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The Effects of Demographic Characteristics, Memory Deficits, and Executive Functioning Impairments in Failure to Respond to Fluvoxamine among Patients with Obsessive-Compulsive Disorder in Iran

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Abstract

Background: Identifying treatment-response predictors could help improve treatment protocols as well as appropriately tailoring them to each subject, leading to a more desirable and accelerated recovery in patients. Thus, the present study aimed to investigate the role of demographic characteristics, memory deficits, and executive functioning impairments in failure to respond to fluvoxamine among patients with obsessive-compulsive disorder (OCD).

Methods: This 2-group design (treatment-responsive and treatment-resistant) experimental study explored 76 participants who had received fluvoxamine monotherapy for OCD for ≥6 months. The study participants were from Iran. Four data collection tools were used in this study (ie, Demographic Data Form, WMS-III, WCST, and Y-BOCS). The achieved data were analyzed in SPSS-16 by descriptive statistics, such as mean and standard deviation and frequency and percentages, as well as an independent samples t-test, a chi-square test, and a Fisher exact test at $P < 0.05$.

Results: The present study findings indicated that 56 (81.2%) out of 76 patients with OCD responded to fluvoxamine treatment. A significant difference between the study groups highlighted age as an influential factor in providing a positive therapeutic response to fluvoxamine (P=0.048). However, the groups did not significantly differ in terms of gender (P=0.272), marital status (P=0.753), educational level (P=0.332), disease duration (P=0.276), and occupational status (P=0.473).

While there was no significant difference between the groups (P=0.639) in terms of memory deficits (P=0.639), the response rate to fluvoxamine treatment was significantly higher in those with a healthy executive functioning, compared with patients with impairments in this respect (P=0.043).

Conclusion: The obtained data suggested that fluvoxamine has a favorable efficacy in the treatment of OCD, and especially in young patients with healthy executive functioning.

Keywords: Obsessive-Compulsive Disorder, Fluvoxamine, Pharmacotherapy, Memory Deficit, Executive Functioning, Treatment Response

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Introduction

Obsessive-compulsive disorder (OCD), as a heterogeneous neuropsychiatric conditio n, affects 3% of the glob-

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↑What is "already known" in this topic:
Only age (younger individuals) was a significant predictor of therapeutic response to fluvoxamine, while all other variables were involved. Treatment with selective serotonin reuptake inhibitors confirmed gender as a predictor of responding to pharmacotherapy.

→What this article adds:
Our study suggested that fluvoxamine has a favorable efficacy in the treatment of OCD, and especially in young patients with healthy executive functioning.

al population and approximately 1.8% of the Iranians (1). The patients with OCD are at risk of experiencing other psychiatric conditions (2). Patients with OCD experience decreased life quality and functional impairment compared with healthy individuals (3). Despite the relatively high prevalence of OCD, only a fraction of the affected people benefit from pharmacotherapy. In other words, 40% to 60% of them fail to respond to such interventions (4-7).

Various effective approaches are available for OCD treatment. Accordingly, identifying treatment-response predictors could help improve treatment protocols as well as appropriately tailoring them to each subject (8), leading to a more desirable and accelerated recovery in patients. However, in a cohort study that followed 144 patients for 40 years, only 20% of the investigated patients demonstrated the recovery criteria (9).

Research studies provided vast amounts of homogeneous data, suggesting significant neuropsychological underpinnings for OCD and that these neuropsychological defects may be related to genetics, age of the disease onset, therapeutic efficacy, symptom profile, patients' insight into the disease, and other primary clinical characteristics (10). Two of the neurological functions that are impaired in OCD and could affect the subsequent response to treatment are memory deficit and functioning impairment (11). Neuropsychological studies strongly supported that certain memory deficits could crucially influence the emergence of OCD-induced rituals (12). Prior research has indicated that OCD patients have difficulty remembering their tasks but encounter fewer issues in remembering other information. Implicit memory, which refers to the recollection of past events, appears to have the strongest association with OCD (13).

