Original Article

Evaluation of Quantitative Electroencephalography in Children with Autistic Disorders in Various Conditions Based on Spectrogram

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Objective: to evaluate the brain signals in children with autism disorder in many different conditions of quantitative Electroencephalography (qEEG) recordings in order to highlight abnormalities and to characterize this group.
Method: In this study, spectrogram was used as a tool for evaluating qEEG in 15 children with autism disorders (13 boys and 2 girls aged between 6 to 11 years old) and in 11 normal children (7 boys and 4 girls with the same age range). Signals of the two groups were recorded in nine conditions.
Results: The recorded signals with the relaxed eye-opened condition in alpha band, those recorded with looking at a stranger's picture condition in beta band, and the ones obtained with children looking at inverted stranger's picture in the same beta band show the best discrimination of 92.3%, 88,9% and 88.9% respectively using spectrogram .
Conclusion: Among the several different EEG recordings, the relaxed eye-opened condition in alpha band had been the best condition for discriminating the two groups using spectrogram. More abnormalities were observed in the prefrontal lobe and the left brain hemisphere in children with autism disorders.
Key Words:
Autistic disorders, quantitative *Electroencephalography (qEEG),Investigative techniques*

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Autism spectrum disorders (ASDs) are devastating conditions with an onset in early childhood and core symptoms of varying degrees involving communication, social and cognitive development, and usually sparing gross motor development (1). In 1943, Kanner first described the case of an autistic individual who developed epilepsy, and since then, multiple case reports and population series have described an association of abnormal EEG findings within autistic individuals (2).
ASD is a highly genetic neurodevelopment disorder affecting approximately 60 per 10,000 of persons (3). In the studies conducted since 1987, Fombonne has reported the prevalence estimates of this disorder raging from 2.5 to 72.6 per 10,000 with a median rate of 11.3 per 10,000 (4). Although EEG abnormalities and clinical seizures may play a role in ASDs, the exact frequency of EEG abnormalities in an ASD population that has not had clinical seizures or prior abnormal EEGs is unknown (5).
Dawson and colleagues recorded EEG in children with ASD and Asperger disorder (AD) during visual attention and found that abnormality decreased the EEG spectral power (using Fourier analysis) over frontal and temporal areas in the delta, theta and alpha frequency ranges, but normal power in the beta range (6). In contrast, Bashina et al. observed a decreased spectral power in alpha/2 bands (7.5-11 Hz), but increased spectral power in delta, alpha3 (11.5-13 Hz) and beta bands, 'at rest' in children with ASD and AD (7). In addition, an abnormal EEG asymmetry was reported in a few studies. Recently Orekhava et al. have obtained an increase of gamma activity under the controlled condition of visual attention and behavioral stillness (8).
Spectrogram (magnitude of short time Fourier transforms, STFT) is very powerful in showing frequency characteristics of signals in the time domain (9, 10). 70 percent of maximum value of spectrogram is used as a threshold to discriminate ASD against the

normal group. This criteria (70 percent of maximum of spectrogram here after the named spectrogram criteria) was employed in many different conditions for recording quantitative EEG signals in frequency bands of delta (0-4 Hz), theta (4-8 Hz), alpha (8-12 Hz), beta (12-36 Hz) and gamma band (36-44 Hz) and the frequency bands showed significant differences in the two groups.

Using spectral power, the alpha activity increased at many electrodes in children with ASD, but not in those who weren't able to discriminate the two groups of ASD and normal children. However, using spectrogram criteria, the alpha activity decreased at many electrodes and also could discriminate between the two groups of normal children and children with ASD with excellent precision (92.3%).

Studies in very young children are of particular interest for understanding the pathogenesis of ASD, but the possibility of functional neuroimaging is limited in the investigations of such young children. In contrast, quantitative EEG can be recorded even in infants. Therefore, this method is of potential interest for both exploratory purposes and early differential diagnosis of ASD.

