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Research / Araştırma

Electroencephalographic Complexity and Decreased Randomness in Drug-Naive Obsessive-Compulsive Patients

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ABSTRACT

Electroencephalographic complexity and decreased randomness in drug-naive obsessive-compulsive patients

Objective: Studies investigating the complexity in electroencephalography (EEG) in various neuropsychiatric disorders have yielded abnormal results. However, few studies have examined EEG complexity in obsessive-compulsive disorder (OCD).

Methods: An eyes-closed scalp EEG series of 3 minutes was recorded in drug-naive patients with OCD and in healthy controls. Each single trial was segmented into multiple identical epochs using two windows of 10 and 30 seconds. Both Kolmogorov Complexity (KC) values and autoregressive (AR) model orders were estimated to quantify the EEG complexity for segmented EEG epochs.

Results: The EEG complexity, measured by both KC and AR model orders and in estimations using window lengths of 10 and 30 seconds, was lower in the patients than in the controls. In the AR model orders, the 10-second window differentiated the patients and controls better than the 30-second window.

Conclusion: OCD is characterized by low EEG complexity, increased regularity, or decreased randomness. Segmentation of EEG signals is useful for their quantitative identification, a smaller window providing a more sensitive characterization of EEG.

Keywords: Autoregressive model order, EEG complexity, Kolmogorov complexity, obsessive compulsive disorder

ÖZET

Tedavi almamış obsesif-kompulsif hastalarda elektroensefalografik karmaşıklık ve azalmış rasgelelik

Amaç: Çalışmalar birbirinden farklı nöropsikiyatrik hastalıklarda elektroensefalografide (EEG) karmaşıklığın anormal olduğunu göstermiştir. Ancak obsesif kompülsif bozuklukta (OKB) EEG karmaşıklığını araştıran çok az çalışma vardır.

Yöntem: OKB'li hastalarda ve sağlıklı kontrollerde gözler kapalı halde 3 dakikalık EEG serileri çekildi. Her bir seri, 10 ve 30 saniyelik pencerelere bölünerek çoklu özdeş epoklara ayrıldı. Kolmogorov karmaşıklığı (KK) ve oto regresif (OR) model kullanılarak segmentlere ayrılmış EEG epoklarının karmaşıklığı hesaplandı.

Bulgular: Gerek KK gerekse OR model, OKB'lilerde karmaşıklığın kontrollere göre anlamlı derecede düşük olduğunu gösterdi. Bu düşüklük hem 10 hem de 30 saniyelik pencereler için geçerliydi, ama OR modelde 10 saniyelik pencere hastalarla kontrolleri 30 saniyelik pencereye göre daha iyi ayırt etti.

Sonuç: OKB'lilerin EEG'lerinde karmaşıklık ve rastgelelik azalmış, düzenlilik artmıştır. Kantitatif bir belirleme yapabilmek için EEG sinyallerinin segmentasyonu faydalıdır. Daha küçük pencereler EEG karmaşıklığını daha duyarlı biçimde gösterir.

Anahtar kelimeler: Oto regresif model düzeni, EEG karmaşıklığı, Kolmogorov karmaşıklığı, obsesif kompülsif bozukluk

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INTRODUCTION

The brain, which comprises billions of neurons and synapses, represents a highly complicated and nonlinear organization characterized by complex spatial and temporal fluctuations in healthy individuals (1) and in pathological conditions (2,3). Its stochastic behavior can be defined through deterministic equations that allow estimating the progression of the system during a certain period of

time (4). In recording the biological signals carrying the aforementioned features, electroencephalography (EEG) has stood out as a useful, non-invasive, and relatively cheap instrument. The extraordinarily entangled organization of human brain (which is full of exceedingly dynamic groups of neurons continuously interacting with each other) manifests itself in EEG as complex temporal fluctuations that are evidence for nonlinear dynamic processes in the brain (5). The fact that human brain produces nonlinear neurophysiological signals indicates the working principles of an individual neuron: first, the threshold (the level of the membrane potential at which an action potential is fired) and, second, saturation (the level arising from the refractory period for firing) (6). Thanks to these two characteristics, the arrival of a stimulus does not essentially require that a neural response ensues. The lack of a direct and linear association between the presence of stimuli and the occurrence of neural responses is the cellular basis of the nonstationary, changeable, and nonlinear property of EEG activity.

