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Differences in Resting State EEG Power Spectrum in Patients with Schizophrenia and Healthy Controls

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Abstract

Background

Schizophrenia is a psychiatric disorder characterized by a heterogeneous syndrome of disorganized thoughts, delusions, inappropriate affect, and hallucinations. There has been a continuous effort to discover and specify the neural correlates of schizophrenia based on spontaneous EEG records.EEG signals can be classified based on certain characteristics, one of them through the power spectral analysis of several brain waves.

Objectiveto investigate EEG changes in chronic medicated schizophrenia patientsby power spectral density analysis during resting state as compared to control subject.

Subject and Method The present study is a case-control study extended from February 2019 to July 2019. Forty subjects were enrolled in this study; 20 patients aging (20-50 years) comprising (9) males and (11) females diagnosed with schizophrenia were analyzed and compared to 20 apparently healthy volunteers comprising (9) males and (11) females.

Results The results of the current studyshowed a significant difference in total delta power spectrum between patients and controls, with patients having higher spectral power($p<0.001$). Moreover, regional delta power spectral activity showed a significant increment in all brain regions in patients than control.Likewise, analysis of theta wave power spectrum revealed significant increment in total theta power spectrum activity as well as in the temporal region($p<0.001$) compared to control.On the other hand, statistical analysis of alpha wave showed a highly significant decrement in the mean total alpha power spectrum as well as the mean alpha power spectrum at the parieto- occipital brain region in patients as compared to controls.

conclusionQEEG analysis of power spectrum of various brain waves in schizophrenic patients demonstrates highly significant increment in slow wave activity of delta and theta frequencies and decrement in fast wave activity of alpha frequency, whether totally or at specific brain regions; which most likely point to a lower cognitive status.

Keyword QEEG, power spectrum, Schizophrenia

Introduction

Schizophrenia is a serious psychiatric disorder and a leading cause of disability worldwide[1].The incidence of schizophrenia remains relatively constant worldwide at 0.1-0.4%. It is higher in men than in women, with the ratio of males to females is 1.4 to 1 [2].It is characterized by a heterogeneous syndrome of delusions, disorganized thoughts, hallucinations and inappropriate affect, according to fifth edition of the Diagnostic and statistical manual of Mental Disorder (DSM-V) published by American Psychiatric Association at 2013[3].EEG is one of the modalities that can detect brain disorders in people with schizophrenia. EEG signals can be classified based on certain characteristics, one of them through the power spectral analysis of several brain waves[4]. The absence of characteristic abnormalities of the raw EEG in

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patients with schizophrenia has led researchers to study quantitative parameters of EEG (QEEG). Previous studies of spectral characteristics of the EEG in patients with schizophrenia have revealed abnormalities in all EEG frequency bands[3].The emergence of QEEG has enabled researchers to extract many variables that can be quantitatively measured by transforming the EEG signals into numerical parameters through a mathematical processing called the Fast Fourier Transformation (FFT). The EEG signal recorded from the scalp is composed of multiple sine waves cycling at different frequencies. Fourier analysis decomposes the EEG into these different sine waves and estimates the spectral power (in mean square microvolts) at each frequency. Power is thought to reflect the excitability of groups of neurons. Power values are usually totaled across frequencies to form measures of power in a specific frequency band [5,6]Abnormal EEG findings are seen in 20% to 60% of patients with schizophrenia [7].A previous study of Di Lorenzo and his colleagues investigated the brain signals in patients with schizophrenia and healthy control, they found increase of delta and theta power during resting eyes closed for schizophrenia when compared with controls [8].

Previous two studies of Moeini and associates, and Yeum & Kang had reported a significant decrease in alpha power spectra at the occipital region in patients compared to normal subjects. The predominant wave in the occipital region of these patients was the delta wave, while it was the alpha wave in normal subjects [6,9]. In another study, spectral analysis of brain waves of schizophrenic patients showed ten times increase in delta power spectrum than healthy subjects, while theta power spectrum in these patients was three times higher than healthy subjects, with significant increase in the activity of delta waves and theta waves in frontal lobe of schizophrenic patients, whereas alpha waves decrement was in the occipital lobe in all patients with schizophrenia [4].The aim of this study is to analyze and quantify EEG changes in patients with schizophrenia using power spectral analysis during resting eyes closed condition, and compare the results to those of normal subjects.

