Seizures in Autism Spectrum Disorder

November 22nd, 2015

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Updated: December 2012

Seizures and Epilepsy

Seizures and epilepsy are fairly common in childhood. Many children will experience a seizure during childhood, and a type of seizure known as a febrile seizure is very common during early childhood. Epilepsy is simply defined as having two seizures without an obvious cause, and approximately 1-2% of children are diagnosed with epilepsy. In most of these children, the seizures resolve within a year or two. A lesser percentage of children with epilepsy go on to have refectory epilepsy that cannot be well controlled with anti-epileptic treatments.

Seizure Types

Seizures are divided into two broad types: generalized and partial seizures. When most people think of seizures, they think of generalized clonic-tonic seizures, in which the whole body shakes rhythmically and convulses. Generalized clonic-tonic seizures are one of the most severe types of clinical seizures and can be dangerous if they continue for 15 minutes or more. However, most people who have generalized clonic-tonic seizures have short seizures that last under five minutes. During a generalized seizure, the entire brain demonstrates abnormal electrical activity. In contrast, during a partial seizure, only one part of the brain experiences abnormal electrical activity. When someone experiences a partial seizure, only one part of his or her body, such as an arm or leg, may demonstrate rhythmic activity. Sometimes seizures can be very subtle and be manifested as only staring episodes.

Seizures in Autism Spectrum Disorder (ASD)

Seizures are a significant concern and are relatively common in individuals with ASD. In fact, seizures are the most prevalent neurological disorder associated with ASD. While 1-2% of children in the general population develop epilepsy, the prevalence of epilepsy in ASD is much higher with estimates varying widely from 5% to 38%. Some individuals with ASD develop seizures in childhood, some at puberty, and some at adulthood. Although the prevalence of seizures by age is not well studied, recent studies suggest the risk of seizure remains high into adulthood. Seizures are associated with increased mortality and morbidity in individuals with ASD and are the leading cause of mortality in adults with ASD. Certain subgroups of individuals with ASD have a higher risk for developing seizures and epilepsy; these subgroups include individuals with comorbid intellectual disabilities, genetic abnormalities, and/or brain malformations.

Diagnosis of seizures in children with autism spectrum disorder

Sometimes it is clear that a person experienced a seizure. However, in some children with ASD, subtle symptoms of seizures are very difficult to differentiate from abnormal behaviors commonly associated with ASD, and in other children with ASD, behaviors that appear to be seizure-like are not seizures. For example, it is common for children with ASD to have staring episodes, motor tics, and stereotyped movements that are not seizures. It is important to determine if these abnormalities are seizures or another neurological abnormality, since they are treated very differently. Thus, in many cases where it is unclear whether the observed behavior is a seizure or not, an extended overnight electroencephalogram should be strongly considered in order to obtain a clear and accurate diagnosis and to capture the suspicious behavior.

Subclinical electrical discharges

Individuals with ASD have a high rate of seizure-like activity when their brain waves are measured with an electroencephalogram. These are referred to as subclinical electrical discharges. The significance of these abnormalities is not clear as they rarely result in symptoms of seizure, but some research studies have shown that they may be associated with cognitive dysfunction in children with epilepsy. There are also specific epileptic syndromes associated with these seizure-like discharges, such as Landau-Kleffner Syndrome and Continuous Spike-wave Activity during Slow-wave Sleep, in which the children affected by these syndromes have characteristics of ASD but do not have ASD. In fact, these syndromes are rare in ASD. Some studies using non-ASD children with epilepsy who have these frequent seizure-

like discharges in the brain have shown improvement in cognition and behavior with anti-epileptic drug treatment; however, no study has been performed in children with ASD. Thus, evidence to support the idea that treatment of these brain wave abnormalities in children with ASD is very limited and recommendations for treatment are highly dependent on the practitioner. Many doctors feel that an empirical treatment trial is reasonable with the newer, safer antiepileptics if the child is closely monitored to ensure a positive response to such treatment. This is clearly an area that requires further research.

Causes of seizures in autism spectrum disorder (ASD)

Specific genetic and metabolic syndromes are associated with both ASD and seizures, although most of the time the cause of the seizures is not discovered even after extensive testing. However, every child with ASD and seizures should have a comprehensive medical workup for known medical disorders.