Due to the nonlinearity of electroencephalographical output of the neural processes in the brain, EEG is a stochastic time series and therefore it requires the application of nonlinear analytical methods. Various nonlinear analytical methods have been used in brain researches, such as correlation dimension, omega-complexity, neural complexity, multiscale entropy, Lempel-Ziv complexity, Lyapunov exponent, Higuchi's fractal dimensions, Shannon entropy, and approximate entropy (2,6,7). These methods have allowed the complex, stochastic, nonlinear activity of the EEG to be quantified. Therefore, a body of literature investigating the complexity or entropy of the electrophysiological activity of the brain has emerged.

The nonlinear analysis of EEG signals has, thus, launched a novel approach in the neuroimaging of brain physiology. The importance of nonlinear analysis techniques rests on the fact that they might successfully reflect the progression of brain oscillations within a given temporal period and thus have the capacity to contribute to our understanding of the dynamical characteristics of mental illnesses. The complexity measures mentioned above are used for this purpose and they reflect two aspects of a bodily mechanism: a) entropy, that is, the extent to which the activity of an organ is predictable, and b) the minimum number of variables allowing the estimation of the activity of the organ under investigation (6).

Although early studies of complexity research have proposed that a healthy organ is characterized by an increased complexity and the process of disease decreases complexity, later studies have produced discrepant results (6). Aberrant EEG complexity has been mostly investigated in schizophrenia (3,8) and Alzheimer's disease (7,9-12). Several studies that have investigated EEG complexity in autism spectrum, (13) mood disorders (5,14-19), posttraumatic stress disorder (PTSD) (20), panic disorder (21) attention deficit and hyperactivity disorder (22,23), with each showing abnormal (increased or decreased) complexity, have also been published. Thus, change in EEG complexity has come on the scene as a biological marker of mental disorders. Interestingly, obsessive-compulsive disorder (OCD), a unique, prevalent, and frequently incapacitating disorder, has rarely been a subject of complexity research.

OCD is characterized by obsessions (unwanted and intrusive thoughts that cause distress) and compulsions (repetitive behaviors or mental acts in most cases as an attempt to relieve the anxiety caused by obsessions). Various neuroimaging methods including functional and structural magnetic resonance imaging, magnetic resonance spectroscopy, positron emission tomography, and single-photon emission tomography have been employed in OCD, denoting anatomical and physiological abnormalities particularly involving the fronto-cortical-striato-thalamic circuitry (24). EEG studies in OCD have usually used quantitative analysis methods and investigated which frequency bands predominate (25-31). The common finding in most of these studies is the involvement of the frontal and frontotemporal areas; nevertheless, frequency analysis has yielded inconsistent results. Some studies have demonstrated that slow activity bands (delta and

theta) predominate in contrast to the other ones showing a preponderance of alpha and beta activity. To our knowledge, however, no study investigating EEG complexity in OCD has been published in English except a former study of ours (32).

We hypothesized that complexity changes (either increases or decreases) in OCD, as the case with other neuropsychiatric disorders. To investigate this, we recruited drug-naive patients with OCD; thus, we were able to exclude the effect of medication on brain physiology and EEG. We employed two different methods to estimate complexity, the Kolmogorov Complexity (KC), and autoregressive orders (AR). The current study differs from our former study in two aspects: 1) we used different methods to measure complexity (approximate entropy, sample entropy, and permutation entropy were used in the previous study); 2) the current study calculated complexity in two different window lengths (a short window of 10-second length and a long window of 30-second length).

