

Study shows that females are more sensitive to external factors that promote alcohol use

April 2 2015, by Ashley Trentrock

A study conducted in rats measuring risk factors that contribute to alcohol abuse suggests females are particularly sensitive to alcohol-related cues and stress which elicits a "craving" response.

"Traditionally, heavy drinking has been shown to be more prevalent in men, though more recent studies point to a narrowing in the gender gap," said Megan Bertholomey, Ph.D., a postdoctoral associate in the laboratory of Mary Torregrossa, Ph.D., at the University of Pittsburgh who conducted the research. "Further, alcohol-dependent women tend to show more negative emotional responses to drinking, including greater stress and anxiety."

To investigate sex differences in the role stress plays in [alcohol abuse](#), the researchers first trained male and female [rats](#) to press a lever, which would then administer alcohol simultaneously paired with an audiovisual cue. After three weeks of drinking, the rats associated the cue with alcohol.

The rats then underwent a period of abstinence with no audiovisual cue and no [alcohol intake](#); regardless of how many times they pressed the lever. However, those original alcohol-cue memories do not go away during abstinence, allowing the researchers to determine factors that can cause the rats to start responding again.

"It's well established that exposure to alcohol-associated cues and to stress can lead to reinstatement of the drug seeking response, which is

thought to be a model of craving or relapse in rats," said Bertholomey, who will present the research at the American Society for Pharmacology and Experimental Therapeutics (ASPET) Annual Meeting during Experimental Biology 2015.

Prior studies show that exposure to both cues and stress can have an additive effect on the propensity to cause craving and relapse in both people and in rats, and that females trained to respond for cocaine may be more sensitive to this effect. Thus, the researchers tested whether reinstatement of alcohol responding was different in male and [female rats](#) in the presence of the alcohol-paired cue with or without an injection of a drug that increases stress. The drug used, yohimbine, also produces a [stress response](#) in humans, which assists in making comparisons across species.

The researchers found that overall, the female rats pressed more on the lever that previously led to alcohol access than the males following either cue or [stress exposure](#) alone. Strikingly, when the cues and stress were combined, females had an even greater increase in alcohol seeking behavior compared to males and when either stimulus was given alone.

The results indicate that females are more influenced by environmental cues and stress in promoting a "craving"-like response that can drive them to seek and consume alcohol. These findings provide the basis for dissecting the brain pathways that causes the interactions between cues, [stress](#) and sex in alcohol seeking and drinking behavior.

"Individuals attempting to maintain abstinence are exposed to a number of factors that elicit craving and can lead to an increased risk of relapse," said Bertholomey. "The next step for us will be to understand the mechanisms responsible for this enhanced sensitivity in females, which will direct further development of pharmacological and behavioral interventions that might reduce craving and prevent relapse."

Alcohol use disorders are diagnosed in approximately 17 million adults in the United States, representing 9.9 and 4.6 percent of men and women in that age group, respectively, according to the National Survey on Drug Use and Health (NSDUH). The Centers for Disease Control and Prevention report that [alcohol](#)-related problems cost the United States \$223.5 billion and represent the third leading cause of preventable death.

Provided by Federation of American Societies for Experimental Biology

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