Neurocognitive dysfunction in patients with obsessive compulsive disorder

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Abstract
Objective: Although a dysfunctional prefrontal-striatal system is presupposed in obsessive–compulsive disorder (OCD), this is not unequivocally supported by neuropsychological studies. This study aims to study the neurocognitive dysfunctions in OCD patients, compared to controls; to study the variations in neurocognitive deficits with the duration of illness, as well as, the severity of the disease. **Method:** Thirty OCD patients were compared with thirty, age and education matched control subjects on computer based tests measuring executive functions, vigilance and spatial working memory. **Results:** OCD patients performed poorly on all the neuro-cognitive parameters as compared to controls. The severity of illness had a positive correlation with poorer performance on CPT. There were no significant correlations between duration of illness and any parameters of cognition. **Conclusion:** The results suggest that OCD patients perform significantly worse on cognitive measures than controls. This is consistent with their poorer functional outcome. The results further indicate that on the basis of severity OCD patients are qualitatively distinguishable in neuropsychological terms, given their difference in the profiles of cognitive impairment.

Keywords: OCD; Cognitive functions; Executive functions; Vigilance; Working memory

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Introduction

Obsessive compulsive disorder (OCD) has emerged from being considered a rare, neglected, untreatable and trivial illness to one of the five most prominent brain based mental disorders and one of the ten medical illnesses associated with greatest worldwide disability. There is now promoted awareness that like schizophrenia, mood disorders and neurological disorders, OCD may be associated with a distinct pattern of cognitive impairment.

Ascertaining whether the cognitive impairment is a function of the present disease state- severity and duration; or a long-term, stable trait has both heuristic and clinical implications. Cognitive deficits could be functioning as an intermediate variable between neurobiological abnormalities and OCD symptoms. Reductions in social competence and the capacity for independent living and vocational success may be the result of neurocognitive compromise.

Brain regions implicated to be involved in the pathogenesis of OCD are orbitofrontal cortex, anterior cingulate cortex, basal ganglion, thalamus and some limbic structures.[1,2] Neuropsychological testing has revealed evidence of impairment in visuospatial abilities[3], non-verbal memory[4,5] and executive function.[6] However, results of the neuropsychological studies, have been inconsistent. Some report deficit in attentional set shifting abilities, response inhibition and trial and error learning.[7,8] Basso et al[8] showed that abnormalities in executive function were related to comorbid depression severity and argued that conflicting findings in past studies regarding executive functioning are due to comorbid depression. Depression is commonly comorbid with OCD. The cognitive dysfunctions that have been demonstrated in the patients of OCD could in part be because of co-morbid depression.

Involvement of fronto-striatal systems is suggested by deficits in executive functioning, especially with respect to flexibility on tasks requiring set shifting. These executive domain deficits may explain partly the performance difficulties seen in patients with OCD in other cognitive domains.[5] Executive function deficits in OCD are also being linked to poor decision making processes related to the orbitofrontal cortex.[10] In contrast, Cohen et al[11] reported that OCD patients showed deficits in visual-constructional area, rather than executive functions. Deckersbach et. al.[12] reported that concurrent explicit and implicit information-processing demands interfere with implicit learning in OCD patients. The patients with OCD showed deficits in cognitive flexibility.[13] Many studies have documented a correlation between OCD and spatial working memory dysfunction, especially for more difficult tasks.[14]

This study had three aims: first was to assess neurocognitive functions in patients with diagnosed OCD and to compare them with healthy controls, on the parameters of executive functioning, working memory and vigilance. Secondly, we studied the impact of severity of the disease on the neurocognitive parameters and finally the impact of duration of OCD on neurocognition was studied. Confounding by comorbid depression was avoided in the present study by excluding patients with depression.

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Methods

The study was a time limited, single-centre study with a case-control design and was conducted from January 2005 to November 2005. Subjects were screened consecutively from the adult psychiatry Out Patient Department, (OPD) of King George Medical University, Lucknow, on specified OPD days.