METHOD

All patients, who apply to Uskudar University Neuropsychiatry Health Practice and Research Center and had never received psychiatric treatment were assessed with EEG in addition to other standard tools of neuropsychiatric evaluation. Out of all the drug-naive patients with OCD, who were examined in the Feneryolu Outpatient Department between August 2008 and March 2012, 10 were appropriate for inclusion in this study (mean age=30.70±8.38, five males and five females). Table 1 shows the mean values of demographic characteristics and clinical measures. OCD, diagnosed according to the Diagnostic Statistical Manual of Mental Disorders, 4th Edition (33), following the Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I) (34) was the major lifetime mental problem suffered by the persons in this study. Exclusion criteria included a history of traumatic head injury, schizophrenia or any other psychotic disorder, bipolar I or II disorder, alcohol, and substance abuse, left-handedness, mental retardation, or any neurological disorder (such as epilepsy or multiple sclerosis) since these criteria may have confounded the electrophysiological activity. EEG data were also acquired for 10 age- and sex-matched healthy controls. The university's Ethics Committee approved the research protocol, and a form of written consent was signed by voluntary participants.

Measures

The severity of OCD was assessed using the Turkish version of the Yale-Brown Obsessive-Compulsive Scale (35-37). The Turkish version of the Hamilton Depression Rating Scale-17 (38,39) was used to measure the severity of depression. The anxiety score was estimated by employing the Turkish version of the Beck Anxiety Inventory (40,41).

Table 1: Descriptive statistics for the patients

	Patients		Controls	
	Mean	**SD**	**Mean**	**SD**
Age	30.70	8.38	30.30	6.43
Years of education	12.80	2.97	12.50	3.84
Duration from the appearance of initial symptoms (years)	11.70	7.13		
Duration from the appearance of obvious symptoms (months)	25.40	21.13		
Yale-Brown Obsession and Compulsion Score	18.70	4.81		
Obsession score	10.60	2.41		
Compulsion score	8.10	5.30		
Hamilton Depression Rating Scale-17	12.30	5.58		
Beck Anxiety Inventory	16.80	8.80		

SD: Standard deviation

Data Collection

Scalp EEG series were recorded from subjects using a 19-channel Neuroscan SynAmps II (Neuroscan Products, Compumedics, USA) recording system. Ag/AgCl surface electrodes were attached to the scalp surface of volunteers in accordance with the international 10-20 recording system, using a quick cap within a light-controlled recording room. During measurements, the temperature was set to approximately 22°C. EEG series of 3 minutes were sampled at a frequency of 250Hz and digitized with a 12-bit analog-to-digital converter.

The impedance values of electrodes were kept less than 5k**Ω**. The rejection level was 50μVolt peak-to-peak for EOG signals to remove artifacts created by eye blinks or movements. An electrode was placed inferior to the right eye, and two electrodes were located on the left and right outer acanthi of the eyes to measure both vertical and horizontal bipolar EOG signals. A low pass filter at 0.5Hz and a high pass filter at 70Hz were applied to the acquired EEG series in Scan Edit 4.3 software. Furthermore, artifacts (blinks, eye movements, muscle activities, etc.) were eliminated by a researcher who carefully inspected the recordings.

Estimation of the Kolmogorov Complexity

In 1965, a definition of algorithmic complexity was presented by Kolmogorov for a given string of zeros and ones (42). Subsequently, a procedure was proposed by Lempel (43) and described by Kaspar (44) in detail to calculate this algorithmic complexity, the so-called Kolmogorov Complexity (KC). The basic principle of this algorithm is that the complexity of a string is correlated by a computer program that is required to generate the string of interest. KC was defined as the descriptive complexity originated by a string denoted by x in the form $KC(x) = \min\{length(p) / T(p) = x\}$ (6).

Here, x is generated by a universal computer, the so-called Turing machine, which is denoted by T with the size of the program considered $length(p)$ (45).

In computing KC, EEG series are considered as binary sequences, and the number of bits of the shortest computer program that can create this binary sequence is estimated to define the complexity of the EEG (46). A detailed description of the algorithm, proposed by Lempel and Ziv (43) to compute the length of the required computer program, is provided in the literature (44). The EEG series is converted to a binary sequence in computing KC. A regular binary sequence generates high KC values.

