

ISSN 1220-8841 (Print)
ISSN 2344-4959 (Online)

ROMANIAN
NEUROSURGERY

Vol. XXXVII | No. 2

June 2023

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DOI: 10.33962/roneuro-2023-041



Electroencephalographic findings in autistic non-epileptic children

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ABSTRACT

Despite the well-acknowledged link between autism spectrum disorders (ASDs) and epilepsy, the prevalence and significance of electroencephalogram (EEG) changes in epileptic children in the absence of clinical seizures remains undetermined.

Aim. The primary goal of this study is to report the prevalence of EEG abnormalities in non-epileptic or pre-epileptic autistic children, investigate their association with a set of pre-determined risk factors, speculate on their significance, and direct future research efforts.

Methods. A case-based sampling for children diagnosed with autism was done. Only patients without a history of epilepsy and those under the age of 15 were included. All patients underwent an EEG study. Children with abnormal EEG findings (case group) were compared to age-matched controls with normal EEG findings using a set of pre-determined factors.

Results. A total of 38 patients were enrolled in our study, of whom 31.6% (n=12) had abnormal EEG readings. Of those, the presence of the following EEG abnormalities were noted – each being present in two patients: frontal sharp waves, frontal slowing, temporal slowing, bitemporal slowing, frontal sharp waves, and generalized sharp waves, Frontal intermittent rhythmic delta activity (FIRDA). Patients with abnormal EEG findings were more likely to have a positive family history of epilepsy and/or autism, with odd ratios of 28.05, and 12.62, accordingly.

Conclusion. Aberrant brain connectivity patterns have been observed in non-epileptic ASD patients, and our findings support these findings. Furthermore, we believe that gender, mother's age, mode of delivery, and speech abnormalities could all have an impact on the EEG results. However, more research is needed to expand on these findings.

INTRODUCTION

Autism spectrum disorders (ASDs) are a broad category of complex neurodevelopmental disorders. ASDs are distinguished by impaired social interaction, deterioration of language skills, and a limited

Keywords
autism spectrum disorders,
EEG



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ISSN online 2344-4959
© Romanian Society of
Neurosurgery



First published
June 2023 by
London Academic Publishing
www.lapub.co.uk

repertoire of interests. Individuals appear to differ in terms of cognitive function decline, the presence of intellectual disability, behavioral changes, and symptom severity and onset. Despite extensive research, the biological factors that govern autism development remain unknown.

The first report on the possible neuronal links of ASD was published in 1943; Kanner examined 11 children with ASD in this report; three of them had seizures, three were mute, and five were macrocephalic (5). However, it was not until 1970 when Gubbay *et al.* published the first report on EEG abnormalities in children with ASD (3). Since then, there has been extensive research into the evidence of neurological involvement in ASD subjects.

Despite the fact that epilepsy is associated with an increased morbidity rates, the clinical significance of EEG abnormalities in the absence of seizures has not been established. Nonetheless, the majority of the evidence points to the presence of hyperexcitable brain regions, which may contribute to aberrant connectivity within the brain, resulting in faulty functioning of neural circuits in the brain responsible for basic information processing (1,4).

As a result, the primary goal of this study is to report the prevalence of EEG abnormalities in non-epileptic or pre-epileptic autistic children, investigate their association with a set of pre-determined risk factors, speculate on their significance, and direct future research efforts.

METHODS

Setting

The study was conducted at Baghdad Teaching Hospital (BTH), Medical City, spanning the period September 2018 to March 2019.

Patient sampling

A case-based sampling for children diagnosed with autism was done. Only patients without a history of epilepsy and those under the age of 15 were included. Patients with medications that might affect EEG readings were excluded. All patients underwent an EEG study. Written informed consent was obtained from the parents for participation in the study. EEG findings were interpreted by two consultant neurophysiologists. The study was approved by the ethics committee of Baghdad Medical City.

Study design

This is a case-control study. Children with abnormal EEG findings (case group) were compared to age-matched controls with normal EEG findings. Both groups had a definite diagnosis of autism and no clinical history of epilepsy.

Study aim

The study was conducted to examine the association between the patient's age, gender, mode of delivery, maternal age at delivery, family history of epilepsy or autism, socioeconomic status, and speech difficulties.

Statistical methods

The odds ratio (OR) was calculated to determine the association of each of the abovementioned factors with the presence of abnormal EEG findings. Fisher exact test was used to determine the significance of association. The significance level was set at a *p*-value of < 0.05.

RESULTS

A total of 38 patients were enrolled in our study, of whom 31.6% (n=12) had abnormal EEG readings. Of those, the presence of the following EEG abnormalities were noted – each being present in two patients - : frontal sharp waves, frontal slowing, temporal slowing, bitemporal slowing, frontal sharp waves, and generalized sharp waves, Frontal intermittent rhythmic delta activity (FIRDA).

