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Multimodal Neuroimaging in the Prediction of Deep TMS Response in OCD

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Abstract

Backgrounds: .Brain morphological biomarkers could contribute to understanding the treatment response in patients with obsessive-compulsive disorder (OCD). Multimodal neuroimaging addresses this issue by providing more comprehensive information regarding neural processes and structures. **Objectives.** The present study aims to investigate whether patients responsive to deep Transcranial Magnetic Stimulation (TMS) differ from non-responsive individuals in terms of electrophysiology and brain morphology. Secondly, to test whether multimodal neuroimaging is superior to unimodal neuroimaging in predicting response to deep TMS. **Methods.** Thirty-two OCD patients who underwent thirty sessions of deep TMS treatment were included in the study. Based on a minimum 50% reduction in Yale-Brown Obsessive Compulsive Scale (Y-BOCS) scores after treatment, patients were grouped as responders (n = 25) and non-responders (n = 7). The baseline resting state qEEG and magnetic resonance imaging (MRI) records of patients were recorded. Independent sample t-test is used to compare the groups. Then, three logistic regression model were calculated for only QEEG markers, only MRI markers, and both QEEG/MRI markers. The predictive values of the three models were compared. **Results.** OCD patients who responded to deep TMS treatment had increased Alpha-2 power in the left temporal area and increased volume in the left temporal pole, entorhinal area, and parahippocampal gyrus compared to non-responders. The logistic regression model showed better prediction performance when both QEEG and MRI markers were included. **Conclusions.** This study addresses the gap in the literature regarding new functional and structural neuroimaging markers and highlights the superiority of multimodal neuroimaging to unimodal neuroimaging techniques in predicting treatment response.

Keywords

deep transcranial magnetic stimulation, magnetic resonance imaging, obsessive compulsive disorder, quantitative EEG, multimodal neuroimaging

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Introduction

Obsessive–compulsive disorder (OCD) is one of the psychiatric diseases with a prevalence of 1% – 3% in adults[1] and a response rate of 40% - 60% to first-line treatments.[2] One of the brain modulation methods, particularly recommended for treatment-resistant OCD, is Transcranial Magnetic Stimulation (TMS). Based on the principle of inducing an electric field in the brain, TMS can modulate the activity of not only the cerebral cortex but also deeper neural circuits by reducing or increasing cortical excitability.[3]

Of note, there are several coil designs categorized under "deep TMS" and approved by the FDA for OCD treatment. A comparative study of two FDA-approved deep TMS interventions with two different coil, i.e, H-7 coil and D-B80, revealed that H-7 coil influences larger and deeper regions in the brain and induces more intense electrical field mostly in "pre-supplementary motor area (pre-SMA), inferior frontal gyrus (IFG), (dorsolateral prefrontal cortex (dlPFC), orbitofrontal cortex (OFC), dorsal anterior cingulate cortex (dACC).[4] The authors interpreted these results as deep TMS with H-7 coil influences brain regions which are considered part of the cortico-striato-thalamic-cortical circuitry (CSTC) associated with the pathology of OCD.[5]

In the treatment of OCD, the endorsed protocol for H-7 coil deep TMS involves high-frequency stimulation (20 Hz) targeting the medial prefrontal cortex (mPFC) and anterior cingulate cortex (ACC). Approximately 72.6% and 52.4% of patients exhibited an initial response and sustained response to deep

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TMS, respectively.[6] This brings the issue of what possible clinical factors could be associated with response to deep TMS in OCD treatment. According to another deep TMS study conducted for OCD treatment, age and severity of illness modulate the treatment response. While older patients show faster response, the severity of OCD is more related to greater treatment benefits from deep TMS stimulated with H-7 coil.[7] Besides, neuroimaging markers are heavily studied for predicting treatment response which is introduced below.

Functional Neuroimaging Markers for OCD in Response to TMS Treatment

There are several functional biomarkers of TMS treatment studied with OCD patients. Douw and colleagues reported that OCD patients who had greater baseline resting-state local connectivity evaluated by functional MRI and less temporal integration of the left dorsolateral prefrontal cortex predicted better benefits from excitatory rTMS applied to left DLPC.[8] Another resting state MRI predictor study to TMS applied 10 Hz stimulation to dorsomedial PFC to 20 treatment-resistant OCD patients. They targeted dmPFC connectivity and found that responders had higher dmPFC-ventral striatal connectivity at baseline. The degree of reduction in this connectivity, from pre- to post-treatment, correlated to the degree of symptomatic improvement concluding that the reductions in fronto-striatal hyperconnectivity were associated with treatment response to dmPFC-rTMS in OCD.[9] A recent study also focused on deep TMS and measured the brain activity of OCD patients during Strop Task by using functional fMRI. The authors stated a significant decrease in the activation of the left caudate nucleus and adjacent white matter after 2 weeks of dTMS treatment[10]

