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Research Article

Quantitative Electroencephalography in Outpatient Children with Autistic Spectrum Disorders: A Case-Control Study in the Child Welfare Teaching Hospital, Baghdad

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Abstract

Background: The diversity of autism spectrum disorder presentation necessitates the use of simple tests. Quantitative electroencephalography is a low-cost, simple instrument that is being investigated as a clinical tool for monitoring abnormal brain development. ***Objective***: To study brain waves by computer-analyzed EEG (quantitative EEG) in autistic children and correlate the changes to the clinical severity of autistic children. ***Methods***: The study involved 65 children; 30 were recruited from the autism center and the pediatric neurology consultant in the child welfare teaching hospital, Medical City, and met the DSM-5 criteria for autism. Another 35 age-matched, normally-developed children ASD children met the DSM-5 criteria, the Childhood Autism Rating Scale, for autism severity. Absolute and relative spectral power measurements were used to investigate brain activity. ***Results***: The absolute and relative delta power increased in the patients as compared to the controls (p<0.05) in all brain regions. There is an association between the disease severity score and absolute and relative delta and theta power in brain areas. The absolute power of the delta wave peaked in the occipital and temporal regions. The relative delta power peaked in the temporal region. ***Conclusions***: The spectrum delta power can aid in the evaluation and classification of ASD. QEEG testing revealed abnormalities in all ASD children and can be a helpful assessment instrument for ASD children.

Keywords: Autistic spectrum disorder, Children, Quantitative electroencephalogram, Power spectrum analysis.

تخطيط كهربية الدماغ الكمي في الأطفال الذين يعانون من اضطرابات طيف التوحد: دراسة حالة وشواهد في مستشفى رعاية الطفل التعليمي، بغداد

الخلاصة

الخلفية: يتطلب تنوع عرض اضطراب طيف التوحد استخدام اختبارات بسيطة. تخطيط كهربية الدماغ الكمي هو أداة بسيطة منخفضة التكلفة يتم التحقيق فيها كأداة سريرية لمراقبة نمو الدماغ غير الطبيعي. **الهدف**: دراسة موجات الدماغ بواسطة EEG الكمي المحسوب بالكمبيوتر في الأطفال المصابين بالتوحد وربط التغييرات بالشدة السريرية. **الطريقة**: شملت الدراسة 65 طفلا. تمت دراسة 30 طفلا من مركز التوحد واستشارية طب أعصاب الأطفال في مستشفى رعاية الطفل التعليمي، مدينة الطب، واستوفوا معايير DSM-5للتوحد. استوفى 35 طفلا آخر مطابقين للعمر وتطوروا بشكل طبيعي معايير DSM-5 ، مقياس تصنيف التوحد في مرحلة الطفولة، لشدة التوحد. تم استخدام قياسات الطاقة الطيفية المطلقة والنسبية للتحقيق في نشاط الدماغ. **النتائج**: زادت قوة دلتا المطلقة والنسبية في المرضى مقارنة بالشواهد في جميع مناطق الدماغ. هناك ارتباط بين درجة شدة المرض وقوة دلتا وثيتا المطلقة والنسبية في مناطق الدماغ. بلغت القوة المطلقة لموجة دلتا ذروتها في المناطق القذالية والزمنية. بلغت قوة دلتا النسبية ذروتها في المنطقة الزمنية. **الاستنتاجات**: أن طاقة دلتا الطيف يمكن أن تساعد في تقييم وتصنيف أضطرابات طيف التوحد. كشف اختبار QEEG عن تشوهات في جميع أطفال ASD ويمكن أن يكون أداة تقييم مفيدة للأطفال المصابين بالمرض.

