

People with increased genetic risk of Alzheimer's may lose sense of smell first, research suggests

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People who carry the gene variant associated with the strongest risk for Alzheimer's disease may lose their ability to detect odors earlier than

people who do not carry the gene variant, which may be an early sign of future memory and thinking problems, according to a study published in the July 26, 2023, online issue of *Neurology*. The gene variant associated with this increased risk of Alzheimer's is called APOE e4.

"Testing a person's ability to detect odors may be a useful way to predict future problems with cognition," said study author Matthew S.

GoodSmith, MD, of the University of Chicago. "While more research is needed to confirm these findings and determine what level of smell loss would predict future risk, these results could be promising, especially in studies aiming to identify people at risk for dementia early in the disease."

The study involved an at-home survey that included testing the [sense of smell](#) of over 865 people—both their ability to detect an odor at all and their ability to identify what odor they were smelling. Tests were given at five-year intervals. People's thinking and memory skills were also tested twice, five years apart. DNA samples gave researchers information about who carried the gene associated with an increased risk of Alzheimer's.

For the test to see if people could detect odors, scores ranged from zero to six based on how many of the different concentrations of odors they could smell.

People who carried the gene variant were 37% less likely to have good odor detection than people without the gene at a single timepoint.

Researchers accounted for other factors that could affect the results, such as age, sex, and [educational level](#). The gene carriers started experiencing reduced smell detection at age 65 to 69. At that age, the gene carriers could detect an average of about 3.2 of the smells, compared to about 3.9 smells for the people who did not carry the gene.

The people carrying the gene variant did not show a difference in their ability to identify what [odor](#) they were smelling until they reached age 75 to 79. Once they started to lose their ability to identify odors, the gene carriers' ability declined more quickly than those who did not carry the gene.

Thinking and [memory skills](#) were similar among the two groups at the start of the study. But as expected, those carrying the [gene variant](#) experienced more rapid declines in their thinking skills over time than those without the gene.

"Identifying the mechanisms underlying these relationships will help us understand the role of smell in neurodegeneration," GoodSmith said.

A limitation of the study is that people with severe dementia were not included.

More information: Matthew S. GoodSmith et al, Association of APOE ϵ 4 Status With Long-term Declines in Odor Sensitivity, Odor Identification, and Cognition in Older US Adults, *Neurology* (2023). DOI: 10.1212/WNL.0000000000207659 , doi.org/10.1212/WNL.0000000000207659

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