- A genetic workup for all children with ASD and seizures should including a chromosomal microarray for both boys and girls and Fragile X testing for boys and Rett syndrome testing for girls.
- Genetic testing for other syndromes should be pursued if characteristics specific to these disorders, such as specific dysmorphic features, are found by the evaluating doctor. These syndromes include Tuberous sclerosis complex and Angelman, Prader–Willi, Velocardiofacial and Smith-Lemli-Opitz syndromes.
- Several metabolic syndromes that have been suggested to have a high prevalence in ASD such as mitochondrial dysfunction and cerebral folate deficiency can also be associated with seizures and should be highly considered in all children with ASD and seizures.
- Other much more rare metabolic disorders should be considered if supporting clinical characteristics exist. Such metabolic syndromes include Succinic Semialdehyde Dehydrogenase Deficiency, Adenylosuccinate lyase deficiency, Creatine Metabolism Disorder, Phenylketonuria, Pyridoxine dependent and responsive seizures, and Urea Cycle Disorders.

Treatment of seizures in autism spectrum disorder (ASD)

Seizures are most commonly treated with antiepileptic drugs (AEDs) but non-AED treatments are used when seizures cannot be controlled with AEDs. While a wide range of AEDs is available to treat epilepsy, few treatments have been specifically studied in children with ASD. If a specific genetic and metabolic syndrome is found to be associated with seizures in a child with ASD, there may be specific treatment. However, for the most part, AEDs are necessary to control seizures even in those children where the underlying genetic or metabolic disorder has been identified.

Antiepileptic Drugs

Although AEDs are first line for treating seizures, no AED has undergone evaluation for efficacy for the treatment of seizures in the ASD population. Recently, to determine whether specific treatments were more beneficial than others for individuals with ASD and seizures, 733 parent of children with ASD and seizures were asked to rate the effect of AEDs on seizures and other clinical factors including sleep, communication, behavior, attention, and mood. Four AEDs – valproate, lamotrigine, levetiracetam, and ethosuximide – were found to provide the best seizure control and worsen other clinical factors the least out of all AEDs examined. Valproate and lamotrigine had the least detrimental effect on mood and lamotrigine appeared to have the least adverse effects overall. These ratings appear to confirm the clinical experience of many clinicians.

Most AEDs have adverse effects, and specific adverse effects are highly dependent on the medication. In general, newer antiepileptic drugs, such as lamotrigine, oxcarbazepine, topiramate and levetiracetam, have few serious adverse effects as compared to older AEDs, such as phenobarbitol, phenytoin, primidone, and carbamazepine. The exception to this is valproate, which is an older antiepileptic medication that appears to have good efficacy for many individuals with ASD. However, the toxicity of valproate acid on the liver, pancreas, and blood cells must be carefully monitored and valproate acid must be avoided in individuals with certain mitochondrial disorders. The adverse effect profiles have not been studied in ASD specifically, so it is not known whether individuals with ASD have a higher incidence of adverse effects than other populations of individuals with epilepsy. However, it is best to avoid older AEDs (phenobarbitol, phenytoin, primidone) that have a high incidence of cognitive and neurological adverse effects, as existing behavioral and cognitive abnormalities could be exacerbated. In general, almost all AEDs can cause neurological side effects (ataxia, tremor, nystagmus), behavioral side effects (hyperactivity, agitation, aggressiveness), gastrointestinal side effects (abdominal pain, nausea), and an allergic reaction which can be severe in some cases. Serious side effects can often be avoided with careful monitoring. It is best to have a practitioner with experience in these medications prescribe an AED and monitor the patient. Care should be taken when using multiple AEDs, as adverse effects can be additive. Since almost all AEDs elevate the rate of birth defects, it is important to carefully consider the choice of AEDs in potentially sexually active females.

