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Cognitive deficits in obsessive–compulsive disorder on tests of frontal lobe functions

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Individuals with obsessive–compulsive disorder (OCD) display frontal lobe deficits, but there are inconsistencies between various tests of frontal lobe functions and between the results from different studies. The objective of this work was to characterize frontal lobe dysfunctions in OCD patients. Fifteen patients and 17 control subjects matched for age, sex and intelligence were tested on classic tests of frontal lobe functions [Wisconsin Card Sorting Test (WCST) and tests of fluency], a smell identification test and one computerized test: the Intra/Extra Dimension test. The Intra/Extra Dimension test showed a significant difference between the two groups in reversal of response. The test of Figural fluency showed a significant difference between the two groups in numbers of produced figures. There were no differences on the WCST, verbal fluency and the smell identification test.

• *Frontal lobe, Neuropsychological tests, Obsessive–compulsive disorder (OCD), Response reversal, Set shifting.*

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Patients with obsessive–compulsive disorder (OCD) display frontal lobe dysfunctions, but neuropsychological studies of OCD have been inconsistent in results. In 10 studies where the Wisconsin Card Sorting Test (WCST) was used, six studies found no significant differences in performance (1–6), whereas the other four studies found a significant difference in the performance between control groups and patients with OCD (7–10). Three of the studies with no significant difference in performance on WCST also included another test, the Object Alternation Test, measuring the patients' ability to reverse a reinforced response (3–5). On this test, all three studies found a significant impairment in patients with OCD. Inconsistencies in the results of the studies have been explained by the sensitivity of the applied tests (3, 4), and it has been suggested that the WCST is sensitive to dorsolateral prefrontal cortex dysfunctions while the Object Alternation Test is sensitive to orbitofrontal cortex dysfunctions. In the studies of Abbruzzese et al. (4, 5), a double dissociation of performance on these two tests was found for patients with schizophrenia compared to patients with OCD. This finding supports that the WCST and the Object Alternation Test are sensitive to and differentiate between different cognitive functions of the frontal lobes. One problem, however, arises by the use of WCST, as it is believed to measure several cognitive functions (11). Computerized tests from the Cambridge Neuropsychological Test Automated Battery (CANTAB) sensitive to frontal lobe dysfunctions have shown promising potential for deciding which cognitive components may be affected in patients with OCD (12, 13). In the study by Veale et al. (12), OCD patients ($n=40$) were significantly impaired in set shifting in a discrimination-learning task. Purcell et al. (13) tested 23 OCD patients on the same tasks as Veale et al., but they failed to replicate the results with a more stringent significance level at $P<0.01$ to protect against type I error.

Other tests have also yielded promising results. Olfactory testing of individuals with schizophrenia (14), Parkinsons disease (15) and sociopathy (16) have shown significant impairments compared to control subjects. It has been suggested that an impaired performance on smell identification may be due to an affected orbitofrontal cortex, which may be a key structure affected in OCD (17). Two studies have tested the ability of olfactory identification in OCD patients (18, 19), and both found a significant impairment. However, the study by Goldberg et al. (19) only included five patients.

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Thus, more studies are needed to characterize cognitive dysfunctions of the frontal lobes in patients with OCD. The objective of this study was to examine OCD patients on several neuropsychological tests thought to be sensitive to various aspects of frontal lobe function.

Materials and Methods

Subjects

Fifteen patients with OCD and 17 controls participated in the study. The patients were recruited via the outdoor psychiatric clinic, an advertisement on the homepage for the Danish Association for Individuals with OCD and an advertisement in a health magazine. Controls were recruited by newspaper advertisement. The patients were screened by a clinical interviewer to exclude other psychiatric and any neurological or medical illness and alcohol or medicine abuse. The patients were rated by one of two senior psychiatrists for OCD and depression. The inclusion criteria were: 1) DSM-IV and ICD-10 criteria for OCD, and 2) absence of psychopharmacological medication in the 4 weeks before testing. The control subjects were screened by the same clinical interviewer to exclude persons with psychiatric, neurological or medical symptoms; persons with first-grade relatives with neuropsychiatric illness and persons taking medication with effects on the central nervous system were also excluded. The study was approved by the local ethics committee. Patients and controls were matched for sex, age and intelligence (estimated according to performance on the Danish Adult Reading Test, DART). The clinical data of the OCD patients and demographic characteristics for the two groups are shown in Table 1. The subjects also took part in a study of regional $5HT_{2A}$ receptor binding, to be published separately.

One subject from the control group showed an arbitrary attitude to the tests. In some of them, the subject declined from doing the test, and in other tests the subject showed signs of inattention and carelessness. Therefore, this subject was excluded.

