Assessing whether voluntary alcohol consumption induces hyperalgesia during withdrawal in mice

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Introduction

- In the United States, 213.2 million adults (84.0%) have consumed alcohol, with 28.6 million adults (11.3%) reporting AUD (NIAAA, 2021)
- While acute alcohol use has been associated with analgesic effects, chronic use is associated with a paradoxical state of hyperalgesia that is exacerbated during periods of abstinence or withdrawal.
- This hyperalgesia is likely a key promoter of continued drinking or relapse behaviors
- Several rodent drinking models, for example, the two-bottle choice paradigm or chronic intermittent exposure to ethanol vapor, have been used to demonstrate hyperalgesia in chronic alcohol users and during ethanol withdrawal
- The drinking in the dark (DID) paradigm may better replicate human drinking behavior, while allowing for in vivo recordings during the drinking period
- <u>Goal</u>: To assess whether the DID paradigm can produce hyperalgesia during withdrawal in adult male and female mice.

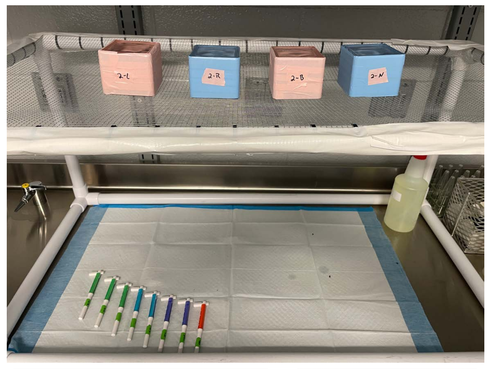
Drinking in the Dark

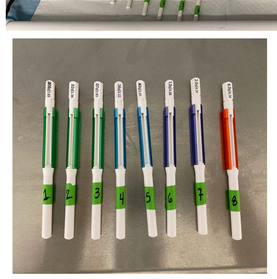
- Capitalizes on natural light/dark circadian rhythm, during which mice tend to consume the most food and drink 2-3 hours into the dark cycle
- 10am – dark cycle begins; 12pm – mice transferred to individual cages, and water bottle replaced with either 20% EtOH or H_2O
- On Monday-Wednesday, the mice are given access for 2 hours. On Thursday, the mice are given access for 4 hours. This is followed by a 3-day abstinent period from Friday-Sunday.

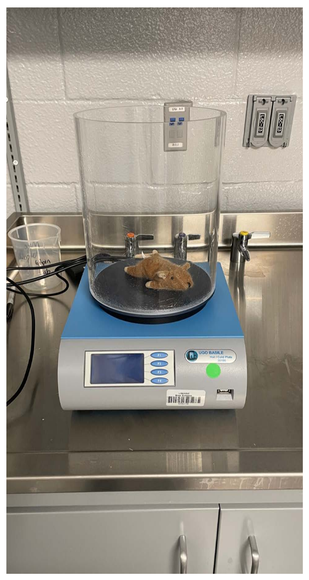
Nociceptive Assays

Von Frey Test

- 8 filaments of varying bending forces are sequentially applied to the center of the plantar surface of each hind paw
- Paw withdrawal latencies are recorded



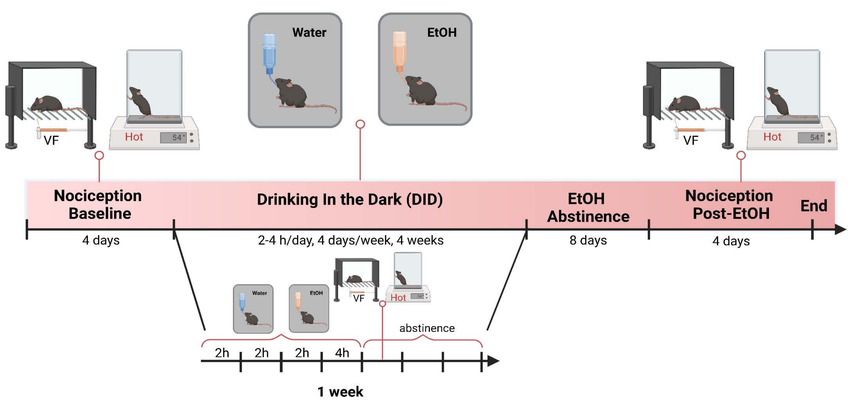




Hot Plate Test

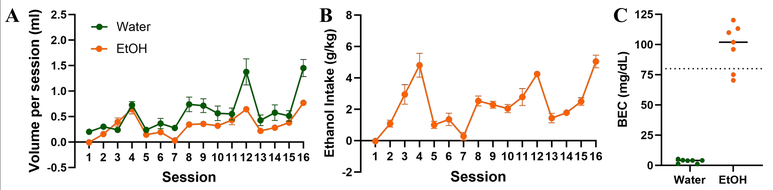
- Plate set to 54ºC
- Latency from the time all four paws touch the surface of the plate until any sign of pain is recorded.
- Repeated 3 times per mouse

Methods



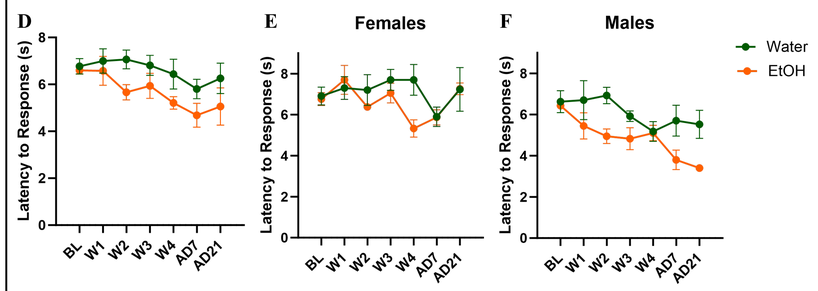
Results

Volume & Ethanol Intake

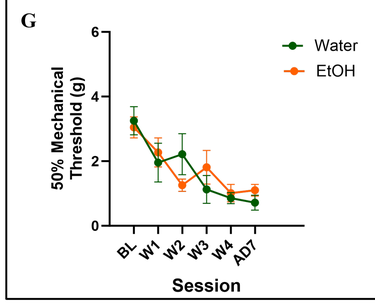


A. Average volumes of Water and EtOH consumed during each session. B. Average intake per session by the EtOH group, accounting for the weight of each mouse. C. During week 3, the majority of the EtOH group had Blood Ethanol Concentrations over 80mg/dL. Sessions 4, 8, 12, & 16 were 4 hour drinking sessions; all other sessions were 2 hours.

Hot Plate



Average thermal nociceptive response latency of all mice (D), just female mice (E), and just male mice (F) from the hot plate set to 54ºC. Lesser latencies indicate increased nociceptive sensitivity (hyperalgesia). Note exacerbation of effect in males after prolonged abstinence.



Von Frey Test

G. Average 50% mechanical nociceptive threshold to the Von Frey test.

Conclusion

- Trends for the hot plate test showed a general increase in sensitivity to thermal stimuli for the EtOH group compared to the H_2O group
- While it appeared as though mechanical sensitivities increased, as well, a similar trend was seen for both groups.
- Next Steps:
  - Increase the number of drinking sessions
  - Single-house the mice for the duration of the study
- Future: Examine neurobiological mechanisms behind this hyperalgesia so that potential pharmacologic targets may be identified

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