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■ **The Doctor Is In**  
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## Epilepsy In Fragile X Syndrome

The association of epilepsy (seizures) with fragile X syndrome (FXS) has been known since the earliest descriptions of affected patients. Its prevalence ranges from 10- to 40 percent, depending on the study design and the number of patients studied. An accepted average prevalence is around 20 percent. Onset of seizures is usually after 2 years of age and rarely after 9.


The most frequent type of epileptic crises reported in children with FXS are simple or complex partial seizures, although other types have also been reported, such as generalized tonic-clonic seizures, staring spells, absence seizures, or temporal lobe seizures. In certain cases, disease progression is benign and has been compared to the benign childhood epilepsy with centrotemporal spikes (BCECTS), suggesting an age-related maturational process. Although these similarities initially suggested that the genetic locus for FXS and BCECTS could be the same, further linkage studies found

no association between the latter and the FMR1 region.

The most frequent EEG pattern in patients with FXS is similar to that of rolandic epilepsy. It includes discharges of sharp waves in centrotemporal regions of the brain, which are activated by sleep. There are FXS patients who have only EEG anomalies without clinical seizures. Other

hypothesized that the excessive neuronal excitation and spiking could be caused by the dendritic spine anomalies observed in the brain of FXS patients. Another theory proposes a dysfunction of GABAergic system related to the absence of FMRP (Fragile X Protein).

Evaluation of children with FXS should include a careful medical history addressing possible seizure episodes, which are sometimes subtle. An EEG should be recommended if seizures are suspected, and should include records during waking and sleeping periods. If signs of focality are seen in the neurological examination, an MRI of the brain should be obtained.

Pharmacological treatment of epilepsy in FXS patients is done with anticonvulsants. Among them, valproic acid and carbamazepine are the most commonly used. Both medications need a medical follow-up that should include blood analyses for white blood cell count, because neutropenia is a common secondary effect of the use of both anticonvulsants. Valproic acid can cause hepatotoxicity or pancreatitis and carbamazepine hypersensitivity reactions with skin rash and fever. New anticonvulsants are now available as adjunct medication for treatment of seizures in epileptic FXS patients. The use of phenobarbital in epileptic FXS patients is not recommended because it may increase hyperactivity. Treatment and follow-up of epileptic FXS patients should be done by a pediatric neurologist, particularly when the child is being treated with anticonvulsants. 

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EEG patterns reported include theta rhythm, diffuse or multifocal spike waves or, more frequently, a diffuse slowing background activity. The frequency of epilepsy is lower in females with FXS, who tend to present unspecific EEG patterns.

Some theories have tried to explain the presence of epilepsy and EEG abnormalities in FXS. One of these