CHARACTERIZING NEUROINFLAMMATORY AND BLOOD-BRAIN BARRIER PROCESSES IN DEMENTIA

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Dementia is one of the leading causes of disability and death among older people worldwide. The chronic and/or progressive nature of dementia results in deterioration of cognitive ability, affecting daily functions and quality of life. There is, as yet, no known cure for dementia; hence, research aiming to understand its pathophysiology is crucial in designing future therapeutic interventions and biomarker studies for early detection. Current literature implicates neuroinflammatory processes in the degeneration of the neuroprotective blood-brain barrier (BBB) in various forms of dementia. Among them, Alzheimer's disease (AD) is the most common form of dementia, accounting for 60-70% of all dementia cases. We hypothesize that alterations in the physiological function of the BBB at an early age can be indicative of disease progression, with potential for development as a biomarker for AD screening. To investigate the interplay between neuroinflammation and BBB dysfunction in AD, we generated a novel transgenic mouse model comprising double knock-in of the two largest genetic risk factors of AD: amyloid precursor protein (*App*) and apolipoprotein E4 (*Apoe4*). Using this double-mutant (DM) mouse model, we characterized the cellular components of the BBB (astrocytes, endothelial cells, microglia) and examined the expression profiles of various BBB-associated tight junction and vasculature proteins across timepoints (3 months, 8 months, and 12 months old) spanning the development of AD-like pathology. Significantly more astrocytes and microglia in the cortices of the DM mice than in wild-type (WT) were observed as early as at 8 months old, suggesting increased neuroinflammatory processes early in disease progression. The DM animals also showed altered expression of specific BBB-related proteins as compared to WT animals, possibly affecting BBB permeability and integrity. Future studies will focus on elucidating how these changes affect the functionality of the BBB, and establishing their feasibility as biomarkers for tracking AD progression.