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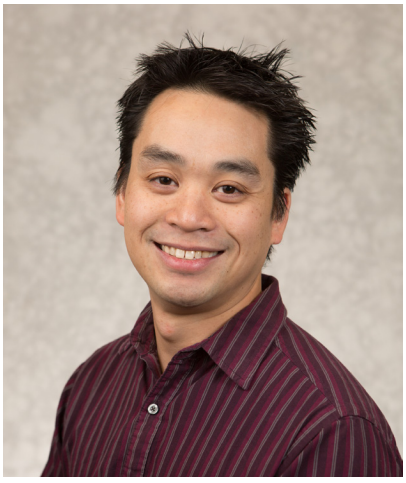

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Alcoholism is estimated to cost the United States a quarter of a trillion dollars annually, including the deaths of 88,000 individuals. Recovering alcoholics often experience a multitude of withdrawal symptoms including long-term mood disturbances. Clinical studies have reported a strong relationship between anxiety and alcohol relapse, which hinders long-term recovery (Hershon, 1977; Cloninger, 1987; De Soto et al., 1989; Annis et al., 1998). Corticotropin-releasing factor (CRF) is a 42-amino acid neuropeptide that regulates the mammalian endocrine, autonomic, and behavioral stress responses. Due to the relationship between anxiety and alcohol relapse, the CRF system is also an important mediator in enhanced alcohol self-administration and anxiety-related behaviors during acute and prolonged alcohol withdrawal. Research has shown that CRF_2 receptor activation alleviates anxiety-related behaviors during acute withdrawal. Due to the long-term mood alterations caused by alcohol withdrawal, this study explored the effects of CRF_2 receptor activation on anxiety-related behaviors during prolonged alcohol withdrawal. We hypothesized that the activation of CRF_2 receptors would decrease anxiety-related behaviors following protracted periods of alcohol withdrawal.

Male and female Wistar rats (n=16) were exclusively fed a liquid diet composed of 10% alcohol or sugar as an isocaloric control -for 25 days with unlimited access. Twenty-four hours after the removal of the ethanol liquid diet, rats were examined for signs of physical withdrawal. Afterward, rats were left undisturbed except for routine husbandry for 5 weeks prior to testing on the elevated plus maze, an animal model of anxiety. Ten minutes prior to testing, all rodents where given either 10 µg of the CRF_2 receptor agonist Urocortin 3 (Ucn3) or vehicle only (control). Rodents were placed on the elevated plus maze for 5 minutes. Every entry and time spent onto each arm of the elevated plus maze were recorded for 5 minutes as measures of general motor activity and anxiety-like behavior.

The results did support our hypothesis. No differences were found in body weight and fluid intake between all groups during liquid diet administration. A two-tail t-test confirmed that ethanol liquid diet fed rats experienced significantly more withdrawal signs compared to controls demonstrating that they were alcohol dependent. A two-way ANOVA was used to analyze behavior in the elevated plus maze with ethanol liquid diet condition and Ucn 3 dose and between-subjects factors. A significant interaction between the ethanol liquid diet and Ucn 3 was found. Alcohol dependent rats that were given Ucn3 prior to testing spent more time on the open arms of the maze compared to those that only received vehicle. This indicates CRF_2 activation alleviates anxiety-like behaviors in rats experiencing prolonged alcohol withdrawal. No differences were found in the number of closed arm entries between groups, suggesting that differences are likely not due to general motor impairment. Limitations of this study involve a low number of subjects. Future research will benefit from larger sample sizes to better indicate external validity. Other animal models of anxiety should also be used to confirm that CRF_2 activation can alleviate anxiety-like behaviors in a multitude of scenarios. If our initial results are supported, this could be an incentive for pharmaceutical companies to invest in the development of therapeutic medications for recovering alcoholics by targeting CRF_2 receptors to prevent anxiety related relapse.

*This scholar and faculty mentor have requested that only an abstract be published.