Table 1. Clinical and demographic characteristics of patients with obsessiv–compulsive disorder (OCD) and control subjects.

	OCD patients ($\pm s$)	Controls ($\pm s$)	*P*
Subjects	15	17	
Males	7	8	
Females	8	9	
Age	39.0 ($\pm$15.6)	32.8 ($\pm$10.4)	0.193
Years of education	12.7 ($\pm$1.9)	14.7 ($\pm$1.7)	0.066
DART	28.1 ($\pm$7.2)	30.3 ($\pm$5.0)	0.473
Y-BOCS	27.2 ($\pm$6.2)		
Obsession	13.7 ($\pm$2.5)		
Compulsion	13.5 ($\pm$4.1)		
HDRS	6.7 ($\pm$3.0)		

s, standard deviation; DART, Danish Adult Reading Test; Y-BOCS, Yale–Brown Obsessive Compulsive Scale; HDRS, Hamilton Depression Rating Scale (17-item version).

Procedures

The neuropsychological testing included WCST, Letter fluency, Figural fluency, a smell identification test and one computerized test from CANTAB: the Intra/Extra Dimension test. The Intra/Extra Dimension test was presented on a Phillips flat monitor with a touch sensitive screen.

WCST, Letter fluency and Figural fluency

WCST, Letter fluency and Figural fluency are widely used tests for frontal lobe dysfunction (11). The WCST was administered according to modified criteria (20). The WCST consists of four stimulus cards with different symbols (circle, triangle, cross and star) and 48 response cards with different combinations of colour, form and number of the symbols. The subject was instructed to place each response card under one of the four stimulus cards according to a certain, but unknown criterion (colour, form and number). The examiner told the subject after each card whether the response was correct or incorrect. After six correct responses in succession, the subject was told that the criterion was changed. The test was scored for number of fulfilled criteria, number of incorrect responses and number of perseverative responses (i.e. card placements according to the previous, now incorrect criterion).

In Letter fluency, the subject had to say as many words as possible beginning with the letter "S" in 1 min. A variation of this test, considered more demanding, combined Letter fluency with Category fluency. In this variation, the subject had to switch between words beginning with the letter "F" and words for animals. We have labelled this test "Shift fluency".

Figural fluency or Design fluency (21) consists of a sheet of paper with identical squares, each with five dots arranged in an X. The subject was instructed to connect any number of dots (two to five dots) with any number of straight lines (one to eight lines), and produce as many unique figures as possible in 3 min.

All tests of fluency were scored according to numbers of unique words and figures. Words or figures that were the same were counted as repetitions.

Smell Identification Test

A short version of a standardized multiple-choice smell test was used to measure olfactory identification ability [University of Pennsylvania Smell Identification Test – Brief (B-UPSIT)] (22). The test consists of a booklet with 12 pages. Each page includes a microencapsulated strip in which the odorant is embedded and elicited by scratching with a pencil. Four possible responses for identifying each odour are provided for each strip on

each page. The subject was instructed to scratch the strip, to smell bilaterally and to make a selection between the four possible responses. B-UPSIT was scored according to number of odours correctly identified (max = 12). History of smoking was registered for all subjects.

INTRA/EXTRA DIMENSION TEST

The Intra/Extra Dimension test measures the ability of the individuals to discriminate between patterns, to reverse a reinforced response and to shift attention from one perceptual aspect of the pattern to another aspect. The test consists of a series of two alternative forced choice patterns presented in nine stages in the same fixed order on the computer. The nine stages are as follows. Stage 1: Simple discrimination between two patterns (SD); stage 2: Reversal of response (SDR); stage 3: Compound patterns (C_D); stage 4: Compound discrimination (CD); stage 5: Reversal of response (CDR); stage 6: Shift to novel exemplars of patterns (IDS); stage 7: Reversal of response (IDR); stage 8: Shift to another perceptual dimension of the patterns (EDS); and stage 9: Reversal of relevant perceptual dimension (EDR). Each stage is passed when the subject correctly responds on the presented patterns six times in succession (12). The subject was instructed to choose one of two patterns shown on the screen and via a feedback from the computer to learn to respond to the correct pattern. The subject was told that the criterion for choosing the correct pattern would change during the course of the test (see reference 12 for further description).

