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Patterns, predictors, and effectiveness of TMS for treatment-resistant OCD: A naturalistic study

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ABSTRACT

Obsessive-Compulsive Disorder (OCD) significantly impairs patients' quality of life and frequently co-occurs with Major Depressive Disorder (MDD), complicating the interpretation of treatment outcomes. Transcranial Magnetic Stimulation (TMS) is FDA-approved for treatment-resistant OCD; however, there is limited naturalistic data on its effectiveness or predictors of response. Additionally, it remains unclear whether improvements in OCD symptoms are driven by concurrent changes in depressive symptoms. This study analyzed naturalistic data from 45 patients receiving TMS treatment with the H7 coil, using the Yale-Brown Obsessive Compulsive Scale (Y-BOCS) and the Quick Inventory of Depressive Symptomatology-16 (QIDS) to examine changes in OCD and MDD symptoms over the course of TMS treatment. A multiple regression analysis showed significant reductions in Y-BOCS scores over time, even when controlling for QIDS scores ($p = 0.0048$), suggesting that improvements in OCD were independent of changes in depressive symptoms. In contrast, QIDS scores did not significantly change when controlling for Y-BOCS scores ($p = 0.82$). The overall OCD response and partial response rates were 28.9 % and 40.0 %, respectively, for patients who received a full course of at least 29 treatments. To account for the high noncompletion rate (48 %), secondary analyses yielded a response rate of 23.0 % for the 74 patients who received at least 10 treatments. Higher baseline Y-BOCS scores and lower baseline QIDS scores were predictive of greater improvements in OCD symptoms, while level of care and symptom-provocation scores did not significantly influence outcomes. Both obsessional and compulsive symptom scores decreased significantly, with no difference in the magnitude of reduction between the subscales. These findings suggest that TMS with the H7 coil is effective in reducing OCD symptoms, independent of improvements in depressive symptoms.

1. Introduction

Obsessive compulsive disorder (OCD) affects approximately 1–2 % of the population (Fawcett et al., 2020; Ruscio et al., 2010) and significantly reduces quality of life (Macy et al., 2013). First-line treatments include psychopharmacotherapy and behavioral interventions, however, only 40–60 % of patients respond to selective serotonin reuptake inhibitors (SSRIs) (Pallanti & Quercioli, 2006). Exposure and response prevention (ERP) therapy has shown efficacy (Hirschtritt et al., 2017) with only small to medium effect sizes (Reid et al., 2021; Yan et al., 2022). Neuromodulatory approaches, such as transcranial magnetic stimulation (TMS), are often pursued when patients do not respond to other interventions (Hirschtritt et al., 2017). However, the patterns and predictors of response remain poorly understood (Boschen et al., 2010). Pivotal TMS trial data found a 38.1 % response rate (Carmi et al., 2019), with a follow-up naturalistic industry-sponsored study reporting a 57.9 % response rate (Roth et al., 2021).

Major depressive disorder (MDD) is the most common psychiatric comorbidity of OCD, affecting 50–90 % of patients (Murphy et al., 2010). There have been inconclusive results regarding whether comorbid depression acts as a predictor of OCD improvement with pharmacologic and behavioral interventions (Hazari et al., 2016; McDonald et al., 2023).

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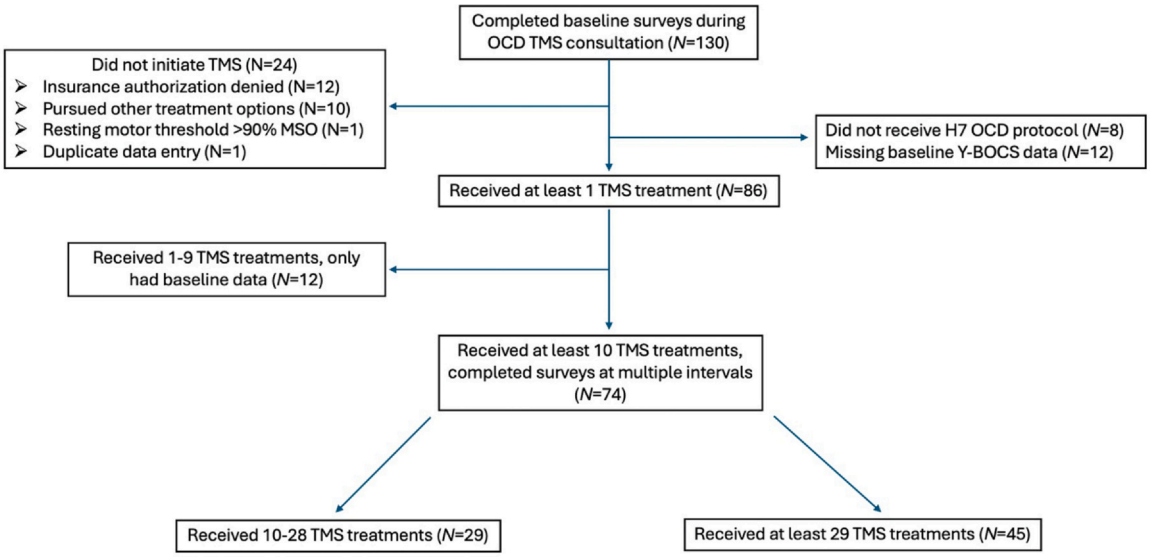

Fig. 1. Flow diagram for the real-world data collection of OCD patients treated with TMS.

Analyses show improvements in both OCD and depressive symptoms when treatment options like pharmacotherapy and neuromodulation are initiated (Hühne et al., 2023). This presents the possibility that improvement in OCD symptoms might be sequelae of primary improvements in depression. While pharmacologic studies have disproven this hypothesis by showing that the OCD response to SSRIs is not impacted by the improvement of depressive symptoms (Goodman et al., 1989; Soomro et al., 2008), the relationship between depressive and OCD symptom change during TMS treatment remains largely unexplored. The present study aimed to determine if the improvement in OCD symptoms is independent or secondary to a MDD response. We hypothesized that the change in OCD symptoms over time would be independent of depression symptoms. Additionally, we aimed to quantify the real-world response rates, predictors of response, and the utility of symptom provocation in OCD-targeted TMS treatment.

