

Executive Functions of Obsessive Compulsive Disorder and Panic Disorder Patients in Comparison to Healty Controls

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ABSTRACT

Introduction: Patients with obsessive compulsive disorder (OCD) have impaired cognitive functions, including attention, verbal and visual memory, and visual-spatial abilities as well as executive function. But some studies did not show any disturbance in executive function of patients with OCD. To date, only few studies have been conducted on neuropsychological functioning of patients with panic disorder (PD). There are limited studies to reach a definite conclusion on executive functions of patients with OCD and those with PD. In this study, we aimed to measure executive functions of patients with OCD and those with PD compared with those of healthy controls. Although there are many studies on cognitive functions of patients with OCD, there appears to be no consistency in results and no findings have been obtained to enable us to reach definite conclusions. Although there are very few studies on neuropsychological functions of patients with PD, impairments on a set of cognitive functions have been demonstrated. To date, no finding with respect to impairment in executive functions of patients with PD has been published. PD and OCD are disorders manifesting similar characteristics, with the presence of anxiety and avoidance behavior. Besides this, patients with OCD also have symptoms such as obsessions and compulsions that are characteristics of this disorder. We aim to compare executive functions in the three groups (patients with OCD, those with PD, and healthy controls) in this study.

Method: Seventeen patients with OCD and 15 patients with PD who were diagnosed according to Diagnostic and Statistical Manual of Mental Disorder

-IV-TR (DSM-IV-TR) and 26 healthy control subjects were included in this study. Patients who used medication as well as those with medical illnesses and Axis-I comorbidities were excluded. The healthy control group subjects were matched with the patients in terms of age, gender, and education. Structured Clinical Interview for DSM-IV Axis-I Disorders-Clinical Version (SCID-I), Hamilton Depression Rating Scale (HDRS), and Yale-Brown obsessive compulsive scale tests (Y-BOCS) were administered to the patients. Trail Making Tests (TMT), verbal fluency tests (Controlled Oral Word Association Test and Categorical Naming), Stroop Test, and Wisconsin Card Sorting Test (WCST) were administered to the study groups.

Results: According to our results, there was no statistically significant difference between the three study groups with respect to executive functions. There was also no significant correlation between executive tests' results and Y-BOCS in the OCD group.

Conclusion: The results of the PD group are in line with that reported in literature. The results of the OCD group can be explained by a lack of medication usage and any comorbidity including depression. A small sample size is the major limitation of our study.

Keywords: Obsessive compulsive disorder; panic disorder; executive function, Wisconsin card sorting test, stroop test

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INTRODUCTION

Obsessive compulsive disorder (OCD) and panic disorder (PD) have some common shared characteristics primarily including anxiety due to threat perception and avoidance behavior. Nevertheless, obsessions and compulsions at a level that disrupts daily routines are descriptive or core symptoms of OCD.

Clinically, OCD and PD are disorders where similar symptoms are presented and they are placed together among anxiety disorders because according to Diagnostic and Statistical Manual of Mental Disorder-IV-TR (DSM-IV-TR), anxiety is considered to be the core symptom (1). In DSM-5, OCD has been excluded from anxiety disorders and has been classified under the title of obsessive compulsive and related disorders along with a group of other disorders (2).

Neuropsychology deals with brain-behavior relationship and examines how the brain controls higher cognitive functions of the brain including language, memory, and visual-spatial skills. Neuropsychological assessments were first developed for paralysis, tumor, or neurological diseases such as degenerative diseases and were later applied for psychiatric disorders, where no lesions were demonstrated in the brain (3). Neuropsychological assessment of psychiatric disorders is thought to contribute toward better understanding of neuroanatomical regions and neurobiological processes related to these disorders.

Upon reviewing neuropsychological studies conducted for OCD and PD, it becomes apparent that more studies are performed on patients with OCD. In OCD, majority of the cognitive functions such as executive functions, visual-spatial skills, attention, and verbal and non-verbal

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memory have been studied. In OCD studies on executive functions are more prominent than those on other cognitive functions; there are also findings that the deterioration in memory and visual-spatial skills are secondary to executive functions (4,5). Executive functions are cognitive functions with the ability to alter behavior when necessary by following the environmental context where planning, organizing, and behavior take place. It is thought that OCD is related to a dysfunction in prefrontal cortex and subcortical brain circuits and that this dysfunction impairs an executive function characteristic, the ability of set-shifting (6). Wisconsin Card Sorting Test (WCST) is a widely used neuropsychological test that measures the ability of set-shifting. There are studies demonstrating the impairment in this function in patients with OCD (6,7,8,9). On the other hand, there are also studies published that conclude that there are no impairments of set-shifting in OCD (10,11,12,13). In 9 of the 19 studies examining fluency, which is another executive function, the OCD group displayed similar performance to healthy controls and in 7 of those studies, patients with OCD performed significantly poorer than healthy controls (14).

