Title
The Paraventricular Nucleus of the Thalamus Contributes to Early-Life Adversity-Induced Disruptions in Reward-Related Behaviors

Journal
NEUROPSYCHOPHARMACOLOGY, 47(SUPPL 1)

ISSN
0893-133X

Authors
Kooiker, Cassandra
Birnie, Matthew
Chen, Yuncai
et al.

Publication Date
2022

P109. The Paraventricular Nucleus of the Thalamus Contributes to Early-Life Adversity-Induced Disruptions in Reward-Related Behaviors

Cassandra Kooiker*, Matthew Birnie, Yuncai Chen, Tallie Z. Baram

University of California - Irvine, Irvine, California, United States

Background: Early-life adversity (ELA) is associated with poor cognitive and emotional health, including an increased risk for a variety of affective disorders, such as depression and substance use disorders. Many of these disorders are characterized by impairments in reward-related behaviors, and we find that these same deficits are provoked by rodent models of ELA. However, the brain regions and processes underlying these long-term consequences of ELA remain largely unknown. The paraventricular nucleus of the thalamus (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-related behaviors in adults.

Methods: We employ TRAP2 mice, which we exposed to a week of simulated ELA in a limited-resource cage between postnatal days 2-9. We induced the TRAP2 system using tamoxifen on P6, triggering Cre-dependent recombination in neurons activated during P6-P8. This leads to permanent labeling of neurons activated during this time frame. We validated our findings using routine cFos immunohistochemistry in WT mice. We then chemogenetically inhibited these ELA-engaged neurons during an adult reward-seeking task with the goal of ameliorating ELA-induced changes in reward-seeking behaviors.

Results: ELA robustly and selectively activates significantly more PVT neurons than typical rearing conditions ($p = 0.0154$, unpaired t-test; $N = 24$), and a large proportion of these ELA-engaged PVT neurons express CRFR1 (40% vs 20% in controls, $p < 0.001$, unpaired t-test; $N = 12$). Silencing ELA-engaged PVT neurons during reward-related tasks in adult female mice ameliorates the observed ELA-induced changes in reward-seeking behaviors ($N = 16$).

Conclusions: The PVT is robustly and almost uniquely activated in response to emotionally salient events in neonatal mice, and inhibition of these ELA-engaged neurons ameliorates ELA-induced changes in reward-seeking. The PVT is thus poised as a potential contributor to deficits in reward-related behaviors following ELA.

Keywords: Paraventricular Nucleus of the Thalamus, Early-Life Adversity, Affective Disorders, Reward Circuitry, Motivated Behaviors

Disclosure: Nothing to disclose.