2. Methods

2.1. Sample and TMS procedure

This study was conducted at McLean Hospital with approval by the Mass General Brigham Institutional Review Board. Patients were referred for TMS treatment and were interviewed by a psychiatrist or psychiatric nurse practitioner at McLean's TMS Clinic. TMS was recommended based on clinical decision-making including the presence of an OCD diagnosis, trials of at least four psychiatric medications, and the absence of any contraindication to safely receive treatment. Patients were receiving ongoing psychiatric care in either outpatient, inpatient, or OCD-intensive residential environments. Treatment used the Brainsway H7 coil at 20 Hz at 100 % resting motor threshold. Each treatment consisted of 50 trains with an intertrain interval of 20 seconds, for 2000 total pulses. Treatment location was set at 4 cm anterior to the foot location of the motor strip to target the dorsomedial prefrontal cortex (dmPFC). Patients often received insurance approval for an acute course of TMS (up to 36 treatments) and received treatment five days per week. Following the FDA-cleared protocol, each patient developed an exposure-based provocation involving distressing thoughts or actions (Carmi 2019). Prior to each treatment, patients participated in their provocations and rated their distress on a visual analog version of the Subjective Units of Distress Scale (SUDS). The aim was a score of 40–70 (out of 100); no additional provocation was performed if distress exceeded 70 upon arrival. SUDS scores across all treatments were averaged. Self-report Yale-Brown Obsessive Compulsive Scale (Y-BOCS) and Quick Inventory of Depressive Symptomatology-16 (QIDS) data were collected at treatments 10, 20, 29, 36, and every subsequent 10 treatments until completion.

Our analyses included data from 130 patients who received a consultation for TMS treatment between 2019 and 2024. Twenty-four patients did not initiate treatment (Fig. 1). Patients who received TMS protocols other than H7 OCD treatment and patients who were missing baseline Y-BOCS data were excluded from analyses. Of the 86 patients who received at least 1 treatment, 12 patients received fewer than 10 treatments and were excluded due to the lack of follow-up data. Seventy-four patients received at least 10 TMS treatments and completed surveys at multiple intervals. To account for premature treatment termination, 29 additional patients who received fewer than 29 treatments were excluded from the primary analyses. Specific reasons for treatment termination among these patients are provided in Table 1. It is important to note that while in some cases, patients stopped treatment for reasons reportedly independent of adverse effects or lack of benefits (Table 1), our decision to include patients who received at least 29 treatments is subject to selection bias. However, it is compatible with previous randomized and naturalistic studies in OCD, which considered 29 treatments an adequate dose of TMS (Carmi et al., 2019; Roth et al., 2021). Moreover, our primary objective was not to simply assess overall response rates as done previously (Roth et al., 2021), but to evaluate these in the context of improvements in depression which acts as an internal control. After the exclusion of these patients, the total sample included 45 patients. Secondary analyses exploring the response rates and trajectory of response were calculated for the 74 patients who received at least 10 treatments. Fig. 1 provides a flowchart of the patients included in these analyses.

2.2. Treatment response rates

We calculated change in Y-BOCS scores as the difference between post-treatment and baseline scores. Treatment response was defined by a $\geq$ 30 % reduction in scores (Carmi et al., 2019), while partial response was defined by a $\geq$ 20 % reduction as in prior studies (Carmi et al., 2019; Roth et al., 2021). Unpaired *t*-tests compared race/ethnicity, gender, level of care, psychiatric comorbidities, age, number of treatments, average SUDS scores, and baseline symptom severity (Y-BOCS and QIDS) between responders and non-responders. To evaluate if TMS was more effective in reducing obsessions versus compulsions, we first used a paired samples *t*-test to see if both subscales improved from treatment onset to treatment completion. Furthermore, we compared percent change in compulsion and obsession Y-BOCS sub-scores using a paired samples *t*-test.

Table 1
Reasons for premature treatment termination in patients excluded from primary data analysis. Many patients begin treatment during inpatient and residential stays at McLean Hospital and stop treatment when leaving the hospital setting (discharging).

Number of treatments received	Insurance coverage denied	Side effects	Symptoms worsened	Ineffective	Discharged or moved*	Restricted to inpatient unit due to safety concerns	Self-discontinued, reason not reported	Other	Total
1–9	0	1	1	0	3	2	4	1	12
10–19	1	0	1	2	1	3	1	1	10
20–28	0	1	1	4	9	0	2	2	19

2.3. Predictors of OCD response with TMS

We used linear regression models to investigate potential predictors of response. Change in Y-BOCS score was used as the outcome variable, while level of care (categorized as “inpatient”, “outpatient”, or “residential”), level of distress during provocation (i.e., average SUDS score), baseline severity of OCD (i.e., pre-treatment Y-BOCS score) and MDD symptoms (i.e., pre-treatment QIDS score) were used as predictors. We hypothesized that patients in residential treatment, with higher distress and higher baseline severity, would respond better to treatment (Guzick et al., 2022; Storch et al., 2021). Given correlations among predictors, we constructed multiple linear regression models to examine them both individually and in combination. Potential collinearity issues were also formally assessed by computing the variance inflation factor (VIF). Interactions between significant predictors were explored through post-hoc analyses. Additionally, we performed a post-hoc analysis categorizing baseline OCD severity as high or low using a Y-BOCS cutoff score of 27, which had been shown to be predictive of response in a previous study (Storch et al., 2021) to try and replicate these results. The relationship of categorical severity with outcome was tested in a regression model, alone and in combination with the above-mentioned predictors.

