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Regular Article

Attention and cognition in patients with obsessive–compulsive disorder

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Abstract Although a dysfunctional prefrontal-striatal system is presupposed in obsessive–compulsive disorder (OCD), this is not sustained by neuropsychological studies. The aim of this study was twofold: (i) to investigate the cognitive deficits in patients with OCD compared to matched healthy controls; and (ii) to relate cognitive performance to clinical characteristics in patients with OCD. In this study, 39 patients with primary OCD according to Diagnostic and Statistical Manual, fourth edition criteria were compared to 26 healthy control subjects on a battery measuring verbal memory and executive functioning. Patients with OCD showed slowed learning on the verbal memory task and made more errors on the Wisconsin Card Sorting Test. Errors were failures to maintain set, which were related to severity of OCD symptomatology. The results show that patients with OCD have cognitive deficits. The authors hypothesize that these deficits may be interpreted by attentional deficits caused by a dysfunctional anterior cingulate cortex.

Key words anterior cingulate cortex, attention, executive functioning, neuropsychology, obsessive–compulsive disorder, Wisconsin Card Sorting Test.

INTRODUCTION

Patients with obsessive–compulsive disorder (OCD) suffer from recurrent anxiety-provoking thoughts (obsessions), and ritualized behaviors directed at reducing this anxiety (compulsions).

Most neurobiological studies in OCD point toward an underlying dysfunctional prefrontal-striatal system. For instance, several structural neuroimaging studies showed reduced orbitofrontal cortex and basal ganglia volumes.[1–3] In addition, functional neuroimaging studies showed hyperactivity in these same regions during rest-state, symptom provocation, and cognitive activity.[4–7] This hyperactivity normalizes after successful treatment with serotonin reuptake inhibitors (SRI) or behavioral therapy.[8–10] Moreover, OCD symptoms might decrease following neurosurgical disruption of prefrontal-striatal circuits.[11]

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If the neurobiological underpinning of OCD is the prefrontal-striatal system, one would expect deficits in domains such as set shifting, spatial working memory, focused attention and verbal fluency.[12–14] However, neuropsychological findings are inconsistent, with some studies finding these deficits,[15–17] some studies finding no deficits,[18–20] and other studies finding no deficits other than slowed performance.[21–23] These conflicting findings can be explained in part by methodological factors such as inadequate matching of patients to controls or lack of control for medication status and the presence of comorbid disorders.

The aim of this study was twofold: (i) to investigate the cognitive deficits in patients with OCD compared to matched healthy controls; and (ii) to examine the relationship between clinical characteristics and cognitive performance in patients with OCD. In this study, patients and controls were carefully matched for age, gender and IQ. All patients with OCD were on stable antidepressant medication and free of major comorbid disorders. The authors hypothesized that patients with OCD would perform worse than healthy controls on the cognitive tests used and the authors expected

negative correlations between performance and OCD severity.

METHODS

Subjects

The study population consisted of 39 severely ill, therapy resistant patients with OCD and 26 healthy controls. The patients with OCD were recruited at the department of psychiatry of the University Medical Center Utrecht, Utrecht, the Netherlands, the controls were recruited by newspaper advertisements. All patients and controls gave written informed consent. This study is part of a larger study, in which the effect of quetiapine addition was investigated. A full description of inclusion and exclusion criteria can be found in the article by Denys *et al*.[24]

Inclusion criteria for patients were: aged between 18 and 65 years, primary OCD according to Diagnostic and Statistical Manual, fourth edition (DSM-IV) criteria, and minimal Yale–Brown Obsessive–Compulsive Scale (Y-BOCS[25,26]) score of 18 or 12 if only obsessions or compulsions were present. All patients showed significant symptoms, despite previous and current treatments. Exclusion criteria were: significant depressive symptoms (defined as a score of 15 or more on the Hamilton Depression rating scale [HAM-D][27]), bipolar disorder, anxiety disorder, schizophrenia or any other psychotic condition, current psychotherapeutic treatment, substance abuse within the past 6 months, primary personality disorder, organic mental disorders, stroke within the last year, epilepsy or other central nervous system disorders. The Mini-International Neuropsychiatric Interview (M.I.N.I.)[28] was given to assess DMS-IV disorders. Patients with OCD were divided into subtypes based on the Y-BOCS checklist, as described by Denys *et al*.[29] Clinical characteristics of the OCD subjects are shown in Table 1.

