EEG abnormalities and severity of symptoms in non-epileptic autistic children

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Received 18 January 2016
Accepted 1 May 2016

Egyptian Journal of Psychiatry
2017, 38:59–64

Background
It has been recently shown that electroencephalogram (EEG) paroxysmal abnormalities are frequently recorded in patients with autism despite the absence of seizures.

Objective
On the basis of the increasing evidence of EEG abnormalities in autism, the aim of this study was to detect the EEG abnormalities in relation to the degree of severity of autism.

Patients and methods
EEG was measured in 40 autistic children aged 2–12 years, in comparison with 40 typically developing matched children. The severity of autism was assessed using the Childhood Autism Rating Scale.

Results
We found that 50% of the autistic children had abnormal EEG findings. There was a statistically significant relation between the EEG abnormalities and the severity of autism. Moreover, there was a statistically significant relation between the site of the wave abnormalities and the severity of autism.

Conclusion
Our study suggests that the use of neurological investigative techniques such as EEG be considered routinely during the evaluation of autistic children.

Keywords:
autism, Childhood Autism Rating Scale, electroencephalogram

Egypt J Psychiatr 38:59–64

1110-1105

Introduction

Autism is a neurodevelopmental disorder that manifests during the first 3 years of life. The group of pervasive developmental disorders (PDDs), also termed autism spectrum disorders (ASDs), includes autism as well as PDD-not otherwise specified and Asperger's disorder (Johnson *et al.*, 2007).

The three core characteristics of the ASDs are impairments of reciprocal social interactions, problems in communication, and a restricted range of behaviors and interests. There is an increased prevalence of both epilepsy and abnormal potentially epileptogenic activity in children with PDDs. The occurrence of epilepsy in autism is variable; nevertheless, electroencephalogram (EEG) paroxysmal abnormalities are frequently recorded in patients with autism (Fombonne, 2009).

EEG was one of the earliest techniques used to investigate the neurobiology of autism. The recognition of a high incidence of EEG abnormalities and seizure disorders in the autistic populations was among the earliest evidence of a biologic basis for this disorder (Minshew, 1991).

On the basis of the increasing evidence of EEG abnormalities in autism, we aimed to detect the relation between the EEG abnormalities and the severity of symptoms of autism measured using the Childhood Autism Rating Scale (CARS).

Patients and methods

This case–control study was conducted on 40 children who had ASD. They were recruited from the Psychiatric Outpatients Clinics, Faculty of Medicine, Zagazig University, Zagazig, Egypt, during their follow-up visits, in the year 2014 (28 male and 12 female patients). Their ages ranged from 2 to 12 years.

The control group comprised 40 age-matched and sex-matched children (32 boys and eight girls). Their ages ranged from 2.5 to 10 years. They were the siblings of children attending this clinic because of a minor illness

 DOI: 10.4103/1110-1105.209676

such as common cold, tonsillitis, acute bronchitis, and gastroenteritis. They were recruited from the Outpatient Clinic of Pediatric Department, Zagazig University Hospital. The control children were not related to the children with autism and had no clinical findings suggesting neuropsychiatric disorders. Informed written consent was obtained from the parents of each participant. The study was explained in simple language to the children and verbal assent was obtained from higher functioning children who were capable of understanding the study process. The study was approved by the ethical committee of Zagazig University Hospital.

Inclusion criteria

(1) Fulfillment of *Diagnostic and Statistical Manual Of Mental Disorders*, 4th ed. criteria for autistic spectrum disorders and a CARS score more than 30.
(2) Both sexes.
(3) Age range of 2–12 years.
(4) All socioeconomic classes.

All participants in the control group were matched for age and sex.

Exclusion criteria

(1) Neurological disorders.
(2) Metabolic disorders.
(3) Head trauma.
(4) Presence of other psychiatric disorders or mental disorder.

Methods

Clinical assessment

Clinical evaluation of autistic children was based on clinical history taking, clinical examination, and neuropsychiatric evaluation, during which the diagnosis of autism was confirmed according to the *Diagnostic and Statistical Manual of Mental Disorders*-IV criteria for research (APA, 2000). CARS: Disease severity was assessed using the CARS (Schopler *et al.*, 1986), which rates the child on a scale from 1 to 4 in each of the following 15 areas: relating to people; emotional response; imitation; body use; object use; listening response; fear or nervousness; verbal communication; nonverbal communication; activity level; level and consistency of intellectual response; adaptation to change; visual response; taste, smell, and touch response; and general impressions. A score of 30–36 points on this scale indicates mild-to-moderate autism (n=31), and a score of 37–60 points indicates severe autism (n=19). EEG: EEG was performed using the type and name of EEG machine in the Outpatient Clinic of Neurological Department, Zagazig University Hospital.