2.4. Relationship between OCD and depression change with treatment

We computed change in QIDS scores as the difference between post-treatment and baseline scores. Response was defined by a $\geq 50\,\%$ reduction in QIDS scores, and remission was defined by a final QIDS score < 6. An unpaired *t*-test compared percent change of QIDS scores between OCD responders and non-responders. We hypothesized that depression response would depend on OCD response, such that OCD responders would show greater improvement in depression compared to OCD non-responders. Response and remission rates were also compared, using a one tailed z-score for two population proportions. Four patients, whose initial QIDS scores were below the clinical cutoff for depression (6), were excluded from this comparison.

The independent effects of treatment on depression and OCD were evaluated using a multiple regression model with QIDS and Y-BOCS as independent variables and time (treatment onset to treatment completion) as the dependent variable. We hypothesized that there would be a significant change in Y-BOCS score over time independent of changes in QIDS score, but that the converse would not be true.

2.5. Post-hoc analyses at interim time points

Through post-hoc analyses, we aimed to determine whether clinical response would differ between patients who received fewer than 29 treatments and those who received at least 29 treatments. To explore the trajectory of response, a one-way analysis of variance ANOVA compared the percent change in Y-BOCS scores at each time point for the entire sample. To explore the dose-response relationship for the OCD protocol, we defined five groups based on the number of completed treatment sessions (i.e., 10–19; 20–28; 29–35; 36; and 37 +) in accordance with the methodology of Hutton et al. (2023). Y-BOCS percent change measured at 10, 20, 29, and 36 sessions, and at the final treatment for those who completed more than 36 sessions, was compared across groups using an ANOVA. Due to the limited sample size of the five groups and the impact of outliers on the data, the Y-BOCS percent change values were rank transformed at each time point prior to conducting the ANOVAs. For the categorical measure of response rate, a Pearson Chi-Square test was used at each time point to compare the five groups.

3. Results

Demographic and clinical data are summarized in Table 2. The sample was primarily White, non-Latino (87 %). The majority were

Table 2
Demographic and clinical data comparing OCD responders and OCD non-responders. There were no differences between the two groups (p's > 0.05).

Demographics		Total	Responders	Non-responders	*p* value
Race/Ethnicity	White, non-Latino	39 (87 %)	11 (85 %)	28 (88 %)	0.80
	Other	6 (13 %)	2 (15 %)	4 (12 %)	
Gender	Male	22 (49 %)	6 (46 %)	16 (50 %)	0.47
	Female	22 (49 %)	7 (54 %)	15 (47 %)	
	Non-binary	1 (2 %)	0 (0 %)	1 (3 %)	
Level of Care	Residential	13 (29 %)	3 (23 %)	10 (31 %)	0.53
	Inpatient	4 (9 %)	1 (8 %)	3 (10 %)	
	Outpatient	28 (62 %)	9 (69 %)	19 (59 %)	
Psychiatric Comorbidities	Diagnosed with comorbid psychiatric disorder	42 (93 %)	12 (92 %)	30 (94 %)	0.86
Comorbid Disorders by type	Depressive	35			
	Anxiety	19			
	Trauma related	10			
	Substance related	3			
	Neurodevelopmental	11			
	Eating	3			
	Personality	4			
	Bipolar	2			
	Obsessive compulsive related	2			
	Dissociative	1			
		Mean (*SD*)			
	Number of psychiatric comorbidities	2 (1.28)	2.03 (1.28)	1.92 (1.32)	0.80
	Age	36.3 (16.2)	42.3 (16.4)	34.3 (15.8)	0.13
	Number of Treatments	36.6 (6.5)	36.7 (3.8)	36.6 (7.4)	0.96
	Baseline Y-BOCS	26.4 (5.0)	26.8 (4.7)	26.3 (5.1)	0.78
	Baseline QIDS	13.5 (5.6)	12.5 (5.8)	13.9 (5.5)	0.44
	Average SUDS	60.9 (10.4)	62.2 (8.0)	60.2 (11.4)	0.57

receiving outpatient care (62 %) and had comorbid psychiatric disorders (93 %). The average number of concurrent psychiatric medications at the time of treatment initiation was 3.0 (SD = 1.8).

The average change in Y-BOCS scores was −17.4 % (SD = 27.1 %), corresponding to a 4.78 (SD = 7.2) point decrease. Thirteen (28.9 %) patients responded while 18 (40.0 %) achieved partial response. For patients who received 20–28 treatments, four (21.1 %) responded while six (31.6 %) achieved partial response with a −7.3 % (SD = 32.2 %) average percent change in Y-BOCS score.

When comparing responders and non-responders (Table 2), there was no difference in demographics including race/ethnicity, gender, level of care, number of psychiatric comorbidities, age, or number of treatments. Additionally, there was no difference in initial Y-BOCS (t = -0.28, p = 0.78) or initial QIDS-16 scores (t = 0.78, p = 0.44). Initial Y-BOCS scores did not differ between patients receiving residential and other levels of care (t = -0.67, p = 0.51). Obsessional (t = 3.33, p < 0.001) and compulsive (t = 3.38, p < 0.001) subscale scores both decreased from the initial to the final treatment, with no significant difference in the percent reduction between the subscales (t = 0.10, p = 0.92).

Across 44 patients, the average SUDS score was 60.85 (SD = 10.4) with each patient's averaged scores ranging from 32 to 80. All but one patient (97.7 %) had an average SUDS score above 40.

3.1. Predictors of response

Using linear regression models, we investigated potential predictors of treatment response. There was no significant association between Y-BOCS improvement and either SUDS (F(1,43) = 1.17, p = 0.29) or level of care (F(2,43) = 0.10, p = 0.90). These results did not change (p_{SUDS} = 0.44, p_{LOC} = 0.75) when additionally accounting for baseline Y-BOCS severity and baseline QIDS scores, leading us to remove SUDS and level of care from the model. Age and gender were included as additional independent predictors and were similarly removed, as they were not significantly predictive of response (p_{age} = 0.82, p_{gender} = 0.62). When focusing on baseline OCD and depressive symptoms, we found a significant association between baseline Y-BOCS scores (F(1,44) = 5.94, p = 0.0192) and baseline QIDS scores (F(1,44) = 4.69, p = 0.0361) with treatment improvement, indicating that higher starting Y-BOCS scores and lower starting QIDS scores were related to a larger change in Y-BOCS (Fig. 2). However, neither predictor was significant when considered in isolation ($p_{Y\text{-}BOCS}$ = 0.15, p_{QIDS} = 0.33).