Materials and Methods

Participants

15 children with ASD (13 boys and 2 girls aged 6 to 11) were studied all of whom had verbal IQ scores of higher than 85 (The Wechsler Intelligence Scale for Children). Each interview and diagnosis was performed by 2 child and adolescent psychiatrists based on DSM-IV-TR criteria (Diagnostic and statistical manual of mental disorders-Text Revision) (1). The subjects were recruited from the autism clinic of Roozbeh Hospital and the private clinic of one of the authors (Tehran). All of the children with ASD were medication-free for at least two weeks prior to EEG recording. The control group consisted of 11 age-matched children without past or present neurological disorders (7 boys and 4 girls).

Handedness was measured using the Edinburgh Handedness Inventory (11). One left-handed and one ambidextrous subject were in the control group and two left-handed were in the ASD group. The remainders were all right-handed.

An informed consent was obtained after the procedures and purpose of the study were described to the parents of normal children and the caregivers or parents of children with ASD. An EEG was recorded under special conditions from every one of the children and also a print of the recorded signal EEG was given to each child's parents.

Conditions of EEG recordings

It has been argued that people with autism disorders have a tendency to focus on the local details of objects (12), that they fail to integrate local and global levels of stimuli (13); or that they pay more attention to the distinguishing features of objects than to their common features (14).

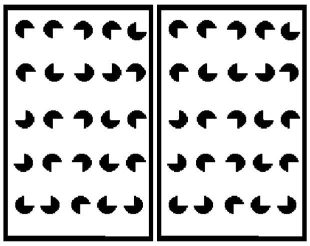


Figure 1. Two Sample of Kanizsa shapes

In this research, the nine conditions that had been introduced are as follows: the eye-closed condition, the relaxed eye-opened condition, looking at the three samples of puzzle shapes as Fig. 1 which is called Kanizsa and has been widely used to investigate the processes underlying perception (15), looking at mother's picture upright and inverted, looking at a stranger's picture upright and inverted.

EEG recordings

The EEG signals were recorded at the sampling rate of 256 Hz with electrodes. Those positioned from the 21 scalp loci according to the international 10–20 system were Fp1, Fp2, F7, F3, Fz, F4, F8, T3, C3, Cz, C4, T4, T5, P3, Pz, P4, T6, O1, O2, A2 electrodes and A1 with both earlobes chosen as common referential electrodes. It was taken aid from additional external electrodes in upper and lower eye-lid dye to extraction eye artefact too. The 10-20 international EEG electrodes placement system is shown in Fig. 2.

EEG recording was conducted only when the child was in a calm state and in many different conditions. More than 20 minutes of data were recorded from each child under different conditions. The recordings were visually inspected by an expert neurologist in encephalography to reject artefacts. Thus, only EEG data which were free from electrooculographic and movement artefacts and had minimal electromyography (EMG) activity were selected. Then, EEGs were organized in 3 second artefact-free epochs (768 points) that were copied for off-line analysis on a personal computer.

In order to remove The artefact-free epochs were selected from each electrode for each subject in nine conditions.

The residual EMG activity and the noise due to the electrical main, all the selected epochs were digitally filtered. A FIR (finite-duration impulse response) band-pass filter with cut-off frequencies at 0.5 and at 100 Hz was used and then data were processed with a notch filter of 50 Hz City electricity interference with Matlab7.1 (The Mathworks, Inc.).

Since frequency bands in EEG signals are very helpful in understanding brain functioning, in this research signals were divided into five frequency bands.

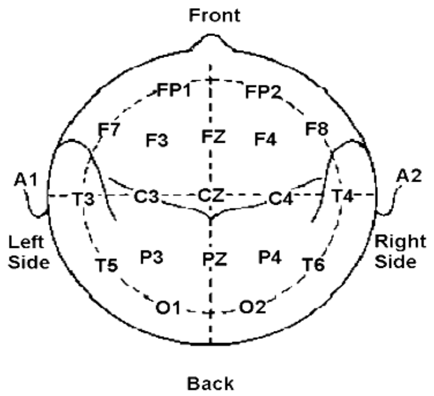


Figure 2. International EEG electrodes placement system

Spectrogram criteria

The STFT of a generic signal $x(t)$ is defined as (16):

$$STFT(t,f)=\int_{-\infty}^{+\infty}x(\tau)w^{*}(\tau-t)e^{-j2\pi f\tau}d\tau \qquad (1)$$

