Association of QEEG Findings With Clinical Characteristics of OCD: Evidence of Left Frontotemporal Dysfunction

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**Objective:** Our objectives were 1) to determine hemispheric asymmetry and regional differences on the EEGs of patients with obsessive–compulsive disorder (OCD); and 2) to investigate the effects of sex, treatment response, illness duration, and Yale-Brown Obsessive Compulsive Scale (Y-BOCS) scores on quantitative electroencephalographic (QEEG) measurements.

**Method:** We recorded EEGs (12-channel) from 22 unmedicated patients with OCD but no depression and from 20 age- and sex-matched control subjects. All patients and control subjects underwent detailed neurological and psychiatric evaluations including the Hamilton Depression Rating Scale (HDRS) and Y-BOCS.

**Results:** QEEG revealed higher frequencies of slow-wave bands and lower frequencies of alpha activity at predominantly left frontotemporal localization in patients with OCD, compared with control subjects. Analysis of variance of QEEG parameters and clinical characteristics showed that sex had a significant effect on delta and alpha frequencies of frontotemporal areas during hyperventilation (HV). Increasing total Y-BOCS score correlated positively with increased frequencies of right parietal delta activity and decreased frequencies of right frontotemporal alpha activity during HV. A significantly increased left frontal slow-wave activity and decreased beta activity during HV in treatment responders led us to consider that frontal lobe functions were better in this group of patients. Illness duration had no important effect on QEEG.

**Conclusion:** Patients with OCD showed important frontotemporal dysfunction, predominantly in the left hemisphere. This was particularly evident in female subjects and in treatment responders. QEEG may be beneficial in understanding the neurobiological basis of OCD.

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**Clinical Implications**
- The finding of left frontotemporal dysfunction observed in visual EEG in patients with obsessive–compulsive disorder (OCD) has been confirmed by quantitative electroencephalographic (QEEG) measurements.
- Left frontotemporal dysfunction was most significant in female patients with OCD and in treatment responders.
- The severity of left frontotemporal dysfunction correlated positively with the severity of OCD.

**Limitations**
- Because specific software was lacking, we performed QEEG analysis by transferring the data obtained from the EEG equipment software to a statistical computer program, and this method may have caused some errors.
- A second QEEG analysis was not performed at the end of the treatment period.
- A single activation method (hyperventilation) was used in EEG.
- The number of male patients was relatively low.

**Key Words:** obsessive–compulsive disorder, electroencephalogram, EEG, quantitative analysis, hemispheric asymmetry, left hemisphere, frontotemporal dysfunction
Obsessive-compulsive disorder (OCD) is characterized by recurrent and disturbing thoughts (obsessions) or repetitive and stereotyped behaviours (compulsions), or both, that the sufferer feels driven to perform but recognizes as irrational or excessive (1,2). Over the past decade, there has been increasing interest in the neurobiological basis of OCD. Neuroradiography and positron emission tomography (PET) studies indicate an increased prevalence of neurologically soft signs and increased metabolism in the frontal cortex, basal ganglia, and cingulate gyrus (3–9).

There are relatively few studies investigating the EEG manifestations of the obsessional syndrome. In the first such study, Pacella and others found that 64% of 31 patients had definite EEG abnormalities, principally in the slow-wave frequencies (10). This was confirmed by Rockwell and Simons, who obtained EEG abnormalities in the same frequency bands in 54% of 24 patients (11). Epstein and Balline described the appearance of temporal spikes during stage 1 and the REM phase of sleep in 3 patients with obsessional symptoms and abnormal waking EEG, but without epilepsy (12).

Flor-Henry and others reported relatively decreased variability in the left temporal region (3). Insel and others reported that, in subjects found to have abnormal EEGs, the abnormality was “nonspecific theta activity” (13). In reviewing EEG data obtained from patients with OCD, Jenike and Brotman concluded that EEG disturbances, when present, were predominantly in the temporal and frontotemporal regions (14).

In a detailed quantitative electroencephalographic (QEEG) study, Khanna found decreased power in the nondominant frontotemporal and posterior temporal regions (15). In an important study using QEEG and brain mapping, Perros and others found significantly increased relative power in the theta-2 band in the left temporal and central regions and significantly reduced variability in frontal and temporal regions (16).

Pritchep and others reported the existence of 2 subtypes of OCD patients within a clinically homogeneous group of patients who met DSM-III-R criteria for OCD. Their QEEG results suggested that Cluster 1 (treatment nonresponders) was characterized by excess relative power in theta, especially in the frontal and frontotemporal regions, and Cluster 2 (treatment responders) was characterized by increased relative power in alpha (9).

