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Drug to treat alcohol use disorder shows promise among drinkers with high stress

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A new medication that targets part of the brain's stress system may help reduce alcohol use in people with alcohol use disorder (AUD), according to a new study by researchers at the National Institute on Alcohol Abuse and Alcoholism (NIAAA), part of the National Institutes of Health.

"Medications have become an important tool for treating alcohol use disorders, but current medications are not effective for all people with AUDs," noted NIAAA Director George F. Koob, Ph.D. "We're committed to developing new medications to provide effective therapy to a broader spectrum of people with AUDs."

As reported online in the journal *Neuropsychopharmacology*, researchers led by Raye Litten, Ph.D., acting director of the NIAAA Division of Medications Development, conducted a randomized clinical trial of a new compound, called ABT-436, designed to block the effects of vasopressin, a neuropeptide produced in the hypothalamus of the brain.

"Vasopressin helps to regulate the pituitary adrenal axis and other brain circuits involved in emotion," explained Dr. Litten. "As such, it plays a role in regulating stress, anxiety, and their interaction with AUD."

Dr. Litten, first author Megan Ryan and their NIAAA colleagues worked with NIAAA's multi-center Clinical Investigations Group, to recruit 144 alcohol-dependent adult men and women for the 12-week study. During a 28-day baseline period, female participants consumed at least 28 drinks per week, while male participants consumed at least 35 drinks per

week. Participants were then randomized to receive either placebo tablets or ones containing the ABT-436 compound. Researchers monitored participants' alcohol consumption, as well as their mood changes and smoking habits, as these are known to co-vary with alcohol consumption.

Researchers found that participants receiving ABT-436 experienced more days of alcohol abstinence than those receiving the placebo. In particular, participants who reported high levels of stress appeared to respond better to ABT-436, in that both the frequency of their drinking and the number of heavy drinking days they experienced decreased.

"Our findings suggest that potential future studies with drugs targeting vasopressin blockade should focus on populations of people with AUD who also report high levels of stress," said first author Ryan, a clinical project manager in the NIAAA Division of Medications Development.

Smokers may be another population that could benefit from ABT-436. In addition to its effects on alcohol consumption, study participants receiving the new compound experienced a reduction in smoking. The researchers suspect that ABT-436 might be targeting the same areas in the brain that relate to withdrawal and stress, and, in the process, influencing both tobacco and alcohol use disorders. Additional research is needed to determine if that is the case.

More information: Megan L Ryan et al. A Phase 2, Double-Blind, Placebo-Controlled Randomized Trial Assessing the Efficacy of ABT-436, a Novel V1b Receptor Antagonist, for Alcohol Dependence, *Neuropsychopharmacology* (2016). DOI: 10.1038/npp.2016.214

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