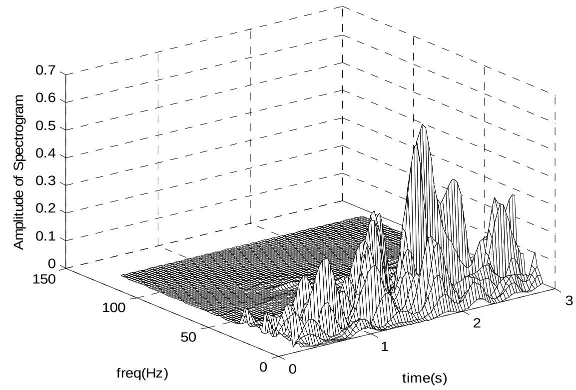
Where * denotes the complex conjugate and $w(t)$ is a window function that has a short time duration. The spectrogram of $x(t)$ is the magnitude of STFT. The result of the transform is a two-dimensional map in time-frequency space that provides a measure of how the frequency content of the signal evolves in time.

In this research, the averaged values of spectrogram greater than 70 percent were used as a discriminating tool for separating the two groups. Averaged spectrogram values greater than 70 percent of maximum (the chosen threshold) were used for comparison 0.49 (0.7×0.7) for Fig. 3(a) and 0.28 (0.7×0.4) for Fig. 3(b).. The 70 percent criteria was arrived by trying many different percentages and 70 percent resulted in best group classifications. It was also used in calculations to decrease cranial bones and skin affects with Z standard normalization.

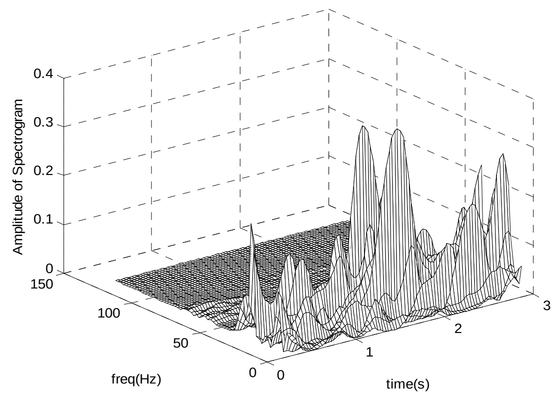
Statistical analysis and classification

The statistical analysis on the two-tailed tests (t-test) with 95% confidence interval was used to compare the data in the two groups. When significant differences between the two groups were found, the effectiveness of this method of analysis in discriminating ASD from normal children was evaluated by using receiver operating characteristic (ROC) curves (17).

The value for the area under the ROC curve can be interpreted as follows: an area of 0.90 (at Fp1 electrode for example) means that a randomly selected individual from the control group has a spectrogram criteria value larger than of a randomly chosen individual from the ASD group in 90% of the time. A rough guide to classify the precision of a diagnostic test is related to the area under the ROC curve. With values between 0.90 and 1, the precision of the diagnostic test is considered to be excellent and good for values between 0.80 and 0.90. Far fair if the results are in the range of



(a)



(b)

Figure 3. Spectrogram of Fp1 electrode for two children a) children with autism b) normal children

0.70-0.79, poor when the value of the area under the ROC curve is between 0.60 and 0.69, and bad for values between 0.50 and 0.59 (18).

For classification between children with ASD and normal children we used the nearest neighbor classifiers called Mahalanobis distance $d_c(x)$ (19):

$$d_c(x)=\sqrt{(x-\mu_c)M_c^{-1}(x-\mu_c)^T} \qquad (2)$$

This leads to a simple yet robust classifier which is suitable for multicasts. Mahalanobis distances define based on correlation between the samples by using average of samples (μ) and co-variance matrix of samples (M_C).

