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Problematic blood clotting contributes to Alzheimer's disease (w/ Video)

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(PhysOrg.com) -- Alzheimer's disease isn't just about twisted brain cells. It's also about the blood vessels that feed those neurons. New research at Rockefeller University has shown how the most common element of the plaque deposits found outside the brain cells of Alzheimer's patients interacts with a blood clotting agent and causes clots to form faster and become harder to break down. The scientists suggest new drugs that would target this association could potentially treat what is increasingly recognized as a crucial element of the disease, the vascular component.

Alzheimer's disease has long been studied primarily as a disease of neurons. But researchers have now shown how the disease may be damaging the brain by choking off blood flow. In experiments published June 10 in *Neuron*, scientists at Rockefeller University reveal that amyloid-β, which builds up around brain cells in Alzheimer's patients, interacts with a common blood clotting agent to increase clotting in the arteries that feed the brain. Such activity could cut off blood flow to neurons, suffocating them over time. A drug that interferes with that process could reduce the memory loss and dementia that are the most wrenching consequences of the disease, the findings suggest.

"There's at least this one very promising therapeutic angle," says Sidney Strickland, head of the Laboratory of Neurobiology and Genetics at Rockefeller. "And
what's nice is that a drug that disrupted this particular interaction would not affect clotting elsewhere like regular anticoagulants, because the amyloid-β peptide is primarily found in the brain."

Postdoctoral fellow Marta Cortes-Canteli led the work in Strickland's lab, conducting test tube experiments and experiments in mice genetically engineered with Alzheimer's disease to investigate the interaction of amyloid-β and the blood-clotting agent called fibrinogen. Normally, when the body is injured, fibrinogen forms fibrin clots to stop uncontrolled bleeding. Once the wound is healed, the blood clot is broken down and blood flow returns to normal.

Strickland, Cortes-Canteli and colleagues found that the blood in mice with the extra amyloid-β produced in Alzheimer's disease clotted more quickly and that the clots were more difficult to degrade. They also found that mice with lower levels of fibrinogen had less buildup of amyloid beta in the walls of their blood vessels and performed better on memory tasks.

This led them to propose a new model for the vascular component of the disease, which is increasingly recognized as a key element in its pathology. "The promotion of blood clots and the difficulty of breaking them down would cause a decrease in cerebral blood flow and increase in inflammation that could eventually lead to the neuronal dysfunction in Alzheimer's patients," Cortes-Canteli says. "Of course, Alzheimer's is a multifaceted disease, and a lot of things are going on, but we do think that targeting the association of amyloid-β and fibrinogen could be a very promising treatment."

More information: Marta Cortes-Canteli et al., Fibrinogen and β-Amyloid Association Alters Thrombosis and Fibrinolysis: A Possible Contributing Factor to Alzheimer's Disease, Neuron 66: 695-705 (June 10, 2010)

Provided by Rockefeller University