

# Predictors of Response to Transcranial Magnetic Stimulation in Obsessive-Compulsive Disorder Patients: A Retrospective Study

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## ABSTRACT

**Objective:** Our study aimed to investigate the factors that can predict the response to repetitive transcranial magnetic stimulation (rTMS) in patients with obsessive-compulsive disorder (OCD).

**Methods:** We conducted a retrospective study of the patients with OCD who underwent rTMS. The patients were categorized into 2 groups based on their Yale–Brown Obsessive-Compulsive Disorder Scale (Y-BOCS) scores before and after rTMS treatment: responders and non-responders. A response for patients with OCD was defined as a decrease of 35% or greater in Y-BOCS scores following rTMS. We compared socio-demographic and clinical variables in 2 groups. Additionally, binary regression analysis was performed to examine the parameters that predict the response to rTMS.

**Results:** The study included 90 patients records. The mean age of the patients was  $34.83 \pm 10.54$  years, and the most patients were female (70%,  $N = 60$ ). After rTMS treatment, 78.9% of patients had a 35% or greater reduction in baseline Y-BOCS score. There was no significant difference in socio-demographic variables between the responder and non-responder groups, while the duration of OCD was statistically significantly longer in the non-responder group than in the responder group ( $12.05 \pm 7.57$  vs.  $8.34 \pm 5.17$ ,  $P = .01$ ). The binary regression analysis could not find any factors that significantly predicted the response to rTMS.

**Conclusion:** The probability of OCD patients responding to rTMS treatment may decrease as the length of the condition increases. Consequently, psychiatrists may employ rTMS therapy at an early stage in patients with OCD, thereby enhancing the efficacy of rTMS.

**Keywords:** Obsessive-compulsive disorder, response, transcranial magnetic stimulation

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## INTRODUCTION

Obsessive-compulsive disorder (OCD) is a severe psychiatric disease marked by intrusive thoughts and repetitive behaviors.<sup>1</sup> Obsessions refer to intrusive ideas, images, or urges that recurrently manifest. Compulsions refer to recurrent, time-intensive, and repeated behaviors or cognitive processes that individuals employ as a means of managing the suffering associated with their obsessions.<sup>1,2</sup> Contemporary primary treatments for OCD involve the administration of clomipramine, high-dose selective serotonin reuptake inhibitors, and cognitive behavioral therapy.<sup>3</sup> Additional treatments,

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such as serotonin and norepinephrine reuptake inhibitors and atypical antipsychotic drugs, are used in individuals with treatment-resistant OCD.<sup>4,5</sup> Despite all these treatments, 60% of OCD patients either cannot tolerate drug treatments or partially recover following treatment. Therefore, there is significant interest in novel treatments for OCD, like repetitive transcranial magnetic stimulation (rTMS).<sup>6,7</sup>

The etiology of OCD is various. Research conducted on both human and animal models has demonstrated that the development of OCD is significantly influenced by functional abnormalities in cortico-striothalamo-cortical circuits and the supplementary motor area (SMA).<sup>8</sup> Furthermore, additional brain regions implicated in pathology include the dorsolateral prefrontal cortex (DLPFC), dorsomedial prefrontal cortex (DMPFC), orbitofrontal cortex, and anterior cingulate cortex (ACC).<sup>9,10</sup> rTMS targeting key regions such as DLPFC, SMA, DMPFC, and ACC are promising for the treatment of OCD.<sup>11,12</sup> Previous research has indicated that rTMS exhibits an average response rate ranging from 35% to 80% in patients with OCD.<sup>6,13</sup> There are few studies investigating the disparities in clinical variables between rTMS responders and non-responders in patients with OCD. One study found that rTMS was more effective in OCD patients using antipsychotics in addition to the serotonergic agent.<sup>14</sup> A recent study found that while low-severity OCD and few comorbidities were associated with a good response to rTMS, higher anxiety and depression scores at the beginning of treatment were associated with a worse response to rTMS.<sup>15</sup>

rTMS has become widespread in Türkiye in recent years. OCD is one of the conditions for which rTMS is most frequently applied. However, research on rTMS and OCD is very limited in our country. In our study, we aimed to examine the factors predicting the response in OCD patients receiving rTMS treatment. We believe our paper will contribute to the few studies in the literature.