As for electrophysiological markers, one study compared the response to 1-Hz TMS applied to the right DLPFC. They found that responsive OCD patients had more QEEG theta activity on the general cortex compared ton non-responsive ones.[11] For Deep TMS treatment, electrophysiological biomarkers were also studied. The first clinical sham-controlled trial of deep TMS on OCD treatment used EEG event-related potentials in addition to clinical outcomes. The results yielded that as the improvement increased, an indicator of electrophysiological activity of ACC, Error Related Negativity (ERN), emerged in the theta band during the Stroop task.[12] Finally, another research showed that resting state QEEG activity changed with thirty sessions of dTMS treatment. Although the electrophysiological change is in theta, alpha, and beta activity, only the decrease in left central beta activity is found to be related to the improvement in OCD symptoms.[13]

Multimodal Neuroimaging in Classification of OCD

Multimodal neuroimaging is an approach that combines data sets obtained using $\geqslant 2$ unimodal modalities, such as EEG and MRI integration to yield more informative, consistent, and reliable results than can be obtained using unimodal neuroimaging. Multimodal neuroimaging contributes to the research in neuropsychiatric diseases by providing more comprehensive information regarding neural processes and structures. Thus, it can play an important role in understanding the treatment response of neuropsychiatric diseases.[14]

As described above, brain morphological and functional biomarkers could contribute to understanding the response to deep TMS as deep TMS can stimulate various brain regions.[4] Existing literature explores the structural and functional correlates of TMS response in standard repetitive TMS[15–21] in patients with MDD. While functional biomarkers have been identified in OCD samples responding to both repetitive TMS[8,9,11] and deep TMS,[10,12,13] a gap exists in the literature concerning structural neuronal predictors of TMS response in patients with OCD. Hence, the aims of the present study are;

1. To investigate whether patients responsive to deep TMS differ from non-responsive individuals in terms of brain morphology measured by magnetic resonance imaging and functionality measured by qEEG.
2. To test whether multimodal neuroimaging can better predict treatment response to deep TMS as opposed to unimodal neuroimaging by comparing the predictive power of only qEEG markers, only MRI markers, and a combination of both qEEG and MRI markers.

Methods

Study Design

This retrospective naturalistic case-control study had emerged from the routinely collected data of the private psychiatry clinic in Istanbul, Turkey. Each patient had been informed of the procedures and potential side effects of deep TMS before informed consent was obtained. Local ethics committee permission was received for the study (61,351,342/MAY 2023-20). The PECO of the study can be seen below:

Population: Patients with OCD, aged between 18–55 years.

Exposure: 30 sessions of deep TMS OCD protocol, applied as five days a week for 6 weeks.

Comparison: Two groups were determined based on response to deep TMS treatment: responders and non-responders. The criteria for groups are: At least 50% reduction in Y-BOCS scores from baseline to endpoint. No healthy control group is included. QEEG and MRI measurements were compared between the two groups.

Observations: Quantitative EEG records, MRI images analyzed by volumetric analysis, Hamilton Depression Rating Scale scores

Subjects were examined by the same psychiatrist between September 2019 and February 2024. The diagnosis of OCD was made in the first interview according to the Diagnostic and Statistical Manual of Mental Disorders, fifth edition (DSM-5).[22]

Data Collection and Filtering

Data collection which includes sociodemographic, clinical information was done by same experienced psychiatrist. All QEEG and MRI measurements were recorded by using same technical equipment. All the data were routinely stored in a private app designed for private use of the psychiatrist. These data anonymized and then converted into SPSS file via another software designed for the private use of the psychiatrist. The files of patients were retrospectively scanned in SPSS file. Inclusion criteria were applied as filters. These criteria are entered sequentially: 1-Receiving 30 sessions of deep TMS treatment (n = 221), 2-Diagnosis of OCD by DSM criteria (n = 102). 3-QEEG recording at baseline (n = 100). 4- MRI recording at baseline (n = 32). 5-Yale-Brown Obsessive-Compulsive Scale (Y-BOCS) scores at baseline and at the end of 30 sessions of deep TMS (n = 32). Exclusion criteria are any neuropsychological or organic diseases (eg, epilepsy), yet some of the patients had also unipolar depression or general anxiety.

After filters, the electronic records of 32 OCD patients (14 female and 18 male) aged at 18–60 (mean ± SD = 34.68 ± 12.77 years) remained for the analysis (Figure 1).

