Quantitative EEG Findings in Patients With Psychogenic Nonepileptic Seizures

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Abstract

Objective. Psychogenic nonepileptic seizures (PNES), is one of the clinical manifestations of conversion disorder that epileptiform discharges do not accompany. Factors capable of increasing susceptibility to these seizures have not been adequately investigated yet. This study aims to investigate the quantitative electroencephalography (QEEG) findings for PNES by evaluating the resting EEG spectral power changes during the periods between seizures. *Methods*. Thirty-nine patients (29 females, 10 males) diagnosed with PNES (group 1) and 47 patients (23 females, 24 males) without any psychiatric diagnosis (group 2) were included in the study. The patients underwent a psychiatric examination at their first visit, were diagnosed and their EEGs were recorded. Using fast Fourier transformation (FFT), spectral power analysis was calculated for delta (0.5-4 Hz), theta (4-8 Hz), alpha (8-13 Hz), beta (15-30 Hz), high-beta (25-30 Hz), gamma-1 (31-40 Hz), gamma-2 (41-50 Hz), and gamma (30-80 Hz) frequency bands. *Results*. Six separate EEG band power, namely (C3-high beta, C3-gamma, C3-gamma-1, C3-gamma-2, P3-gamma, P3 gamma-1), were found to be higher in the patients diagnosed with PNES than in the control group. *Conclusion*. Our findings show that PNES correlate with high-frequency oscillations on central motor and somatosensory cortices.

Keywords

electroencephalogram (EEG), seizures, epilepsy, EEG, electroencephalography

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Introduction

Conversion disorder is a functional neurological disorder characterized by a wide variety of sensory and motor symptoms, including psychogenic nonepileptic seizures (PNESs), tremor, movement disorders such as dystonia and gait abnormalities, loss of motor functions such as leg or arm paresis, blindness, deafness, and loss of sensation in the limbs, which cannot be explained by a neurological disease. In addition, known medical causes cannot explain these symptoms or the impairment they cause.¹

PNESs are among the clinical manifestations of conversion disorder and are most commonly observed in females aged 15 to 35 years.² Early diagnosis of these nonepileptiform seizures is important because patients can be incorrectly treated for epilepsy. Three-quarters of patients with PNES receive long-term antiepileptic treatment due to incorrect diagnosis of epilepsy, unnecessarily subjecting them to the side effects of antiepileptic drugs.^{3,4} In addition, 10% of patients with PNES can also have epilepsy, experiencing both epileptic and nonepileptic seizures.⁵ PNES patients with comorbid epilepsy can be over medicated, which can increase the number and severity of antiepileptic medication–related adverse effects. Furthermore, prolonged nonepileptic seizures can be inadvertently treated as

status epilepticus; thusly, PNES should be considered in all patients with seizure that present to emergency departments.⁶

The diagnosis of PNES is difficult and challenging for neurologists and psychiatrists. Some patient and seizure characteristics can lead to clinician suspicion of PNES. For instance, PNESs usually last longer than epileptic seizures, and are associated with eye closure and asynchronous movements. Additionally, during a PNES patients are commonly aware of their surroundings during the ictal state and do not experience postictal confusion.⁷ Although these characteristics are indicative of PNES, alone they are not diagnostic. The gold standard for the diagnosis of PNES is video-electroencephalography (vEEG).⁸⁻¹¹ Documented absence of epileptiform activity during a seizure is necessary for the diagnosis of PNES; however, vEEG is expensive and not all patients have a seizure while

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undergoing the procedure, even when vEEG is performed for \geq 24 hours.