Result

Information and demographic factors on the two groups, aged 6 to 11 years old is presented in Table 1. Since the assumptions of normal distribution and similarities were valid, statistical analysis of two-tailed tests (t-test) with 95% confidence interval was used to compare the data in the two groups. The results of the t-test on age demonstrate that there were not any significant differences between the two groups.

The spectrogram criteria values were obtained for Fp1, Fp2, F7, Fz, F4, F8, T3, C3, Cz, C4, T4, T5, P3, Pz, P4, T6, O1 and O2 electrodes. The results have been

Table 1. Characteristics of two groups: children with autism disorder (ASD) and normal children

Sample	ASD (15)	Normal (11)	t (df)
Age (years)	Mean=9.41 Range: 6.16- 10.75	Mean=8.75 Range: 6.33- 10.66	0.638 (24)
Sex	Male (13) Female (2)	Male(7) Female (4)	-----
Handedness	Right (13) Left (2)	Right (9) Left (1) Ambidextrous(1)	-----

averaged based on all the artefact-free 3 second epochs within the 20 minutes period of EEG recording.

This criteria of spectrogram for EEG recording was evaluated in frequency bands of delta (0-4 Hz), theta (4-8 Hz), alpha (8-12 Hz), beta (12-36 Hz) and gamma (36-44 Hz). It was observed that there is a little abnormality in beta and gamma frequency bands. The beta frequency band showed a significant difference in Fp1 and T6 in gamma band with ($p<0.05$). The criteria of spectrogram values and standard deviations for the ASD and normal children and the corresponding p values for alpha band in the relaxed eye-opened condition are summarized in Table 2. The ASD had significant lower spectrogram criteria values ($p<0.01$) at Fp1, Fp2, F3 and T5 electrodes and lower values ($p<0.05$) at T3, P3 and O1 electrodes.

Spectral power values in the two groups showed significant differences ($p<0.01$) with higher at F3 (0.167±0.023, 0.124±0.027 ASD and normal children respectively), O2 (0.165±0.037, 0.164±0.039), F8 (0.154±0.021, 0.153±0.028) and ($p<0.05$) with lower T6 (0.168±0.043, 0.169±0.068), C4 (0.151±0.041, 0.153±0.031) and Pz (0.154±0.043, 0.155±0.042) in alpha band. However, the values of spectral power in contrast to the spectrogram criteria were almost higher in children with ASD.

We evaluated the effectiveness of spectrogram criteria to discriminate ASD from normal children at the electrodes in which significant differences were found using ROC plots. Table 3 summarizes the results. The values of the area under the ROC curve for F3, T5, Fp2, Fp1, P3 and O1 electrodes had the most validation for classifying the two groups. According to Table 3, value of F3 has an excellent precision level (area under the ROC curve is more than 0.9) and T5, Fp2, Fp1, P3 and O1 have a somewhat good precision level for distinguishing the two groups.

Classifications of results with Mahalanobis distance in alpha band and in the relaxed eye-opened recording condition were obtained. We found that the spectrogram criteria have been able to classify correctly fourteen out of fifteen ASD children and ten out of eleven normal children. The beta and gamma bands didn't provide a proper sensitivity and specificity using ROC curve for classifying the two groups whereas an excellent distinction (92.3%) was obtained between two groups in alpha band.

Table 2. The average spectrogram criteria values of the EEG for the autism (ASD) and normal children in alpha band (8-12Hz).

Electrodes	ASD children (mean±SD)	Normal children (Mean± SD)	Statistical analysis (p value)
Fp1**	0.166±0.072	0.345±0.156	0.005
Fp2**	0.169±0.089	0.378±0.158	0.006
F7	0.252±0.154	0.372±0.157	0.115
F3**	0.178±0.077	0.429±0.118	0.000
Fz	0.201±0.094	0.277±0.170	0.238
F4	0.249±0.182	0.295±0.131	0.546
F8	0.250±0.138	0.352±0.112	0.098
T3*	0.242±0.135	0.384±0.154	0.047
C3	0.238±0.143	0.348±0.148	0.119
Cz	0.264±0.158	0.350±0.153	0.243
C4	0.249±0.189	0.285±0.204	0.699
T4	0.291±0.163	0.357±0.221	0.466
T5**	0.207±0.132	0.397±0.128	0.005
P3*	0.239±0.102	0.384±0.125	0.013
Pz	0.265±0.172	0.377±0.127	0.132
P4	0.294±0.205	0.411±0.159	0.190
T6	0.285±0.157	0.383±0.146	0.179
O1*	0.223±0.112	0.307±0.150	0.013
O2	0.253±0.119	0.269±0.159	0.811

