

How to Know if You Have a Genetic Risk for Alzheimer's

Chris Hemsworth recently revealed that he's predisposed to dementia. Here's how to find out if you're at risk — and what to do if you are.

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The actor Chris Hemsworth announced last week that he's taking a break from acting to focus on his health. The news came after Mr. Hemsworth learned through genetic testing that he has two copies of the APOE4 gene variant, which is associated with increased odds of developing Alzheimer's disease, the most common form of dementia. The 39-year-old star of "Thor" has not reported having any symptoms, but he told Vanity Fair that he wanted to focus on mitigating his risk as much as possible.

Should you, like Mr. Hemsworth, undergo genetic testing to assess your risk for Alzheimer's? And if you have the variant, what options are available to prevent or delay the condition? Here's what to know.

What is APOE4?

The APOE gene is important for the formation of a protein that helps carry cholesterol through the bloodstream. Nearly 30 years ago, scientists learned that APOE also influences a person's chances of developing Alzheimer's.

There are three variants of the gene, each conferring a different risk. People with the APOE2 variant appear to have a decreased risk of Alzheimer's; the APOE3 variant — the most common type — is "neutral," meaning it does not increase or decrease risk; and the APOE4 variant raises a person's risk. Everyone has two versions of the gene, one inherited from their mother and one from their father.

About 25 percent of people carry one APOE4, increasing their chance of developing Alzheimer's by two or three times. Another 2 to 3 percent of people have two copies of APOE4, as Mr. Hemsworth does. This is associated with a roughly 10-fold higher risk. Having APOE4 is also linked to earlier onset of the disease.

Scientists aren't exactly sure why a gene involved in capturing cholesterol plays such a large role in Alzheimer's disease. It's possible that changes in cholesterol can damage brain cells or cause inflammation in the brain, which could lead to dementia.

Having the APOE4 gene variant, either one or two copies, does not mean you will definitely get Alzheimer's disease. Some conditions, such as Huntington's disease, are directly caused by a specific gene mutation. Alzheimer's disease and APOE4 don't work like that. The gene is just one factor that contributes to people's risk. Some people with the gene variant are never diagnosed with the disease, and many people without APOE4 develop Alzheimer's.

How do you know if you have the APOE4 variant?

If you're interested in knowing your status, you can ask your doctor or a genetic counselor about getting tested. You can also order a kit directly from 23andMe, which includes APOE4 on its health panel. However, Alzheimer's experts are divided about whether testing for the gene is helpful for most people.

"Generally, in my clinical practice, I dissuade people from getting the test and getting the information," said Dr. Gary Small, chair of psychiatry at Hackensack University Medical Center in New Jersey. If you have a family history of dementia, you should assume you have an increased risk, he said, "so getting the genetic test is not going to tell you much more."

Dr. Richard Isaacson, an adjunct associate professor of neurology at Weill Cornell Medical College, disagreed. "The reason that I believe in testing for APOE4 is that some people really want to know more about themselves, and it really democratizes the ability to learn about those risks," he said. "Not about if they're going to get the disease, but what we can do about it."

If you do decide to get tested, Margaret Pericak-Vance, director of the John P. Hussman Institute for Human Genomics at the University of Miami Miller School of Medicine, said she would "suggest having a meeting with a genetic counselor afterward, because the risk is not straightforward."

"By having one copy or two copies, it gives you an important part of the picture, but it's

just one part of a very complex risk picture,” Dr. Isaacson said. “Genes are not your destiny. You can win the tug of war against your genes.”

How can you reduce your chance of getting Alzheimer’s?

All the experts interviewed for this article agreed that regardless of your genetic status, it is possible to reduce your overall risk of dementia, including Alzheimer’s. Studies show that tried and true healthy habits — exercise, eating well, limiting your alcohol intake, getting enough sleep, not smoking and being socially engaged — are key to fending off neurodegenerative disease.

Exercise, both endurance and strength training, helps the brain grow new connections between cells, particularly in the hippocampus, an area important for memory. Scientists think that building up more connections can be protective against memory loss. Dr. Small said that if you have the APOE4 variant, “physical exercise still can be helpful. There’s some studies showing that may even be more helpful for people with a genetic risk.”

There’s also evidence that a healthy diet, such as the Mediterranean diet, can be beneficial. In particular, it helps to eat fruits and vegetables, which are high in antioxidants, and fish, which contain omega-3 fats that can reduce inflammation. “These kinds of diets can have a tremendous effect on brain health,” Dr. Small said.

While the importance of vitamins and healthy fats in your diet is clear, the case for taking supplements for brain health is weak. Dr. Isaacson said that a person’s genes may play a role in whether supplements can be beneficial. For example, research suggests that people with two copies of APOE4 can’t absorb omega-3 fats from their diet as well as people without the genetic variant. Taking an omega-3 supplement may be advantageous for that specific group of people, but likely isn’t helpful for others, he said.

Finally, higher education has consistently been shown to be one of the best ways to lower a person’s risk for dementia. The hypothesis is that education helps people’s brains become more resilient, a concept known as cognitive reserve. Even if there are visible changes to a person’s brain, the more education they have, the less likely they are to display dementia symptoms. “If you look at numerous studies, level of education is correlated with lower risk, even within families,” Dr. Pericak-Vance said. “It all has to do with cognitive reserve. You build up more cognitive reserve the more schooling you get.”

Studies on identical twins, who share nearly all the same genes, have shown just how much lifestyle behaviors influence brain health. In one of the largest studies of its kind, which looked at 392 pairs of twins aged 65 and up where one or both had Alzheimer’s

disease, genes accounted for 58 percent of a person's risk. The rest depended on lifestyle and environmental factors.

Who else is at risk for developing Alzheimer's?

Age is the number one risk factor for Alzheimer's disease. As we get older, chronic diseases associated with aging — such as high blood pressure, high cholesterol and diabetes — start to take their toll on the brain as well as the body.

Women are more likely than men to get Alzheimer's, for multiple possible reasons. Women generally live longer than men, so they might have more time to develop the condition. Historically, women did not receive as much education as men, which experts surmise could have increased the risk for earlier generations. There also appears to be an interplay between the loss of estrogen during menopause and Alzheimer's; research is ongoing into whether hormone replacement therapy could be beneficial.

Black and Latino Americans also have an elevated risk for Alzheimer's — two- and 1.5-times higher than white Americans. One recent study found that the brains of Black Americans aged faster than white Americans' brains, with more neurodegeneration at an earlier age, which could contribute to risk of disease. The authors theorize that one reason for these disparities is the additional stress Black and Latino Americans experience because of systemic racism.

Race also appears to play a role in the risk associated with the APOE4 variant. People of Asian descent have the greatest increased risk of developing Alzheimer's if they have APOE4, while people of African descent with APOE4 have the lowest elevated risk. Dr. Pericak-Vance said this is likely because of differences in the DNA that surrounds the APOE gene and influences how it acts.

If you think you have an elevated risk of Alzheimer's, either because of your genes or other factors, Dr. Isaacson recommended talking to your doctor sooner rather than later. And regardless of your individual risk, everyone can benefit from incorporating more healthy habits, he said. "It's almost never too early, in my opinion, to adopt brain-healthy choices."