Drake and others compared EEG spectral measures in patients with OCD and in healthy control subjects and reported that modal alpha frequency (MAF) and maximal alpha frequency (MxAF) were reduced in the frontal regions in patients, compared with control subjects (17). Most of these observations support the hypothesis that obsessions and compulsions have a physiologic basis and frontal lobe disturbance in their pathophysiology. However, studies conducted so far have described EEG changes obtained from restricted region recordings. The association of EEG findings with the clinical characteristics of OCD and with patients’ sex has not been clarified.

This study investigates EEG changes at resting state (RS) and during hyperventilation (HV) in unmedicated OCD patients without depression and in healthy control subjects. It also investigates the possible association of clinical characteristics of OCD and QEEG findings.

Method

Subjects

The patients and the control subjects were matched for age and sex. Table 1 gives their demographic characteristics. We selected 22 right-handed OCD patients as the study group and 20 right-handed healthy subjects as the control group. Patients were consecutively selected from among those applying to the psychiatric outpatient clinic of Mersin University Faculty of Medicine. Twelve patients had never taken treatment for OCD. Ten patients had previous treatment periods but had not taken psychotropic drugs for at least 2 weeks prior to the study, either from noncompliance or because of adverse effects. None of the control subjects had a history of any psychiatric disorder, and none had ever taken drugs affecting the central nervous system (CNS). Inclusion criteria for the study were as follows: 1) a strict DSM-IV diagnosis of OCD, 2) the presence of symptoms for at least 1 year, 3) being free of psychotropic drugs for at least 2 weeks prior to the study, 4) being neurologically intact (that is, without epilepsy, stroke, head injury, dementia, or sleep disorder), 5) being free of concomitant severe or chronic medical illnesses (for example, hepatic failure or chronic renal failure) or comorbid psychiatric disorders (for example, other anxiety disorders, depression, schizophrenia, or substance abuse), and 6) having no history of psychosurgery or any other neurosurgical procedure. All patients received treatment for OCD. Depressive symptoms on the Hamilton Depression Rating Scale (HDRS) were absent or mild (that is, scores were below 15) (18). Validity and reliability of the Turkish version of the HDRS has been tested by Akdemir and others (19). Patients reported a wide range of obsessions and compulsions. Most often, these included hand-washing, checking, and hoarding compulsions and contamination, aggressive, somatic, and religious obsessions, as well as pathological doubt. Eight patients showed obsessional thoughts without significant compulsions. We administered
Table 1 Demographic and clinical characteristics of the groups

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>OCD patients (n = 22)</th>
<th>Control subjects (n = 20)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td>5 men, 17 women</td>
<td>6 men, 14 women</td>
</tr>
<tr>
<td>Age (years)</td>
<td>28 (SD 7, range 14 to 47)</td>
<td>30 (SD 2, range 18 to 39)</td>
</tr>
<tr>
<td>Duration of education (years)</td>
<td>10.1 (SD 4.2)</td>
<td>9.4 (SD 2.8)</td>
</tr>
<tr>
<td>Age at onset of symptoms</td>
<td>23 (SD 4)</td>
<td>—</td>
</tr>
<tr>
<td>Duration of illness (year)</td>
<td>5.2 (SD 4.1)</td>
<td>—</td>
</tr>
<tr>
<td>Y-BOCS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Obsession subscore</td>
<td>12.6 (SD 3.03, range 6 to 18)</td>
<td>—</td>
</tr>
<tr>
<td>Compulsion subscore</td>
<td>9.6 (SD 5.2, range 0 to 20)</td>
<td>—</td>
</tr>
<tr>
<td>Total score</td>
<td>22.3 (SD 6.2, range 14 to 38)</td>
<td>—</td>
</tr>
</tbody>
</table>

*χ² test: P > 0.05; **t-test: P > 0.05

the Yale-Brown Obsessive Compulsive Scale (Y-BOCS) to assess the severity of obsessive-compulsive symptoms (20,21). Validity and reliability of the Turkish version of Y-BOCS has been tested by Tek and others (22).

After clinical evaluation, patients were started on pharmacotherapy (11 patients on fluvoxamine [dosage range, 100 to 300 mg daily], 4 on fluoxetine [dosage range, 20 to 80 mg daily], and 5 on sertraline [dosage range, 100 to 200 mg daily]). Treatment drugs were determined on the basis of previous treatment and adverse effects. Dosages were adjusted according to each patient’s clinical condition and adverse-effect status. At the end of month 3, we evaluated treatment response, using the Clinical Global Impression Scale (CGI) (23). Responders were defined as very much improved or much improved, and nonresponders as those who showed minimal or no change on CGI; 13 patients were responders and 7 patients were nonresponders. Two patients discontinued drug therapy and were excluded from the treatment-response analysis.

