GABA mediated aggression in female mice

Matthew Bicakci, Meghan Lauze, Emily Newman, Klaus Miczek, Joseph DeBold

Tufts University, Psychology Dept., Medford, MA, 02155

Background

Alcohol and Violence
Most violent crime involves the consumption of alcohol. While most violent crime is committed by men, women can also become more aggressive under the influence of alcohol.

Individual Variability
Only a subset of individuals become aggressive after intake of alcohol. This can be seen in humans, as well as in animals ***(Miczek et al ,1998).***

Brain Mechanisms
Alcohol and benzodiazepines have a facilitating effect on $GABA_A$ receptors, the main inhibitory receptor in the brain. At low doses, these can alter an individual's perception of social cues which leads to increases in aggressive behavior. However, most research on heightened aggression in mammals has been conducted in males.

Objectives

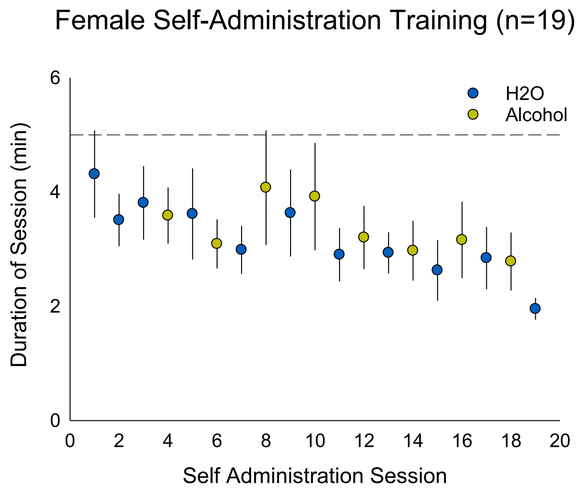
Aim 1: To determine if GABA-mediated heightened aggression can be modeled in female mice using alcohol and the benzodiazepine midazolam

Aim 2: To determine any differences in expression of heightened aggression between the sexes

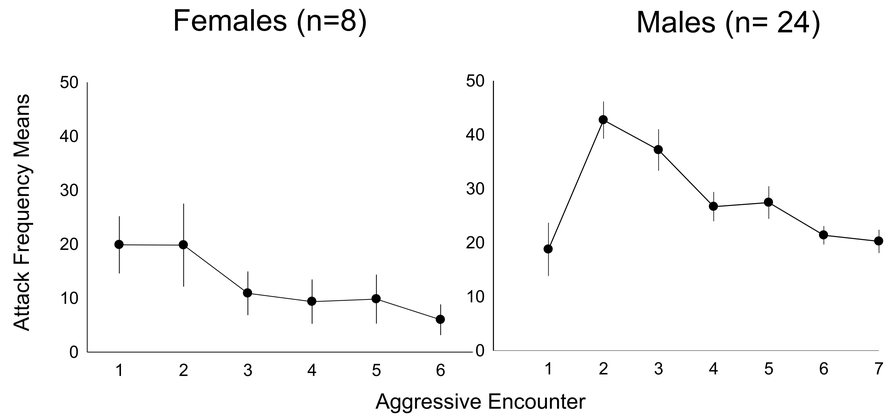
Results

A.

Over time, mice learn to take in fluid at higher rates

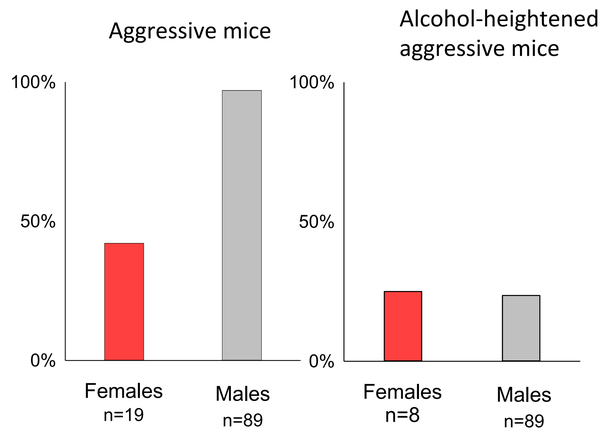


Female aggression stabilized in six confrontations, but at a much lower level than male aggression