Regarding time sequences such as EEG signals, every sample is compared with the mean value of the sequence (mvs). Then, if the sample is greater than the mvs, 1 is addressed to this sample. Correspondingly, if the sample is less than the mvs, the sample takes a value of zero. As a result of this primary mapping, KC can be computed from a digitized sequence consisting of zeros and ones (44). From a theoretical point of view, the expected value of KC matches the Shannon entropy (47).

Estimation of the Auto Regressive Model Order

An auto regressive (AR) model was introduced to obtain high resolution power spectral density (PSD) without spectral leakage for a stationary time series ($x(n)$). This series is assumed to be the output of a linear system driven by white noise ($w(n)$) in parametric spectral estimation of the form $x(n) = -\sum_{k=1}^{p} a(k)x(n-k)$, where p is the model order (48). Here, the estimation of p is crucial. Many computer-based algorithms have been proposed to estimate the model order. Among them, Akaike Information Criteria and Forward Prediction Error were combined to estimate the accurate model order in representing $x(n)$ into the algorithm of ARfit, which is not heuristic and is less computationally complex.

AR modeling was used to model nonlinear EEG series in the past (49,50). To compute the AR model orders, Matlab modules in ARfit algorithm were used (48).

EEG Analysis

In the literature, EEG series is assumed to be stationary within just one second (51). Therefore,

single trial EEG measurements were segmented by using a constant length window covering a very short time interval such as 2 seconds in linear EEG analysis to understand the functional status of the brain (52-58). Regarding the common manner in these works, each single channel EEG measurement of 3 minutes was segmented by using two specified windows of 10 seconds and 30 seconds in nonlinear EEG analysis in the present study. Since the sampling frequency is 250Hz, the number of the samples in segments was 2500 and 7500 for the windows of 10 seconds and 30 seconds, respectively.

EEG data collected from 10 patients and 10 controls were analyzed in Matlab 11.0. For each recording channel, the following steps were performed for each participant.

1. A single trial EEG signal of 3 minutes was segmented using a window size of 10 seconds. Then, each scalp measurement was divided into 15 consecutive epochs: a) for each epoch, both the individual AR model order and the value of KC were estimated as proposed in (45). And, then, the estimated AR model orders and the estimated KC values of those 15 epochs were averaged to obtain the mean order and the mean value of KC, respectively.
2. A single trial EEG signal of 3 min was segmented using a window size of 30 seconds. Then, each single channel EEG series was divided into 5 consecutive epochs having the same number of samples, and the first step was performed for these 5 epochs.

Statistical Analysis

The analyses were performed by using the R Foundation for Statistical Computing (3.2.3). Analysis of normality was performed with the Kolmogorov-Smirnov test. Normally distributed continuous variables were expressed as mean±SD and non-normally distributed variables as median min.-max. Differences in normally distributed continuous variables were analyzed by the Independent t-test for two groups. Differences in non-normally distributed continuous variables were analyzed by the Mann-Whitney U test for two groups and by the Kruskal-Wallis test after the Bonferroni-corrected pairwise tests for more than two groups. Statistical significance tested for the level of alpha was 0.05. Electrode variable statistical significance tested for the level of alpha set at 0.002632 due to the Bonferroni correction.

RESULTS

KC for all participants within each group for time intervals of 10 and 30 seconds are shown in Figures 1-a and 1-b, respectively. Patients produced significantly lower EEG complexity in comparison to controls in both window lengths ($p<0.001$). For the 10-second window, KC ranged from 5.92 (minimum) to 7.88 (maximum) within controls (mean complexity=6.64 [SD=0.20], median=6.62) and from 11.09 (minimum) to 11.68 (maximum) within patients (mean complexity=11.33 [SD=0.11], median=11.32) ($p<0.001$). For the 30-second window, KC ranged from 5.89 (minimum) to 7.09 (maximum) within controls (mean complexity=6.40 [SD=0.12], median=6.42) and from 12.89 (minimum) to 13.11 (maximum) within patients (mean complexity 12.89 [SD=0.03], median=12.84) ($p<0.001$). In both patients and controls, no significant difference was observed among scalp locations in both figures ($p=1.00$).

