New method could aid Alzheimer's research by predicting risk before symptoms start

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Researchers have developed a new method to identify people who are at greater genetic risk of developing Alzheimer's disease before any symptoms appear—which could help speed creation of novel treatments. Manish Paranjpe of the Broad Institute of MIT and Harvard in Cambridge, Massachusetts, United States, and colleagues present these findings in the open-access journal *PLOS Genetics* on September 1.

People with Alzheimer's disease experience gradual loss of memory and other cognitive functions. While some treatments can ease symptoms, it has been challenging to develop treatments to prevent or slow disease progression. Some clinical trials investigating potential treatments may have been unsuccessful because they involved patients whose disease was too advanced to be treated. Better methods to identify people at high risk of developing Alzheimer's could aid treatment research.

To help meet that need, Paranjpe and colleagues analyzed data on 7.1 million common DNA variants—alterations to the standard DNA sequence—from an earlier study that included tens of thousands of people with or without Alzheimer's. They used this data to develop a novel method that predicts a person's risk of Alzheimer's, depending on which DNA variants the person has. Then, they refined and validated the method with data from more than 300,000 additional people.

The researchers note that their DNA-based method is unlikely to be suitable for doctors to predict a patient's risk of Alzheimer's because it may be less accurate for non-European populations, it could impact insurance, and it could cause anxiety without the relief of reliable preventive treatments. However, it could be applied to speed Alzheimer's research.

To demonstrate the potential of the new method, the researchers applied it to determine the risk of Alzheimer's for each of 636 blood donors and examined whether blood levels of any of 3,000 proteins were higher or lower than normal for those identified as being high-risk. The analysis surfaced 28 proteins that could be linked to Alzheimer's risk, including several that have never been studied in Alzheimer's research. Studying these proteins could uncover new directions for drug development.

Future research could help replicate and confirm these findings and expand on them, such as by considering populations with non-European ancestry.

Senior author Dr. Amit V. Khera adds, "We developed a genetic predictor of Alzheimer's disease associated with both clinical diagnosis and age-dependent cognitive decline. By studying the circulating proteome of healthy individuals with very high versus low inherited risk, our team nominated new biomarkers of neurocognitive disease."

Provided by Public Library of Science

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