</td>
<td>37.5 (8.5)</td>
<td>40.8 (12.9)</td>
<td>.72</td>
</tr>
<tr>
<td>Handedness, No. of right:left</td>
<td>26:4</td>
<td>28:2</td>
<td>19:1</td>
<td>27:3</td>
<td>.73</td>
</tr>
<tr>
<td>Education, y</td>
<td>12.6 (2.3)</td>
<td>12.1 (1.8)</td>
<td>13.5 (1.6)</td>
<td>12.9 (1.9)</td>
<td>.10</td>
</tr>
<tr>
<td>Estimated verbal IQ</td>
<td>105.5 (9.0)</td>
<td>105.1 (6.0)</td>
<td>107.7 (8.2)</td>
<td>109.1 (7.3)</td>
<td>.17</td>
</tr>
<tr>
<td>Clinical characteristics</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Length of illness, y</td>
<td>20.5 (12.9)</td>
<td>10.5 (9.4)</td>
<td>6.4 (6.6)</td>
<td>0.0</td>
<td>&lt;.001†</td>
</tr>
<tr>
<td>Receiving medication, No. of yes:no‡</td>
<td>23:7</td>
<td>19:11</td>
<td>12.6</td>
<td>0.0</td>
<td>.39</td>
</tr>
<tr>
<td>YBOCS total score</td>
<td>24.1 (8.1)</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td></td>
</tr>
<tr>
<td>YBOCS obsessions score</td>
<td>12.6 (4.3)</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td></td>
</tr>
<tr>
<td>YBOCS compulsions score</td>
<td>12.5 (6.2)</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td></td>
</tr>
<tr>
<td>HAM-D score§</td>
<td>10.5 (5.4)</td>
<td>11.1 (5.0)</td>
<td>22.6 (5.8)</td>
<td>1.8 (2.0)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>HARS score</td>
<td>13.3 (8.3)</td>
<td>20.6 (6.8)</td>
<td>15.1 (4.4)</td>
<td>1.2 (1.6)</td>
<td>&lt;.001¶</td>
</tr>
</tbody>
</table>

*Data are given as mean (SD), unless otherwise indicated. OCD indicates obsessive-compulsive disorder; YBOCS, Yale Brown Obsessive Compulsive Scale; HAM-D, 24-item Hamilton Depression Rating Scale; HARS, 17-item Hamilton Anxiety Rating Scale; and ellipses, not applicable.
†OCD > panic > depression.
‡Patients had been withdrawn from medication for at least 6 weeks before undergoing testing.
§HAM-D item 21 (Obsessional and Compulsive Features) was not included in the scores of patients with OCD.
||Depression>panic, OCD, controls.
¶Panic>depression, OCD, controls.

Figure 1. Displays of screens for each executive function task. A, Spatial span task (subjects are required to remember and reproduce the sequence in which the boxes changed color); B, spatial working memory task (subjects are required to search boxes to locate blue tokens without returning to a box that has previously yielded a token); C, Tower of London copying move (subjects are instructed to rearrange their balls in the lower half of the screen, so that they match the position of the balls in the top half of the screen in the specified minimum number of moves); and D, Tower of London following move (subjects are required to move the position of a single ball, 1 position at a time, in the bottom half of the screen, so that it matches the position of the ball in the top half of the screen).
depression (50%) ($\chi^2=6.32; df=3; P=.01$), patients with depression vs controls) (Figure 5). Group performance at each stage was then compared noncumulatively; that is, only those subjects who actually attempted each stage were included in the analysis. Percentage of subjects passing at the ID shift (IDS) stage ($\chi^2=3.31; df=3; P=.28$) or the ED shift (EDS) stage ($\chi^2=4.62; df=3; P=.24$) did not differ between groups. The mean number of noncumulative trials required to reach the criterion at each stage of the task was also examined (Figure 5, B). The number of trials required at the IDS stage differed between groups, although there were no differences at the EDS stage of the task (Table 2).

CORRELATIONS BETWEEN COGNITIVE IMPAIRMENT AND PATIENT CHARACTERISTICS

Correlations were performed to examine the relationship between impaired cognitive performance and the demographic and clinical characteristics of the patients with OCD and depression. For the group with OCD, there were no correlations between impaired function and patient age, education, estimated IQ, length of illness, or ratings on the HAM-D and HARS. However, total scores on the YBOCS correlated negatively with the subsequent movement time ($r=-0.59; P<.001$) of the patients with OCD, indicating that increased OCD symptom severity was associated with faster motor execution. For the group with depression, there was no relationship between impaired attentional set shifting and patient age, education, IQ, duration of illness, or ratings on the HAM-D and HARS. The ANOVA demonstrated that, irrespective of medication status, patients with OCD or depression did not differ by cognitive performance (data not shown).

COMMENT

Our study demonstrated selective cognitive deficits in patients with OCD that were not observed in matched controls or in patients with unipolar depression or panic disorder. The patients with OCD demonstrated impaired spatial working memory, speed of motor initiation and execution, and spatial recognition. These deficits did not correlate with the demographic or clinical characteristics. As such, the impairments in neuropsychological function observed in the group with OCD appeared to relate specifically to the illness processes associated with the disorder.

