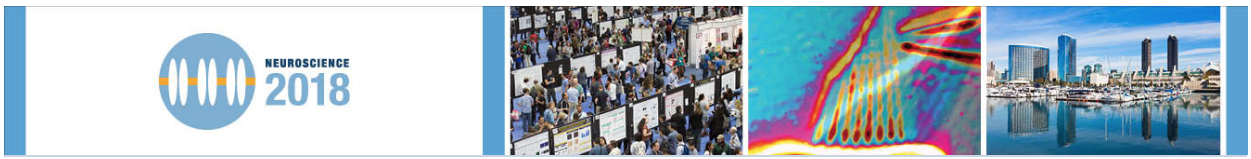

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Session 746 - Alzheimer's Disease and Other Dementias: ApoE and Associated Pathways

Add To Itinerary

746.06 / T1 - Effects of diet induced obesity and APOE genotype on Alzheimer-related pathology in female EFAD mice

November 7, 2018, 1:00 PM - 5:00 PM | SDCC Halls B-H

Presenter at Poster
Wed, Nov. 7, 2018, 2:00 PM - 3:00 PM

Grant Support
NIA Grant P01 AG26572

Grant Support
NIA Grant T32 AG052374

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Disclosures
A. Christensen: None. C.J. Pike: None.

Abstract
Alzheimer's disease (AD) risk is significantly influenced by genetic and environmental risk factors. The greatest genetic risk factor for late onset AD is APOE genotype, with E4 carriers being at a greater risk than E2 or E3 carriers. This increased risk in APOE4 carriers is exacerbated in females. Further, obesity in midlife has been shown to significantly increase AD risk in late life. To investigate whether APOE genotype and obesity interact to affect AD pathogenesis in females, we studied the effects of diet-induced obesity in the EFAD mouse model of AD. EFAD mice have knock-in of human APOE3 (E3FAD) or APOE4 (E4FAD) in the presence of 5xFAD genes. Female EFAD mice were maintained on either Western diet (WD; 45% fat, 21% sugar) or a control diet (10% fat, 7% sugar) for 12 weeks. E3FAD mice showed greater metabolic impairments after WD including increased glucose dysfunction and increased circulating leptin. E4FAD mice did not show impairments after WD, but had poorer metabolic function at baseline than E3FAD mice. E3FAD mice on WD were impaired on cognitive tasks and showed increased beta-amyloid pathology. E4FAD mice were more impaired on the behavior tests and had greater beta-amyloid neuropathology in comparison to E3FAD mice, but showed no further impairment by WD. Microglia are believed to play an important role in the progression of AD neuropathology and are implicated in the effects of both APOE4 and obesity. We assessed the activation of microglia in the hippocampus. As with beta-amyloid pathology, E3FAD mice showed increased microglial activation after WD. E4FAD mice had more activated microglia than E3FAD mice, but no further impairment after WD. Overall, these findings demonstrate significant gene-environment interactions between APOE and obesity in female EFAD mice.

Abstract Citation