Methods

Subjects

The present study is a case-control study conducted in the Neurophysiology Unit at Al-Imamain Al- Kadhimain Medical City, Baghdad, Iraq for the period extended from February 2019 to July 2019. All the selected subjects were enlightened about the electrophysiological examination and an informed consent for participation in the study was provided. The study was approved by the Institute Review Board of the College of Medicine, Al-Nahrain University.

The study included 20 chronic medicated schizophrenic patients diagnosed clinically as per Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition, Text Revision (DSM V-TR) criteria, aging (20-50 years) who were collected and referred from psychiatric clinic in Al-Imamain Al- Kadhimain Medical City hospital by a psychiatrist. Those were compared with 20 age and sex matched healthy controls with no history of any medical, psychiatric or organic disease.

Materials

1. Electroencephalography DeviceNihon Kohden (1200J/K) Electroencephalography machine.
2. The surface electrodes conduct electrical potentials to the Junction box, where a montage selector permits signals to pass into the amplifiers. After amplification of the signals, filtering and other controls regulate signal output.
3.

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Quantitative Electroencephalography

The study was conducted in a quiet and dark room. The room temperature was controlled to be between 25-30˚C. The EEG examination started usually after 10 minutes of patient's rest on a comfortable chair, during which 21 EEG electrodes were placed on both hemispheres at the frontal, temporal, parietal and occipital sites according to the international 10-20 system.

Both cases and controls were subjected to EEG for 20 minutes during awakened state with eyes closed. EEG recordings were performed with typical longitudinal bipolar montage (double banana montage). The ground electrode was placed on the forehead. All electrode impedances were kept <5 k_{ohm}. EEG epochs that contained different types of artifacts were automatically excluded from further analysis.

Statistical Analysis

This is a case control study, most of data were continuous and expressed as mean ± standard deviation, comparison of these data were done by using unpaired Student t-test. Sex was expressed as frequency and percentage, comparison of these data was done using Fisher exact test. P value less than 0.05 was considered as significant. The software used were Microsoft excel 2019 and SPSS (statistical package for social sciences) version 23(Property of IBM Corp. Copyright IBM Corporation and licenses 1989,2015).

Results

Demographic characteristics

Forty subjects were enrolled in this study; 20 patients diagnosed with schizophrenia and 20 apparently healthy volunteers were analyzed. The mean age of patients was (35.6±12.44years); comprising (9) males and (11) females, with duration of disease (9.12±7.61years), Compared to (37.1±7.86years) of apparently healthy volunteers comprising (9) males and (11) females and years of education (14.05±2.06years) (Table 1).

Table (1): Comparison of Age , Sex, , Duration of Educations, Duration of Disease and Duration of Treatment Between Patients and Controls

Parameters		**Patients N=20 Mean±SD**	**Controls N=20 Mean±SD**	**P value**
Age (yr)		35.6±12.44	37.1±7.86	0.651 *
		N (%)	**N (%)**	
Sex*	Female	11 (55.0)	11 (55.0)	1.000**
	Male	9 (45.0)	9 (45.0)	
Education (yr)		6.15±5.36	14.05±2.06	**<0.001**
Disease (yr)		9.12±7.61		
Treatment (yr)		5.85±6.16		

* unpaired ttest ** Fisher exact test

A highly significant difference were found in the years of education between patients and controls (*p* value = <0.001) with no significant difference to be noticed regarding age or gender(p= 0.651 ,1.000; respectively).

Spectral analysisof the total delta activity using unpaired t-test revealed highly significant difference in the power spectrum between patients and controls, with the patients having higher

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spectral power (p<0.001). Moreover, regional delta power spectral activity showed significant increment in the frontal, temporal and parieto-occipital areas in patients than control (p value = 0.021, 0.009and 0.029respectively)(Table 2).

