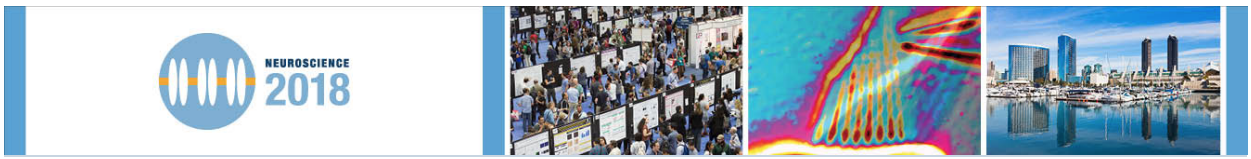

(https://www.abstractsonline.com/pp8/#!/4649)

Session 205 - Altered Energy Homeostasis in Alzheimer's Disease

Add To Itinerary

205.11 / H1 - Effects of APOE genotype and obesity on metabolic and inflammatory outcomes in male mice

November 4, 2018, 1:00 PM - 5:00 PM | SDCC Halls B-H

Presenter at Poster
Sun, Nov. 4, 2018, 3:00 PM - 4:00 PM

Grant Support
NIH Grant AG26572

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Disclosures
C.H. Sample: None. **V.A. Moser:** None. **C.J. Pike:** None.

Abstract
Genetic and environmental factors interact to regulate Alzheimer's disease (AD) risk. The strongest genetic risk factor for the development of late-onset AD is the ε4 allele of apolipoprotein E (*APOE*4). *APOE* encodes the apolipoprotein (apoE) cholesterol transporter, which has a role in lipid homeostasis. Obesity and the metabolic syndrome are primary modifiable risk factors for AD and may exacerbate these genetic vulnerabilities. Indeed, recent research from our lab demonstrated a significant interaction between obesity and *APOE* genotype in the regulation of AD-like pathology in EFAD mice in which obesogenic diet increased pathology in *APOE4* but not *APOE3* genotype. Because increased inflammation is implicated in driving AD pathogenesis and is associated with the deleterious effects of both obesity and *APOE4*, inflammation represents a compelling candidate mechanism by which obesity and *APOE4* interact to accelerate the development of AD. To gain insight into this possibility, the current research compared the effects of normal and obesogenic diet in male mice with *APOE3* versus *APOE4* genotype on inflammatory indices systemically and in brain. Further, we considered downstream effects of these interactions, focusing on metabolic and behavioral outcomes. Experimentally, adult male mice (N = 34) with knock-in of human APOE3 (E3) or APOE4 (E4) were maintained on Western diet (WD; high in saturated fat and sugars) or standard chow for 12 weeks beginning at age 3 months. Expression of microglia/macrophage markers, cytokines, and immune response factors were determined peripherally (e.g., plasma, adipose tissue) and in brain. In addition, mice were assessed on a range of metabolic (e.g., adiposity, glucose tolerance, fasting levels of glucose, insulin, and leptin) and behavioral (e.g., spontaneous alternation behavior, elevated plus maze) measures. Results from this investigation will provide novel insight into the interactions between *APOE* and diet-induced obesity, which will inform on the mechanisms contributing to their cooperative actions in regulating AD pathology.

Abstract Citation