

Study suggests earliest brain changes associated with the genetic risk of Alzheimer's disease

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What are the earliest brain changes associated with the risk of developing Alzheimer's disease? A scientific report published in the October *Journal of Alzheimer's Disease* finds reduced activity of an energy-generating enzyme in deceased young adult brain donors who carry a common genetic risk factor for Alzheimer's disease—before the protein changes or microscopic abnormalities commonly associated with the disease and almost five decades before the age at which they might have developed memory and thinking problems.

Arizona researchers studied tissue from a vulnerable part of the brain in 40 young adults who had died and donated their brains for research. 15 of the brain donors carried a common [genetic risk](#) factor for [Alzheimer's disease](#), known as APOE4, and 25 of the brain donors did not. With the exception of a person with two copies of the APOE4 gene, none of the deceased young adults had the microscopic abnormalities or elevated amyloid protein levels long associated with Alzheimer's disease. However, the activity of an enzyme known as cytochrome oxidase, an energy-making enzyme found in the power-packs of the brain cells, was slightly reduced in the group at increased genetic risk for Alzheimer's disease.

A team of researchers from several institutions in the Arizona Alzheimer's Consortium had previously used a brain imaging technique called PET to detect reduced brain activity in living young adults at

genetic risk for Alzheimer's disease. They had also shown reductions in cytochrome oxidase activity and the expression of energy-making genes in deceased brain donors with Alzheimer's symptoms. Based on these findings, they had proposed that individuals at genetic risk for Alzheimer's disease might have alterations in energy utilization, or some other abnormality in the mitochondria (the power packs inside each cell) long before the progressive [brain](#) changes associated with Alzheimer's disease had even started.

"Our findings suggest that mitochondrial [brain changes](#) contribute to the risk of Alzheimer's disease," said Jon Valla, Assistant Professor of Biochemistry at Midwestern University and the study's lead author. He conducted the cytochrome oxidase activity analysis at the Barrow Neurological Institute. "While our findings do not suggest ways in which to predict or reduce a person's risk at this time, they provide a foundation for studies seeking to do just that."

Provided by IOS Press

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