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INTRODUCTION

Autism spectrum disorders (ASD) are a group of early-onset neurodevelopmental disorders characterized by persistent deficits in social communication and social interaction and stereotypic, restricted, and repetitive behaviors that cause functional impairment with onset before the age of 3 years [1,2]. It is estimated that worldwide, about 1 in 100 children has autism [3]. Autism's etiologic hypotheses implicate a significant genetic component as well as environmental risk factors associated with early fetal development [4]. Identification of ASD is based on the developmental history and behavioral and cognitive observations of autistic children [5]. This must satisfy specific criteria agreed upon by specialists and outlined according to the fifth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) published by the American Psychiatric Association [6]. ASD diagnosis is a difficult and time-consuming process, owing to the vast variability in symptom types, intensity, and changes related to age [7]. ASD is diagnosed using DSM5 criteria, which include central symptoms that are required to present prior to establishing the diagnosis of diseases; other scales take more time and require collaboration between the researcher and the data supplier, such as the patient's parents, teachers, or caretakers. This makes the system susceptible to errors due to insufficient collaboration, misinterpretation of questions, caregivers' failure to recall responses, and other issues. Moreover, the specificity of instruments was susceptible to bias risk [8,9]. QEEG is a technique for evaluating the neurophysiological basis of neurodevelopmental disorders. (QEEG) is defined by the American Academy of Neurology as digital electroencephalogram (EEG) mathematical processing. This processing provides absolute and relative power, coherence, amplitude asymmetry, phase lag throughout a range of frequency bands, and other necessary patterns for optimal mental function [10]. According to QEEG studies, excessive slow-wave activity (delta, theta) and rapid-wave activity (alpha, beta) in children with ASD is associated with hyper- or hypofunction of the localized region [11]. When compared to other neuroimaging procedures, QEEG has the advantages of being less costly, easier to conduct, and noninvasive. It has been suggested that it be used as a possible clinical evaluation tool for neurological and mental problems [12,13]. Additionally, QEEG has the possibility to monitor and reevaluate the treatment outcomes of children with ASD [14]. The aim of this study is to assess QEEG findings in children with ASD and to evaluate if QEEG analysis is a marker of the severity score of ASD.

METHODS

Study design and setting

A case-control study was carried out at the Autism Center, Pediatric Hospital, and Baghdad Teaching Hospital in Medical City for the period from October 5, 2022, to April 1, 2023. The study involved a total of 65 children, comprised of 30 children ages 2–12 who were recruited from the autism center and the pediatric neurology consultant in the child welfare teaching hospital in Medical City and met the DSM-5 criteria for autism. Another 35 age- and gender-matched normally-developed children (2–12 years) who do not fulfill the criteria of any pervasive developmental disorder serve as the control group, recruited from the children's consultant in a child welfare teaching hospital. A full physical and medical history was taken, and patient demographics were registered. In addition, neurological and psychiatric examinations were conducted for the clinical assessment of ASD according to DSM-5 criteria. ASD severity was determined using the Childhood Autism Rating Scale (CARS), an observational scale in which each item is given a rating ranging from 1 (within the normal boundaries) to 4 (abnormally severe), and ratings take into consideration the "peculiarity, frequency, and length" of the behavior being rated. It can result in a total score somewhere between 15 and 60. Autism ranging from mild to moderate severity is indicated by a score between 30 and 36.5, and scores between 37 and 60 indicate severe autism [15]. The EEG signals were recorded using the 10-20 international system for electrode location [16,17], by an EEG machine (Nihon Kohden Company, Japan, Serial No. VNCT617201). The EEG recording was done during induced sleep with 50 mg/kg of chloral hydrate [18]. Nineteen scalp electrodes were attached to the following sites (Fp1, Fp2, F3, F4, Fz, Cz, Pz, F7, F8, T3, C3, C4, T4, T5, T6, P3, O1, P4, O2) utilizing montage (bipolar), and the time of recording varies from 20 to 30 minutes; all electrode impedances were kept <5 Kohm.

Patients' selection

Outpatient children were admitted to a pediatric hospital to an autism center, and the patients were randomly selected using a simple random sampling technique. The number of autistic children of the male gender was greater than the female gender, and they were selected randomly from the list of patients, one patient per day.

Inclusion criteria

Diagnostic and Statistical Manual of Mental Illnesses, 5th edition, standards of ASD and CARS score of greater than 30. Both gender male and female. Age between 2-12 years. Every social and economic class.

Exclusion criteria

Presence of other neurological, metabolic, mental, and psychiatric disorders.

