Binge drinking affects male and female brains differently

September 10 2018

Credit: CC0 Public Domain

Gene expression in an area of the brain linked to addiction is affected differently by repeated binge drinking in males and females, finds a new study published today in *Frontiers in Genetics*. It reveals for the first time that genes associated with hormone signaling and immune function are affected by repeated binge drinking in female mice, whereas genes

associated with nerve signaling are affected in males. These findings have significant implications for the treatment of alcohol use disorder as they emphasize the importance of tailoring effective therapies towards male and female patients.

"We show that repeated binge drinking significantly alters molecular pathways in the nucleus accumbens, a region of the brain linked to addiction. A comparison of activated pathways reveals different responses in each sex, similar to that reported in recent research on male and female mice tested during the withdrawal phase following chronic alcohol intoxication," says Deborah Finn, a Professor of Behavioral Neuroscience at Oregon Health & Science University and a Research Pharmacologist at the VA Portland Health Care System, USA.

She continues, "These findings are important as they increase our understanding of male and female differences in molecular pathways and networks that can be influenced by repeated binge drinking. This knowledge can help us identify and develop new targeted treatments for alcohol use disorder in males and female patients."

Repeated binge drinking can be a risk factor for the development of alcohol dependence. Finn and her colleagues wanted to determine whether repeated binge drinking produced different responses in the brains of male and female mice, as has been found in alcohol-dependent mice tested during the withdrawal phase.

To do this, they analyzed gene expression in an area of the brain linked to addiction, the nucleus accumbens. Gene expression is the process where specific genes are activated to produce proteins for use by the cell, e.g. as building blocks for new tissues or hormones. Gene regulation governs the amount and timing of gene expression.

"We examined the effect of repeated binge drinking on the expression

of 384 genes previously identified as important in addiction and mood disorders," says Finn. "Of a total of 106 genes regulated by binge drinking, only 14 were regulated in both males and females, representing common targets to binge drinking. Interestingly, only 4 of these 14 genes were regulated in the same direction and the top 30 genes regulated by binge drinking in each sex differed markedly."

The researchers analyzed the data further, to examine the likely overall effect the regulation and expression of these genes would have on males and females.

"Our results suggested repeated binge drinking had a very different effect on the neuroadaptive responses of the nucleus accumbens in males and females, with different pathways being activated in each sex. Pathway analysis suggests hormone signaling and immune function were altered by binge drinking in females, whereas nerve signaling was a central target of binge drinking in males," reports Finn.

This has important implications for the treatment of alcohol addiction and emphasizes the need to tailor individual pharmaceutical treatments for male and female patients.

Finn explains, "We have shown that pharmacologically manipulating a pathway in both sexes that only was affected by binge drinking in males did not decrease binge drinking in females; binge drinking was only decreased in males. A consideration of sex is critical in the development of potential pharmacological therapies for the treatment of alcohol use disorder."

She concludes, "Future studies will determine whether the current gene expression changes correspond to behavioral and/or physiological differences."

More information: Deborah A. Finn et al, Binge Ethanol Drinking Produces Sexually Divergent and Distinct Changes in Nucleus Accumbens Signaling Cascades and Pathways in Adult C57BL/6J Mice, *Frontiers in Genetics* (2018). DOI: 10.3389/fgene.2018.00325