Table 1. Clinical characteristics of patients with obsessive–compulsive disorder ($n = 39$) and controls ($n = 26$)

	OCD Mean ± SD	Controls Mean ± SD	*F*	*P*
Gender distribution (male : female)	10:29	10:16	$\chi^2 = 1.20$	0.289
Age	36.1 ± 12.2	34.0 ± 11.5	0.51	0.477
NART IQ	102.0 ± 10.2	106.2 ± 6.3	3.55	0.064
Range	81–118	94–118		
Medication at time of testing				
Paroxetine $n = 14$ dose	47 ± 15	NA		
Citalopram $n = 11$ dose	52 ± 13	NA		
Venlafaxine $n = 5$ dose	300 ± 0	NA		
Fluoxetine $n = 4$ dose	35 ± 19	NA		
Fluvoxamine $n = 3$ dose	150 ± 86	NA		
Imipramine $n = 1$ dose	150	NA		
Clomipramine $n = 1$ dose	75	NA		
Duration of illness (years)	21.6 ± 10.9	NA		
Y-BOCS				
Obsessions	13.4 ± 4.0	NA		
Compulsions	13.9 ± 3.4	NA		
Total	27.3 ± 5.4	NA		
HAM-D	12.0 ± 6.0	NA		
HAM-A	13.7 ± 5.9	NA		
Number of previous SRI treatments	2.8 ± 1.0	NA		
Number of previous CBT treatments	1.1 ± 1.0	NA		
OCD subtype				
Contamination and cleaning	$n = 7$	NA		
Aggressive, sexual and religious obsessions	$n = 6$	NA		
Somatic obsessions and checking	$n = 5$	NA		
Symmetry and counting/arranging	$n = 10$	NA		
High risk-assessment and checking	$n = 11$	NA		

CBT, Cognitive Behavioral Therapy; HAM-A, Hamilton Anxiety rating scale; HAM-D, Hamilton Depression rating scale; NA, not applicable; NART IQ, National Adult Reading Test Intelligence Quotient; OCD, obsessive–compulsive disorder; SD, standard deviation; SRI, Serotonin Reuptake Inhibitor; Y-BOCS, Yale–Brown Obsessive–Compulsive Scale.

Exclusion criteria for the healthy control group were: neurological illness or other disorders of the central nervous system and substance abuse within the past 6 months. Further exclusion criteria were history of psychiatric disease (assessed by Comprehensive Assessment of Symptoms and History [CASH][30]), history of personality disorder (assessed by Structured Interview for DSM-IV Personality Disorders [SIDP-IV])[31] and psychiatric disease in first or second degree relatives (assessed by Family Interview for Genetic Study [FigS]).[32] Healthy controls and patients with OCD were matched groupwise for age, gender, handedness and IQ (measured by the Dutch version of the National Adult Reading Test[33,34]).

As can be seen in Table 1, patients with OCD and controls did not differ with respect to demographic and clinical characteristics.

Cognitive measures

National Adult Reading Test[33,34]

In this test, known to be a good indication for verbal IQ, subjects are asked to read aloud a list of phonetically irregular words. The authors transformed the raw scores into IQ scores, which were then used to match the two groups.