Statistical analysis

IBM SPSS statistics (version 22.0, 2013; IBM Corp., Armonk, New York, USA) was used for data analysis. Data was expressed as median and percentiles for quantitative nonparametric measures. The ranked Spearman correlation test was used to study the possible association between each two variables for nonparametric data. The following tests were carried out when appropriate: t-test for independent samples, Pearson's correlation coefficient, the χ^2-test, and analysis of variance test. The probability of error at 0.05 was considered significant, while at 0.01 and 0.001 are highly significant.

Results

Table 1 displays the demographic and EEG data of the participants. The mean age (mean± SD) of children with ASD included in the study was (4.97±2.9), and (5.06±2.2) years for typically developing controls. In the ASD group, 28 participants (70%) were boys. EEG abnormalities were significantly higher in children with ASD in comparison to control groups (P<0.05) as 50% of the autistic group had abnormal EEG findings,

Table 1 The demographic and electroencephalogram data of the studied groups

Variables	Control group (N=40)	Autistic group (N=40)	Tests of significance	P
Child age (years)				
X±SD	5.06±2.2	4.97±2.9	t=0.1	0.91
Range	2.5–10	2–12		
Sex [n (%)]				
Male	32 (80.0)	28 (70.0)		
Female	8 (20.0)	12 (30.0)	χ^2=1.06	0.53
EEG abnormalities [n (%)]				
Generalized	0 (0.0)	11 (27.5)	χ^2=10.4	<0.05
Focal	0 (0.0)	9 (22.5)		
Total	0 (0.0)	20 (50.0)		

EEG, electroencephalogram. P>0.05, nonsignificant.

Table 2 Electroencephalography pattern in relation to the severity of autism

Severity of autism	EEG pattern[N (%)]			χ^2	*P* value
	Generalized	Focal	Total		
Mild	1 (9.1)	1 (11.1)	8 (40.0)	11.05	0.02*
Moderate	3 (27.3)	2 (22.2)	9 (45.0)		
Severe	7 (63.6)	6 (66.7)	3 (15.0)		

EEG, electroencephalogram.

Table 3 Type and site of the abnormalities (wave type and site) in relation to the severity of autism

Site of abnormalities	*N*	Mild [*N* (%)]	Moderate [*N* (%)]	Sever [*N* (%)]	χ^2	*P*
Wave site						
Bicentrotemporal	2	0 (0.0)	0 (0.0)	2 (33.3)	9.0	0.029*
Bitempofrontal	3	0 (0.0)	0 (0.0)	3 (50.0)		S
Centroparietal	2	1 (100.0)	1 (50.0)	0 (0.0)		
Frontotemporal	2	0 (0.0)	1 (50.0)	1 (16.7)		
Wave type						
Spike	4	1 (50.0)	1 (20.0)	2 (15.4)	1.14	0.49
Slow	13	1 (50.0)	3 (60.0)	9 (69.2)		NS
Sharp	3	0 (0.0)	1 (20.0)	2 (15.4)		

NS, nonsignificant; S, significant. $P<0.05$, significant.

divided as 27.5% had generalized and 22.5% had focal EEG abnormalities while there were no EEG abnormalities in the control group.

Table 2 demonstrates the relation between EEG pattern and severity of autism in autistic group. Our study found that 50% of the autistic group had abnormal EEG findings: 27.5% had generalized and 22.5% had focal EEG abnormalities. However, there were no EEG abnormalities in the control group. Thus, there was a statistically significant difference between the autistic and the control group with regard to EEG abnormalities ($P<0.05$).

Table 3 shows the EEG pattern in relation to the severity of autism measured using the CARS in the autistic group. There was a statistically significant relation between the EEG results and the severity of autism measured using CARS ($P=0.02$), as the EEG abnormalities increased with the increase in the severity of autism. Moreover, there was agreement between the EEG results and the CARS results.

Table 3 shows the relation between the site of abnormalities (wave site) and the CARS. There was a statistically significant relation ($P=0.029$) between the site of the wave abnormalities and the severity of autism measured using CARS.

Discussion

EEG are frequently recorded in patients with autism despite the absence of seizures. Multiple case reports or population series have described an association of abnormal EEG findings within autistic individuals (Chez *et al.*, 2006; Amiet *et al.*, 2008).

