National Ataxia Foundation

Fragile-X Associated Tremor/Ataxia Syndrome Information (FXTAS)

What is FXTAS

Fragile X–associated tremor/ataxia syndrome (FXTAS) is a rare neurodegenerative disorder. It is caused by a CGG triplet repeat expansion in the FMR1 gene. The prevalence of FXTAS is approximately 1 in 8,000. The risk of someone developing FXTAS is influenced by the number of CGG repeats in their FMR1 gene, their sex (men are at greater risk), and age (symptoms are more common in older individuals).

What are the symptoms of FXTAS?

Like many other forms of Ataxia, FXTAS is marked by poor balance and coordination. In fact, the word Ataxia means incoordination. There can also be problems coordinating muscles that control speech and swallowing.

The major symptoms used to diagnose FXTAS include intention tremor (when someone is actively moving), poor balance and coordination, changing of white matter in the brain, and neuropathology findings called “FXTAS inclusions” inside of brain cells. Minor symptoms used to diagnose FXTAS include tremors at rest (called Parkinsonism), short term memory problems, problems with decision making, and other brain imaging findings.

Other symptoms commonly associated with FXTAS include neuropathy, mood instability, cognitive difficulties, bowel or bladder issues, and irritability.

t is t e o nosis o FXTAS

FXTAS symptoms usually begin after the age of 50. Males tend to have more severe symptoms than females. The progression of symptoms varies between individuals. Some FXTAS patients have multiple symptoms and rapid progression, while others have a few symptoms which remain mild.

Treatments such as mental health support, medication to treat specific symptoms, physiotherapy, occupational therapy, and speech-language therapy can significantly improve the lives of people with FXTAS.

s FXTAS enetic

FXTAS is a genetic disorder which means that it is an inherited disease. The abnormal gene responsible for this disease is passed along from generation to generation by family members who carry it. Genetic diseases like FXTAS occur when one of the body’s 0,000 genes does not work properly. Genes are microscopic structures within the cells of our bodies that contain instructions for every feature a person inherits from his or her parents.

FXTAS is an X-linked disorder, meaning that the mutated gene is found on the X chromosome called FMR1. Since males only have one X chromosome, they are more likely to develop X-linked disorder like FXTAS.

Females can also develop FXTAS, but they usually have milder symptoms since they have two X chromosomes. Since females have two X chromosomes, all cells in their body will randomly “turn off” one copy of the X chromosome through a process call x-inactivation.

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FXTAS enetics (continued)

Research suggests that if most cells in a woman's body have turned off the X chromosome containing an FMR1 mutation, she will have no symptoms or mild symptoms. owever, if the X chromosome containing an FMR1 mutation is turned on, the woman will have more severe symptoms. More research is being done to better understand FXTAS symptoms in women.

FXTAS is caused by a mutation called a CGG triplet repeat expansion in the FMR1 gene. The number of repeats you have influences your risk of developing FXTAS or other Fragile X disorders.

- **Between 55-40 CGG Repeats:** This is the typical number of repeats in the FMR1 gene. People with this number of repeats are usually healthy.

- **Between 55-200 CGG Repeats:** This length of repeats is called an FMR1 gene premutation. People with the FMR1 gene premutation are more likely to develop FXTAS or Fragile X-Associated Primary Ovarian Insufficiency (FXPOI). owever, some people with the FMR1 gene premutation will develop FXTAS and/or FXPOI, while others do not. Researchers are trying to better understand the variability in why some people develop symptoms and others do not.

- **Over 200 CGG Repeats:** People with more than 00 repeats usually develop a condition called Fragile X Syndrome, which causes intellectual disability, behavioral difficulties, learning challenges, and various physical characteristics. Fragile X syndrome affects young children, mainly boys.

Gene tests can be performed for diagnostic purposes to determine what kind of Ataxia is within a person or family. Genetic testing also can be done, in some circumstances, even before there are symptoms to determine whether a person carries the abnormal gene or genes that cause Ataxia. This is called predictive or presymptomatic testing. A gene test also can be used to determine whether a fetus has an abnormal Ataxia gene. This is called prenatal testing. Anyone who is considering a predictive or prenatal test should consult with a genetic counselor to discuss the reasons for the test, the possible outcomes, and how those outcomes might affect the person emotionally, medically, or socially.

Since FXTAS, FXPOI, and Fragile X Syndrome are all caused by mutations in the FMR1 gene, a diagnosis in one family member can have implications for the whole family. If someone is diagnosed with FXTAS, their family members (particularly grandchildren) may want to consider genetic testing for Fragile X Syndrome. Likewise, if a child is diagnosed with Fragile X Syndrome, older family members may want to consider genetic testing for FXTAS or FXPOI.

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How is FXTAS diagnosed?

A neurologic examination can determine whether a person has symptoms typical of FXTAS. This suspected diagnosis is then verified through brain imaging, such as MRI, and genetic testing to detect the presence of the FMR1 gene premutation that causes FXTAS. A neurologist is often the most helpful specialist in recognizing symptoms and diagnosing the disease that causes Ataxia.

You may see a FXTAS diagnosis described as "definite", "probable", or "possible". This classification depends on the number of major or minor clinical symptoms someone has. To learn more about FXTAS diagnosis classifications, visit the National Fragile X Foundation.

What kind of support is available after the diagnosis?

As Ataxia research moves into the clinical phase, pharmaceutical companies will begin recruiting participants for clinical trials. NAF provides accurate information for you, your family, and your physician about Ataxia. Please visit the NAF website at www.ataxia.org for additional information, including a listing of ataxia support groups, physicians who treat Ataxia, social networks, and more. For questions contact NAF directly at (763) 552-0020 or naf@ataxia.org.