Evaluation of quantitative electroencephalogram changes in the assessment of anxiety disorders among children and adolescents

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Background
Anxiety disorders are considered a major health problem affecting children and adolescents with high incidence and prevalence in different societies.
Aim
The present study aimed at detecting the quantitative electroencephalogram (QEEG) changes in children and adolescents with anxiety disorders compared with healthy children. It also aimed to estimate sensitivity and specificity of QEEG in the identification of children with anxiety disorders.
Patients and methods
This is a case–control study, which was conducted on 20 children and adolescents with anxiety disorders and 20 healthy children and adolescents. Children were initially screened with the Arabic version of Screen for Child Anxiety Related Disorders and then furtherly subjected to interviewing children and caregivers and finally psychological testing using questionnaires for both the child and parents to verify diagnosis of anxiety disorder according to the Diagnostic and Statistical Manual of Mental Disorders criteria. QEEG recording: QEEG recording was performed to cases and controls under comfortable light and calm room without artifacts to assess spectrum power.
Results
Using receiver operating characteristic curve analysis, theta wave spectrum power can significantly detect anxiety disorders in children and adolescents at cutoff less than or equal to 65.4 with a sensitivity and specificity of 80 and 65%, respectively. High-frequency beta wave spectrum power can significantly detect children and adolescents with anxiety disorders at a cutoff more than 23.7 with a sensitivity and specificity of 65 and 90%, respectively.
Conclusion
Children and adolescents with anxiety disorders have QEEG changes that coincide with their symptomatology proving that QEEG is a useful method in the assessment and diagnosis of anxiety disorders.

Keywords:
alpha wave, beta waves, Diagnostic and Statistical Manual of Mental Disorders, quantitative electroencephalogram, Screen for Child Anxiety Related Disorders, theta wave

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Introduction

Anxiety disorders are considered a serious health problem that affects children and adolescents. Anxiety disorders are said to be one of the most common psychiatric disorders in the childhood age group, with an incidence rate of nearly 5–18% of all children and adolescents (Robert *et al.*, 2019). Its prevalence is between 10 and 30% in the United States with a higher prevalence in females (Ghandour *et al.*, 2019). The prevalence of social anxiety disorder is 7–13% and it may be increased up to 18.75% in adolescents in Egypt (Ragheb *et al.*, 2008). Although the age of onset varies according to the specific disorder, most anxiety disorders are first recognized in late childhood to early adolescent years. Many other psychiatric and medical disorders may be comorbid with anxiety disorders, so these comorbidities severely affect normal daily activities (Melton *et al.*, 2016).

Anxiety is considered a brain response to different stimuli. This brain response is a basic emotion already present in infants and children, so anxiety is not totally pathological as it is an adaptive method in different situations when it helps in avoiding danger.

So, it is considered maladaptation when it is frequent, severe, or persistent causing interference with normal daily activities (Beesdo *et al.*, 2009).

Anxiety disorders include generalized anxiety disorder, social anxiety disorder (social phobia), specific phobia, separation anxiety disorder, panic disorder, selective autism, agoraphobia, and post-traumatic stress disorder (American Psychiatric Association, 2013a).

Electroencephalogram (EEG) is used to detect any changes in electrical activity in the brain (Giannakakis *et al.*, 2015). It is widely used in the diagnosis of different neurologic and psychiatric disorders such as epilepsy, learning disorders, autistic spectrum disorders, and attention-deficit hyperactivity disorders (Runyon *et al.*, 2018).

In the last few years, several studies were conducted to determine the role of quantitative electroencephalogram (QEEG), as a new modality in the diagnosis of neuropsychiatric disorders in children including the diagnosis of stroke, dementia, epilepsy, anxiety, and traumatic brain injury (Popa *et al.*, 2020).

Accurate diagnosis and assessment of anxiety disorders in children and adolescents is very important for both treatment and research (Acharya *et al.*, 2018).

