Understanding Alzheimer's Disease Genes

National Institute on Aging

FACT SHEET

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Many people wonder if Alzheimer's disease runs in their family. Is it in your genes? This question isn't easy to answer. Researchers have identified several genetic variants that are associated with Alzheimer's and may increase or decrease a person's risk of developing the disease. What does that mean? Let's first learn about the role of genes.

What Are Genes?

Human cells contain the instructions needed for a cell to do its job. These instructions are made up of DNA, which is packed tightly into structures called chromosomes. Each chromosome has thousands of segments called genes.

Genes are passed down from a person's biological parents. They carry information that defines traits such as eye color and height. Genes also play a role in health and disease. Variations in genes — even small changes — can affect the likelihood of a person developing a disease, such as Alzheimer's.

Do Changes in Genes Cause Diseases?

Permanent changes in one or more specific genes are called genetic variants. Some variants are quite common in the human population. While most genetic variants don't cause diseases, some do. In some cases, a person inherits a genetic variant that will almost certainly lead to that individual developing a disease. Sickle cell anemia, cystic fibrosis, and some cases of early-onset Alzheimer's are examples of inherited genetic disorders. However, other variants may simply increase or decrease a person's risk of developing that disease. Identifying genetic variants and their effects can help researchers uncover the most effective ways to treat or prevent diseases in an individual.

Additionally, factors such as exercise, diet, and smoking can have positive or negative effects by changing the way certain genes work. In the field of epigenetics, researchers are studying how such factors can alter a cell's DNA in ways that affect gene activity.

Genetic research is a component of precision medicine, an emerging approach that considers individual variability in genes, environment, and lifestyle. Precision medicine will enable researchers and doctors to predict more accurately which treatment and prevention strategies will work in particular groups of people.

Genes and Alzheimer's Disease

In most cases, Alzheimer's does not have a single genetic cause. Instead, it can be influenced by multiple genes in combination with lifestyle and environmental factors. A person may carry more than one genetic variant or group of variants that can either increase or reduce the risk of Alzheimer's.

Importantly, people who develop Alzheimer's do not always have a history of the disease in their families. Still, those who have a parent or sibling diagnosed with the disease have a higher risk of developing Alzheimer's than those who don't have a close relative with the disease.

Genetic Variants That Affect Alzheimer's Disease Risk

Scientists have identified multiple genetic regions associated with Alzheimer's. Understanding which genes play a role — and what role they play — may help identify new methods to prevent, delay, or treat dementia.

One well-known gene that influences Alzheimer's risk is the apolipoprotein E (*APOE*) gene. The *APOE* gene is involved in making a protein that helps carry cholesterol and other types of fat in the bloodstream. Problems in this process are thought to contribute to the development of Alzheimer's. *APOE* comes in several forms, called alleles (for example, *ε2* and *ε3*).

- ***APOE ε2*** may provide some protection against the disease. If Alzheimer's occurs in a person with this allele, it usually develops later in life than it would in someone with *APOE ε4*. Roughly 5% to 10% of people have this allele.
- ***APOE ε3***, the most common allele, is believed to have a neutral effect on the disease — neither decreasing nor increasing risk of Alzheimer's.
- ***APOE ε4*** increases risk for Alzheimer's and is associated with an earlier age of disease onset in certain populations. About 15% to 25% of people have this allele, and 2% to 5% carry two copies. Having two copies of *APOE ε4* is associated with a higher risk of Alzheimer's than having one copy. While inheriting *APOE ε4* increases a person's risk of Alzheimer's, some people with an *APOE ε4* allele never develop the disease.

Researchers are also finding other genetic variants, in addition to *APOE ε2*, that appear to provide some protection against developing Alzheimer's.

The prevalence of *APOE* alleles and other genetic variants, and the risk associated with these genetic changes, may not be the same across all population groups. Research suggests that the degree of risk may be affected by genetic ancestry — the global geographic region from which a person is biologically descended — and differ among people of African, Asian, American Indian, and European descent.

