Electroencephalographic Findings In Children With Autism Spectrum Disorder

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Abstract

Introduction: Autism Spectrum Disorder is a neurodevelopmental disorder characterized by impairments in social communication, reciprocal social interaction, and repetitive behaviors and interests. It was previously known as Pervasive Developmental Disorders. It affect 1 in 88 children, Males are affected four times more than females. It has a complex and multifactorial aetiology. It is known to be highly heritable. It is frequently associated with comorbid psychopathology as high as 70%. The most common are intellectual disability, ADHD, Eating disorder, depression, sleep disorder and Anxiety disorder. There is no "gold standard" measure for assessing ASD so Diagnosis takes place typically from a complete history, physical and neurological evaluation. EEG has been the primary measure used to capture and characterize epileptiform and abnormal paroxysmal activity through the detection of focal spikes, which occur with increased frequency in ASD.

Methods: Cross sectional descriptive study, conducted on 32 children attending the outpatient clinic of Special Need Center, Institute of Postgraduate Childhood studies, Ain Shams University. They underwent Thorough Full medical history, clinical examination, Clinical Psychiatric assessment using CARS, IQ test and EEG.

Results: ASD is more common in males than females, although 53.1% had positive history of consanguinity but no statistically significant difference. As regarding EEG findings, 56.3% of children had normal EEG Finding; while 43.8% had abnormal EEG Findings. 50% with abnormal EEG Findings had subcortical Dysrythmia, 14.3% Generalized Epileptic Dysrythmia. There was no statistically significant relationship between different EEG Findings and CARS in the studied children with ASD.

Conclusion: ASD is a neurodevelopmental disorder with altered brain connectivity. There is no agreement on EEG features in ASD. Although clinical EEG studies generally agree on the high prevalence of epileptiform abnormalities in children with ASD.

Key words: Autism Spectrum Disorder, Electroencephalograhy, EEG.

نتائج رسم المخ الكهرباني المصاحبه لاضطراب طيف التوحد في الأطفال

مقدمة: يعد اضطراب طبف التوحد أحد الأضطرابات النمائيه ويتم تشخيصه خلال مرحلة الطفولة المبكرة ويتميز بالعجز المستمر في التواصل والتفاعل الاجتماعي عبر سياقات متعددة، ويشمل الاتصال اللفظي وغير اللفظي المستخدم، وتتمثل نسبته بين الأطفال ١ لكل ٨٨ طفل، ويتأثر الذكور أربع مرات أكثر من الإناث. والمسببات المرضية له معقدة وليست محدده. ومن المعروف أنه وراثيا وكثيرا ما يرتبط بأمراض نفسيه أخرى بنسبه تصل الى ٧٠% وتشمل الإعاقة الذهنية، فرط الحركه وتشتت الأنتباه، اضطرابات الأكل، والاكتئاب، واضطراب النوم واضطراب القلق. ليس هناك "معيار ذهبي" أو مقياس لتشخيص التوحد ولكن التشخيص عادة من خلال التاريخ المرضى الكامل والفحص الأكلينيكي والتقييمات النفسيه. ويعتبر رسم المخ الكهربائي المقياس الأساسي المستخدم لالتقاط وتمييز أنشطة المخ غير الطبعية.

منهج البحث: الدراسة وصفية مقطعية، أجريت على ٣٢ طفلا حضروا العيادة الخارجية بمركز ذوى الأحتياجات الخاصه، معهد الدراسات العليا للطغولة، جامعة عين شمس. وقد خضع المرضى للتاريخ المرضى الطبى والفحص السريرى والتقييم النفسى باستخدام اختبار كارز ورسم المخ.