Conceptual thinking and planning are also considered within executive functions. These functions are mostly assessed by employing the Tower of London or Hanoi Tower Test. Although deterioration of comprehension in patients with OCD was demonstrated in some studies, there are also views that this impairment may be due to a problem in the spatial process memory (6,15).

It is apparent that the number of studies researching on cognitive functioning in general and in particular, on executive functions are far less in patients with PD. Purcell et al. (16) have compared cognitive functioning of patients with OCD, PD, and unipolar major depression with those of healthy controls and have not found any significant differences between the groups. Boldrini et al. (17) have assessed verbal fluency and set-shifting among executive functions and demonstrated that these functions were similar among healthy controls and patients with PD; however, these functions were more impaired in patients with OCD than in healthy controls. In a research where OCD and PD groups were compared and no healthy controls were included, it was demonstrated that in PD, set-shifting and interference inhibition functions remained unaffected (18). Although there are many studies showing frontal-striatal dysfunction affecting executive functions in OCD, there is no data on the etiology of PD suggesting any such impairment.

It has not been determined whether OCD and PD are similar or different compared with each other and compared with healthy controls with respect to cognitive functioning, symptoms for which may be both similar as well as different. Although impairment in executive functions in OCD has been shown in many studies, there is insufficient data on PD. Also there is no consensus on the impairment in executive functions of patients with OCD. This study aims to show that there is no impairment in executive functions in patients with PD compared with healthy controls and that executive functions manifest differently in patients with OCD compared with healthy controls. For both disorders, patients without comorbidity and use of medicine are targeted to be included into the study.

METHOD

Sample and Control Group: Seventeen patients with OCD and 15 patients with PD between the ages of 18 and 60 years who had applied to the Marmara University Education and Research Hospital's Psychiatry Clinic between February 2012 and March 2013 as well as healthy controls matched with the patients for age, education level, and gender were included. An approval was obtained for this research from Marmara

University Education and Research Hospital Local Ethics Committee on 02.23.2012 (protocol number 09.2012.0014). In addition, all participants were informed about the study and processes to be performed, and volunteer's approval forms were collected.

Of the individuals who were included in the patient groups, those with comorbid Axis-I psychiatric disorder according to DSM-IV-TR, those who have a medical condition requiring the use of psychotropic medicine within the past 1 month, those who scored ≥ 8 on the Hamilton Depression Rating Scale as well as those who were illiterate were excluded from the study. Healthy controls were also excluded if diagnosed with Axis-I disorder according to DSM-IV-TR, presence of a medical condition requiring permanent use of medicines, and for being illiterate.

Following psychiatric assessment of the patient and healthy control groups, obtaining their socio-demographic data, and making a diagnosis, a Structured Clinical Interview for DSM-IV Axis-I Disorders-Clinical Version (SCID-I-CV) was applied. Then, all participants were assessed using the Hamilton Depression Rating Scale (HAM-D) and patients with OCD were assessed using the Yale-Brown obsessive compulsive scale (YBOCS). Then, executive function tests were performed. Trail making tests (TMTs) A and B, verbal fluency tests, Stroop Test, and WCST were applied. The assessment lasted for approximately 2-2.5 hours for each participant.

Data collection tools

SCID-I-CV: It is a test for screening and diagnosing Axis-I disorders structured in accordance with DSM-IV-TR (19). Its validity and liability in Turkish has been performed (20).

Hamilton depression rating scale (HAM-D): HAM-D is a clinician rated scale to assess patients' depression levels. It includes 17 items. A score of ≥ 14 indicates depression. Its validity and liability in Turkish was performed by Akdemir et al. (21); test and re-test reliability was found to be $r=0.85$; and similar scales validity was found to be $r=0.48$.