Post-hoc analyses further explored this combined effect of baseline OCD and depression symptoms on Y-BOCS change. Despite a positive correlation between baseline Y-BOCS and QIDS scores (Pearson r = 0.53, p = 0.0002), no evidence of multicollinearity was found in our regression model (VIF = 1.38). There was also no significant interaction between these variables (F(1,44) = 0.025, p = 0.87).

In a separate post-hoc analysis, we classified patients into high or low baseline severity groups using a Y-BOCS cutoff score of 27, as done previously (Storch et al., 2021). This was linearly predictive of treatment outcome, whether considered as sole predictor (F(1,44) = 5.52, p = 0.0235), or analyzed alongside baseline depressive symptoms (F(2,44) = 6.19, p = 0.0017).

3.2. Patterns of response

Forty-one patients met the clinical cutoff for depression (baseline QIDS > 6), of which 11 (26.8 %) were OCD responders. The average change in QIDS score was −2.8 points (SD = 4.3), corresponding to an average percent change of −21.8 % (SD = 31.3 %). Of the eight patients (19.5 %) who achieved a response in depressive symptoms, four (50.0 %) also achieved a response in OCD symptoms. One patient whose QIDS score improved from 6 to 4 was excluded in the remission calculation, as they artificially inflated the remission rate due to their small score change, yielding a remission rate of 15.0 %. On average, OCD responders experienced a larger reduction in their QIDS scores compared to non-responders (44.7 % (SD = 30.7 %) vs. 13.4 % (SD = 27.5 %), respectively) (t = 3.13, p = 0.003; Fig. 3). The depression response (36.4 %) and remission (40.0 %) rates for the OCD responders were higher than the depression response (13.3 %) and remission (6.7 %) rates of the OCD non-responders (z = 1.65, p = 0.049; z = 2.56, p = 0.005, respectively).

A multiple regression model showed that improvement in Y-BOCS occurred independently of improvement in QIDS. Y-BOCS scores changed significantly over time when controlling for QIDS (t = -2.89,

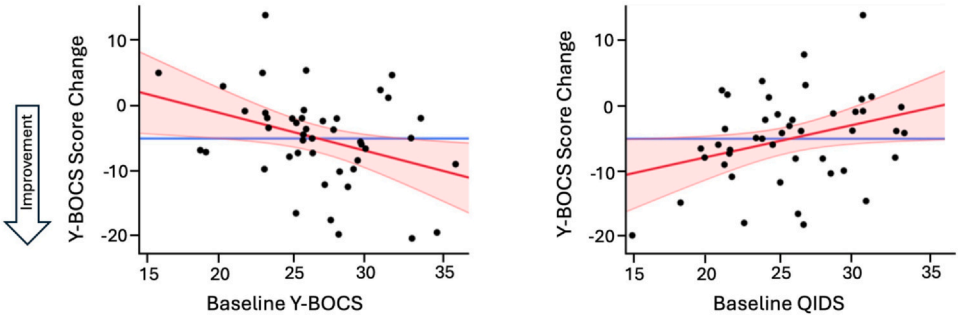

Fig. 2. Treatment Predictors of OCD Response. In a multiple linear regression model using Y-BOCS (treatment completion – treatment onset) as the dependent variable and initial Y-BOCS and initial QIDS as independent variables, the left panel shows the relationship between initial Y-BOCS scores and Y-BOCS change Leverage residuals ($p = 0.0192$), while the right panel shows the relationship between initial QIDS scores and Y-BOCS change Leverage residuals ($p = 0.0361$). The red lines represent the fitted regression lines with shaded areas indicating 95 % confidence intervals. Blue lines show the reference line of no effect.

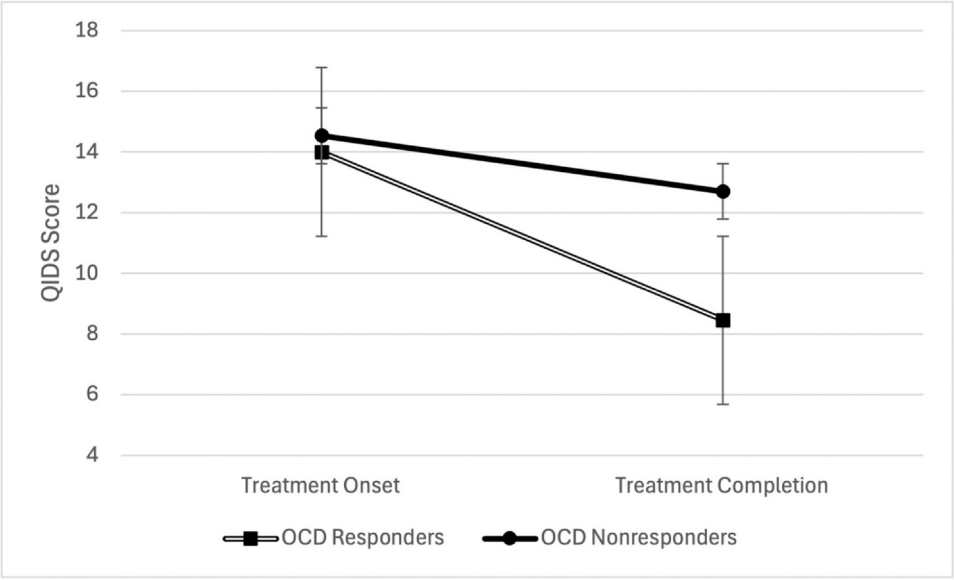

Fig. 3. Depression Changes in OCD Responders and Non-responders. Patients were classified as OCD responders if their Y-BOCS scores decreased at least 30 % from treatment onset to completion. The change in depression symptoms was larger for patients who reached OCD response ($p = 0.003$).