Statistical analysis

Data were plotted into Excel calculation sheets. Descriptive and inferential statistics were performed with SPSS 11.5 (Statistical Package for the Social Sciences). *t*-tests were performed for measures on the WCST, Intra/Extra Dimension test and B-UPSIT, except for number of sets in WCST and number of smokers in B-UPSIT, which were analysed by chi-square test. Statistics were one-tailed for the Intra/Extra Dimension test, as it was hypothesized that patients with OCD would show a significantly impaired performance. Statistics were two-tailed for the rest of the tests. As four independent tests were used, significance levels were adjusted to alpha = 0.01 to protect against type 1 error.

Results

Table 2 shows the results for the performance on tests of frontal lobe functions. In WCST, there was no significant impairment on the three measures: sets completed [chi-squared(31) = 2.17, $P = 0.14$], total errors [$t(30) = 1.41$, $P = 0.17$] and perseveration errors [$t(30) = 0.45$, $P = 0.65$]. There was no significant difference in the performance in Letter fluency [$t(30) = 0.89$, $P = 0.35$] or in Shift fluency [$t(30) = 1.56$, $P = 0.13$]. There was a significant difference in the performance in Figural fluency for patients with OCD compared to controls [$t(30) = 3.72$, $P = 0.001$]. The smell identification test showed no impairment for OCD patients in their ability to identify the 12 odours correctly compared to controls [$t(30) = 0.79$, $P = 0.43$], and there was no significant difference in the number of smokers in each group [chi-squared(31) = 0.75, $P = 0.39$].

In the Intra/Extra Dimension test, the OCD patients did not differ from the control group in number of stages [$t(29) = 1.32$, $P = 0.10$, one-tailed]. In number of errors in the Intra Dimension Shift (IDS), the OCD patients made 6.9 ($\pm$2.8), whereas the controls made 4.9 ($\pm$1.4). This was a significant difference [$t(29) = -2.55$, $P = 0.008$, one-tailed]. In number of errors in the Extra Dimension Shift (EDS), before criterion the patients made 15.7 ($\pm$12.6), and the controls made 8.6 ($\pm$9.1). This difference was insignificant [$t(29) = -1.81$, $P = 0.04$, one-tailed].

Details in the results on the Intra/Extra Dimension test

The analysis of the Intra/Extra Dimension test was undertaken to examine where in the nine stages the impaired performance of the OCD patients took place. All subjects passed up to and including stage 7 (IDR). On stage 8 (EDS), three subjects (19%) of the control group did not manage to shift their attention to the other perceptual aspect in the patterns, whereas six subjects (40%) of the OCD group failed to do this. On stage 9 (EDR), one additional subject in each group failed to reverse his responses on the patterns. Fig. 1 shows the number of errors on each of the nine stages for subjects who passed each stage. Thirteen subjects in the control group made 8.6 errors ($\pm$9.1) before they managed to shift their attention to the other perceptual aspect, whereas nine subjects in the OCD group made 15.7 errors ($\pm$12.6). In a close up (Fig. 2) of the performance in the Intra Dimension stages (stages 1–7), it is seen that the greatest impairment for the OCD patients happened at stage 2 (SDR). At this stage, patients made 1.60 errors ($\pm$0.83) before they managed to reverse their response on the reinforced patterns, whereas controls made 1.06 errors ($\pm$0.25). This difference did not reach significance [$t(29) = 2.27$, $P = 0.015$]. The other impaired performance is seen at stage 3 (C_D), when an irrelevant feature in the patterns was introduced. This difference was not significant [$t(29) = 1.44$, $P = 0.081$]. In the remaining stages (stages 4, 5, 6, 7 and 9), when features and the reversal of responses and attention on the reinforced patterns are introduced for the second time, the OCD group performed as well as the control group (Figs. 1 and 2).

Table 2. Mean performance of patients with obsessive–compulsive disorder (OCD) and controls on tests of frontal lobe functions.

Tests	OCD patients ($\pm s$)	Controls ($\pm s$)	Statistic	*P*
WCST (20)				
Sets completed	5.0 ($\pm$1.9)	5.9 ($\pm$0.3)	$\chi^2(31) = 2.17$	0.14
Total errors	8.9 ($\pm$7.4)	5.2 ($\pm$2.3)	$t(30) = 1.41$	0.17
Perseveration	1.7 ($\pm$2.6)	1.1 ($\pm$1.1)	$t(30) = 0.45$	0.65
Tests of fluency				
Letter fluency	18.1 ($\pm$6.2)	19.9 ($\pm$5.8)	$t(30) = 0.89$	0.35
Shift fluency	6.3 ($\pm$2.0)	7.2 ($\pm$1.3)	$t(30) = 1.56$	0.13
Figural fluency	31.4 ($\pm$8.6)	42.3 ($\pm$8.0)	$t(30) = 3.72$	0.001
Smell identification				
Identifications	9.9 ($\pm$1.0)	10.2 ($\pm$1.2)	$t(30) = 0.79$	0.43
Number of smokers	6/40.0%	10/58.8%	$\chi^2(31) = 0.75$	0.39
Years of smoking	19.3 ($\pm$11.4)	13.5 ($\pm$11.7)	$t(14) = 0.97$	0.35
Intra/Extra Dimension				
Number of stages	8.1 ($\pm$1.0)	8.6 ($\pm$0.8)	$t(29) = 1.32$	0.10
IDS trials	6.9 ($\pm$2.8)	4.9 ($\pm$1.4)	$t(29) = -2.55$	0.008
EDS trials	15.7 ($\pm$12.6)	8.6 ($\pm$9.1)	$t(29) = -1.81$	0.04