In this study, we aimed at detecting QEEG changes in children and adolescents with anxiety disorders compared with healthy children. Also the study aimed to estimate sensitivity and specificity of QEEG in the identification of children with anxiety disorders.

Patients and methods

The sample size was divided into two groups. Patients were 40 children and adolescents, group 1 (cases): 20 children and adolescents with anxiety disorder. Group 2 (controls): 20 matched healthy children and adolescents. The cases were recruited from Child Psychiatry and Neurology Outpatient Clinic at Alexandria University Children's Hospital. A matched control group for age and sex were selected from the General Paediatric Outpatient Clinics at Alexandria University Children's Hospital.

Inclusion criteria of cases

Children and adolescents diagnosed with anxiety disorder according to Diagnostic and Statistical Manual of Mental Disorders criteria.

Inclusion criteria of the control groups

Healthy children and adolescents matched for age and sex.

Exclusion criteria of cases

Children diagnosed with mental disorders other than anxiety disorders such as bipolar disorders, autistic spectrum disorder, and depression, children diagnosed with any chronic neurological disease such as epilepsy or attention-deficit hyperactivity disorder and children with chronic non-neurologic diseases such as type I diabetes mellitus or bronchial asthma.

Methods

Recruitment phase

Parents of children attending the study were subjected to a structured interview questionnaire to collect the following data: child demographic data (age and sex) and child medical history of chronic diseases. Children fulfilling study eligibility criteria according to data collected from parents were furtherly subjected to the following: full clinical examination which included general examination (body systems review to exclude chronic disease) with emphasis on neurological examination. Intelligence quotients using Stanford-Binet scale to exclude cases and controls with intelligence quotients less than 80 (Janzen *et al.*, 2004).

The Arabic version of Screen for Child Anxiety Related Disorders (SCARED) (Arab *et al.*, 2016).

The SCARED includes (41 items), each scored as a Likert-type scale of 0–2 ('not true or hardly ever true,' 'somewhat true or sometimes true,' and 'very true or often true'). The total score is from 0 to 82.

Case–control study phase

Children initially screened with SCARED were then furtherly subjected to the following:

Full psychiatric evaluation: (Norman *et al.*, 2015) description of the present symptoms, parent and family health information to exclude precipitating factors of anxiety, developmental history of the child, information about school performance, friends and family relationships, interviewing the child or adolescent to evaluate speech, language, intelligence, thinking and emotions, and interviewing parents or guardians and finally psychological assessment using questionnaires for both the child and parents to verify diagnosis of anxiety disorder according to the Diagnostic and Statistical Manual of Mental Disorders criteria (American Psychiatric Association,

2013b). QEEG recording: QEEG recording was performed to cases and controls under comfortable light and calm room without artifacts to assess spectrum power. Nineteen electrode caps according to the 10–20 international QEEG configuration to measure absolute power of each band in all areas. Gel was applied to each electrode site (parietal, frontal, temporal, occipital, and central) (Thakor and Tong, 2004). Analysis: QEEG spectral power is estimated by separating the EEG recordings using computerized algorithms including the fast Fourier transform [this is an algorithm that computes the discrete Fourier transform of a sequence; so, its analysis converts a signal (either a space or time) to a frequency domain] into activities within narrow frequency bands.

QEEG was recorded for each patient. Power of channel and frequency bands including delta (1 to <4 Hz), theta (4 to <8 Hz), low beta (12 to <20 Hz), high beta (20 to <30), and alpha (8 to <12 Hz) with frontal, temporal, central, and occipital areas were recorded. Finally, all the EEG data were analyzed to reject artifacts as eye movements, blinking, or muscle activity (Sterman and Kaiser, 2008).

The software provides mathematical processing of the received data. The settings were set on low-pass filters of 35 Hz, high-pass filters of 5 Hz, and a 50 Hz notch filter (Jeste *et al.*, 2015).