$p = 0.0048$), while QIDS scores did not significantly change when controlling for Y-BOCS ($t = 0.22$, $p = 0.82$). Raw and adjusted scores are shown in Fig. 4.

3.3. Post-hoc analyses of clinical outcomes at interim time points

The overall response rate for the 74 patients who received at least 10 treatments was 23.0 %. The average percent change at each time point is shown in Fig. 5. The average improvement in Y-BOCS scores at session 10 was 7.16 % ($SD = 19.8$) and at session 36 was 16.6 % ($SD = 32.6$). For patients who received exactly 36 treatments, the final response rate was 38.5 %. There was no statistical difference in percent change of Y-BOCS scores across the time points ($F(4,211) = 1.27$, $p = 0.28$). Analyses of TMS response grouped by number of treatments received at interim time points are summarized in Fig. 6. One-way ANOVAs indicated that these groups did not differ in Y-BOCS score percent change at any of the time points, including prior to treatment completion (p's > 0.34) and after completion of treatment course ($p = 0.09$). Chi-square tests also revealed no significant difference in the response rates between groups at all time points (p's > 0.07) (Table 3).

4. Discussion

In this naturalistic sample of patients with treatment-resistant OCD undergoing TMS to augment their ongoing OCD treatment, 28.9 % of patients achieved response, and 40.0 % achieved partial response. This corresponded to an average reduction in Y-BOCS scores of 4.8 points, compared to 6.0 points from the pivotal clinical trial (Carmi et al., 2019). This response rate is lower than reported in the clinical trial (38.1 %) (Carmi et al., 2019) and observed in a naturalistic industry-sponsored study (57.9 %) (Roth et al., 2021). This difference may be attributable to the greater clinical complexity of our patient population, 93 % of whom had a comorbid psychiatric diagnosis, compared to 66 % in the previous naturalistic sample. (Roth et al., 2021). Additionally, the level of treatment resistance in our sample was high, with the majority of patients failing at least five prior psychiatric medications. Although the severity of our patients likely influenced the response rates, we were unable to quantify the impact of level of treatment-resistance due to inconsistent documentation of past medication trials. While most pharmaco- and psychotherapy studies investigating OCD treatment consider a 35 % reduction in Y-BOCS a clinical response (Farris et al., 2013), our decision to adopt 30 % was in accordance with the 2019 pivotal TMS OCD study (Carmi et al., 2019). Using the 35 % response cutoff, our results are comparable to pharmacologic augmentation data (28.4 % response rate) for treatment-resistant OCD (Dold et al., 2013). While some pharmacologic trials have had limited success in treating compulsive symptoms (Nematizadeh et al., 2023; Tilaki et al., 2023), we found similar reductions in patients' compulsive and obsessional symptoms, thus supporting the efficacy of TMS as a modality that treats both dimensions.