Yale-Brown obsessive compulsive scale (YBOCS): It was developed for assessing the frequency and severity of obsessive compulsive symptoms (22). It includes 19 items. The points of the first 10 items assess the severity of OCD. Its validity and liability in Turkish has been performed (23).

Executive function test: These neuropsychological tests selected for assessing participants' executive functions were conducted by the researcher who had received training in this field from a consultant psychologist prior to the implementation. For TMT and WCST, the versions that were used in Neuropsychological Test Battery for Cognitive Potentials (BİLNOT) study were employed. Standardization of BİLNOT for our society has been performed (24,25,26). For verbal fluency and Stroop Tests, the version standardized by Tumaç was used (27).

Trail making test (TMT): It consists of two parts (A and B). In part A of the test form, individuals are requested to connect consecutive numbers (1-2-3-4-...) in the correct order by drawing a line. In part B, participants are requested to connect consecutive numbers and letters on the test form, connecting a number to a letter (1-A, 2-B, 3-C-...), in the correct order by drawing a line. TMT-A is used for measuring psychomotor speed; among executive functions, TMT-B is used for measuring complex attention, planning, set-shifting, and interference. The duration of the test completion time is recorded. (26).

Verbal fluency tests: (K, A, and S test and Counting Animal Names Test): Participants are requested to count a word (lexical) or a categor-

ically linked name of an animal (semantics) beginning with letters K, A, and S. These tests are used to assess perseverance, fluency, and mental recollection. During standardization of the test to Turkish, the letters K, A, and S were used (27). This test is commonly used for assessing semantic memory; the study to obtain the norms for the Turkish population was done (28,29). The total number of remembered words, uncategorized words, and perseverance are recorded.

Stroop test: In this test, a state of interference is created by requesting to say the color of a set of words consisting of red-blue-green words; however, these words are printed in colors discordant with the words. The objective is to suppress the automatic tendency to read the word but say the color of the text. Reading mistakes indicate a disability to suppress the tendency to give more automatic answer in a state of interference. This is a neuropsychological test that measures the speed of information processing, ability to switch focus of perception on demand, and resistance toward disruptive effects of automatic processes, parallel processing of focused and unfocused stimulants (30).

Wisconsin card sorting test (WCST): The WCST test used in this research was applied in a specific program format prepared on a computer. One of the four stimulant cards (each with a different color, number, and shape) is expected to be matched with a fifth card. After 10 correct matches, the category is switched (31). The participant's ability to access information to match cards based on color, shape and number requires abstract thought and conceptualization skills. Even if the participant succeeds, he/she may still make errors in relation to complex attention processes. There are two types of errors: "perseverance type of error" and "failure to maintain set-shifting." In studies, mostly "incomplete number of category," "number of perseverance type of error," and "failure to maintain set-shifting" are being used.

Statistical Analysis

Statistical Package for the Social Sciences version 12.0 (SPSS Inc.; Chicago, IL, USA) statistics software was used for assessments. On evaluating qualitative data, mean and standard deviation values were obtained and the chi-square test was used for comparing such values. On evaluating quantitative data, if there were two groups and they were normally distributed on analysis of data distribution, the parametrical t-test was used; if they were not normally distributed, non-parametrical Mann-Whitney U test was used. If there were three groups when evaluating quantitative data and they are normally distributed on analysis of data distribution, the parametrical test one-way ANOVA was used; if they were not normally distributed, the non-parametrical Kruskal-Wallis test was used.

RESULTS

Seventeen patients with OCD, 15 patients with PD, and 26 volunteer healthy controls matched with the patient group in terms of age, education, and gender were included. Mean ages of the OCD, PD, and control groups are shown in the Table 1. On analyzing gender distribution of the participants, it was observed that the OCD group included 94.1% (n=16) women and 5.9% (n=1) men, the PD group included 73.3% (n=11) women and 26.7% (n=4) men, and the healthy control group included 80.8% (n=21) women and 19.2% (n=5) men (Table 2). On examining the education levels of participants, it was observed that the number of primary school graduates was the highest in the OCD group (35.3%); the number of secondary school graduates was the highest in the PD group (33.3%), and primary school and university graduates were equal in number of samples and percentage (30.8%) in the control group (Table 2).

