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Adaptations in the Parabrachial Nucleus After Chronic Opioid Exposure and Withdrawal

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Understanding how neural circuits involved in aversive states altered across the opioid-use cycle may provide us with an opportunity to identify novel mechanisms to break on the cycle. The parabrachial nucleus (PBN) acts as a hub for processing information about aversive states. Cells in the PBN, such as calcitonin gene-related peptide (CGRP) neurons, have been demonstrated to be critical in avoidance learning. Yet, whether neurophysiological or molecular adaptations in the PBN neurons help regulate symptoms of opioid withdrawal has yet to be elucidated. The PBN may be a critical hub in the processing of aversive states associated with OUDs. Discovering how the PBN is altered throughout the OUD cycle can lead to a new understanding in the progression of OUDs. We hypothesized that the PBN is involved in aversive states associated with opioid withdrawal. Using in vivo fiber photometry to profile calcium activity dynamics across the opioid-exposure cycle, we found that opioids reduce PBNCGRP neuron population activity and opioid withdrawal increases activity. Chemogenetically inhibiting PBN neurons during opioid withdrawal reduces overall withdrawal score. Using in situ hybridization, we found that there is altered expression of Oprm1 expression after induction of opioid dependence in the PBN. We found that there are neurophysiological and molecular adaptations in the PBN at different stages of the opioid-use cycle. We are currently performing bulk RNA sequencing from PBN tissue collected across the opioid-exposure cycle to determine how gene expression is altered to regulate these neurophysiological states.