Ethical considerations

The study protocol was approved by the Ethics committee of Faculty of Medicine, University of Alexandria. The caregivers were asked to provide written consents for their children to take part in the study, after explaining the purpose of the study. All data and information from the participants were kept confidential.

IRB NO (Institutional Review Board Number): 00012098.

Results

As regards the delta wave spectrum power, the two study groups showed a *P* value of 0.71, 0.62, 0.31, 0.20, and 0.75 in the areas of right temporal (anger), left frontal polar (irritability), right temporal (emotion content), right parietal (personality), and right frontal polar (emotion inhibition), respectively. This was statistically not significant (Table 1).

Concerning the delta wave amplitude, the anxiety group showed a significantly higher amplitude of left frontal polar (irritability) compared with the control group (P=0.031). There was no statistically significant difference between the two study groups in right temporal (anger), right temporal (emotion content), right parietal (personality), and right frontal polar (emotions inhibition) categories in delta amplitude (P>0.05) (Table 2).

There was a statistically significant difference regarding the theta spectrum power. The anxiety group showed a significant low power of right temporal (anger) (P=0.007), right temporal (emotion content) (P=0.032), and right parietal (personality) (P=0.01) categories compared with the control group. However, there was no statistically significant difference between

Table 1 Comparison between the two study groups regarding delta spectrum power

	Mean	SD	SE	95% confidence interval for mean		Minimum	Maximum	*t*	*P* value
				Lower bound	Upper bound				
Right temporal (anger) (A1-T4)									
Controls	62.270	13.4902	3.0165	55.956	68.584	39.7	88.5	0.376	0.709
Cases	64.140	17.7163	3.9615	55.849	72.431	27.5	94.9		
Left frontal polar (irritability) (A1-Fp1)									
Controls	75.530	11.0583	2.4727	70.355	80.705	45.4	92.8	0.495	0.623
Cases	73.495	14.6791	3.2823	66.625	80.365	38.8	97.1		
Right temporal (emotion content) (A1-T6)									
Controls	61.130	19.9581	4.4628	51.789	70.471	21.0	96.4	1.038	0.306
Cases	67.100	16.2132	3.6254	59.512	74.688	30.4	95.0		
Right parietal (personality) (A1-P4)									
Controls	59.315	17.9832	4.0212	50.899	67.731	21.2	89.6	1.314	0.197
Cases	66.650	17.3211	3.8731	58.543	74.757	32.1	94.6		
Right frontal polar (emotion inhibition) (A1-Fp2)									
Controls	72.115	12.6746	2.8341	66.183	78.047	40.9	90.0	0.322	0.749
Cases	73.445	13.4227	3.0014	67.163	79.727	30.8	96.1		

P value less than or equal to 0.05 is considered statistically significant; analysis was done by independent *t* test.

the two study groups in left frontal polar (irritability) (P=0.166) and right frontal polar areas (emotions inhibition) (P=0.102) (Table 3).

The theta wave amplitude in the anxiety group showed a significant lower amplitude of right temporal (anger) (P=0.004), left frontal polar (irritability) (P=0.03), right temporal (emotion content) (P=0.017), and right parietal (personality) (P=0.007) categories compared with the controls. However, there was no statistically significant difference between the two study groups in right frontal polar (emotions inhibition) (P=0.05) (Fig. 1).

Concerning the alpha spectrum power, there was no statistically significant difference between the two study groups in right temporal (anger), right temporal (emotion content), right parietal (personality), right frontal polar (emotions inhibition) categories, and left frontal polar (irritability) (P=0.414, 0.148, 0.140, 0.358, 0.75, and 0.683, respectively) (Table 4).

