Effects of Sex and Ethanol on Approach-Avoidance Conflict Resolution: Including Females in a Preclinical Model of Alcohol Use Disorder

Danzell Lopez, Tanner McNamara, and Rutsuko Ito
Department of Psychology, University of Toronto Scarborough

Introduction:
- Alcohol use disorder (AUD) is characterized by excessive alcohol consumption, inability to control alcohol seeking during unavailability, and compulsive-seeking.
- AUD prevalence in females is increasing and they are more susceptible than males to the negative health consequences of alcohol use. However, they are underrepresented in preclinical models of AUD.
- Cocaine pre-exposed animals showed greater tendencies to approach conflicting cues of appetitive and aversive valences compared to cocaine naïve animals. This study aimed to include females in assessing the effects of ethanol to approach-avoidance decision-making and in evaluating a proposed preclinical model of AUD.

Methods:
Subjects: 40 Long Evans rats, 20 males and 20 females.

Radial Y-Maze: Half of the animals self-administered ethanol in their home cages for 5 weeks prior to this test.

Operant Training & Challenges:
- Ethanol Self-Administration (FR3 15-minute)
- Progressive Ratio (PR)
- Foot Shock Co-Delivery

Resistance to Foot Shock:
- Both sexes had similar percent baseline lever pressing.
- There was a trend for females to consume more ethanol at higher foot shock intensities than males.

Discussion:
- Females relative to males displayed reduced approach of conflict, although ethanol history did not affect approach-avoidance decision making unlike cocaine.
- Females consumed more ethanol, displayed greater motivation, and had a trend to be more persistent in ethanol seeking and more resistant to extinction and foot shock compared to males.
- Future directions of interest include analyses of ventral hippocampal projection activity to the median prefrontal cortex and nucleus accumbens which are involved in approach-avoidance decision making and affected by ethanol.


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