THE EFFECT OF ADVANCED AGE AND ALZHEIMER'S DISEASE NEUROPATHOLOGY ON LEVELS OF THE TIGHT JUNCTION PROTEIN OCCLUDIN IN THE BRAIN MICROVASCULATURE

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ABSTRACT: The Blood-Brain Barrier (BBB) is a physiologic interface between the bloodstream and the brain. The BBB has tight junction proteins (TJPs) that restrict blood and toxins from entering the brain and allow important nutrients and biomolecules, like glucose and amino acids, to diffuse through the membrane and supply energy for neural processes. This interface plays an important role in the health of our brains and helps protect against an array of neurodegenerative diseases. However, it is possible for diseases like Alzheimer's Dementia (AD) to impact this interface and cause it to be less functional as a barrier. In recent studies, we found a significant increase in the TJP, occludin, located in microvessels (MVs) isolated from the parietal lobe of female subjects of advanced age with Alzheimer's Dementia (AD) relative to age-matched females (F) without Alzheimer's Dementia (NAD) (n=8 AD, n=8 NAD; age range: 79-99; mean: 93 years for both groups). There were no significant differences in occludin between MVs of male subjects with and without dementia, who were of a much younger average age (mean: 74 years old). To further evaluate this finding, we examined MVs in cross-cuts of the superior parietal lobes of a separate group of F subjects, both AD and NAD, via immunohistochemistry (IHC) techniques (n=12 AD, age range: 82-93; n= 5 NAD, age range: 83-98). We additionally measured levels and distribution of occludin in isolated MVs from the original group of female subjects with AD and NAD (n=8) utilizing immunofluorescence (IF) techniques. Preliminary analysis of IHC was not able to detect differences in occludin levels, but initial IF studies suggest that higher levels of occludin in MV derived from F AD subjects. Current studies are evaluating occludin localization in both groups of brain MVs. In summary, our data suggested that occludin is increased in brain MVs from female subjects of advanced age with AD, relative to those NAD participants. Ongoing studies with IHC and IF confirm differences in levels and determine localization. The increase of occludin in F AD MVs is an unexpected finding and could reflect a compensatory mechanism within brain MV in the context of both advanced age, and Alzheimer's Dementia. Based on our findings, we could potentially develop methods to create therapies that mimic the compensatory mechanism used to protect our BBB and preventative care for patients.

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