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Autism and epilepsy: Cause, consequence, comorbidity, or coincidence?

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Abstract

Autism is associated with epilepsy in early childhood, with evidence suggesting that individuals with both autism and more severe cognitive impairment are at higher risk. However, the incidence of an abnormal electroencephalogram and/or epilepsy in the full range of pervasive developmental disorders (PDDs) is not well defined. This naturalistic study addresses the incidence of epilepsy and electroencephalographic abnormalities in children with PDDs. The clinical history and electroencephalograms of 56 children diagnosed with PDD—not otherwise specified, autism, or Asperger syndrome were retrospectively reviewed. Forty percent of children with autism were diagnosed with epilepsy. Abnormal electroencephalograms and epilepsy occurred at significantly higher rates in children in the more impaired range of the autism spectrum ($P < 0.05$). These findings suggest that the use of neurological investigative techniques such as electroencephalography should be a consequence of careful clinical evaluation and should be considered routinely during evaluation of more impaired individuals.

Keywords: Autism; Children; Diagnosis; Electroencephalography; Epilepsy

1. Introduction

Epilepsy occurs in 10–30% of individuals with autism. This association was mentioned in the first description of autism by Kanner. However, the association between autism and specific epileptiform electroencephalography (EEG) abnormalities is not firmly established; neither is the prevalence of epileptiform abnormalities in the broader range of pervasive developmental disorders (PDDs) [1].

There is an increased prevalence of both epilepsy and abnormal potentially epileptogenic activity in children with PDDs [2,3]. About 10% of children given a diagnosis of autism are found to have either a paroxysmal EEG pattern, as seen in acquired epileptic aphasia (Landau–Kleffner syndrome), or electrical status epilepticus during sleep, as seen in some children with childhood disintegrative disorder [4]. Any association between concomitant new onset of epilepsy and behavioral or functional regression is unknown, because there is usually a significant delay between the report of regression and the diagnosis of epilepsy [5]. However, in children with a history of language regression, seizures were actually less frequent in children in the autism spectrum than in children with regression of language who did not meet criteria for autism [5]. It has been suggested that the routine awake EEG frequently shows epileptiform abnormalities in adolescents and young adults with autism [6].

Requesting EEG studies for children with autism only is not, however, routine practice. EEG is not recommended in the practice parameters for autism, either by pediatricians or by the Psychiatric Associations of America, unless there is evidence of clinical seizures or regression or a high index of suspicion for epilepsy [7]. There is considerable variability between pediatric neurologists, pediatricians, and psychiatrists with respect to referral for EEG (practice parameter).

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This retrospective study addressed the utility of routine EEG in the evaluation of children with PDDs, including diagnoses of pervasive developmental disorders—not otherwise specified (PDD-NOS), autism, and Asperger syndrome.

2. Methods

2.1. Design

Retrospective review of EEG (including video/EEG) data and independent review of medical record charts were employed.

2.2. Study background and subject characteristics

In the suburban academic tertiary care center in which this study was performed, children with autism were found to be frequently referred for routine EEG as part of a normal assessment process. However, certain clinical features in the child's history seemed more likely to prompt referral for EEG based on our observation of reasons for referral. These included a history of regression of language or an episodic event, as well as a clear history of repetitive abnormal movements with or without altered consciousness. Other reported reasons for referral were a history of staring episodes, repetitive behaviors, and other episodic events, such as temper tantrums and rage. To delineate separate clinical groups by cause of referral for the purposes of this study, history of any event, other than routine evaluation, that prompted the EEG study, was regarded as a symptom and classified as "potentially symptomatic." Those children for whom EEG was requested merely as part of the evaluation of autism were classified in this study as "routine evaluation."

2.3. Subjects

Children with a clinical diagnosis of PDD referred for elective EEG during the years 1999 and 2000 were included. Charts were independently reviewed, and based, on available clinical information, diagnoses were made according to DSM-IV-TR [8] criteria. As many of the referrals had come from a specialist autism center, highly structured records and clinical evaluation reports were often available, and approximately 50% of the subjects had received an Autism Diagnostic Observational Schedule (ADOS) [9] evaluation to further validate the diagnosis. Children were included in the study only if there was unequivocal evidence for a diagnosis of PDD. A diagnosis of autism was made only in children who clearly met DSM-IV-TR [8] criteria for deficits in the areas of communication, social interaction, and repetitive behaviors. Children who met criteria in only two areas (always meeting criteria in the social domain) or had deficits in all three areas but below diagnostic threshold were diagnosed as having PDD-NOS. In the presence of no significant language deficits, a diagnosis of Asperger syndrome was made (in keeping with present diagnostic practice [8]).

2.4. EEG study

EEG was performed at one location (State University of New York at Stony Brook). EEG recordings were reviewed by one of the authors. Electroencephalograms of all patients were recorded on 18-channel instruments with electrodes placed according to the international 10–20 system, using a digital tracing monitor that enables review of both referential and bipolar montages. The recording was done while awake and asleep, as well as with photic stimulation and hyperventilation, when possible.