Estimated AR model orders for all participants within each group for 10- and 30-second time intervals are shown in Figures 2-a and 2-b, respectively. For the 10-second window, AR model orders ranged from 10 (minimum) to 23.94 (maximum) within controls (mean complexity=12.81 [SD=3.47], median=11.59) and from 25.06 (minimum) to 37.27 (maximum) within patients (mean complexity=29.42 [SD=2.90], median=29.13) ($p<0.001$). For the 30-second window, the range of the estimated AR orders becomes larger within both groups. Therefore, the 30-second window could not discriminate the patients and controls as well as the 10-second window. We could not measure any differences in the degree of EEG complexity among the different locations on the scalp ($p=1.00$).

In patients, for the 10-second window, some differences were detected among AR model orders created by 15 epochs. For the 30-second window, however, no significant differences were found among AR model orders originated by 5 epochs in patients.

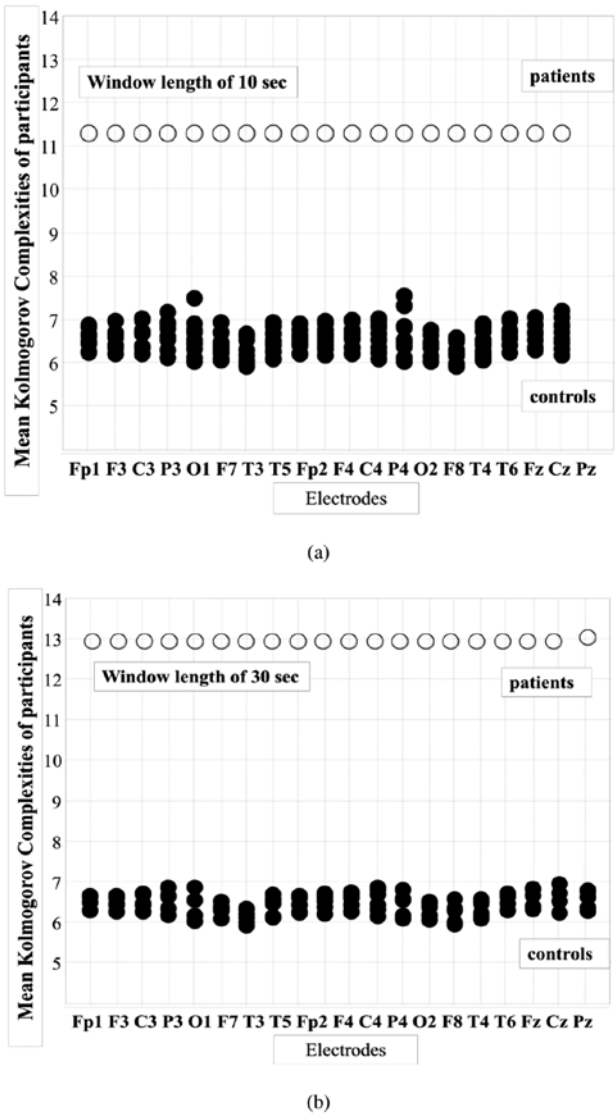

Figure 1: Estimated KC (Kolmogorov Complexity) values of patients and controls (filled markers in black) for the windows of 10 seconds (a) and 30 seconds (b). In Figure 1-a, it seems that all patients exhibit quite similar numeric values. This results from the fact that we showed both the patient and the control groups in the same axis; therefore, the scale could not be adjusted in line with in-group sensitivity. It should be considered that the standard deviations of the two groups are different.

DISCUSSION

We found a decrease in EEG complexity in drug-naive obsessive-compulsive patients. To the best of our knowledge, the only other study investigating EEG complexity in OCD was conducted by us (32). In our former study, we used different measures (approximate entropy, sample entropy, and permutation entropy) to estimate the complexity in OCD patients who were drug-naive as the patients of the current study were and we found that patients had significantly lower complexity than controls. Therefore, two studies detecting the EEG complexity

