Low to moderate, not heavy, drinking releases 'feel-good' endorphins in the brain

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Scientists know that alcohol affects the brain, but the specifics remain unclear. One possibility is that alcohol may increase or decrease the release and the synthesis of endogenous opioid peptides - endorphins, enkephalins and dynorphins - in distinct brain regions important for drug addiction. For the first time, a rodent study has confirmed that low to moderate levels of alcohol alter beta-endorphin release in the midbrain/Ventral Tegmental Area (VTA) region, producing the pleasant effects that likely reinforce alcohol consumption.

Results will be published in the June issue of *Alcoholism: Clinical & Experimental Research* and are currently available at Early View.

"Some of the functions of opioid peptides are similar to those of the opiate morphine," explained Christina Gianoulakis, a professor in the departments of psychiatry and physiology at McGill University, and the study's corresponding author. "Like morphine, endogenous opioid peptides can induce analgesia and a mild euphoric effect, reduce anxiety, and may lead to a general feeling of well being. Therefore, increased release of endogenous opioid peptides in response to drinking could be partially responsible for the mild euphoric and anxiolytic effects associated with low to moderate amounts of alcoholic beverages." Gianoulakis is also with the Douglas Mental Health University Institute.

"The brain's natural opioids have been implicated in many physiological functions such as pain and pleasure," added Dzung Anh Le, a senior scientist at the Centre for Addiction and Mental Health, University of

Toronto. "Alcohol has long been thought to release these peptides, but previously the only way to confirm this was to rely on test tube experiments using extracted tissue samples, and findings from these studies were indirect and offered extremely limited interpretation."

Le said that researchers suspected that dopamine was a key brain chemical in one of the most heavily implicated pathways likely involved in drug and alcohol addiction, the VTA.

"One mechanism by which alcohol produces its euphoric or rewarding effects is through the stimulation of natural opioid peptides in the VTA, which consequently activates dopamine in this critical pathway," Le said. "Until now, no one has been able to answer whether alcohol is actually capable of triggering opioid release in the VTA."

Researchers injected male Sprague-Dawley rats with either saline or alcohol (0.8, 1.2, 1.6, 2.0, and 2.4 grams alcohol/kg of body weight). Using an in vivo microdialysis technique, study authors tracked the response of endorphins, enkephalins, and dynorphins at the level of the midbrain, including the VTA.

"We found that low to moderate but not high doses of alcohol increase the release of beta-endorphin in the VTA, one of the brain regions shown to be important for mediating the rewarding effect of alcohol," said Gianoulakis. "This supports a role of beta-endorphin in mediating some of the rewarding effects of alcohol. However, the same doses of alcohol that increase beta-endorphin release in the VTA have no significant effect on the release of enkephalins and dynorphins, the other two families of endogenous opioid peptides we examined."

Gianoulakis said that readers should remember that it is the low to moderate doses of alcohol that are associated with mild euphoria, decreased anxiety and a general feeling of well being. "On the other

hand, high doses of alcohol are known to induce sedative and hypnotic effects, and often increase rather than decrease anxiety."

"This research has confirmed a role of endogenous opioids in mediating alcohol addiction, and has delineated a pathway within which they may be involved," said Le. "It also goes further to specifically isolate an opioid peptide that may be most critically involved in a specific region of the brain. Endorphins are the natural peptides that most closely mimic the pharmacological properties of morphine, and of the three opioid families, they likely produce the greatest 'high.'"

Furthermore, Le added, methods used in this study are groundbreaking. "Dr. Gianoulakis and her team can track changes over time in living and freely moving animals," he said. "This has a profound implication on research in this area, as the effects of alcohol can be measured from an intact 'living' brain, in animals that are relatively uninhibited and unstressed within their environment."

Both Gianoulakis and Le said these findings will help future treatment options.

"VTA beta-endorphin appears to play a significant role in alcohol reinforcement, and may partially explain the effectiveness of naltrexone - an opioid receptor antagonist currently used as treatment of alcoholism - in reducing alcohol consumption by some individuals," said Gianoulakis.

"While current alcoholism treatment blocks opioids in a nonspecific fashion, this research suggests that a more targeted approach would be more beneficial," said Le. "Researchers now have to specifically target endorphins in the VTA to see if it really does affect alcohol abuse and craving."

"Readers should understand that drinking only low amounts of alcohol will increase endorphin release and produce pleasant effects," said Gianoulakis. "Thus, if after consumption of about two drinks of alcohol an individual does not experience the pleasant effects of alcohol, he or she should stop drinking. Consumption of high amounts of alcohol will not only fail to increase the release of endorphins, but may stimulate other systems in the brain that may lead to the development of anxiety and depression."

Source: Alcoholism: Clinical & Experimental Research