Ataxia

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Adopted for use by the ERN-RND by Dr Mary Kearney European Patient Advocate in 2022

INTRODUCTION

Ataxia is a very rare disease which effects people's balance. It is a neurological disorder, meaning that it is caused because of the deterioration of a particular part of the brain, spinal cord and nerves (known as peripheral nerves) in the body. Even though the disease is related to the brain it does not affect intelligence. Ataxia is most often a progressive disorder and slowly worsens to the point that patients need a wheelchair. There is no cure yet but research is on-going.

I am going to talk about what causes ataxia, how it is diagnosed.

WHAT IS ATAXIA?

The word ataxia comes from the Greek word "ataxis" which means "without order" or "unco-ordinated". The disease usually starts with the person being clumsy, things fall out of one's hands, one would prefer to walk by a wall. Ataxia usually affects the fingers and hands, the arms and legs, the body, speech, swallowing or eye movement. There are many types of ataxia. It can be a system of many disorders and can be due to brain disease as a result of:

- Infection
- Injury
- Degenerative changes in the brain or nerves in the body
- Inherited from one's parents

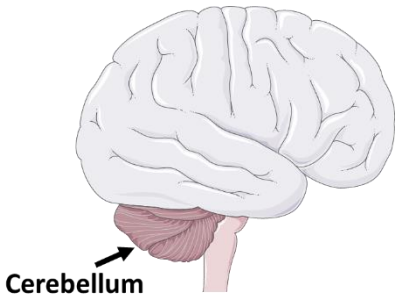
The hereditary nature of ataxia has been known since the late 19th century but as there were no genetic tests or MRI scan until the later 1990's it was very difficult to know the exact cause of ataxia. As a result, there are a myriad of names given to ataxia all over the world. With increasing knowledge, classification of ataxia is becoming more accurate.

Initially ataxia as a disease was categorized in two ways:

- if ataxic symptoms developed at an early age, you had Friedreich's ataxia
- if ataxic symptoms developed at a later age you had Marie's ataxia.

However today this is not how ataxia is classified now. In 1996 the gene for Friedreich's ataxia was discovered. People then realized that you could present with symptoms at any age. They realized that every case of ataxia was different. Friedreich's ataxia is the most common inherited ataxia and is just one type of 50 or more ataxias.

Ataxia is caused by the loss of function of a particular part of the brain, the coordination area, which is known as the cerebellum. This loss of function causes the cerebellum not to sends messages to the spinal cord and the peripheral nerves. The deterioration of this part of cerebellum is what causes the loss of coordination.



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With increasing knowledge and research, the hereditary ataxias are now divided into two main groups:

1) Dominant ataxias
2) Recessive ataxias

Inherited ataxias are caused by a defect in a certain gene in our chromosomes. These chromosomes are present at the start of a person's life.

DOMINANT ATAXIA

In dominant ataxia, the condition develops when a faulty gene is passed from one parent to the child. Each child born from a parent with dominant ataxia has a 50% chance of develop ataxia. If the child does not inherit the faulty gene, his or her children cannot become affected, and future generations will be free of the disease. Children of either sex are equally likely to inherit the abnormal gene and thus inherit ataxia. By chance, all offspring in one ataxic family may have ataxia while offspring in another ataxic family may be free.

