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EEG abnormalities and epilepsy in autistic spectrum disorders: Clinical and familial correlates

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ABSTRACT

Our aim was to examine the characteristics of EEG findings and epilepsy in autistic spectrum disorders (ASD) and the associated clinical and familial risk factors. Fifty-seven children (86% male) with ASD, mean age 82 ± 36.2 months, were included in the study. Thirty-nine (68.4%) children had the diagnosis of autism, 15 (26.3%) had Pervasive Developmental Disorder Not Otherwise Specified, and 3 (5.3%) had high-functioning autism. One hour of sleep and/or awake EEG recordings was obtained for each child. All patients were evaluated with respect to clinical and familial characteristics and with the Childhood Autism Rating Scale, the Autism Behavior Checklist, and the Aberrant Behavior Checklist. The frequency of interictal epileptiform EEG abnormalities (IIEAs) was 24.6% ($n = 14$), and the frequency of epilepsy was 14.2% ($n = 8$). IIEAs were associated with a diagnosis of epilepsy ($P = 0.0001$), Childhood Autism Rating Scale Activity scores ($P = 0.047$), and a history of asthma and allergy ($P = 0.044$). Epilepsy was associated with a family history of epilepsy ($P = 0.049$) and psychiatric problems in the mother during pregnancy ($P = 0.0026$). Future studies with larger samples will help to clarify the possible associations of epilepsy/IIEAs with asthma/allergy, hyperactivity, and familial factors in ASD.

1. Introduction

Autistic spectrum disorders (ASD) are devastating conditions with an onset in early childhood and core symptoms of varying degrees involving communication and social and cognitive development, and usually sparing gross motor development. In 1943, Kanner was the first to describe the case of an autistic individual who developed epilepsy [1]. The frequency of epilepsy in autism ranges from 4% to 42% according to different studies [2–6]. It is known that a significant majority of patients with ASD without seizures have interictal epileptiform EEG abnormalities (IIEAs) on routine EEG studies [5,6]. The incidence of IIEAs in autistic individuals was found to be between 6% and 74% [5,6–8].

Previous studies have reported age, mental status and neurological findings as risk factors for epilepsy in ASD. There is a bimodal age distribution of seizures in autism: one peak occurs before 5 years of age and the other in adolescence after age 10 [7,9,10]. Individuals with ASD who have profound mental retardation and/or cerebral palsy are at high risk for epilepsy [5,7]. However, whether there are other factors associated with epilepsy and epileptiform EEG abnormalities in ASD remains unknown. Indeed, although not previously shown, the factors associated with epilepsy and IIEAs may differ. The aim of this study was to examine the characteristics of EEG findings and epilepsy in ASD subtypes and the association between epilepsy and EEG abnormalities and clinical, psychiatric, developmental, and familial risk factors.

2. Methods

Fifty-seven patients between the ages of 2 and 18 years who were diagnosed with ASD (autism, Asperger syndrome, Pervasive Developmental Disorder Not Otherwise Specified [PDD-NOS], high-functioning autism [HFA]) according to DSM-IV [11] criteria were included in the study. For all patients, 1-hour recordings of sleep and/or awake EEGs were obtained. Patients with a diagnosis of schizophrenia, schizophrenic disorder or any other psychotic disorder, Rett syndrome, childhood disintegrative disorder, and severe mental retardation (Total IQ <25) were excluded from the study. The study period was from June 2007 to April 2008.

The EEGs were performed in three university hospitals in Istanbul. However, all of the EEGs were reevaluated blindly by the same pediatric neurologist who has expertise in pediatric epilepsy (U.I.). Electrodes were placed according to the international 10–20 system; 18 electrodes were used and recorded with bipolar and referential

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montages. The EEGs were classified as normal, abnormal nonepileptiform (e.g., inadequate or abnormal sleep architecture, focal or generalized slow waves), and abnormal epileptiform (focal, multifocal, generalized or secondarily generalized epileptiform abnormalities). The foci of epileptiform EEG abnormalities were also recorded. An epilepsy diagnosis was confirmed (unprovoked, two or more seizures) by the same pediatric neurologist.

The Autism Behavior Checklist (AuBC) and Aberrant Behavior Checklist (ABC) were completed by the children's parents under the supervision of a child psychiatrist. The Childhood Autism Rating Scale (CARS) was administered by the child psychiatrist taking care of the child. The Ankara Developmental Screening Test (AGTE in Turkish) and the Weschler Intelligence Scale for Children-Revised (WISC-R) were administered by psychologists qualified to perform these tests at Marmara University Hospital. The AuBC and ABC were translated into the Turkish language and adjusted to standards for Turkish children [12,13]. The Ankara Developmental Screening Test is widely used in Turkey to determine the developmental status of children between 0 and 6 years of age. It consists of 154 parameters that examine language, fine motor, gross motor, and social skills in addition to overall developmental level [14]. The WISC-R was translated and adjusted for Turkish children by Savaşir et al. [15].

2.1. Statistical analysis

SPSS Version 11.5 was used for statistical analysis. The χ^2 test was used for comparison of categorical variables, and Student's *t* test was used for comparison of continuous variables. Fisher's exact test and the Mann–Whitney *U* test were used as nonparametric tests where appropriate. Variance was determined with the Kolmogorov–Smirnov Test, and 0.05 was determined as statistically significant.

