Cerebral Amyloid Angiopathy and Microhemorrhages in the Occipital Cortex of Aging Adults with Down Syndrome

Alex Helman [1] • *Michael P Murphy, PhD* [1] • *Katie Mccarty* [2] • *Fred Schmitt, PhD* [2] •

Elizabeth Head, PhD [2]

[1]Biochemistry, University of Kentucky • [2]Sanders-Brown Center on Aging, University of Kentucky

People with Down syndrome (DS), or trisomy 21, consistently have sufficient neuropathology for a diagnosis of Alzheimer's disease (AD) by age 40, including both amyloid plaques and neurofibrillary tangles. Cerebrovascular pathology is a known contributor to sporadic AD, but has been virtually unexplored in people with DS who have AD. This is because people with DS are often thought to be protected from vascular risk factors, like atherosclerosis and hypertension. However, cerebral amyloid angiopathy (CAA) is consistently seen in brains of people with DS as they age and studies from our lab have shown that people with DS have significant microhemorrhages in the frontal cortex. Additionally, preliminary imaging studies from our Aging in Down syndrome cohort show significant microbleeds in the occipital cortex. Therefore, we hypothesized that there may be an age-dependent increase in CAA in the occipital cortex in people with DS and that this is driving an increase in microhemorrhages in this region. We counted the number of microhemorrhages in the occipital cortex using Prussian Blue stained slides in several autopsy groups: DS without AD, DS with AD, sporadic AD, and their age matched controls. This tissue was also stained for total amyloid (6E10) and CAA severity was scored. Microhemorrhage counts in DS cases without AD were not significantly different from their age-matched controls. However, sporadic AD cases did have significantly higher microhemorrhage counts than their age matched controls. Additionally, DS with AD cases had the highest overall microhemmorhage counts compared to all other groups, and had significantly higher counts than the AD group alone. This data matches what we have seen in the frontal cortex. Additionally, we saw that the DS with AD group had significantly higher amounts of CAA than other groups. Our results suggest a high frequency of microhemorrhages in DS adults with AD, moreso than sporadic AD. This along with the increased amount of CAA suggests that cerebrovascular pathology may be an under-recognized, yet significant contributor to aging and the development of dementia in people with DS.