TriHealth

Precision Medicine

Genetics of Alzheimer's Disease

What is Alzheimer's disease and what's my risk?

Alzheimer's disease (AD) is the most common cause of dementia. The main features are memory loss, disorientation, and mood or behavior changes that worsen over time. In the general population, the lifetime risk of developing AD is 10-12%. Age is the strongest risk factor for developing the disease. Regarding family history, a person with a first degree relative with AD (parent, sibling) has about a two to three times higher risk of developing the illness compared to someone without a family history.

Is Alzheimer's disease genetic?

There are two types of AD:

- Early onset Alzheimer's disease (EOAD) - diagnosed before age 65 – accounts for 1-5% of all AD cases
- Late onset Alzheimer's disease (LOAD) - diagnosed at age 65 or later – the predominant form of AD

Family history of AD may be consistent with sporadic, familial, or autosomal dominant AD.

- Sporadic AD (75% of all cases) is characterized by an isolated case in the family. The AD occurred sporadically or randomly.
- Familial AD (15-25% of all cases) is characterized by disease that occurs in more than 1 individual in a family. The AD in the family happened due to an interaction between environmental and minor genetic factors (multifactorial).
- Autosomal dominant AD (<5% of all cases) is characterized by disease that occurs in at least 3 individuals in two or more generations. The AD in the family is caused by pathogenic variants or mutations in one of three genes: *APP*, *PSEN1*, or *PSEN2*.

One of the well-known genes that influences AD risk is the *APOE* gene. Problems in this gene can contribute to the development of AD. *APOE* comes in several forms, called alleles (e2, e3, e4). Each person inherits two *APOE* alleles, one from each biological parent. The *APOE* e4 allele increases the risk for AD, but does not guarantee one will develop AD. About 25% of the general population will have one e4 allele.

What are my options for genetic testing for Alzheimer's disease?

For unaffected individuals: Genetic testing for sporadic or familial AD provides limited information about a person's chances of developing or preventing the disease. *APOE* variant testing is not recommended due to limited usefulness in medical care. If you have a relative with a known mutation in *APP, PSEN1, or PSEN2*, predictive genetic testing can be considered only after pre-test counseling in a specialized clinic that includes a neurologic evaluation.

For individuals concerned they have dementia-like symptoms: In order to consider genetic testing for AD, you must have a diagnosis. Please ask your primary care physician to refer you to a neurologist for an evaluation.

For individuals diagnosed with Alzheimer's disease: Your neurologist may refer you for *APOE* genetic testing depending on their treatment recommendations. Genetic testing for early onset AD can be considered and discussed with a genetic counselor. Please ask your neurologist about a receiving a referral.

Additional Resources:

https://www.alz.org/alzheimers-dementia/what-is-alzheimers/causes-and-risk-factors/genetics
https://www.nia.nih.gov/health/alzheimers-disease-genetics-fact-sheet

References:

Goldman JS, Hahn SE, Catania JW, et al. Genetic counseling and testing for Alzheimer disease: joint practice guidelines of the American College of Medical Genetics and the National Society of Genetic Counselors [published correction appears in Genet Med. 2011 Aug;13(8):749]. Genet Med. 2011;13(6):597-605. doi:10.1097/GIM.0b013e31821d69b8

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