Consensus of the Fragile X Clinical & Research Consortium on Clinical Practices

Seizures in Fragile X Syndrome

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Seizure disorder, or epilepsy, is defined as a disorder of recurrent, spontaneous episodes consisting of abnormal electrical discharges in neural networks associated with alterations in consciousness, movement, and/or sensation. Seizure disorder is diagnosed in about 15% of males with fragile X syndrome (FXS). In keeping with the generally milder manifestations of FXS in females, their seizure frequency is estimated at only 6-8% . Most cases of seizure disorder in FXS develop in childhood and remit by adulthood. Some individuals with FXS may have just one seizure that never reoccurs.

Individuals with FXS are most likely to be diagnosed with focal seizures and complex partial seizures. However, generalized tonic-clonic or grand mal seizures are also reported in this population. Some individuals may have both types. Partial seizures may occur frequently or primarily during sleep.

While a routine EEG is indicated to help guide treatment for the patient suspected of seizure disorder, it may not be diagnostic. Many patients with FXS and seizure disorder have an EEG pattern characterized by centrotemporal spikes, which is also seen commonly in benign rolandic epilepsy of childhood. However, nonepileptic patients with FXS may also have this or other abnormal EEG patterns. Patients with FXS and seizure disorder may show other abnormalities on EEG, or no abnormalities at all.

Patients with FXS should be treated after the second clinical seizure, as is the typical guideline for seizure disorders in other conditions. Most individuals with FXS and seizure disorder can achieve good seizure control on a single anticonvulsant. While a discussion of the pros and cons of all the various anticonvulsants is beyond the scope of this writing, oxcarbazepine (Trileptal), levetiracetam (Keppra), and lamotrigine (Lamictal) are medications with relatively good profiles in terms of cognitive side effects that do not require standard blood monitoring in children, and thus may be viewed as first-line choices. Valproic acid may be good for certain EEG patterns and when there are seizures and mood/aggression or language regression issues; it may also be effective in cases where seizures are not responsive to the first-line medications. Phenobarbital is generally avoided because of its tendency to worsen hyperactivity and other behavioral issues.

Seizures in FXS do not seem to be correlated with lower cognitive function, but do appear to be more common in individuals diagnosed with autism. Additional research is needed to clarify the reasons for this finding.

Common Q & A:

Q: *My patient isn't having any seizure-like symptoms, but his family would like me to do an EEG anyway. Is this necessary?*

A: The EEG is generally used to provide data to support or detract from a clinical suspicion. As discussed above, however, many nonepileptic individuals with FXS have striking abnormalities on EEG, while some individuals with seizures and FXS may have mild or no abnormalities on this study. If your patient is having a significant unexplained change in sleep habits, decline in communication skills, or dramatic increase in aggression, it may be appropriate to order an EEG even though these symptoms are not typically epileptic.

Q: My patient's teacher is reporting that she "stares into space" frequently and does not respond when her name is called. The teacher has to touch her shoulder to get her attention. The staring lasts for several minutes and does not seem to be associated with any focal motor symptoms. The parents, who have never seen these spells at home, know about the association between FXS and seizures and are concerned.

A: Although staring and inattentive episodes are universal in students, they are more common in children with ADHD and intellectual disabilities. They may be more likely in less stimulating environments or when the child is overwhelmed or fatigued. The parents' description of these episodes is not highly concerning for seizure, as the child becomes alert when she is touched. In addition, the symptoms seem dependent on environment, whereas seizures tend to occur across environments.

Additional resources:

Berry-Kravis E, Raspa M, Loggin-Hester L, Bishop E, Holiday D, Bailey D. Seizures in fragile X syndrome: characteristics and co-morbid diagnoses. Am J Intellect Dev Disabil 2010;115:461-472

www.epilepsyfoundation.org/
The Epilepsy Foundation of America's website has updates on recent developments in epilepsy care and links to epilepsy research opportunities. For your patients and their families, there are clearly written explanations about seizure types, medications, and other options for treatment. Some content is translated into Spanish.

Seizures and Epilepsy in Childhood: A Guide (Johns Hopkins Press Health Book)
John M. Freeman MD, Eileen P. G. Vining MD, Diana J. Pillas
Family-friendly book reviewing the medical and psychological issues related to seizures

Author: This guideline was authored by Dianne McBrien, MD and was reviewed and edited by consortium members both within and external to its Clinical Practices Committee. It has been approved by and represents the current consensus of the members of the Fragile X Clinical & Research Consortium.

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The Fragile X Clinical & Research Consortium *was founded in 2006 and exists to improve the delivery of clinical services to families impacted by any Fragile X-associated Disorder and to develop a research infrastructure for advancing the development and implementation of new and improved treatments. Please contact The* ***National Fragile X Foundation*** *for more information. (800-688-8765 or www.fragilex.org)*