All subjects gave informed consent after a full explanation of the study and the EEG testing procedure.

Procedure
Each subject was seated in a soundproof, light-controlled, well-ventilated resting EEG recording room while 30 minutes of eyes-closed resting EEG data were collected from the 14 monopolar electrode sites of the International 10/20 system, referred to Cz. We used the following 12-channel and Ag/AgCl disk electrodes (Medelec, Oxford, England) for the data collection: O₁, P₃, P₅, T₃, T₅, T₇, T₉, F₃, F₄, F₇, F₉, T₄, T₆, T₈, T₁₀, O₂, and P₃, O₂ (transverse montage). Electrodes were applied with collodion and impedance was kept below 5 KΩ. EEG recordings were made with Medelec Profile equipment and software (24). The EEG amplifiers had a bandpass from 0.3 to 70 Hz (3 decibel points), with a 60-Hz notch filter. Recordings were made during RS and HV.

After performing visual analysis, a series of 2-second epochs of raw EEG data were inspected on the computer screen to eliminate artifact eye movements and muscle activity. To enter the study, each subject was required to provide at least 10 artifact-free epochs for each of the 2 experimental conditions (RS and HV). All the patients and control subjects met this requirement.

We analyzed the artifact-free epochs using frequency analysis of basic wave forms (alpha 8.5 to 12 Hz, beta 12.5 to 30 Hz, delta 0.5 to 3 Hz, theta 3.5 to 8 Hz). Hemispheric asymmetry and regional differences (frontal F₃, F₄, F₇, F₉, temporal T₃, T₄, T₅, T₆; parietal P₃, P₄) were evaluated with frequency analysis. For illustrative purposes, we constructed maps of probabilities based on t-test values from comparisons at each electrode site.

Statistical Analysis
We used SPSS 7.0 software for the statistical analyses (25). We conducted repeated measures analysis of variance (ANOVA), with Greenhouse-Geisser correction, for the absolute values and evaluation of clinical and demographic parameters and QEEG results. In the analysis, we used a model of 6-factor ANOVA. The factors were transverse montage (12-channel), recording state (RS or HV), wave forms (alpha, beta, theta, and delta), group (patient and control), hemisphere (right and left), and region (frontal, temporal, and parietal). In addition, we used Student’s t-test and Fisher’s exact test where appropriate. The effects of sex, treatment response,
duration of illness, and Y-BOCS scores on QEEG were analyzed in the same regression analysis model. P-values less than 0.05 were considered statistically significant.

Results
In visual analysis of EEG recordings, 1 control subject showed nonspecific intermittent irregular left temporal slow-wave activity. In the patient group, 3 women showed nonspecific intermittent left temporal sharp-wave activity. Two patients (1 man and 1 woman) with abnormal EEGs showed left hemisphere bursts of rhythmic theta activity. None of the patients had epileptiform discharges.

As shown in Table 2, QEEG analysis of RS showed a considerable increase in delta and theta activity and a decrease in alpha activity of left frontotemporal regions—differences not observed during HV. A decrease in beta activity was significant only in left frontal recordings during HV (P = 0.01).

When the associations of clinical characteristics and QEEG findings were considered, increased left temporal theta activity in RS was associated with increasing illness duration. The relative EEG power of delta and theta waves was significantly higher in patients than in control subjects (Figure 1). However, this was not observed in HV recordings (Figure 2). Female patients showed significantly decreased alpha and beta
Figure 2 Relative EEG power of patient and control subject recordings during hyperventilation

activity in RS and increased theta activity in the left frontal region. In female patients, increased left frontotemporal delta activity and frontal theta activity was associated with decreased frontal alpha activity. In the treatment-responder group, increased left frontal delta activity was associated with moderately decreased beta activity in the right parietal region (Table 3 and Table 4). In treatment responders, decreased right parietal beta activity changed to left frontal beta activity during HV.

Increased left temporal theta activity in RS correlated significantly with increasing Y-BOCS scores, but such a correlation was not observed during HV. Decreased alpha activity became significant in bilateral frontal recordings during HV.

Initial YBOCS scores of the treatment responders and nonresponders were 20.7 (SD 5.7) and 23.4 (SD 8.9), respectively. The difference was not statistically significant ($P = 0.43$).

