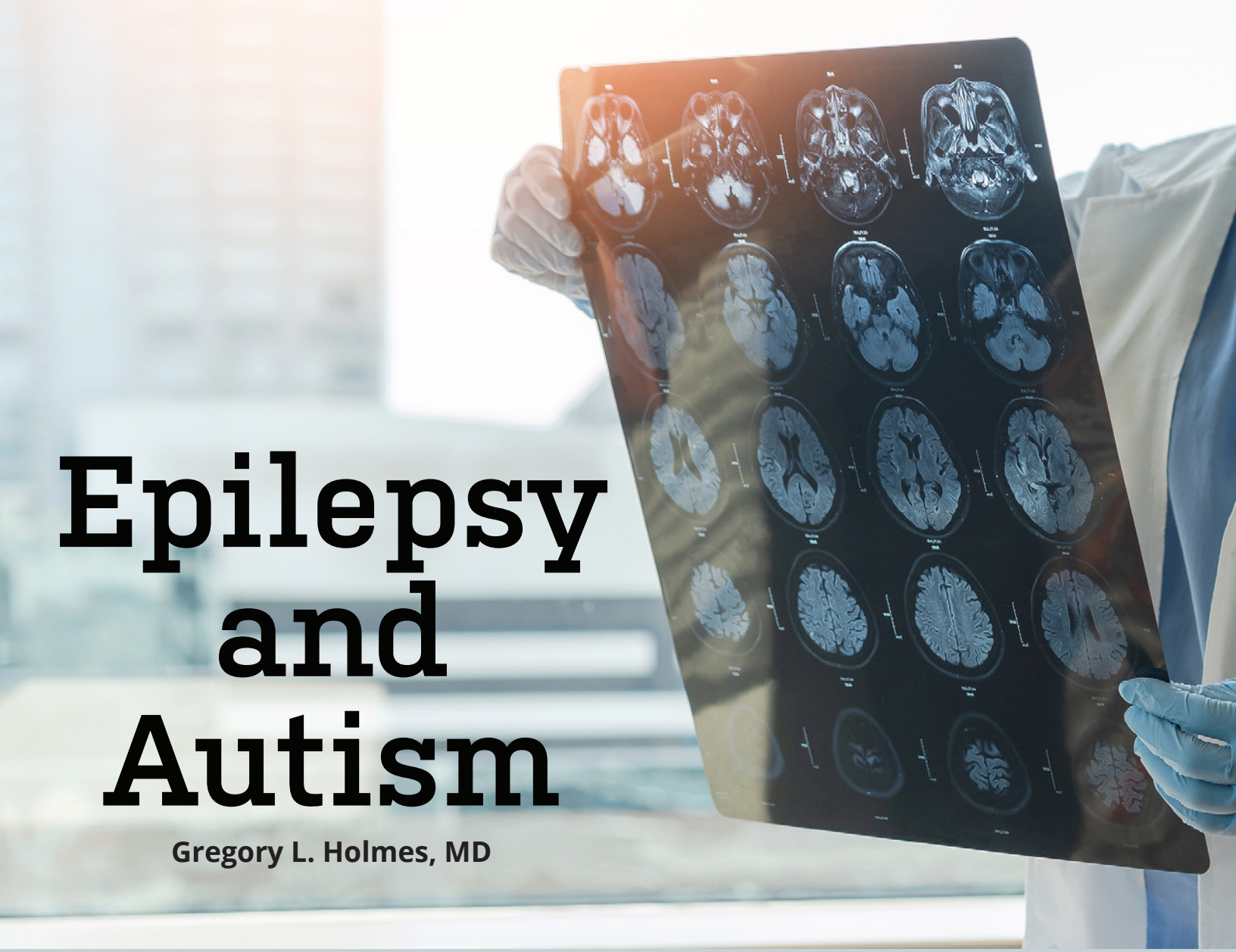


Epilepsy and Autism

Gregory L. Holmes, MD

I recently saw six-year-old Emily in the ER after she experienced a likely convulsion. Her parents were awakened around 6:00 a.m. by gasping sounds coming from her bedroom. When they entered her room, they found her rigid with rhythmic jerking of the arms and legs. Her eyes were open, but she was unresponsive. She was gasping for air, and her lips were blue. The panicked family called 911. Upon arrival at the home, the EMS team found the child limp and largely unresponsive to questions. After transport to the hospital, Emily became increasingly aware of her surroundings but had a severe headache and intermittent vomiting.

When I saw Emily, she was gradually coming around but was terrified and could provide little detail of what had happened to her. Her parents, while quite distraught, provided me with a detailed history. I learned that Emily was diagnosed with Autism Spectrum Disorder (ASD) at age four. While she had no prior documented seizures, the family noted that she had recently had episodes of unexplained nocturnal bed-wetting associated with morning headaches. This raised the question in my mind as to whether or not she had experienced prior nocturnal seizures. Her evaluation included an MRI, which was normal, and an EEG, which showed left frontal spikes, an abnormality likely indicating her seizures began in the left frontal part of the brain.