The age range was (3-10) years with a mean of 6.1 years. The male-to-female ratio was 32.6. As for the mother age, 26.3% (n=10) were 35 years or older. The percentage of patients that were delivered by cesarean section was 47.4% (n=18). A family history of epilepsy and autism was documented for 10.5% (n=4), and 5.3% (n=2) of the patients, respectively. Speech difficulty was present in 47.4 (n=18) of the participants, and 10.5% (n=4) of them belonged to high socioeconomic group. (Table 1). Patients with abnormal EEG findings were more likely to have a positive family history of epilepsy and/or autism, with odd ratios of 28.05, and 12.62, accordingly. The other parameters under study, including patient and mother age, gender, mode of delivery, socioeconomic status, and the presence of speech difficulties failed to achieve statistical significance in this study. (Table 2).

Table 1. Patients' characteristics.

Characteristic	% (n)
Age range	3-10 yrs
Age mean	6.1 yrs
M:F	32:6
Mother age of 35 +	26.30% (10)
C/S delivery	47.40% (18)
FHX epilepsy	10.50% (4)
FHX autism	5.30% (2)
High SES	10.50% (4)
Speech difficulty	47.40% (18)
EEG +	31.60% (12)

Table 2. Odds ratios, 95% confidence intervals, and P-values for the association of abnormal EEG readings with the parameters understudy.

	OR	95% CI	P-value
Gender (M)	0.9	0.14 - 5.81	1
Maternal age (35+ years)	0.45	0.08 - 2.5	0.5
Delivery (CS)	3.2	0.76 - 13.5	0.2
FHX of epilepsy	28.05	1.37 - 576.2	0.002
FHX of autism	12.62	0.56 - 285.6	0.03
SES (high)	0.2	0.01 - 4.03	0.3
Speech difficulties	1.4	0.35 - 5.4	0.73

DISCUSSION

The high rate of co-existence of epilepsy and ASD is well recognized, pointing to a possible shared pathophysiology. However, the prevalence, nature, and clinical implications of abnormal EEG findings in the absence of clinical seizure activity in ASD children have received less attention. The existence and potential value of such abnormalities are indicated by data from scattered reports, but their exact nature and clinical significance remain unknown.

In our cohort of 38 non-epileptic ASD patients, 31.6 percent (n=12) had abnormal EEG findings, which is consistent with the published literature. Having a positive family history of epilepsy and/or autism showed a significant association with the presence of abnormal EEG findings among the factors studied. The non-significance of the other factors may be due to the fact that the study is underpowered, and expanding the scope of the study to include more participants or a control group such as children with ASD and epilepsy may reveal statistically significant associations. Follow-up is also required to determine the persistence or absence of the observed EEG abnormalities.

Aside from the abovementioned, well-designed longitudinal studies are also required to determine the role, if any, of these bioelectrical abnormalities in the development and natural course of autistic symptoms, language, and cognitive decline. The presence of epileptic discharges in patients with non-epileptic ASD may represent an endophenotype with treatment and prognostic implications, and it aids in the precise characterization of study samples.

The results of this study as well as the available literature over the span of the previous four decades highlights a set of key questions to be addressed. First, is the cost-effectiveness of extensive initial EEG, and/or follow-up EEG in non-epileptic ASD patients justified? Currently, there is no data on the cost-effectiveness of EEG testing in children exhibiting ASD symptoms. However, if early intervention can prevent or ameliorate a life-long disorder, even a low yield may be justified not only economically, but also in terms of avoided suffering for patients and their families.

The second question is whether the lack of an epileptic discharge detected by EEG or magnetoencephalography (MEG) technology indicates the absence of such an abnormality. According to data published by Small (6) and Frye et al. (2) different study designs that used alternate detection protocols, such as EEG monitoring units, will result in higher yield. Furthermore, comparing electroencephalography (EEG) and magnetoencephalography (MEG) readings reveals that the latter is superior, with detection rates of 68 percent and 82 percent, respectively. This means that while an EEG test may produce "negative results," this does not imply that there is no abnormality, and it also highlights the significant false negative problem, which is especially common in EEG studies.

Another unanswered question is whether the nature of EEG abnormalities influences the course of clinical symptomatology and whether the location of the EEG abnormality is causal. Hashimoto et al. found that the coexistence of frontal and temporal lobe abnormalities had a significant impact on the rate of emergence of autistic features in their study.

Unraveling the clinical significance of these findings in terms of how they might inform treatment decisions is critical, and it is the starting point for answering the questions raised above.

CONCLUSION

Aberrant brain connectivity patterns have been observed in non-epileptic ASD patients, and our findings support these findings. Furthermore, we believe that gender, mother age, mode of delivery, and speech abnormalities could all have an impact on the EEG results. However, more research is needed to expand on these findings.

ABBREVIATIONS

ASDs: autism spectrum disorders;
EEG: electroencephalogram;
FIRDA: frontal intermittent rhythmic delta activity;
MEG: magnetoencephalography.

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