High-frequency (HF) beta wave spectrum power showed significantly higher power of right temporal (anger) and right parietal (personality) categories in children and adolescents with anxiety compared with

Table 2 Comparison between the study groups regarding delta amplitude

	Mean	SD	SE	95% confidence interval for mean		Minimum	Maximum	*t*	*P* value
				Lower bound	Upper bound				
Right temporal (anger) (A1-T4)									
Control	36.260	7.5973	1.6988	32.704	39.816	25.3	55.8	3.475	0.070
Diseased	31.685	7.9203	1.7710	27.978	35.392	18.8	46.0		
Left frontal polar (irritability) (A1-Fp1)									
Control	41.590	8.1192	1.8155	37.790	45.390	27.4	57.8	5.028	0.031
Diseased	35.880	7.9862	1.7858	32.142	39.618	20.7	48.8		
Right temporal (emotion content) (A1-T6)									
Control	35.805	9.2161	2.0608	31.492	40.118	22.7	59.6	2.716	0.108
Diseased	31.575	6.8421	1.5299	28.373	34.777	19.9	44.6		
Right parietal (personality) (A1-P4)									
Control	34.905	7.2533	1.6219	31.510	38.300	22.1	49.1	1.810	0.186
Diseased	31.945	6.6486	1.4867	28.833	35.057	18.8	44.8		
Right frontal polar (emotion inhibition) (A1-FP2)									
Control	40.475	8.3345	1.8637	36.574	44.376	22.6	58.5	2.351	0.133
Diseased	36.660	7.3720	1.6484	33.210	40.110	21.1	47.7		

Table 3 Comparison between the study groups regarding theta spectrum power

	Mean	SD	SE	95% confidence interval for mean		Minimum	Maximum	*t*	*P* value
				Lower bound	Upper bound				
Right temporal (anger) (A1-T4)									
Control	16.810	6.0052	1.3428	13.999	19.621	9.5	30.7	2.854	**0.007**
Diseased	12.085	4.3310	0.9684	10.058	14.112	1.7	19.9		
Left frontal polar (irritability) (A1-Fp1)									
Control	12.270	5.9479	1.3300	9.486	15.054	3.2	32.1	1.419	0.166
Diseased	10.075	3.5337	.7902	8.421	11.729	1.2	16.2		
Right temporal (emotion content) (A1-T6)									
Control	17.120	7.9863	1.7858	13.382	20.858	2.0	34.9	2.241	**0.032**
Diseased	12.355	5.1581	1.1534	9.941	14.769	1.6	25.4		
Right parietal (personality) (A1-P4)									
Control	17.675	7.5557	1.6895	14.139	21.211	3.7	39.8	2.737	**0.010**
Diseased	12.125	5.0128	1.1209	9.779	14.471	1.8	24.1		
Right frontal polar (emotion inhibition) (A1-FP2)									
Control	13.480	5.0237	1.1233	11.129	15.831	3.7	21.8	1.675	0.102
Diseased	11.145	3.6947	0.8262	9.416	12.874	1.7	18.6		

P value less than or equal to 0.05 is considered statistically significant; analysis done by independent *t* test.

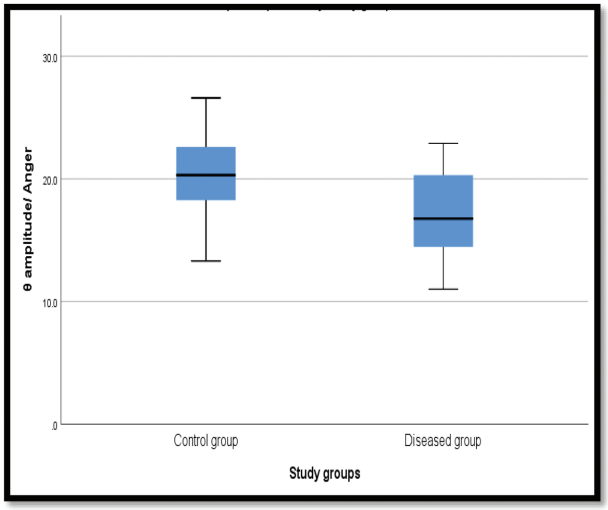
controls (*P*=0.037 and 0.038, respectively). Nevertheless, there was no statistically significant difference between the two study groups in left frontal polar (irritability) (*P*=0.103), right temporal (emotion content) (*P*=0.08), and right frontal polar (emotions inhibition) (*P*=0.296) (Table 5).