Table 1. Demographics, clinical symptoms and results of psychiatric scales (age, duration of illness, YBOCS, HAM-D)

	OCD (n=17)	PD (n=15)	Control group (n=26)		
	Mean±SD	Mean±SD	Mean±SD	f	p
Age	32.76±9.07	30.73±8.63	31.53±8.46	0.225	0.799
Duration of illness (year)	3.79±4.11	2.96±4.04			
YBOCS (total)	26.56±4.87				
HAM-D	2.58±1.83	1.86±2.41		t	p
				0.959	0.398

SD: standart deviation; OCD: obsessive compulsive disorder; PD: panic disorder; Y-BOCS: Yale-Brown obsessive compulsive scale; HAM-D: Hamilton depression rating scale

Table 2. Demographics, clinical symptoms and results of psychiatric scales (gender, marital status, education, treatment history)

	OCD (n=17) n (%)	PD (n=15) n (%)	Control Group (n=26) n (%)		
				χ ²	p
Gender				2.543	0.280
Female	16 (94.1)	11 (73.3)	21 (80.8)		
Male	1 (5.9)	4 (26.7)	5 (19.2)		
Marital status					
Married	13 (76.4)	9 (60)	12 (46.1)		
Single	4 (23.6)	6 (40)	14 (53.9)		
Education				4.238	0.835
Literate	1 (5.9)				
Primary school	6 (35.3)	3 (20.0)	8 (30.8)		
Secondary school	3 (17.6)	5 (33.3)	6 (23.1)		
High school	3 (17.6)	3 (20.0)	4 (15.4)		
University	4 (23.5)	4 (26.7)	8 (30.8)		
Treatment history					
Yes	6 (35.3)	4 (26.7)			
No	11 (64.7)	11 (73.3)			

OCD: obsessive compulsive disorder; PD: panic disorder

The mean duration of illness was 3.79±4.11 years in the OCD group and 2.96±4.04 years in the PD group. The average of the total HAM-D score for the OCD group was 2.58±1.83 and for the PD group was 1.86±2.41. Majority of both patient groups included individuals who have not received any treatment in the past. The average of the total YBOCS score for the OCD group was 26.56±4.87 (Table 1).

It was determined that neither of the three groups were different in terms of age, education, and gender (Table 1, 2) Upon comparing HAM-D scores of OCD and PD groups, no statistically significant difference was found (Table 1). No difference in neuropsychological tests was determined between OCD, PD, and control groups (Table 3). On analyzing the correlation of neuropsychological test results and YBOCS scores of patients with OCD, no significant relation was established (p>0.05).

Table 3. Neuropsychological tests scores in OCD, PD and healthy controls, correlation between YBOCS scores and neuropsychological tests for OCD group

	OCD Mean±SD	PD Mean±SD	Control group Mean±SD	p
WCST				
WCST-toc	76.70±21.02	71.40±19.10	79.73±24.39	0.51
WCST-tne	51.29±21.02	56.60±19.10	48.26±24.39	0.51
WCS-tp	32.41±21.34	35.86±15.71	30.38±20.82	0.69
WCST-npe	23.47±15.80	25.06±7.98	21.00±15.86	0.66
WCST-pe	27.82±16.40	31.66±12.44	26.53±16.00	0.58
WCST-cc	4.05±2.63	3.53±2.82	4.73±2.86	0.40
WCST-ppe	21.73±12.81	24.74±9.72	20.70±12.47	0.57
WCST-rfc	23.25±19.78	26.57±18.82	23.14±20.90	0.86
WCST-clr	47.75±22.66	42.81±19.29	51.39±26.89	0.54
WCST-fsm	1.23±1.48	1.33±1.11	1.50±1.56	0.68
TMT				
TMT-A	55.35±39.48	36.40±13.29	38.07±15.93	0.05
TMT-B	149.37±112.33	113.80±79.23	108.69±45.94	0.24
TMT-B-TMT-A	99.68±95.54	76.73±69.59	70.65±39.40	0.39
Verbal fluency				
VF-Ac	17.35±4.75	19.46±5.27	19.84±5.18	0.27
VF-Ap	0.23±0.43	0.26±0.59	0.23±0.51	0.96
KAS-n	29.52±12.83	34.20±13.70	37.34±15.91	0.23
KAS-p	0.47±0.94	0.33±0.81	0.34±0.56	0.83
Stroop test				
ST-dd	49.52±27.55	45.46±13.72	40.96±13.89	0.34
ST-e	4.47±4.97	4.06±3.34	4.06±3.34	0.29
ST-sc	2.47±2.60	3.13±2.87	1.73±1.40	0.15
SD: standard deviation; OCD: obsessive compulsive disorder; PD: panic disorder; WCST: Wisconsin card sorting test; WCST-tnc: WCST-total number of correct; WCST-tne: WCST-total number of errors; WCST-tp: WCST-total perseverative responses; WCST-npe: WCST-total number of non-perseverative errors; WCST-pe: WCST-total number of perseverative errors; WCST-cc: WCST-number of completed categories; WCST-ppe: WCST- percentage of perseverative errors; WCST-rfc: WCST-number of responses to finish the first category; WCST-clr: WCST-number of conceptual level responses; WCST-fsm: WCST-failure in set-maintenance; TMT: trail making test; TMT-A: duration of complete TMT-A (second); TMT-B: duration of complete TMT-B (second); TMT-B-TMT-A: difference of completion time; VF-Ac: number of counting names of animals; VF-Ap: number of perseverative errors (animal names); KAS-n: number of words counting with K, A, S; KAS-p: number of perseverative errors (K, A, S); ST: stroop test; ST-dd: difference of duration (second); ST-e: number of errors stroop test; ST-sc: number of spontaneous correction stroop test				