Further demographic information can be seen in Table 1. The primary clinical measure of OCD was Yale-Brown Obsessive-Compulsive Scale (Y-BOCS).[23] Patients were grouped as responders and non-responders. Response was defined as at least a 50% reduction in Y-BOCS scores from baseline to endpoint since 50% reduction criterion is appropriate for predicting mild illness at posttreatment.[24] In addition to Y-BOCS, depressive and anxiety symptoms evaluated by Hamilton Depression Rating Scale (HDRS),[25] Hamilton Anxiety Rating Scale[26] at baseline and endpoint were also measured.

QEEG Recording

All subjects underwent QEEG recording before paroxetine treatment. Resting-state QEEG recordings were taped in a silent, dim room with well air-conditioning. A 19-channel (FP1, F7, T3, T5, F3, C3, P3, O1, FZ, CZ, PZ, F4, C4, P4, O2, FP2, F8, T4, and T6) electro-cap was positioned onto the head of the participants according to the 10–20 international system. A transparent electro-gel was injected into the scalp to increase conductivity. The ground electrode was placed in the FPz position. Reference electrodes were positioned to both earlobes and average of both electrodes were used as reference. The impedance of electrodes was controlled whether they were <5000 ohm for each electrode.

A Neuron-Spectrum-4/P device was utilized to record resting-state QEEG activity while patients were in a comfortable sitting-positioned, closed-eye state. The total duration of records was approximately 7 min, consisted of a 3- minute background recording, a 30-s open eyes condition, and a 3.5-min closed-eyed condition. Data were sampled at 500 Hz rate; signals were bandpass filtered at 0.15–70 Hz and notch filtered at 50 Hz.

QEEG Analysis

Offline muscle artefacts were removed by an automatic artifact rejection in Neuroguide software (Applied Neuroscience, Inc.; Neurogude Deluxe version 3.8.2). Samples with artifacts were deleted and a minimum of 3-min edited data was obtained. Each patients' data were averaged across the recording epochs for each electrode, and the absolute power was computed for the following bands: delta (1-4 Hz), theta (4-7 Hz), alpha (8-12 Hz), alpha1 (8-10 Hz), alpha2 (10-12 Hz), beta (12-25 Hz), beta1 (12-15 Hz), beta2 (15-18 Hz), beta3 (18-25 Hz), high beta (25-30 Hz), gamma (30-50 Hz), gamma1 (30-35 Hz), gamma2 (35-40 Hz), high gamma (40-50 Hz). As qEEG data were highly skewed, natural log-transformation was applied. However, some qEEG parameters of high-frequency bands were between 0 and 1; therefore, "1" was added to qEEG parameters before natural log transformation to prevent negative log transformed values. The calculated data were transferred to SPSS.

MRI Recording

MR imaging was performed by using a 3T MR Scanner (Magnetom Lumina, Siemens Healthcare, Erlangen, Germany) and acquired with only head matrix coil. 180 sections high-resolution T1-weighted images (magnetization-prepared rapid gradient-echo [MPRAGE]) were obtained in axial and sagittal planes under the following parameters: echo time (TE) 3.50 ms, repetition time (TR) 1800 ms, flip angle 8 °, field of view (FOV) 250 × 250 mm^2, matrix 320 × 80 mm^2.

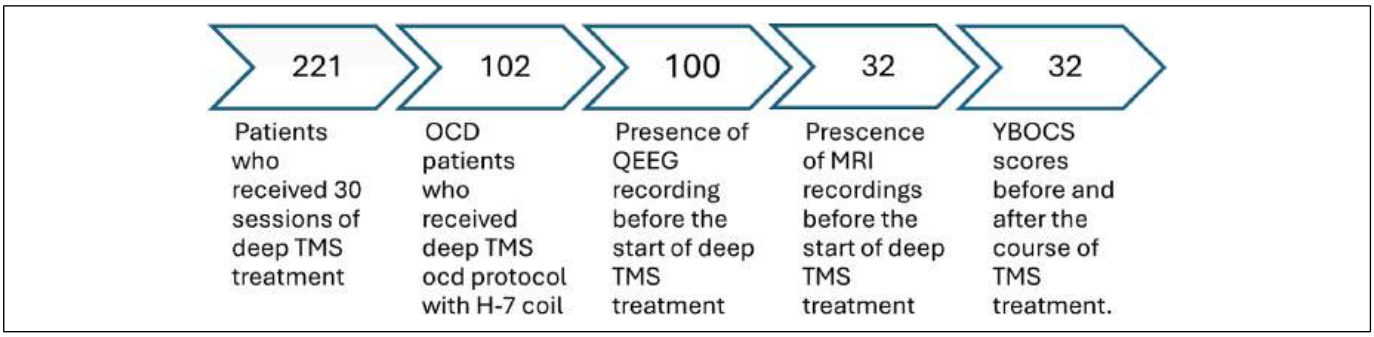

Figure 1. Participants remained for analysis after applying filters.