Table (2): Power Spectral Analysis of Delta Wave between Patients and Control by Unpaired T-Test

Delta wave	Patients N=20 Mean±SD	Control N=20 Mean±SD	P value
Total delta	15.33±9.9	7.87±1.27	**0.003**
Frontal	14.46±9.56	8.89±3.04	**0.021**
Central	4.81±5.96	2.22±0.8	0.069
Temporal	22.75±20.53	9.46±1.88	**0.009**
Parieto-occipital	14.98±13.99	7.55±2.1	**0.029**

Analysisof theta wave power spectrum by unpaired t-test revealed higher spectral activities in patients' group compared to control, whether totally or at different brain regions, and the difference was highly significant in total theta power spectrum activity as well as in the temporal region (p<0.003, p<0.005; respectively), while, it was less significant in the central and parieto-occipital regions (p value = 0.045and 0.010; respectively)(Table 3).

Table (3):Power Spectral Analysis of Theta Wave between Patients and Control by Unpaired T-Test

Theta wave	Patients N=20 Mean±SD	Control N=20 Mean±SD	P value
Total theta	16.35±11.34	7.57±1.51	**0.003**
Frontal	12.66±11.71	8.51±3.24	0.141
Central	3.98±3.84	2.11±0.75	**0.045**
Temporal	24.72±22.95	8.27±2.14	**0.005**
Parieto-occipital	18.92±16.37	8.31±3.39	**0.010**

On the other hand, statistical analysis of alpha power spectrum showed a highly significant decrement in the mean total alpha power spectrum as well as the mean alpha power spectrum at the parieto- occipital brain region in the patients as compared to controls (p<0.001), with no other significant differences at other brain regions between patients and control (Table 4).

Table (4): Power spectral Analysis of alpha wave between Patients and Control by Unpaired T-test

Alpha wave	Patients N=20 Mean±SD	Control N=20 Mean±SD	P value
Total alpha	8.87±2.35	12.89±2.54	**<0.001**

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Frontal	6.16±2.79	7.26±2.12	0.167
Central	2.13±1.54	2.36±1.23	0.612
Temporal	10.88±4.34	11.35±2.91	0.690
Parieto-occipital	12.46±5.16	24.57±7.43	**<0.001**

Discussion

In the current study, no significant difference was noticed regarding gender and age between the two studied groups, however, highly significant difference was found in the years of education between patients and controls. This can be explained that most schizophrenic patients had their first onset in early adulthood, then, recurrent hospitalizations would deprive the patient from completing his or her educational life. It had been stated that schizophrenia is often associated with recurrent hospitalizations, poor social functioning, low education, and high-unemployment rates. Evidence highlights that not completing primary school and receiving low school marks were associated with a higher risk of schizophrenia[9,10].

The QEEG analysis of delta wave in the current study revealed highly significant increase in the delta power spectrum activity in schizophrenia patients than control group, whether along the whole brain or at different brain regions; Abnormal slow wave activity has been attributed to a 'dysfunctional state' of the generating neuronal tissue. Delta activity in the waking state was strongly associated with CNS depression, as seen in coma, anesthesia, toxic and metabolic encephalopathy and all conditions characterized by decreased levels of consciousness [11,12]. The highly significant increase in the delta power spectrum activity in patients than control group in this study could be most likely consistent with depressed central neuronal functions leading to poor cognitive performance of these patients. These findings are in accordance with several studies which found significantly increased resting QEEG spectral power in delta frequency in schizophrenia patients compared to healthy controls [3,4,13].

In the current study the distribution of delta wave activity was higher at frontal and temporal area in patients than control, which is consistent with previous studies that found abnormal increase in delta activity in frontal and temporo-parietal regions in schizophrenic patient than healthy control. The authors believed that abnormal slow wave in schizophrenia is of clinical interest, predicting symptom severity and cognitive impairments [11,14].In a meta-analysis by Boutros and his collaborators, they suggested that EEG low-frequency oscillatory abnormalities in schizophrenia are primarily localized to frontal regions and that increased frontal low-frequency EEG power is a unique endophenotype for schizophrenia [15].Therefore, slow wave frequency increment and their possible relations with the above histopathological findings could interpret poor cognitive performance of such patients.