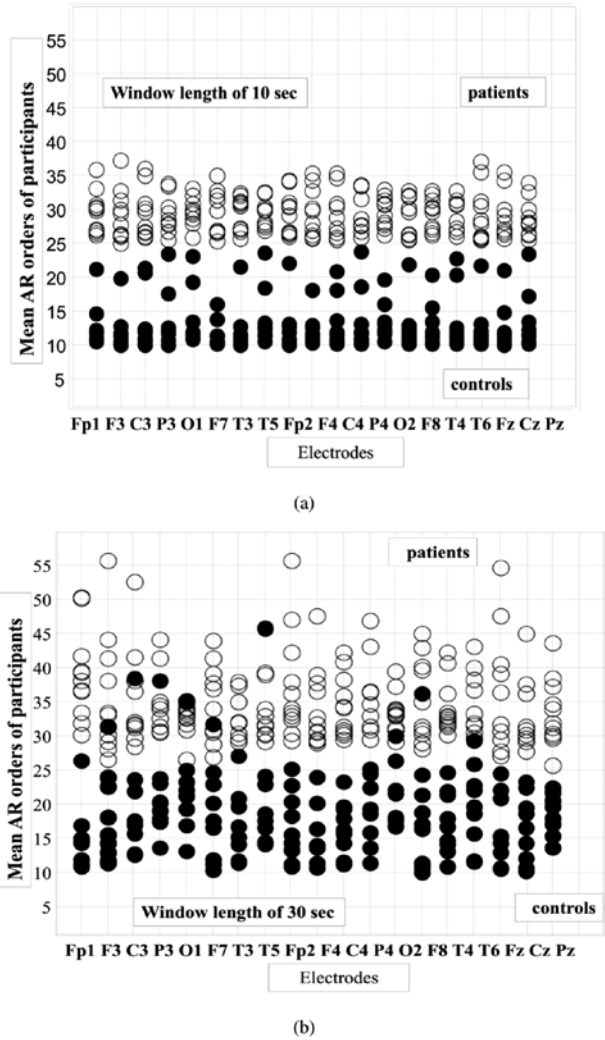

Figure 2: Estimated AR (autoregressive) orders of patients and controls (filled markers in black) for the windows of 10 seconds (a) and 30 seconds (b).

in OCD patients having similar clinical characteristics produced consistent results by using five different measures of complexity.

Studies on various neuropsychiatric disorders have shown different patterns of complexity. An increased complexity has been observed in relatively younger patients with recent-onset schizophrenia with positive symptoms, whereas relatively older schizophrenics with negative symptoms and chronic illness exhibited a decreased complexity (7,8). It seems that schizophrenia is characterized by increased complexity that decreases with age, protracted illness, and medication. While several studies have demonstrated a higher complexity in depression (8,17,26), Pezard et al. (15) found that, in first-episode depression, EEG complexity was decreased and after treatment returned to levels observed in controls. Manic patients have shown an increased complexity (5). In ADHD, Fernández et al. (59) found an increased complexity whereas Chenxi et al. (23) detected a lower complexity in delta and theta bands and higher complexity in the alpha band. During a cognitive task, complexity was observed to be decreased in the study by Sohn et al. (60) and increased by Zarafshan et al. (61). EEG was found to be of a low complexity in Alzheimer's disease (2,9,12), autism spectrum disorders (13), dissociative states (62), anorexia nervosa (63), PTSD (20), and panic disorder (21).

Hypotheses about the role of disconnectivity in mental disorders greatly rely upon electrophysiological studies. It has been suggested that, as a result of aberrant neural connectivity, abnormal complexity behavior might be detected by EEG (2,6). Sporns et al. (64) proposed that the more connected the brain, the more complex it's functioning. This proposal is in contrast to the views of Friston (66,66), who has elaborated the disconnection hypothesis in schizophrenia. This discrepancy might be related to the fact that complexity is not necessarily related to only connectivity. On the other hand, altered connectivity patterns differ among neuropsychiatric disorders and also differ among different clinical appearances of the same disorder (as the case with schizophrenia as mentioned above), manifesting themselves as a variety of neuroimaging and EEG patterns. Thus, pathological process might represent itself as a decreased complexity in some conditions such as OCD, Alzheimer's disease (2,9,12), or chronic residual schizophrenia (3,8) and increased complexity in other conditions such as mania (5), some types of depression (15,17,18,67) and ADHD (23,59-61), or recent-onset schizophrenia with positive symptoms (3).

