

# Researchers connect gene to pre-Alzheimer's

Cornell University

Cornell scientists have shown a significant correlation for the first time between a human gene and people's risk for mild cognitive impairment (MCI), often a precursor to Alzheimer's disease and related forms of dementia.

The findings could help doctors to recommend simple preventative measures for at-risk patients, including healthy diet, exercise and intellectual activity -- all of which could forestall and even prevent chronic symptoms associated with the disease, said lead author Charles Brainerd and Valerie Reyna, professors of human development in Cornell's College of Human Ecology.

The professors, with researchers at the Mayo Clinic in Rochester, Minn., linked the  $\epsilon 4$  allele of the apolipoprotein E (APOE) genotype to a greater likelihood of the onset of MCI in the July 4 issue of the journal *Neuropsychology*.

"We're excited about these findings, because they help identify the segment of the population who will most benefit from effective treatments to prevent Alzheimer's-type dementia," Brainerd said.

The clinical applications of linking this genetic marker with MCI are far-reaching, Brainerd said, because genetic testing can now be added to the neuropsychological tests that are currently the only way to identify MCI.

"What is at stake is whether genetic testing is useful for determining MCI susceptibility and candidacy for treatments that are designed to prevent or forestall/treat MCI (and therefore prevent Alzheimer's dementia)," the authors write. "If not, neuropsychological testing remains the only reliable means of identification."

Prior studies have been inconclusive owing to limits of their subject populations. In the new study, the researchers identified the link between the  $\epsilon 4$  allele and the risk of MCI by analyzing a large data set from the National Institute on Aging, the Health and Retirement Study (HRS), that accurately represents older adults from all regions and racial and ethnic groups in the United States.

Classifying subtypes of MCI was also critical to the study's success. Led by Dr. Ronald C. Petersen and Glenn E. Smith at the Mayo Clinic, the authors successfully identified subtypes of MCI, only one of which is the precondition for Alzheimer's. The paper outlines how criteria for the different MCI subtypes developed by the Mayo researchers helped control for errors that have plagued previous studies that have attempted to identify an  $\epsilon 4$ -MCI link.

By sorting the HRS subjects who have the  $\epsilon 4$  gene into subtypes of impairment identified in Petersen's and Smith's work, the Cornell researchers were able to show

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a significant correlation the  $\epsilon 4$  gene and risk of the Alzheimer's precondition, known as amnesic MCI (or a-MCI). The results specifically show that 32 percent of study subjects who had been diagnosed as a-MCI were carriers of the  $\epsilon 4$  APOE biomarker, as compared to only 20 percent of study subjects who had been diagnosed as normal and healthy.

The Cornell part of the research was supported by the National Institutes of Health.

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