Inherited ataxias

Understanding this group of genetic disorders.

Summary

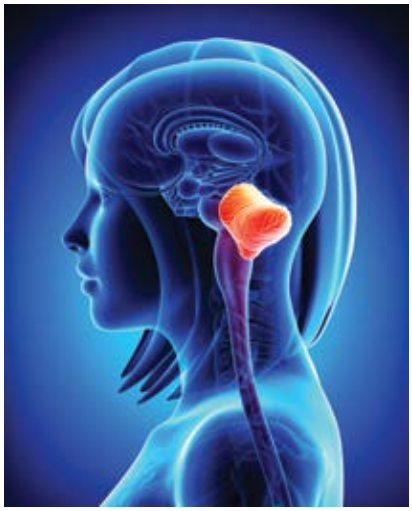
Inherited ataxias is an umbrella term for a group of rare genetic disorders characterised by slowly progressive incoordination of gait and often associated with poor coordination of hands, speech, and eye movements. Frequently, atrophy (wasting) of a part of the brain called the cerebellum occurs - the cerebellum is where movement, posture, and balance are coordinated.

MDANZ covers all types of inherited ataxias. These rare conditions include Friedreich's ataxia (FA), all types of spinocerebellar ataxia (SCA) and a condition known as CANVAS; cerebellar ataxia with neuropathy and bilateral vestibular areflexia syndrome.

Symptoms

There are many different types of hereditary ataxias and each may have unique signs and symptoms. However, in general, it is difficult to differentiate among the different types, and all are characterised by problems with movement that tend to get worse over time. Affected people may experience the following:

- Problems with coordination and balance (ataxia)
- Uncoordinated walk
- Poor hand-eye coordination



Wasting of the cerebellum frequently occurs.

- Speech difficulties (dysarthria)
- Involuntary eye movement
- Vision problems
- Difficulty processing, learning, and remembering information

Depending on the type of condition, signs and symptoms can develop anytime from childhood to late adulthood. Over time, the affected nerve cells begin to function poorly and ultimately degenerate. As the disease progresses, muscles become less and less responsive to commands from the brain, causing coordination problems to become more pronounced. Those affected by poor coordination will notice poor balance when walking, inability to run, clumsiness of the hands, a change in speech, or unusual eye movements.

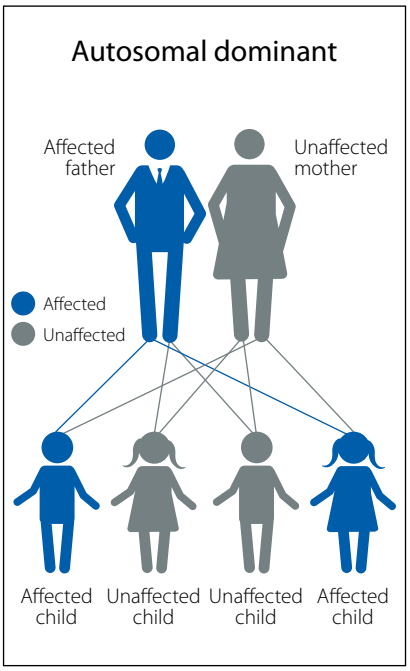
Individuals with inherited ataxias may develop a variety of other symptoms as their condition progresses, such as: numbness, tingling, or pain in the arms and legs (sensory neuropathy); uncontrolled muscle tensing (dystonia); muscle wasting (atrophy), muscle twitches (fasciculations), rigidity, tremors, seizures, tinnitus, vertigo, and involuntary jerking movements (chorea). The condition may be complicated by vision disorders and eye movement paralysis, or have association with heart disease, breathing problems, bone abnormalities and diabetes depending on the type.

FA is associated with cardiac problems, depression and type 2 diabetes. Cardiac complications include cardiomyopathy, myocardial fibrosis, heart failure, tachycardia or heart block. Many of these symptoms can be treated with medication.

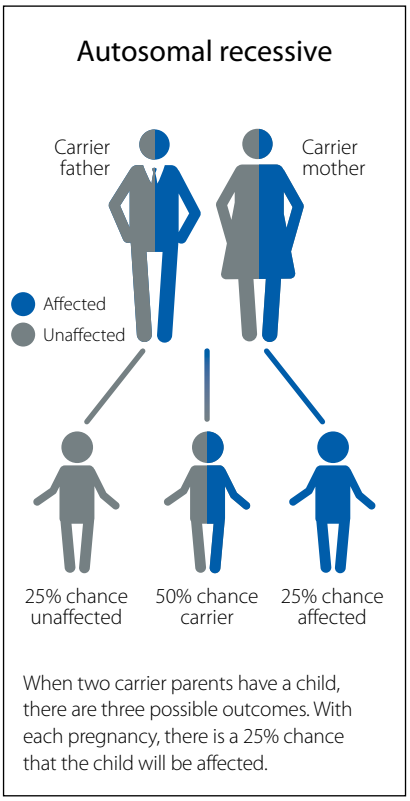
CANVAS is associated with a dry cough.