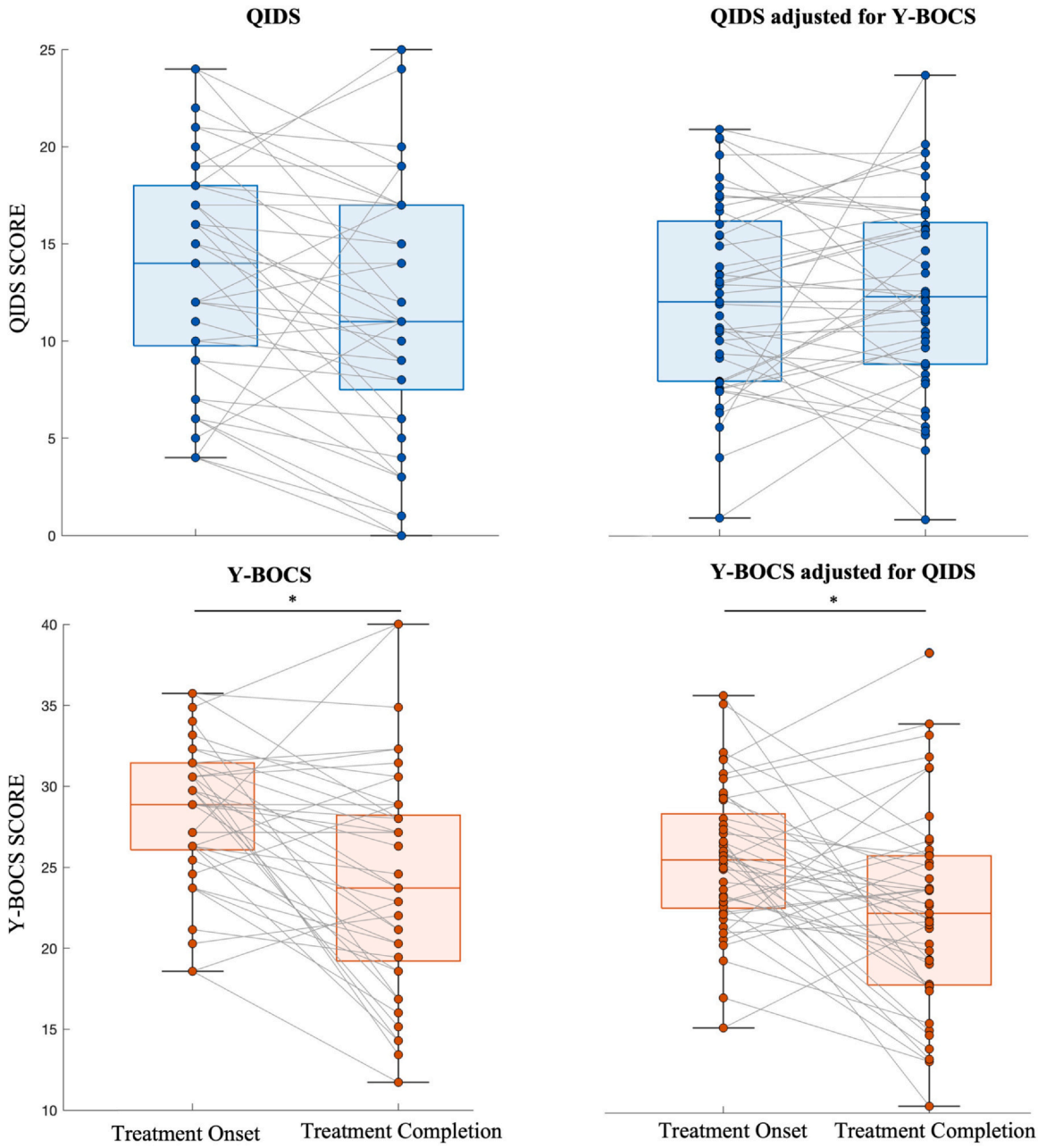

Fig. 4. Independence of OCD Response. Raw QIDS and Y-BOCS scores (left panels) are compared to adjusted QIDS and Y-BOCS scores (right panels) from treatment onset to treatment completion. A linear regression model with time as the dependent variable found that Y-BOCS scores were independent of QIDS scores ($p = 0.0048$) and that QIDS scores were not independent of Y-BOCS scores ($p = 0.82$).

Linear regression models revealed no effect of SUDS scores or level of care on treatment outcome. We hypothesized that patients in residential treatment would have more severe OCD, with possibly inflated initial Y-BOCS scores due to concurrent ERP treatments. However, these patients did not have higher initial Y-BOCS scores, and we found no influence of level of care on treatment response. Concurrent treatment may still impact response rates, as specific details about patients' ongoing psychiatric care were not available in this naturalistic sample.

The inclusion of symptom provocation prior to treatment was based on data supporting the importance of state-dependency in neuronal responses to TMS (Silvanto et al., 2008) and its impact in psychiatric treatments (Dinur-Klein et al., 2014; Isserles et al., 2013). One study found that patients with higher levels of distress during exposure had a larger OCD symptom response to TMS overall. They attributed this to a sub-population with a higher severity of OCD having a greater treatment response (Guzick et al., 2022). However, randomized controlled trials comparing treatment outcomes with and without symptom provocation are lacking. Without a control group, it is difficult to truly evaluate the provocation's utility or to determine if there is a minimum level of neurocircuitry activation required for optimal TMS treatment. However, our results suggest that the provocation does not impact clinical response in a dose-dependent manner.

These provocations are a form of exposure that could have contributed to the response rates to sham treatment during the clinical trials (Carmi et al., 2019). Given the severity of our patient population, some patients reported SUDS scores in the target range at baseline – prior to any intentional provocation. While the provocation is proposed to facilitate activation of the OCD neural networks, some patients with severe and consistent OCD symptoms may not require additional provocation to reach the prescribed SUDS level. The distress elicited by the

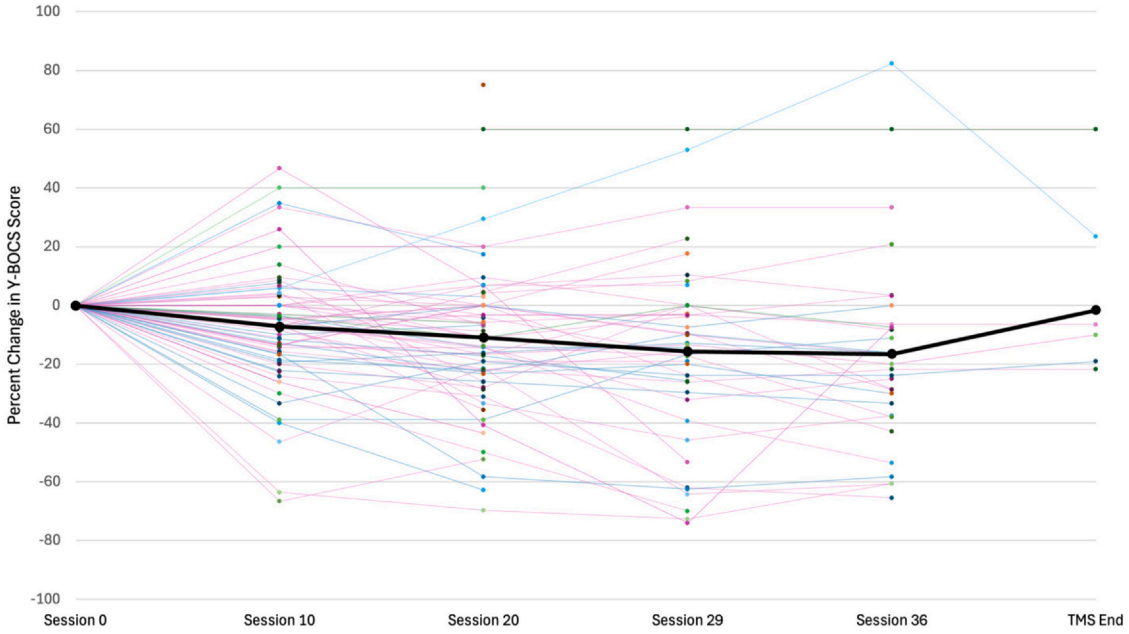

Fig. 5. Trajectory of Response. Percent change in Y-BOCS scores compared to baseline scores for each individual patient at fixed time points. The average percent change in Y-BOCS scores across all 74 patients is shown in black.

provocation could have led some patients to prematurely terminate treatment, contributing to our 48 % noncompletion rate. However, the most common reason for premature termination was discharging or relocation as many patients admitted to McLean Hospital's OCD Institute for residential care choose to continue their acute TMS course locally after returning home.