Table 1. Descriptive Statistics and Group Comparisons on Demographic and Clinical Variables.

Demographics	Diagnostic Groups		*N*	*M*	*SD*	*p*
Gender	Responder	Female	8			0.027[a]
		Male	17			
		Total	25			
	Non-responder	Female	6			
		Male	1			
		Total	7			
	Total	Female	14			
		Male	18			
Age	Responder		25	35.28	12.88	0.628[b]
	Non-responder		7	32.57	13.13	
	Total		32			
YBOCS baseline	Responder		25	29.08	11.16	0.466[b]
	Non-responder		7	32.71	12.84	
	Total		32			
HDRS-17 Baseline	Responder		25	7.88	6.38	0.580[b]
	Non-responder		7	6.29	7.72	
	Total		32			
HARS Baseline	Responder		25	10.88	8.94	0.874[b]
	Non-responder		7	10.29	7.54	
	Total		32			
YBOCS Second visit	Responder		25	2.84	3.35	0.000[b]
	Non-responder		7	26.43	12.49	
	Total		32			
HDRS-17 Second visit	Responder		25	1.32	1.86	0.006[b]
	Non-responder		7	8.43	11.91	
	Total		32			
HARS Second visit	Responder		25	1.44	1.50	0.004[b]
	Non-responder		**7**	9.29	12.66	
	Total		32			
Duration of illness (years)	Responder		25	14.70	8.94	0.702[b]
	Non-responder		7	13.07	11.05	
	Total		32			
Drug Free	Responder	Yes	17			0.667[a]
		No	8			
	Non-Responder	Yes	4			
		No	3			
	Total		32			
Duration of Disease Onset	Responder		25	21.32	10.08	0.538[b]
	Non-Responder		7	18.79	5.54	
	Total		32			

Note: YBOCS = Yale-Brown Obsessive Compulsive Rating Scale. HDRS = Hamilton Depression Rating Scale. HARS = Hamilton Anxiety Rating Scale.
[a]Fisher's Exact test result.
[b]Independent Sample t-test result.

First, all MRI series of the patients were examined. Patients with lesions that would cause changes in the cortical thickness and volume of other brain structures, such as intracranial space-occupying lesions (tumor, arachnoid cyst, etc), previous cerebral infarcts, were excluded. Then, T1-weighted MPRAGE images were downloaded from the scanner.

MRI Analysis

MPRAGE images were processed and saved in NIFTI format. The NIFTI images of all subjects (33 patients with OCD, 56 HCs) were uploaded to VolBrain (https://VolBrain.upv.es).[27] VolBrain is a fully automatic pipeline for volumetric brain analysis based on multiatlas label fusion technology that is able to provide accurate volumetric information. This method is publicly, freely accessible and without the need for any infrastructure. The vol2brain option was selected in this system. The vol2 brain option is a more developed version of the previous volBrain pipeline, and with this option, segmentation analysis of all intracranial structures is performed and labeled intensively ($N > 100$). This method is based on a multiscale multiatlas label fusion technology.[28]

After MPRAGE images are uploaded to Vol2Brain, the results of analysis are downloaded. In the analysis in csv

format, intracranial structures are divided into separate segmentations as right and left, and volume (mm^3) and thickness measurement results are included. Total measurements of intracranial structures (cortex and subcortical gray matter, white matter, cerebrospinal fluid), right and left separate results, asymmetry between both sides, macrostructure volume, structure segmentation, volume calculation of cortical, subcortical structures and cerebral lobes, subsegments along with cortical thicknesses are obtained. The obtained data were transferred to SPSS.

Deep TMS Intervention

For the deep TMS sessions, Brainsway's H7 coil deep TMS System was used (Brainsway, Har Hotzvim, Jerusalem, Israel). OCD protocol was applied according to the guidelines of the manufacturing company.

The measurement of the motor threshold and the intervention were conducted by two certified clinical practitioners. The motor threshold (MT) was measured with the H7 coil positioned over the leg area of the motor cortex and a minimum threshold was detected when an observable twitch is seen in either resting leg. The motor threshold was reassessed in each treatment session. The treatment position of the coil for OCD is 4 cm anterior the location where maximum stimulation is observed for the motor threshold measurements.

