Name: Cassandra Kooiker
Email: ckooiker@uci.edu
PI Name: Tallie Z. Baram, MD, PhD
PI email: tallie@uci.edu

Genetic tagging uncovers a role for the thalamic paraventricular nucleus in mediating aberrant reward behaviors following adverse experiences early in life

Cassandra L. Kooiker[1], Sophia C. Levis[1], Yuncai Chen[2], Matthew T. Birnie[2], Stephen V. Mahler[3], Tallie Z. Baram[1,2]

[1]Department of Anatomy and Neurobiology, University of California – Irvine, Irvine, CA; [2]Department of Pediatrics, University of California – Irvine, Irvine, CA; [3]Department of Neurobiology and Behavior, University of California – Irvine, Irvine, CA

Early-life adversity (ELA) is associated with poor emotional health, including risk for substance use disorders later in life. We have identified a striking opioid addiction-like phenotype and augmented pursuit of natural rewards in females reared in our rodent model of ELA. However, the brain regions and processes underlying these long-term consequences remain unclear. The paraventricular thalamic nucleus (PVT) is an important node of the reward circuit that encodes remote emotionally salient experiences to influence future motivated behaviors. We hypothesize that the PVT encodes adverse experiences as remote as the early postnatal period in mice, and that ELA-engaged PVT neurons subsequently contribute to alterations in reward behaviors in adults. To investigate this hypothesis, we employed genetic tagging: TRAP2 mice were reared in control or ELA in a limited-resource cage between postnatal days 2-9, and we induced the TRAP2 system using tamoxifen on P6, triggering Cre-dependent recombination in neurons activated during P6-P8. This leads to permanent Fos-promoter dependent labeling of neurons activated during this time frame. We then chemogenetically inhibited these ELA-engaged neurons during an adult reward behavior task to test for their contribution to ELA-induced exuberant reward behaviors. ELA robustly and selectively activated more PVT neurons than typical rearing conditions, validated by quantifying FOS expression in wild-type mice. Silencing ELA-engaged PVT neurons during reward-related tasks in adult female mice normalized their behavior, ameliorating ELA-induced changes.

Conclusion: The PVT, likely through selective activation by ELA and consequent transcriptional cascades may contribute crucially to aberrant reward behaviors following ELA, with significant translational impact.