Abstract

Drinking at a young age—especially heavy episodic binge drinking—is associated with reductions in white matter, cognitive abilities, and an increased risk of stress-related disorders such as addiction in adulthood. This suggests that experiences with alcohol may alter adolescent brain development and have long-lasting effects on mental health risk in adulthood. Alternatively, these neural and behavioral characteristics may be present prior to—and potentially lead to—heavy drinking early in adolescence. To help delineate these two possibilities we developed a preclinical model of voluntary binge drinking in adolescent rats. This operant self-administration model uses sweetened alcohol and a dynamic, intermittent drinking schedule to stimulate high voluntary intake of alcohol early in adolescence in outbred Wistar rats, i.e., animals without a predisposition for alcohol abuse or dependence. The model was used to explore the effect of adolescent alcohol on myelinated axons in male rats. We found evidence of myelin loss and damage in the prefrontal cortex of alcohol-exposed animals, which related to higher relapse-like drinking in adulthood. Finally, animals that consumed the highest amount of alcohol during adolescence showed the worst performance on a working memory task in adulthood. These findings establish a causal role of voluntary alcohol intake on myelin and give insight into specific prefrontal axons that are both sensitive to alcohol and could contribute to the behavioral and cognitive impairments associated with early onset drinking and alcoholism.