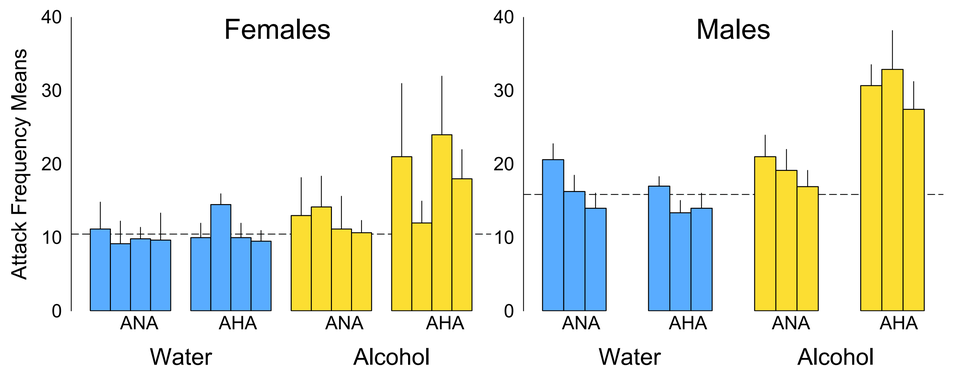


B.

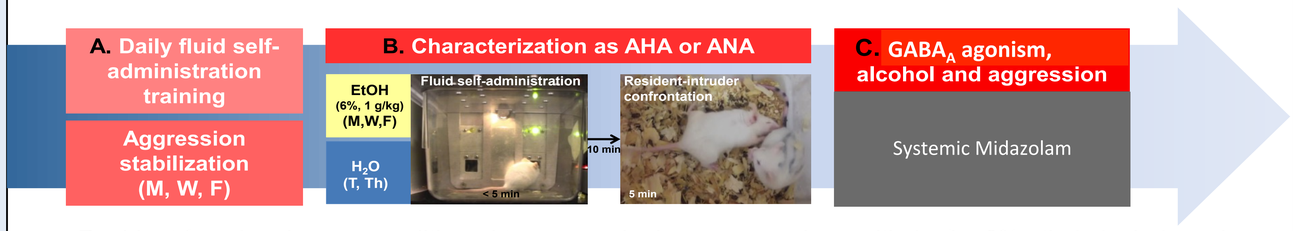
40% of females mice showed aggression



Female and male mice that are classified as alcohol-heightened aggressors show similar increases in aggressive behavior



Methods



A. Resident female mice are conditioned to nose-poke in an operandum, with 1 g/kg 6% ethyl alcohol serving as a reinforcer. Every other day, the same residents are exposed to a submissive female intruder mouse (5 minute session), and the resident's aggressive behavior is measured.

B. Residents were identified as expressing alcohol-heightened aggression (AHA) or alcohol non-heightened aggression (ANA) via aggressive encounters 10 minutes after self-administration, alternating between water and alcohol sessions.

C. A future direction of this study will be to asses the effects of midazolam (0 – 1.0 mg/kg) on aggressive behavior.

Conclusions

- Fewer females than males are aggressive, and their levels of aggression are much lower, as measured by bites and threats.
- Non aggressive females do not show aggressive behavior following alcohol intake

- The proportion of females that show alcohol-heightened aggressive behavior is similar to that of males
- AHA mice in both sexes show similar increases in aggressive behavior when they consume alcohol

References: Miczek et al. (1998) *Alcoholism-Clinical and Experimental Research 22*: 1698

Acknowledgements

We would like to thank the Summer Scholars program, as well as the NIAAA for the funding of this project (NIH Grant# NIH R01 AA013983).

NIAAA National Institute on Alcohol Abuse and Alcoholism