** $p<0.01$ and * $p<0.05$

The values of the area under the ROC curves for spectral powers of F3, O2, F8, T6, C4 and Pz (0.122, 0.633, 0.444, 0.433, 0.600 and 0.522 respectively) didn't have proper precision levels for classifying the two groups. Therefore, spectral power was not able to discriminate the two groups.

Finally, this method of classification of ASD and normal children was extended to nine conditions of EEG recordings in five frequency bands. These conditions were the eye-closed condition, the relaxed eye-opened condition, looking at three samples of Kanizsa shapes, looking at mother's picture upright and inverted, looking at stranger's picture upright and inverted in frequency bands. The results are summarized in Table 4.

According to Table 4, in the relaxed eye-opened condition, it is found that in children with ASD, Fp1, Fp2, F3 and T5 have significant differences ($p<0.01$) and T3. P3 and O1 also have significant differences ($p<0.05$). The ASD children have significant differences ($p<0.01$) at F3 and T3 electrode and at T4, T5 and O1 electrodes ($p<0.05$) in looking at mother's picture inverted. F7 and F3 have significant differences ($p<0.01$) and Fz and Cz ($p<0.05$) in looking at a stranger's picture upright condition. In looking at a stranger's picture inverted it is seen that C4, Fz and F8 ($p<0.01$) and Fp2 ($p<0.05$) have significant differences. The best results of the classification were observed in relaxed eye-opened condition and looking at stranger's picture upright and inverted.

From the five frequency bands, delta and theta didn't show any significant differences, but alpha and beta bands did show great distinctions in relaxed eye-opened condition. Alpha band gave 92.3% distinction for the relaxed eye- opened condition, whereas beta band provided 88.9% distinction in looking at a stranger's picture upright and inverted.

Table 3. Area of receiver operating characteristic (ROC) curves for electrodes that had significant differences

	Electrodes	Area of under the ROC curve
Spectrogram criteria	FP1	0.822
	FP2	0.844
	F3	0.967
	T3	0.778
	T5	0.878
	P3	0.811
	O1	0.800

The eye-closed recording condition was disregarded because the subjects were not completely cooperative. We did not notice any significant differences in the two groups in looking at mother's picture upright and Kanizsa shapes.

Discussion

In this study, the qEEG of 11 normal children and 15 children with ASD were analyzed, and the results of groups were compared against one another conditions. using spectrogram criteria in the nine recording the two Our results demonstrate that children with ASD have significant lower values ($p<0.01$) at Fp1,

Fp2, F3 electrodes and T5 and T3, P3 and O1 electrodes ($p<0.05$) in alpha frequency band using spectrogram criteria in the relaxed eye-opened condition.

We observed that all of electrodes with significant differences are in the left brain hemisphere (the electrodes with odd index). This funded in autism with right handedness is in agreement with the finding of Chandana and colleagues that obtained using the measurement of brain serotonin synthesis in a large group of autistic individuals with positron emission tomography (PET) (20).

Table 4: The spectrogram criteria of the EEG for the autism (ASD) and normal children in frequency bands with recording conditions those had significant differences

Recording conditions	Affected bands frequency and percent of discriminate	Fp1	Fp2	F7	F3	Fz	F4	F8	T3	C3	Cz	C4	T4	T5	P3	Pz	P4	T6	O1	O2
Relaxed eye-opened	Alpha (92.3%)	**	**		**				*					**	*				*	
	Beta (0%)	*																		
	Gamma (0%)																	*		
Looking at mother's picture inverted	Alpha (83.3%)								**					*					*	
	Beta (72.2%)				**								*							
Looking at a stranger's picture upright	Delta (0%)										*									
	Alpha (0%)					*														
	Beta (88.9%)			**	**															
Looking at a stranger's picture inverted	Delta (0%)							*												
	Alpha (77.8%)		*			**		*												
	Beta (88.9%)							**				**								

** $p<0.01$ and *$p<0.05$

children using spectrogram criteria.