There was a statistically significant difference regarding HF beta amplitude in the anxiety group compared with the controls. The cases showed significantly higher amplitude of right temporal (anger) (*P*=0.004), left frontal polar (irritability) (*P*=0.016), right temporal (emotion content) (*P*=0.007), and personality (*P*=0.004) categories compared with the control group. However, there was no significant statistical difference between the study groups in right frontal polar (emotions inhibition) (*P*=0.296) (Fig. 2).

Concerning the low-frequency (LF) beta amplitude, the anxiety group showed a significantly higher amplitude of right temporal (anger), right temporal (emotion content), and personality with *P* value of 0.008, 0.015, and 0.012, respectively, compared with the control group. However, there was no statistically significant difference between the two study groups in left frontal polar (irritability) (*P*=0.074) and right frontal polar (emotion inhibition) (*P*=0.195) (Fig. 3) regions.

There was a strong correlation between HF beta spectrum power and anxiety symptoms. The receiver operating characteristic curve analysis for HF beta wave was found to be accurate in discriminating between children and adolescents with and without anxiety disorders with a sensitivity and specificity of 55 and 90%, respectively (area under the curve=0.771, *P*=0.001) (Table 6, Fig. 4).

Figure 1



Boxplot showing comparison between study groups regarding anger amplitude.

Discussion

Many studies have reported the value of QEEG as a new tool for the assessment of anxiety disorders (Arikan *et al.*, 2006; Jones and Hitsman, 2018; Gregory *et al.*, 2020).

The present study highlighted the significance of studying QEEG changes in anxiety disorders in this group of children and adolescents.

Table 4 Comparison between the study groups regarding alpha wave spectrum power

	Mean	SD	SE	95% confidence interval for mean		Minimum	Maximum	*t*	*P* value
				Lower bound	Upper bound				
Right temporal (anger) (A1-T4)									
Control	13.600	9.1144	2.0380	9.334	17.866	1.8	37.1	0.826	0.414
Diseased	11.300	8.4857	1.8975	7.329	15.271	2.1	35.7		
Left frontal polar (irritability) (A1-Fp1)									
Control	6.675	3.5690	0.7981	5.005	8.345	1.4	14.4	-0.413	0.683
Diseased	7.410	7.1222	1.5926	4.077	10.743	0.8	35.6		
Right temporal (emotion content) (A1-T6)									
Control	15.500	13.0738	2.9234	9.381	21.619	1.1	43.5	1.489	0.148
Diseased	10.615	6.6612	1.4895	7.497	13.733	2.1	26.1		
Right parietal (personality) (A1-P4)									
Control	17.850	13.1334	2.9367	11.703	23.997	1.4	43.7	1.512	0.140
Diseased	12.325	9.7247	2.1745	7.774	16.876	2.5	37.2		
Right frontal polar (emotion inhibition (A1-FP2)									
Control	7.475	4.2460	0.9494	5.488	9.462	2.5	16.2	0.930	0.358
Diseased	6.330	3.5019	0.7830	4.691	7.969	1.1	13.4		

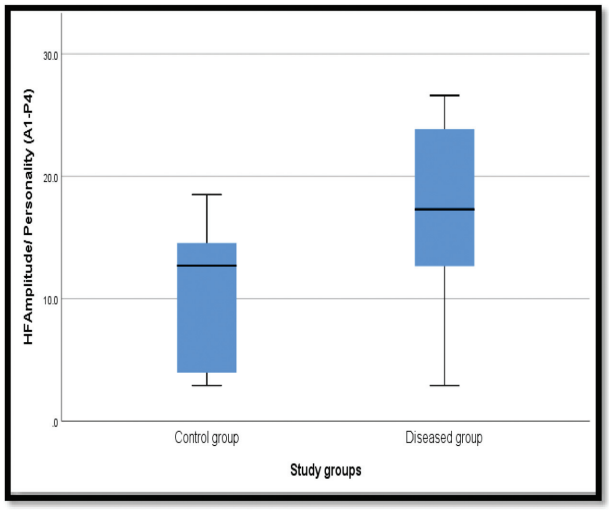
P value less than or equal to 0.05 is considered statistically significant, analysis done by independent *t* test.