Discussion

The results of the present study indicate a reduced electrical activity in patients with OCD, predominantly in left frontotemporal regions of the cortex. The increase in EEG power was confined to delta, and to a lesser extent, theta bandwidths. However, alpha powers decreased in some of the samples from frontotemporal and, more rarely, from right parietal areas. These findings partly agree with the opinion that the frontal lobes are involved in OCD; some evidence has located delta bandwidth wave generators in deep frontal regions (10,26).

Significant irregular theta activity observed by visual EEG analysis of recordings from frontotemporal regions—particularly the left—were similar to reports from other authors (3,10–13,16). As similarly reported by Jenike and Brotman (14), 5 patients (1 man and 4 women) showed abnormal non-specific EEG patterns in their left frontotemporal EEG recordings. Although Rapoport and others reported no alterations in EEG pattern of patients with OCD, abnormalities in our patients ranged from the irregular theta rhythm to sharp-wave activity (27).

QEEG analysis supported our visual observation of increased slow-wave activity, predominantly in the left frontotemporal region. In their power-spectral EEG analysis of 10 patients with OCD, Flor-Henry and others reported temporal and parietal abnormalities, predominantly in the left hemisphere (3). Studies by Perros and others and Pritchep and others also support these findings (9,16). However, Kuskowsky and others reported reduced electrical activity predominating over the right hemisphere, according to QEEG and neuropsychological parameters (28). Contrary to our finding of decreased alpha power, Kuskowsky and others reported generally increased alpha power (28).

As an activation method in EEG studies, HV consists of deep and regular respiration at a rate of about 20/min for a period of
Table 3 The relation between clinical characteristics and qualitative electroencephalographic (QEEG) variables in resting state recordings of patients with OCD

<table>
<thead>
<tr>
<th>Electrode localizations</th>
<th>Δ (2–4 Hz)</th>
<th>θ (5–7 Hz)</th>
<th>α (8–12 Hz)</th>
<th>β (13–18 Hz)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex (women or men)a</td>
<td></td>
<td>F3↑</td>
<td>F3↑</td>
<td>F3↓</td>
</tr>
<tr>
<td>Responder or nonresponderb</td>
<td>F7↑</td>
<td></td>
<td></td>
<td>P4↓</td>
</tr>
<tr>
<td>Duration of illnessb</td>
<td></td>
<td>T3↑ (R:0.46)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total score of Y-BOCSb</td>
<td></td>
<td>T3↑ (R:0.39)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

↓, ↑: P < 0.05; ↓↑: P < 0.01.
a Differences are given with reference to the second item (women or men, responder or nonresponder). b Data are taken as continuous variables into the logistic regression model, no cut-off point determined.

Table 4 The relation between clinical characteristics and QEEG parameters of patients with OCD during hyperventilation

<table>
<thead>
<tr>
<th>Electrode localizations</th>
<th>Δ (2–4 Hz)</th>
<th>θ (5–7 Hz)</th>
<th>α (8–12 Hz)</th>
<th>β (13–18 Hz)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex (women or men)a</td>
<td></td>
<td>T4, T6, F3, F7↑</td>
<td>F7↑</td>
<td>F3↓</td>
</tr>
<tr>
<td>Responder or nonresponder</td>
<td></td>
<td>F3↑</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Duration of illnessb</td>
<td></td>
<td></td>
<td></td>
<td>F7↓</td>
</tr>
<tr>
<td>Total score of Y-BOCSb</td>
<td>P4↑</td>
<td></td>
<td>F4, F6, T6, P4↓</td>
<td>T3↓</td>
</tr>
</tbody>
</table>

↓, ↑: P < 0.05; ↓↑: P < 0.01.
a Differences are given with reference to the second item (women or men, responder or nonresponder). b Data are taken as continuous variables into the logistic regression model, no cut-off point determined.

2 to 4 minutes. The characteristic EEG response to HV consists of a fluctuating increase in bilaterally synchronous slow-wave activity and slowing of alpha and beta rhythms (29). Delta waves tend to appear initially in frontal regions and spread backward in the older age group (17,30). In patients with OCD, the changes observed in response to HV and the neurobiological basis of these changes have not been very clear in the previous studies. We observed that female patients had significantly increased left frontotemporal slow-wave activity during HV, compared with the control subjects. The significance of this finding is not yet known. We are cautious about interpreting this finding in terms of sex, because our sample had fewer male OCD patients. One may speculate that the frontal hypermetabolism (4,31,32) or hypometabolism (5,33) found in PET studies, associated with sensitivity to hypoxia or hypercapnia, may be related to increased slow-wave activity predominantly in left frontotemporal regions after HV (28).