## MATERIAL AND METHODS

### Study Procedure

Our study is a retrospective study based on patients' medical records. It includes the records of patients diagnosed with OCD from March 2021 to October 2023 who underwent rTMS. The inclusion criteria were as follows: Yale–Brown Obsessive–Compulsive Disorder Scale (Y-BOCS) and Hamilton Depression Rating Scale 17 (HDRS-17) must be complete in the patient file before rTMS treatment (pre-treatment) and after post-treatment, Y-BOCS score of 16 points and above (moderate OCD), including information on sociodemographic data in the patient file. The exclusion criteria were the absence of Y-BOCS and HDRS-17 in the patient files and those with a Y-BOCS score below 16 points. Upon scanning the files, we identified 138 patient files. Of these, 39 lacked Y-BOCS and HDRS-17 data, and crucial sociodemographic information thus was not included. Furthermore, the study excluded 9 patients due to their Y-BOCS scores being below the threshold of 16. The study was conducted on a total of 90 patient files. Figure 1 presents the flowchart of our study. We identified those who responded to treatment by comparing the Y-BOCS scores of all patients before and after rTMS sessions (baseline vs. last scores). We accepted the Y-BOCS value as a response if it decreased by 35% or more compared to the baseline score. This decline rate is recognized as a cut-off value for response in OCD treatment guidelines and many clinical studies. Our study was approved by University of Health Sciences, Erzurum Faculty of Medicine Scientific Research Ethics Committee (Approval no: 2023/05-51, Date: September 13, 2023).

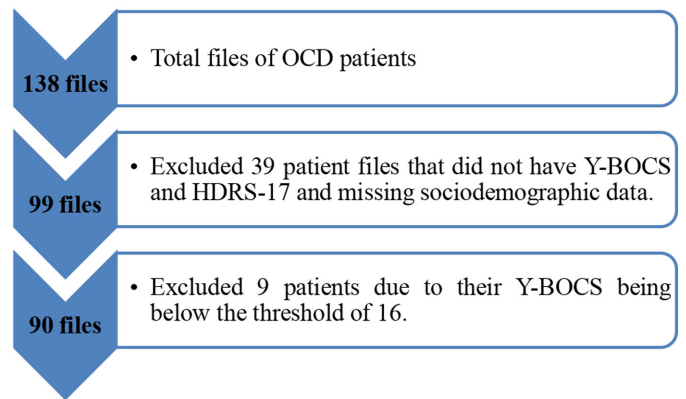


Figure 1. Study Flowchart.

### rTMS Treatment Parameters

rTMS was applied utilizing DCC-03-125-C coil (double cone) using Neuro-MS rTMS equipment from Neurosoft in Russia.<sup>16</sup> The US Food and Drug Administration (FDA) has cleared certain combinations of devices, protocols, and brain target areas for treating OCD. The FDA-cleared “recipe” for OCD treatment using TMS involves a deepTMS device, specifically the BrainsWay deepTMS H7 coil, the MagVenture cool DB80 coil devices, or the Neuro-MS/D (CloudTMS) and DCC-03-125-C coil, using high-frequency stimulation (20 Hz) targeting the DMPFC or ACC.<sup>17</sup> However, despite FDA approval, TMS applications to bilateral DLPFC and SMA regions are also frequently used in OCD patients, and there is still not a clear consensus on which protocol should be recommended in clinical practice.<sup>18</sup> In our study, we used rTMS-SMA, rTMS-bilateral DLPFC, or rTMS-DMPFC/ACC stimulation in the patients. The rTMS-SMA protocol was applied 1 Hz, 110% MT, 900 pulses for 19 min. The rTMS-bilateral DLPFC was administered to the right and left DLPFC, respectively. Initially, a 15-minute session of 1 Hz inhibitory stimulation was administered to the right DLPFC, delivering a total of 750 pulses. Following the right DLPFC stimulation, the left DLPFC was then stimulated with 10 Hz excitatory stimulation. The rTMS-DMPFC/ACC was administered at 20 Hz, 100% MT, 2000 pulses for 18 min. rTMS sessions were administered by a nurse certified in TMS.