EEG is a low-cost and noninvasive method for measurement of brain activity. Neurologists usually examine EEG data via visual inspection to detect epileptiform discharges. Interictal EEG is routinely employed in patients that present with a seizure-like episode; however, absence of epileptiform activity does not rule out the possibility of epilepsy. Another method primarily used by psychiatrists—is quantitative EEG (qEEG),¹² which can be utilized to estimate the frequency of brain oscillations as power values and for calculating indices of connectivity in clinical populations.¹³⁻¹⁵

The literature includes only a limited number of randomized controlled studies on resting qEEG findings during the interictal state in PNES patients. It was reported that PNES patients have decreased gamma synchronization between the frontal and posterior regions¹⁶ and decreased functional connectivity between the widespread cortical regions and the basal ganglia in the alpha band,¹⁷ as compared with healthy controls. It was also reported that gamma-band spectral power is higher in the left parietal region and lower in the right temporal region in adolescent PNES patients than in healthy controls.¹⁸ These studies indicate that although interictal qEEG may not be a reliable tool for the diagnosis of PNES, it can identify qEEG alterations that would help understand the neural mechanisms of PNES.

The present study aimed to identify qEEG findings associated with PNES by evaluating resting qEEG spectral power changes during the periods between seizures. Alterations in neural oscillations in PNES patients were analyzed in order to (1) identify neurobiological correlates of PNES that could shed light on pathophysiology and (2) identify targets for the treatment of PNES. Identification of targets for the treatment of PNES is especially important because our current understanding of the pathophysiology of PNES remains inadequate and because psychotherapy is, to date, the only available treatment for PNES. It is hypothesized that the data obtained from the present study might lead to novel biological interventions for PNES, such as transcranial magnetic stimulation.

Materials and Methods

Participants

The study included individuals that presented to Kemal Arıkan Psychiatry Clinic (a private psychiatric practice), Istanbul, Turkey, that were diagnosed as PNES (PNES group) and those without a psychiatric diagnosis (control group). In the psychiatric interview (Structured Clinical Interview for *DSM-5* [SCID-5]) conducted with the participants in the control group, it was detected that they did not have any neuropsychiatric diseases.¹⁹ It was not questioned whether there were any neuropsychiatric diseases in the family history of the participants in the control group. PNES was diagnosed based on International League Against Epilepsy (ILAE) Commission on Neuropsychobiology Nonepileptic Seizures Task Force criteria.¹¹ Based on the ILAE criteria, patients were diagnosed as probable PNES.¹¹ Other

psychiatric diseases in the PNES group were excluded with SCID-5.¹⁹ None of the patients were previously diagnosed with epilepsy. For all patients diagnosed as PNES, we witnessed their seizures firsthand or observed video recordings of their seizures. In all PNES cases, the semiology was atypical for an epileptic seizure. All PNES patients' interictal qEEG recordings were normal. The participants underwent a psychiatric examination at their first visit to the clinic, as well as qEEG recording. Only the first qEEG recordings of the participants were taken into consideration. Controls consisted of individuals without a neuropsychiatric diagnosis who volunteered to have a qEEG recording.

EEG Recording

All the participants underwent qEEG recording following the first psychiatric examination and all were free of neuropsychiatric medications for at least 1 month during recording. The participants were informed about the procedure prior to qEEG recording. In order to reduce anxiety, the participants were allowed to rest in a quiet room for 30 minutes prior to the procedure. qEEG recording was performed in a soundproof, dimly light, and well-ventilated room. 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 that was compatible with each participant's head measurements was properly fixed to the head of each participant. Electro-gel was used between the electrodes and the scalp to increase conductivity and the signal-to-noise ratio. A sufficient amount of gel was applied to each electrode area using a blunt tip injector. The ground electrode was placed in the FPz position. Reference electrodes were extra electrodes attached with qEEG paste to both earlobes, which had first been cleaned with cleansing gel and alcohol.

A vertical electrooculogram (v-EOG) and horizontal EOG (h-EOG) were recorded to determine simultaneous eye movements in qEEG imaging; the Ag-AgCl disc electrodes used for this purpose were attached to the relevant area using the qEEG paste and fixed to the area with a plaster. Following these procedures, all electrodes were checked for impedance, and additional electro-gel was used, as necessary. qEEG recording was initiated when impedances were <5000 ohm. qEEG recordings were made using a Neuron-Spectrum-4/P device, and only while the participants were at rest; no activation method was applied. The participants were instructed to sit comfortably, remain awake, and blink as little as possible during qEEG recording.