Cause

Mutations in many different genes are known to cause the different types of spinocerebellar ataxia (SCA). For some types, the gene known to cause it has been identified, while in others, the genetic cause is still unknown (about 40 percent to 25 percent of the cases).



Mode of Inheritance for the majority of SCA's (autosomal dominant inheritance). Also Friedreich Ataxia and some SCA'S (autosomal recessive inheritance).



When two carrier parents have a child, there are three possible outcomes. With each pregnancy, there is a 25% chance that the child will be affected.

In 1863, Nikolaus Friedreich (1825-1882), a German pathologist from Heidelberg, described a new spinal disease for the first time, which came to carry his name 'Friedreich's Ataxia'. It took a 120 years to discover the genetic defect underlying Friedreich Ataxia (FRDA) in 1996 named 'frataxin'.

The cause of CANVAS is currently unknown – this condition was only described in 2011 and work has been underway ever since trying to find the genetic cause of it.

Inheritance

Inheritance can be either autosomal dominant as in many of the SCA's, autosomal recessive as in FA or X-linked recessive. The inheritance pattern of CANVAS is yet to be fully understood but is considered likely to be autosomal recessive.

For some types of SCA and for CANVAS, the genetic cause is still unknown.

Diagnosis

A diagnosis of hereditary ataxia is often suspected when certain signs and symptoms, such as a poorly coordinated gait (walk) and uncoordinated hand/finger movements, are present.

Genetic testing is the best way to confirm FA and SCA and identify the specific type, however, this is only an option if the disease-causing gene for that particular condition or sub-type of condition has been identified. Genetic testing can confirm a clinical diagnosis or it can predict that an individual is likely to go on and develop the condition. Testing is available for many different genes known to cause spinocerebellar ataxia (SCA) and is also available to test for FA. Carrier testing for at-risk relatives and prenatal testing are possible if the disease-causing mutations in the family are known.

For some types of SCA and also for CANVAS, the genetic cause is still unknown. Genetic testing is not available for families with these types of conditions until the genetic cause is identified. In these cases, imaging studies such as computed tomography (CT scan) and/or magnetic resonance imaging (MRI scan) may be helpful in establishing a diagnosis. A CT scan is an imaging method that uses x-rays to create pictures of cross-sections of the body, while an MRI scan uses powerful magnets and radio waves to create pictures of the brain and surrounding nerve tissues.

Treatment

There is no known cure for any types of hereditary ataxia. The best treatment options for SCA and FA vary by type and will depend on the signs and symptoms present in each person. The most common symptom of hereditary ataxias is ataxia (a condition in which coordination and balance are affected). Physical therapy can therefore help strengthen muscles, while mobility aids (e.g., walking stick, walker, or wheelchair) can

CANVAS is associated with a dry cough.

Many will eventually need assistance to perform daily tasks.

assist in mobility and other activities of daily life. Many people with SCA have other symptoms in addition to the ataxia such as tremors, stiffness, muscle spasms, and sleep disorders; medications or other therapies may be suggested for some of these symptoms. One report described some improvement in the symptoms with zolpidem 10 mg in four out of five family members with SCA type 2, and a trial of 20 patients with SCA3 found that varenicline led to improvement in some, but not all of the symptoms.

Prognosis

The long-term outlook (prognosis) for people with CANVAS, FA or spinocerebellar ataxia (SCA) varies.

Most available information on the prognosis of SCA is based on the four most common types: SCA1, SCA2, SCA3 and SCA6. People affected by one of these types of SCA usually require a wheelchair around 10-15 years after the onset of symptoms. Many will eventually need assistance to perform daily tasks. Similarly the prognosis of FA is reasonably well described and is constantly being updated as more research is carried out.

Research

Research helps us better understand diseases and can lead to advances in diagnosis and treatment.

Clinical Research Resources

The US government website 'Clinicaltrials.gov' lists all clinical trials and some other research studies. Enter the condition that you're interested in into the search bar and then click on the generated list to read descriptions of these studies.

Please note: *We strongly recommend that you talk with a trusted healthcare provider before choosing to participate in any clinical study.*

Patient Registry

The NZ NMD Registry covers all neuromuscular conditions including all forms of SCA, CANVAS and FA. Talk to your fieldworker or contact info@mda.org.nz to find out more.