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Contact: Elizabeth Streich

eas2125@columbia.edu

212-305-6535

[Columbia University Medical Center](#)

Diabetes and elevated levels of cholesterol linked to faster cognitive decline in Alzheimer's patients

Heart disease and stroke linked to increased cognitive decline only in Alzheimer's patients who carry the APOE-e4 gene -- previously implicated in late-onset disease

NEW YORK – A history of diabetes and elevated levels of cholesterol, especially LDL cholesterol, are associated with faster cognitive decline in patients with Alzheimer's disease, according to a new study from Columbia University Medical Center researchers. These results add further evidence of the role of vascular risk factors in the onset and progression of Alzheimer's disease.

The study will be published in the March 2009 issue of *Archives of Neurology*. This special issue, titled, *Archives of Neurology: Neurological Disorders Related to Obesity, Diabetes Mellitus, the Metabolic Syndrome, and Other Comorbidities*, is part of a special JAMA/Archives focus on diabetes and metabolic disorders.

"These findings indicate that controlling vascular conditions may be one way to delay the course of Alzheimer's, which would be a major development in the treatment of this devastating disease as currently there are few treatments available to slow its progression," said Yaakov Stern, Ph.D., a professor at the Taub Institute for the Research on Alzheimer's Disease and the Aging Brain and director of the Cognitive Neuroscience Division of the Gertrude H. Sergievsky Center at Columbia University Medical Center, and senior author of the paper.

"Preventing heart disease, stroke and diabetes – or making sure these conditions are well managed in patients diagnosed with them – can potentially slow the disease progression of Alzheimer's," said Dr. Stern.

Dr. Stern and the research team used longitudinal data for a mean of 3.5 years (up to 10.2 years) for 156 people diagnosed with Alzheimer's disease who were participants in the Washington Heights/Inwood Columbia Aging Project, a 10-year multi-ethnic, prospective, epidemiological study of cognitive aging and dementia in northern Manhattan.

“Through the Washington Heights/Inwood Columbia Aging Project, we were able to follow patients before they began to show symptoms of Alzheimer’s and for several years following their diagnosis. This makes our estimates of progression much more powerful, since we were able to know exactly when cognitive decline began,” said Dr. Stern.

They found that a history of diabetes and higher cholesterol levels (total cholesterol and LDL-C) was associated with faster cognitive decline. A history of heart disease and stroke was found to be associated with cognitive decline only in carriers of the apolipoprotein E ϵ 4 (APOE- ϵ 4) gene, which has been implicated in late-onset Alzheimer’s disease.

Researchers from Columbia’s Taub Institute have previously demonstrated a link between stroke, diabetes, smoking, hypertension and a higher risk of Alzheimer’s disease. While vascular risk factors have been studied as predictors of Alzheimer’s, few studies have assessed their influence on disease progression. As the authors write, “There has been intense interest in identifying modifiable Alzheimer’s disease risk factors such as cardiovascular risk factors, with the goal of preventing or at least delaying disease onset. However, little attention has been given to the influence of these factors on disease progression.”

Dr. Stern and the research team theorize that the link between vascular risk factors and faster cognitive decline in patients with Alzheimer’s disease may occur because vascular diseases may increase oxidative stress or activate inflammation in the brain, thereby triggering the production of amyloid, and/or triggering the formation of neuron tangles – known as neurofibrillary tangles – which are believed to be a primary cause of Alzheimer’s disease.

Dr. Stern and his colleagues are continuing to study the basis of the links between vascular risk factors and Alzheimer’s disease using epidemiologic and imaging approaches.

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