Electroencephalographic pattern among autistic children and their relatives

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Introduction
Autism and related autism spectrum disorders (ASDs) are lifelong, often severely impairing neurodevelopmental syndromes involving deficits in social relatedness, language, and behavior. There is good evidence that electroencephalographic (EEG) changes are common in children with autism and these EEG changes are considered to be signs of cerebral dysfunction.

Aim of the work
The aim of this study was to study specific EEG patterns in autism and to correlate severity of autism to EEG patterns.

Participants and methods
The study was conducted on 30 children who met the DSM-IV-TR criteria for autism aged 3 years and above, and 30 siblings of them not fulfilling criteria of any pervasive developmental disorder. Participants of this study were recruited from the private centers of developmentally handicapped children, and the neuropsychiatry outpatient clinic of Alexandria University Hospital. All studied children were subjected to the following: first: full history taking and physical, neurological, and psychiatric examination for clinical assessment of ASD according to DSM-IV-TR criteria. Second: psychological testing using the Childhood Autism Rating Scale (CARS). Third: EEG for all sampled children.

Results
Prevalence of EEG abnormalities among autistic cases was 66.7%, whereas in the sibling group was 20%, which was significantly different from cases group. Generalized symmetrical spike wave complexes and focal centrotemporal spikes were the most prevalent EEG changes among autistic cases. There was a significant relationship between CARS and generalized EEG abnormalities.

Conclusion
Generalized symmetrical spike wave complexes and focal centrotemporal spikes were the most prevalent EEG changes among autistic cases. The lack of similarity between cases and sibling EEGs suggests that the epileptiform activity found in children with ASDs is more than just a familial pattern or a typical childhood finding. There was a significant relationship between CARS and generalized EEG abnormalities.

Keywords:
autism, autism spectrum disorder, Childhood Autism Rating Scale, electroencephalography, epilepsy, epileptic, pervasive developmental disorder, seizures

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Introduction

Autism, also referred to as autism spectrum disorder (ASD), constitutes a neurodevelopmental disorder characterized by impairment in communication, including language, social skills, and comportment often involving rigidity of interests and repetitive, stereotypical behavior (American Psychiatric Association, Washington, DC, 2000). It is clearly evident today, as substantiated by both MRI (including functional MRIs) and PET scan studies, that the brains of children with autism are different. Electroencephalograms (EEGs) and magnetoencephalography have also been used to measure fluctuations in electrical and magnetic responses generated by neural activity in the brain. The evidence suggests that there are abnormalities in both the structure and the function of the brains of individuals with autism (Fidler *et al.*, 2000; Brambilla *et al.*, 2003; Ecker *et al.*, 2012).

The EEG is a leading tool in the evaluation of ASDs (Ekinci *et al.*, 2010). The EEG is most commonly thought of in the conventional medical community to be utilized with seizure disorders, which coincidently, are present in about one-third of children with autism. Because of its ease of availability and noninvasive nature, EEG may be the most helpful in identifying the areas of unique variability in the brains of children with autism (Tuchman and Rapin, 2002). Recently, there have also been reports of high rates of epileptiform EEGs in children with autism without a history of seizures or epilepsy; these EEG changes are considered to be signs of cerebral dysfunction (Chez *et al.*, 2006; Kim *et al.*, 2006).

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Aim of the work

The aim of this work was to study specific EEG patterns in autism as it can indicate specific areas of cerebral dysfunction and to correlate severity of autism to EEG patterns.

Participants and methods

This case–control study was conducted in private centers of developmentally handicapped children having special classes for autistic children and the child psychiatry outpatient clinic of Alexandria University Hospital. The studied sample comprised 30 children aged 3 or more who met the DSM-IV-TR criteria for ASD, and 30 sibling of them not fulfilling criteria of any pervasive developmental disorders or epilepsy. Children with other ASDs, with gross dysmorphic features, with severe degrees of head asymmetry and those who experienced single or more seizures were excluded. All studied children were subjected to the following: first: full history taking and physical, neurological, and psychiatric examination for clinical assessment of ASD according to DSM-IV-TR criteria. Second: psychological testing using the Childhood Autism Rating Scale (CARS). Third: EEG for all sampled children. The procedure was done using Nihon Kohden 92 (Hamburg, Germany). The study was approved by the Ethics committee of Alexandria Faculty of Medicine, November 2013.