Deep TMS was administered at 100% of the resting leg motor threshold in 20-Hz 2 s trains, with 20-s intertrain intervals, for fifty trains totaling 2000 pulses. OCD symptoms were induced by asking patients to think about or visualize their obsessions during the TMS sessions.[29]

Statistical Analysis

All the statistical analyses were conducted in SPSS (version 25). The normality control of the groups, i.e, responders and non-responders was performed with the Shapiro wilk test and was observed that the normality assumption was met.

Chi-square or Fisher's exact test was selected to check the distribution of categorical variables, ie, gender and drug-use. Clinical variables namely, severity of obsession, depression, and anxiety severity were compared between responders and responders by independent sample t-test. The possible confounding variables (age, severity of obsessive-compulsive, depressive and anxiety symptoms at baseline, duration of illness, age at disease onset, use of medications) were checked groups but did not show significant differences. Therefore, they were not taken as confounding variables in MRI and EEG analysis.

Brain structure, thickness and general brain measurements, i.e, white matter, gray matter volumes were compared among responders and non-responders. For all the related regions, total volume (cm^3) and total thickness (mm) values were compared for both left and right areas separately. Brain structure and cortical thickness were compared with independent samples t-test. The variables with significant differences in the t-test were included in logistic regression analysis and the results were reported. The level of statistical analysis (alpha) was determined as 1% for independent sample t-test to avoid data dredging and 5% for logistic regression.

Results

Demographic and Clinical Variables

Demographic and clinical variables between responders and non-responders can be seen in Table 1. The groups did not differ from each other with respect to age (Table 1). As Chi square test indicates, the groups are not homogenous for gender ($p < .05$) meaning the females constitute the majority of non-responders to dTMS while males constitute the majority of responders to dTMS. (Table 1).

Other clinical variables were investigated for only responder and non-responder groups. Both patient groups were similar for baseline scores of YBOCS, HDRS-17, HARS, duration of illness, and use of medication, however, they had distinct YBCOS, HDRS-17, HARS scores at the end of dTMS treatment as expected (Table 1).

Structural Volumes of Brain Regions

As independent sample t-test indicates OCD patients responsive to deep TMS had similar cortical thickness and overall brain morphology compared to non-responsive patients. However, they differ in structural volume of various brain regions, namely bilateral parahippocampal gyrus, entorhinal area and left temporal pole ($p < .01$) (Table 2 and Figure 2).

QEEG Absolute Power

The independent sample test revealed that the responders differed from non-responders in electrode band pairs in that they had more qEEG Alpha-2 spectral power in T5 region compared to non-respnders ($p < .01$) (Table 2).

Logistic Regression Analysis

Logistic regression analysis was separately conducted for only MR predictors, only qEEG predictor and both MR and qEEG predictors together (Figure 3). Based on Nagelkerke R Square values, it can be concluded that both MR predictors, i.e, bilateral parahippocampal volume, left temporal pole and entorhinal area volume, and qEEG predictor T5 Alpha-2 power had better predictive power (0.581) (Table 3) than only MR predictors (0.421) (Table 4) or only qEEG predictors (0.268) (Table 5).

Discussion

Predicting treatment response in psychiatric disorders, particularly in obsessive-compulsive disorder (OCD) and depression,

Table 2. QEEG and MRI Measurements Significantly Differed Between dTMS Responders and non-Responders.

	Nonresponders: 0		Responders:1				
	n = 7		n = 25		Between Subject		
Variables	*M*	*SD*	*M*	*SD*	*t*	*df*	*p*
T5 Alpha-2 Absolute Power	1.49	0.13	2.31	0.87	-4.55	27.13	0.00
Temporal pole Left	7.67	2.04	9.79	1.62	-2.53	8.23	0.03
Entorhinal area Total	3.53	0.81	4.19	0.72	-1.94	8.80	0.09
Parahippocampal gyrus Total	4.72	1.02	5.74	0.82	-2.43	8.28	0.04
Parahippocampal gyrus Right	2.37	0.53	2.82	0.43	-2.11	8.31	0.07
Parahippocampal gyrus Left	2.35	0.53	2.91	0.44	-2.55	8.37	0.03