Data Conditioning

Neuron-Spectrum.NET software was used for qEEG impedance measurement, as follows: notch filter, on; scale, 10 mV/mm; sweep, 30 mm/s. As used for standard qEEG recording, high pass filter (HPF) was set to 0.5 Hz and low-pass filter (LPF) was set to 70 Hz. The qEEG range was reinforced using a 0.5- to 70-Hz bandpass filter, with the resistance of the electrodes set at <5000 ohm, and the sampling rate was 250 Hz. All qEEG recording data were transferred to a computer hard drive. qEEG recordings were made with the participants' eyes open during 2 individual 5-minute periods and with their eyes closed during 2 other 5-minute periods. Continuous qEEG recordings that were made during 20-minute periods were cleared of qEEG ranges contaminated by both eye movement and motion-related artifacts using a combination of visual inspection and a computer-ized artifact identification algorithm.²⁰

Data Analysis

Fast Fourier transformation (FFT) was used for spectral analysis of qEEG ranges without artifacts.¹⁹ Spectral analysis is a standard method for qEEG quantification²¹ that facilitates determination of the distribution of power according to frequency,²² which provides information about the frequency content of a signal. For each of the 19 monopolar derivations, absolute (μ V²) and relative (%) power, mean frequency, interand intrahemispheric coherence, bilateral symmetry, intrahemispheric distribution of power, and total spectral power were calculated for the delta (0.5-4 Hz), theta (4-8 Hz), alpha (8-13 Hz), beta (15-30 Hz), high beta (25-30 Hz), gamma-1 (31-40 Hz), gamma-2 (41-50 Hz), and gamma (30-80 Hz) frequency bands.²²⁻²⁴

Statistical analysis

Log-transformation was used because the qEEG data were skewed to a large degree. Furthermore, as some of the qEEG measurements produced values between 0 and 1, 1 was added to all qEEG results before log-transformation was applied. The normality of the distribution of data was determined based on log-transformation results. Student's *t* test was applied to the transformed qEEG values, with the diagnosis of PNES as the dependent variable. So as to remain conservative and achieve a high level of significance, $\alpha = 0.001$ was accepted as the level of statistical significance.

Results

The PNES group included 39 patients (29 female and 10 male) diagnosed as PNES and the control group included 47 individuals (23 female and 24 male) without a psychiatric diagnosis. PNES group contained significantly more females, and was slightly younger; however, the age difference did not reach significance (Table 1). In terms of qEEG findings, C3-high theta band (P = .0002), C3-gamma band (P = .0001), C3-gamma-1 band (P = .0001), C3-gamma-2 band (P =.0001), P3-gamma band (P = .0006), and P3 gamma-1 band (P = .0006) log-transformed absolute power measurements differed significantly between the PNES and control groups (Table 2). There was no significant difference in the mean frequency, inter- and intrahemispheric coherence, bilateral symmetry, intrahemispheric distribution of power and total spectral power between the PNES and control groups. These results were obtained using the back-log-transform procedure; as 2

 Table 1. Demographic Characteristics in the PNES and Control Groups.

	Gender			Ago (Yoors)
	n	Female (n)	Male (n)	Mean \pm SD
Group I (PNES)	39	29	10	34.9 ± 10.5
Group 2 (control)	47	23	24	40.8 ± 15.9
Total	86	52	34	
Р		.016ª		.054ª

Abbreviation: PNES, psychogenic nonepileptic seizures.

^aThere was no statistically significant difference between the groups.

Table 2. Log-Transformed Absolute Power According to Group.

EEG Band	PNES	Control	Р
C3-high-beta	1.929	1.014	.0002a
C3-gamma	1.202	0.499	.0001ª
C3-gamma-I	0.969	0.404	.0001ª
C3-gamma-2	0.303	0.104	.0001ª
P3-gamma	0.834	0.466	.0006ª
P3-gamma-I	0.668	0.372	0,0006ª

Abbreviation: PNES, psychogenic nonepileptic seizures. ^aStudent's *t* test; the difference between the groups was found to be statistically significant.