How autosomal dominant ataxia is inherited

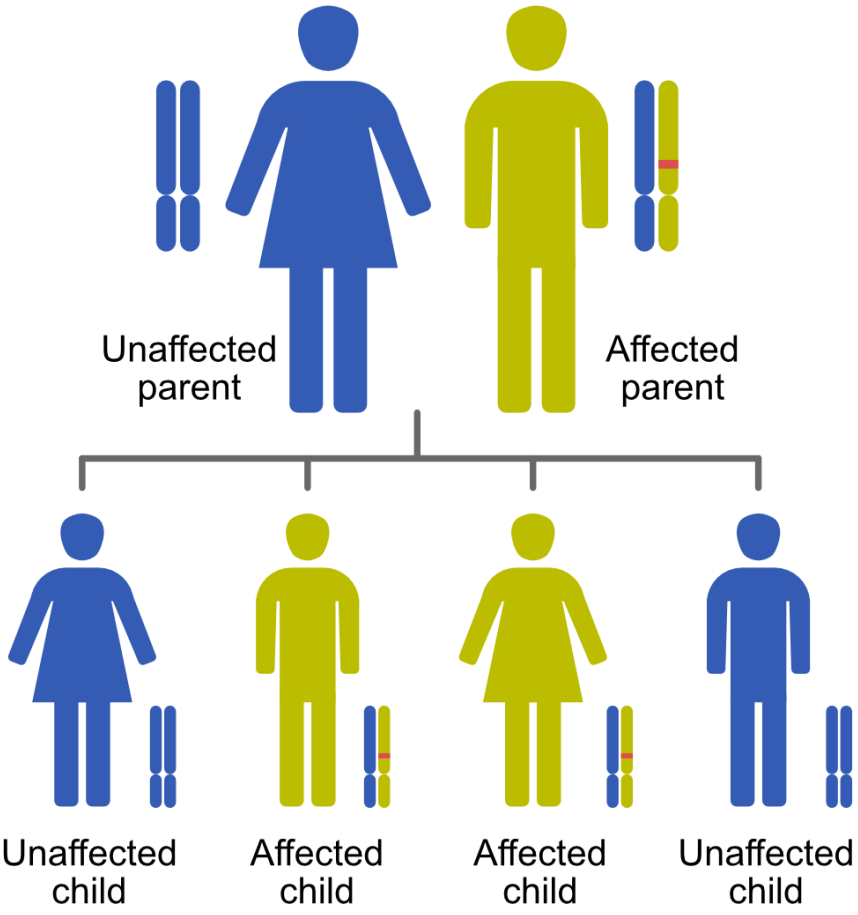

Figure 1: Courtesy of Annemarie Post Feb 2022
European Reference Network - Rare Neurological Disease group

RECESSIVE ATAXIA

In recessive ataxia, the condition is passed on by receiving the faulty gene from both parents. The parents, themselves, don't have symptoms but each carries a gene which may cause ataxia in their offspring. *A* recessive gene may be passed down for generations, the family would not be aware that they had the faulty gene until people with the same abnormal gene have children together. Symptoms of the recessive ataxias usually appear in the 1st or 2nd decade of life.

How autosomal recessive ataxia is inherited

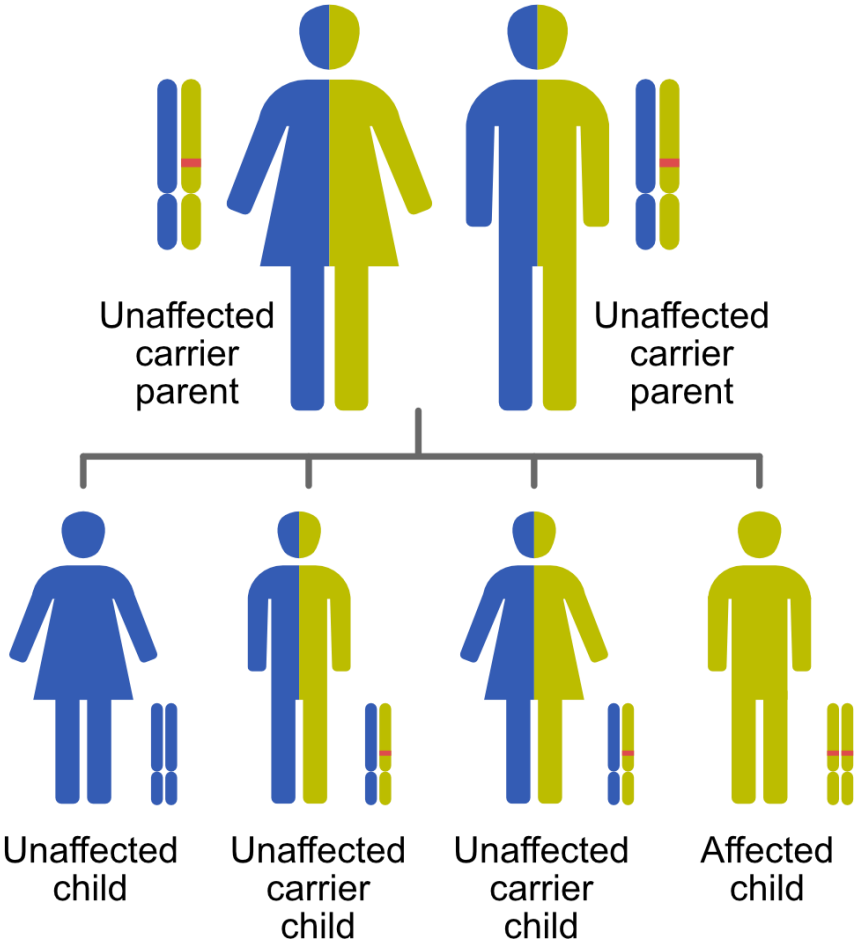

Figure 2 Courtesy of Annemarie Post Feb 2022
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Affected patients with the recessive ataxia genes have the following genetic odds for each child that they might have:

1) a 25% chance of not having the disease,
2) a 50% chance of being a carrier without showing symptoms and
3) a 25% chance of having the disease.