Verbal fluency

The authors measured verbal fluency with a word-generation tasks in which subjects are given 1 min to retrieve as many words as possible in response to letter ('N', 'A') and semantic ('animals', 'professions') cues. These four trials result in four scores: number of unique words. The scores for the two phonemic trials are added and so are the scores for the two semantic trials. Verbal fluency is considered to be a measure of executive function.[35]

Trail Making Test[36]

In this task the time required to track a number sequence (Trail Making Test [TMT] A) and a sequence of alternating numbers and letters (TMT B) is measured. Time needed for part A and part B can both be considered a measure of visual scanning and mental speed, where part B focuses more on alternated attention. Since performances in both parts exhibit a close linear relationship, an outcome measure for set shifting measured by the TMT is time B divided by time A.[37]

California Verbal Learning Test[38]

The California Verbal Learning Test (CVLT) is a verbal memory task that consists of five presentations of an identical list of words. Subjects are asked to reproduce as many words as they can. By repeating the same list five times, the examiner can study the learning curve (i.e. the amount of words remembered for each presentation). The test also yields information on the subject's memory capacity, encoding strategy, recall after a long and short delay and recognition. The first presentation of the list is generally regarded as a test of immediate word span, more closely related to attention than to memory per se.[39] The measures used in analysis were: total recall in five trials, number of words learned over five trials (trial 5 minus trial 1), semantic clustering index, retrieval after short delay, retrieval after long delay, number of hits on recognition trial. To prevent practice effects due to the two administrations, the authors used the parallel version of this test in a counterbalanced design.[40] A Dutch version of the CVLT was used.[41]

Wisconsin Card Sorting Test[42]

The Wisconsin Card Sorting Test (WCST) is one of the most widely used tasks in the assessment of neurocognitive function, it measures so called 'frontal' functions, such as set-shifting, category formation and set maintenance.[39] In the WCST, the subject has to discover criteria by which to sort cards (according to three 'sets': color, shape, or number). After 10 consecutive sorts, the examiner changes the set unbeknown to the subject (this is only indicated by feedback from the examiner). The authors used the version as described by Milner[43] in which two packs of 64 cards are used and the test is discontinued when the subject reaches six categories. For each subject, the authors calculated the number of categories completed (10 consecutive correct sorts), percentage of errors made, percentage of perseverative errors and failure to maintain set (five to nine consecutive correct sorts followed by an error) as described in the manual.

Clinical characteristics

The clinical characteristics included in the analyses were: age, duration of illness, number of previous treatments, OCD severity measured by the Y-BOCS (obsessions and compulsions subscales, total), anxiety symptoms measured by the Hamilton Anxiety Rating Scale (HAM-A),[44] depressive symptoms measured by the HAM-D, OCD symptom subtype.

Statistical analyses

Data were analyzed using the Statistical Package for the Social Sciences (SPSS) version 11.5 (SPSS Inc.,

Chicago, IL, USA). The authors used multivariate ANOVA (factor is *Group* with two levels: *OCD* and *healthy controls*) to compare patients with OCD and healthy controls, and used Pearson's coefficients to calculate correlations between clinical characteristics and neuropsychological performance. *P*-values under 0.05 were considered significant.

RESULTS

Patients with obsessive–compulsive disorder versus healthy controls

Table 2 summarizes the group mean performance and statistical comparisons for each task.

The patients with OCD and healthy controls did not differ in the two timed tasks, verbal fluency and TMT. The ratio between part A and part B of the TMT, which is a measure of set shifting, showed no abnormalities either.

Patients with OCD showed greater learning on the CVLT (measured by the 'number of words learned over five trials' variable), this was caused by a significantly lower performance on the first trial (see Table 2: recall 1st trial). The performance on the other four trials did not differ.

The patients with OCD performed worse on the WCST compared to the controls: they completed significantly fewer categories; the percentage of errors was higher as was the number of failures to maintain set. The percentage of perseverative errors was not elevated in the OCD group.