Figure 1. Log-transformed absolute power according to group.

transformations were applied, sharing the standard deviation values was not considered appropriate (Figure 1).

Discussion

In the present study, resting-state qEEG findings were compared between PNES patients and controls. In the present study 6 qEEG band power (C3-high beta, C3-gamma, C3-gamma-1, C3-gamma-2, P3-gamma, and P3-gamma-1) were higher in the PNES group than in the control group. The P3 qEEG band not only corresponds to the somatosensory and receptive language area of the brain,²⁵ but it also overlaps areas such as inferior parietal lobule and intraparietal sulcus, which is a part of frontoparietal executive network, whereas the C3 band corresponds to the motor and expressive language area.^{26,27} Processes involving activation of the cortical brain regions are associated with the higher frequency qEEG bands (alpha, beta, and gamma).¹ Our results, therefore, indicate overactivation in somato-motor and language areas and possibly in parietal executive areas.

One pilot study conducted with 3 PNES patients investigated qEEG spectral power changes that occurred just prior to nonepileptic seizures in an effort to identify a biomarker for PNES. All 3 of the PNES patients exhibited a decrease in beta power (desynchronization) before nonepileptic seizures, which was not observed in any of the patients with epilepsy. The findings of this pilot study indicate that desynchronization of beta power might be a marker for impending nonepileptic seizures.²⁸

In a QEEG study conducted on 15 adolescents diagnosed with PNES and 10 healthy controls, EEG gamma-band spectral power was found to be higher in the left parietal regions in patients with PNES in comparison with the control group. This result is consistent with our study. Furthermore, lower gamma-band spectral power in the right temporal region and decreased current source distribution in the right superior temporal gyrus were found in the PNES group compared to the control group. These regions are important for the neural process of emotional salience and social-emotional cognition thanks to their connections. In the PNES group, gamma band source density decreased in the right posterior parietal cortex, posterior cingulate cortex, and superior temporal gyrus compared to the control group.¹⁸ Experiencing movement as a conscious action is associated with increased activity in the posterior parietal cortex.²⁹

In a resting-state MEG study, which was conducted with 6 participants diagnosed with PNES and 9 healthy controls, alpha power reduction in the posterior occipital region and delta and theta power increase in the frontotemporal region were found in the PNES group compared to the control group. These results are consistent with frontotemporal limbic hyperexcitability. Furthermore, focal coherence in the left caudate and putamen was significantly higher in the PNES group than in the control group, and this situation was associated with motor symptoms in PNES.³⁰

There are other studies showing frontal lobe dysfunction in PNES and changes in frontostriatal loop. Orbitofrontal cortex dysfunction may lead to dissociation by disrupting the ability to integrate positive and negative emotions.³¹ Episodes in PNES patients may be observed as a result of a supersensitive limbic-frontal loop and unstable/hyperexcitable cognitive-emotional attention system.³²

Conversion disorder is diagnosed based on inconsistency between symptoms and clinical findings, and neurological and medical status.³³ Conversion disorder was historically defined psychodynamically,³⁴ but Sigmund Freud was the first to suggest that the origin of conversion disorder involves psychological as well as biological factors, and such biological factors might include impaired cerebral hemispheric communication and excessive cortical arousal.³⁴⁻³⁶

It is known that conversion patients are unable to adequately describe their symptoms.³⁷ The presence of high activity in

motor and somatosensorial regions could be associated with over focusing on somatosensorial input. For instance, one might speculate that conversion patients overactivate somatomotor regions in an effort to cope with emotional distress associated with the inability to adequately verbalize their emotional experience. This hypothesis is in line with the psychodynamic formulation of conversion disorder, which posits that unconscious conflict and affective motive are transformed into bodily complaints.³⁸