s, standard deviation; WCST, Wisconsin Card Sorting Test; IDS, Intra Dimension Shift; EDS, Extra Dimension Shift.

Discussion

Performance on the smell identification test did not show any differences between the two groups. This is opposite to the results from the two existing studies with OCD and smell identification (18, 19). A possible explanation is that Barnett et al. (18) and Goldberg et al. (19) used the long 40-item version of the smell test, whereas our study used the short 12-item version. The 40-item version may be more sensitive to olfactory inacuity. That it has to be a higher level processing area, which lies behind the olfactory deficit, is supported by studies showing that OCD patients have no problems with detecting (18, 24) or discriminating smells (25).

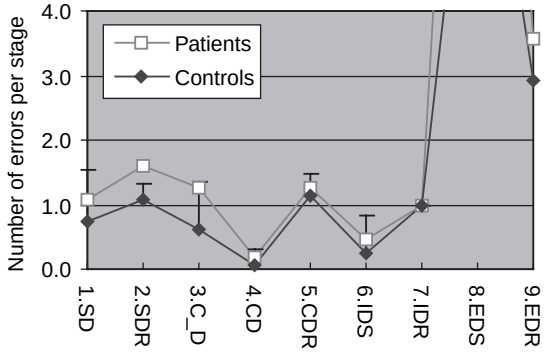

Fig. 1. Number of errors made by the patient group and the control group on the stages in the Intra/Extra Dimension test. The curves for stage 8 (EDS) and stage 9 (EDR) exceed the figure. Stage 1: Simple discrimination between two patterns (SD); stage 2: Reversal of response (SDR); stage 3: Compound patterns (C_D); stage 4: Compound discrimination (CD); stage 5: Reversal of response (CDR); stage 6: Shift to novel exemplars of patterns (IDS); stage 7: Reversal of response (IDR); stage 8: Shift to another perceptual dimension of the patterns (EDS); and stage 9: Reversal of relevant perceptual dimension (EDR).

On the Letter fluency and Shift fluency, our group of OCD patients did not differ from the controls, but the patients showed an impaired performance on Figural fluency. A similar result has been found by Schmidtke et al. (26). One reason for patients differing in performance on Figural fluency and Letter fluency may be that the former test is more sensitive to frontal lobe functions (27). Phillips (27) argued that Letter fluency depends on retrieval from long-term memory, whereas the Figural fluency truly depends on strategies to generate novel figures. In her study, she found that Letter and not Figural fluency correlated significantly with measures for intelligence (i.e. performance on the Weschler Adult Intelligence Scale, WAIS).

Performance on the WCST did not differ significantly between the two groups. Earlier investigations have shown contradictory results on this test. The question is whether the WCST (20) is too easy and therefore insensitive to the cognitive dysfunctions in OCD patients or whether WCST is irrelevant for the cognitive deficits in OCD. The first seems to be a possible explanation, as the examiner noticed that the sorting principles used in WCST were easily recognized by the subjects. After the instruction, some subjects spontaneously exclaimed, "Well, then the cards have to be sorted according to colour and form." This implicates less demand on the subjects' cognitive function of planning and executing new strategies. The other possible explanation that WCST is irrelevant for the deficits in OCD is elaborated on below.