المتنابع: مرض طيف التوحد كثر شيوعا في الذكور حيث أن ٣٠٣٠% من الأطفال في العينه ذكور ٣٠،٨٠% من الإناث، كما أن ٣٠٠٠% لديهم قرابة بين الأبوين ولكن لا يوجد فرق نو دلالة إحصائية. وأما نتائج رسم المخ كان ٣٠،٣٠% من الأطفال لديهم رسم مخ طبيعي و٣٠.٤% لديهم رسم مخ غير طبيعي. وكان متوسط معدل الذكاء للأطفال ٣٠ ومعظمهم نسبته من بسيط إلى شديد ولكن لا يوجد فرق ذو دلالة إحصائية بينه وكذلك بين نتائج رسم المخ وشدة أعراض التوحد باستخدام اختبار كان :

الخلاصة: يعتبر اضطراب طيف التوحد هو اضطراب في نمو الجهاز العصبي للطفل وطرق الاتصال بينه ولا يوجد اتفاق على ملامح العلاقه بين اضطراب التوحد ونتائج رسم المخ على الرغم من أن بعض الدراسات يتفقون على ارتفاع معدل انتشار التشوهات الصرعيه في الأطفال الذين يعانون من التوحد.
الكلمات المفتاحية: اضطراب طيف التوحد, رسم المخ الكهربائي.

Introduction:

Autism spectrum disorder (ASD) is a lifelong neurodevelopmental disorder that is often diagnosed during early childhood and is characterized by impairments in social communication, reciprocal social interaction, and repetitive or restricted behaviors and interests (APA, 2013). It had a complex aetiology However; an etiological factor has been identified in only (15- 20)% of persons with ASD (Schaefer and Mendelsohn, 2008). Typical diagnosis occurs at (3- 4) years of age (Matson et.al.; 2008).

It is frequently associated with intellectual impairment, structural language disorder, psychiatric symptoms, ADHD, developmental coordination disorder, anxiety disorders, depressive disorders, specific learning difficulties, medical conditions, avoidant- restrictive food intake disorder (APA, 2013).

Electroencephalography is defined as electrical activity recorded from the scalp surface by metal electrodes and conductive media (Niedermeyer and Lopes da Silva, 1993). it is used to assess functional connectivity between different brain regions over time via EEG coherence, and quantitative measurement of the relationship of frequency spectra between two EEG signals (Olejiczak, 2009).

Many studies suggested that ASD was a connectivity disorder (Assaf et.al., 2010). While a number of previous studies have reported underconnectivity in ASD cortex (Coben et.al., 2008), others had indicated mixed or overconnectivity (Shih et.al., 2011) and/or aberrant lateralization in ASD brain connectivity (Lee et.al., 2009).

Aim Of The Study:

- 1. To assess EEG findings in children with autism spectrum disorder.
- To correlate between different levels of Autism Spectrum Disorder and EEG findings.

Subjects And Methods:

- ☐ Type Of The Study: Cross Sectional Descriptive Study
- Subjects: The study was conducted on 50 children diagnosed as ASD according to DSM-V. The children attended the outpatient clinic of Special Need Center, Institute of Postgraduate Childhood, Ain Shams University from the period January 2014 till July 2015. The study enrolled only 32 children because of lack of detailed data or dropping out during the study.
 - Inclusion Criteria
 - 1. Age: from age of (3-10 years).
 - 2. Gender: Both Sexes.
 - 3. Cases diagnosed as Autism Spectrum Disorder according to DSM- v.
 - II Exclusion Criteria
 - 1. Children with autism spectrum disorder and epilepsy.
 - 2. Children suffering from chronic medical diseases.
 - 3. Children with other neurological or psychiatric diseases.
- $\mbox{\em \mathbb{H}}$ Methods" All children were subjected to the following:
 - 1. Full medical history Focusing on age of onset, Course and

