National Ataxia Foundation
Connecting Ataxia families, researchers, clinicians and the community

Gene Testing for Hereditary Ataxia

This fact sheet provided an overview of gene testing for Ataxia. It also addresses commonly asked questions about gene testing for Ataxia, and offers general guidelines for testing of the hereditary Ataxias. Keep in mind that the answers and information given here are general. Your physician and a genetic counselor should be consulted for more specific recommendations pertaining to your care and genetic testing.

What is Ataxia?

The word "Ataxia" refers to clumsiness or a loss of balance and coordination that is not due to muscle weakness, but rather a symptom of many diverse conditions that affect the nervous system. People affected by Ataxia may experience problems with using their fingers and hands, arms, legs, speaking or moving their eyes. This loss of coordination may be caused by a number of conditions. For this reason, is it important that a person with Ataxia seek medical attention to determine the underlying cause of the symptom and to receive the appropriate treatment.

What is hereditary Ataxia?

Ataxia is one of the symptoms in more than 300 hereditary conditions. However, inherited conditions where Ataxia is the primary symptom are much less common. These inherited forms of Ataxia are often referred to as "hereditary Ataxias". Hereditary Ataxia means the condition is caused by changes in genes that are inherited from parents .

What is genetic information?

We are all born with genetic instructions of how to grow and develop. We inherit our genetic information through chromosomes passed to us from out parents. We have 23 pairs of chromosomes because we receive one copy of each chromosome from our mother and one from our father. Males and females each receive 22 pairs of the same chromosomes and are called autosomal chromosomes. The 23rd pair differs between males and females and the chromosomes in this pair are called the sex chromosomes.

There are a number of different genes that can cause Ataxia and, at this time, most are located on autosomal chromosomes. Chromosomes are made up of substances known as nucleotides. These nucleotides, identified by letters, are linked together in chains. A group of nucleotides together form genes. There are thousands of genes located on each chromosome.

Many of the genes that cause dominant forms of Ataxia have a mutation resulting from expanded sections in these nucleotide chains called "trinucleotide repeat expansions." For instance, a mutation in the SCA1 gene on the sixth chromosome results in extra copies of a series of nucleotides identified by the letters C-A-G. In some conditions, the number of trinucleotide repeats is associated with the severity of the disease and the age of onset.

For which of the hereditary Ataxia is gene testing available?

Discovery of specific Ataxia genes makes it possible to develop blood tests to facilitate the diagnosis of both symptomatic individuals and at risk family members. In 1993, the first Ataxia gene was identified by a research team led by Drs. Harry Orr and Huda Zoghbi. This gene is responsible for Spinocerebellar Ataxia Type 1 (SCA1) Its discovery paved the way for the identification of many additional Ataxia genes. The list continues to grow as we discover new forms of Ataxia.

New genetic testing technologies have enabled the discovery of many new ataxia genes and the list of available tests is constantly growing.

What is the preparations for gene testing?

NAF recommends that you research your family tree and record as much health information as possible about your family, including your parents, siblings, grandparents, uncles, aunts, and cousins. Family research can help your physician as he or she tires to determine the cause of Ataxia in your family. NAF also highly recommends that you consult with a genetic counselor as you consider genetic testing for diagnostic or predictive purposes.

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A counselor can help collect your family history and discuss how Ataxia is being inherited in your family. In addition, a genetic counselor will discuss the risks, capabilities, limitations, accuracy, costs, and requirements of genetic testing. Genetic counseling should be made available to all family members because genetic testing has direct implication for the affected individual as well as other family members, particularly siblings, parents, and children.

Meeting with a genetic counselor allows you the opportunity to explore important issues such as the reason for pursing testing at this time, possible outcomes of learning the results, clarification of your support system, and appropriate timing for testing.

What are the purposes of genetic testing?

Diagnostic testing—Testing is performed when symptoms are present. The purpose of diagnostic testing it to confirm or rule out a specific hereditary Ataxia. A careful evaluation by a physician will help determine which genetic tests to perform and rule out the possibility of other medical problems. If a gene test has already shown the specific type of Ataxia present in a family, it is not necessary to test every affected person. However, if for any reason the diagnosis is uncertain in a family member, a diagnostic test will be useful. When ataxia is sporadic (there is no known family history of affected relatives), gene testing should be considered only after non-genetic causes of Ataxia have been excluded. In these cases, tests for known Ataxia genes often come back normal. However, as more genes are identified, gene tests may provide a definitive diagnosis in a greater number of cases.

Predictive testing— Testing is performed when there are no Ataxia symptom in an individual, but they are at risk of developing a known form of Ataxia. The purpose of predictive testing is to determine whether a gene mutation is present and whether your will develop symptoms or not. People elect predictive testing to help plan and prepare for their future. To be eligible for predictive gene testing, you must know which specific type of Ataxia runs in your family and be 18 years or older.

There are a number of other issues to consider before having predictive gene testing, including the possible psychological effects of the results on you or your family and the impact of results on your insurance and employment. It is best not to rush into a predictive test. Once you know the answer, you can never "unknow" it. Predictive testing will not tell you when symptoms of Ataxia will begin or how severe your symptoms will be.

