Arterial stiffening linked to Alzheimer's disease

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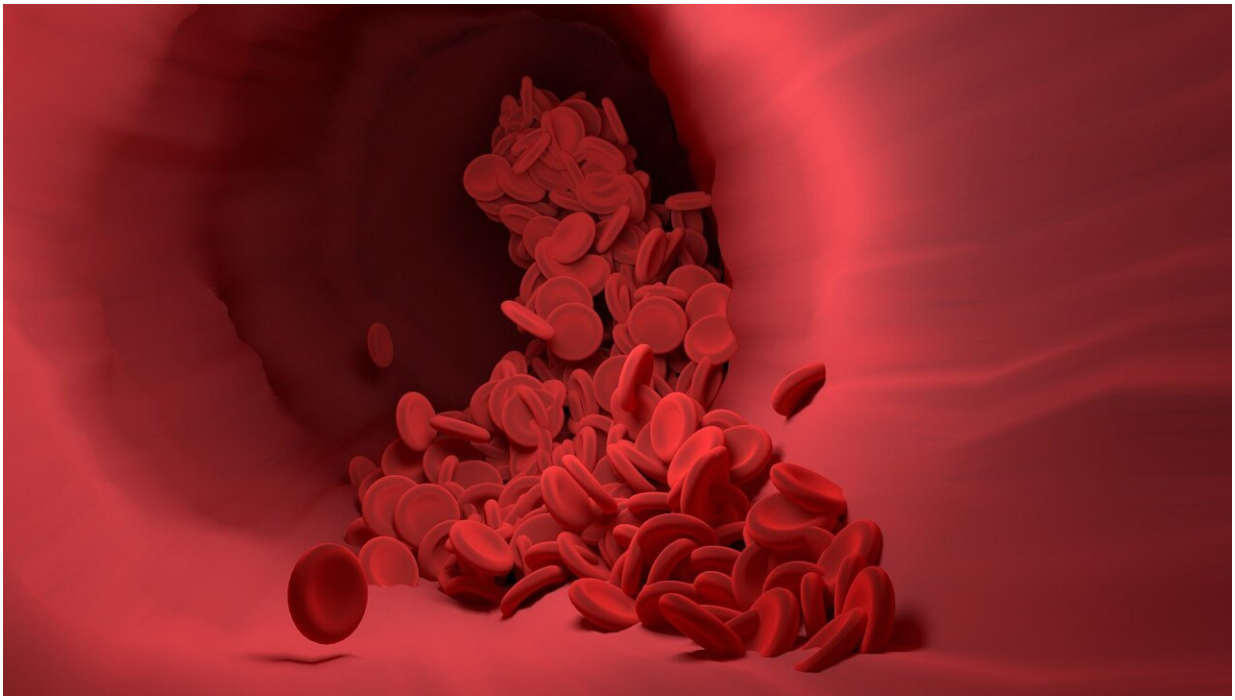

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A research team from Vanderbilt University Medical Center reports in *Neurology* that greater stiffening of the aorta, the main artery in the human body, is associated in older adults with increased Alzheimer's disease (AD) pathology as reflected in a range of neurochemical indicators measured in cerebrospinal fluid.

"These results have major implications for Alzheimer's disease prevention," said Angela Jefferson, Ph.D., professor of Neurology and founding director of the Vanderbilt Memory and Alzheimer's Center, who led the study with Elizabeth Moore, an MD/Ph.D. student who recently completed a Ph.D. under Jefferson's mentorship.

"Building on our previous research, we have identified specific pathological pathways by which cardiovascular health relates to cognitive decline in aging," Jefferson said. "With this study we have discovered new associations between greater arterial stiffness and biomarkers of inflammation, synaptic injury, neurofibrillary tangles and neurodegeneration, all pathological processes that are present in Alzheimer's disease.

"As our understanding of the impact of cardiovascular health on Alzheimer's biomarkers increases, so do the potential prevention and treatment options for this devastating and costly disease."

The new findings are based on examination of 146 patients aged 60 to 90 who were free of dementia and neurological disease. The patients are a subset of participants in the Vanderbilt Memory and Aging Project, an expanding observational cohort study led by Jefferson, focused on uncovering pathways of injury that accelerate or ameliorate the clinical manifestation of AD.

While there may be no single cause of Alzheimer's, a range of neurochemical indicators are thought to define not only AD core pathology and the ultimate progression of the disease, but also AD risk in asymptomatic patients. Previous studies have found associations between aortic stiffness and two of these AD biomarkers—increased amyloid-beta and deposits of phosphorylated tau.

The new findings from VUMC, which are based on a more sensitive

measure of arterial stiffness, run counter to the first of these earlier findings, support the second, and identify three new associations between aortic stiffness and biomarkers thought to be implicated in AD.

In asymptomatic subjects age 74 and older, the study finds associations between greater aortic stiffness and greater cerebrospinal fluid concentrations of four out of seven AD biomarkers tested: phosphorylated tau and total tau, considered indices of neurodegeneration in AD; neurogranin, considered an index of synaptic dysfunction in AD; and a glycoprotein called YKL-40, considered an index of neuroinflammation in AD.

While it's long been understood that age-related arterial stiffening carries risk of events like heart attack and stroke, more recent studies have found associations with cognitive impairment, changes in brain structure and cerebral small vessel disease. Previous studies led by Jefferson and colleagues have found increased aortic stiffness and reduced cardiac output to be associated with decreased cerebral blood flow and increased risk of cognitive decline.

"We previously showed greater arterial stiffness reduces blood flow to the cerebral microcirculation, which may cause cognitive decline," Jefferson said. "This new study adds paradigm-shifting evidence that vascular risk factors might also contribute to the molecular pathology thought to drive core Alzheimer's disease and concomitant pathologies."

More information: Elizabeth E Moore et al, Association of Aortic Stiffness With Biomarkers of Neuroinflammation, Synaptic Dysfunction, and Neurodegeneration, *Neurology* (2021). DOI: 10.1212/WNL.0000000000012257

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