Electroencephalograms were classified as: normal, abnormal but not epileptiform (e.g., background slowing), abnormal epileptiform with focal onset, and abnormal epileptiform with generalized onset.

Epilepsy was diagnosed by a pediatric neurologist in children with more than one unprovoked seizure and/ or an epileptiform EEG.

3. Results

Fifty-six children with PDD were referred for EEG during the 2 years. After review of diagnostic criteria, 35 children met criteria for autism, 3 were diagnosed with Asperger syndrome, and 18 children were diagnosed with PDD-NOS.

3.1. Demographic information

Forty-three were males (77%): 29 with autism (83% of the autism group), 3 (100%) with Asperger syndrome, and 11 with PDD-NOS (61% in the PDD-NOS group). Thirteen were females: 6 with autism and 7 with PDD-NOS. The children were between 1 and 14 years old. Presenting symptoms and corresponding EEG findings are listed in Tables 1 and 2; Table 1 summarizes the findings for all subjects, and Table 2 lists the findings only for subjects with epilepsy.

3.2. Data for the whole group

Epilepsy was diagnosed in 28.6% of children in the PDD spectrum referred for EEG. The electroencephalogram was abnormal in 30.3% of children. In 2 children with autism (11.8%), the abnormal electroencephalogram showed slowing; one was diagnosed with epilepsy based on video/EEG and description of symptoms, and the other child was not diagnosed with epilepsy. Among the abnormal electroencephalograms, 29.4% showed generalized spike activity, and 58.8% showed abnormal epileptiform activity with focal onset. The remaining 69.9% of the children had normal electroencephalograms.

Table 1
Diagnosis of epilepsy according to presenting symptoms, all subjects

	Autism group[a]		Asperger syndrome group, no epilepsy[a]	PDD-NOS group[a]		Total[b]	
	No epilepsy	Epilepsy		No epilepsy	Epilepsy	No epilepsy	Epilepsy
Number of Patients	21	14	3	16	2	40	16
Male	54.3% (19)[c]	28.6% (10)	100% (3)	55.6% (10)	5.6% (1)	57.1% (32)	19.6% (11)
Referred for routine evaluation	31.4% (11)	5.7% (2)	33.3% (1)	61.1% (11)	5.6% (1)	41.1% (23)	5.4% (3)
Potential symptoms	28.6% (10)	34.3% (12)	66.6% (2)	22.2% (5)	5.6% (1)	30.4% (17)	23.2% (13)
Abnormal EEG	5.7% (2)	37.1% (13)	0% (0)	0% (0)	11.1% (2)	3.6% (2)	26.8% (15)
Normal EEG	54.3% (19)	2.9% (1)	100% (3)	88.9% (16)	0% (0)	67.9% (38)	1.8% (1)

[a] Data are given as percentages of the group.
[b] Data are given as percentages of the whole subject cohort.
[c] *n* given within parentheses.

Table 2
Presenting symptoms and corresponding electroencephalographic findings of subjects with epilepsy

	Autism group[a]	PDD-NOS group[a]	Total[b]
Number of patients	14	2	16
Male	28.6% (10)[c]	5.6% (1)	19.6% (11)
Referred for routine evaluation	5.7% (2)	5.6% (1)	5.4% (3)
Potential symptoms	34.3% (12)	5.6% (1)	23.2% (13)
Convulsion	20% (7)	5.6% (1)	14.3% (8)
Staring episodes	11.4% (4)	0% (0)	7.1% (4)
Fainting episode	0% (0)	0% (0)	0% (0)
Febrile seizure	0% (0)	0% (0)	0% (0)
Medical history of regression	14.3% (5)	0% (0)	8.9% (5)
Rage episodes	0% (0)	0% (0)	0% (0)
Breath holding	0% (0)	0% (0)	0% (0)
Abnormal EEG	37.1% (13)	11.1% (2)	26.8% (15)
Epileptiform focal	22.9% (8)	11.1% (2)	17.9% (10)
Epileptiform generalized	11.4% (4)	0% (0)	7.1% (4)
Not epileptiform	2.9% (1)	0% (0)	1.8% (1)
Normal EEG	2.9% (1)	0% (0)	1.8% (1)

[a] Data are given as percentages of the group.
[b] Data are given as percentages of the whole subject cohort.
[c] *n* given in parentheses.