Subjects

Patients from an outpatient section of the department of psychiatry, K.G's Medical University, Lucknow, were screened. The potential cases were interviewed by a psychiatric resident, and their medical records were reviewed whenever relevant. A consultant psychiatrist audited the first phase results and confirmed or rejected the diagnosis. Finally, two psychiatrists set the diagnosis, blind to each other's classification, using written information collected about the patients. Only the patients who received the diagnosis of OCD, according to ICD-10 DCR[15], were included. Retrospective assessments in both the groups were based on records and history given by reliable informants. Patients without records or informants were not taken for study. The patients between 18 to 45 years of age and at least 10 years of education were included in the study. Patients having severe OCD which is incapacitating (Y-BOCS score>31), psychotic symptoms and co-morbid psychiatric illness including any co-morbid anxiety disorders, concurrent major illness or systemic dysfunction (including seizures), history of head injury severe enough to cause unconsciousness, history of substance abuse or dependence and patients with history of electroconvulsive therapy (ECT) in the past 6 months were excluded. Patients who were on a stable dose of a single SSRI for the past 3 months were included. Patients currently taking other psychotropic medications were excluded. Patients were also screened on Hamilton Rating Scale for Depression (HAM-D)[16] and patients with a score of >17 were excluded. All the subjects were assessed for intellectual capacity by a clinical psychologist on Bhatia's Battery[17] and subjects with IQ < 70 were excluded from the study. The severity of illness was assessed using the Yale-Brown Obsessive Compulsive Scale (Y-BOCS).[18]

The controls were taken from the friends and caregivers who were not blood related to the patient and were matched for education. The ethnic background of the patient and controls was similar. Those having a present, past or family history (in first degree relatives) of psychiatric illness and history of substance abuse were excluded from control group. The 12 item General Health Questionnaire (GHQ)[19] was administered to healthy subjects. Those with a score of more than 3 were excluded from the study.

Protocol and procedure

Informed consent was obtained from all the subjects and the study was undertaken in accordance with the Ethical guidelines for biomedical research on human subjects of Indian Council for Medical Research (ICMR) (2000).[20] As the data for the study was collected as a part of a thesis dissertation. The protocol was approved by the university review board before any subjects were recruited.

Assessment was undertaken on a semi-structured socio-demographic proforma which required patient information regarding demographic and personal details of the patients and informants, complaints of the patients, history of present illness, details of medical or surgical interventions, past history, family history, personal history, premorbid personality, details of physical examination, mental status examination and diagnostic formulation. The diagnosis was made using ICD-10 DCR. Patients were then screened on Y-BOCS for severity and Y-BOCS symptom checklist, and, inclusion and exclusion criteria were applied. Computer based cognitive tests included Wisconsin Card Sorting Test, Spatial Working Memory Test and Continuous Performance Test. The 12 item General Health Questionnaire (GHQ) 18 was used for the selection of controls.

Cognitive assessments took place in both the groups between 1 pm and 4pm, to minimize the confounding factors of drowsiness. It was further ascertained that they had not taken benzodiazepines (known to impair cognition) in the 8 hrs preceding the cognitive assessments.

All the three tests have been used for research purposes and have been well authenticated for the study of cognitive functions. The psychologist, who administered the tests in our study, was formally trained in their usage during the previous multicenter study. The tests were explained to the patients at the start of each test and all possible queries were answered promptly. They were made to relax and asked to concentrate on the tests, as much as possible. To accomplish this, the tests were administered in a quiet room, with minimal disturbance. Each test was preceded by a mock test series to check the understanding and involvement of the patient in the test. Throughout the tests, the researcher conducted the tests and the patients were not required to do any computer based operation (except in SWMT, where the patients had to press a predetermined keyboard button, in response to a target stimulus). The patients were not required to have any knowledge of computers for the tests. Any queries regarding the tests were addressed, without giving them any clue about the possible solutions. The tests were conducted in a single sitting in all the patients, sequentially with an interval of 15 minutes between each test.

