

## New evidence ties gene to Alzheimer's

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Of dozens of candidates potentially involved in increasing a person's risk for the most common type of Alzheimer's disease that affects more than 5 million Americans over the age of 65, one gene that keeps grabbing Johns Hopkins researchers' attention makes a protein called neuroglobin.

Adding to a growing body of evidence about the importance of this protein for the health of the aging [brain](#), researchers at the McKusick-Nathans Institute of Genetic Medicine of the Johns Hopkins University School of Medicine canvassed the genetic neighborhood of neuroglobin and, for the first time in a human population, linked variation there with a risk for Alzheimer's.

Ever so slight genetic variations between individuals can and do influence the amounts of particular proteins that each specific gene ultimately produces. In this case, the team has found that individuals with genetic variations equating to less neuroglobin production have an increased risk for Alzheimer's.

"An intriguing part of this study was the high levels of neuroglobin that we found in the Alzheimer's brain, which was exactly the opposite from what we expected," says Dimitrios Avramopoulos, M.D., Ph.D., an associate professor in Hopkins' Institute of Genetic Medicine and the Department of Psychiatry.

Referring to data published in *Neurobiology of Aging*, Avramopoulos explains that his team measured levels of gene product in 56 different

samples of human [brain tissue](#): 30 from confirmed cases of Alzheimer's and 26 without brain disease.

The scientists found that neuroglobin levels decreased with advancing age, which, Avramopoulos points out, is consistent with risk of Alzheimer's increasing with advancing age. They also found that levels of neuroglobin were lower in women than in men, which is consistent with the fact that women have a slightly higher risk of Alzheimer's. About two times as many patients in the general population with Alzheimer's are women which, in part, can be attributed to the fact that women live longer and therefore have more of a chance to get Alzheimer's. Having corrected for that disparity, researchers have noted a slightly higher risk in women than in men.

They were surprised to find that neuroglobin levels were higher in the brain tissue from Alzheimer's patients than that of the control group.

Counter-intuitive though it seemed at first, it actually makes sense, Avramopoulos says, especially in light of previously published studies that indicated a protective function for neuroglobin and showed that mouse brains respond to stress — in this case, a lack of oxygen — by producing more neuroglobin.

The scientists think that neuroglobin production also ramps up in reaction to the insult of the [Alzheimer's disease](#). They hypothesize that maybe in some people it's simply not enough of a protective response to effectively defend the brain.

"The older we get, the less neuroglobin this particular gene produces in our brains — unless something stimulates the gene to produce more," Avramopoulos explains. "That something could be a stressor such as a lack of oxygen resulting from stroke or emphysema, for instance. And it looks like it also could be Alzheimer's disease."

"Further work on this gene will likely provide intervention targets for a multitude of very common conditions including Alzheimer's."

Source: Johns Hopkins Medical Institutions

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