DISCUSSION

In our research, executive functions of patients with OCD were found to be similar to those of patients with PD and of healthy controls. There are studies in the literature that show impaired executive functions of patients with OCD compared with those of healthy controls as well as studies that show no difference between effective functions of patients and healthy controls (5,7,8,9,10,11,12,13).

There may be various explanations for not reaching consistent conclusions in researches. Comorbidities along with OCD and particularly high rates of depression that accompany this disorder appear to be a significant

reason. In a study that compares patients with OCD, who do not use medication, and who do not have any comorbidity in terms of frontal lobe functions, no difference was determined between the groups in WCST and verbal fluency tests (32). In their research using WCST and TMT tests among others, Basso et al. (33) demonstrated that performances of patients with OCD were more impaired than those of healthy controls; however, when evaluations were repeated by taking patients' depression levels into consideration, it was revealed that executive functions of the patients were similar to those of healthy controls. Moritz et al. (34), have found differences in WCST and creative verbal fluency test scores between OCD patients with high Beck Depression Inventory and HAM-D levels, OCD patients with low Beck Depression Inventory and HAM-D levels and healthy controls. Executive functions of patients with OCD with low depression levels were found to be similar to those of healthy controls. Similarly, Ayçiçeği et al. (35) also showed that the difference discovered in executive functions between the patient and healthy control groups disappeared after the effect of the depression was controlled. In the same study, the correlation between impairment in neuropsychological tests and severity of symptoms lost its significance upon repetition, after taking the effect of depression into consideration. In this study, it was emphasized that depression does not affect all areas of neuropsychological evaluation, but only affects executive functions. Therefore, impairment in executive function may develop in OCD as a result of depression and the because of the effects of other comorbidities. Whether patients use any medications during the assessment is another issue that requires to be taken into account when evaluating neuropsychological functions. There are studies published in the literature that show that variances within the serotonergic system affect cognitive functions. There are reports on patients developing serious cognitive problems because of selective serotonin reuptake inhibitors (36). For instance, a young patient with OCD has been presented, who developed apathy, indifference, impaired attention and perseveration after using fluoxetine (37). Besides this, clomipramine, which is often used for treating OCD, causes sedation and with its anticholinergic side effects, is an antidepressant that can impair cognitive functions. It has been reported that shortly after the application of clomipramine, patients experience slowness in reaction time, impairment in verbal learning, and remembering (38, 39). In a research conducted in India, attention, memory, and executive functions of 31 patients with OCD, who have not received any treatment and do not have recent or past major depression, were compared with healthy controls (40). In this study, executive functions were measured using the Controlled Oral Word Association (FAS) Test, WCST, Stroop Test, and a set of evaluation tools that were not used in the present study. Executive functions of patients with OCD who did not use medication were found to be similar to those of healthy controls. In a review, it was concluded that the results of TMT and WCST may show variances between patients who use medication and those who do not (14).

