Cerebrovascular Pathology in Down syndrome and Alzheimer Disease

Elizabeth Head, PhD [1] • Michael Phelan, PhD [2] • Eric Doran, MS [3] • Ronald Kim, MD [4] • Wayne Poon, PhD [5] • Frederick Schmitt, PhD [1] • Ira Lott, MD [6]

[1]Sanders Brown Center on Aging, University of Kentucky • [2]Statistics, University of California at Irvine • [3]Pediatrics, University of California at Irvine • [4]Pathology, University of California at Irvine • [5]Institute for Memory Impairments and Neurological Disorders, University of California at Irvine • [6]Neurology, University of California at Irvine

People with Down syndrome (DS) are at high risk for developing Alzheimer disease (AD) with age. Typically, by age 40 years, most people with DS have sufficient neuropathology for an AD diagnosis. Interestingly, atherosclerosis and hypertension are atypical in DS with age, suggesting these vascular risk factors may reduce some forms of vascular pathology in DS. However, because the extra copy of APP leads to increased beta-amyloid peptide (Aβ) accumulation in DS, we hypothesized that there would be higher levels of cerebral amyloid angiopathy (CAA) with age in DS relative to sporadic AD. To test this hypothesis CAA, atherosclerosis and arteriolosclerosis were used as measures of cerebrovascular pathology and compared in post mortem tissue from individuals with DS (n=32), sporadic AD (n=80) and controls (n=37). CAA was observed with significantly higher frequencies in brains of individuals with DS compared to sporadic AD and controls. Atherosclerosis and arteriolosclerosis were rare in the cases with DS. CAA in DS may be a target for future interventional clinical trials. Funding: National Institutes on Aging P50AG16573 (E.D., R C.K., W.W.P., I.T.L.); National Institutes on Aging R01AG 21912 (E.D., I.T.L.); National Institutes on Aging R01HD065160 (E.D., I.T.L.); National Institutes on Child Health and Development R01HD064993 (E.H., F.A.S.). The authors are grateful to the donors and families who contributed to the study.