Outcome measurements

Quantitative EEG is the application of numerous algorithms and displays to digital EEG. Frequency content can be calculated and compared to prior or normative values by calculating the quantity of EEG in each major frequency band and displaying the results in a numeric table or a topographic scalp map. The data gathered was converted into computer-generated frequency domains (Fourier transform and Welch method), and frequency-band maps of the scalp were created. Following the elimination and removal of artifacts. The record was split into 8–10-second chunks called epochs. Fourier power spectral analysis and the Hanning window bandpass were then used to figure out the size of each frequency band in microvolts. The frequency bands were classified into delta (0.5–3.5 Hz), theta (4–7.5 Hz), and alpha (8–12 Hz) bands. The findings were used to compute the following QEEG measures: (i) absolute power (the amount of energy in Uv2); (ii) relative power (the percentage of total power within each frequency band) [19]. A topographical illustration of spectral power (delta [0.1–2 Hz], fast theta [2–4 Hz], alpha [4–8 Hz frequency bands]) for the ASD patient was evaluated. In the central and parietal regions, the highest power value appeared red, whereas the lesser value appeared blue in the frontal regions. As a result of ASD, the delta band had the highest value, while the theta and alpha bands had the lowest value because alpha waves are slower and less complex, as shown in Figure 1.

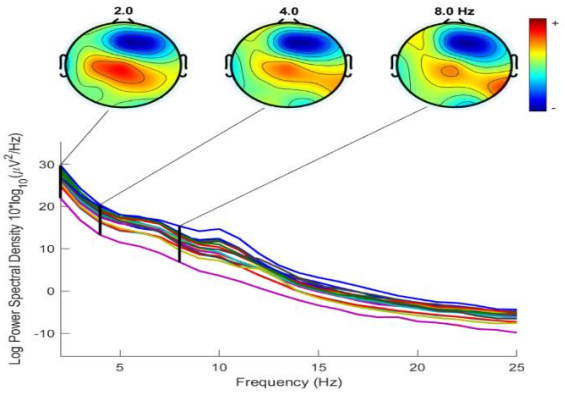

Figure 1: Topographical illustration of spectral power.

Ethical consideration

The study was approved by the ethical committee of the College of Medicine, University of Baghdad. Written consent was obtained from the patient his/her parents after the nature of the procedure had been fully explained.

Statistical analysis

SPSS statistical software, version 22, was utilized for all of the statistical analyses that were conducted (IBM Corporation, USA). Normally distributed variables were shown as mean ± standard deviation (SD) and were compared between two groups using a student t-test, an unpaired t-test between two continuous variables. Or more than two groups using an analysis of variance (ANOVA). Chi-square analysis was used to determine the counts and percentages of categorical variables. In the first ANOVA session, a two-way ANOVA was performed; the group factor (mild, moderate and severe ASD children) was the independent variable and the relative power RP (δRP, θRP, αRP) are the dependent variable. The significance level was established at $p<0.05$. The Duncan test was utilized for post-hoc analysis. The significance level was set at $p<0.05$ for all statistical tests. A two-way analysis of variance (ANOVA) was used in a second session on absolute power. We looked at the statistically significant differences between the five categories of brain regions and the absolute power of Ab (δAbs, θAbs, αAbs) as a dependent variable. Duncan's test was used for the post-hoc comparison. The significance level was set at $p<0.05$.

ESULTS

A total of sixty-five children were included in this study; 30 were diagnosed to have ASD (23 males and 7 females), and 35 were normally developed children (25 males and 10 females). No significant difference was noticed between the two groups regarding gender ($p=0.632$). Also, no significant difference ($p=0.994$) was found between the ages of children with ASD and the normally-developed children, as shown in Table 1.