Table 5 Comparison between the study groups regarding the power of high-frequency Beta wave

	Mean	SD	SE	95% confidence interval for mean		Minimum	Maximum	*t*	*P* value
				Lower bound	Upper bound				
Right temporal (anger) (A1-T4)									
Control	3.255	3.0604	0.6843	1.823	4.687	0.0	12.5	2.218	**0.037**
Diseased	8.005	9.0744	2.0291	3.758	12.252	0.1	28.8		
Left frontal polar (irritability) (A1-Fp1)									
Control	2.510	2.0285	0.4536	1.561	3.459	0.0	7.4	1.671	0.103
Diseased	5.410	7.4907	1.6750	1.904	8.916	0.1	27.8		
Right temporal (emotion content) (A1-T6)									
Control	2.760	2.9183	0.6525	1.394	4.126	0.0	11.9	1.822	0.080
Diseased	5.670	6.5176	1.4574	2.620	8.720	0.1	24.0		
Right parietal (personality) (A1-P4)									
Control	2.065	1.4500	.3242	1.386	2.744	0.0	4.9	2.208	**0.038**
Diseased	4.790	5.3262	1.1910	2.297	7.283	0.1	21.9		
Right frontal polar (emotion inhibition) (A1-FP2)									
Control	3.305	3.6709	0.8208	1.587	5.023	0.1	16.3	1.059	0.296
Diseased	5.370	7.9066	1.7680	1.670	9.070	0.1	31.2		

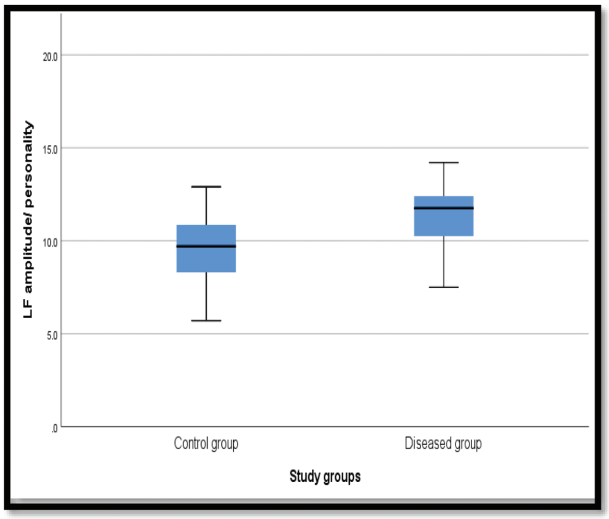
P value less than or equal to 0.05 is considered statistically significant, analysis done by independent *t* test.

Figure 2



Boxplot showing comparison between study groups regarding HF amplitude/personality. HF, high frequency.

Figure 3



Boxplot showing comparison between study groups regarding LF amplitude/personality. LF, low frequency.

Table 6 High-frequency beta wave validity

Spectrum power	Cutoff value	AUC	Sensitivity	Specificity	PPV	NPV	*P* value
HF beta wave	>23.7	0.771	65.0%	90.0%	86.5%	72.0%	<0.001

AUC, area under the curve; HF, high frequency; NPV, negative predictive value; PPV, positive predictive value.

