Brain Microvessels from Dementia and No Dementia Subjects

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Background

The brain microvasculature is the foundation of the blood-brain barrier (BBB), an interface that regulates passage between the circulatory system and the brain parenchyma. Tight junction (TJ) proteins function as cell-cell adhesion molecules at the BBB and have been shown to differ in subjects with dementia (D) versus those without dementia (ND), with most studies showing an overall decrease in Alzheimer's Disease (AD).

Methods

We measured levels of TJ proteins (occludin, claudin-5) and protein markers of neurovascular unit cells (endothelial cell PECAM, pericyte PDGFR, astrocyte foot process GFAP, associated neuronal MAP2 and NeuN) in brain microvessels (MV) to determine the association with dementia. MV were isolated from the superior parietal lobe cortex of female (F) (n=8 D and 8 ND, age range 79-99, mean 93 for both groups) and male (M) (n=7 D and 7 ND, age range 53-93, mean 74 for both groups) subjects. Within each sex, D and ND subjects were matched by age and AD neuropathologic change. Protein levels were assessed by western blot (WB). Additional unique MV samples from fresh brains of female subjects (n=3 D, age range 92-94; n=3 ND, age range 51-92) were examined by WB and immunofluorescence (IF). A separate set of unique parietal cortex sections from female subjects (n=12 D, age range 82-93; n= 5 ND, age range 83-98) were examined by immunohistochemistry (IHC) to confirm the WB and IF data.

Results

WB and IF results showed no detectable differences in claudin-5, PECAM, GFAP, MAP-2 or NeuN in M or F regardless of dementia status but demonstrated significant increases in occludin in F D versus ND. IHC results demonstrated that brain microvascular density was similar in D versus ND samples by PECAM staining with no detectable differences in claudin-5, but again showed an increase in occludin in F D versus ND.

Conclusions

The significant increase in occludin observed only in F D, which was unexpected, could reflect a compensatory response in the brain MV of D subjects of advanced age (mean age 93) or changes in total protein that do not represent cellular localization to the TJ.

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