In one of the first QEEG studies in unmedicated OCD patients, Locatelli and others analyzed temporal lobe activity at rest and during olfactory stimulation. They found a difference in delta-1 and alpha-2 powers at rest and detectable differences in slower beta frequencies during olfactory stimulation (34). The findings of these authors have supported previous reports of EEG abnormalities in the temporal lobe of patients with OCD. Our findings of increased left temporal delta activity predominantly in women during HV, and decreased right temporal alpha activity in patients with higher Y-BOCS scores, also point to an abnormal electrophysiologic activity in the temporal lobes of our OCD patients.

In treatment responders, significantly increased left frontal slow-wave activity and decreased beta activity during HV led us to consider that frontal lobe functions were better in this group of patients. However, Prichop and others reported that alpha activity was increased in treatment responders (82.4% of their entire OCD group), whereas frontotemporal theta activity was increased in nonresponders (9). The discrepancy between the above-mentioned study and our study may be explained partly on the basis of a younger study group in our study (28.7 years vs 40.6 years) and possible genetic differences between the study populations.

The low number of male patients is a major limitation of this study. The ratio of men to women is approximately 1 to 3,
although it is approximately 1 to 1 in most epidemiological studies. This discrepancy may be due to the selection of patients from among those applying to our outpatient clinic. In our country, men and women may differ in psychiatric help-seeking behaviour, leading to a predominance of women in the study group. In a previous study we reported that, compared with male patients, 4 times as many female patients with depressive disorders applied to our outpatient clinic (35).

In addition, the finding that treatment responders and those with high initial Y-BOCS scores showed most dysfunction may raise the question whether treatment response was more likely to be quantitatively apparent in those patients. However, analysis showed no statistical difference between initial Y-BOCS scores of treatment responders and non-responders. Therefore, this finding is not simply a result of higher initial Y-BOCS scores.

In conclusion, we found that OCD showed a significant frontotemporal dysfunction, compared with control subjects. This left frontotemporal dysfunction was most prominent in female patients, in treatment responders, and in patients with higher Y-BOCS scores. These findings may contribute to understanding the neurobiological basis and clinical subtypes of OCD. Methodological limitations and controversial findings observed in studies may be eliminated in well-designed, larger, and more systematic studies.

References


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Résumé : Association des résultats des mesures EEGQ avec les caractéristiques cliniques du trouble obsessionnel-compulsif : preuve de la dysfonction frontotemporale gauche

Objectif : Nos objectifs étaient les suivants : 1) déterminer l’asymétrie hémisphérique et les différences régionales sur les EEG des patients souffrant du trouble obsessionnel-compulsif (TOC); 2) examiner les effets du sexe, de la réponse au traitement, de la durée de la maladie et des scores obtenus à l’échelle obsessionnelle-compulsive de Yale-Brown (Y-BOCS) sur les mesures électroencéphalographiques quantitatives (EEGQ).

Méthode : Nous avons enregistré les EEG (12 canaux) de 22 patients non médicamenteux souffrant du TOC mais pas de dépression, et de sujets témoins âgés d’au moins 20 ans et assortis selon le sexe. Tous les patients et les sujets témoins ont fait l’objet d’évaluations neurologiques et psychiatriques détaillées, dont l’échelle de dépression de Hamilton (HDRS) et la Y-BOCS.

Résultats : Les mesures EEGQ ont révélé des fréquences plus élevées de bandes d’ondes lentes et des fréquences moins élevées d’activité alpha dans une localisation à prédominance frontotemporale gauche chez les patients souffrant du TOC, comparativement aux sujets témoins. L’analyse de variance des paramètres EEGQ et des caractéristiques cliniques a démontré que le sexe avait un effet significatif sur les fréquences delta et alpha des régions frontotemporales durant l’hyperventilation (HV). Le total croissant des scores de la Y-BOCS avait une corrélation positive avec les fréquences accrues d’activité delta dans le pariétal droit et avec les fréquences réduites d’activité alpha du frontotemporal droit durant l’HV. Une activité des ondes lentes significativement accrue dans le frontal gauche et une activité bêta réduite durant l’HV chez les répondants au traitement nous ont poussés à envisager que les fonctions du lobe frontal étaient meilleures chez ce groupe de patients. La durée de la maladie n’avait pas d’effet important sur les mesures EEGQ.

Conclusion : Les patients souffrant du TOC présentaient une importante dysfonction frontotemporale, surtout dans l’hémisphère gauche. Cela était particulièrement évident chez les sujets féminins et chez les répondants au traitement. Les mesures EEGQ peuvent être utiles à la compréhension du fondement neurobiologique du TOC.