- duration of disease- Symptoms of ASD- Severity of symptoms-Prenatal, natal and postnatal history- Developmental history-Family and past history- History of consanguinity.
- Thorough clinical examination focusing on neurological assessment.
- Clinical Psychiatric interview: All children were diagnosed according to DSM-V criteria of ASD (APA, 2013).
- 4. Assessment Of Children Through:
 - a. Childhood Autism Rating Scale (CARS) (Schopler et.al., 1986): It is a behavior rating scale help to diagnose ASD and Assessment of severity of autistic symptoms (Ozonoff et.al., 2011). It rates the child on a scale from 1 to 4 in each of 15 areas. It is completed by a clinician based upon observations and/or caregiver reports. Intellectual ability and language level are included as part of the total score (Hong et.al., 2011).
 - The possible range of scores is (15-60). A total score classifies children's behavior as having no autism (15-29.5), mild to moderate autism (30-36.5) and severe autism (37-60) (Rellini et.al., 2004).
 - b. Electroencephalography (EEG): It is done using (compumedics- E series Device- Type 5CP70- Serial J11D725). It is a fully digital amplifier system with a standard network interface that is compatible with most current personal computers. With 22 channel configurations, these amplifier systems are appropriate for both full sleep and EEG data collection.
 - c. IQ test using Stanford- Binet Intelligence Scales- fivthEdition,
 The Arabic version (۲۰۱۱ (ابو النيل،): It is used to assess
 intellectual ability between ages 2 and 16 years. It consists of
 10 subscales. The three areas assessed are general cognitive
 functioning, verbal and nonverbal intelligence and five factors
 formed into groups along verbal\ nonverbal measures: fluid
 reasoning, knowledge, quantative reasoning, visual- spatial
 processing, and working memory together (Roid, 2003).
- Limitation Of The Study: The study conducted on about 50 children many of them excluded due to:
 - 1. Refusal of parents of children to participate in the study.
 - Incomplete data as regards EEG which could be defective or in apparent.
- Ethical Aspect: Informed written consent was obtained from parents
 after explanation of the aim of the study and its benefits.

Results:

Table (1) Demographic characteristics of the studied Children with ASD (n= 32)

		n	%	x^2	P- Value	
Sex	Male	18	56.3	0.500	0.400	
	Female	14	43.8	0.500	0.480	
Age		Mean+SD	Min.	Max.	Range	
		5.30+1.96	3.0	10.0	(3.0-10.0)	

As shown in table (1), The sample ages range from (3-10) years and it

affects males more than female as shown in table

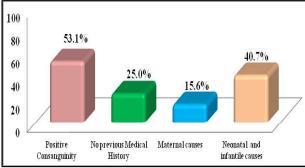
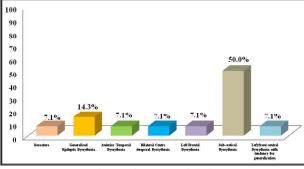


Fig (1) Previous Medical History of studied children with ASD

As shown in figure (1) (53.1%) of the studied children had positive history of consanguinity; (40.7%) due to Neonatal and infantile causes (25.0%) had no previous medical history (15.6%) had maternal causes.

Table (2) EEG Findings in the studied patients with ASD (n= 32)

Eeg Finding	n	%			
Normal Eeg Finding	18	56.3			
Abnormal Eeg Finding	14	43.8			



Fig(2) Types of Abnormal EEG Findings

As shown in table (2) (56.3%) of children had normal EEG; while (43.8%) had abnormal EEG Findings. The abnormal EEG findings were (50%) had sub cortical Dysrythmia (14.3%) Generalized Epileptic Dysrythmia (7.1%) Immature ECG finding, Anterior Temporal Dysrythmia, Bilateral Centro temporal Dysrythmia, Left Frontal Dysrythmia and Left front central Dysrythmia with tendency for generalization as shown in figure (2).

Table (3) Description of IQ and CARS in Children with ASD (n= 32)

IQ	Mean + Sd	Min.	Max.	Range
	65 + 10	40	78	(40- 78)
CARS	Mean + Sd	Min.	Max.	Range
	32.2 + 3.2	29.50	45.0	(29.50-45.0)

As shown in table (3) the mean IQ of children was (65) and The mean CARS was (32.2 + 3.2).

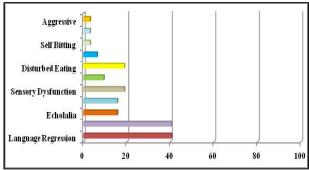


Fig. (3) Symptomatology in the studied Children with ASD (n= 32)

As shown in figure (3) (40.6%) of children had Language Regression (40.6%) were hyperactive (15.6%) had Echolalia, Poor social interaction (18.8%) had sensory dysfunction, disturbed eating (9.4%) had symptomatology of ASD only (6.3%) had disturbed sleep (3.1%) experienced self- Injurious behavior, poor attention, aggression.