Yang and Tsai (68), in an attempt to solve this dichotomy, suggested that complexity does not denote 'randomness' (69). Any complex structure must essentially include a remarkable amount of information, and complexity may increment proportionally with increasing information. As an example, Yang and Tsai gave a Shakespearean text that is both complex and highly informative. By contrast, a text produced aimlessly by a monkey typing should be referred to as 'random' rather than 'complex' because it conveys no information. By analogy, delusions of a schizophrenic person are conveniently called random as opposed to complex. According to Yang and Tsai, the healthy, complex brain deteriorates in two opposing ways: randomness or orderliness. The nervous system enables the organism to adapt to constantly changing environmental challenges; mental disorders impair that adaptation and produce either random or ordered behavior. If deterioration occurs toward randomness, symptoms of, for example, positive schizophrenia may arise; if the direction of impairment is towards excessive order, obsessive-compulsive-related symptoms may emerge. Therefore, a clearer terminology would involve changing the terminology by substituting 'increased orderliness' for 'decreased complexity.' Based on macroscopic observations, persons with obsessive-compulsive personality disorder show highly ordered behavior and avoid random situations. Those observations can be extended to OCD that is characterized by preoccupation with a single theme and inflexible rituals. For example, an OCD patient with contamination obsessions exhibits highly regular and predictable behaviors. His major activity is to wash his hands, body, and objects around him because the

major subject in his mind is the anxiety of being contaminated with bodily secretions, microorganisms, environmental pollutants, and so forth. As OCD becomes more severe, thoughts of contamination and washing activities take increasingly longer time periods in the patient's life and a variety of all other activities such as working, reading, doing sports or chores, going out with friends, and having sex remain limited to a relatively much shorter duration. Such a clinical picture defined by a lifestyle represented by the same apprehensions, the same anticipations, and very same practical reactions every day is consistent with increased regularity or decreased randomness seen in the EEG of patients with OCD. The same monotonous type of thoughts and activities is also true for other symptom dimensions of OCD. Blasphemous or sexual obsessions outweigh most (or even all in some patients) other considerations and imaginations. Checking sockets, electrical devices, taps, and windows overshadow all other activities of everyday life. Certainly, we do not have sufficient evidence to establish a direct relationship between the microscopic processes within the brain and their physiologic outputs, such as EEG.

The fact that our patients were drug-naive is important in that suspicion about the modifying effect of medications on brain function has already been relieved. EEG studies on schizophrenia (70) and fMRI studies on OCD (71,72) have shown that pharmacotherapy reversed brain activity. Beucke et al. (71) and Nakao et al. (72) recruited OCD patients who had been non-medicated for some time, but not drug-naive. It cannot be excluded, however, that previous medication alters brain activity. Therefore, the present study reports clear electrophysiological pathology that is not confounded by medical interference.

Why do some disorders, such as schizophrenia, manifest themselves with increased EEG complexity while others, such as OCD, present with decreased complexity? Neuroimaging studies other than EEG have shown that frontal lobe activity decreases in schizophrenia (73) and increases in OCD (72). Therefore, it is plausible that different disorders can be characterized by completely different EEG patterns. Studies using fMRI have found a high degree of connectivity or hyperactivity in the orbitofrontal cortex and the basal ganglia (74,75) in non-medicated OCD patients; this connectivity decreased after using antidepressant drugs (71,72). Untreated schizophrenia that is characterized by a hypoactive and disconnected brain manifests as increased complexity in EEG, whereas OCD that is characterized by a hyperactive and overconnected brain comes out as a decreased complexity in EEG. This finding is consistent to some extent with research on epilepsy that has shown markedly decreased complexity in EEG taken during seizures, although epilepsy is an illness of overexcitation of the neural tissue (76).