3.3. Symptoms indicative of epilepsy

The number of children who presented with symptoms that the referring physician felt were suggestive of epilepsy, and the number of children referred as part of the routine evaluation for PDD were almost equal. Autism was the only reason for referral in 39% of the children; the remaining (61%) children with autism had symptoms that prompted EEG. In 39% staring or convulsions were reported; for the remainder, history of regression, rage episodes, and breath holding spells were the reasons for requesting EEG (potential symptoms). With respect to presenting symptomatology, there were important differences in the likelihood of detecting epilepsy. When the presenting symptom was history of convulsions, regression of normal development, or staring episodes, the likelihood of a diagnosis of epilepsy was high and represented as much as 20% of the autism group. However, none of the children who presented with ''unlikely symptoms,'' such as febrile convulsions, breath holding spells, and rage episodes, were diagnosed with epilepsy. As many as 40% of the total group with autism had epilepsy, which was symptomatic in most children. Half of the children presented with convulsions, and they all had abnormal electroencephalograms and were diagnosed with epilepsy. About one-quarter of the children presented with staring episodes, half of whom had epilepsy.

All children with convulsions as the referring symptom had an epileptiform electroencephalogram and were diagnosed with epilepsy. One patient had clinical seizures with a normal electroencephalogram and was diagnosed with epilepsy as well, based on review of the seizure on videotape. Half of the patients with staring episodes and autism had abnormal electroencephalogram and were diagnosed with epilepsy.

Eight children were referred for EEG because of autistic regression; five of them were diagnosed with epilepsy. None of the children with episodes of rage or breath holding spells had epilepsy. From the routine evaluation group, one child had a generalized discharge and two children had abnormal background slowing. Two children from the initially routine evaluation group were diagnosed with

epilepsy based on EEG, additional history, and video/EEG monitoring. From the review of records, both children were in the very low functioning autism range.

3.4. Diagnostic subtype and epilepsy

Two-thirds of the girls with autism and one-third of the boys had epilepsy. Eighteen children with a diagnosis of PDD-NOS were referred for EEG. Only two were diagnosed with epilepsy, and one had history of a convulsion. The electroencephalogram was epileptiform with focal onset in both children. The remaining 88.9% of the children in the PDD-NOS group were not diagnosed with epilepsy, although one-third of them had additional suggestive symptoms, such as staring episodes, fainting spells, and an event described by the parents as an apparent convulsion. In all those children, EEG was normal.

Three children with Asperger syndrome had normal electroencephalograms, and epilepsy was ruled out clinically and by EEG.

4. Discussion

This is a retrospective study of the EEG findings for 56 children in the PDD spectrum referred for routine EEG, either because of events raising suspicion of seizures, or because of regression, or as part of their evaluation for a PDD. Our study did not evaluate the cognitive function of the patients, but examined only differences in prevalence of epilepsy between diagnostic subgroups. A study comparing autistic and nonautistic dysphasic children found no difference in the risk of epilepsy, once the risk attributable to associated cognitive and motor dysfunction was eliminated [10]. However, compared with patients with PDD-NOS and Asperger syndrome, our study shows that the prevalence of epilepsy in children with autism was significantly higher than chance ($P < 0.05$), supporting prior studies showing that epilepsy and autism are comorbid phenomena and may be related to a common brain abnormality. Girls with autism had a higher incidence of epilepsy than boys, and this is possibly also correlated to lower cognitive ability in autistic girls [10].

Epilepsy should be suspected in children in the autism spectrum who have paroxysmal events. Review of home or school videos in addition to routine EEG may help in clarifying the diagnosis. Our results, which indicate that clinical suspicion for epilepsy should be high if there is a history of convulsion and staring episodes, are in agreement with other studies showing that nearly all autistic children with seizures also exhibit epileptiform activity on electroencephalograms [2,11]. Regression of normal development was found to be another important clinical suspicion for epilepsy and is in accordance with other studies showing that autistic regression is significantly associated with the presence of epilepsy [12,13]. Episodic events that are considered potentially symptomatic (e.g., breath holding spells, rage) rarely relate to epilepsy, especially if they occur in children who have a milder form of PDD, such as PDD-NOS or Asperger syndrome.

In our study of children with autism, an abnormal epileptiform electroencephalogram without clinical seizures or history of regression was seen in only two children, both in the lower functioning range of autism. In comparison, three children with Asperger syndrome (one routinely evaluated, one with staring episodes, and one with history of febrile seizures), had normal electroencephalograms and did not have epilepsy. It has been shown that adults with infantile autism without epilepsy have higher IQ scores than adults with autism and epilepsy [14].

In children who are low-functioning or severely impaired, a history of potential epileptic symptoms is more difficult to accurately ascertain, and routine EEG should be considered in their comprehensive evaluation. There is little support for performing routine EEG in higher-functioning children in the autism spectrum without significant symptoms suggestive of epilepsy and without regression of language and communication.

In our study we retrospectively reviewed the children who underwent EEG according to the referral physician, but we do not have information on how many children with autism are seen by each practice. EEG results and epilepsy incidence are presented as incidence by diagnostic group (autism, PDD-NOS, Asperger). The main limitation of our study is the lack of information with respect to cognitive function.

This review is retrospective, based on a list generated from the EEG laboratory database, and does not represent percentages of findings in a population with PDD. The results are limited to the group referred for performance of EEG.

The findings should be further examined in a larger cohort of children in the autism spectrum, with consideration of the subclassification of the children within the spectrum.

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