Spatial Working Memory Test (SWMT)

In the SWMT[21,22], which is a test of memory for spatial locations, the subject views a brief presentation of black circle on a computer screen and is then asked to point the location of circle after a delay of '0' second and 20 seconds, randomly. During the 20 second delay, the subject was engaged in a distraction task (by repeating continuously a 3 digit number, appearing on the screen).The result in the SWMT is obtained from the number of correct responses and the number of non-adjacent errors at 0 second and at 20 second delay respectively.

Continuous Performance Test (CPT)

Sustained attention, vigilance and impulse control is assessed by CPT.[23,24,25] The test requires a participant to respond to a specified target when it is presented spontaneously within a stream of interfering visual stimuli. The task involves monitoring a random series of geometrical figures. It requires one to distinguish targets from non-targets (an ability known as sensitivity). The results obtained are in terms of correct responses, wrong responses, missed responses and the reaction or response time. In the test, the target stimulus is rare in frequency and presentation latency is brief. A total of 328 stimuli are presented, of which 28 are for practice. Stimulus duration and interstimulus latency are 50 milliseconds and 1000 milliseconds respectively.

Wisconsin Card Sorting Test (WCST)

The WCST can be considered a measure of executive function requiring the ability to develop and maintain an appropriate problem-solving strategy across changing stimulus conditions in order to achieve a future goal.[21,26,27] It is the classic test for dorsolateral prefrontal cortex function.[28] There are 4 stimulus cards. These stimulus cards reflect three stimulus parameters-colour, form and number. The response cards display figures of varying forms (crosses, circles, triangles or stars), colours (red, blue, yellow or green) and number of figures (one, two, three or four). These cards are numbered from 1 to 64 on the lower left corner of the reverse side to ensure a standard order of presentation. It can be applied to subjects in the age group of 6½ to 89 years.

The tests used (WCST, CPT, and SWMT) are independent of language. They are based on symbols only. The instructions were given in Hindi. The computer based tests have been used in other multi-center multinational studies. They were not adapted in any form for the current study.

Data analysis

The mean scores of the patients and the controls were compared using Student's t – test (two tailed), which is a statistical hypothesis test based on the t-distribution and is used to test for a difference between the means of two groups. A p value of <0.05 was considered significant. Correlation coefficients were obtained between severity of illness and various parameters of cognition tests. Similarly correlation coefficients were obtained between duration of illness and parameters of cognition tests. There was no change in the significance or the analyses on application of the Bonferroni corrections.

Results

110 patients were screened in OPD. 30 patients with OCD were included in the study. Similarly, 60 control subjects were screened, out of whom 30 fulfilled the selection criteria and were assessed in the study. 26 patients were taking fluoxetine, while 4 were taking sertraline. Both the subject group and the control group were matched for age, sex and education.

As shown in Table I there was no significant difference between the two groups on the parameters of age, sex and education. The control group (n=30) had a mean age of 34.26 years, 80% of them were females with a mean 10.80years of education. In the patient group (n=30), mean age was 34.98 years, 82% of them were female with a mean of 11.91 years of education. 21 patients and 23 controls had an urban background, 12 patients and 15 controls were married and 7 members in each group had family income of less than Rs 5000/month, while the rest had family income more than that. None of the parameters were significantly different, when compared using a chi-square test.

The mean duration of illness (MDI) for the patient group (n=30) was 4.77 years (S.D. =3.53), the mean severity of illness (MSI) for the patient group was 23.87 on Y-BOCS (S.D. =5.15). The mean score on the HAM-D of the patients was 10.93 (S.D. = 3.23).

Table II shows the results of comparison of the patient group and the control group on the CPT, SWMT and WCST. The control group and the patient group showed significant differences on various parameters, as shown.