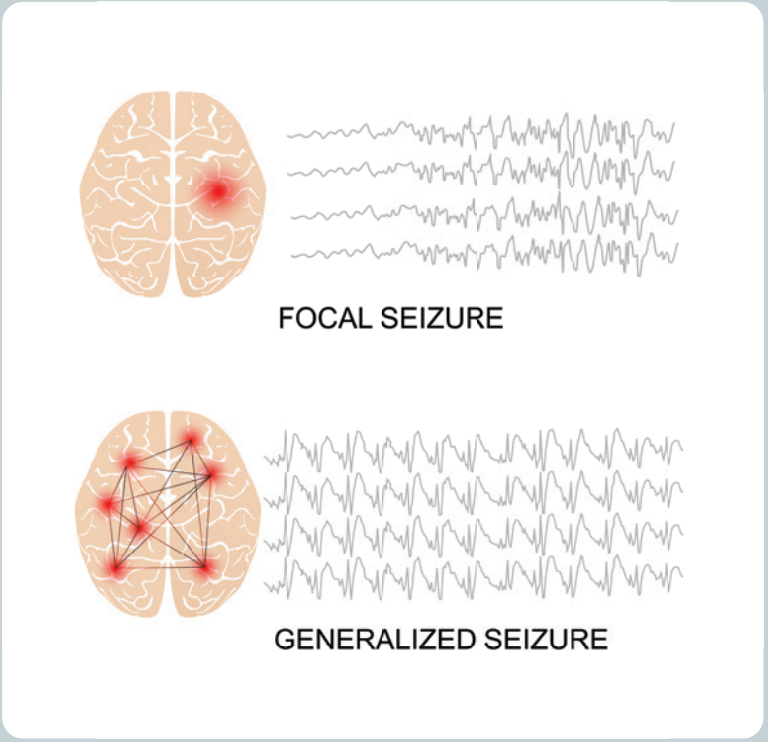
When I told the family that I thought Emily had epilepsy, I was met with fear, grief and anger. Their words still ring in my mind: "First we are told we have a child with autism, and now you are telling us she also has epilepsy? This is so unfair. How can we possibly manage?"

The parents' concerns were understandable. Seeing your child have a seizure, especially a generalized convulsion, is frightening. Many parents believe their child is dying. In addition, the diagnosis of epilepsy is scary as it conjures up mistaken beliefs that epilepsy causes brain damage. Fortunately, these beliefs are incorrect. Most seizures are short, lasting only a few minutes, and benign, with no detrimental effects on intelligence or behavior.

What is a Seizure?

When talking about ASD and epilepsy, it is helpful to start with a few definitions. A seizure is a burst of uncontrolled electrical activity between brain cells that causes temporary abnormalities in behaviors, sensations or states of awareness, and in muscle tone or movements, such as stiffness, jerking, twitching or limpness. Seizure symptoms vary from simple brief lapses of consciousness to episodes of confusion with stereotypical behaviors — known as automatisms — like chewing, swallowing or hand gestures. They also include involuntary twitching or stiffness of the body with loss of consciousness, or convulsion.

The two major classes or groups of seizures are focal seizures and generalized onset seizures. Focal onset seizures start in one area and can spread across the brain. They cause mild or severe symptoms depending on how the electrical discharges spread. Generalized seizures can start as focal seizures that then spread to both sides of the brain. They can also occur as generalized onset seizures in which seizure activity starts simultaneously on both sides of the brain. In general, any seizure type can occur in children with or without autism, although most children with autism have focal seizures that may generalize.



While epileptic seizures are the quintessential element of epilepsy, there is a spectrum of cognitive, behavioral, and psychiatric disorders that accompany epilepsy. Epilepsy is now defined as "a disease characterized by an enduring predisposition to generate epileptic seizures and by the neurobiological, cognitive, psychological, and social consequences of this condition."[1] A comorbid condition is defined as a greater than coincidental association of two conditions in the same individual. One common comorbid condition of epilepsy is autism.

Epilepsy and Autism

The strong relationship between epilepsy and autism is well established. Indeed, the American child psychiatrist Leo Kanner — who is credited with coining the term infantile autism — reported epilepsy in a third of the 11 children with symptoms of autism that he studied for his ground-breaking 1943 paper on autism.[2] In recent studies, the percentage of individuals with ASD who also had epilepsy has varied widely, but is thought to be in the range of 30 to 50 percent. Likewise, the prevalence of ASD in individuals with epilepsy is higher than in the general population, with up to 20 percent of individuals with epilepsy also having ASD.[3]

The fact that epilepsy is a comorbid condition with ASD does not mean that epilepsy causes autism or that autism causes epilepsy. There is strong evidence to the contrary. There are indications that autism and epilepsy, rather than being causative, share a common susceptibility. Recent research indicates that a shared feature of both autism and epilepsy is hyperexcitability in which connections between brain cells are overly active.[4] This overactivity has been thought to explain the seizures, as well as several of the features of ASD.

Recent research indicates that a shared feature of both autism and epilepsy is hyperexcitability in which connections between brain cells are overly active.