### Instruments

The Y-BOCS is a self-report measure consisting of 10 items. Every item is assigned a score ranging from 0 to 4, and the overall score ranges from 0 to 40. A response for patients with OCD is defined as a decrease of 35% or greater in Y-BOCS scores following treatment.<sup>19,20</sup> The HDRS-17 is a measurement tool employed by healthcare professionals to assess depressive symptoms. The severity of depression is commonly evaluated using this scale in the literature. The assessment consists of 17 items, with higher scores indicating greater severity of depression. The Turkish version of HDRS-17 showed good psychometric properties.<sup>21</sup>

### Statistical Analysis

We showed descriptive statistics such as mean, standard deviation, and percentage. We divided all patients into 2 groups: responders and non-responders. When comparing continuous values between the responders and non-responders groups, we used the *t*-test for normally distributed values and the Mann–Whitney *U*-test for non-normally distributed values. We showed the changes in Y-BOCS and HDR17 scores between groups before and after treatment using a violin graph. We used Jamovi 2.3.28 for the violin graphs. We preferred binary regression analysis to

identify variables that predict responses. A statistically significant *P* value <.05 was considered.

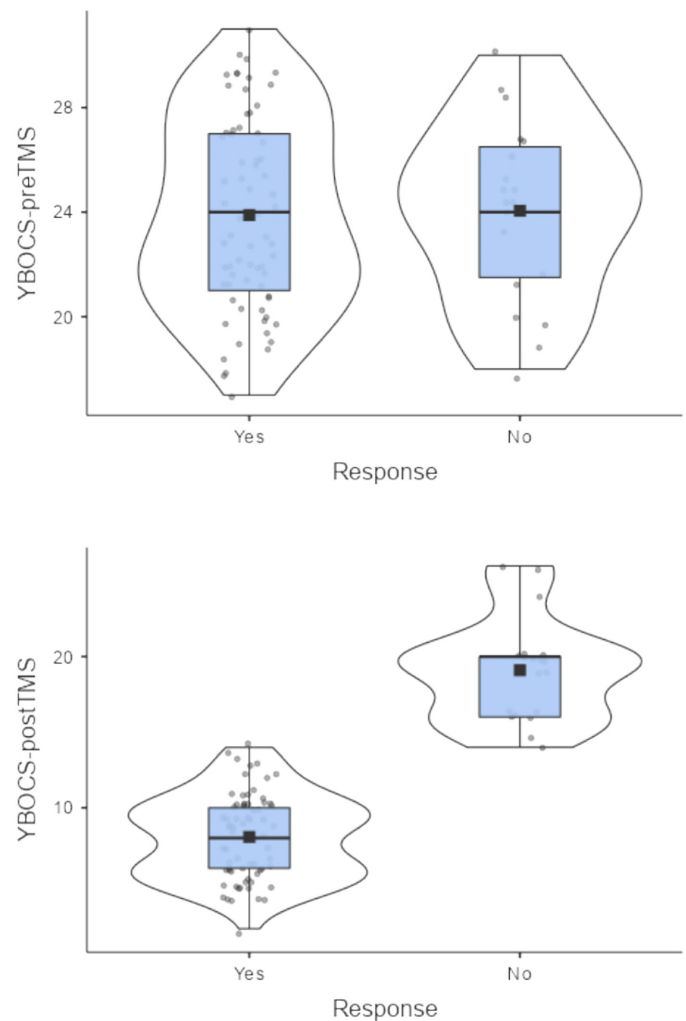
## RESULTS

A total of 90 patient files were included in the analysis. Most of the patients were female (70%, *N* = 60). The mean age of the patients was  $34.83 \pm 10.54$  (age range: 19-67). The mean duration of OCD was  $9.12 \pm 5.91$  years. More than half of the patients, 53.4% (*N* = 48), had contamination and doubt obsessions. At least religious obsessions were present in 7.8% (*N* = 7). The mean Y-BOCS score of the patients before rTMS was  $23.92 \pm 3.54$ . The mean HDRS-17 score of the patients before rTMS was  $16.83 \pm 14.22$ . The regions where TMS was applied to the patients were as follows: DMPFC/ACC in 31 patients, SMA in 30 patients, and bilateral