The potential is amplified about a million times, and presented for interpretation as an ink trace on a moving paper. Recording is done over a short period of time, usually 20–40 min. Visual analysis is done by an expert epileptologist who was blinded for data.

Statistical analysis

Data were fed to the computer and analyzed using IBM SPSS software package version 20.0. Qualitative data were described using number and percent. Quantitative data were described using mean and SD, median, minimum and maximum.

Comparison between different groups regarding categorical variables was tested using χ^2-test. When more than 20% of the cells have expected count less than 5, correction for χ^2 was conducted using Fisher's exact test or Monte Carlo correction. The distributions of quantitative variables were tested for normality using Kolmogorov–Smirnov test, Shapiro–Wilk test and D'Agostino test, and also histogram and QQ plot were used for vision test. If it reveals normal data distribution, parametric tests were applied. If the data were abnormally distributed, nonparametric tests were used.

For normally distributed data, comparison between two independent populations was done using independent *t*-test. Correlations between two quantitative variables were assessed using Pearson coefficient. For abnormally distributed data, comparison between two independent populations was done using Mann–Whitney test. Significance test results are quoted as two-tailed probabilities. Significance of the obtained results was judged at the 5% level.

Results

Sociodemographic characteristics of the autistic children and their sibling: The distribution of the autistic children and their siblings according to their sociodemographic characteristics is shown in Table 1.

Severity of autistic symptoms according to Childhood Autism Rating Scale

The severity of autistic symptoms according to CARS is shown in Table 2.

The distribution of cases and siblings according to psychiatric comorbidities is shown in Table 3.

The distribution of cases and siblings according to medical history is shown in Table 4.

The comparison between cases and siblings according to perinatal history is shown in Table 5.

Table 1 Comparison between cases and siblings according to demographic data

	Cases (n = 30) [n (%)]	Sibling (n = 30) [n (%)]	Test of significance
Sex			
Male	24 (80.0)	16 (53.3)	P = 0.028 (χ^2)*
Female	6 (20.0)	14 (46.7)	
Age			
Minimum–maximum	3.0–11.0	3.0–20.0	^{MW}P = 0.003*
Mean ± SD	5.50 ± 2.76	8.10 ± 3.74	
Median	5.0	7.50	
Residence			
Urban	25 (83.3)	25 (83.3)	—
Rural	5 (16.7)	5 (16.7)	
Education level			
No	3 (10.0)	2 (6.7)	^{MC}P < 0.001*
Special education	20 (66.7)	1 (3.3)	
Primary	7 (23.3)	24 (80.0)	
Secondary	0 (0.0)	2 (6.7)	
College	0 (0.0)	1 (3.3)	

χ^2, χ^2-test; MC, Monte Carlo test; MW, Mann–Whitney test; P, P value for comparing between the two studied groups; *Statistically significant at $P \leq 0.05$.

Details on neurological examination are shown in Table 6.

Comparison between cases and sibling groups according to electroencephalography

Details regarding background (symmetry) are shown in Table 7.

Information regarding sleep paroxysmal activity are shown in Table 8.

Table 2 Distribution of the autistic children and the severity of autistic symptoms according to Childhood Autism Rating Scale

	n (%)
CARS	
Autistic trait	8 (26.7)
Mild to moderate	16 (53.3)
Severe	6 (20.0)
Minimum–maximum	24.0–48.0
Mean ± SD	33.20 ± 5.52
Median	33.0

CARS, Childhood Autism Rating Scale.