Table (4): CARS in children with different EEG findings (n = 32)

Eeg Finding	CARS	x ²	P- Value
Normal	Mean± Sd		
Normai	31.9± 3.6		
Immeture	Mean± Sd		
Immature	29.5±0.0		
Conception d Englantic Dynamic	Mean± Sd		
Generalized Epileptic Dysrythmia	35.0±0.0		
Anterior Temporal Dysrythmia	Mean± Sd	1.192	0.344
America Temporal Dysryumna	33.3±0.9		
Bilateral Centrotemporal Dysrythmia	Mean± Sd		
Bhaterai Centrotemporai Dysrytiinia	34.0±0.0		
Left Frontal Dysrythmia	Mean± Sd		
Len Frontai Dysrytimia	38.9±0.0		
Subcortical Dysrythmia	Mean± Sd		
Subcortical Dysrythinia	31.0± 1.3		
Left frontocentral Dysrythmia with tendency for	Mean± Sd		
generalization	36.0±0.0		

As shown in table (4) Left Frontal Dysrythmia had got the highest CARS (38.9), Left frontocentral Dysrythmia with tendency for generalization was (38.9), while Immature, Normal and subcortical dysthrymia (29.5, 31.9, 31.0) respectively

Discussion:

The number of reported cases of ASD increased dramatically in last years. This increase is attributable to changes in diagnostic practices, referral patterns, availability of services, age at diagnosis, and public awareness (Chawarska and Volkmar, 2005). The clinical signs of ASD are known to emerge concurrently with a period of abnormal brain and head "overgrowth" occurring within approximately the first year of life and plateaus into adulthood (Hazlett et.al., 2011). Our results pointed to the higher risk of ASD in boys than girls about (56.3%) of the studied children were males, while (43.8%) were females and there was no statistically significant difference between the studied children with ASD as regard their ages (P>0.05). This finding was consistent with that reported by Itzchak et.al. (2010) who found 461 children (81%) out of 564 participants were male autistic patients. Fombonne (2009) showed a marked male preponderance, with the male- to- female ratio ranging 4:1. Another study conducted from a pediatric hospital at Ain Shams University and found that boys had higher risk of autism than girls (El- Baz et.al., 2011). Levy et.al. (2009) found that Males are affected four times more frequently than females.

The causes of ASD are still unclear, although results from twin and family studies provide evidence for a strong genetic contribution (Paul et.al., 2010). Despite significant research on prenatal, perinatal, neonatal, and other risk factors in autism, the causal nature of these associations is still disputed due to several current methodological limitations of studies

(Gardener et.al., 2009). It is known to be highly heritable with a recurrence rate of 19% in siblings (Ozonoff et.al., 2011).

We found that (53.1%) had positive history of consanguinity but there was no statistical significance but El baz et.al. (2011) found that Positive family history was found to be significantly associated with the risk of ASD (16% of cases versus 1% of controls). Similar findings was reported by Bilder et.al. (2009).

Higher prevalence of ASD also had been associated with obstetric and neonatal factors that result in NICU admission (Kuban et.al., 2009). Schendel and Bhasin (2008) found a twofold increase in ASD risk as a result of lower birth weight and gestational age. El baz et.al. (2011) found a history of low birth weight and using instrumental tools during delivery were significantly higher in cases than controls. Postnatal factors as history of hypoxia, resuscitation, history of neonatal jaundice were also statistically significantly increased in autistic patients. Kolevzon et.al. (2007) suggested the presence of non-heritable prenatal and perinatal risk factors for autism. Bolton et.al. (1992) demonstrated an association between autism and obstetric complications, prenatal or intrapartum use of medications.

The mean IQ of the studied children was (65) as most of them had mild to severe retardation, as El Baz et.al. (2011) found that 55% of children had mild to severe retardation and Baron- Cohen et.al. (2006) who reported that autistic children had spectrum of IQ ranged from 0to 60.

There is no "Gold standard" measure for assessing ASDs (Kleinman et.al.; 2008); however, best practice involves utilizing various methods of garnering information including interviews, observation, and rating scales that involve multiple informants such as parents, teachers, and alternative caregivers (Haynes and O'Brien, 2000).