Our results also demonstrated that patients with OCD do not exhibit generalized cognitive dysfunction.
Although selective deficits in executive and visual memory processes and response slowing were observed, other functions within each cognitive domain were not compromised. For example, the patients showed a normal ability to organize and execute a series of goal-directed moves on the planning task. However, they were significantly impaired in the organization and execution of a sequence of selections on the spatial working memory task. An important difference between these 2 executive function measures is whether external validation of ongoing performance is provided. On the planning task, subjects could monitor their performance, as the goal arrangement remained on the screen throughout each trial. In contrast, ongoing performance on the working memory task had to be monitored internally, as no information was provided concerning the accuracy of selections. The patients' pattern of performance suggests that executive processes related to organizing and executing a series of responses were facilitated by the presence of external information. However, when patients with OCD had to rely on internal representations to guide their selections, performance was compromised. An impaired ability to use internal representations to guide ongoing behaviors may have clinical relevance to OCD. For example, checking compulsions may reflect impaired internal representations of behavior (eg, locking the door), which necessitate external verification (eg, checking the door). This hypothesis is supported by studies reporting reduced confidence in memories and increased deficits in memory for actions in patients with OCD.

Our results also indicated a distinction in visual memory processes in OCD. Although the patients showed normal recognition and recall of pattern material, recognition of spatial locations was impaired. This distinct-
tion in memory function may reflect differences in the type of memory stimulus, but may also reflect the influence of verbal mediation. For example, on the pattern recognition and DMTS tasks, stimuli can be classified verbally according to color and shape components. In contrast, verbal representations cannot be applied easily to spatial memory tasks; instead, greater reliance is placed on visual representations of the stimulus location. The patients' performance suggested that, whereas verbal representations may facilitate memory processes, the use of visual representations is problematic in this disorder. Zielinski et al. also reported that patients with OCD showed deficits on a recognition task when verbal mediation was limited. These results were consistent with reports of visual memory and visuospatial deficits in OCD, although our results emphasized a selective deficit related to memory of spatial information.

Our results also supported previous findings of response slowing in OCD. The patients exhibited a slowing of motor initiation and execution on the Tower of London task, indicating deficits in the speed of simple movements. This motor slowing is unlikely to reflect obsession-related doubt, as the patients were not impaired in their response latencies on any other measure. By separating...
cognitive from motor response latencies, our results suggested a specific deficit of motor slowing in OCD. Our findings also demonstrated that patients with more severe OCD symptoms show faster motor execution than patients with mild OCD, although it is unclear what type of symptoms may be associated with faster or slower motor execution (eg, meticulousness, doubting).

The patients with depression in our study were impaired only for attentional set shifting. Only half of this group completed all 9 stages of the task, with particular deficits at the IDS stage who had to maintain attention to new examples within the reinforced stimulus dimension. This result was consistent with previous studies reporting deficits in patients with depression on the same set-shifting task and the Wisconsin Card Sorting Test.

This finding also suggested that set-shifting ability is disrupted more in patients with depression than in those with OCD. This has important implications for neuropsychological studies of OCD, as several studies have reported deficits on set-shifting tasks, while others have found no differences between patients and controls. Importantly, these studies not reporting group differences have assessed the severity of depression symptoms and have excluded patients with OCD showing notable depressive features (ie, HAM-D score >16). In contrast, studies that have identified set-shifting deficits have not assessed depressive symptoms, which suggests that these studies may have been confounded by depressive features among the sample. Future research should explicitly measure comorbid depressive symptoms in patients with OCD to examine any relationship between depressive symptoms and set-shifting deficits.

A notable finding was the absence of cognitive deficits in our patients with panic disorder. Few studies have assessed neuropsychological performance in these patients, and the results from these investigations have been inconsistent. One study reported deficits only in verbal learning and memory, whereas another study failed to replicate this result, instead finding impaired visual memory. Our results suggest that there are no attentional, memory, or planning deficits in this group, although further research will be required to determine whether other cognitive functions are disrupted.

Current theories regarding the pathophysiological features of OCD emphasize the involvement of the prefrontal cortex, subcortical structures, and the distributed neural circuits that connect these regions. Our findings of selective deficits in OCD on tasks of executive function, spatial memory, and motor speed also supported a frontal-subcortical disturbance in the disorder. Normal spatial working memory performance has been associated with increased activation in mid dorsolateral prefrontal cortex (DLPFC) during positron emission tomographic (PET) investigations. The patients’ deficits on this task suggested that DLPFC may be involved in the pathophysiological features of OCD. However, the patients performed normally on the set-shifting task, which has demonstrated sensitivity to DLPFC function. Furthermore, abnormal activation of DLPFC is rarely reported in PET studies of OCD, making hypotheses about its role in the disorder speculative. Instead, most PET studies of OCD have reported increased metabolism or blood flow in orbitofrontal and anterior cingulate cortex and the caudate nucleus. Similar patterns of activation, however, have been observed in patients with simple phobia, indicating that orbitofrontal and anterior cingulate regions may mediate anxiety per se, rather than specific OCD phenomena. Furthermore, many of these investigations have reported evidence of symptom provocation (with its attendant elevated anxiety and resistance to obsessions) or have examined the resting state (which fails to control the patient’s cognition during scanning). Future neuroimaging studies of OCD will benefit from the use of cognitive activation paradigms to examine activation while controlling the mental state of patients.

Several limitations associated with our study may restrict the generalizability of our results. First, patients with varying medication status were included, although no differences between clinical characteristics or neuropsychological performance according to medication status were found. Second, although all patients were receiving treatment, we did not control for variation in treatment status (ie, recent vs long-term or relapse treatment). Finally, given differences in the patterns of illness onset across disorders (ie, frequent childhood onset of OCD vs predominately adult onset of depression and panic disorders), it was not possible to adequately match the patient groups according to illness duration. Nonetheless, the specificity of the deficits found in the patients and the homogeneity of variance for performance measures across the groups suggested that the influence of these factors was minimal.

In conclusion, we have demonstrated selective deficits in executive function, visual memory, and motor slowing that were specific to patients with OCD, which may help elucidate the pathophysiological features of the disorder.

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