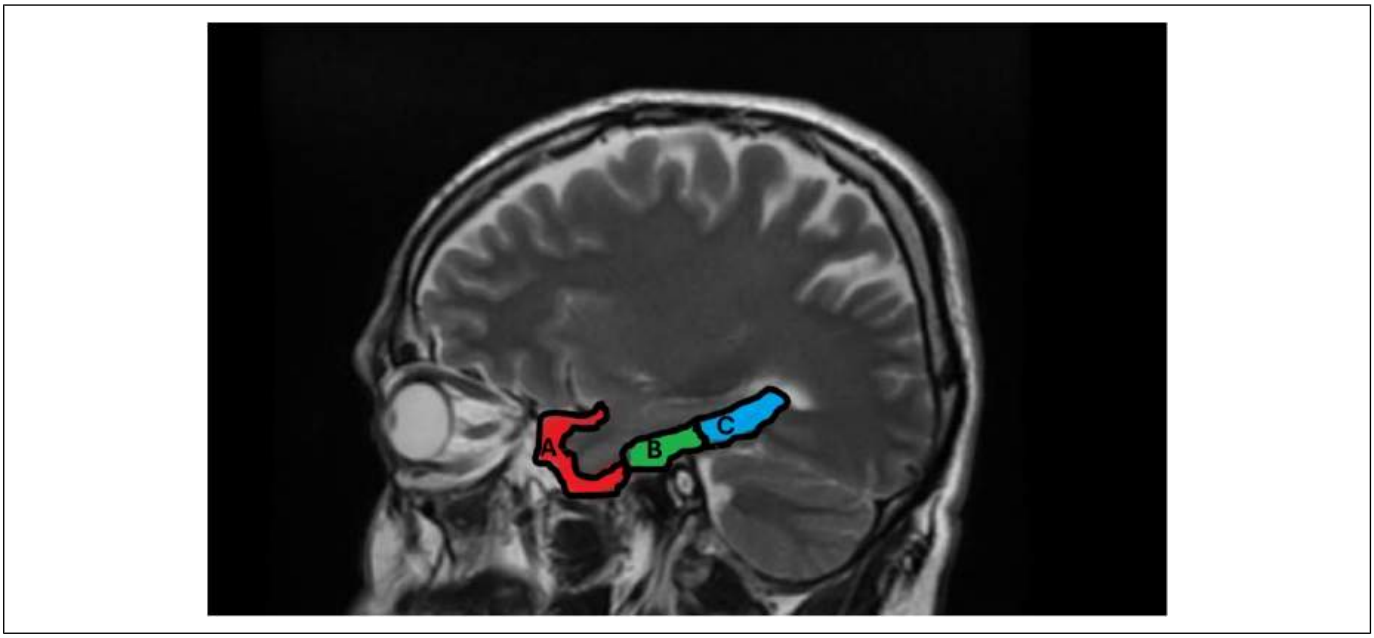

Figure 2. Lateral view of the brain presenting predictors of MRI model. *Note.* A = Temporal Pole. B = Entorhinal Cortex. C = Parahippocampal gyrus.

holds significant ethical and clinical importance. In OCD, this importance is further emphasized due to the necessity of administering high doses of SSRIs, highlighting the importance of preventive medicine.

Accurate prediction can save time for the patient, prevent economic losses such as disability, and avoid unnecessary side effects. For these reasons, scientists are heavily invested in identifying markers to predict treatment response. Some of these markers include electrophysiological and morphological indicators.

Among these, electrophysiological markers are of special importance because they are frequently repeatable, cost-effective, and non-invasive. Although the use of MRI for prediction in OCD is not common, morphological analyses are routinely employed to identify the etiology of the disorder. It is well known that various anatomical pathological conditions can lead to OCD.[30]

Since MRI is already used clinically before treatment, the collected data can be analyzed as a potential predictor of response. Although not common, MRI data is indeed used to predict pharmacotherapy, cognitive behavioral therapy, and electroconvulsive therapy response in psychiatric disorders[31–36] including OCD.[37,38]

In the present study, firstly, we found a substantial association among increased left temporal alpha 2 activity along with greater volume of left temporal pole, entorhinal area, and bilateral parahippocampal area and good response to deep TMS treatment in OCD. Then, we used existing data to evaluate the predictive power of qEEG and MRI separately. Additionally, we examined whether the combination of these two modalities enhanced predictive power. We found that both electrophysiological and MRI approaches individually possess significant predictive value in regression analyses. When we combined these approaches (multimodal brain imaging), we observed a higher predictive power compared to the individual strengths of the biological markers alone. This

