

Where did you get those eyes and that brain?

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A family history of Alzheimer's disease significantly increases the risk for developing this disorder, but a new study in *Biological Psychiatry* suggests that which of your parents has the disease is very important.

Alzheimer's is the most common form of <u>dementia</u> in late-life, affecting over 5 million elderly in the United States alone. In order to develop preventative treatments, it is necessary to identify those individuals who are at highest risk for developing Alzheimer's.

Although individuals with a parental history of Alzheimer's are at increased risk for developing the disease, the specific biological and genetic mechanisms accounting for this increased risk are not known.

An important consideration may be a phenomenon called genomic imprinting, where the pattern of the inherited disease differs based on whether the risk genes are inherited from the mother or the father. Imprinting is a type of epigenetic regulation, meaning that long lasting changes in gene function are produced through regulatory mechanisms rather than by altering the sequence of the <u>DNA</u>.

In this new study, researchers set out to evaluate Alzheimer's risk in healthy, cognitively normal individuals by measuring their cerebrospinal fluid proteins, which are known to be altered in Alzheimer's. They compared individuals with a maternal or paternal history of Alzheimer's to individuals with no family history.

Only individuals whose mothers had Alzheimer's showed altered levels



of a protein called amyloid, a major hallmark of Alzheimer's pathology, as well as proteins involved with oxidative stress (i.e., free radicals, which are harmful to the brain as well as the rest of the body). In contrast, individuals whose fathers had Alzheimer's and those with no family history had protein levels within normal range.

"Our data indicate that adult children of mothers with Alzheimer's may be at increased risk for developing the disease," explained Dr. Lisa Mosconi, the first author on the study. "It is therefore extremely important to understand the genetic mechanisms involved in maternal transmission of Alzheimer's disease, which are currently unknown. Identifying a genetic predictor for the disease might lead to preventive treatments years before the onset of clinical symptoms."

Dr. John Krystal, Editor of <u>Biological Psychiatry</u>, added: "This study is very important because we are just beginning to understand the epigenetic control of particular genes. In theory, some day, one might develop a medication that reduces the risks associated with a maternal history of Alzheimer's disease."

The authors cautioned that additional follow-up research is now needed to test the usefulness of these <u>protein</u> measures for predictive purposes and to investigate potential susceptibility genes for Alzheimer's disease.

More information: The article is "Oxidative Stress and Amyloid-Beta Pathology in Normal Individuals with A Maternal History of Alzheimer's" by Lisa Mosconi, et al. The article appears in *Biological Psychiatry*, Volume 68, Issue 10 (November 15, 2010)

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