DLPFC in 29 patients. Table 1 displays the sociodemographic and clinical variables of the patients. The number of patients whose scores on the Y-BOCS scale decreased by at least 35% or more before and after rTMS was 71 (78.9%). Figures 2 and 3 present the decline in Y-BOCS and HDRS-17 scores among the responder and non-responder groups. When comparing responders and non-responders, no significant difference was detected in terms of age, gender, and marital status. Details of the comparison of sociodemographic variables of OCD patients who responded and did not respond to rTMS are shown in Table 2. We found no significant difference between responders and non-responders in terms of OCD severity, depression level before rTMS treatment, rTMS applied brain region, and otojen obsession. Y-BOCS and HDRS-17 scores were significantly lower after rTMS in the responder group than in the non-responder group. Patients who did not respond to rTMS had a significantly longer disease duration than those who responded to rTMS. Details of the comparison of clinical variables of OCD patients

**Table 1. Sociodemographic and Clinic Variables of Patients (N = 90)**

Age (years) (minimum–maximum)	34.83 ± 10.54 (19-67)
Sex (female)	60, 70%
Marital status (married)	58, 64.4%
Working (unemployed)	51, 56.7%
Family OCD history (yes)	40, 44.4%
OCD disease duration	9.12 ± 5.91
Obsession types	
Contamination	24, 26.7%
Doubt	24, 26.7%
Symmetry and order	15, 16.7%
Religious	7, 7.8%
Sexual	9, 10%
Aggression	11, 12.2%
rTMS total session numbers	15.29 ± 7.19
rTMS applied regions	
DMPFC/ACC	31, 34.4%
SMA	30, 33.3%
Bilateral DLPFC	29, 32.3%
Y-BOCS <sub>Pre-rTMS</sub>	23.92 ± 3.54
HDRS-17 <sub>Pre-rTMS</sub>	16.83 ± 14.22
Y-BOCS <sub>Post-rTMS</sub>	10.40 ± 5.39
HDRS-17 <sub>Post-rTMS</sub>	8.61 ± 7.63

ACC: anterior cingulate cortex; DLPFC: dorsolateral prefrontal cortex; DMPFC: dorsomedial prefrontal cortex; SMA: supplementary motor area; HDRS-17, Hamilton Depression Rating Scale 17; OCD, obsessive-compulsive disorder; Y-BOCS, Yale–Brown Obsessive-Compulsive Disorder Scale.



