National Ataxia Foundation

Spinocerebellar Ataxia Type 4 (SCA4)

What is SCA4?

Spinocerebellar Ataxia type 4 (SCA4) is a rare neurodegenerative disorder. It is caused by a GGC triplet repeat expansion in the ZFHX3 gene. SCA4 is very rare worldwide. However, SCA4 is more common in the Skane region of Sweden, as well as areas around the world with Swedish ancestry. This includes parts of the United States and Germany.

SCA4 Symptoms

Like many other forms of Ataxia, SCA4 is marked by poor balance and coordination. In fact, the word Ataxia means incoordination. There can also be problems coordinating muscles that control speech, swallowing, and vision.

People with SCA4 also develop neuropathy, which is the progressive loss of feeling in the hands and/or feet. Other potential symptoms include decreased reflexes and problems with bowel or bladder control. People with late stage SCA4 may also experience significant weight loss or muscle wasting.

Prognosis

SCA4 symptoms usually begin around age 40. However, symptoms can begin as young as 12 years old and as late as 65 years old. About 10% of people with SCA4 experience their first symptoms before the age of 25. The severity of SCA4 symptoms may varies considerably, even within families.

SCA4 usually progresses very slowly, with patients eventually needing the use of a wheelchair. Lifespan generally is not shortened by the disease. Treatments such as physiotherapy, occupational therapy, and speech-language therapy can significantly improve the lives of people with SCA4.

SCA4 Genetics

SCA4 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 SCA4 occur when one of the body's 20,000 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.

SCA4 is an autosomal dominant disease, meaning individuals of either sex are equally likely to inherit the gene and develop the disease. Each child of a person with SCA4 has a 50% chance of inheriting the gene that causes SCA4.

In the case of SCA4, it is caused by a mutation called a GGC repeat expansion in the *ZFHX3* gene. Whether or not you develop SCA4 depends on how many repeats you have.

- **Fewer than 31 GGC Repeats:** This is the typical number of repeats in the *ZFHX3* People with this number of repeats are healthy.
- **Between 31 and 41 GGC repeats:** Due to limited data, it is not clear what this number of repeats means. It doesn't seem that people with this length of repeats will develop SCA4, however, their children may be at risk. There is active research to understand what this number of repeats does to the body, but right now there is still uncertainty.
- **Over 42 GGC repeats:** People with more than 42 repeats usually develop SCA4.

Genetics (continued)

More repeats are associated with an earlier age of onset of symptoms and more severe symptoms. GGC repeats can expand or increase in number between generations. This results in each subsequent generation typically developing SCA4 symptoms at a younger age.

Gene tests can be performed for diagnostic purposes to determine what kind of Ataxia is within a person or family. Genetic testing can also 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 can also 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.

Diagnosis

A neurologist is often the most helpful specialist in recognizing symptoms and diagnosing the disease that causes Ataxia. A neurologic examination can determine whether a person has symptoms typical of SCA4. There are several potential follow-up tests. MRI brain imaging may be used to confirm cerebellar atrophy. Electromyography (EMG) may be used to test for neuropathy.

A definitive diagnosis of SCA4 is established following genetic testing. This confirms that someone has a mutation that causes SCA4 in their *ZFHX3* gene. The gene causing SCA4 was only recently discovered in 2024. Thus, previously, SCA4 was diagnosed based on symptoms, family history, MRI data, and EMG data. People who we diagnosed with SCA4 prior to 2024 are encouraged to speak with their doctor about accessing *ZFHX3* genetic testing.

What kind of support is available after the diagnosis?

The National Ataxia Foundation (NAF) is committed to providing information and education about Ataxia, support groups for those affected by Ataxia, and promoting and funding research to find the cause for the various forms of Ataxia, better treatments, and, hopefully someday, a cure. As Ataxia research moves into the clinical phase, pharmaceutical companies will begin recruiting participants for clinical trials. Individuals with Ataxia or who are at-risk for Ataxia are encouraged to enroll in the CoRDS Ataxia Patient Registry. To access the Registry, go to NAF's website www.ataxia.org and click on the "Enroll in the Patient Registry" tab and follow the directions on the CoRDS website.

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 the NAF directly at (763) 553-0020 or naf@ataxia.org.