Table 1: The demographic data of the studied groups

Parameter	ASD (n=30)	Control (n=35)	p-value
***Sex n*(%)**			
Male	23(47.9)	25(52.1)	0.632
Female	7(41.2)	10(58.8)	
Child age (years)			
Mean±SD	6.17±2.5	6.29±2.5	0.994
Range	2-12	3-12	

The absolute power spectral analysis of the QEEG waves (delta, theta, and alpha) was calculated collectively and in different brain regions (frontal, central, temporal, parietal, and occipital) for children with ASD and controls (Table 2). The absolute power of the delta wave was significantly increased in the patients as compared to the controls ($p=<0.05$) in all brain regions. Similarly, the absolute power of the theta wave was significantly higher in the autistic children than in the controls (in the frontal and temporal regions,

p=<0.05; in the central region, p=0.001; in the occipital region, p=0.01) except for the parietal region (p=0.147), where there is no statistically significant difference between ASD and controls.

Table 2: QEEG parameters absolute power in patients and controls by unpaired *t*-test

Brain Regions	Absolute powers (μV2)	ASD (n=30)	Control (n=35)	*p*-value
Frontal	Delta	45.8±4.95	41.33±4.30	0.05
	Theta	37.4±4.32	34.18±3.2	0.05
	Alpha	32.52±3.68	30.50±3.93	0.001
Central	Delta	41.48±5.18	36.00±5.84	0.05
	Theta	33.79±4.33	30.37±4.11	0.001
	Alpha	29.01±3.78	27.35±3.87	0.065
Parietal	Delta	43.39±6.21	39.41±5.65	0.006
	Theta	34.97±5.1	33.32±4.37	0.147
	Alpha	30.24±4.21	30.53±3.95	0.76
Occipital	Delta	49.35±4.17	44.13±5.01	0.05
	Theta	39.98±3.64	37.25±3.43	0.01
	Alpha	34.55±2.75	34.44±3.57	0.897
Temporal	Delta	47.51±3.86	42.3±4.55	0.05
	Theta	38.88±3.41	35.58±2.91	0.05
	Alpha	33.50±2.41	32.36±3.4	0.047

Values are presented as mean±SD.

The absolute power of the alpha wave was significantly increased in the patients as compared to the controls (in frontal p=0.001; in temporal p=0.047). On the contrary, the regional central, parietal, and occipital absolute powers were not significantly different between the two groups. The relative power spectral analysis of the QEEG waves (delta, theta, and alpha) was calculated collectively and in different brain regions (frontal, central, temporal, parietal, and occipital) for children with ASD and controls (Table 3).

Table 3: QEEG parameters relative power in patients and controls by unpaired *t*-test

Brain Regions	Relative powers (μV2)	ASD (n=30)	Control (n=35)	*p*-Value
Frontal	Delta	0.76±0.11	0.67±0.11	0.05
	Theta	0.12±0.04	0.15±0.05	0.002
	Alpha	0.05±0.02	0.08±0.05	0.05
Central	Delta	0.74±0.12	0.59±0.17	0.05
	Theta	0.14±0.05	0.17±0.06	0.011
	Alpha	0.05±0.03	0.11±0.08	0.05
Parietal	Delta	0.76±0.12	0.61±0.18	0.05
	Theta	0.12±0.05	0.16±0.07	0.004
	Alpha	0.05±0.02	0.12±0.11	0.05
Occipital	Delta	0.82±0.09	0.658±0.2	0.05
	Theta	0.11±0.05	0.15±0.06	0.026
	Alpha	0.04±0.02	0.12±0.11	0.05
Temporal	Delta	0.79±0.10	0.63±0.18	0.05
	Theta	0.12±0.05	0.15±0.05	0.023
	Alpha	0.04±0.02	0.10±0.09	0.05

Values are expressed as mean±SD.

