TACSM Abstract

Diet and Sex Differences Induce Unique Alterations of Markers for Blood Brain Barrier Integrity in Age-Accelerated Mice

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ABSTRACT

The role of diet on brain health has received significant attention, with the Western diet (WD) contributing to cerebrovascular alterations and neurodegenerative disease. The blood-brain barrier (BBB) may play a particularly important role as it forms the interface between the peripheral circulation and the central nervous system. The WD has been shown to negatively impact the BBB. Whether there are sex specific differences with diet on BBB integrity remains unclear. **PURPOSE**: To determine the effect of diet and sex on the mRNA expression of markers of BBB integrity in an age-accelerated mouse model. **METHODS**: Male and female Senescence Accelerated Mouse-Prone 8 (SAMP8) mice were randomly assigned to a standard diet (SD) or WD formula for a 32-week period, matched for sex, ending at 12-months of age (n=10-14/group). At 12-months of age, cortical brain tissue was evaluated for the expression of mRNA for targets associated with BBB integrity (Cldn-1, Cldn-3, Cldn-5, Cldn-12, F11r, Lsr, Msfd2a, Ocln, Tjp) using quantitative RT-PCR. A two-way ANOVA was used to identify whether mRNA expression of these targets differed with sex, diet, and their interaction. **RESULTS**: A significant ($p<0.05$) sex effect was observed, where female mice had significantly ($p<0.05$) higher expression of Cldn-5 (23%), Cldn-12 (18%), F11r (72%), Lsr (18%), Mfsd2a (60%), Ocln (62%), and Tjp (20%) than male mice, demonstrating better BBB integrity in female mice. Interestingly, a significant ($p<0.05$) diet effect was observed, where mice fed the WD had significantly ($p<0.05$) lower expression of Cldn-1 (22%), Cldn-12 (33%), F11r (286%), Lsr (37%), Mfsd2a (169%), Ocln (180%), and Tjp (51%) than mice fed the SD, showing impaired BBB integrity with a Western diet. A significant ($p<0.05$) interaction between sex and diet was observed for F11r and Ocln. F11r and Ocln were significantly ($p<0.05$) lower in female mice fed the WD when compared to female mice fed a SD. **CONCLUSION**: Overall, female mice presented with higher expression of mRNA markers for BBB integrity, which may be a protective factor. Furthermore, mice fed the WD had lower mRNA expression of markers of BBB integrity suggesting that a Western diet may accelerate the pathogenesis of the disease state.