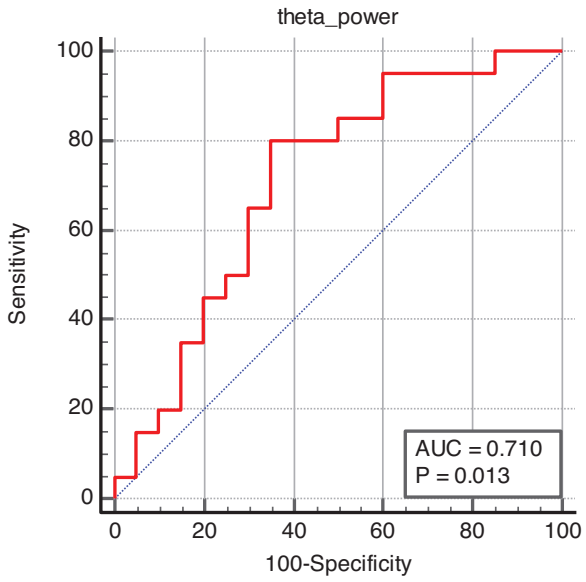
In the present study, we recorded spectrum power and amplitude changes of delta, theta, alpha, LF beta, and HF beta waves.

Regarding theta wave, cases showed statistically significant lower values than the control group according to spectrum power in right temporal and right parietal regions.

The explanation of low values of theta waves spectrum power is that theta waves (>4–8 Hz) are related to early sleep or when preparing to sleep and so, low values of spectrum power of theta waves mean less relaxation and more irritability (Ribas *et al.*, 2018).

The HF beta spectrum power wave was significantly higher in cases than controls in right temporal (anger)

Figure 4



Receiver operating characteristic curve of theta wave for the detection of children and adolescents with anxiety disorders.

and right parietal (personality) regions. In accordance with our study, Ribas *et al.* (2018) indicated that there was a statistically significant positive association between anxiety symptoms and beta wave spectrum power.

In partial agreement with the present work, a study conducted by Knott *et al.* (1996) utilized the QEEG to compare patients with panic disorder with the control. The study revealed significant higher spectrum power of HF beta waves in right temporal and right parietal, and lower spectrum power of theta waves among cases than controls, which is similar to the current study results of HF beta waves. However, there were lower spectrum power values regarding delta and alpha and LF beta waves among cases compared with controls (Knott *et al.*, 1996).

These differences between the two studies can be attributed to the difference in associated comorbidities and use of different QEEG program recording in 1996 when the study was done or even different environmental factors and societies.

The LF beta wave power showed no statistically significant difference between cases and controls, but the anxiety group showed a significantly higher amplitude in the right temporal and right parietal region.

This is different from Jalali *et al.* (2018) who reported a significantly higher absolute power of LF beta waves in the central region and LF beta wave in the occipital area among cases compared with controls.

Regarding alpha wave, there was no statistically significant difference between cases and controls according to amplitude and spectrum power.

On the contrary, a study conducted by Runyon *et al.* showed a higher right frontal alpha activity in cases with anxiety than controls (Runyon *et al.*, 2018).

As regards the delta wave spectrum power, there was no statistically significant difference between cases and controls. This matches a study by Kim *et al.* (2021) to measure the wave's absolute power changes in anxiety in adults. They concluded that there was no significant correlation between delta wave absolute power and anxiety scores. On the other hand, they found no statistically significant difference in the alpha, theta, and beta wave power, which is different from the current study results (Kim *et al.*, 2021). This difference might be explained by the difference in the age group.

Findings of the current study support the validity of QEEG in discriminating between children with and without anxiety disorders.

Conclusion

Children and adolescents with anxiety disorders have QEEG changes that coincide with their symptomatology proving that QEEG is a useful method in the assessment and diagnosis of anxiety disorders.

Limitation of the study

There are not enough studies to validate the QEEG role in the diagnosis of anxiety in children.

Further studies and larger sample size are required to evaluate the role of QEEG in the assessment of anxiety disorders in children and adolescents.

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Conflicts of interest

There are no conflicts of interest to declare.

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