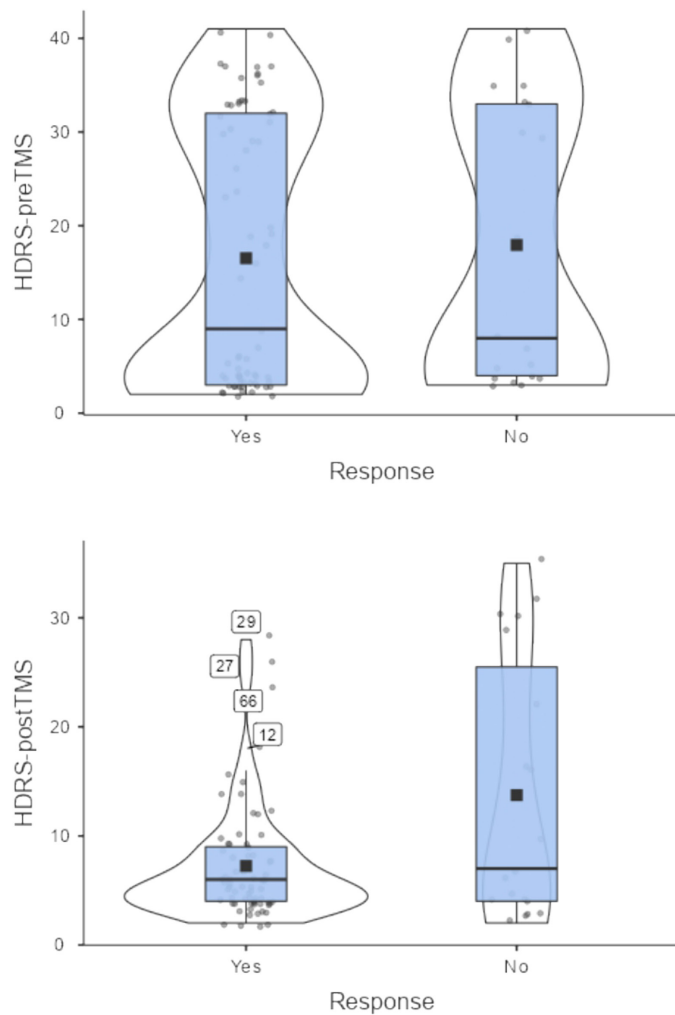
**Figure 2. The Decline of Y-BOCS after rTMS among Responder and Non-responder Groups.**

who responded and did not respond to rTMS details are presented in Table 3. When we examined the demographic and clinical variables that predicted treatment response in binary regression analysis, we found no demographic or clinical values that predicted response to rTMS treatment. Table 4 presents details of the regression analysis regarding the response to rTMS.

## DISCUSSION

The present study was a retrospective analysis of the patients with OCD who underwent rTMS. We classified patients who experienced a minimum 35% reduction in Y-BOCS following rTMS as treatment-responsive patients. This decline rate is accepted as a cutoff value for response in OCD treatment guidelines. We analyzed sociodemographic and clinical differences between individuals who responded and those who did not respond. Then, we aimed to identify factors that predict responses through regression analysis. As far as we know, our research is the initial retrospective research that focuses on this issue in Türkiye.

Nowadays, when medications are not sufficient for the treatment of OCD and access to psychotherapy services is still difficult, the search for different treatments for OCD has always aroused interest rTMS has been a highly effective and widely utilized treatment for OCD in



**Figure 3. The Decline of HDRS After rTMS among Responder and Non-responder Groups.**

recent years. The number of publications on rTMS in OCD is growing rapidly in the literature. The designs of these studies exhibit significant heterogeneity.<sup>18</sup> rTMS parameters such as the applied brain area, number of sessions, number of pulses, and motor threshold vary widely in rTMS studies.<sup>22,23</sup> These differences may make the outcomes very different. Several studies have documented different rates of treatment response in patients with OCD who have received rTMS. The response to treatment in previous studies was determined by calculating the Y-BOCS measurements before and after rTMS. Some studies accepted a response to treatment as a 25% or 30% decrease in the Y-BOCS scale after rTMS, and some studies accepted a response to treatment as a 50% decrease.<sup>11,13,24</sup> In a study that accepted a 50% decrease in Y-BOCS as a response after rTMS, the

**Table 2. Comparison of Sociodemographic Variables Between Responders and Non-responders Groups**

	<b>Responders N = 71 (78.9%)</b>	<b>Non-responders N = 19 (21.1%)</b>	<b>P</b>
Age	33.90 ± 10.02	38.32 ± 11.93	.10
Gender (female) n (%)	52 (73.2)	11 (57.9)	.19
Marital status (married) n (%)	48 (67.6)	10 (52.6)	.22
Working (unemployed) n (%)	43 (60.6)	8 (42.1)	.14