To confirm the diagnosis of ASD in this study and to distinguish the severity of ASD symptoms, the CARS was applied. The results demonstrated that 40% of the autistic group scored severe (>36), whereas 35% scored moderate (range from 33 to 36) and 25% scored mild (range from 30 to 33).

The results of this study were slightly closer to the scores yielded by Kotoury *et al.* (2009), who found that 18% of cases were classified as mild, 29% as moderate, and the rest 53% were of severe forms. Moreover, in the study by El-Baz *et al.* (2011), they found that 15% of their autistic patients had mild degree of autism with CARS, 28% had moderate degree of autism, and 57% had severe autism (≥34). A similar finding was reported by many authors (Bilder *et al.*, 2009; Mamidala *et al.*, 2013).

In this study, a higher rate of ASD diagnosis was reported in boys (70%) than in girls. Their ages ranged from 2 to 12 years.

In agreement with our study, Fombonne (2009) found that the male prevalence was 4 : 1 in autism.

Moreover, Cohen *et al.* (2006) mentioned that autism is four times more likely to appear in boys than in girls. This finding is in agreement with that of Hassan (2008), who studied caregivers' awareness with

regard to autistic children and found that the majority of children were boys.

There was a statistically significant difference between male and female autistic children as regards the severity of autism measured using CARS (P=0.02), as the severity of autism increased in boys compared with girls.

In agreement with our results, Hartley and Sikora (2009) and Lai *et al.* (2011) reported greater difficulties in communication and more restricted/repetitive/stereotyped behaviors in autistic boys than in autistic girls.

In contrast, Holtmann *et al.* (2007) and Allison *et al.* (2008) found that there was no difference with regard to severity of autistic symptoms. This may be due to the sampling and methodological differences.

Carter *et al.* (2007) reported that significant differences in children's behaviors with regard to sex were reported by parents, but no significant differences emerged on direct assessment of social and language functioning. Specific to the study of ASD, Holtmann *et al.* (2007) reported the possibility of 'interpreting bias' among parents of children with ASDs, who may expect more socially desirable behaviors from daughters than from sons.

In addition, our result revealed that there was no statistically significant difference between male and female autistic children as regards the EEG results (P=0.76).

In agreement with our finding, Hara (2007), who studied the relation between the autistic child sex and the EEG abnormalities, reported no significant differences in sex ratios.

Moreover, others suggested the increased risk for EEG abnormalities in girls as opposed to boys (Danielsson *et al.*, 2005; Hughes and Melyn, 2005), and this probably reflects the greater severity of associated MR in female patients with a diagnosis of autism.

Amiet *et al.* (2008) found that the male-to-female ratio in autism with EEG abnormalities was close to 2 : 1 versus 3.5 : 1 in autism without EEG abnormalities, and a higher pooled prevalence of EEG abnormalities in female than in male patients (34.5 vs. 18.5%).

In our study, we found that there was a statistically significant difference between the autistic and the control group as regards the EEG abnormalities, as there was a high rate of subclinical epileptiform abnormalities in the autistic group (50%) compared with (0%) the control group (P<0.05).

These results are in agreement with the study by Yasuhara (2010), who found that abnormal EEG discharges occur in 85.8% (870/1014) of patients with ASD.

Our study is in agreement with the study by Elsayed and Sayyah (2012), who studied 47 patients diagnosed with idiopathic autism without epilepsy (age range 3–12 years) and 24 normal children of matched age and sex. They found a high rate of epileptiform abnormalities in children with autism (51.1%) compared with (8.3%) the control group (P=0.002).

In agreement with our study, a study by Tamarah *et al.* (2005) for screening of EEG in ASD (1986–2005) indicated that the prevalence of EEG abnormalities irrespective of clinical seizure history was 38.3–60.8%.

Chez *et al.* (2006), in a sequential screening of 1268 ASD children between 1996 and 2005, found that 64.7% had EEG abnormalities. In the study by Hara (2007), 33 of the 130 (25%) patients developed epilepsy during the follow-up period [epileptics (n=33); nonepileptics (n=97)] and 21% of nonepileptic children with autism exhibited epileptic discharges on EEG.

In contrast, Hardlicka *et al.* (2004) reported a lower rate (38%) of their sample (63) children with EEG abnormalities. This may be attributed to the differences in the type of EEG recording routine; awake EEG was used in their studies, whereas in the present study sedation and induced sleep EEG was used.

The exclusion of both severely retarded individuals and those who had or were having clinical seizures removes the bias of some prior studies that may have increased the percentages of abnormal EEG activity (Canitano *et al.*, 2005; Danielsson *et al.*, 2005; Hughes and Melyn, 2005).

