Autism Spectrum Disorders and Epilepsy

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Abstract: *Epileptic seizures are frequent in children with ASD with a reported prevalence between 7% and 46%. These figures are higher than those reported for the normal pediatric population but the true prevalence remains uncertain because studies examining this have included comorbid conditions.Aim: Study the prevalence of epilepsy in children diagnosed with ASD. Methods: Retrospective study of 30 children diagnosed with ASD in the National Center for Growth, Development and Rehabilitation of Children. The clinical history and electroencephalograms of these children were reviewed. The children were from 2 years old until 8 years old.Results: 7 out of 30 children diagnosed with ASD were also diagnosed with epilepsy or abnormal electroencephalograms with a prevalence of 23%. These children showed more profound intellectual impairment and regression in cognitive development than those with ASD, but no epilepsy. Conclusion: ASD in early childhood is associated with high rate of epilepsy . These findings suggest that neurological investigative techniques such as EEG should be considered during evaluation of children with ASD with more impaired cognition.*

Keywords: ***Autism, ASD, Epilepsy***

Introduction

Autism spectrum disorder (ASD) and autism are both general terms for a group of complex disorders of brain development. Autism is a disorder of neurodevelopment characterized by core deficits in three major domains: social interaction, communication and restricted interests with repetitive behavior.

The diagnostic criteria require that symptoms become apparent before a child is three years old. The Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) defines autism as a spectrum disorder encompassing autistic disorder, pervasive development disorder not otherwise specified (PDDNOS), Asperger's syndrome, childhood disintegrative disorder and Rett syndrome.

DSM-V proposes to use just one general term: autism spectrum disorders, leaving out of the spectrum the Rett syndrome. The criteria to be met to be included in the spectrum will be as followed:

Autism Spectrum Disorder

Must meet criteria A, B, C, and D:

A. Persistent deficits in social communication and social interaction across contexts, not accounted for by general developmental delays, and manifest by all 3 of the following:

1. Deficits in social-emotional reciprocity; ranging from abnormal social approach and failure of normal back and forth conversation through reduced sharing of interests, emotions, and affect and response to total lack of initiation of social interaction,
2. Deficits in nonverbal communicative behaviors used for social interaction; ranging from poorly integrated- verbal and nonverbal communication, through abnormalities in eye contact and body-language, or deficits in understanding and use of nonverbal communication, to total lack of facial expression or gestures.
3. Deficits in developing and maintaining relationships, appropriate to developmental level (beyond those with caregivers); ranging from difficulties adjusting behavior to suit different social contexts through difficulties in sharing imaginative play and in making friends to an apparent absence of interest in people

B. Restricted, repetitive patterns of behavior, interests, or activities as manifested by at least two of the following:
   1. Stereotyped or repetitive speech, motor movements, or use of objects; (such as simple motor stereotypies, echolalia, repetitive use of objects, or idiosyncratic phrases).
   2. Excessive adherence to routines, ritualized patterns of verbal or nonverbal behavior, or excessive resistance to change; (such as motoric rituals, insistence on same route or food, repetitive questioning or extreme distress at small changes).
   3. Highly restricted, fixated interests that are abnormal in intensity or focus; (such as strong attachment to or preoccupation with unusual objects, excessively circumscribed or perseverative interests).
   4. Hyper-or hypo-reactivity to sensory input or unusual interest in sensory aspects of environment; (such as apparent indifference to pain/heat/cold, adverse response to specific sounds or textures, excessive smelling or touching of objects, fascination with lights or spinning objects).

C. Symptoms must be present in early childhood (but may not become fully manifest until social demands exceed limited capacities)

D. Symptoms together limit and impair everyday functioning.

In Albania apart from DSM, ICD 10 criteria are also used to establish a diagnosis for autism. These criteria are similar to DSM –IV criteria.

The number of observed cases of autism is increasing rapidly, about 1 in 88 children has been identified with an autism spectrum disorder (ASD) according to estimates from CDC's Autism and Developmental Disabilities Monitoring (ADDM) Network. ASDs are reported to occur in all racial, ethnic, and socioeconomic groups. ASDs are almost 5 times more common among boys (1 in 54) than among girls (1 in 252). Studies in Asia, Europe, and North America have identified individuals with an ASD with an average prevalence of about 1%. A recent study in South Korea reported a prevalence of 2.6%.