The spectrogram criteria were employed in nine conditions in five frequency bands. The electrodes that had been significantly different between the two groups are presented in Table 5. This table demonstrates that recorded signals with relaxed eye-opened condition in alpha band, those recorded with looking at a stranger's picture upright condition in beta band and the ones obtained with subjects looking at a stranger's picture inverted in the same beta band show the best discrimination of 92.3%, 88.9% and 88.9% respectively.

Table 5 demonstrates that there are more abnormalities in alpha band than in beta, and more in beta band than in gamma. Abnormalities in alpha and beta bands are in agreements with the Bashina et al. study (7). In another study, using spectral power, it was reported that there are not any differences in children with autism under controlled conditions (22). However, in our study ,using spectrogram criteria, it is shown that there are abnormalities in alpha and beta bands. Whereas alpha band reflects the co-ordination of wider areas of the brain, beta band shows an integrating role in the areas of the brain that are neighbors (23, 24). Therefore, it seems that abnormalities in ASD can be reflected to co-ordination in areas of the brain.

We observed a few abnormalities in ASD in gamma band (T6 electrode in relaxed eye-opened condition). Our results do not agree in induced gamma band regions of ASD (25, 26). This difference can be related to our subjects that were in autism with low functioning activity whilst they tested autism disorders with high functional or with Asperger disorder. The gamma band plays a synchronization role of cortical nets region especially in recognition and perception task (27). The results of this study demonstrate that there are not abnormalities in gamma band and so suggest abnormalities can not related to synchronization cortical nets in children with autism disorders.

Using spectrogram criteria in looking at the three samples of Kanizsa shapes have proven not to be effective in discriminating ASD from normal children. However, our findings differ from other studies showing that these shapes can not be effective in significant differences in delta and alpha bands (15).

This inconsistency may well be as a result of well known heterogeneity in ASD, different age range, IQ and sex of the subjects and/or dissimilarity in the behavioral conditions during EEG recordings. Groups of autism usually comprise both autism and Asperger disorder whilst we have only studied children with ASD. Another difference between our study and others is how we evaluated EEG signals. In this study, we used spectrogram criteria with more information of signal in two dimensional maps (time-frequency) instead of spectral power.

One of the limitations of our study that merits consideration is that the sample size was small. In the other words, it is better that subjects be with the same handedness (for example they be only with right handed) because in our result it is shown there are abnormalities in the left hemisphere of children with autism. As a result, our findings are preliminary and require more replications in a larger disorder population before any conclusive valuable clinical diagnostic can be made. This study to the best of our knowledge is the first to employ spectrogram value to qEEG in children with ASD and using it for classification and diagnosis of ASD. However, since no other researchers have used the method in this area, we were unable to assess our results. Another limitation was that the ASD children could not be taken off their medication for a long time; all of these children were only medication-free for at most two weeks prior to EEG recording.

Conclusions

In this research it is shown that qEEG can be used for discriminating and diagnosing children with ASD from normal children using spectrogram criteria. In many different recordings of conditions, it is obtained that qEEG with relaxed eye-opened condition and looking at a stranger's picture in upright and inverted positions had the most distinction in the frequency bands. Among the frequency bands, alpha and beta bands had the most differences in ASD children. These can be a reason for abnormalities in synchronization cortical nets and disorganization of various parts of activities especially in wider areas of the brain and those areas of the brain that are neighbors. Furthermore, it has been shown that there are abnormalities in the prefrontal lobe and more abnormalities in the left brain hemisphere than the right. Future research with more participants and trials should be undertaken to replicate and increase the depth of this study; in addition, the use of spectrogram criteria for evaluation of EEG in other disorders is also recommended.

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