Table I: Demographic profile

	Control group (n=30)	*Experimental (n=30)*
Age (in years) Mean(SD)	34.26(11.11)	34.98 (10.63)
Sex Male Female	20 (%) 80 (%)	18 (%) 82 (%)
Years of education Mean (SD)	10.80 (2.49)	11.91(3.61)

Table II: Comparison of scores on various tests

	Control group N=30 Mean (SD)	*Experimental N=30 Mean (SD)*	*Significance t*	*p*
Continuous Performance Test (CPT)				
Correct Responses	34.07 (3.33)	26 (8.16)	4.95	<.0001
Wrong Responses	5.27 (2.41)	12.00 (6.17)	5.51	<.0001
Missed Responses	10.00 (3.39)	17.00 (8.43)	4.16	<.0001
Response Time	0.74 (0.09)	0.88 (0.21)	1.19	0.2389
Spatial Working Memory Test (SWMT)				
Correct Responses at Zero second delay	22.86 (0.86)	22.50 (0.99)	1.48	0.1443
Non adjacent errors at Zero second delay	0.27 (0.57)	0.30 (0.46)	0.25	0.8035
Correct Responses at 20 second delay	22.46 (0.81)	18.00 (3.21)	7.86	<.0001
Non adjacent errors at 20 Second delay	0.40 (0.61)	0.83 (1.15)	1.78	<.0001
Wisconsin Card Sorting Test (WCST)				
Categories completed	4.17 (1.81)	2.35 (1.15)	3.99	<.0002
Perseverative error	26.06 (15.30)	44.50 (21.88)	3.72	<.0005

d.f. for all comparisons was 58

Table III depicts correlation coefficients between the severity of illness as indicated by YBOCS score and various parameters of cognition tests utilized in the study. Only one correlation coefficient was found to be statistically significant. Missed responses on CPT were found to have a significant correlation with the YBOCS score.

Table IV shows the coefficient scores between various parameters of cognition tests with duration of illness. None of the correlation coefficients were found to be statistically significant.

Table V gives the details of the types of obsession and compulsions in the patients .

Table III: Correlation coefficient between severity of illness (YBOCS score) and parameters of cognition tests

Cognition Test Parameters	*Correlation coefficient*	*p value*
Continuous Performance Test (CPT)		
Correct Responses	- 0.031	0.872
Wrong Responses	0.008	0.966
Missed Responses	0.519	0.003
Response Time	- 0.203	0.282
Spatial Working Memory Test (SWMT)		
Correct Responses at Zero second delay	0.164	0.386
Non adjacent errors at Zero second delay	0.026	0.893
Correct Responses at 20 second delay	0.298	0.110
Non adjacent errors at 20 Second delay	- 0.090	0.636
Wisconsin Card Sorting Test (WCST)		
Categories completed	0.152	0.423
Perseverative error	- 0.192	0.310

Table IV: Correlation coefficient between duration of illness and parameters of Cognition tests

Cognition Test Parameters	*Correlation coefficient*	*p value*
Continuous Performance Test (CPT)		
Correct Responses	- 0.062	0.744
Wrong Responses	0.224	0.235
Missed Responses	0.155	0.414
Response Time	- 0.064	0.738
Spatial Working Memory Test (SWMT)		
Correct Responses at Zero second delay	- 0.028	0.885
Non adjacent errors at Zero second delay	0.053	0.780
Correct Responses at 20 second delay	0.060	0.752
Non adjacent errors at 20 Second delay	0.027	0.889
Wisconsin Card Sorting Test (WCST)		
Categories completed	- 0.294	0.115
Perseverative error	0.030	0.876

Table V: Details of clinical characteristics

Type of Obsessions:		*Type of Compulsions:*	
Single	26.67%	Single	26.67%
Multiple	73.33%	Multiple	73.3%
Contamination	80%	Cleaning/Washing	80%
Doubt	60%	Checking	53.3%
Aggressive	0%	Repeating	40%
Sexual	20%	Counting	33.3%
Hoarding	0%	Ordering	13.3%
Religious	20%	Hoarding	0%
Symmetry and exactness	13.3%		
Somatic	6.67%		

Discussion

The main finding in the study was impairment in executive functioning, working memory and attention in OCD patients, which was significantly affected by increasing severity, but not by the duration of the disease. The current sample consisted of depression-free patients with OCD, with a mean Hamilton–Depression score of 10.93, which is indicative of mild depressive symptoms.

