When a premutation or full mutation is present, it can result in a Fragile X-associated Disorder (FXD). These include:

- Fragile X syndrome (FXS): A condition that can affect intellectual, behavioral, and social development. It occurs in both males and females who have a full mutation of the FMR1 gene.
- Fragile X-associated tremor/ataxia syndrome (FXTAS): An adult onset (over 50 years of age) neurological condition, seen in males and females, but more common and more severe in some male premutation carriers. It can cause tremors, memory, and balance issues.
- Fragile X-associated primary ovarian insufficiency (FXPOI): A condition affecting ovarian function that can lead to infertility and early menopause in some female premutation carriers.
- Other issues may be present in premutation carriers, and this is an ongoing area of study for researchers.

What is a Seizure?

- A seizure is a single event characterized by an abrupt change in behavior (e.g., staring without response, dropping to the ground, or twitching a part or all of the body).
- What you don’t see is that the behavior is accompanied by a burst of electrical discharges that comes from neurons in the brain, i.e., the behavior appears in association with the burst and then goes away when the burst is over.
- A seizure occurs either as primary excess electrical excitability in an otherwise normal brain or secondary to another disorder.
- In fragile X syndrome (FXS) the excess electrical excitability is most likely related to the effects of the genetic change in the fragile X gene (FMR1) and the resultant loss or reduction of the fragile X protein (FMRP) on activity in neurons.
- Other causes of seizures have to be considered in a person with FXS as there could be another diagnosis in addition to the FMR1 gene mutation.

Classification of Seizures

Seizures are classified according to the International League Against Epilepsy (ILAE). There are Focal Seizures (also known as Partial Seizures), Generalized Seizures, Status Epilepticus Seizures, and Febrile Seizures.

Evaluation of Seizures

- In the evaluation of seizures, it is important to collect a detailed moment by moment history of the event (activity, body position, progression, duration, loss of sphincter tone resulting in urination or a bowel movement, tongue biting, visual/auditory/olfactory auras).
- This will help determine if the event was likely an epileptic seizure versus a non-epileptic spell that might include things like shuddering, breath-holding, benign nocturnal myoclonus (twitching when falling asleep), night terrors, migraine, panic attack, fainting, hyperventilation or heart arrhythmia.

Typically, patients would be referred to neurology to manage seizures although in uncomplicated cases the primary care physician may handle the problem.
It is important to recognize that while a routine EEG is indicated to help guide treatment for a person suspected of seizure disorder, it may not be diagnostic and then one has to rely on clinical judgement.

**Frequency of Seizures in FXS**
Recently the largest and most definitive study yet published on seizures in FXS was completed using the Fragile X Online Registry with Accessible Research Database (FORWARD). In this study the overall chance of having at least one seizure was 12% overall in FXS, 13.7% in males and 6.2% in females.

**Age of Onset and Resolution of Seizures in FXS**
- In the group with seizures, the average age of the first seizure was 6.4 years of age with the great majority (86.7% of males and 81.8% of females) having the first seizure before age 10 years.
- The age of the last seizure followed a similar age dependence to age of first seizure, with 70.9% of seizures in males and 63.6% of seizures in females resolving by age 10 years.

**Types of Seizures in FXS**
Partial (focal) seizures were reported in 25% and generalized seizures in 31% of those with seizures, with febrile seizures in 8% and the remainder of seizures being of unknown type. Males and females did not show a different distribution of seizure types.

**Association of Seizures with Other FXS Characteristics**
As compared to individuals with FXS without seizures in FORWARD, those with seizures were more likely to have more severe intellectual disability, current sleep apnea, delayed acquisition of expressive language, autism spectrum disorder (ASD), hyperactivity, irritability, and stereotyped movements.

**Treatment of Seizures in FXS**
Treatment and management of seizures in FXS is similar to seizure treatment in other conditions associated with seizures. There is no FXS-specific medication or approach to treating seizures.

**Medications for use in FXS**
A person with seizures is usually treated with medications, known as anticonvulsants, after two (or sometimes more if there is a long time between seizures) seizures.

**Conclusion**
In summary, based on the FORWARD data, 12% of people with FXS have seizures. Treatment and management of seizures in FXS is similar to seizure treatment in other conditions associated with seizures. There is no FXS-specific medication or approach to treating seizures, but the approach is to try to use the medications expected to have the least side effects first and those not requiring blood monitoring. In general seizures are easily controlled in FXS and most patients grow out of their seizures before their twenties, although infrequently seizures can be a more challenging problem.