Table 3 Distribution of studied cases and siblings according to psychiatric comorbidities

Comorbidities	Cases (*n* = 30) [*n* (%)]	Sibling (*n* = 30) [*n* (%)]
None	15 (50)	28 (93.3)
ADHD	6 (20)	0 (0)
Tic disorder	1 (3.3)	0 (0)
Elimination disorder	3 (10)	2 (6.7)
Sleep disorders	5 (16.7)	0 (0)

Table 4 Comparison between cases and siblings according to medical history

Medical history	Cases (*n* = 30) [*n* (%)]	Sibling (*n* = 30) [*n* (%)]	Test of significance
Medical history			
–	12 (40.0)	29 (96.67)	$P < 0.001$ (χ^2)*
+	18 (60.0)	1 (3.3)	
URTIs	8 (44.4)	0 (0.0)	$^{FE}P = 0.495$
GIT	3 (16.7)	0 (0.0)	$^{FE}P = 1.000$
Asthma	3 (16.7)	0 (0.0)	$^{FE}P = 1.000$
Febrile seizures	2 (11.1)	0 (0.0)	$^{FE}P = 1.000$
Allergic sinusitis	2 (11.1)	0 (0.0)	$^{FE}P = 1.000$
Allergy skin	2 (11.1)	0 (0.0)	$^{FE}P = 1.000$
Favism	1 (5.6)	0 (0.0)	$^{FE}P = 1.000$
Falling from height	1 (5.6)	0 (0.0)	$^{FE}P = 1.000$
Congenital heart	1 (5.6)	0 (0.0)	$^{FE}P = 1.000$
Meningitis	0 (0.0)	1 (100.0)	$^{FE}P = 1.000$

χ^2, χ^2-test; *P*, *P* value for comparing between the two studied group; *Statistically significant at $P \leq 0.05$; URTIs, upper respiratory tract infection; GIT, Gastrointestinal tract .

Details on distribution of cases and siblings according to EEG abnormalities are shown in Table 9.

As regarding relation between CARS and paroxysmal activity, Table 10 shows that: in cases group we found a significant relationship between CARS and generalized EEG abnormalities.

Table 5 Comparison between cases and siblings according to perinatal history

Perinatal history	Cases (*n* = 30) [*n* (%)]	Sibling (*n* = 30) [*n* (%)]	*P*
Prenatal			
Normal	15 (50.0)	27 (90.0)	0.005*
Hyperemesis gravidarum	5 (16.7)	0 (0.0)	
Twin	3 (10.0)	3 (10.0)	
History of still birth	2 (6.7)	0 (0.0)	
Exposure to anesthesia	1 (3.3)	0 (0.0)	
HTN	1 (3.3)	0 (0.0)	
Maternal depression	1 (3.3)	0 (0.0)	
Threatened abortion	1 (3.3)	0 (0.0)	
Premature rupture of membrane	1 (3.3)	0 (0.0)	
Natal			
Normal	20 (66.7)	25 (83.3)	0.118
CS	6 (20.0)	5 (16.7)	
Complicated vaginal delivery	4 (13.3)	0 (0.0)	
Postnatal			
Normal	20 (66.7)	30 (100.0)	0.001*
Pneumonia	2 (6.7)	0 (0.0)	
Jaundice	4 (13.3)	0 (0.0)	
Asphyxia	3 (10.0)	0 (0.0)	
Preterm (<38 week)	1 (3.3)	0 (0.0)	

CS, cesarean section; HTN, hypertension; *P*, *P* value for monte carlo test for comparing between the two studied groups; *Statistically significant at $P \leq 0.05$.

Table 6 Comparison between the two studied groups according to neurological examination in cases group

Neurological examination	Cases (*n* = 30) [*n* (%)]	Siblings (*n* = 30) [*n* (%)]	χ^2	*P*
Neurological examination				
Normal	18 (60.0)	29 (96.7)	11.882*	0.001*
Exaggerated reflexes	7 (23.3)	0 (0.0)	7.925*	$^{FE}P = 0.011$*
Unsteady gait	1 (3.3)	0 (0.0)	1.017	$^{FE}P = 1.000$
Equivocal plantar	5 (16.7)	1 (0.0)	2.963	$^{FE}P = 0.195$
Hypertonia	5 (16.7)	0 (0.0)	5.455	$^{FE}P = 0.052$

χ^2, value for χ^2; FE, fisher exact test; *Statistically significant at $P \leq 0.05$.