Furthermore, deficits in executive functioning have also been observed in several studies conducted on OCD patients. Studies have found that certain neuropsychological domains, particularly those related to executive functioning, such as planning, cognitive flexibility, response inhibition, decision-making, and attentional bias/vigilance, are impaired in OCD patients. However, there is no consensus between the scholars in this regard (14).

Executive functioning includes a series of interconnected abilities, consisting of cognitive flexibility, concept development, and self-control. The evaluation of executive functioning could be beneficial in estimating a patient's capacity to take health-related measures. Treatment response is better in OCD patients with higher neuropsychological baseline performance (15). In addition, functional deficits associated with OCD significantly impact patients' behaviors, which could disrupt response to treatment. Numerous investigations have been conducted in this area; however, the results of these studies are inconsistent.

There is a great body of literature available on OCD, its appropriate and effective therapies, and the predictors of OCD treatment response. Prior research suggested that 40% to 60% of patients with OCD fail to respond to Selective serotonin reuptake inhibitors (SSRIs) (16) adequately. Researchers have also reported that a subset of patients with OCD do not respond to cognitive behavioral therapy (CBT) and pharmacotherapies.

For instance, some authors stated that OCD patients who typically enjoy a better baseline cognitive and executive abilities are more susceptible to respond to CBT and fluoxetine. Studies supported that more severe OCD symptoms are correlated with baseline functional deficits, leading to poorer treatment response; they suggested that children with higher OCD severity may require more intensive longer treatments (11).

The OCD patient appears to fall into a vicious circle during the course of illness that exacerbates the condition; the neurodegenerative defects adversely impact the disease, and subsequently impair the medical care. Such disturbances return the patient to the previous stage of illness or prevent them from progression in treatment. Therefore, identifying predictors affecting treatment progression is necessary. Such measures help to detect potentially effective and destructive variables and design an appropriate treatment plan for the patient. Thus, the present study aimed to investigate the role of demographic characteristics, memory deficits, and executive functioning impairments in failure to respond to fluvoxamine among patients with OCD.

Methods

This was a 2-group design experimental study. The study population consisted of all OCD patients referring to selected psychiatric centers in Tehran, Iran.

The inclusion criteria for the treatment-responsive group were as follows: age 20 to 50 years, ≥6 months of psychotherapy, and obtaining 50% of the recovery, as per Yale-Brown Obsessive-Compulsive Scale (Y-BOCS) scores. Besides, the inclusion criterion for the group of treatment response failure was obtaining <30% of the recovery in the symptoms after pharmacotherapy, as per Y-BOCS values.

In addition, the primary inclusion criterion for both study groups was receiving the appropriate type and dose of the medication. In other words, by initiating an effective dose of 50 to 100 mg of fluvoxamine for OCD, the drug dose increases according to the patient's therapeutic response.

The exclusion criteria of the study included the existence of a comorbid axis I disorder, failure to regularly consume medications prescribed by a psychiatrist, concurrent consumption of medications other than those prescribed for OCD, the presence of other systematic conditions, affecting the pharmacodynamics/pharmacokinetics of drugs, the presence of neurological diseases (eg, a history of head trauma) impairing the cognitive functions, receiving nonpharmacological treatments, and smoking cigarettes.

Applying a purposive sampling method and considering that 40% to 60% of patients fail to respond to SSRIs (16), the sample size was estimated as 69 patients. Moreover, considering sample dropouts, we enrolled 76 participants as the final samples who were assigned into 2 groups of treatment-responsive and treatment nonresponsive for further comparisons (each group consisted of 38 patients).

To collect the required data, 4 questionnaires were used in this study.

1. Demographic Data Questionnaire: This researcher-designed inventory was implemented to determine the study patients' age, gender, marital status, educational level, occupational status, and the duration of illness.