The poor performance shown by the patients on various parameters of the WCST, CPT and SWMT demonstrated that they had poor executive functions viz. deficits in set shifting, inhibition control and trial & error learning; poor attention and poorer working memory as compared to the control group. In patients with OCD, one would expect to find a profile of deficits associated with prefrontal-striatal dysfunction.[2,8,29] 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 dysfunction in the orbitofrontal cortex may lead to cognitive changes that might include executive deficits leading to, namely; errors in set shifting, focused attention and working memory.[30] The most prominent feature of executive/frontal dysfunction is perseverative behavior. It has been shown that tasks like WCST and CPT activate a neural network that includes important areas of the brain such as dorsolateral region of prefrontal cortex.[31,32] These regions have numerous connections with the cortical systems involved in information processing. Thus, our findings are suggestive of a frontal lobe dysfunction as indicated by impaired performance on WCST.

The 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.[33] Studies in OCD patients consistently showed hypermetabolism of the ACC during symptom provocation[34] at rest[35] and during the execution of neuropsychological tasks.[36] 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.[37,38] 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.

The findings on SWMT are consistent with earlier studies.[14,39] Nevertheless, a link between OC behaviour and working memory deficits has not been clearly demonstrated 10,39 thus inviting future studies. Vander Wee et al.[14] suggested the deficits in SWMT in patients with OCD was significant only for a region involving the anterior cingulate cortex hence suggesting that the abnormal performance pattern may be secondary to another aspect of executive dysfunctioning of OCD.

On analysis it was found that the missed responses on CPT

had a significant and positive correlation with the YBOCS score. This indicates that the severity of illness is associated with greater attention deficits. One possible speculation for the cognitive deficits could be that the frontal and the cingulate cortex are crucial for the activity of generating internal cues for initiating, planning and monitoring behavioural responses. The basal ganglia, in turn, are partly responsible for the gating mechanisms of both inner and external sensory input (Baxter et al[2]). As a consequence of the hyperactivity of the circuit, OC patients might be overwhelmed by internal cues, and might take longer to choose those relevant to the ongoing task and to exclude the irrelevant ones.

The cognitive profile did not vary with the duration of the disease, thus signifying the relative stability of the brain dysfunction with time, unless the disease severity increases. However, these findings need to be replicated in larger studies.

In the current study, the control group was well matched for age, gender and education so that the confounding factors for assessment of cognitive functions and functional disability would be minimized. The selection criteria were made stringent to minimize the confounding factors in evaluation of cognitive functions. Such confounding factors could have been extremes of age, comorbid psychiatric or significant physical disorders, significant substance use or use of medications associated with cognitive changes. Severe and extreme OCD were not included as they were found to be too affected (both emotionally and cognitively) to complete the assessment during the preliminary stage of study i.e. before the recruitment of patients in this study.

The specified tests were chosen because; evidence has suggested differential impairment especially in the cognitive domain related to the frontal system, executive and attentional systems and medial temporal memory system. Moreover, these measures are important in regard to functional outcome. The computerized version of these tests ensured greater reliability, objectivity and standardization, as well as a less confrontational and formal approach.

As the selection criteria were rigid, only multicenter studies can provide a larger sample base. Premorbid IQ of the patients was not assessed. All the patients in our study were receiving anti-OCD medications and the effect they can have on cognition is yet to be ascertained completely. Finally, to come to a concrete conclusion a long term follow up study would have been better but time as well financial constraints have to be taken into consideration.

Conclusion

The finding from the study suggest that OCD patients perform significantly worse on the selected cognitive measures than controls. The poorer cognitive functions in the patients may contribute to the functional impairment seen in OCD. The results further indicate that on the basis of severity, OCD patients are qualitatively distinguishable given their difference in the profiles of cognitive impairment.

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