Table 7 Comparison between cases and sibling groups according to electroencephalographic background

EEG background	Cases (n = 30) [n (%)]	Sibling (n = 30) [n (%)]	Test of significance
Background symmetry			
Symmetrical	29 (96.7)	30 (100.0)	^{FE}P = 1.000
Asymmetrical	1 (3.3)	0 (0.0)	
Organization			
Well formed	28 (93.3)	30 (100.0)	^{FE}P = 0.492
Slow for the age	2 (6.7)	0 (0.0)	
Dominant rhythm			
Mixed alpha and theta	14 (46.7)	17 (56.7)	^{MC}P = 0.019*
Mixed alpha and beta	1 (3.3)	6 (20.0)	
Mainly alpha	8 (26.7)	6 (20.0)	
Mixed theta and delta	5 (16.7)	0 (0.0)	
Mixed alpha, delta and theta	2 (6.7)	0 (0.0)	
Mixed alpha, theta and beta	0 (0.0)	1 (3.3)	

*Statistical significance $P < 0.05$

Table 8 Comparison between cases and siblings according to paroxysmal activity

Paroxysmal activity	Cases [n (%)]	Sibling [n (%)]	Test of significance	χ^2
Focal (36.67%)				
Normal	10 (33.3)	24 (80)	<0.001*	
Unilateral spikes				
Centro temporal	6 (20)	0 (0.0)	^{FE}P = 0.024*	6.667*
Anterior temporal	0 (0.0)	2 (6.6)	^{FE}P = 0.492	2.069
Orbitofrontal	1 (3.3)	0 (0.0)	^{FE}P = 1.000	1.017
Parietal	1 (3.3)	0 (0.0)	^{FE}P = 1.000	1.017
Bilateral spikes				
Temporal	2 (6.6)	1 (3.3)	^{FE}P = 0.612	0.386
Parietal	1 (3.3)	0 (0.0)	^{FE}P = 1.000	1.017
Generalized (36.67%)				
Symmetrical				
Spike wave complex	10 (33.3)	3 (10)	0.028*	4.812*
Poly spike wave	0 (0.0)	0 (0.0)	—	—
Asymmetrical				
Burst of poly spikes	1 (3.3)	0 (0.0)	^{FE}P = 1.000	1.017

χ^2, χ^2-test; FE, fisher exact test; MC, monte carlo test; P, P value comparing between the two studied groups; *Statistically significant at $P \leq 0.05$.

Discussion

Although many studies have attempted to clarify the pathogenesis of autism and related disorders, causes remain unclear (Courchesne and Pierce, 2005).

The present work spots light on EEG changes in autistic children and their siblings. Thirty children with autism aged 3–11 years — all of them fulfilling criteria of the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-IV-TR) — and their siblings, were included in the study (American Psychiatric Association, Washington, DC, 2000). The mean age of our children was 5.53 ± 2.73 years, which is in accordance with the school age at which the diagnosis is well established.

In our study the majority of the studied cases were males (80%), whereas the rest (20%) were females that reflects male to female ratio of 4: 1, respectively. The excess of boys was always noted in all studies on autism since Kanner's 1943 original paper (Kanner, 1968).

The cause for this observed sex difference is still debatable. It is possible that males have a lower threshold for expressing the disorder and that more severe neurodevelopment abnormalities are required to cause autism in a girl (Gillberg *et al.*, 1991). Another theory is that high fetal testosterone levels have been associated with autistic traits in toddlers and older children. This supports the extreme male brain theory of autism (Auyeung *et al.*, 2010).

As regards residence of both cases and siblings 83.3% were urban, whereas 16.7% were rural. Malhotra *et al.* (2003) found a statistically significant association between autism and coming from a family from the upper socioeconomic status, and contributed this to the availability of healthcare services for those families (Malhotra *et al.*, 2003).

On the contrary, Wing (1980) did not support this idea, and reported that autism and other ASD are observed in families of all socioeconomic and educational levels, and the impression of association with high socioeconomic level was the result of selection bias. This group of higher levels is more likely to seek referral (Wing, 1980).

The CARS was applied to distinguish the severity of ASD symptoms in the present study, results demonstrated that more than half of the sample scored mild to moderate 30 to <37 (53.3%), whereas 20% scored severe ≥37, and about 26.7% scored <30 with a mean 33.20 ± 5.52. Koenig and Scahill (2001) conducted a multisite study of using CARS on ASD children. Results indicated excellent sensitivity and specificity of the tool (Koenig and Scahill, 2001).

