

A maternal link to Alzheimer's disease

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People who have a mother with Alzheimer's disease appear to be at higher risk for getting the disease than those individuals whose fathers are afflicted, according to a new study by NYU School of Medicine researchers.

The study is published in this week's online edition of the *Proceedings of the National Academy of Sciences*. It is the first to compare brain metabolism among cognitively normal people who have a father, a mother, or no relatives with Alzheimer's disease, and to show that only individuals with an affected mother have reduced brain metabolism in the same brain regions as Alzheimer's patients.

Over the last two decades a number of studies have shown that people with the disease have significant reductions in brain energy metabolism in certain regions of the brain. In some recent research studies these reductions are evident in healthy people years before symptoms of dementia emerge.

The researchers wanted to evaluate people with a family history of Alzheimer's because that is one of the biggest risk factors for the disease. Alzheimer's affects more than 5 million Americans and is the most common form of senile dementia. People with an affected parent have a 4- to 10-fold higher risk compared to individuals with no family history. It isn't known why people with a family history are more susceptible to the disease.

Likewise, it isn't known why individuals with a history of the disease on their mother's side are at increased risk for Alzheimer's, and this observation must be replicated in larger studies before it could be of use in the clinic to perhaps identify people who may be more vulnerable to the disease, says Lisa Mosconi, Ph.D., Research Assistant Professor of Psychiatry at NYU School of Medicine, who led the new study. She speculates that genes that are maternally inherited might alter brain metabolism.

The new study involved 49 cognitively normal individuals, from 50 to 80 years old, who underwent a battery of neuropsychological and clinical tests, and PET (positron emission tomography) scans of their brains using a technique that labels glucose—the brain's fuel—with a special chemical tracer. Sixteen subjects had a mother with the disease, and eight had a father with Alzheimer's. The remaining subjects didn't have a family history of the disease.

People with a maternal history of the disease had the largest reductions in glucose metabolism in several areas of the brain, including the medial temporal lobes and the posterior cingulate cortex, two brain regions involved with memory storage and retrieval. Brain energy metabolism was reduced by 25 percent in the posterior cingulate cortex in this group.

There weren't any reductions in brain energy metabolism in the people without a family history and in those with a father who had the disease. The effects in glucose metabolism among subjects with a maternal history remained significant after accounting for possible risk factors for Alzheimer's, including age, gender, education, Apolipoprotein E genotype, and subjective memory complaints.

"This is a preliminary study and the results have to be replicated," says Dr. Mosconi. "What we need even more is to follow subjects over time until they develop clinical symptoms, and we really need to assess whether the metabolic reductions predict and correlate with disease progression," she says.

"Energy metabolism hasn't been a major focus of research in Alzheimer's, so we hope that this study will stimulate further discussion on brain activity and disease risk, which could also be important for planning targeted therapeutic interventions," says Dr. Mosconi.

"This is an intriguing finding," says Mony de Leon, Ed.D., Professor of Psychiatry and Director of the Center for Brain Health at NYU School of Medicine.

"It points to the need for more research to investigate the mechanisms of maternal transmission of this observed glucose metabolism deficit as well as to learn of any direct or indirect relationship to Alzheimer's disease," said Dr. de Leon.

Source: New York University Medical Center

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