To further examine the impact of an incomplete TMS course, we calculated the response rates in patients who received 20–28 treatments, finding a 21.1 % response and 31.6 % partial response rate. Due to the large number of patients who discontinued TMS prior to completing a full treatment course, we included them in post-hoc analyses; we evaluated OCD symptoms throughout the treatment course for all patients with follow-up Y-BOCS data. While differences in response rates between the five groups of patients at each treatment interval did not reach statistical significance, those who received more treatments show a trend toward higher response rates after 20 treatments. Similarly, although there was no significant difference in the percent change of Y-BOCS scores between the five groups, the median improvements were the greatest for the 36 treatments group, with a response rate of 38.5 %. Given our limited sample size, we may not have been adequately powered to detect a dropout bias; there may still be a differential response in those who discontinued TMS, impacting our overall response rate in the primary analysis. Furthermore, the present sample was not large enough to detect whether treatment response plateaued over time. The largest variance of Y-BOCS scores occurred among the group of six patients who received greater than 36 TMS treatments. These patients are likely more complex, as their extended treatment courses were driven by clinical judgment in the setting of failing to reach response criteria. Future studies should explore the timeline of improvement and determine if there is a sub-population of patients who would benefit from an extended course of TMS.

Initial Y-BOCS and QIDS scores were predictive of treatment response when acting together as independent variables. Higher initial Y-BOCS scores were predictive of a larger improvement in OCD symptoms aligning with previous research that a larger magnitude of symptom reduction occurred in higher severity patients (Storch et al., 2021). Post-hoc analyses applying the same cutoff for high severity (Y-BOCS > 27) revealed that higher baseline OCD severity can act as an independent predictor of treatment response. This finding may support the clinical significance of this initial Y-BOCS value, although previous classifications define moderate-severe symptoms as Y-BOCS scores of 26–34 and severe symptoms as 35–40 (Storch et al., 2015). Patients with higher initial Y-BOCS scores may represent a subgroup more sensitive to stimulation, their scores could be regressing to the mean over time, or there may be more room for improvement without a floor effect.

Initial QIDS scores were inversely associated with OCD treatment response, with lower depression scores predicting better OCD outcomes. This could be indicative of the challenges in treating patients with additional psychiatric comorbidities. Alone, initial QIDS and initial Y-BOCS scores were not significant predictors, suggesting that they explain different yet complementary aspects of symptomatic improvement. Since the mechanism behind their complementary contributions to post-treatment outcomes remains unclear, it is important to independently investigate depression outcomes.

Some patients experienced a reduction in their depressive symptoms during OCD treatment, with a 19.5 % response rate and 15.0 % remission rate. This TMS protocol has been shown to ameliorate depressive symptoms, with an average decrease of 38 % in MDD scores (Tendler et al., 2021). This aligns with evidence that the H7 coil targeting the dmPFC and ACC can also treat depression (Tendler et al., 2017; Zangen et al., 2023) by targeting a large brain area impacting multiple neuronal circuits (Tzirini et al., 2022). Furthermore, TMS biotyping has mapped anxiety/insomnia symptom clusters of depression to the dmPFC, with preferential psychosomatic responses occurring when using symptom-specific targets (Siddiqi et al., 2020). This suggests a potential mechanism of treatment through improvements in mental rumination and obsessional anxiety. However, in our sample, OCD responders had larger reductions in their depression symptoms, which could indicate that the depression response is secondary to the reduction in OCD symptom burden.

Our results suggest that the improvement in OCD symptoms was independent of the improvement in depression, while the improvement in depression symptoms depended on the OCD response. The lack of an independent depression response could be attributed to the site of stimulation as TMS outcomes are target dependent, with potential symptom-level changes occurring based on treatment location (Siddiqi & Fox, 2024). Imaging studies have found that OCD impacts the orbitofrontal cortex and the ACC (Saxena & Rauch, 2000; Yang et al., 2024), with OCD treatments like ERP modulating both of these brain regions

