Adolescent binge drinking reduces brain myelin, impairs cognitive and behavioral control

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Binge drinking can have lasting effects on brain pathways that are still developing during adolescence, say neuroscience researcher Heather N. Richardson and her colleagues at the University of Massachusetts Amherst and Louisiana State University. Results of their study using a rodent model of adolescent drinking appear in the October 29 issue of The *Journal of Neuroscience*.

Richardson says, "Adverse effects of this physical damage can persist long after adolescent drinking ends. We found that the effects of alcohol are enduring." She adds, "The brains of adolescent rats appear to be

sensitive to episodic alcohol exposure. These early experiences with alcohol can physically alter brain structure, which may ultimately lead to impairments in brain function in adulthood."

She and her colleagues believe their study is the first to show that voluntary alcohol drinking has these effects on the physical development of neural pathways in the prefrontal cortex, one of the last brain regions to mature.

In humans, early onset of alcohol use in young teenagers has been linked to memory problems, impulsivity and an increased risk of alcoholism in adulthood. Because adolescence is a period when the prefrontal cortex matures, Richardson adds, it is possible that alcohol exposure might alter the course of brain development. Rodent models used in this study are documented to have clinical relevance to alcohol use disorder in humans.

The prefrontal cortex is the center of decision-making and regulates emotions and impulses. Specifically, the researchers explored the physical damage to fatty myelin sheaths that wrap and insulate axons, the "wires" that transmit information from one neuron to another. Myelin increases the speed at which electrical impulses travel along axons, enhancing information-processing and cognitive performance.

Richardson and her colleagues doctoral candidate and first author Wanette Vargas, Lynn Bengston and Brian Whitcomb of UMass Amherst, with Nicholas Gilpin of Louisiana State University, conducted this study with support of a two-year grant from the National Institute on Alcohol Abuse and Alcoholism at the National Institutes of Health.

The researchers used preclinical rodent models to explore how alcohol affects myelin in the prefrontal cortex. They gave male rats in early adolescence, several bouts of access to sweetened alcohol or, in controls,

the same amount of sweetened water daily for two weeks. Like teenagers, rats love sweet beverages and are willing to work for this reward by pressing on a lever in an operant box. This approach supported the development of a behavioral reinforcement circuit and generated a high amount of voluntary alcohol consumption during the rats' early adolescent developmental period.

The researchers examined myelin at the end of the binge-drinking period and found that it was reduced in the prefrontal cortex of the binge drinking adolescent rats. In a separate experiment, they examined myelin several months later after testing for adult drinking behaviors and found that adolescent alcohol drinking caused significant white matter loss and damage to myelin in the prefrontal cortex.

They also noted that the effects of adolescent alcohol were comparable to what was observed after alcohol dependence in adulthood. The duration and amount of alcohol exposure was much less in the adolescent drinking model compared to the adult dependence model. This shows that the adolescent brain may have heightened sensitivity to alcohol, Richardson and colleagues say.

Another interesting finding, they note, is that prefrontal white matter loss was greatest in the animals that showed the most robust increases in drinking after short periods of abstinence in relapse drinking tests in adulthood. This suggests that "perhaps this prefrontal fiber track is important for controlling behavior and may help keep animals from over-doing it when they are given the chance to drink again after taking short breaks from alcohol," the authors point out.

In a final experiment, the researchers found that heavy adolescent alcohol drinking, but not sweetened water, predicted poor performance on a working memory task in adulthood. This supports the idea that the enduring effects of alcohol may not only be structural but could also

affect cognitive functions that are dependent on a healthy prefrontal cortex.

Overall, they conclude, "These findings establish a causal role of voluntary alcohol on myelin and give insight into specific prefrontal axons that are both sensitive to alcohol and could contribute to behavioral and cognitive impairments associated with early onset drinking and alcoholism."

Richardson says she and her colleagues hope their findings lead to new therapeutic strategies in treating alcohol use disorder and new approaches for families and professionals who work with adolescents. Further, "results from this work focusing on the prefrontal cortex could also help us better understand the function of myelin and how myelin deficits may contribute to other psychiatric conditions associated with prefrontal impairments such as impulsivity, Tourette syndrome and schizophrenia."

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