3. Results

The mean age of the total sample was 82 ± 36.2 months (range: 30–192 months). The mean age of children with autism was 79 ± 32 months, whereas the mean ages of those with PDD-NOS and HFA were 87 ± 42.7 and 108 ± 44.4 months, respectively. Fifty-nine percent of children with autism were under the age of 6 years, whereas 73% of patients with PDD-NOS were above 6 years of age. Forty-nine patients (86%) were boys and 8 (14%) were girls. Thirty-nine patients (68.4%) were diagnosed with autism, 15 (26.3%) with PDD-NOS, and 3 (5.3%) with HFA (Table 1).

The time of the first EEG was a mean of 17.73 ± 30.3 months after diagnosis. Of all EEGs, 84.2% were ordered by the Child Psychiatry Department, and the remainder (15.8%) were ordered by the Pediatric Neurology Department. Seventy-seven percent of EEGs were ordered as a routine screening test, 10.5% were ordered on suspicion of epilepsy, and 10.5% were ordered as follow-up EEGs for an existing epilepsy diagnosis. Eighty-six percent of patients had only a sleep EEG. The rate of performance of sleep EEGs was 94.9% for children with autism, 60% for those with PDD-NOS, and 100% for those with HFA. Forty percent of children with PDD-NOS had an awake EEG; this rate was only 5.2% for the autistic children.

Overall, 14.2% ($n = 8$) of patients were diagnosed with epilepsy. Six of these eight children were from the autism group, and two were from the PDD-NOS group. None of the patients with HFA had an epilepsy diagnosis. Among the study group, 24.6% ($n = 14$) of patients, among the autism group 30.8% ($n = 12$), and among the PDD-NOS group 13.3% ($n = 2$) had IIEAs. None of the three children with HFA had IIEAs (Table 2).

Table 1
Age, sex, and EEG features of patients according to ASD type.

	All patients	Autism	PDD-NOS	HFA *N*
N	57	39 (68.4%)	15 (26.3%)	3 (5.3%)
Sex (male)	49 (86%)	34 (87%)	12 (80%)	3 (100%)
Age (months)				
Mean ± SD	82 ± 36.2	79 ± 32	87 ± 42.7	108 ± 44.4
Range	(30–192)	(30–183)	(30–192)	(68–156)
Age <6 years	28 (49.1%)	23 (59%)	4 (26.7%)	1 (33.3%)
Reason for EEG referral				
Routine screening	44 (77%)	29 (74.4%)	12 (80%)	3 (100%)
Suspicion of epilepsy	6 (10.5%)	5 (12.9%)	—	—
Epilepsy follow-up	6 (10.5%)	4 (10.3%)	2 (13.3%)	—
EEG type				
Sleep	49 (86%)	37 (94.9%)	9 (60%)	3 (100%)
Awake	4 (7%)	1 (2.6%)	3 (20%)	—
Sleep/awake	4 (7%)	1 (2.6%)	3 (20%)	—

Note. Values are *N* (%) except where otherwise noted. PDD-NOS, Pervasive Developmental Disorder Not Otherwise Specified; HFA, high-functioning autism.

Table 2
EEG results and epilepsy diagnoses among the total group and diagnostic subgroups.

	Total ($N = 57$)	Autism ($N = 39$)	PDD-NOS ($N = 15$)	*P*
Nonepilepiform EEG abnormalities	6 (10.5%)	4 (10.3%)	1 (6.7%)	0.684
Epileptiform EEG abnormalities	14 (24.6%)	12 (30.8%)	2 (13.3%)	0.302
Epilepsy				
Present	8 (14.2%)	6 (15.4%)	2 (13.3%)	0.322
Absent	44 (77.1%)	28 (71.8%)	13 (86.7%)	

Note. Values are *N* (%). PDD-NOS, Pervasive Developmental Disorder Not Otherwise Specified.

3.1. Lateralization and localization of epileptiform EEG abnormalities

Of all 14 patients with IIEAs, 8 patients (14%) had left-sided, 2 (3.5%) had right-sided, 2 (3.5%) had bilateral, and 2 (3.5%) had central (vertex) abnormalities. IIEAs were distributed evenly in all 14 patients: 2 temporal, 2 frontal, 2 central, 2 occipital, 2 centrotemporal, 3 frontocentral, and 1 temporo-occipital.

3.2. Seizure types

Among the eight patients with epilepsy, four had complex partial seizures, one had generalized seizures, and three had multiple types of seizures. Four patients had an active ongoing seizure disorder, and in four patients, seizures were in remission (seizure free for the last 6 months). Eleven patients were on an antiepileptic medication (eight of them were diagnosed with epilepsy, and the other three were on antiepileptic medication for behavioral symptoms). Nine were on valproic acid, one on carbamazepine, and one on multiple drugs.

3.3. Use of psychotropic medications

Forty percent of children were on a psychotropic medication before or during evaluation. Twenty-seven of 39 patients with autism (69.2%), 10 of 15 patients with PDD-NOS, and all 3 patients with HFA were on a psychotropic medication. More than half of the patients (56.1%) were on risperidone treatment (59% in autism, 53% in PDD-NOS).