2. Wechsler Memory Scale-Third Edition (WMS-III): This 18-item scale has 18 subscales and is available in 13 age groups from 16 to 89 years. It takes 55 to 75 minutes to complete the WMS-III, depending on the respondent's ability and the examiner's skills. The WMS-III has high reliability and validity (17). Considering the present study purposes, only the verbal paired associated subscale was used to assess the verbal memory, the visual memory span subscale was used to assess the visual memory, and the digit span subscale was used to evaluate the auditory attention and the working memory capacity.

3. The Wisconsin Card Sorting Test (WCST): The WCST consists of 2 card packs having 4 stimulus cards and 64 response cards in each. A number of stimulus cards are presented to the participant. The participant is told to match the cards, but not how to match; however, they are told whether a particular match is right or wrong. The original WCST used paper cards and was performed with the experimenter on one side of the desk facing the participant on the other. The test takes approximately 12 to 20 minutes to carry out and generates a number of psychometric scores, including numbers, percentages, and percentiles of categories achieved, trials, errors, and perseverative errors. The WCST is a neuropsychological test of "set-shifting," that is, the ability to display flexibility in the face of changing schedules of reinforcement. This inventory is considered to be among the most sensitive tests related to the function of the prefrontal cortex and the lateral dorsal region of the frontal. The validity of this test in measuring cognitive impairments (post-brain injury) has been reported to be >0.86 in Lezak's (2004) research (18). Besides, Naderi, 1994 (19), using the test-retest method, calculated the validity of this test in the Iranian population as 0.85. Earlier research also confirmed the validity and reliability of this tool (20).

4. The Yale-Brown Obsessive-Compulsive Scale (Y-BOCS): The Y-BOCS is a 10-item ordinal scale (0–4) that rates the severity separately for both obsessions and compulsions of OCD according to the time occupied, the degree of interference, subjective distress, internal resistance, and the degree of control. This scale is a semi-structured interview to evaluate the severity of obsessions and compulsions, regardless of the number and content of current obsessions and compulsions. Unlike other relevant questionnaires, the Y-BOCS is highly sensitive to therapeutic changes. Furthermore, it is widely used to evaluate the effects of OCD pharmacological and psychological therapies, as a "golden criterion" for assessing the severity of OCD symptoms at the end of the treatment course. The interrater and test-retest reliability of the Y-BOCS have been reported to be desirable for evaluating the changes in OCD symptoms, and not in other anxiety disorders or depressive disorder. According to studies, the Y-BOCS has high reliability and validity in the Iranian population. Scholars have confirmed the reliability and validity of this tool in Iran (21). To collect the required data, we initially referred to the selected clinics and identified the patients who had received fluvoxamine monotherapy for OCD for ≥6 months.

To confirm the diagnosis, the patient's medical records and the specialist's diagnosis were considered. Then, the samples were selected according to the inclusion/exclusion criteria of the study. Participation in the research project was completely voluntary and written informed consent to participate in the research was obtained from all patients. The Y-BOCS was then administered to all individuals. Those who received a score <17 (Y-BOCS's cutoff point) were assigned into the treatment-responsive group, and those who obtained a score of ≥17 were enrolled in the nonresponsive group. Next, all patients completed the demographic data questionnaire. With the researcher's assistance, all study samples completed the WMS-III and the WCST. The collected data were analyzed in SPSS-16 (SPSS Inc). The qualitative variables were analyzed by frequency and percentage values; the quantitative variables were analyzed using mean and standard deviation. The normality distribution of the study variables was established using the Kolmogorov-Smirnov test, which revealed a normal distribution in this respect. Other implemented statistical tests included an independent samples t-test, a chi-square test, and a Fisher Exact test. The significance level was set at $P < .05$.

Results

The present study data suggested that 56 (81.2%) of the studied patients with OCD responded to fluvoxamine treatment (Table 1).

