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NEWS

RSNA Press Release

Gene Variation Associated with Brain Atrophy in Mild Cognitive Impairment

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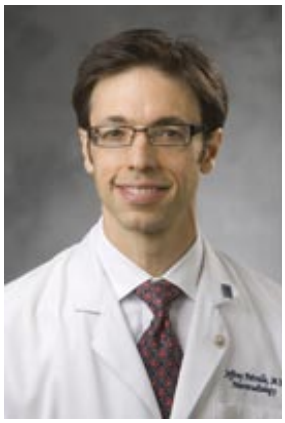
At A Glance

- A gene variant in people with mild cognitive impairment (MCI) is associated with accelerated rates of brain atrophy.
- Analyzing data from the Alzheimer's Disease Neuroimaging Initiative, researchers used MRI to measure brain atrophy rates in 237 patients with MCI over a 12- to 48-month period.
- The researchers hope the findings will aid in developing and testing drugs that modify the Alzheimer's disease process.

OAK BROOK, Ill. – The presence of a gene variant in people with mild cognitive impairment (MCI) is associated with accelerated rates of brain atrophy, according to a new study published online in the journal *Radiology*.

The study focused on the gene apolipoprotein E (APOE), the most important genetic factor known in non-familial Alzheimer's disease (AD). APOE has different alleles, or gene variations, said the study's senior author, Jeffrey R. Petrella, M.D., associate professor of radiology at Duke University School of Medicine in Durham, N.C.

"We all carry two APOE alleles, and most people have at least one copy of the APOE epsilon 3 (ε3) variant, which is considered neutral with respect to Alzheimer's risk," Dr. Petrella said.


Jeffrey R. Petrella, M.D.

The less common epsilon 4 (ε4) allele, in contrast, is associated with a higher risk for development of AD, earlier age of onset, and faster progression in those affected, as compared with the other APOE alleles.

Dr. Petrella and colleagues recently analyzed data from the Alzheimer's Disease Neuroimaging Initiative (ADNI) involving 237 patients, mean age 79.9, with MCI, a slight but noticeable decline in cognitive ability that is tied to a higher risk of AD. The researchers used MRI to measure brain atrophy rates in these patients over a 12- to 48-month period.

The ε4 carriers in the study group exhibited markedly greater atrophy rates than ε3 carriers

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in 13 of 15 brain regions hypothesized to be key components of the cognitive networks disrupted in AD.

"The results showed atrophy in brain regions we know are affected by AD, in a population of patients who do not have AD, but are at risk for it," Dr. Petrella said. "This suggests the possibility of a genotype-specific network of related brain regions that undergo faster atrophy in MCI and potentially underlies the observed cognitive decline."

The researchers did not explore why APOE ε4 might accelerate atrophy, but the affect is likely due to a combination of factors, noted Dr. Petrella.

"The protein has a broad role in the transport and normal metabolism of lipids and a protective function on behalf of brain cells, including its role in the breakdown of beta-amyloid, one of the proteins implicated in the pathophysiology of AD," he said.

With MRI playing an increasingly prominent role in MCI research, Dr. Petrella predicted that increased knowledge about the effects of APOE will improve the design and execution of future clinical trials. For instance, researchers could enrich their samples with ε4 patients in MCI prevention trials to better determine potential treatment effects on brain regions vulnerable to degeneration.

The advances in knowledge will also help expand the role of MRI measures in clinical trials investigating novel drugs with potentially disease-modifying capabilities.

"Current FDA-approved drugs treat symptoms, but don't modify the underlying cause of the disease," Dr. Petrella said. "We want to make continued inroads toward the goal of developing and testing drugs that modify the disease process itself."

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"Mapping the Effect of the Apolipoprotein E Genotype on 4-Year Atrophy Rates in an Alzheimer's Disease-related Brain Network." Collaborating with Dr. Petrella were Christopher A. Hostage, M.D., Kingshuk Roy Choudhury, Ph.D., and P. Murali Doraiswamy, M.B.B.S., FRCP. For the Alzheimer's Disease Neuroimaging Initiative.

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