Association of Electroencephalographic Alpha-2 Activity With Fluoxetine Response in Obsessive-Compulsive Disorder

To the Editors:

Obsessive-compulsive disorder (OCD) is one of the most common mental problems with an estimated lifelong prevalence of 1.3% in the community.[1] Regarding the treatment of OCD, selective serotonin reuptake inhibitors (SSRIs) and/or cognitive behavior therapy are suggested as first-line treatments.[2] Selective serotonin reuptake inhibitors demonstrate similar therapeutic results on OCD, for example, fluoxetine with a 45% to 60% success rate.[3] According to the study of the World Health Organization, a considerable number of patients suffering from mental disorders (57.3% for the OCD) have difficulty in accessing the right treatment despite the expansion of the effective treatment techniques.[4] Thus, appropriate prediction measures are necessary to decrease OCD morbidity and to use medical resources economically.

Several quantitative electroencephalography (QEEG) studies conducted within OCD patients have found that alpha activities in the frontal, posterior, and temporal regions predicted response to SSRI medications.[5,6] Considering the right treatment fit for each patient is a long process, treatment response predictors have a timesaving role in clinical practice. The primary aim of this study is to explore whether there are electrophysiological markers associated with the response of OCD patients to fluoxetine treatment by using QEEG, a cheap, noninvasive, user-friendly, and repeatable technique in psychiatric practice.

The present study consisted of patients consulted to Kemal Arıkan Psychiatry Clinic (a private psychiatric practice), Istanbul, Turkey. Totally, 34 OCD patients (18 women and 16 men) aged 18 to 77 years (mean ± SD, 28.6 ± 10.1 years) providing the following criteria were recruited for the study: (1) diagnosed as OCD, determined by *Diagnostic and Statistical Manual of Mental Disorders, Sixth Edition* criteria (American Psychiatric Association, 2013); (2) medication free for 3 weeks or longer; (3) a 10-item Yale-Brown Obsessive Compulsive Scale (Y-BOCS)[7] score before and maximum 12 weeks after the fluoxetine treatment; (4) a QEEG before the fluoxetine treatment.

None of the patients were acknowledged to be treatment-resistant OCD patients before the fluoxetine treatment. They did not have any neurological or organic diseases (eg, epilepsy). Yale-Brown Obsessive Compulsive Scale was used to assess OCD symptomatology. The mean pretreatment Y-BOCS scores were 25.1 ± 10.3 (range, 13–40). All patients used fluoxetine as a monotherapy. All fluoxetine responders manifested at least 35% decrease in Y-BOCS scores compared with fluoxetine nonresponders at posttreatment. The local ethics committee approved this study.

Before the medical treatment, patients underwent QEEG recording in a silent, well-aired room with dim light. A 19-channel (FP1, F7, T3, T5, F3, C3, P3, O1, FZ, CZ, PZ, F4, C4, P4, O2, FP2, F8, T4, and T6) electrocap was placed according to the 10–20 international systems onto the head of each subject. By using blunt tip injectors, a transparent electrogel was injected into the electrodes to increase conductivity. The ground electrode was placed in the FPz position. Reference electrodes were extra electrodes attached with QEEG paste to both earlobes. All electrodes were checked for impedance, QEEG recording was initiated after impedances were less than 5000 Ohm. A Neuron-Spectrum-4/P device was used to record resting state QEEG data under a comfortable, closed-eye, awake state. The duration of the records was approximately 7 minutes. Data were sampled at 500 Hz rate; signals were bandpass filtered at 0.15 to 70 Hz and notch filtered at 50 Hz. Muscle artifacts were eliminated from the raw QEEG data. 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).[8]

The QEEG data were analyzed by Neuroguide Deluxe v.2.5.1 program (Applied Neuroscience, Largo, FL). The QEEG data were checked for normality, and it was not validated because of the small sample size; therefore, log transformation was not applied. Because we aimed to define which of the QEEG measurements are related to treatment response, absolute power for each band was counted as a dependent variable, and response to treatment was taken as an independent variable. Nonparametric independent sample Mann-Whitney *U* test was chosen because of the small sample size, and the significance level was set at *P* less than 0.01 value. Mean differences between treatment responders and nonresponders regarding absolute powers for all bands were explored.

Among the 34 OCD patients who received fluoxetine treatment for a maximum of 12 weeks, the treatment-resistant patients constitute 70% of the sample (N = 24), whereas the number of patients responding to treatment was 10 (30%). Groups based on treatment response were homogenous for sex and age. Nonparametric independent sample Mann-Whitney *U* test found that there was a significant difference between fluoxetine-resistant OCD patients and fluoxetine responders in terms of alpha2 absolute powers in FP1, FP2, F3, Fz, and F7 regions (Table 1). Pretreatment QEEG recordings demonstrate that OCD patients who responded to fluoxetine medication had greater alpha2 activity in frontal regions, particularly on the left side. As for the pretreatment Y-BOCS scores varying from 13 to 40 (mean ± SD = 25.1 ± 10.3); treatment response groups were homogenous ($P = 0.889$). Nonparametric correlation analysis was applied to Y-BOCS scores and significant alpha2 powers (in FP1, FP2, F3, FZ, F7 regions). No significant correlation was observed.