Our study showed that there was a statistically significant relation between the EEG abnormalities and the severity of autism. The children with severe autistic symptoms present epileptiform activities, mainly generalized and bitempofrontal, and slow-wave predominates. These findings may represent that the severity of autistic symptoms has an underlying neurological basis.

The incidence of generalized EEG abnormalities was only 9.1% in children with mild autism and 27.3% in children with moderate autism, whereas there was a higher incidence (63.6%) in children with severe autism. Moreover, the focal EEG abnormalities predominate (66.7%) in severe cases of autism. Thus, in mild cases, EEG was commonly normal, whereas generalized and focal EEG patterns were common in moderate and severe cases.

These results are in agreement with a study conducted by Gabis *et al.* (2005), who found that abnormal EEG occurred at significantly higher rates in children in the more impaired range in ASD ($P<0.05$). Canitano *et al.* (2005) and Chez *et al.* (2004) supported this conclusion and added that children with ASD without clinical seizures have EEG changes that may be the cause of their marked deficit with regard to their cognitive, language function, and behavioral profile.

In agreement with our study, Elsayed and Sayyah (2012) found that the pattern of epileptiform abnormalities is highly correlated to the severity of autism ($P=0.000$).

Moreover, they found that EEG was abnormal in 21.7% children with mild autism but there was a higher incidence of generalized EEG changes in children with moderate autism (53.5%), whereas focal EEG predominates in severe cases of autism (72.7%).

Hughes and Melyn (2005), McVicar *et al.* (2005), Kim *et al.* (2006), and Akshoomoff *et al.* (2007) reported that epileptiform EEGs appear to be more common compared with nonepileptiform abnormalities.

Our results showed that generalized EEG abnormalities were predominant (27%), followed by bitempofrontal (7.5%); however, the other regions in this study (bicentrotemporal, frontotemporal, and centroparietal) had the same distribution (5%).

Moreover, our results reveal that there was a statistically significant relation ($P=0.029$) between the site of wave abnormalities and severity of autism measured using CARS.

In severe autism, the generalized abnormalities were more predominant, followed by the bitempofrontal, the bicentrotemporal, and the frontotemporal. In moderate autism, the generalized abnormalities were more predominant, followed by the frontotemporal and centroparietal. In mild autism, there was only one case with generalized and one case with centroparietal abnormalities.

Moreover, our finding showed that 50% of autistic children had EEG abnormalities and were divided on the basis of the wave type as follows:32.5% with slow wave, 10% with slow spike wave, and 7.5% with sharp wave.

Thus, in mild cases, EEG was commonly normal, whereas generalized and focal EEG abnormalities were common in moderate and severe cases.

Hara (2007) reported that paroxysmal EEG activities in the frontal area were common abnormalities in autism, which could be related to frontal lobe dysfunction in ASD.

Chez *et al.* (2006) found that the right temporal site is the most common locus. This suggests that the right hemisphere, with the potential to be involved in social deficits, is a site of dysfunction. Bitemporal and left temporal abnormalities are also consistent with sites of potential language dysfunction. The generalized epileptiform discharges may represent inherited patterns or perhaps different subgroups within autism.

Baird *et al.* (2006) suggested that temporal abnormalities may be more common. However, Kim *et al.* (2006) do not support this view.

In the study by Yasuhara (2010), patients' abnormal EEG was most often located in the frontal lobe. In another study, the EEG abnormalities in ASD children localized in the central and temporal regions (Chez *et al.*, 2006).

In the study by Chez *et al.* (2004), patients with ASDs have predominantly rare or infrequent posterior central parietal and temporal sleep-activated spikes and complexes. They suggested that the presence of EEG abnormalities in the autistic population is truly unique and not just a familial pattern. This further indicates that abnormal EEG spikes are not just a genetic risk for a type of epilepsy but that autistic individuals have a unique increased risk for epileptiform activity compared with their normal siblings.

In our study, the slow wave contributed the higher percentage (32.5%). This is in agreement with the study by Rondeau (2010), who said that the first pattern seen often in ASD is the excess slow-wave

activity (delta, theta). There may also be excess fast (alpha, beta) brainwaves present relating to hyperfunctioning or hypofunctioning of the localized area.

Conclusion

Our study revealed that there was a significant relation between the EEG abnormalities and the severity of autism. This suggests that the use of neurological investigative techniques such as EEG should be considered routinely during the evaluation of autistic individuals.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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