While the reason why children have both epilepsy and autism is unclear in many cases, there are several genetic conditions that put children at risk for both conditions. Genetic disorders that impact the development of the brain, or how brain cells communicate, are the most likely to cause both ASD and epilepsy. For example, ASD and epilepsy co-exist in such genetic disorders as tuberous sclerosis complex (TSC), Rhett syndrome and fragile X syndrome.[3] It is difficult to predict which children with these conditions will develop ASD or epilepsy, or both. It is known that genetic disorders that cause significant neurological injury have the highest risk for both ASD and epilepsy. For instance, children with TSC who develop infantile spasms — a severe form of childhood epilepsy — are at higher risk for ASD than children who have less severe seizures. This does not mean that infantile spasms cause ASD, but rather that children with the most severe brain injury are at the highest risk for both ASD and epilepsy.

Treatment



There is no difference in treatment approach to epilepsy for children with or without autism.[5] For the most part, the treatment of all types of epilepsy uses anti-seizure medications. Such medications work about 70 percent of the time, and are as effective in children with ASD as in those who do not have ASD. For those children who do not respond to the drugs, other therapies are available, including dietary therapy, such as a ketogenic diet, and, in rare cases, surgery. It is important that the physician treating the child not use drugs that could exacerbate symptoms of ASD. Typically, drugs in the benzodiazepine family, such as clonazepam, diazepam and clobazam, and the barbiturate family, such as phenobarbital, are avoided. However, parents of a child with ASD should be aware that any of the seizure medications could lead to undesirable behavioral changes in a particular child. It is also important to know that seizures do not exacerbate any of the behaviors of ASD.

Returning to the experience of Emily, she was started on the anti-seizure medication lamotrigine despite having had only one documented seizure. Given the abnormal EEG and history suggesting nocturnal seizures in the past, Emily was deemed to be at high risk for a subsequent seizure, and therapy was recommended. In addition, the family was given a rescue medication — rectal diazepam gel — to be used if she had any seizures lasting longer than five minutes. A seizure action plan was provided to the school with instructions on how to manage a seizure. The plan recommended that Emily avoid climbing on the playground equipment, and that Emily have one-on-one supervision when swimming. The main message to the family, however, was that Emily's life did not need to change because of the diagnosis of epilepsy.

References

1. Fisher R. S. (2015). Redefining epilepsy. *Current Opinion in Neurology*, 28(2), 130–135.

2. Kanner L. (1943). Autistic disturbances of affective contact. *Nervous Child*, 2:217-50.

3. Buckley, A. W., & Holmes, G. L. (2016). Epilepsy and Autism. *Cold Spring Harbor Perspectives in Medicine*, 6(4), a022749.

4. Buckley, A. W., Scott, R., Tyler, A., Mahoney, J. M., Thurm, A., Farmer, C., Swedo, S., Burroughs, S. A., & Holmes, G. L. (2015). State-Dependent Differences in Functional Connectivity in Young Children With Autism Spectrum Disorder. *EBioMedicine*, 2(12), 1905–1915.

5. Holmes G. L. (2021). Drug Treatment of Epilepsy Neuropsychiatric Comorbidities in Children. *Paediatric Drugs,* 23(1), 55–73.



Gregory L. Holmes, MD, is an internationally renowned pediatric neurologist with an expertise in pediatric epilepsy. His research in the laboratory and clinic has resulted in an understanding of the pathophysiological basis of cognitive impairment and other comorbidities in children with epilepsy. Dr. Holmes studied at Washington & Lee University (B.S.) and the University of Virginia School of Medicine (M.D.), followed by residencies in pediatrics at Yale and pediatric neurology at the University of Virginia. Dr. Holmes spent 16 years at Children's Hospital Boston and Harvard Medical School, where in 1996 he became Professor of Neurology and was bestowed an honorary M.A. degree. Prior to becoming the Chair of Neurological Sciences at UVM in 2013, Dr. Holmes was the inaugural Chair of Neurology at Dartmouth Medical School. His research is inspired by his patients and their families. He has over 500 peer-reviewed research articles, books, book chapters and review articles. He has enjoyed continuous funding for more than 40 years from federal agencies, primarily the National Institutes of Health. Dr. Holmes served on the editorial boards of 12 epilepsy and neurology journals and has been on multiple NIH study sections and FDA advisory committees. He is the past president of the American Epilepsy Society and has received many honors, including research awards from the American Epilepsy Society, NIH, American Clinical Neurophysiology Society, International League Against Epilepsy and the Child Neurology Society. From 2010–2012 he was a member of the National Academy of Science-sponsored Committee on the Public Health Dimensions of the Epilepsies, culminating in the book *Epilepsy Across the Spectrum*.

For information only. Views, recommendations, findings and opinions are those of the author and do not necessarily reflect the opinion of Autism Advocate Parenting Magazine Inc. or anyone otherwise involved in the magazine. The magazine and others are not responsible for any errors, inaccuracies or omissions in this content. The magazine provides no guarantees, warranties, conditions or representations, and will not be liable with respect to this content. Please read our full terms here.