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"Assessing whether voluntary alcohol consumption induces hyperalgesia during withdrawal in mice"

BACKGROUND: Acute alcohol use is known to have analgesic properties and has been used by many as a form of self-medication for acute or chronic pain. However, chronic alcohol use is associated with inducing a paradoxical state of hyperalgesia, an increased sensitivity to nociceptive stimuli. This effect is further exacerbated during periods of alcohol withdrawal. Alcohol withdrawal hyperalgesia has been demonstrated using several rodent drinking models, for example, chronic intermittent exposure to ethanol vapor protocol or two-bottle choice paradigm. However, it has not been shown in paradigms that better replicate human binge drinking behaviors while allowing for in vivo recordings during the drinking period such as the drinking in the dark (DID) paradigm.

OBJECTIVES: The objective of this study is to assess the presence of hyperalgesia in male and female mice following voluntary alcohol consumption using the DID paradigm, followed by a sustained period of withdrawal.

METHODS: Adult male and female C57BL/6 mice were exposed to a 20% ethanol solution (EtOH) for 2 hours, three days a week, and for 4 hours, one day a week, followed by 3 days of abstinence. The control group was exposed to water (H_2O). This cycle was repeated 4 times making a total of 16 sessions of EtOH or H_2O exposure. Nociceptive testing occurred on Fridays. Mechanical sensitivity was assessed using the von Frey test, which involves applying a series of filaments with different bending forces to the mice's hind paws and recording their withdrawal responses. Thermal sensitivity was assessed using the hot plate test, during which the mice were placed onto a hot plate set to 54ºC and the latency to exhibit a pain response was measured.

RESULTS: Over the course of the study, the mice in the EtOH group generally increased their drinking, though the water group exhibited a similar trend. During week three, the majority of the EtOH group had blood alcohol concentrations over 80mg/dL. Mice exposed to chronic EtOH developed increased thermal sensitivity to the hot plate test when compared with the control group, and this effect was potentiated across abstinence days in males.

CONCLUSION: While no clear relationship was observed for the von Frey mechanical testing in this study, trends for the hot plate test showed a general increase in sensitivity to thermal stimuli, as was hypothesized. Future experiments will look to further examine these relationships to allow for testing of the neurobiological mechanisms behind this paradoxical hyperalgesia to identify potential pharmacologic targets to help treat individuals experiencing alcohol withdrawal and those at risk of developing AUD.