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Research illuminates link between Alzheimer's and stroke

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For years, neuroscientists have known that the risk of Alzheimer's disease is nearly doubled among people who have had a stroke. Now researchers at Columbia University Medical Center have found a process in the brain that may help explain the link between Alzheimer's and stroke. Findings are published in the March 13, 2008 issue of *Neuron*.

After a stroke, it is known that there is an increase in the production of the toxic amyloid beta (Aβ) peptides that are believed to cause Alzheimer's disease. In this study, results showed that Aβ production rises when there is an increase in production of a peptide called p25, which is known to occur, both in rodent models and in human post-mortem tissue, following a stroke. Columbia researchers and their colleagues identified a pathway, known as p25/cdk5, whereby higher levels of p25 led to enhanced activity of a molecule called cdk5, which in turn led to a rise in the production of Aβ.

When lead author Karen Duff, Ph.D. and her colleagues reduced the activity of cdk5 either using an inhibitor, or by genetic manipulation, they found a decrease in Aβ production in the brain. These results indicate that the p25/cdk5 pathway may be a treatment target for Alzheimer's disease – in particular, inhibitors of cdk5 are particular candidates for therapeutic development.

"This finding connects the dots between p25 and increased production of amyloid beta, and this p25/cdk5 pathway could explain why the risk of Alzheimer's disease is significantly higher following a stroke," said Dr.

Duff, professor of pathology (in psychiatry and in the Taub Institute for Research on Alzheimer's Disease and the Aging Brain) at Columbia University Medical Center and the New York State Psychiatric Institute. “However, we still need to verify that this pathway is actually set in motion after a stroke; right now the data is still circumstantial.”

Duff’s laboratory is currently working on experiments to verify this pathway’s involvement using human post-mortem tissue of stroke patients.

The specific pathway investigated was shown to be most active in young mice, as compared to older mice suggesting that p25/cdk5 may not be implicated in late-onset Alzheimer’s disease, the most common form of this neurodegenerative disease.

Alzheimer’s disease, which affects 4.5 million Americans, is differentiated as either early-onset or late-onset. The early-onset form is rare and tends to affect those between the ages of 30-60. Most cases of early-onset are genetic, caused by a mutation of the APP gene. The late-onset form is much more common – accounts for 90 percent of all cases of Alzheimer’s – and tends to affect those aged 65 and older. With aging baby boomers, the prevalence of late-onset Alzheimer’s is expected to double in the next 25 years as the population ages.

Source: Columbia University