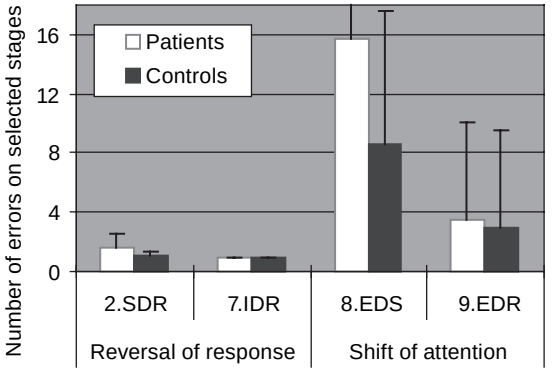

Fig. 2. Comparing number of errors made by the patient group and the control group, on the first and second time they reverse their response and shift their attention. On stage 2 (SDR), subjects have to do their first reversal of response and on stage 7 (IDR), they do their second reversal of response. On stage 8 (EDS), subjects have to do their first shift of attention and on stage 9 (EDR), they do their second shift of attention. The standard deviation ($\pm$12.6) for the patient group in stage 8 (EDS) exceeds the figure. Stage 2: Reversal of response (SDR); stage 7: Reversal of response (IDR); stage 8: Shift to another perceptual dimension of the patterns (EDS); and stage 9: Reversal of relevant perceptual dimension (EDR).

IntralExtra Dimension test

The Intra/Extra Dimension test from CANTAB was used under the hypothesis that it probed more specific functions of the frontal lobes, and our results tended to support this hypothesis. On the Intra/Extra Dimension test, the OCD patients showed an impairment in the shift of attention. The impairment was not due to visual problems, as patients without error discriminated between the different patterns. Also, the patients were not distracted by irrelevant features in the patterns [stages 3 (C_D) and 4 (CD)]. This means that they possess a filtering mechanism that keeps their attention focussed on the relevant features of the patterns, but at the moment they were required to shift their attention to the irrelevant features, one half of the patients failed and the other half showed impairments. The second time the patients should shift their attention, i.e. back to the former feature in the patterns, they were not impaired.

In the reversal of response, the patients tended to be impaired too. Detailed analysis showed that patients were impaired only in the initial learning. Other studies have shown the same deficit in OCD patients on the Object Alternation Test (3–5), but in the two previous studies with the Intra/Extra Dimension test, the researchers failed to find any significant impairment of the OCD patients on response reversal [i.e. stage 2 (SDR)] (12, 13). The reason for this discrepancy might be that the Object Alternation Test draws on an internal behaviour system, whereas the Intra/Extra Dimension test draws on an external behaviour system, and that the mental components being associated in the two tests are different. In the Intra/Extra Dimension test, a visual gestalt is associated with a reward, whereas in the Object Alternation Test, it is a motor act that is associated with a reward. Seen in relation to the frontostriatal loops, it may mean that the loop processing sensory inputs and rewards is less affected than the loop processing motor output and rewards.

Inhibitory control and prepotent response in the prefrontal cortex

The results showed that once the patients had learned the reversal of response and shift of attention, they performed as well as the controls [i.e. performance on stages 5 (CDR), 7 (IDR) and 9 (EDR)]. Roberts & Wallis (28) have used the Intra/Extra Dimension test in an animal model to investigate the cognitive functions of the prefrontal cortex. According to Robert & Wallis, suppression of prepotent responses is an intrinsic property of the prefrontal cortex as a whole. If several prepotent responses are available, the responses are controlled by the lateral prefrontal cortex, and if only one prepotent response is available, the response is controlled by the orbitofrontal cortex.

The number of prepotent responses or familiarity with test responses therefore may be an explanation for the different results on the various frontal lobe tests: the performance of OCD patients on the Letter fluency and WCST may be normal because the materials or principles in these tests were familiar to the patients or did not involve a prepotent response, whereas the performance on tasks in Intra/Extra Dimension and on the Figural fluency may be impaired because the material or principles in the tests were unfamiliar to the patients or involved a shift relative to the prepotent response. Familiarity with the tasks implies that the subjects have several prepotent responses attached to a given performance on the test, and subjects having an intact lateral prefrontal cortex will therefore not fail on these tasks. The opposite will be the case for unfamiliar tasks, where the subjects have to associate reward with a new stimulus or new act. OCD patients can do this, but they exhibit problems with breaking this association afterwards.

Conclusion

In this study, we have employed several tests of frontal lobe functions in patients with OCD compared to normal controls. The smell identification test sensitive to affected areas in the orbitofrontal cortex did not show any significantly impaired performance in the OCD patients. In the Letter fluency and WCST, there were no significant impairments in the patient group, but performance on the Figural fluency showed a significant impairment. We suggest that the latter test actually demanded the ability to generate new strategies, whereas the former two tests relied on already established strategies in the subjects.

In the Intra/Extra Dimension test, patients were impaired in reversing their response on reinforced patterns and they were impaired on shifting their attention to other perceptual aspects of the patterns. We suggest that an affected orbitofrontal cortex gave patients problems reversing responses and shifting attention in the first round, but as patients had their second round on the tasks, they could perform the reversals and shifts without problems.

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