Rellini *et al.* (2004) found complete agreement between CARS and DSM-IV criteria regarding the diagnosis and screening for ASD on a sample size of 65 children aged between 2 and 11 years; the results showed 0%

Table 9 Distribution of cases and siblings as regards electroencephalographic abnormalities

EEG abnormalities	*n* (%)
Normal cases normal sibling	10 (33.3)
Abnormal cases normal sibling	14 (46.4)
Abnormal sibling normal cases	1 (3.3)
Both abnormal cases and sibling	5 (16.7)

Table 10 Relation between Childhood Autism Rating Scale and paroxysmal activity in cases group

Paroxysmal activity	CARS		
	Minimum–maximum	Mean ± SD	Median
Normal	25.0–38.0	31.70 ± 3.80	31.50
Focal			
Abnormal	24.0–40.0	31.36 ± 4.67	31.0
P	0.859		
Generalized			
Abnormal	29.0–48.0	36.45 ± 6.01	5.52
P	0.045*		
Overall			
Normal	25.0–38.0	31.70 ± 3.80	31.50
Abnormal	24.0–48.0	33.95 ± 6.16	33.0
P	0.301		

CARS, Childhood Autism Rating Scale; *P*, *P* value for Student *t*-test for relation between CARS and normal and abnormal of each parameter; *Statistically significant at $P \leq 0.05$.

false negative diagnosis with CARS compared with other tools (Rellini *et al.*, 2004).

In our study eight children were diagnosed with autism according to DSM-IV criteria but had a score less than 30; this can be explained by the early intervention they received as they improved in some aspects, also Mayes *et al.* (2012) in their study on the use of the CARS for children with high functioning autism or Asperger syndrome suggested a cutoff point of 25.5 in high functioning autism.

As regards psychiatric comorbidities in the studied sample, 30% exhibited hyperactivity and inattention, which may be attributed to a general underlying brain pathology, in comparison with other researchers; Frazier *et al.* (2001) reported 83% of children with combined disorders. Goldstein and Adam (2004) in their attempt to determine the comorbidity of ASD and attention deficit hyperactive child (ADHD), they found that 60% met symptom criteria for both ASD and ADHD. The higher rate in the first study may be explained by their sample collection from hospitalized children where higher rates of mental morbidities are expected.

The rate of ADHD in autism reported by other investigators has varied from 29 to 73%. The convergent findings of our study and the studies of other investigators suggest that impairing ADHD syndromes are common, but not universal phenomena, in autism (Leyfer *et al.*, 2006).

Children with autistic disorder have been reported to have a higher-than-expected incidence of upper respiratory infections and other minor infections. Gastrointestinal symptoms commonly found among children with autistic disorder include excessive burping, constipation, and diarrhea. Also seen is an increased incidence of allergy in children with autistic disorder (Sadock and Sadock, 2007); in our study about 44.4% of the studied autistic sample had repeated upper respiratory tract infections, 16.7% had repeated gastrointestinal problems as gastroenteritis and loose bowel motions, 16.7% had asthma, 11.1% had febrile seizures and about 22.2% for allergic sinusitis and skin allergy.

As regards prenatal factors, history of hyperemesis gravidarum, history of fetal loss, twin pregnancy and exposure to medication during pregnancy (anesthetics, antihypertensive) were significantly higher among our cases than controls ($P = 0.005$) .Our results dealing with postnatal factors such as history of hypoxia, preterm labor, history of neonatal jaundice and pneumonia were also statistically significantly increased in autistic patients ($P = 0.001$). On the other hand our study did not show a statistically significant difference between patients and control as regards cesarean delivery and obstructed labor.

Kolevzon *et al.* (2007) suggested the presence of nonheritable prenatal and perinatal risk factors for autism. A possibility supported by the study of Bolton *et al.* (1992) demonstrated an association between autism and obstetric complications, prenatal or intrapartum use of medications. Burd *et al.* (1999) reported that perinatal risk factors as breech presentation, low Apgar score (≤7) at 5 min, low birth weight (≤2500 g), gestational age at birth of less than 35 weeks, and being small for gestational age were associated with a statistically significantly increased risk of autism.