The mean age of the patients in the groups that responded to the treatment was 30.9 years, while the same rate in the nonresponsive group to treatment was 33.8 years; thus, such statistically significant difference between these groups signifies age as an effective factor on a positive therapeutic response to fluvoxamine (P=0.048).

Furthermore, the response rates to treatment with fluvoxamine was 75.8% and 86.1% in men and women, respectively, suggesting no gender-wise significant difference (P=0.272). Similarly, no significant difference was detected between the married (84.6%) and single (79.1%) participants in terms of therapeutic response to fluvoxamine (P=0.753) (Table 2).

Table 1. Frequency of Response to Fluvoxamine Treatment in the Studied Patients

Response	Number	Percent	Valid Percent	Cumulative Percent
Valid positive	56	81.2	81.2	81.2
Negative	13	18.8	18.8	100
Total	69	100	100	100

The same pattern was observed concerning the rate of response to treatment with fluvoxamine across the study groups with less than a high school diploma (88.9%), a high school diploma (74.3%), and above high school diploma (87.5%) (P=0.332) (Table 2).

Additionally, the response rate to treatment was 85.2% in the studied patients with <2 years of disease duration, 75% in patients with 2 to 5 years of disease duration, and 100% in the study samples with >5 years of disease duration, which revealed no statistically significant difference in this regard (P=0.276) (Table 2).

In terms of occupational status, the therapeutic response rates to fluvoxamine was 84.2% and 77.4% in the employed and unemployed participants, respectively, demonstrating no statistically significant difference between the groups (P=0.473) (Table 2).

Table 3 presents that the therapeutic response rates to fluvoxamine was 82% in the investigated patients with a healthy memory and 75% in those with memory impairment. Accordingly, there was no statistically significant difference between these groups (P=0.639).

The response rate to fluvoxamine treatment was 84.4% in those with a healthy executive functioning and 40% in the study participants with deficits in executive functioning. Thus, there was a significant difference in responding to treatment with fluvoxamine between the studied OCD patients with and without deficiencies in executive functioning (P=0.043) (Table 4).

Discussion

The current study examined the effect of demographic characteristics, memory deficit, and executive functioning impairment in failure to respond to fluvoxamine pharmacotherapy in patients with OCD. The relevant results highlighted a significant relationship between non-responsiveness to treatment with fluvoxamine and the older age of patients. We also observed a significant correlation between healthy executive functioning and a more desirable therapeutic response to fluvoxamine in the explored patients with OCD. According to prior research, only age (younger individuals) was a significant predictor of therapeutic response to fluvoxamine, while all other variables were involved (11). This finding is consistent with that of our research. Based on another study (14), older patients responded better to fluoxetine; however, younger patients with less severity of OCD symptoms demonstrated a more desirable response to the same medication, which is in line with our study findings.

Furthermore, some scholars argued that a longer course of the disease (which may be related to age) could be associated with the development of bioneurological abnormalities that make the disorder more resistant to pharmacotherapy (22). However, the present study results revealed no correlation between the disease course and the therapeutic response to fluvoxamine. However, an experiment on the fluoxetine response (23) suggested an association between older age and treatment failure, which is consistent with our results.

Table 2. Relationship between demographic characteristics and response rate to fluvoxamine among the studied patients with OCD

Variable		Response Rate Positive	response Rate Negative	P Value
Gender	Male	25 (75.8)	8 (24.2)	
	Female	31 (86.1)	5 (13.9)	
	Total	56 (81.2)	13 (18.8)	0.272
Marital status	Single	22 (84.6)	4 (15.4)	
	Married	34 (79.1)	9 (20.9)	
	Total	56 (81.2)	13 (18.8)	0.753
Educational level	<diploma	16 (88.9)	2 (11.1)	
	Diploma	26 (74.3)	9 (25.7)	
	>diploma	14 (87.5)	2 (12.5)	
	Total	56 (81.2)	13 (18.8)	0.332
Disease duration (years)	<2	23 (85.2)	4 (14.8)	
	2-5	27 (75)	9 (25)	
	>5	6 (100)	0 (0)	
	Total	56 (81.2)	13 (18.8)	0.276
Occupation	Employed	32 (84.2)	6 (15.8)	
	Non employed	24 (77.4)	7 (22.6)	
	Total	56 (81.2)	13 (18.8)	0.473