Ever since its original description by Leo Kanner in I943, autism has been generally defined by its clinical characteristics and core symptoms. Over time, it has become apparent that autism is a heterogeneous disorder with regard to its clinical presentation, etiology, underlying neurobiology, and degree of severity. With advancements in clinical care, there has come the appreciation that many ASD children, adolescents, and adults may have medically relevant disorders that may negatively impact their developmental progress and behavior, but which frequently go undetected. Many of these medical conditions are treatable, often resulting in improved developmental gains and quality of life for the patient and family. In addition, the possibility exists that some of these medical conditions may suggest the presence of important genetic and/or biologic markers, which, if identified, can refine our ability to be more precise in categorizing clinical and genetic subtypes within the autism spectrum.

Neurological co-morbidities include motor impairments, epilepsy, and sleep dysfunction. These impairments have been receiving more attention recently, perhaps because of their significant impact on the

behavior and cognitive function of children with ASDs. Autism affects information processing in the brain by altering how nerve cells and their synapses connect and organize; how this occurs is not well understood.

The International League Against Epilepsy (ILAE) and the International Bureau for Epilepsy (IBE) have come to consensus definitions for the terms epileptic seizure and epilepsy. An epileptic seizure is a transient occurrence of signs and/or symptoms due to abnormal excessive or synchronous neuronal activity in the brain. Epilepsy is a disorder of the brain characterized by an enduring predisposition to generate epileptic seizures and by the neurobiologic, cognitive, psychological, and social consequences of this condition. The definition of epilepsy requires the occurrence of at least one epileptic seizure.

Epilepsies are classified in five ways:

1. By their first cause (or etiology).
2. By the observable manifestations of the seizures, known as semiology.
3. By the location in the brain where the seizures originate.
4. As a part of discrete, identifiable medical syndromes.
5. By the event that triggers the seizures, as in primary reading epilepsy or musicogenic epilepsy.

In 1981, the International League Against Epilepsy (ILAE) proposed a classification scheme for individual seizures that remains in common use. This classification is based on observation (clinical and EEG) rather than the underlying pathophysiology or anatomy and is outlined later on in this article. In 1989, the ILAE proposed a classification scheme for epilepsies and epileptic syndromes. This can be broadly described as a two-axis scheme having the cause on one axis and the extent of localisation within the brain on the other. Since 1997, the ILAE have been working on a new scheme that has five axes:

1. ictal phenomenon, (pertaining to an epileptic seizure)
2. seizure type,
3. syndrome,
4. etiology,
5. impairment.

The relationship between epilepsy and ASD has been studied since decades by neurologists although areas for ongoing debate still exists. This association was also mentioned in the first description of autism by Leo Kanner. Studies suggest that epilepsy is more common in children with ASD than in the general pediatric population. Studies also show that the prevalence rates of epilepsy among the general pediatric population is between 2 to 3% compared to as high as 30% among children with ASD.

Even in children with ASD who have no other risk factors such as perinatal disorders, cerebral palsy or other medical conditions or those who have normal intelligence or no family history of epilepsy, still the prevalence of epilepsy is 2 to 3 times higher than in typically developing children.This strongly supports the association between the two disorders.

Epilepsy and autism are both heterogeneous clinical disorders associated with an array of etiologies and pathologies, many of which are common to both group of disorders.

Research Methodology

The aim of the study is to find out the prevalence of epilepsy in children diagnosed with ASD (2-8 years old).

2.1 Method

The study was conducted retrospectively. Selection of the method and instrument for data collection was selected in compliance with the aim of the study.

2.2 Instrument

The instrument used in this study was data collection from the medical records of the children diagnosed with ASD. The diagnosis of autism was established using DSM- IV criteria and/or ADOS or ADI-R. Children with Asperger syndrome or PDD-NOS were not included in the study. Their medical records related to IQ, co morbid conditions, perinatal conditions, behavior, language development, regression in cognitive development and several epilepsy factors including EEG were reviewed. SON-R (Snijders OOmen non verbal intelligence test, revised version) psychometric test was administered to all the children in the study to determine their cognitive profile.

Participants

A total of 30 children diagnosed with ASD in the National Center for Growth, Development and Rehabilitation of children were included. All these children were referred for EEG as part of a routine examination. All the cases were chosen randomly. The children aged from 2 to 8 years old. 18 of the children were boys and 12 girls. All participants came from different parts of Albania and represent children from different economic, social and cultural and religious background.

EEG study

EEG was performed in one location, at a private clinic in Tirana. EEG recording was reviewed by one of the authors. Electroencephalograms of all the patients were recorded on an 18 channel instrument. The electrodes were placed by the technicians according to the international 10-20 system, using a digital tracing monitor. The recording was done while the children were in natural sleep for the younger children or awake for the older ones when possible. Hyperventilation and light stimulation were also used when possible.
EEG were classified as normal, abnormal but not epileptiform (for example slow waves), abnormal epileptiform with focal onset and abnormal epileptiform with generalized onset.
The diagnosis of epilepsy was established if the child had more than one unprovoked seizure and/or an epileptiform EEG.

