ALYSSA IHLENFELD, Department of Biomedical Research, Joan C. Edwards School of Medicine, Marshall University, Huntington, WV, USA, and Neurobiology Research Laboratory, Hershel 'Woody' Williams Veterans Affairs Medical Center, Huntington, WV, USA. NL-1 Can Reverse Cognitive Deficits and Restore Astrocyte Function Following Adolescent Intermittent Ethanol Exposure

Adolescent binge drinking produces neurobiological changes that increase the risk of cognitive impairment. The objective of this study was to determine whether NL-1, a mitoNEET-targeting ligand that regulates mitochondrial function, can restore astrocyte function and improve behavioral outcomes following adolescent intermittent ethanol (AIE) exposure. Male and female Sprague Dawley rats were exposed to AIE from postnatal day 30 to 45 using an intermittent intragastric ethanol paradigm modeling adolescent binge drinking. After a 26-day washout period, animals received NL-1 or vehicle, generating four treatment groups: water + vehicle, water + NL-1, AIE + vehicle, and AIE + NL-1. Contextual fear conditioning and extinction were used to assess hippocampal-dependent learning. Astrocyte calcium dynamics were measured using astrocyte-specific GCaMP6f imaging in the mPFC, and circuit activation was evaluated using cFos immunohistochemistry. Preliminary findings indicate that AIE exposure produces deficits in contextual fear conditioning, as evidenced by reduced freezing behavior during extinction compared with water controls. AIE animals also exhibit reduced astrocyte calcium responsivity in the mPFC, suggesting impaired signaling. These results support the hypothesis that AIE produces astrocyte dysfunction that contributes to cognitive deficits. Ongoing analyses will determine whether NL-1 treatment restores mitochondrial function, normalizes astrocyte calcium signaling, and reverses AIE-induced behavioral impairments.