Core diagnostic features are evident in the developmental period but Manifestations of the disorder also vary depending on the severity of the autistic condition, developmental level, and chronological age; hence, the term spectrum (APA, 2013). In this study, as regarding symptomatology of ASD about (40.6%) of the studied children had Language Regression (15.6%) had Echolalia (18.8%) had sensory dysfunction (9.4%) had symptomatology of ASD only. El-baz et.al. (2011) found that (72) of children presented with delayed speech (11%) play alone (9%) inattention, and (8%) with loss of eye contact.

Also, we found that (3.1%) experienced self injurious behavior (3.1%) had inattention (3.1%) were aggressive.

Maladaptive behaviors frequently associated with ASD include hyperactivity/inattention, aggression, and motor stereotypies. Prior studies have also shown that ID is a strong predictor of greater severity in ASD (Matson and Shoemaker, 2009) and is associated with various maladaptive behaviors (Emerson et.al.; 2001).

Also (40.6%) of children were hyperactive. Sturm et.al. (2004) found that ADHD symptoms are present in about 20- 80% of children with ASD. Also, the severity of ASD correlates with the co- occurrence of

ADHD symptoms (Holtmann et.al.; 2007). Impairment of motor control, including neurological soft signs is common in ASD (Price et.al.; 2012).

In this study (9.4%) had Delayed Milestones. El baz et.al. (2011) found that all studied developmental milestones were delayed in autistic children than control group. The difference was statistically significant. Mc Partland (2006) found that children with autism may be delayed in acquiring motor activity.

Also, we found that (18.8%) had disturbed eating. Children with ASD were found to have significantly more feeding problems and eat significantly a narrower range of foods than children without ASD which may be due to food allergies or intolerances or from autistic features (Schreck et.al.; 2004).

We found that (6.3%) had sleep disorders. Krakowiak et.al. (2008) found that Sleep problems are present in 80% of children with ASD. Rzepecka et.al. (2011) found that 77.2% of children with ASD had sleep problems. Mannion et.al. (2013) found that 80.9% of children and adolescents with ASD presented with sleep problems. Mayes and Calhoun (2009) found that sleep problems were not related to age, IQ, gender, race, parent occupation, neuropsychological functioning and learning ability and increased with severity of autistic symptoms and with severity of parent reported symptoms.

We found that (40.6%) of the studied children had Language Regression which is defined as a period of normal development followed by a significant change in which there is a loss of previously acquired language and other skills, this is in accordance with Baird et.al. (2008) that found Regression occurs in 15- 40% of children with autism but Luyster et.al. (2005) found that this pattern associated with about a quarter of the ASD population.

Also, we found (43.8%) of children had abnormal EEG most commonly subcortical Dysrythmia and Generalized Epileptic Dysrythmia. El baz et.al. (2011) had 31% of autistic children epileptic focus in EEG, with and without a history of convulsions. Ballaban and Tuchman (2000) found that 64 patients with autism out of 316 children evaluated for ASD had EEG findings. These findings confirm the importance of ongoing medical follow- up for children with ASDS, especially for those with abnormal EEG results. Also, Kanemura et.al. (2013) found that EEG paroxysmal abnormalities were present in 11 to 21 patients (52.4%).

Chez et.al. (2006), found that the incidence of abnormal epileptiform activity on EEG is high as many as 60-75% of individuals with autism. Epileptiform activity itself might contribute to dysfunction of language and social regions of the brain (Ballaban and Tuchman, 2000).

As regarding relationship between different EEG Findings and CARS in there was no statistically significance although children with left frontal dysrythmia had got the highest CARS (38.9), and left frontocentral dysrythmia with tendency for generalization was (36).

Conclusion:

ASD is a neurodevelopmental disorder with no agreement on the EEG

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features of ASD. Although clinical EEG studies generally agree on the high prevalence of epileptiform abnormalities in children with ASD.

Recommendation:

- Early detection of abnormalities in EEG signals may allow early intervention to prevent or ameliorate lifelong conditions.
- Long term EEG is required is required to allow better findings and events.
- Follow up of children with normal EEG is required to detect any changes.

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