**Table 3. Comparison of Clinical Variables Between Responders and Non-responders Groups**

	<b>Responders N = 71</b>	<b>Non-responders N = 19</b>	<b>P</b>
Y-BOCS <sub>Pre-rTMS</sub>	23.89 ± 3.60	24.05 ± 3.40	.10
Y-BOCS <sub>Post-rTMS</sub>	8.07 ± 2.78	19.11 ± 3.46	<.01
HDRS-17 <sub>Pre-rTMS</sub>	16.54 ± 14.06	17.95 ± 15.14	.70
HDRS-17 <sub>Post-rTMS</sub>	7.24 ± 5.30	13.74 ± 11.99	<.01
OCD disease duration	8.34 ± 5.17	12.05 ± 7.57	.01
Family OCD history (yes)	30 (42.3%)	10 (52.6%)	.41
Total numbers of rTMS sessions	15.66 ± 7.28	13.89 ± 6.87	.34
rTMS applied regions			
DMPFC/ACC	22 (31%)	9 (47.4%)	
SMA	26 (36.6%)	4 (21.1%)	.32
Bilateral DLPFC	23 (32.4%)	6 (31.6%)	
Otojen obsession (yes)	22 (31%)	5 (26.3%)	.69

ACC: anterior cingulate cortex; DLPFC: dorsolateral prefrontal cortex; DMPFC: dorsomedial prefrontal cortex; SMA: supplementary motor area; HDRS-17, Hamilton Depression Rating Scale-17; OCD, obsessive-compulsive disorder; Y-BOCS: Yale-Brown Obsessive-Compulsive Disorder Scale.

**Table 4. Binary Regression Analysis for Predictive Factors in Response to rTMS**

	<b>B</b>	<b>SE</b>	<b>Wald</b>	<b>Sig.</b>	<b>Exp(B)</b>
Age	0.038	0.035	1.215	0.270	1.039
Gender (1)	-0.747	0.706	1.119	0.290	0.474
Marital status (1)	0.852	0.750	1.291	0.256	2.345
Working (1)	-0.636	0.633	1.009	0.315	0.529
Otojen (1)	-0.501	0.659	0.579	0.447	0.606
Disease duration	0.094	0.069	1.869	0.172	1.099
Family History (1)	-0.112	0.689	0.026	0.871	0.894
Y-BOCS <sub>Pre-rTMS</sub>	-0.011	0.093	0.014	0.907	0.989
HDRS-17 <sub>Pre-rTMS</sub>	-0.017	0.023	0.580	0.446	0.983
Number session	-0.052	0.044	1.390	0.238	0.950
Constant	-1.650	2.552	0.418	0.518	0.192

HDRS-17, Hamilton Depression Rating Scale-17; Y-BOCS: Yale-Brown Obsessive-Compulsive Disorder Scale.

response rate was found to be 50%.<sup>24</sup> Another study, which accepted a 25% Y-BOCS decrease after rTMS as a response, found the response rate to be 80%.<sup>13</sup> Another sham-controlled study, which considered a 25% Y-BOCS decrease after rTMS as a response, found the response rate to be 67%.<sup>25</sup> In another study, 46.2% of all patients responded to rTMS based on the criterion of at least a 30% reduction in Y-BOCS scores.<sup>11</sup> In our study, we accepted a decrease of at least 35% in Y-BOCS after rTMS as the response. About 78.9% (71/90) of patients responded to rTMS treatment. This rate is difficult to compare due to heterogeneity in other studies, but it was close to the study that considered response to treatment as a 25% decrease in Y-BOCS. If we had accepted the response rate to treatment as higher, our response rate would probably have been lower. The study, which found an 80% response rate to treatment, is a multi-center study conducted in Türkiye and Bulgaria. The mean Y-BOCS of the patients included in this study from Türkiye before rTMS was 28 ± 4, and the mean OCD disease duration was 18 ± 12. In our study, the mean Y-BOCS before rTMS was 23.92, and the OCD disease duration was 9.12 ± 5.91.