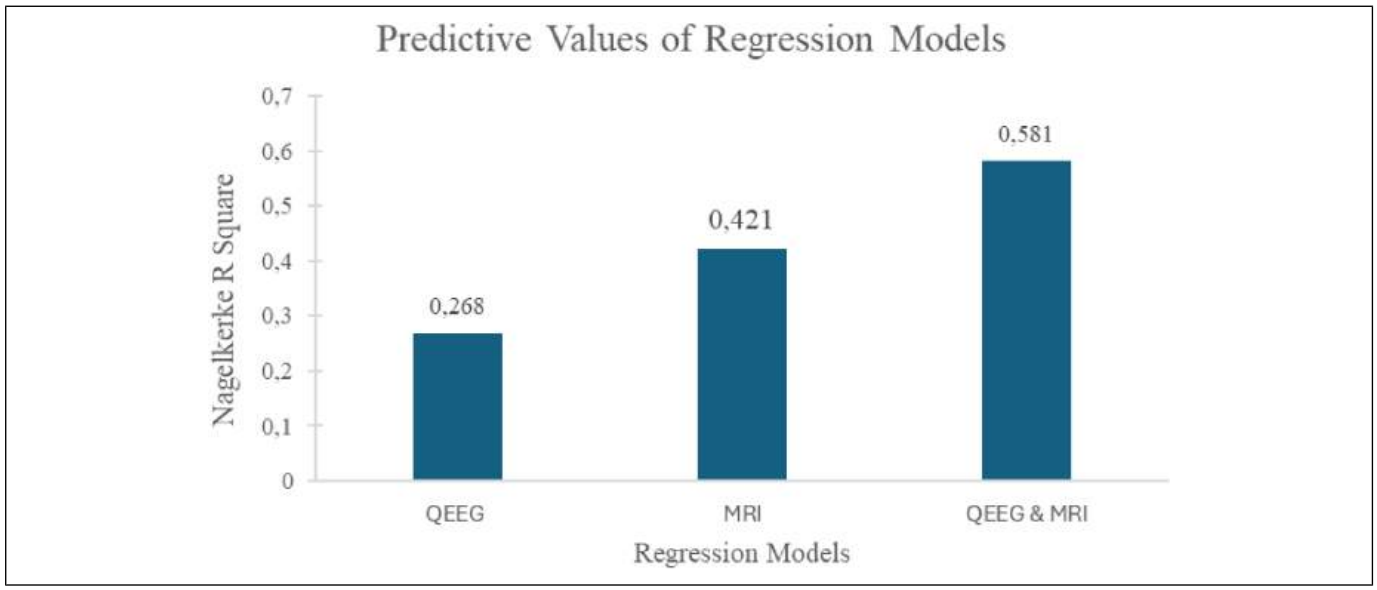

Figure 3. The graph of nagelkerke R square values for three logistic regression models. *Note.* QEEG model includes T5-Alpha 2 absolute power as predictor. MRI model includes left temporal pole volume, entorhinal area total volume; left, right and total Parahippocampal gyrus total volume as predictors. QEEG & MRI includes all predictors of QEEG and MRI models.

Table 3. Logistic Regression Analysis for dTMS Treatment Response of OCD Patients by qEEG Predictor.

							95% C.I.		
Predictors	B	S.E.	Wald	df	p	Exp(B)	Lower	Upper	Nagelkerke R Square
T5 Alpha-2	1.55	0.73	4.41	1	0.03	4.71	1.11	20.04	0.26
Constant	-1.63	1.32	1.51	1	0.21	0.19			

Table 4. Logistic Regression Analysis Result for dTMS Treatment Response of OCD Patients by MRI Predictors.

							95% C.I.for		
Predictors	B	S.E.	Wald	df	p	Exp(B)	Lower	Upper	Nagelkerke R Square
Temporal pole Left	0.72	0.49	2.18	1	0.14	2.05	0.78	5.33	0.42
Entorhinal areaTotal	−1.07	1.24	0.74	1	0.39	0.34	0.03	3.93	
Parahippocampal gyrus Total	100.90	159.82	0.40	1	0.53	6.58	0.00	7.23	
Parahippocampal gyrus Right	−101.19	159.91	0.40	1	0.53	0.00	0.00	1.50	
Parahippocampal gyrus Left	−98.76	159.60	0.38	1	0.54	0.00	0.00	9.07	
Constant	−5.64	3.57	2.50	1	0.11	0.00			

Table 5. Logistic Regression Analysis Result for dTMS Treatment Response of OCD Patients by MRI and qEEG Predictor.

							95% C.I.for		
Predictors	B	S.E.	Wald	df	p	Exp(B)	Lower	Upper	Nagelkerke R Square
Temporal pole Left	0.36	0.52	0.47	1	0.49	1.43	0.51	4.07	0.581
Entorhinal area Total	0.06	1.62	0.00	1	0.97	1.06	0.04	25.37	
Parahippocampal gyrus Total	64.08	173.13	0.14	1	0.71	6.77	0.00	1.57	
Parahippocampal gyrus Right	−65.20	172.84	0.14	1	0.70	0.00	0.00	6.42	
Parahippocampal gyrus Left	−60.57	173.28	0.12	1	0.72	0.00	0.00	1.55	
AP T5 LE Alpha 2	2.04	1.14	3.18	1	0.07	7.70	0.81	72.49	
Constant	−12.09	6.93	3.04	1	0.08	0.00			

was demonstrated by showing the percentage of the population represented by the predictive value of these biological markers.