Clinical characteristics and neuropsychological performance

The authors performed exploratory correlational analyses to examine the relationships between the clinical measures. These analyses showed that HAM-A and HAM-D scores correlated significantly ($r = 0.784$, $P = 0.000$), HAM-D was also related to age ($r = 0.376$, $P = 0.018$). Duration of illness was related to age ($r = 0.819$, $P = 0.000$) and HAM-A score ($r = 0.399$, $P = 0.013$). Number of previous SRI and CBT treat-

Table 2. Performance on neuropsychological measures

	OCD ($n = 39$) Mean ± SD	Controls ($n = 26$) Mean ± SD	*F*	*P*
Verbal fluency				
Phonemic	24.46 ± 7.93	24.68 ± 8.24	0.01	0.916
Semantic	42.92 ± 9.54	44.04 ± 8.02	0.24	0.629
TMT				
Time A	30.72 ± 10.05	28.39 ± 9.72	0.86	0.357
Time B	65.49 ± 21.59	63.45 ± 23.42	0.13	0.720
Time B/time A	2.24 ± 0.77	2.28 ± 0.51	0.57	0.811
CVLT				
Total recall 5 trials	53.90 ± 13.08	56.38 ± 9.37	0.70	0.406
Recall 1st trial	6.74 ± 2.07	8.15 ± 1.87	7.79	0.007
Recall 2nd trial	10.15 ± 2.98	11.04 ± 2.69	1.49	0.228
Recall 3rd trial	11.51 ± 3.32	11.96 ± 1.82	0.40	0.532
Recall 4th trial	12.56 ± 2.92	12.38 ± 2.26	0.07	0.792
Recall 5th trial	12.90 ± 2.88	12.85 ± 2.33	0.01	0.940
Number of words learned over 5 trials	6.15 ± 2.13	4.69 ± 2.00	7.70	0.007
Semantic clustering index	2.28 ± 1.00	2.31 ± 0.87	0.01	0.924
Retrieval after short delay	0.62 ± 1.48	1.46 ± 1.33	3.34	0.074
Retrieval after long delay	0.38 ± 1.18	0.77 ± 1.17	1.04	0.313
Number of hits on recognition trial	15.00 ± 1.59	14.81 ± 1.77	0.21	0.649
WCST				
Number of categories completed	4.64 ± 1.87	5.54 ± 1.27	4.56	0.037
% errors	31.64 ± 14.54	22.32 ± 14.08	6.57	0.013
% perseverative errors	15.95 ± 7.29	12.88 ± 9.77	2.10	0.152
Failure to maintain set	1.03 ± 1.16	0.42 ± 0.81	5.30	0.025

CVLT, California Verbal Learning Test; OCD, obsessive–compulsive disorder; SD, standard deviation; TMT, Trail Making Test; WCST, Wisconsin Card Sorting Test.

ments correlated significantly ($r = 0.433$, $P = 0.006$). These relationships were taken into account in further analyses, the authors corrected for factors by means of partial correlations.

Correlations between clinical and neuropsychological variables are shown in Table 3.

Severity of OCD symptomatology, measured by the Y-BOCS, correlated significantly with failure to maintain set on the WCST. Depressive symptomatology, measured with HAM-D was also related to failure to maintain set. When corrected for age (which correlates with both failure to maintain set and HAM-D), this effect disappeared ($r = 0.270$, $P = 0.101$). WCST number of categories completed was negatively related to number of previous SRI treatments.

Duration of illness correlated significantly with several CVLT measures: total recall, semantic clustering index, retrieval after a long delay and number of hits on recognition. After correction for age (since duration of illness is closely linked to age), the significant results disappeared (total recall: $r = –0.130$, $P = 0.443$; semantic clustering index: $r = –0.277$, $P = 0.097$; retrieval after long delay: $r = 0.133$, $P = 0.327$; number of hits on recognition: $r = –0.111$, $P = 0.521$). The authors interpreted these results as an artifact, because verbal memory is known to be related to age, as can also be seen in Table 3.[39]

Severity of anxiety symptoms, measured by HAM-A, correlated significantly with several CVLT measures: total recall, semantic clustering index and long-term retrieval. Again, these effects could be explained by duration of illness and age. After correction for duration of illness, all significant results disappeared (total recall: $r = –0.277$, $P = 0.093$; semantic clustering index: $r = 0.271$, $P = 0.099$; retrieval after long delay: $r = –0.329$, $P = 0.044$). Because of the direct relationship between duration of illness and age, the authors interpreted the results as an artifact.