Maimburg and Vaeth (2007) conducted a population-based matched case–control study of 473 children with autism and 473 matched controls. They found an almost four-fold risk for infantile autism in infants who had hyperbilirubinemia after birth. Their findings suggest that hyperbilirubinemia in the neonatal period is an important factor to consider when studying causes of infantile autism. However, Croen *et al.* (2005) reported that neonatal hyperbilirubinemia is not a risk factor for ASDs.

Although not proven as independent risk factors for autism, these variables should be examined in future

studies that use large, population-based birth cohorts with precise assessments of exposures and potential confounders.

On performing neurological examination for both the cases and siblings, we found several abnormalities as exaggerated reflexes, hypertonia, unsteady gait, and equivocal planter with an overall prevalence about 40% in comparison with 6.6% in sibling, which was a statistically significant difference.

Presence of neurological signs suggested an underlying brain pathology in ASD children. These are in agreement with Ardila, (1996). Bauman (1999) and McPartland and Klin (2006) suggested that 40–100% of autistic children show at least one of these signs with a controversial agreement to the causative underlying brain damage.

As regards the EEG changes among the autistic children, it was found that abnormal EEG findings in children with autism provide evidence that autism is a neurobiological disorder. Epileptiform abnormalities may further impair cognitive function (Galanopoulou *et al.*, 2002).

In the present study, 20 (66.6%) autistic children had EEG changes. EEG changes are considered to be signs of cerebral dysfunction. Rates as high as 60% have been reported by some investigators who propose that these abnormalities may play a causal role in the autism (Spence and Schneider, 2009).

Lewine *et al.* (1999) and Chez *et al.* (2006) have reported frequency of 64.7 and 68%, respectively, of EEG changes in autistic children, which are consistent with the result found in the present study (66.6%).

On the other hand, several studies (Canitano *et al.*, 2005; Giannotti *et al.*, 2008; Ekinci *et al.*, 2010) have demonstrated an average frequency of 30.8–40.5% of EEG changes in children with autism. These results were lower than those detected in our study.

There is a variation of the rate of EEG abnormalities. This was demonstrated by a study done by Tamarah *et al.* (2005). Screening EEG in autistic spectrum of disorders, indicated that the prevalence of EEG abnormalities, irrespective of clinical seizure history, was 38.3 to 60.8% (Tamarah *et al.*, 2005) these variations may be explained by methodological and sample differences. Some samples were purely idiopathic (Giovanardi Rossi *et al.*, 2000; Hara, 2007), others employed routine EEGs rather than prolonged studies. It should be noted that only 20 min EEG recordings were obtained in our study.

These higher rates of EEG abnormalities among autistic children suggest that this activity may be a factor in the pathology of cognitive impairment, behavioral problems, language dysfunction, and increase the possibility of development of clinical seizures later on (Bonde, 2000).

Regarding the character of EEG changes 50% generalized and 50% focal, as regarding localization of focal abnormalities the majority was centrotemporal (about 54.5% of focal changes), about 18.18% of focal changes were bitemporal and 9.1% for each of other sites, parietal, orbitofrontal and biparital. As regarding generalized abnormalities, which constitute 50% of changes about 91% were symmetrical spike wave complexes and about 9% asymmetrical bursts of polyspikes.

Comparing these results with the study conducted by Chez *et al.* (2006) in a sequential screening of 1268 ASD children between 1996 and 2005 they found 64.7% had EEG abnormalities, many different localization patterns, instead of one locus were observed in their study, right temporal region was the most common site, followed by bitemporal, and generalized epileptiform discharge, and equal percentage for remaining locations (Chez *et al.*, 2006), which was in accordance to our study.

Lewine *et al.* (1999); Tuchman and Rapin (1997); and Giovanardi Rossi *et al.* (2000) reported that localization of the EEG abnormalities in ASD children is variable ranging from centrotemporal spikes to similarities to benign focal epilepsies (Tuchman and Rapin, 1997; Giovanardi Rossi *et al.*, 2000).

