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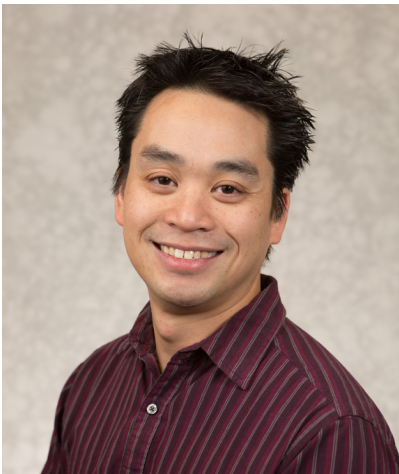
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The Effect of CRF2 Receptor Regulation on Depressive-Like Behaviors During Protracted Ethanol Withdrawal*



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There are many times in which stress plays an influential role in alcohol addiction, but it is most influential during the time of relapse, in which there are cycles of heightened anxiety, depressive mood, and negative affect (Logrip et al., 2011). Clinical studies have suggested that the most common reason for relapse is the ability for alcohol to relieve these negative mood symptoms experienced during withdrawal (Hershon, 1977; Cloninger, 1987). The target of this study is the corticotropin-releasing factor (CRF) system, which is understood to play a central role in regulating the behavioral stress response within the body (Dunn & Barridge, 1990). It is our hope that by regulating the depression experienced, we can begin the foundation for long-term strategies in the prevention of relapse following protracted abstinence. Urocortin 3 (Ucn 3) is a highly selective CRF₂ receptor agonist (Lewis et al., 2001), and studies have shown that Ucn 3 has the ability to reduce behaviors associated with depression in animal models (Tanaka & Telegdy, 2008). However, the ability of Ucn 3 to diminish depressive-like behaviors during protracted withdrawal has yet to be studied.

In order to examine the effects of Ucn 3 following protracted abstinence, male and female Wistar rats (n=24) were given a liquid diet consisting of a chocolate nutritional shake, vitamins, minerals, and 10% ethanol as their sole source of nutrition for 25 days. Those in the control group were given sugar as a caloric substitute for the ethanol and were fed the average amount of the liquid diet that the ethanol group consumed the previous day. The results showed that there were no statistical differences found between diet and the body weight or fluid intake for either male or female rats. This ensures that any potential behavioral differences cannot be attributed to nutritional deficiency or dehydration. The amount of ethanol consumed by the rats has been previously shown to produce blood ethanol levels of 150-225 mg/dl (Macey, 1996). One day after removal of the liquid diet, the rats were observed for physical signs of alcohol withdrawal. The results from this assessment showed that ethanol liquid diet fed rats had significantly higher withdrawal scores, confirming physical dependence to

alcohol. After five weeks during which rats were left undisturbed with the exception of routine husbandry, the rats were examined in the forced swim test. The results from the test did not show a statistically significant interaction between diet, drug, and time spent immobile. However, post hoc analysis did show a trend of less time spent immobile when injected with Ucn 3 during ethanol withdrawal that approached statistical significance $F(1,19) = 3.72$ $p = .07$. Further studies would need to be conducted in order to confirm the hypothesis that Ucn 3 has the ability to alleviate depression experienced during withdrawal, but the trend shows that there is reason to be cautiously optimistic about the future pharmaceutical opportunity to help those going through long term withdrawal in their path to remaining abstinent.

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