This suggested that the OCD patients in our study had less severe OCD. Therefore, although we considered the decrease in Y-BOCS for response to be higher than in this study, it was understandable that our response rate was close to 80%. In a study that found a response rate of 67.7%, compared to our study, the mean Y-BOCS scores of the patients before rTMS were higher ( $26 \pm 5.4$ ). In another study that found a 50% response rate, Y-BOCS scale scores before rTMS were also higher than the initial Y-BOCS mean scores in our study ( $30.5 \pm 4.3$ ). The fact that the initial Y-BOCS scale scores were relatively lower in our study than in other studies proved that our response rate was compatible with the literature.

Potential predictive variables for response in OCD include age, gender, age of OCD onset, disease duration, obsessive-compulsive symptom severity, and co-occurring depressive symptoms.<sup>26</sup> In studies examining the predictors of response to TMS, factors that negatively affect response to treatment include comorbidity, longer duration of disease, higher initial depression and anxiety levels, and high resistance against compulsions.<sup>15,27</sup> In this study, regression analysis did not find any sociodemographic or clinical variables as predictors of response. However, upon comparing responders and non-responders, it was observed that patients with a longer duration of disease exhibited a lower response to treatment. There was no significant difference in baseline depression scores between the responder and non-responder groups. However, post-rTMS depression scores were significantly lower in the responder group than in the non-responder group. This was consistent with previous studies.<sup>13</sup> In addition to the significant decrease in Y-BOCS scores, the depression scores of those who responded to treatment also decreased significantly.<sup>6,11,23</sup> This may be related to the fact that TMS is effective in the treatment of both depression and OCD, and it may also be related to the simultaneous decrease in depressive symptoms of patients whose OCD improve.

#### Limitations and Future Recommendations

Our study has several limitations. Firstly, our research is based on retrospective patient files and did not include a sham TMS group. The ideal sham group in rTMS treatment is controversial due to the combined effects of sound, intracranial stimulation, and sensation on the scalp during rTMS application. In addition, the existing sham coils are expensive and not available for every TMS clinic.<sup>28</sup> Secondly, most of the patients were female. Thirdly, since some variables were missing in the patient files, such as comorbidity, age at disease onset, and drug treatments used, we could not include these variables in the analysis. Fourthly, there are differences in the rTMS protocols applied to the patients, such as the brain region and the number of sessions. However, the lack of a standard rTMS protocol in OCD is among the important limitations of other studies. Fifthly, response rates were determined according to the Y-BOCS scale administered immediately after treatment. This response rate may change during long-term follow-up. Despite all these limitations, our study contributes to the literature investigating response predictors related to OCD. Future studies should examine factors that predict response to rTMS treatment by considering more sociodemographic and clinical variables. In addition, it would be beneficial to have data on the continuation of this well-being. A detailed study on the continuation of well-being after rTMS may be planned in the future.

In conclusion, the extended duration of the disease in OCD is linked to an inadequate response to rTMS. Therefore, OCD patients may benefit more from rTMS in an earlier stage of the disease.

Psychiatrists should be able to use TMS in OCD patients before drug resistance develops, even at the beginning of treatment. Treatment guidelines and insurance companies may include TMS treatment in the early stages of OCD.

**Ethics Committee Approval:** The study was approved by the Health Sciences University, Erzurum Faculty of Medicine Noninterventional Clinical Research Ethical Committee (Approval no: 2023/05-5, Date: September 13, 2023).

**Informed Consent:** The authors declared that it was not considered necessary to get consent from the patients because the study was a retrospective data analysis.

**Peer-review:** Externally peer-reviewed.

**Author Contributions:** Concept – S.Z., H.U.; Design – S.Z., H.U.; Data Collection and/or Processing – S.Z.; Analysis and/or Interpretation – H.U. Literature Search – S.Z. Writing – S.Z., H.U.

**Declaration of Interests:** The authors have no conflict of interest to declare.

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