

November 27, 2018

Dear Dr. Koob,

Please consider the attached manuscript “Repeated binge drinking causes plastic increases in central amygdala corticotropin releasing factor neurons in vivo” by Irving, Aroni et al for submission to *Neuropsychopharmacology*. We declare no competing financial interests. This work has not been published and is not submitted for publication elsewhere.

Alcohol use disorder is a **severe public health crisis**, which costs the United States over 200 billion dollars annually, more importantly, binge drinking accounts for 75% of this cost. Corticotropin releasing factor neurons residing within the central amygdala (CeA) are involved in the modulation of binge drinking. However, the CeA is heterogeneous with many different neurotransmitter and neuropeptide containing neurons, making it difficult to examine CeA CRF neurons on a circuit level. In this current study, we combined *in vivo* electrophysiology with optogenetics to record from CeA CRF neurons during binge alcohol sessions. **This is the first study to identify and record from CeA CRF neurons in freely behaving mice.** We found that CeA CRF neurons display distinct firing characteristics to a lick of alcohol. Of these different groups, we found that CeA CRF neurons that increase firing immediately before a lick of ethanol increase their firing throughout a binge drinking session. Additionally, the activity of these neurons are enhanced after repeated binge drinking, indicating possible synaptic plasticity. Overall these data show that the CeA CRF neurons are not uniform and quite diverse in response to binge drinking. We believe these findings will be of broad interest to the neuroscience community and are well-suited for publication in *Neuropsychopharmacology*.

The following reviewers are well suited to review this manuscript:

Dr. Nicholas Gilpin

Dr. Paul Phillips

Dr. Thomas Kash

Dr. Marissa Roberto

Dr. Amy Lasek

Dr. Woody Hopf



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Due to conflict of interests, we would like to exclude the following reviewers:

Dr. Klaus Miczek

Thank you for your consideration of our manuscript as well as your time and effort. We look forward to your response.

Sincerely,



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