It may be thought that the use of medication may have affected the results in studies where executive functions of patients with OCD were found to be different from those of healthy controls. Another reason for inconsistent results of studies conducted in this field may be the clinical variance of patients with OCD included into the studies. In a study that compared 59 patients with OCD with 59 healthy controls using a wide neuropsychological test battery, an error in spatial working memory, slowness in task planning and starting speed, and recollection error was observed in the "checker group"; an error in spatial recollection was observed in the "obsessive" group; and slowness in task planning and starting speed and an error in recollection was observed in the "mixed" group (41). In this study, "checker" patients with OCD manifested impairment in more areas on neuropsychological tests than the other OCD subgroups; this finding

supports the view that clinical symptom types of OCD may be affecting the results of neuropsychological assessment. In another study, when the patients with OCD were compared according to their YBOCS symptom subtypes, it was determined that "checker" patients had significant deterioration in Hanoi Tower Test measuring executive functions (42). In a review, it was suggested that studies in this field were often conducted on "checker" patients and that fewer studies were being conducted on relatively rare patients with hoarding or patients with obsessional slowness (43). In a recently published meta-analysis, it was emphasized that in OCD, the "washer" subtype was far better in most cognitive fields than the "checker" subtype and that "checker" patients manifested substantial deterioration in executive functions (44). In summary, neuropsychological test performance in OCD appears to be affected by the type of symptoms.

In our study, no correlation was observed between neuropsychological test findings and YBOCS scores in OCD patients. In a recent study, executive functions of 40 patients with OCD were assessed; no correlation was determined between severity of illness and neuropsychological findings (45). Similarly, in another study, no correlation was found between neuropsychological test scores and YBOCS scores of patients with OCD (46). Failure to determine a correlation between YBOCS scores and neuropsychological findings appears to be the common conclusion of many studies (5,14,47,48).

Another result of our study is that executive functions of patients with PD are no different from those of healthy controls. The PD group comprising patients with and without agoraphobia has not performed differently in WCST, TMT-A and -B verbal fluency tests, and Stroop Test compared with the healthy control group. These results are consistent with those reported in literature. Cognitive functions that were impaired in patients with PD were not executive functions. Boldrini et al. (17) have found that patients with PD manifested error in spatial learning compared with healthy controls. In this study too, this function was impaired in patients with OCD; however, they were different from patients with PD and healthy controls because they also manifested errors in visuoconstruction, verbal fluency, spatial working memory, and set-shifting (17). Boldrini et al. (17) have indicated that the error in spatial learning supports the temporal hippocampal system dysfunction hypothesis suggested in relation to anxiety. In a study where cognitive impairment was established in patients with OCD, it was demonstrated that none of the patients with PD who were included in the control group were different from the healthy controls in any of the cognitive fields (6). Another remarkable finding of this study was that neuropsychological performances of patients with anxiety disorders except acute stress disorder and post-traumatic stress disorder were compared with those of control group.

Trail making test performance of patients with PD was found to be impaired in that study and this finding was interpreted in favor of impairment in executive function (46). However, after controlling the effect of alcohol abuse and addiction comorbidity and repeating the evaluations, it was discovered that executive functions of patients were no different than those of healthy controls. Most of the studies suggest that there is no impairment in executive function in patients with PD. Therefore, our results may be deemed consistent with literature.

Limitations

The strength of this study was that it was conducted on a patient group without use of medicine and comorbid mental illness. On the other hand, a study from our country was recently included into those studies that found that executive functions of patients with OCD were impaired compared with those of healthy controls (5). The said research was conducted

with a wider sample group than the present study. Patients not using medicines and without comorbidity were included into this study that compared 72 patients with OCD with 54 healthy controls. In our study, the number of required patients in order to obtain statistically significant differences between groups has not been full field. The low patient number may be deemed as a limitation of the study. Difficulty to identify patients in the clinic without comorbidity and without use of medicines may be the reason for this situation.

No impairment in executive functions that differentiates patients with OCD and those with PD from each other as well from healthy controls was detected in our study. It was seen that OCD and PD groups were not different in terms of executive functions. It may be suggested that additional studies are needed, conducted over larger patient groups without comorbidity and use of medicines and where subgroups of disorders are taken into consideration to overcome the existing contradictory results in this field.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of Marmara University Training and Research Hospital Local Ethics Committee (02.23.2012/09.2012.0014).

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