Adverse effects of specific antiepileptic drugs (AEDs)

- Lamotrigine: Lamotrigine has a low incidence of serious adverse effects and is generally well tolerated. The most serious adverse effect of lamotrigine is a life-threatening whole-body rash known as a Steven-Johnson's reaction. Increasing the lamotrigine dose slowly towards the target dose can reduce the risk of this reaction occurring.
- Levetiracetam:Levetiracetam has a low incidence of serious adverse effects and is probably one of the safest antiepileptic drugs. The most prevalent adverse effects are behavioral, including agitation, aggressive behavior, and mood instability. Levetiracetam has been linked to suicide in a few individuals without ASD. Co-treatment with pyridoxine (vitamin B6) helps reduce adverse behavioral effects in some cases.
- Valproate: The most serious adverse effects are hepatotoxicity (liver toxicity), hyperammonemia (high ammonia), and pancreatitis (inflammation of the pancreas). Precautions can be taken to prevent these adverse effects from occurring. In general, complete blood count, liver function tests, and amylase and lipase should be monitored during the initial period of starting the medication and if the patient experiences gastrointestinal symptoms. Once a stable dose has been selected, the patient can be monitored approximately every three months. Hepatotoxicity is believed to be more prevalent in children under two years of age, so it is best to avoid prescribing valproate to very young

children. In children with Alpers' syndrome, a syndrome caused by depletion of mitochondrial DNA, valproate can be fatal. In general, L-carnitine may mitigate liver damage resulting from valproate, and thus, co-treatment with L-carnitine is recommended. Common adverse effects of valproate include weight gain and thinning of the hair. The latter is believed to respond to selenium (10-20 mcg per day) and zinc (25-50 mg per day). Long-term use of valproate has been linked to bone loss, irregular menstruation, and polycystic ovary syndrome.

- Oxcarbazepine: Hyponatremia (low blood sodium) can develop in some individuals.
- Topiramate: Common adverse effects include weight loss and cognitive and psychomotor slowing. Topiramate is minimally metabolized by the liver and is excreted mostly unchanged by the kidney. Topiramate can cause a metabolic acidosis (high blood acid), nephrolithiasis (kidney stones) and oligohidrosis (decreased sweating). This medicine should be avoided in individuals with kidney disorders and extra care during hot weather is necessary. Glaucoma (increased eye pressure) has occurred in rare cases, so any vision symptoms should be evaluated.
- Vigabatrin: Vigabatrin is associated with a progressive and permanent vision loss. Thus, its use is usually restricted to control of a special type of seizure known as infantile spasms in a specific condition known as Tuberous Sclerosis.

A guide to selecting antiepileptic drugs (AEDs).

ASD Symptoms	Avoid	Possible Alternative
Gastrointestinal Disorders	Valproate	Lamotrigine
Mitochondrial Disorders	Valproate	Levetiracetam, Lamotrigine
Poor growth	Topiramate	Lamotrigine
Overweight	Valproate	Topiramate, Lamotrigine, Levetiracetam
Behavioral problems	Levetiracetam	Lamotrigine, Valproate, Topiramate

Non-antiepileptic drug treatments

Non-AED treatments are typically used to treat seizures when AEDs are not effective by themselves. None of these treatments has undergone evaluation for efficacy for the treatment of seizures in the ASD population. In our recent survey of 733 parents of children with ASD and seizures, we found that certain non-AED treatments were rated as having a favorable effect on seizures and other clinical factors including sleep, communication, behavior, attention, and mood. The best treatments appear to be low-carbohydrate diets such as the ketogenic and Atkins/modified Atkins diets. These diets are also thought to be effective in individuals with epilepsy without ASD. Information regarding several non-AED treatments is outlined below.