DISCUSSION

The present study found an increased alpha2-specific electrical activity in OCD patients responding to fluoxetine treatment, exclusively at prefrontal and left frontal regions. It seems that alpha bands should be investigated by classifying into subgroups because more precise frequencies in the alpha band bring about some advantages, reducing the probability of fishing expedition and presenting more reliable repeatable results. Although the alpha band is associated with SSRI treatment response in previous studies,[5,6] they did not specify subgroups of that band. As more studies are conducted with the alpha band in particular frequencies, we suppose that the role of alpha2 oscillations in SSRI treatment response will be comprehended clearly.

Our study has some strong points with respect to the characteristics of the OCD patient population: no comorbid disorder, drug-free before the treatment, and receiving monotherapy (ie, only fluoxetine); being

TABLE 1. Pretreatment Alpha2 Absolute Power Difference Between Treatment Responders and Nonresponders at FP1, FP2, F3, Fz, and F7 Regions

AP Alpha 2	Groups	N	Mean	Std. Deviation	Std. Error Mean	*P*
AP FP1 Alpha 2	Nonresponse	24	1.47	0.71	0.14	0.001
	Response	10	2.59	1.03	0.33	
AP FP2 Alpha 2	Nonresponse	24	1.59	0.60	0.12	0.008
	Response	10	2.24	0.62	0.20	
AP F3 Alpha 2	Nonresponse	24	1.71	0.61	0.12	0.005
	Response	10	2.40	0.61	0.19	
AP Fz Alpha 2	Nonresponse	24	1.79	0.66	0.13	0.005
	Response	10	2.51	0.68	0.22	
AP F7 Alpha 2	Nonresponse	24	1.32	0.59	0.12	0.002
	Response	10	2.02	0.54	0.17	

AP, absolute power.

classified as either treatment responder or nonresponders groups which are homogenous in terms of age, sex, and pretreatment Y-BOCS scores. Further, the lack of correlations between Y-BOCS scores and QEEG measurements in the pretreatment period demonstrates that electrophysiological biomarkers of patients are independent of their severity of OCD symptoms, which aids in clarifying the association between high alpha2 activities with treatment response.

It should be noted that the age range (18–77 years) is wide in this study. However, we did not suppose this would impact the results as treatment groups are homogenous concerning age. As for the main limitation of this study, the small sample size along with no placebo condition and no control groups should be pointed out. Although nonparametric tests for analyses and small significant values ($P < 0.01$) are determined as precautions, the 10-patient treatment response group decreases the generalizability of the results. Therefore, a larger, placebo-controlled prospective study with posttreatment QEEG recordings is recommended to conclude that improvements are independent of other factors.

AUTHOR DISCLOSURE INFORMATION

The authors declare no conflicts of interest.

Received July 23, 2020; accepted after revision October 14, 2020.

Mehmet Kemal Arıkan, MD, PhD
Kemal Arıkan Psychiatry Clinic
Istanbul, Turkey
Department of Psychology
Uskudar University
Istanbul, Turkey
mkarikan46@gmail.com

Mehmet Güven Günver, PhD
Department of Biostatistics
Istanbul University
Istanbul, Turkey

Reyhan İlhan, BA
Kemal Arıkan Psychiatry Clinic
Istanbul, Turkey

REFERENCES

1. Fawcett EJ, Power H, Fawcett JM. Women are at greater risk of OCD than men: a meta-analytic review of OCD prevalence worldwide. *J Clin Psychiatry*. 2020;81:19r13085.
2. Koran LM, Simpson HB. Guideline watch: practice guideline for the treatment of patients with obsessive-compulsive disorder. *Arch Gen Psychiatry*. 2013.
3. Ghoreishizadeh SMA, Herizchi S, Jamloo R, et al. Comparing factors associated with primary treatment response to fluoxetine in patients with obsessive-compulsive disorder. *J Med Res*. 2017;3:1–5.
4. Kohn R, Saxena S, Levav I, et al. The treatment gap in mental health care. *Bull World Health Organ*. 2004;82:858–866.
5. Prichep LS, Mas F, Hollander E, et al. Quantitative electroencephalographic subtyping of obsessive-compulsive disorder. *Psychiatry Res Neuroimaging*. 1993;50:25–32.
6. Hansen ES, Prichep LS, Bolwig TG, et al. Quantitative electroencephalography in OCD patients treated with paroxetine. *Clin Electroencephalogr*. 2003;34:70–74.
7. Goodman WK, Price LH, Rasmussen SA, et al. The Yale-Brown Obsessive-Compulsive Scale I: development, use, and reliability. *Arch Gen Psychiatry*. 1989;46:1006–1011.
8. Arikan MK, Metin B, Günver MG, et al. Borderline personality and bipolar disorders cannot be differentiated electrophysiologically. *Clin EEG Neurosci*. 2019;50:383–388.