Although semiological indicators help differentiate PNESs from epileptic seizures, the gold standard for the diagnosis of PNES is vEEG.³³ vEEG is very effective as a diagnostic tool, however it requires that patients remain in hospital for 24 hours.³⁶ Furthermore, patients can have PNESs and epileptic seizures at the same time, and observation of only epileptic seizures during vEEG monitorization can complicate the diagnostic procedure further. Accordingly, the PNES misdiagnosis rate is between 11% and 25%, 10,39 even with vEEG monitorization. It should be noted that the present study's PNES patients did not undergo vEEG monitorization, but a clinician capable of differentiating PNESs from epileptic seizures witnessed the event or watched a video recording of the event. While this might be considered a potential limitation of the study, it was concluded that PNES was diagnosed as probable PNES based on ILAE criteria in all patients, as none had a history of epilepsy and interictal qEEG findings were normal in all cases.11

The ratio of female patients in the PNES group is high, and the PNES and control groups do not match in terms of gender. Although the average age of the PNES group was lower, this was not statistically significant. In a study investigating the effects of age and gender on qEEG, it was determined that the global absolute power in the delta band was affected by age, that there was higher global absolute power in the delta, theta, and beta bands in women than in men, and that the relative and absolute power values in the beta band increased with increasing age.⁴⁰ These results suggest that genders not matching between the groups is a limitation of our study.

It was not questioned whether there were neuropsychiatric diseases in the family history of the participants in the control group. The presence of neuropsychiatric diseases in the family history may affect the QEEG results of a clinically healthy individual. In twin and family studies, the heritability of some EEG parameters such as alpha peak frequency and alpha spectral power density was demonstrated.⁴¹ In comparison with the control group, in relatives of bipolar patients, reduced alpha-1, beta-3, and gamma sources in the temporal gyrus and cingulate and an increase in the right frontotemporal areas in the gamma band were observed.⁴² In a study conducted with 37 men and 27 women with a family history of alcoholism, a decrease in the relative and absolute alpha power in the occipital (O1, O2) and frontal (F3, F4, Fz) regions and an increase in the relative beta power in both regions were found.⁴³ Epileptic EEG abnormalities were observed in 37% of individuals having relatives diagnosed with epilepsy, and the ratio of epileptic abnormalities to clinical manifestation is approximately 4:1.⁴⁴ In summary, the fact that the family history of the patients in the control group was not questioned may affect the QEEG results, and this is one of the limitations of our study.

In conclusion, the present findings show that PNES is correlated with increased activation of higher frequency qEEG bands, possibly relating to overactivation in brain areas mediating somatic and motor functions. These findings could play an important role in the development of novel treatment strategies, including transcranial magnetic stimulation. The present study has some limitations, including a small study population and lack of objective measurement/psychometric evaluation of verbalization ability. As such, additional larger scale studies based on objective measurement of verbalization ability in PNES patients are warranted.

Author Contributions

KA substantially contributed to conception or design; critically revised the manuscript for important intellectual content; gave final approval; agrees to be accountable for all aspects of the work in ensuring that questions relating to the accuracy or integrity of any part of the work are appropriately investigated and resolved. ÖÖ substantially contributed to conception or design; drafted the manuscript; gave final approval; agrees to be accountable for all aspects of the work in ensuring that questions relating to the accuracy or integrity of any part of the work are appropriately investigated and resolved. BM contributed to acquisition, analysis, or interpretation of data; critically revised the manuscript for important intellectual content; gave final approval; agrees to be accountable for all aspects of the work in ensuring that questions relating to the accuracy or integrity of any part of the work are appropriately investigated and resolved. GG contributed to acquisition, analysis, or interpretation of data; agrees to be accountable for all aspects of the work in ensuring that questions relating to the accuracy or integrity of any part of the work are appropriately investigated and resolved. HLC contributed to acquisition, analysis, or interpretation of data; agrees to be accountable for all aspects of the work in ensuring that questions relating to the accuracy or integrity of any part of the work are appropriately investigated and resolved. TE contributed to acquisition, analysis, or interpretation of data; agrees to be accountable for all aspects of the work in ensuring that questions relating to the accuracy or integrity of any part of the work are appropriately investigated and resolved. NT contributed to acquisition, analysis, or interpretation of data; agrees to be accountable for all aspects of the work in ensuring that questions relating to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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