Prenatal testing—Prenatal testing is another form of predictive testing. When a family has a history of a specific hereditary Ataxia, prenatal testing will determine whether the abnormal gene is present in the fetus. If you are at risk of having a child with Ataxia and are of childbearing age, NAF recommends that you talk to your physician and genetic counselor regarding reproductive options. A variety of options currently exist for couples at risk who are of hereditary Ataxia.

Pre-implantation genetic diagnosis (PDG)—Genetic screening for mutations associated with Ataxia can be performed on embryos produced through invitro fertilization . If you are at risk of having a child with Ataxia, invitro fertilization is a technology that can be used to conceive embryos outside of the body. Embryos can be tested for genetic mutations before they are implanted into the uterus. This screening process allows a couple at risk for hereditary Ataxia to greatly reduce the risk of their child inheriting the condition. In order to perform PGD, physicians will need to know the type of Ataxia that is in your family.

Exome or Genome sequencing—Some individuals have a family history of Ataxia, but diagnostic testing for known Ataxia genes cannot explain the Ataxia in their family. In recent years, scientists have developed technologies to sequence thousands of genes at the same time. This allows specialists to find Ataxia-causing genetic mutations in many families. However, since these tests provide such a large amount of genetic information, they may identify some unexpected findings in your genes.

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If you are considering exome or genome sequencing, it is important to consider the following possibilities:

- Variants of uncertain significance—Exome or genome sequencing may identify changes in genes that are difficult to interpret. In some cases, these changes may be the cause of a person's Ataxia. In other cases, these changes turn out to be normal variants. It often takes years to figure out the significance of these findings.
- Incidental findings—When looking at such a large amount of genetic information, it is possible that the results will show the presence of a genetic mutation that is not linked to Ataxia, but may provide you with information about other serious health concerns. For example, the testing may find a genetic variation that increases your risk for cancer or heart disease.
- Portions of the genome not sequenced—Current testing cannot completely analyze all of your genes. There may be variants or mutations in your genome sequencing which impacts your condition that testing will not detect.

What are the key considerations before undergoing gene testing?

If you are considering predictive gene testing of Ataxia, it is important to locate a clinic that provides the following services:

- **Genetic Counseling**—Before gene testing, a geneticist or genetic counselor should explain genetic principles important for understanding the test and its results. They should clarify what the test does and does not provide, the implication of the results, and the alternatives to genetic testing. The reasons for seeking predictive testing, in particular, are complex and the outcome of such a test (favorable or unfavorable) can potentially impact many aspects of life, including work, ability to obtain life and health insurance, and relationships with family and friends. Finally, the logistics (cost and payment, clinical protocol, resources, etc.) of a gene test should be reviewed.
- **Psychological assessment/counseling**—prior to testing, psychological evaluation is recommended to ensure the person being tested is as prepared as possible to receive the test results, and to ensure a professional , is available in the event that further support is needed after the results are given. As part of the assessment, the psychologist or psychiatrist will review support resources and stress management, as well as anticipated benefits of the gene test results. In some cases, this may be provided by a genetic counselor and does not require an additional visit to a psychologist.
- **Neurologic evaluation**—Before gene testing is ordered, the coordinating physician may choose to perform neurologic examinations, MRI scans, or other tests. It is important to be informed about the reason for the exam or tests, the possible outcomes, and the nature of information the test will provide.
- **Time**—It is wise to allow a span of time between the request for genetic testing and the actual drawing of blood to proceed with the test. This provides the opportunity to carefully consider the input from the counseling sessions before deciding to actually proceed with the test.
- **Results and follow-up**—Predictive test results favorable or unfavorable, should always be given face-to-face rather than by telephone, mail or email. Follow-up should be discussed at that time. A physician or counselor should be available, or called on, to respond to additional questions or concerns. If tests results indicate the presence of an abnormal gene, the person tested should be referred to a neurologist or Ataxia center for a baseline neurological evaluation.

Where can I find more information?

NAF does not endorse any specific physician or genetic testing center, but can help you find a health care professional in your area who can provide the services you need. Some neurologists work with a genetic counselor, and most medical schools have one or more geneticists or genetic counselors who can help you obtain more information about gene testing.

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What is GINA?

The Genetic Information Nondiscrimination Act of 2008, also referred to as GINA, is a federal law that protects Americans from being treated unfairly because of differences in their DNA that may affect their health. The law prevents discrimination from health insurers and employers. In general, Title I of GINA prohibits health plans from discriminating against covered individuals based on genetic information. "Genetic information" includes family medical history and information regarding individuals, and family members, genetic tests and genetic services. Title II of GINA prohibits employers from discriminating against employees based on genetic information. There are exceptions to this law. To find out more of what the law provides and does not provide, please visit the National Human Genome Research Institute's web site, at www.Genome.gov and select the "issues" tab.

How does the National Ataxia Foundation Help?

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. NAF has been at the forefront funding promising worldwide research to find answers.

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 e 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.

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