Analysis of the delta activity revealed a significant increment in patients' relative power of QEEG versus controls in all brain regions (p=<0.05). The relative power of the theta wave was significantly greater in autistic children than in controls (in frontal p=0.002; in central p=0.011; in arietal p=0.004; in occipital p=0.026; in temporal p=0.023). The relative power of the alpha wave was significantly decreased in the patients compared to the controls in all brain regions. There was a statistically significant difference between ASD and controls (p=<0.05). According to the autism severity score, 12 cases (40%) have mild ASD, 12 cases (40%) have moderate ASD, and only 6 cases (20%) have severe forms of ASD. An obvious association was demonstrated between the disease severity score and the absolute power of delta and theta waves in brain regions. Table 4 shows the absolute power in delta δ ($\theta Abs_{Severe} > \theta Abs_{Moderate} > \theta Abs_{Mild}$) significantly increased and peaked delta values at the occipital and temporal area, a statistically significant difference between the absolute power of delta at the temporal and occipital region with severity score (p=0.05), and also a clear association between disease severity score and the absolute power of delta wave in the frontal region (p=0.02). There is a significant increase in theta absolute power θAbs ($\theta Abs_{Severe} > \theta Abs_{Moderate} > \theta Abs_{Mild}$) with their highest values at the central regions, a statistically significant difference between theta absolute power at the central region and ASD severity (p<0.05). On the contrary, there is no statistically significant difference between the alpha absolute power (αAbs) and ASD severity score.

Table 4: Association of CARS with QEEG parameters (Absolute powers) by ANOVA

Brain Regions	Absolute powers (μV2)	ASD severity			*p*-value
		Mild	Moderate	Severe	
Frontal	Delta	43.7±3.43	46.09±6.59	46.91±3.26	0.02
	Theta	36.03±4.14	37.66±5.25	38.04±3.15	0.14
	Alpha	31.49±2.68	33.01±4.98	32.72±2.47	0.21
Central	Delta	39.63±2.77	41.74±6.94	42.45±4.19	0.34
	Theta	32.99±3.99	33.94±5.06	34.19±3.92	0.05
	Alpha	28.63±2.58	29.26±4.83	29.02±3.42	0.9
Parietal	Delta	42.15±4.89	42.48±8.32	45.12±4.09	0.32
	Theta	33.99±5.36	34.51±6.24	36.07±3.48	0.5
	Alpha	29.71±4.02	29.88±5.50	30.94±2.74	0.67
Occipital	Delta	47.93±3.33	49.99±5.49	49.64±3.11	0.05
	Theta	38.80±4.64	40.39±3.32	40.37±3.37	0.58
	Alpha	33.87±2.21	34.86±2.84	34.69±3.12	0.72
Temporal	Delta	45.56±2.31	48.24±4.89	48.07±3.13	0.05
	Theta	37.53±3.99	39.65±3.29	39.01±2.95	0.15
	Alpha	32.68±1.42	34.15±3.02	33.41±2.14	0.16

Values are expressed as mean±SD.

Table 5 shows the relative power in delta wave δ ($\delta RP_{Severe} > \delta RP_{Moderate} > \delta RP_{Mild}$) significantly increased and peaked values at the temporal area, a statistically significant difference between the relative power of delta wave at the temporal region with ASD severity score (p=0.025), and also a statistically significant difference in delta relative power at the frontal region (p=0.05). Relative theta power has its greatest values in the central regions (p=0.05). On the contrary, power

decreased ($\alpha RP_{Severe} > \alpha RP_{Moderate} > \alpha RP_{Mild}$). There is no statistically significant difference between the alpha relative power (αRP) and ASD severity score.

Table 5: Association of CARS with QEEG parameters (Relative powers) by ANOVA

Brain Regions	Relative powers (μV2)	ASD severity			*p*-value
		Mild	Moderate	Severe	
Frontal	Delta	0.70±0.08	0.76±0.13	0.81±0.06	0.05
	Theta	0.14±0.07	0.12±0.02	0.12±0.04	0.08
	Alpha	0.05±0.02	0.05±0.03	0.04±0.02	0.072
Central	Delta	0.68±0.06	0.73±0.17	0.79±0.07	0.066
	Theta	0.17±0.06	0.13±0.03	0.13±0.04	0.055
	Alpha	0.06±0.02	0.06±0.04	0.04±0.02	0.227
Parietal	Delta	0.73±0.07	0.73±0.18	0.81±0.06	0.081
	Theta	0.14±0.07	0.12±0.04	0.12±0.03	0.422
	Alpha	0.05±0.01	0.05±0.03	0.04±0.02	0.305
Occipital	Delta	0.80±0.05	0.81±0.13	0.83±0.07	0.78
	Theta	0.12±0.06	0.10±0.04	0.12±0.04	0.633
	Alpha	0.04±0.01	0.04±0.03	0.04±0.02	0.939
Temporal	Delta	0.74±0.05	0.78±0.13	0.82±0.06	0.025
	Theta	0.14±0.07	0.12±0.03	0.12±0.04	0.23
	Alpha	0.04±0.01	0.04±0.02	0.04±0.02	0.321

Values are expressed as mean±SD.