Findings and Discussion

Rates of epilepsy among the children with ASD in this study was 23% compared to 1% reported for children with typical neurodevelopment. For most of the children there is not an identified cause for either the conditions, epilepsy or autism.

All the children diagnosed with ASD and epilepsy expressed the following characteristics: males or females, first EEG examination at 2-8 years of age, onset of initial chief complaint at 2 to 3 years old, spike and wave EEG abnormalities.

Children diagnosed with autism and epilepsy showed more marked impairment in verbal and receptive language being compared with children with ASD but not epilepsy. Also they showed more impaired cognitive development than children with only ASD.

Distinguishing seizures from non-seizures is difficult especially in young children and especially in children with autism. This is because of the communication difficulties and impaired intellectual function these children have. Stereotypy, aggressive behavior, neurological deficits. odd behaviors and diminished responsiveness may be present in a person with autism with or without epilepsy.
Another big difficulty rises from the fact that children with ASD are very difficult to cooperate with tests and investigations such as EEGs. CT and MRIs. Normal CTs and MRIs suggest that there are not structural abnormalities in the brain but they don't explain the seizures.

In some of the children there was evidence in EEG of subclinical epileptic activity going on but not manifested as clinical episodes. Not all seizures are noticeable, some may be subclinical and difficult to detect by observation by physicians or parents and caregivers. Possible signs of subclinical seizures include regression of both behavior and cognition, deterioration in behavior especially aggression, temper tantrums, self injurious behavior, staring episodes, breath holding spells, fainting episodes, plateauing in academic achievement. It is very important to identify such abnormalities and treat them if necessary to improve the overall functioning of the child.

One of the more complicated implications of the children involved in the study was that the children having epilepsy showed in some cases developmental regression associated with the onset of the seizures. The having of epilepsy itself does not necessary deteriorate the overall performance. But we know from experience and evidence that untreated seizures, apart from being potentially dangerous can lead to serious bad effects on the levels of functioning.

In Albania there is a considerable variability between pediatric neurologists, general pediatricians and psychiatrists with respect to referral for EEG. EEG is not routinely recommended in the practice parameters for autism unless there is evidence of clinical seizures or a high index suspicion for epilepsy.

All children with convulsions as the referring symptom had an epileptiform encephalogram and were diagnosed as epilepsy.

A history of potential epileptic symptoms is more difficult to ascertain in very young children and in children who are low-functioning or severely impaired. Routine EEG should be considered as crucial part of the evaluation of these children.

Another point to discuss is the treatment of seizures in children with ASD. The use of antiepileptic drugs to control seizures is controversial to the aim of treating autism through special intervention programs. Children with ASD and epilepsy require intensive, highly structured special education support, behavior therapy, speech and language therapy than children with ASD alone.

When autism and epilepsy coexist the quality of life of these children is severely impacted. Another important point is that autism is not an epileptic encephalopathy and that epilepsy and epileptiform activity are more likely to be associated with language regression than autistic regression in these children.

Autistic children with epilepsy also tended to be more impaired than those without epilepsy. About 48 percent of those with treatment-resistant epilepsy had motor skills delays, compared to 32 percent of those with treatable epilepsy. Also, those with treatment-resistant epilepsy had more language delays (69 percent versus 51 percent), and were somewhat more likely to experience development regression. The relationship between epilepsy and autism, and specifically the effects that abnormal electrical activity may have on the developing brain, may provide some valuable insights into the type of studies that are needed to help us understand the pathophysiology of autism.

This retrospective study is based on the children diagnosed with ASD who also performed EEG and does not represent percentages of seizures in the pediatric population of children with ASD. The findings should be further examined in a larger cohort of children with ASD.

Conclusion

The study suggests that the use of the neurological investigative techniques such as electroencephalography should be considered routinely during evaluation of the young children with ASD and performed as soon as a diagnosis of ASD is being done.

Epilepsy can directly affect cognition and behavior and there are several epileptic disorders that may cause behavioral and language regression with a behavioral phenotype similar to autism. Thus it is important to make an accurate differential diagnosis.

From this rather small study and from other reports from the literature another big question rises and should find answers in may be future studies. Is autistic brain more prone to seizures or is the epileptic brain

more prone to autism? Are they often in combination or do they represent a manifestation of a broader, larger disorder? Is epilepsy a cause, consequence a coincidence or co morbidity of autism?

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