When HAM-D scores were corrected for age, semantic verbal fluency showed a significant relationship with depressive symptoms ($r = –0.328$, $P = 0.045$), but the relationship with CVLT total recall disappeared ($r = –0.167$, $P = 0.316$).

No other effects achieved significance. In particular, OCD severity did not have any effect on cognitive measures other than the WCST. Depressive symptomatology and anxiety symptoms did not relate to any of the cognitive measures. There were no differences

Table 3. Pearson correlation coefficients between clinical and neuropsychological variables in the obsessive–compulsive disorder group ($n = 39$)

	Age	Duration of illness	No. previous SRI treatments	No. previous CBT treatments	Y-BOCS	HAM-A	HAM-D
Verbal fluency							
Phonemic	0.14	0.23	0.03	–0.28	–0.10	0.11	–0.01
Semantic	–0.12	–0.14	0.17	–0.04	–0.20	–0.29	–0.35*
TMT							
Time B/time A	0.04	–0.05	0.09	0.22	0.26	–0.05	–0.10
CVLT							
Total recall 5 trials	–0.54**	–0.53**	0.17	0.07	–0.30	–0.38*	–0.33*
Number of words learned over 5 trials	0.00	0.01	0.11	0.01	–0.09	–0.15	–0.10
Semantic clustering index	–0.29	–0.41*	0.21	0.14	–0.30	–0.39*	–0.24
Retrieval after short delay	0.10	0.15	0.08	0.02	0.19	0.13	0.15
Retrieval after long delay	0.28	0.32*	0.04	–0.12	0.01	0.33*	0.27
Number of hits on recognition trial	–0.44**	–0.43**	–0.03	0.00	–0.20	–0.13	–0.06
WCST							
Number of categories completed	–0.31	–0.32	–0.34*	0.07	–0.27	–0.03	–0.07
% errors	0.20	0.16	0.31	–0.13	0.09	–0.08	0.01
% perseverative errors	0.21	0.09	0.25	–0.21	0.18	–0.11	0.03
Failure to maintain set	0.38*	0.28	–0.09	0.09	0.57**	0.28	0.38*

* Correlation is significant at the 0.05 level (two-tailed).

** Correlation is significant at the 0.00055 level (Bonferonni corrected α).

CBT, Cognitive Behavioral Therapy; CVLT, California Verbal Learning Test; HAM-A, Hamilton Anxiety rating scale; HAM-D, Hamilton Depression rating scale; SRI, Serotonin Reuptake Inhibitor; TMT, Trail Making Test; WCST, Wisconsin Card Sorting Test; Y-BOCS, Yale–Brown Obsessive–Compulsive Scale.

between the five symptom subtypes for any of the cognitive measures.

DISCUSSION

The main finding in the present study is that patients with OCD showed slowed learning on the CVLT and deficits in set maintenance as measured by the WCST, the latter being related to severity of OCD symptoms.

In contrast to many studies;[16,17,45] the present study failed to find slower performance on timed tests (TMT, verbal fluency). The slower performance of patients in other studies might be explained by depressive comorbidity, approximately 50% to 80% of patients with OCD suffer from comorbid depression, a disorder renowned for its slowness of thought and movement.[46] Schmidtke *et al.*,[17] for instance, found deficits in patients with OCD on timed tests. Eight of the 29 patients (28%) had a lifetime diagnosis of major depressive disorder. In 2001, Basso *et al.*[16] showed that abnormalities in executive function were related to comorbid depressive severity and argued that conflicting findings in past studies regarding executive functioning are due to comorbid depression. The current sample consisted of depression-free patients with OCD, with a mean Hamilton–Depression score of 12, which is indicative of mild depressive symptoms. This could explain their normal performance on timed tests.