For centrotemporal spikes predominance in focal EEG changes in those studies as well as our study may strengthen a theory done by Baron-Cohena *et al.* (2000) and Grelottia *et al.* (2004) that abnormal functioning of the brain areas that participate in face processing and social cognition has been consistently demonstrated in persons with autism and reflects hypoactivation in the amygdala and fusiform gyrus. The fMRI studies of individuals with autism judging expressions from another person's eyes did not activate the amygdala, whereas people without autism did show amygdala activation. Because autism involves deficits in 'social intelligence' it is plausible that an amygdala deficit could be involved (Baron-Cohena *et al.*, 2000; Grelottia *et al.*, 2004).

As regards EEG changes found among the sibling group, we found six (20%) had EEG changes, which was significantly different from the autistic group and near but slightly higher to the range of EEG changes in

normal children (8–18.6%) (Shelley *et al.*, 2008), which open the floor for further research on EEG changes of autistic siblings on a larger sample size.

In our study distribution of cases and siblings as regards EEG abnormalities was as follows:

(1) We found only five cases (16.67%) in which both cases and siblings had EEG changes, whereas the majority 14 (46.4%) only autistic cases had changes in their EEG with normal EEG of their siblings.
(2) Also the lack of similarity between cases and sibling EEGs suggests that genetics alone does not explain the higher frequency of EEG abnormalities reported in ASDs. The results suggest that the epileptiform activity found in children with ASDs is more than just a familial pattern or a typical childhood finding.

This suggests a lower frequency of EEG abnormalities than is seen in ASD patients. We conclude that normally developing siblings of children with ASDs have less frequent epileptiform activity than is present in the ASD population. It remains to be studied whether the normal preschool childhood population would exhibit the same incidence of spike activity with prolonged ambulatory EEGs. This finding was in accordance with the study of Chez *et al.* (2004).

As regards relationship between the EEG changes and the severity of autistic symptoms our study demonstrated a significant relationship between generalized EEG abnormalities and severity of autistic symptoms. While our data did not support a significant relationship between focal abnormalities and severity of autistic symptoms, an explanation can be derived from EEG findings in the present work, that the multiple location of the EEG changes in the form of epileptiform activity indicated the multisite affection in the brain. This consequently explains the higher rate among the severe autistic children who actually presented with severe impairments across different domains, as behavior, social adaptively and cognition functions.

These results were in agreement with a study of Gabis *et al.* (2005) who found that abnormal EEG occurred at significantly higher rates in children in the more impaired range among ASD (P<0.05); they suggested the use of EEG recording routinely during evaluation of more impaired individuals.

Several researchers, Tuchman (2000); Chez *et al.* (2004); Canitano *et al.* (2005) and others supported this conclusion and added that children with ASD without clinical seizures have EEG changes that may be the cause of their marked deficit regarding their cognitive, language function and behavioral profile.

To the best of our knowledge regarding researches concerned with this hypothesis, no study was against it.

In our study there was a significant relationship between generalized EEG changes and mental retardation. This may show the underlying cause of mental retardation that pointed to the brain pathology either for the multifocal affection or the bitemporal pattern that concerned more with the language dysfunction that considered the main obstacle during the assessment of IQ level among the autistic children. This is supported by our results as we noticed that the two cases who had bitemporal epileptiform activity their IQ were untestable.

These results were in agreement with Olsson *et al.* (1988); Kasteleijn-Nost (1995); Tuchman (2000); Daniellson *et al.* (2005) and others in that, the incidence of EEG changes depending on the level of mental retardation, and these changes may only manifest itself in the form of cognitive dysfunction.

Limited studies were available in detecting the specific pattern of localization of EEG changes and particular dysfunction among autistic individuals. Chez *et al.* (2004) suggested the link between localization of EEG abnormalities and language dysfunction if localization mainly bitemporal, social impairment in right temporal, generalized represented an inherited pattern and associated more with behavioral problems and cognitive impairments.

These results were presented also in the sibling group as there was a significant relationship between IQ and EEG changes, which support the link between intellectual disability and EEG abnormalities.

Conflicts of interest

None declared.

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