MedicalXpress

Study shows that major Alzheimer's risk gene causes alterations in shapes of brain protein deposits

July 14 2010

Researchers at Mount Sinai School of Medicine have used a newly discovered class of biomarkers to investigate the possibility that the shape of brain protein deposits is different in people with Alzheimer's who have the highest-risk gene type than in those with the condition who have a neutral risk gene type. The study is being presented July 14 at the 2010 Alzheimer's Association International Conference on Alzheimer's Disease in Honolulu, Hawaii.

Sam Gandy, MD, PhD, the Mount Sinai Professor in Alzheimer's Disease Research, Professor of Neurology and Psychiatry, and Associate Director of the Alzheimer's Disease Research Center at Mount Sinai School of Medicine, led the study. Mount Sinai labs led by Patrick R. Hof, MD, Regenstreif Professor of Neuroscience and Vice-Chair for Translational Neuroscience of the Department of Neuroscience and Dara L. Dickstein, PhD, Assistant Professor, Neuroscience also collaborated on the study.

Apolipoprotein E (APOE) is a gene containing instructions needed to make a protein that helps carry cholesterol in the bloodstream. The APOE gene, which comes in several different forms, is related to increased risk of developing Alzheimer's disease. People with APOE ε4/ε4 gene type have the highest risk of developing the disease and people with APOE ε3/ε3 have a neutral risk. Discovering the important mechanisms underlying how APOE ε4/ε4 increases Alzheimer's risk has

been one of the most vexing mysteries facing Alzheimer's researchers for over a decade.

Luminescent conjugated oligothiophenes (LCOs) or luminescent conjugated polymers (LCPs), the newly discovered class of biomarkers, can stick to protein structures in the body and emit colors reflecting the different shapes or forms of the proteins. Among other uses, LCPs/LCOs are currently being employed in test tubes, animal models, and autopsied Alzheimer's brains to study the structure of proteins deposits caused by the disease. The new markers bind to the two well-established hallmarks of Alzheimer's - beta amyloid plaques and tau tangles - and glow different colors depending on which forms of the deposits they "stick" to (e.g., plaques often "glow" orange, while tangles "glow" yellowish green).

In the study, frozen brain sections from people who died with Alzheimer's were stained using two LCPs/LCOs: pentamer formyl thiophene acetic acid (pFTAA) and polythiophene acetic acid (PTAA). Using PTAA, the researchers observed that Alzheimer patients with APOE ε4/ε4 gene type had core and cerebrovascular amyloid of different shapes, while in people with APOE ε3/ε3, the two amyloid structures had the same shape. Using pFTAA revealed that tau tangle densities in ε4/ε4 Alzheimer patients that were apparently greater than those with ε3/ε3.

"The findings support our hypothesis that APOE genotype changes amyloid structure," Dr. Gandy said. "This is important because the different shapes might respond differently to treatments that attempt to clear amyloid deposits from the brain. We already know, for example, that APOE ε4/ε4 patients respond less well to anti-amyloid antibody with bapineuzumab."

Provided by The Mount Sinai Hospital