Alcohol exposure in aged mice: Effects on recognition memory and compulsive-like behaviors

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Introduction

- Alcohol use is an identified risk factor for aging-related memory impairment[1] and increases the prevalence of anxiety-related disorders.[3,7]
- Binge-drinking in older adults[2] as well the prevalence of Alcohol Use Disorder (AUD) in women[5] has seen a relative increase. Thus, it is important to assess whether alcohol exposure during aging affects memory impairment and anxiety-related behaviors and whether it differs between sexes.
- However, human findings are complicated due to individuals often having lifetime alcohol consumption. Animal models on the other hand allow for controlled examination of how alcohol affects memory at specific time points. This study uses the following behavioral models:
- Drinking in the Dark (DID): Procedure aimed to induce binge levels of ethanol intake as mice have their highest ingestive behavior at night.[6]
- Marble Burying (MB): Assesses anxiety-related compulsive burying behaviors.[8]
- Object Recognition Memory Test (ORM): Assesses recognition memory as mice tend to explore novel objects more if they remember the familiar objects.[4]

Hypotheses: Alcohol will induce greater cognitive impairment in females than males. Male mice at baseline will have more compulsive-like behavior, however, alcohol will increase compulsive-like behavior in both sexes.[8]

Experimental Setup

Figure 1: Marble Burying

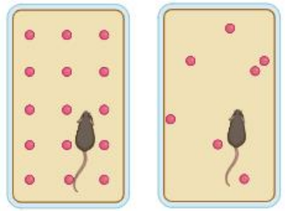


Figure 2: Object Recognition Memory

Methods

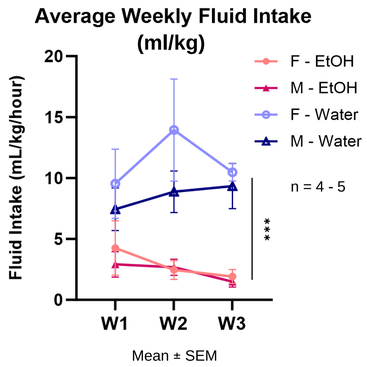
Subjects: 18 15-month-old mice with low alcohol preference (LAP); 8 females, 10 males.

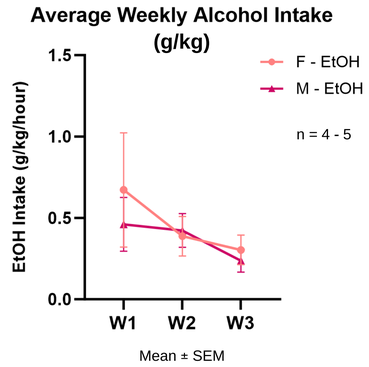
DID: For 3 weeks:
- Day 1 – 3: 20% alcohol (EtOH) or water for 2 hours.
- Day 4: 20% alcohol (EtOH) or water for 4 hours.

MB: Placed in tank with 20 marbles for 30 min.
- MB 1: 1 day after the last DID.
- MB 2: 10 days after MB1.

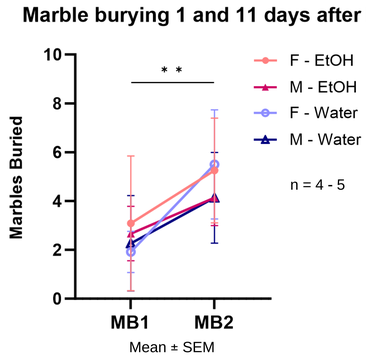
ORM:
- Habituation: Explore empty box for 5 min (3 days).
- Training: Explore 2 identical objects for 10 min.
- Testing: Explore 1 familiar object (from train day) & 1 novel object for 10 min.

DID & MB Results



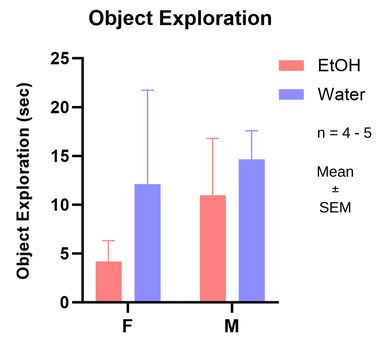


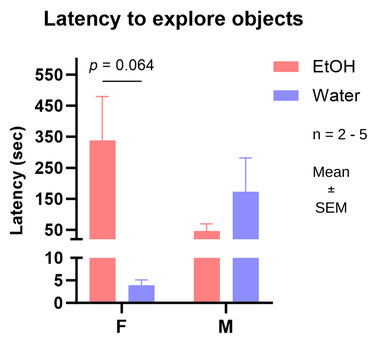
- EtOH LAPs drank less fluid (ml/kg) than Water LAPs, $p < 0.001$.
- No significant effect of weeks and sex on fluid intake and alcohol intake.
- On average, LAPs displayed low but physiologically relevant alcohol intake (0.41 g/kg/hour).



- LAPs had greater marble burying at MB2 than MB1, $p = 0.005$.
- No significant effect of EtOH exposure or sex.

ORM Results





Train day:
- No significant effect of EtOH or Sex on object exploration time.
- Significant EtOH x Sex interaction effect on latency to explore, $p = 0.047$. EtOH-Females had longer latency to explore than Water-Females, $p = 0.064$. This trend wasn't present in males, $p = 0.331$.

Test day: Many LAPs did not reach the criteria for reliable assessment of memory.

		> 3s explorarion during Train AND Test	
		Yes	No
Female	EtOH	2	2
	Water	1	3
Male	EtOH	2	3
	Water	4	0

Discussion and Acknowledgements

- Alcohol exposure did not affect marble burying.
- LAPs displayed very low levels of object exploration. LAPs' exploration is lower than their High Alcohol Preferring (HAP) counterparts (unpublished data) potentially due to differences in motivation.
- Higher exploration latency in EtOH than Water females could be due to alcohol-induced anxiety and/or neophobia towards objects.
- Larger sample size is needed to confirm these results.
- Other memory tests that do not rely on exploration may be suitable for aged LAP mice.

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