Analysisof theta wave power spectrum in the current study revealed significantly higher total spectral activity in patient's group compared to control group. Several studies had found increased power of the slow EEG oscillations including theta power spectrum in schizophrenic patients compared to healthy subjects which, again, most claimed that increase resting state theta power is an indicator of cognitive deficit in patients with schizophrenia and associated especially with memory deficits [3,16,17]In the current study the pattern of distribution of theta wave activity was highest at the temporal lobe region in schizophrenic patients than control. Several previous studies had revealed increased theta activity in subjects with schizophrenia, most prominent in the temporal lobe[3,14,18]. The temporal lobes which include the hippocampus and amygdala play roles in memory and emotion[19]. Atrophy to the amygdalohippocampal network

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of the temporal lobe with its resulting memory deficits were found to be reliably associated with abnormal increase in theta activity of the QEEG in resting state [20,21]In the present study, the parieto-occipital brain region was the second brain region having high theta activity as compared to controls, a finding which is in line with a number of other studies which had found more focal theta activity during rest, most pronounced in the temporal and parietal areas [15,22]. On the other hand, few studies found contradictory results as decreased theta power in resting state in patients with schizophrenia [20,23].John and his colleagues studied (28) neuroleptic-naïve recent onset schizophrenia patients compared to control subjects, they found decreased theta power in these patients stating that this reflects an underlying dysfunction of the frontal-midline theta activity [20].Whereas, Koychev and his colleagues acquired 20 chronic medicated schizophrenic patients and 20 healthy volunteers and revealed decrease theta power spectrum during WM task [23]. QEEG recordings were conducted during WM task not during resting state as in the current study, not to mention that patients who participate in the current study were all chronic medicated and not neuroleptic-naïve recent onset schizophrenia, which most likely might explain the difference in the results.

Regarding alpha wave power spectrum, the present study revealed significant decrement in the mean of the total alpha power spectral activity as well as parieto- occipital area which is consistent with the finding of other studies [4,6,17,24,25]. The increase in alpha activity during resting state has been correlated with internal mental processing and social cognition, therefore, the decrease in peak alpha frequency in schizophrenia patients indicates cognitive impairment [26].A recent study by Ishii and his fellow workers suggested that a decrease in alpha oscillations in the occipital areas during an eyes-closed resting-state, with a concomitant increase in delta current density had been associated with a lower cognitive status [27].

Therefore, such findings indicate diminished mental and intellectual processing of neural information related to cognitive functions in schizophrenic patients compared to controls. It was stated that alpha brain activity in the resting state can reflect the health of the brain to a certain extent. Alpha waves may have an important role in the mechanisms of attention and consciousness, which is associated with memory performance and cognitive function [6].Occipital alpha power is known to be impaired in schizophrenia patients, during both the resting state and during cognitive task activation [28]. According to Kustermann and Ahn and their associates, alpha band activity is a sensitive marker in the progress of schizophrenia. Kustermann and his colleagues revealed that alpha power is also reduced during verbal working memory task in schizophrenia patients [29].Ahn and his fellow workers, applied transcranial alternating current stimulation to enhance alpha oscillations and modulate network dynamics that are reduced in schizophrenia. They justified their choice to target alpha oscillations since previous studies had reported reduced alpha oscillations in patients with schizophrenia compared to healthy participants. They concluded that an increase of alpha activity is related to clinical improvement of auditory hallucinations in schizophrenia [30].

Yet, some studies had contradictory results; a higher alpha activity had been reported in schizophrenic patients over temporal and frontal regions in resting state with eyes opened [31]. In another study, no evidence of alpha impairments was found in patients with first episode schizophrenia [32]. Nevertheless, resting state EEG in the current study was performed with eyes closure as in most studies focused on QEEG and schizophrenia, also, patients included in the current study were recruited having chronic schizophrenia not in the acute state.

In conclusion QEEG analysis of power spectrum of various brain waves in schizophrenic patients demonstrates highly significant increment in slow wave activity of delta and theta

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frequencies and decrement in fast wave activity of alpha frequency, whether totally or at specific brain regions. This might indicate impaired processing of neural information related to cognitive functions, leading to a lower cognitive status in these patients.

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