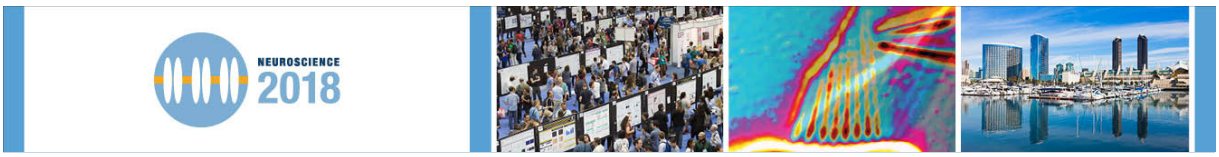

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Session 474 - Neurotoxicity, Inflammation, and Neuroprotection: Mechanisms of Neurot...

474.10 / S15 - Environmental toxicants, ApoE and sex interaction in human cognitive aging and in mice transgenic for Alzheimer-associated genes

November 6, 2018, 8:00 AM - 12:00 PM | SDCC Halls B-H

Presenter at Poster
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Abstract
Cigarette smoke and air pollution are strong risk factors of Alzheimer's disease (AD) and other age-associated chronic diseases. While many effects of these environmental toxicants are well documented, less is known about their interactions with sex and ***ApoE*** alleles (Cacciottolo et al. 2017, PMID:28140404). This study investigates the pathways of interactions of sex, ***ApoE*** genotype, and environmental toxicants that contribute to cognitive decline and neurodegenerative diseases. We evaluate correlations of human genomic and phenomic data from the Health Retirement Survey (HRS, U.S. sample) with transcriptomic data from male and female ***ApoE*** transgenic mice exposed to air pollution. Results from the HRS cohort show ***ApoE4*** and smoking are risk factors of accelerated cognitive aging (Method from Levine et al. 2018 under review) with stronger trends in women. To complement these human studies, we applied Weighted Gene Co-Expression Network Analysis (WGCNA) to identify gene networks differentially expressed in the mouse cerebral cortex as a function of sex, ***ApoE***, and environmental toxins. One WGCNA module enriched for nervous system-associated signaling pathways showed significant interactions among sex, ***ApoE*** and air pollution. These genes had high overlap with 215 previously-defined polygenic genes for predicting long-lived human smoking survivors. This suggests cigarette smoke and air pollution have convergent molecular toxicities that mediate gene environment interactions in cognitive aging. We further analyzed AD associated genes for susceptibility to each factor and possible genotype-environment interaction. These findings suggest influences of ***ApoE4*** allele in sex difference of cognitive aging vulnerability to environmental toxins.

Abstract Citation