DISCUSSION

The QEEG results, which were modified in 2009, found six subgroups of autism. They are as follows: I) High beta activity (over-focused or over-aroused pattern); II) Abnormal EEG or seizure pattern; III) High delta, theta, which corresponds to cortical slowing and inattention, impulsivity, and hyperactivity; IV) Mu activity, which corresponds to social skills; V) Coherence abnormalities; and VI) metabolic or toxic pattern of decreased overall activity [20]. Our QEEG results fall within the third subgroup, high delta/theta. The absolute and relative power of delta-theta activity were significantly higher in patients versus controls. This may be due to the hyper- or hypo-functioning of the localized region, particularly the frontal lobe, indicating a lack of neural integration between the frontal and posterior areas. Our study revealed a statistically significant rise in the delta wave power in various parts of the brain compared to normally developed children, and there was a statistically significant rise in the delta wave power in various parts of the brain as ASD severity progressed according to the CARS score. Cantor's research from 1986, which was one of the initial investigations, found that children with ASD had more delta-band activity than control subjects of the same mental age [21]. Similar to the results of this study, a greater absolute EEG of the delta frequency band across the scalp and theta activity was demonstrated [22–24]. Previous studies have shown that neurons in the frontal cortex are not as healthy as they should be [25], brain connections are not arranged normally, and the frontal lobes get bigger in people with autism [26]. Our study revealed the same, as many studies showed an enhanced delta wave at the frontal area and proposed that it reflects a dysfunction in the frontal lobe [22,27,28]. The researchers reported that the increased prefrontal delta was not unique to autism; it was detected in children with mental retardation, learning problems, and social disadvantages who didn't have autism. Some studies find enhanced delta in the central and peripheral regions [29]. Delta rhythm prevalence in children beyond infancy has been linked to learning problems and attention deficiencies [30]. Contradictory to these results, a pattern of excess midline beta and insufficient delta over the frontal brain was observed [31,32]. Our study shows an increase in theta band wave, especially in the central brain region. Some studies reported higher left frontal and prefrontal theta activity in participants with ASD, which is associated with reduced capacity for switching among mental sets and high-level regulated operation [28,33]. Children with executive functioning and mental activity issues, such as attention deficit hyperactivity disorder and learning impairments, frequently exhibit excessive theta activity [24]. Our study revealed the relative power of alpha band waves in ASD decreases in all brain regions as compared to normally developed children. This may indicate aberrant mirror neuron activity, a variant that may explain ASD children's behavioral imitative deficit and inability to imitate a directed task [34]. In the study conducted by Sheikani *et al.* (2010), children with ASD had significantly lower values at many electrodes in the alpha band waves of the left brain. Furthermore, the data revealed differences in beta and gamma rhythms between the control and ASD groups. Alpha represents the coordination of larger portions of the brain, whereas beta represents the integration of surrounding areas of the brain. They found that the alpha and beta discrepancies demonstrated that ASD problems were likely connected to the synchronization of larger brain regions [35]. Finally, in a recent study, QEEG findings were strongly correlated with symptoms severity as measured by the calibrated severity score [36].

Conclusion

QEEG testing revealed abnormalities in all children with ASD. QEEG abnormalities underlie the symptomatology of children with ASD. Our findings lead us to conclude that the spectrum power of delta activity can aid in the evaluation and classification of ASD. A QEEG test can be a useful assessment instrument for children with ASD since it is a simple, uncomplicated, and affordable procedure.

Conflict of interests

No conflict of interest was declared by the authors

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Data sharing statement

Supplementary data can be shared with the corresponding author upon reasonable request.

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