

FREQUENTLY ASKED QUESTIONS ABOUT...

Spinocerebellar Ataxia Type 3 (SCA3)/ Machado-Joseph Disease (MJD)

What is spinocerebellar ataxia type 3?

Spinocerebellar ataxia type 3 (SCA3), also known as Machado-Joseph disease (MJD), is one type of ataxia among a group of inherited diseases of the central nervous system. As in many of the inherited ataxias, SCA3 results from a specific genetic defect that leads to impairment of nerve cells in the brain and nerve fibers carrying messages to and from the brain. In SCA3, the impairment of nerve cells and nerve fibers results in degeneration of the cerebellum (the coordination center of the brain) and related brain regions.

What are the symptoms of SCA3?

The word ataxia means incoordination. As in other forms of inherited ataxia, SCA3 is marked by incoordination. Impaired balance is usually the first symptom, followed later by incoordination of the hands and slurring of speech. Some individuals with SCA3 will notice double vision, and an examining physician might note limitation of eye movements, abnormally slow eye movements, or a “staring” appearance of the eyes. As the disease progresses, it is common to experience spasticity, rigidity, loss of muscle bulk and strength, and slowness of movement. In general, SCA3 symptoms tend to be more wide-ranging than those in many other forms of ataxia. The age of onset and the range of symptoms can vary widely in SCA3, even among affected persons in the same family. This variability reflects the type of disease-causing genetic defect in SCA3: an expansion of a DNA triplet repeat. The repeat expansion in SCA3 varies in size among affected persons. In general, the longer the repeat the more powerful the effect of the mutation, resulting in earlier onset disease. The greater the expansion, the more severe the disease is likely to be.

What is the prognosis for SCA3?

The symptoms of SCA3 usually appear in middle adult life and progress over several decades, with some patients surviving for almost 30 years after the onset of symptoms. Onset in adolescence or as late as age 70 also can occur. This extreme range in age of onset reflects differences in the size of the disease-causing DNA repeat.

How is SCA3 acquired?

SCA3 is a genetic disorder, which means that it is an inherited disease. The abnormal gene responsible for this disease is passed from generation to generation by family members who carry it. Genes are heritable microscopic structures that comprise our genetic makeup and contain instructions for the features a person inherits from his or her parents. Genetic diseases like SCA3 occur when there is an abnormal change or mutation in the DNA that makes up one of the body's approximately 25,000 genes. In SCA3, the mutation is an expansion of a DNA triplet repeat in the ATXN3 gene. Genes are made up of molecules known as nucleotides linked together in highly ordered chains. Each nucleotide is identified by one of four letters (C,A,G, or T). In SCA3, the mutation results in extra copies of a triplet repeat of the nucleotides C-A-G. Thus SCA3 is due to a CAG repeat expansion. SCA3 is inherited in a dominant fashion, which means that it passes directly from one generation to the next without skipping generations. Each child of a person with SCA3 has a 50 percent chance of inheriting the disease gene that causes SCA3. Individuals of either gender are equally likely to inherit the gene and develop the disease.

How common is SCA3?

Machado-Joseph disease was identified in 1972, and researchers first described SCA3 in 1983. The discovery of the disease gene revealed that these two are actually the same disease. Although SCA3 was once thought to be very rare and found only in certain isolated ethnic groups, studies have since shown that SCA3 may be the most common dominantly inherited ataxia in many regions of the world. The ratio varies among populations depending on geographical location and ethnic background.

How is the diagnosis made?

A neurologic examination can determine whether a person has symptoms typical of SCA3, and a simple gene test can accurately detect the presence of the mutation that causes the disease. A neurologist is often the most helpful specialist in determining the cause of symptoms that might indicate SCA3. Most people who develop SCA3 have a family history of ataxia with similar symptoms, which is an important clue to the diagnosis. It is important to rule out other diseases and to consider other forms of ataxia. When SCA3 is suspected, DNA-based testing can confirm the diagnosis. The DNA test for SCA3 involves analysis of the mutation in the ATXN3 gene.

What can be done to move research in SCA3/MJD forward?

Individuals with SCA3 or who are at-risk for SCA3 are encouraged to enroll in the CoRDS Ataxia Patient Registry. This can be done by going to the NAF website's homepage and clicking on the "Ataxia Patient Registry" button. This is a secure site to complete the enrollment process in the patient registry for recruitment into clinical trials. The National Ataxia Foundation funds research studies around the world. Supporting NAF's research funding efforts will help move us closer to treatments and a cure for SCA3.

What kind of support is available after the diagnosis?

Research in many laboratories is leading to a better understanding of the disease mechanism in SCA3. Despite these research advances, there is no specific treatment to delay or halt the progression of SCA3. Supportive medical therapy, however, is available to help manage many disease symptoms. These symptoms can include stiffness or spasticity, slowed movements, restless legs, fatigue, sleep problems, double vision, and depression. In addition, there are resources to provide emotional support. *Living With Ataxia: An Information and Resource Guide*, published by the National Ataxia Foundation, includes a range of practical information and lists additional resources. NAF also provides and participates in local ataxia support groups, an on-line chat room and social networking groups. Visit the Web site at www.ataxia.org for a listing of these groups. For a more complete listing of resources provided by the National Ataxia Foundation, contact: naf@ataxia.org.