Regarding the CVLT, the authors did not find any deficits in verbal memory, other than a slightly slower learning curve. The patients in the current sample showed a lower performance on the first trial, probably reflecting a lack of attention.[39] They made up for this in later trials, where they performed at the same level as controls, therefore, the authors conclude that these patients do not suffer from a verbal memory deficit. Almost all studies investigating verbal memory tasks (like the CVLT) show normal performance in patients with OCD,[47–49] confirming that there is no mnemonic deficit. When the material is non-verbal (e.g. Rey complex figure test), most studies do find differences in recall scores between patients with OCD and healthy controls, but this is most often explained in terms of a failure to use organizational strategies.[17,50–55]

In patients with OCD, one would expect to find a profile of deficits associated with prefrontal-striatal dysfunction.[1–11] To be more precise, the structures that are most consistently shown to be involved in OCD are the orbitofrontal cortex and basal ganglia structures (especially caudate nucleus). A cognitive profile matching dysfunction in these structures, might include executive deficits leading to, namely; errors in set shifting, focused attention and verbal fluency.[12–14] The most prominent feature of executive/frontal dysfunction is perseverative behavior. The deficits found in the current patient sample did not fit this profile. First of all, the authors did not find deficits in tasks such as verbal fluency and TMT (set shifting, attention). Furthermore, the authors did find a deficit in WCST performance (set shifting), but failed to find the expected elevated level of perseverative errors. In summary, the cognitive deficits found in patients with OCD do not fit the profile of deficits associated with prefrontal-striatal dysfunction.

An alternative line of explanation is that the current results on the CVLT and the WCST can be explained by a deficit in the attention system. The deficit found on the WCST is a failure to maintain set. Failure to maintain set occurs when the subject makes an error after five or more consecutive correct responses (the subject 'loses' the set) and is often explained as reflecting difficulty in sustaining attention and remaining 'on task'.[56,57] As mentioned earlier, the lower performance on the first presentation of the CVLT can also be explained in terms of an attention deficit.[39] The authors did not find deficits on the TMT, a task sometimes considered to be a measure of attention. However, several authors argue that the TMT should be seen as a measure of cognitive flexibility, visual scanning and simple motor skills.[58] Therefore, it is plausible to assume that the CVLT and WCST data indicate a deficit in the attention system of the subjects with OCD.

This attention deficit could be due to abnormal functioning of the anterior cingulate cortex (ACC), a structure involved in attention functions and conflict monitoring in information processing (for an overview see References59,60). Studies in OCD patients consistently showed hypermetabolism of the ACC during symptom provocation,[4,6,7,61] at rest,[8,62] and during the execution of neuropsychological tasks.[63–65] Structural studies found abnormalities in the ACC as well: more total gray matter[66,67] and white matter abnormalities.[68] In line with this, event-related potential studies demonstrated an increased error-related negativity (a negative waveform time-locked to incorrect responses) in patients with OCD.[69–71] This error-related negativity is attributed to the action-monitoring function of the ACC. Many authors argue that an overactive action-monitoring system leads to constant feelings of erroneous performance, which in its turn leads to the doubt and checking behavior characteristic for OCD.

Monchi *et al.*[72] showed that receiving negative feedback during the WCST leads to activity in the dorsal part of the ACC of healthy subjects. This is another argument for the hypothesis that the deficits in WCST performance in the current sample might be due to ACC abnormalities. Furthermore, failure to maintain set correlated significantly with the Y-BOCS, suggest-

ing that patients with more severe symptoms showed more attentional dysfunction.

In summary, in a sample of 39 patients with OCD the authors found deficits in set maintenance and slightly slower learning on a verbal memory task. These deficits seem to be indicative of attention dysfunction in patients with OCD, possibly related to abnormal ACC functioning. The ACC is involved in action-monitoring, which could be linked to doubt and checking behavior. Therefore, it would be interesting to investigate the ACC functioning in different OCD-subgroups, for example 'checkers', 'washers', and patients with 'pure obsessions'.

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