QEEG Alpha Power and Treatment Response

Alpha waves are neural oscillations within the 8–12 Hz frequency range, detectable via electroencephalography (EEG). Typically, there is an inverse relationship between resting-state alpha power and the local activation of a brain region.[39] Numerous studies have reported an association between elevated baseline alpha oscillations and responsiveness to various antidepressant medications[40–44.]

Moreover, a reduction in alpha power after several weeks of treatment has been documented in responders to various selective serotonin reuptake inhibitors (SSRIs).[42,45,46] Based on these findings, greater baseline alpha power and a reduction in alpha activity in responders appear to be common across different treatment modalities, suggesting that these patterns could serve as general markers of response to antidepressant treatments, including cognitive behavioral therapy (CBT).[47]

This phenomenon may also apply to patients with obsessive-compulsive disorder (OCD), as they are often treated with antidepressants. For instance, increased left frontal alpha power at baseline is associated with a positive response to fluoxetine,[48] and elevated relative alpha power is linked to a favorable response to paroxetine in OCD patients.[49]

Temporal Area, Parahippocampus, Entorhinal Area Morphology and Treatment Response

The temporal pole, or temporopolar area, is a region of the anterior temporal lobe associated with several high-level cognitive processes. These include visual processing for complex objects and face recognition, autobiographical memory, naming and word-object labeling, semantic processing across all modalities, and socio-emotional processing, as demonstrated in both healthy subjects and patients with neurological or psychiatric conditions.[50] Specifically, the left temporal pole, also known as Brodmann area 38, is implicated in various language functions such as semantic processing, speech comprehension, and naming.[51]

The parahippocampal gyrus, located along the ventromedial edge of the temporal lobe adjacent to the hippocampus, has been recognized as a prominent structure of the limbic lobe since early human neuroanatomical research. Studies in both non-human animals and humans indicate that the parahippocampal gyrus is involved in complex emotive processes and is significantly interconnected with other cortical limbic structures as well as the amygdala.[52] The entorhinal area, part of the parahippocampal region, constitutes a major component of the medial temporal lobe memory system. It is involved in higher-order cognitive processing, particularly memory processes.[53]

Similar to our findings, the smaller entorhinal area along with the parahippocampal area were associated with treatment-resistant depression,[54] failure to reach remission with antipsychotic treatment in first-episode schizophrenia,[55] and conversion from mild cognitive impairment to Alzheimer's disease.[56] These brain regions have also been previously studied in patients with obsessive-compulsive disorder (OCD). For instance, treatment response to CBT in OCD patients has been predicted by brain activity patterns in these regions.[37] As for the response to pharmacotherapy in OCD, cortical morphology-based networks including language network with the temporal area, and limbic network with parahippocampal gyrus predicted the pharmacotherapy responders and non-responders with an accuracy of 89.0%.[38]

Limitations

Two main limitations of the study harden the interpretation of the results. The first one is the small sample size which makes the replication of the findings harder. The second one is the distribution of gender on responder-non responder groups, where almost half of the females responded to treatment and only one male responded. Parahippocampal gyrus, entorhinal cortex, and temporal pole are all known to be larger in males than females. However, when there is no full consensus on this subject in the literature and that different results have been obtained in the studies.[57–59]

Conclusion

The advantages of multimodal neuroimaging are evident. "Each of these techniques has advantages and disadvantages related to resolution, safety, availability, and accessibility. Thus, multimodal neuroimaging overcomes the limitations of unimodal techniques and play an important role in the detection, diagnosis, prognosis, and treatment of some diseases like neuropsychiatric diseases"[14(pp4-5)]

In conclusion, this study demonstrates the clinical importance of routine daily electrophysiological and morphological analyses, preventing the wastage of valuable data. Lastly, it highlights that multimodal neuroimaging techniques are superior to unimodal neuroimaging techniques in differentiating treatment response of patients with OCD.

Data Availability Statement

The data that support the findings of this study are not publicly available. However, the data are available on request from the corresponding author (M.K.A)

Declaration of Conflicting Interests

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Ethical Statement

All subjects gave their informed consent for inclusion before they participated in the study. The study was conducted in accordance with the Declaration of Helsinki, and the protocol was approved by the Ethics Committee of Uskudar University (61351342/MAY 2023-20).

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