Table 3. Relationship between memory status and therapeutic response to fluvoxamine among the investigated patients with OCD

Variable		Response Rate Positive	Response Rate Negative	Total	P Value
Cognitive function	Normal	50 (82)	11 (18)	61 (100)	
	Abnormal	6 (75)	2 (25)	8 (100)	0.639
	Total	56 (81.2)	13 (18.8)	69 (100)	

Table 4. Relationship between executive functioning and therapeutic response to fluvoxamine in the explored patients with OCD

Variable		Response Rate Positive	Response Rate Negative	Total	P Value
Executive functioning	Normal	54 (84.4)	10 (15.6)	64 (100)	
	Abnormal	2 (40)	3 (60)	5 (100)	0.043
	Total	56 (81.2)	13 (18.8)	69 (100)	

A similar study concerning treatment with SSRIs confirmed gender as a predictor of responding to pharmacotherapy (11). Consistently, in our study, gender was not associated with treatment outcomes. Accordingly, gender does not appear to influence the odds of response to treatment in OCD. However, men and women may differ in the metabolism of psychotherapeutic medications, including those prescribed to manage OCD. Besides, the aggravation rate of the OCD symptoms at the premenstrual phase was reported to range between 20% and 42%, which could significantly affect the response to treatment (24). In most relevant experiments, variables that demonstrated no significant association with therapeutic response included medication implementation, OCD onset age, OCD-related beliefs, and academic level (25); the latter was similar to our achieved data.

Additionally, some researchers (26) believed that the behavioral dimensions observed in patients with OCD indicate memory issues (difficulty in properly deciphering memories for personal tasks). However, similar studies documented no evidence of defects in these areas; empirical data on the relationship between OCD symptoms and memory problems are contradictory. Memory deficit also suggested no significant effect on responding to fluvoxamine pharmacotherapy in our study.

Studies have also reported that better cognitive functioning (including intelligence, verbal memory/inhibitory control, and learning) predicts a more efficient response to OCD management, regardless of treatment approach (14), which is inconsistent with the current research results. Some research revealed that adolescents with OCD were poorly able to plan and organize tasks, which implicitly addresses impairments in the prefrontal executive functioning skills (26). This finding is consistent with that of the current study. In addition, executive functioning, or high-level cognitive functions, has been suggested to depend on the integrity of the prefrontal cortex; numerous investigations have reported impaired executive functioning in OCD patients (26). Overall, several possible predictions have been proposed in various studies in this area; however, there is limited consensus on the main predictive factor of the therapeutic response to fluvoxamine in patients with OCD.

The key limitation to the current research was the small sample size, which reduced the power of the study as well as its generalizability. In addition, some patients were reluctant to collaborate in the research and discontinued participation in the study. Implementing fluvoxamine pharmacotherapy is recommended for patients with OCD, especially those at younger ages and with healthy executive functioning. Future investigations are suggested to conduct multicenter studies with higher sample sizes and compare relevant results with those of other available treatments to improve treatment outcomes in patients with OCD.

Conclusion

The obtained data suggested that fluvoxamine has a favorable efficacy in the treatment of OCD, especially in young patients with healthy executive functioning.

Ethical Approval

All procedures performed in the study involving human participants were in accordance with the ethical standards of the institutional and national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. The required approval was obtained from the Ethics Committee of the University of Social Welfare and Rehabilitation Sciences before conducting the research project (IR.USWR.REC.1397.017). Moreover, participating in the study was voluntary, and the study results are available to the study samples upon request.

Informed Consent

A relevant, informed consent form was obtained from all study participants.

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Conflict of Interests

The authors declare that they have no competing interests.

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