GRACE ANGELONA, DARSHAN SANGANI, ALYSSA IHLENFELD, MIKA JONES, TRISTAN MUCK, HANNAH SEXTON, OLIVIA COULTER, and MARY-LOUISE RISHER. Department of Biomedical Research, Joan C. Edwards School of Medicine, Marshall University, Huntington, WV and Neurobiology Research Laboratory, Hershey 'Woody' Williams Veterans Affairs Medical Center, Huntington, WV. Sex Dependent Rescue of Astrocyte-Synaptic Remodeling by Rosiglitazone Following Adolescent Binge Ethanol Exposure.

Binge drinking typically begins during a critical period of adolescent brain maturation and is associated with long-term behavioral dysregulation and increased risk for alcohol use disorder. Using the adolescent intermittent ethanol (AIE) rat model, our laboratory has shown long-term, sex-dependent behavioral deficits that are associated with astrocyte reactivity and dysregulation of bioenergetics and oxidative stress within dorsal hippocampal (dHipp). Rosiglitazone (ROSI) has been shown to have anti-inflammatory and metabolic regulatory properties that may mitigate AIE-induced neurobiological dysfunction. We therefore tested whether ROSI could rescue AIE-induced astrocyte and synaptic alterations and oxidative stress. Male and female rats underwent AIE or $H_2O$ exposure for 10 doses (5g/kg, i.g.). Animals then received 20 doses of ROSI or Vehicle. On PND 72, immunohistochemistry was performed on dHipp tissue to evaluate the effects of AIE+ROSI on oxidative stress (4-HNE, PPLN), astrocyte reactivity (GFAP), and tripartite synapse integrity. Imaging was performed using STED or confocal microscopy and analyzed with Synbot and Imaris. AIE increased peripheral astrocyte process (PAP) proximity to inhibitory synapses and reduced proximity at excitatory synapses in the male dHipp, both of which were rescued by ROSI. In females, AIE had no effect on synaptic proximity. ROSI reduced oxidative stress in females but increased oxidative stress in AIE males. ROSI had no effect on GFAP expression in either sex. These results indicate that ROSI influences AIE-induced astrocyte and synaptic remodeling in a sex-specific manner, highlighting astrocyte metabolic pathways as potential therapeutic targets for the long-term neurobiological consequences of adolescent binge drinking.