More research is needed to better understand how certain genetic variants might affect a person's or group's risk for Alzheimer's and to identify treatment and prevention strategies that will work best for that particular group.

Genetic Variants That Cause Alzheimer's Disease

Of the genetic variants so far associated with Alzheimer's, three rare single-gene variants are known to cause the disease:

- Amyloid precursor protein (***APP***) on chromosome 21
- Presenilin 1 (***PSEN1***) on chromosome 14
- Presenilin 2 (***PSEN2***) on chromosome 1

A person who inherits a variant in one of these genes has a very strong probability of developing Alzheimer's before age 65 and sometimes much earlier. When someone develops Alzheimer's before age 65, it is known as "early-onset Alzheimer's" or sometimes "younger-onset Alzheimer's" or "earlier-onset Alzheimer's." Less than 10% of all people with Alzheimer's develop symptoms this early. Of those who do, 10% to 15% can be attributed to changes in *APP*, *PSEN1*, or *PSEN2*.

People with Down syndrome also have a higher risk of developing early-onset Alzheimer's. This is because they have an extra copy of chromosome 21, which carries the *APP* gene. Estimates suggest that 50% or more of people living with Down syndrome will develop Alzheimer's, with symptoms appearing in their 50s or 60s.

Genetic Testing for Alzheimer's Disease

Genetic tests are not routinely used in clinical settings (such as a doctor's office or hospital) to diagnose or predict the risk of developing Alzheimer's or a related dementia. In some cases, if a person has symptoms at an early age with a strong family history of Alzheimer's, a neurologist or other medical specialist may order a genetic test for *APP*, *PSEN1*, and *PSEN2*.

Although *APOE* testing is also available, the results can't fully predict who will or won't develop Alzheimer's. Rather, this type of testing is used primarily in research settings to identify study participants who may have an increased risk of developing Alzheimer's. This approach helps scientists look for early brain changes and compare the effectiveness of possible treatments for people with different *APOE* alleles.

Some people learn their *APOE* status through consumer genetic testing. While at-home genetic tests are convenient, people considering them can benefit from talking with a doctor or genetic counselor to better understand this type of test and their results.

Alzheimer's Genetics Research

Discovering as much as possible about the role of Alzheimer's genetic risk and protective factors across populations is an important area of research. NIA funds several major genetics research programs. Understanding more about the genetic basis of the disease will help researchers:

- Answer a number of basic questions, such as: What makes the disease process begin? Why do some people with memory and other thinking problems develop Alzheimer's while others don't?
- Determine how genetic risk and protective factors may interact with other genes and lifestyle or environmental influences to affect Alzheimer's risk in an individual.
- Identify people who are at high risk of developing Alzheimer's so they can benefit from new interventions and treatments as much and as soon as possible.
- Explain differences in Alzheimer's risks and protections among racial groups and genders.
- Use individual gene discoveries to develop potential therapies to prevent or treat the disease.

Research needs volunteers of all different races, ethnicities, ancestries, ages, and genders to participate in clinical trials and studies. If you're interested in participating in Alzheimer's research, talk with a doctor or search the Alzheimers.gov Clinical Trials Finder at **www.alzheimers.gov/clinical-trials**.

For More Information

NIA Alzheimer's and related Dementias Education and Referral (ADEAR) Center
800-438-4380
adear@nia.nih.gov
www.nia.nih.gov/alzheimers

The NIA ADEAR Center offers information and free print publications about Alzheimer's and related dementias for families, caregivers, and health professionals. ADEAR Center staff answer telephone, email, and written requests and make referrals to local and national resources.

Alzheimers.gov
www.alzheimers.gov

Explore the Alzheimers.gov website for information and resources on Alzheimer's and related dementias from across the federal government.

ClinicalTrials.gov
www.clinicaltrials.gov

MedlinePlus — National Library of Medicine
www.medlineplus.gov

National Human Genome Research Institute
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