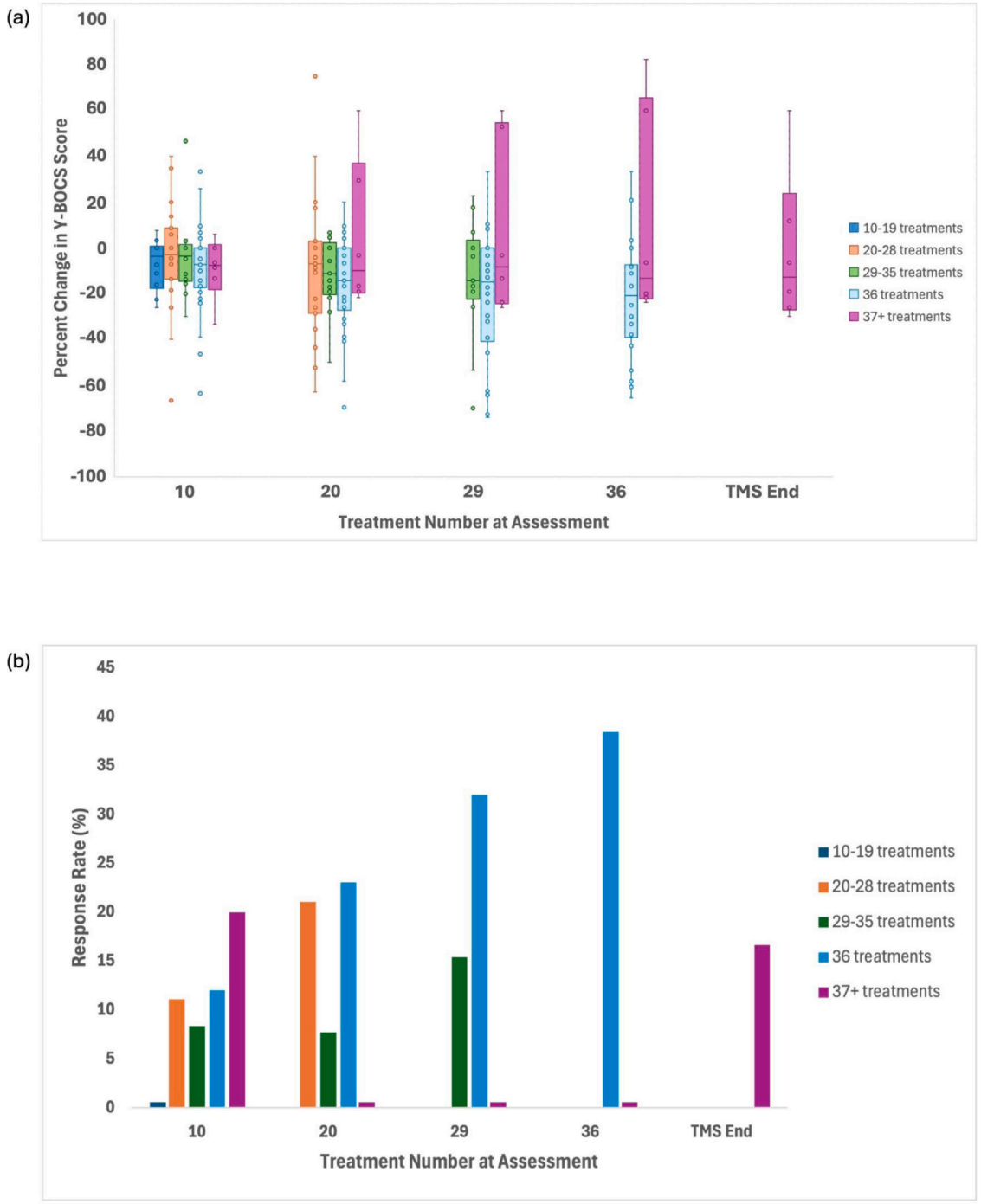

Fig. 6. Response Rates by Number of Treatments Completed. Categorical clinical outcomes for the five groups who received different number of treatments after 10, 20, 29 and 36 sessions and at endpoint in the group with extended treatment (> 36 sessions). (a) Percent change in Y-BOCS scores for the five groups at the fixed time points. (b) Response rates (> 30 % improvement) for the five groups at the fixed time points.

(Yan et al., 2022). The dmPFC and dorsal ACC (Harmelech et al., 2023) are thus the targets for TMS treatment for OCD.

Site specificity was highlighted in a deep brain stimulation trial for OCD. Differences in stimulation to the ventral capsule/ventral striatum, which was functionally connected to the medial orbitofrontal cortex, had a greater impact on mood than stimulation to the anteromedial subthalamic nucleus, with no differences between the two in OCD response (Tyagi et al., 2019). Even with deep TMS protocols, selection of stimulation site remains an essential consideration, requiring further efforts to identify symptom-specific targets to improve clinical outcomes for patients with comorbid psychiatric disorders.

These results bear clinical significance for the management of patients with OCD and comorbid depression. This protocol has been shown to reduce depression symptom severity in MDD (Zangen et al., 2023), although in our sample, patients' OCD response was independent of their MDD response. Future studies should optimize TMS protocols to treat patients with symptoms of OCD and MDD. Additionally, further efforts should explore the durability of symptom response, as this would be a clinically significant factor in optimizing treatment protocols.

This study builds upon other naturalistic studies that support the utility of TMS in treating OCD by showing that OCD improves

Table 3
Y-BOCS clinical outcomes for patients grouped by differing durations of treatment after 10, 20, 29, 36, and TMS end.

Total Treatments	10–19 N = 10	20–28 N = 19	29–35 N = 13	36 N = 26	37 + N = 6
Assessment after 10 Sessions					
N	10	18	12	25	5
Average Percent Change (*SD*)	−7.24 (11.4)	−3.73 (25.0)	−3.81 (18.9)	−10.4 (20.3)	−11.2 (14.3)
Median Percent Change	−3.7	−3.69	−4.17	−7.41	−8.7
Response Rate (%)	0	11.1	8.33	12	20
Assessment after 20 Sessions					
N		19	13	26	6
Average Percent Change (*SD*)		−8.01 (32.4)	−11.8 (16.1)	−16.2 (20.7)	4.79 (33.0)
Median Percent Change		−6.9	−11.11	−14.29	−9.95
Response Rate (%)		21.1	7.69	23.1	0
Assessment after 29 Sessions					
N			13	25	6
Average Percent Change (*SD*)			−13.4 (25.9)	−22.4 (28.1)	7.75 (38.7)
Median Percent Change			−14.29	−16.67	−8.28
Response Rate (%)			15.4	32	0
Assessment after 36 Sessions					
N				26	6
Average Percent Change (*SD*)				−23.1 (25.2)	11.7 (47.0)
Median Percent Change				−20.83	−13.23
Response Rate (%)				38.5	0
Assessment at TMS End					
N					6
Average Percent Change (*SD*)					−1.64 (33.8)
Median Percent Change					−12.75
Response Rate (%)					16.7

independently of improvement in depressive symptoms. The study's limitations include the absence of control groups, high non-completion rate, low racial and ethnic diversity, and a limited sample size. These gaps highlight the need for future studies with larger sample sizes across multiple sites to optimize TMS for patients with OCD and utilize predictors of treatment response.

CRediT authorship contribution statement

Micah Breiger: Writing – review & editing, Writing – original draft, Visualization, Validation, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Samantha Baldi:** Writing – review & editing, Visualization, Validation, Methodology, Investigation. **Sarah Perlo:** Writing – review & editing, Writing – original draft, Data curation, Conceptualization. **Brian P. Brennan:** Writing – review & editing. **Joshua C. Brown:** Writing – review & editing, Methodology, Conceptualization. **Shan H. Siddiqi:** Writing – review & editing, Supervision, Methodology, Investigation. **Mahdi Razafsha:** Writing – review & editing, Writing – original draft, Supervision, Methodology, Investigation, Conceptualization.

Declaration of Competing Interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Joshua C. Brown reports a relationship with Elsevier Inc that includes: consulting or advisory and serves as the Editor-in-Chief of *Transcranial Magnetic Stimulation*. If there are other authors, they declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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