- Low Carbohydrate Diets: Low carbohydrate diets, such as the ketogenic diet, have been very effective at controlling seizures in some children with refractory epilepsy. The ketogenic diet is a very restrictive diet, so some have tried the modified Atkins diet and found it to be effective. Any dietary treatment should be conducted under the guidance of a trained professional. The ketogenic diet can cause acidosis (high blood acid), so anyone on this diet needs to be carefully monitored.
- Intravenous Immunoglobulin: Regularly scheduled infusion of intravenous immunoglobulin may help in refractory epilepsy, particularly epileptic encephalopathy syndromes. Common adverse effects include rash, headache, and fever and require prophylactic pretreatment. This treatment is contraindicated in individuals with kidney or heart problems and should be administered by a practitioner familiar with the treatment. Many individuals develop increasingly severe allergic reactions to intravenous immunoglobulin treatment. In such cases, changing the brand may reduce adverse effects.
- Steroids: One-time treatment or regularly scheduled treatments of high-dose steroids may help in refractory epilepsy, particularly epileptic encephalopathy syndromes. Daily steroids may also be effective, but are difficult to maintain because of the high risk of adverse effects. Common adverse effects include weight gain, edema, mood instability, and insomnia. Serious adverse effects include hypertension, immunosuppression, gastrointestinal ulceration, glucose instability, and osteoporosis. Anyone on steroids for an extended period should be closely monitored for serious adverse effects.
- Elimination Diets: Isolated cases of improvement in seizures with elimination of certain foods or preservatives have been reported, but no large studies have confirmed this practice as effective. Any dietary treatment should be conducted under the guidance of a trained professional.
- Vagus Nerve Stimulator: The vagus nerve stimulator is a small device that is implanted under the skin that has a wire that wraps around the vagus nerve. The device stimulates the vagus nerve, which has neural inputs into the brain. It is believed that stimulation of the brain results in changes in several levels of neurotransmitters, particularly gamma-aminobutyric acid, which can help control seizures. This device can cause alternations in vocalization, coughing, throat pain, and hoarseness. More serious side effects include spasms of the vocal cords, obstruction of the airway, and sleep apnea.
- Corticetomy: If seizures are found to arise from one small area of the brain, it is possible for a neurosurgeon to remove the dysfunctional part of the brain. In order to determine if one portion of the brain is generating seizures, a patient must typically go through several extended hospitalization. Brain surgery can have serious adverse effects, so this option is typically reserved for the most refractory patients.
- Multiple Subpial Transection: If a dysfunctional portion of the brain is found but cannot be removed, it is possible for a neurosurgeon to make small cuts in the brain areas surrounding the dysfunctional areas. Like corticetomy, this requires brain surgery, which can have serious adverse effects and requires an extended in-hospital workup. This particular therapy is not widely used and there are only a few cases published to support its use.

Emergency Treatments

Individuals with epilepsy, especially those with frequent or prolonged seizures, should have an emergency medication readily available to stop any generalized seizure that is sustained for 5 minutes or more. The most common emergency

medication is rectal diazepam. The most common adverse reaction is drowsiness. Respiratory depression can occur if high doses or multiple doses are given. If it is necessary to use this medication, medical personnel should be called to evaluate the patient.

Other websites with important information about seizures and epilepsy

- **The Epilepsy Foundation of America:** www.epilepsyfoundation.org
- **American Epilepsy Outreach Foundation:** www.epilepsyoutreach.org
- **Autism Research Institute:** www.autism.com
- **Autism Speaks:** www.autismspeaks.org

Tags: epilepsy, fit, medical, seizure, seizures

7 Responses

1. *Autism Spectrum Disorder and Seizure Disorder of Epilepsy* says:
   April 3, 2013 at 6:18 am
   […] Read the entire article HERE (1) […]

2. *Life is what happens to you while you're busy making other plans | Lisa Ackerman - Real Help Now* says:
   July 31, 2013 at 4:42 pm
   […] Fore more information regarding seizures visit http://www.tacanow.org/family-resources/seizures […]

3. *Max goes to the Neurologist – Part 1 of 3 | Lisa Ackerman - Real Help Now* says:
   August 14, 2013 at 4:13 pm
   […] yourself: Start reading. Start with TACA's website. 1. Seizure page: http://tacanow.wpengine.com/family-resources/seizures/ 2. Rossignol's Simplified Mitochondria, Immune and Neuro Approach Papers: […]

4. *Reflection #3: Autism Spectrum Disorder – Parent Blogs | SPED301(MCENTEGART)* says:
   October 3, 2013 at 1:32 pm
   […] information, advice, and additional resources just for individuals with Autism and Epilepsy. TACA (Talk About Curing Autism) also had many alternative non-drug treatments which I think the family […]

5. *Epilepsy and Autism | Epilepsy Talk* says:
   October 6, 2013 at 7:09 pm
   […] http://tacanow.wpengine.com/family-resources/seizures/ […]

6. *A Beginners Guide To Medical Interventions for ASD - Talk About Curing Autism (TACA)* says:
   November 23, 2015 at 5:58 pm
   […] – Seizures are the most prevalent neurological disorder associated with ASD. While 1-2% of children in the […]

7. *What Autism Symptoms Mean - Talk About Curing Autism (TACA)* says:
   December 4, 2015 at 11:39 pm
   […] Seizures. Get a 24-hour non-medicated EEG. […]

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