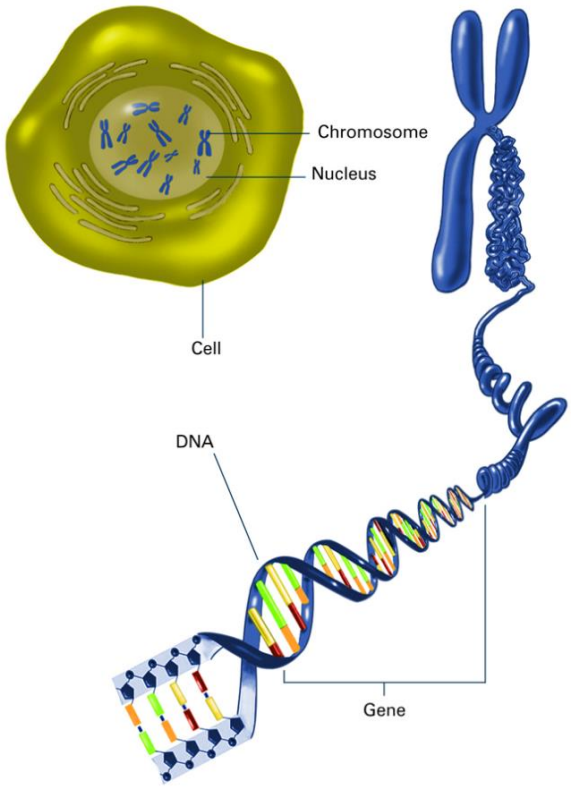
CHROMOSOMES & GENES

Chromosomes are thread like structures located inside the nucleus of animal and plant cells (see figure 3). Each chromosome is made of protein and DNA (deoxyribonucleic acid).. DNA contains the specific instructions that make each type of living creature unique (i.e. dictate the colour of our eyes, hair etc). Several sections of DNA form a gene.

We all start off in life as one single cell which contains 46 chromosomes, often referred to as 23 pairs as one gets half of the chromosomes from each parent.

During growth, the cells in our body divide to produce new cells, thus a single cell evolve into billions of cells. Not all the information in the different cells is used at once.

Inherited ataxias are caused by a defect in a certain gene in our chromosomes.



Source: National Institute of General Medical Sciences (CC BY-NC-SA3.0)

Figure 3: Cell nucleus showing where the chromosomes are kept and details of a gene

Genes are too small to be seen even with the most powerful microscope. *As* tiny as they are, genes play a powerful role. There are roughly 4000 genes on each chromosome. We have about 100,000 genes in total. We all have up to 20 defective genes in our body. Most of the time people are unaware of their defective genes.

DIAGNOSIS

When a patient presents with symptoms resembling those of ataxia it is important to be checked out by a neurologist. Generally, an evaluation will involve:

1. Medical examination
2. Blood test
3. Brain MRI to search for abnormalities in the brain and spinal cord.

Figure 4: MRI scanner

Occasionally, tests are done to rule out other possible causes of the ataxia symptoms. Tests that could be included, depends on the symptoms the person with ataxia has:

a) CT scan (a sophisticated x-ray technique for imaging of the brain and spinal cord),
b) EMG (electromyography, a test that records the electrical activity of muscle and nerve)
c) Analysis of spinal fluid

If the person has a genetic ataxia, family members are offered genetic counselling. This often helps to answer the many questions about the chances of other family members acquiring the disease.

Regarding the ataxia, it is advisable that patients find a doctor, usually it will be a neurologist, who is familiar with the ataxia or is willing to educate themselves about the ataxia. The neurologist would review the patient on a regular basis, assess disease progress, and advise about preventative care where possible and clinical trials into the ataxia. Some patients will find it helpful to have psychological counselling or to participate in support groups.

For more details on Rare Neurological Disease network please see ern-rnd.eu.

This information was reviewed by Prof Sylvia Boesch, Innsbruck, Austria, Dr Isabella Moroni, Milan, Italy and Dr Lucie Stovickova, who are all members of the European Reference Network for Rare Neurological Diseases - Project ID No. 739510