The nonlinear dynamical methods to analyze the complicated and hierarchical organization of neuronal networks have up to date produced some information helpful to enhance our understanding of the pathological processes of mental illnesses. Nevertheless, it seems that findings are far from being consistent and precise. The present-day limitations of complexity research might be due to several issues. First, it is well-known that a certain mental disorder has a heterogeneous nature in clinical manifestations and in neuroanatomical, pathophysiological, and biochemical abnormalities (as the case with schizophrenia which has quite distinctive subtypes). Although OCD is also apparently heterogeneous in symptom dimensions and biological aspects, without any exception, all of our patients showed a decreased complexity that greatly differed from controls. Second, different methods of analysis can result in different estimations of complexity, a rationale for the fact that we employed two different methods to measure complexity. Both methods, the KC and AR model orders, revealed consistent findings. Furthermore, our former study (32) utilizing three different methods to analyze the EEG of OCD patients congruently demonstrated a decrease in complexity. The homogeneity of the findings of our patients in both studies (who were clinically not homogeneous except being drug-naive adults) might indicate that OCD represents a fruitful area in the research of complexity.

Past studies using quantitative EEG in OCD have mostly evaluated the frequency bands of delta, alpha, theta, and alpha. The most persistent finding is an increase in the slow frequency bands of either theta or delta waves (26-29,31) whereas only one study found an increased current source density in the beta frequencies (30). Coherence analysis, which is another approach to the electrophysiological investigation of OCD, has shown a decrease in interhemispheric coherence (31). The studies of frequency and coherent analysis have revealed the involvement of the frontotemporal regions predominantly (26,27,29,31), followed by the cingulate gyrus (27,28,30), adjacent limbic structures (27,31), insula (31), and parietal lobe (31). Low-resolution electromagnetic tomography (LORETA), a special application of quantitative EEG, has been used in some of these studies as it allows the assessment of localization relatively more precisely than other electrophysiological methods. The involvement of the anterior brain regions is principally consistent with a vast body of literature using a variety of neuroimaging techniques (77).

The EEG findings in our study did not show a preference of certain localizations. This contradicts the literature and is difficult to explain. Despite the fact that neuroimaging researches of OCD have chiefly denoted abnormalities in the frontotemporal regions, it has been understood that the parietal and posterior areas are also involved, though to a lesser extent (77). The measurement techniques we employed might have enabled the estimation of posterior abnormalities more definitely than other methods to the degree that differences between the anterior and other regions become less discernible. Another factor might be the great difference between our patients and the controls in all electrode sites, rendering the comparison of regional variations relatively unimportant. The low spatial resolution of EEG should also be always considered when anatomical involvement is discussed.

Our small sample size is a shortcoming of the study, which could be to some degree offset by the highly significant finding that all patients, with no exception, showed quite obvious difference from controls. Our criterion of artifact rejection was another, perhaps more important, shortcoming. Independent component analysis would be a better way for the quantitative detection of artifacts for a study on complexity. Comparisons of drug-naive patients to medicated and chronic patients and of pre- and post-treatment results with regard to complexity will be highly valuable. OCD is a disorder usually comorbid with a variety of other mental illnesses, and therefore the investigation of EEG after data that differentiates co-occurring conditions (not allowed by our small sample size) may present interesting knowledge. Using more measures of complexity in the same patient and control groups will shed further light on the area under research as different complexity measures may produce different results. Comparing the electrophysiological data of patients having OCD with those suffering from other neuropsychiatric disorders, such as schizophrenia, will enhance our understanding of connectivity or disconnectivity in the central nervous system.

In conclusion, the brains of drug-naive OCD patients are electrophysiologically less complex, more regular, and more random than the brains of controls. Investigating EEG trace in smaller window lengths may be more successful in differentiating patients and controls. These findings may contribute to the discussions of increased or decreased brain connectivity in the pathologies of the central nervous system when evaluated together with the former and future studies in this area.

Contribution Categories	**Name of Author**
Development of study idea	O.T., S.A.
Methodological design of the study	O.T., S.A.
Data acquisition and process	O.T., S.A.
Data analysis and interpretation	O.T., S.A.
Literature review	O.T., S.A.
Manuscript writing	O.T., S.A.
Manuscript review and revisation	S.A.

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