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Permalink

https://escholarship.org/uc/item/1cp713br

Journal

NEUROPSYCHOPHARMACOLOGY, 45(SUPPL 1)

ISSN

0893-133X

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Publication Date

2020

Copyright Information

Peer reviewed

W28. A Novel CRH-specific Projection from Basolateral Amygdala to Nucleus Accumbens Depresses Reward-Seeking Behaviors

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Background: The reward circuit executes the encoding and seeking of rewarding experiences, and disrupted reward circuit function is thought to underlie mental health problems including depression and drug and alcohol use disorders. The nucleus accumbens (NAc) is a major component of the reward circuit and key structure mediating pleasure, motivation, and emotional processes. Multiple inputs converge onto the NAc to modulate reward-seeking behaviors, including the basolateral amygdala (BLA). The BLA mediates associate learning for both aversive and appetitive stimuli, and stimulation of glutamatergic projections from the BLA to NAc selectively promotes appetitive, but not aversive behaviors. We have identified a BLA-NAc projection expressing corticotropin-releasing hormone (CRH). CRH is an evolutionarily conserved stress reactive neuropeptide that plays context dependent roles in the reward circuit. In the NAc, CRH+ axon terminals modulate reward and motivational behaviors, yet their origin is unclear. CRH+ BLA-NAc projections are uniquely poised to influence reward behaviors during current or prior stress, Here, we identify the role of this CRH+ BLA-NAc projection in reward seeking behavior in naïve and stress-experiencing mice.

Methods: To identify CRH+ projections onto the NAc, we utilized viral-genetic approaches to map these pathways using Cre-dependent viruses injected into CRH-IRES-Cre mice. To determine the function of the novel CRH+ BLA-NAc projection we employ chemogenetic and optogenetic strategies in both control and early-life adversity experiencing mice. In CRH-IRES-Cre mice, we injected excitatory or inhibitory Cre-dependent DREADD (hM3Dq and hM4Di) and optogenetic (ChR2 and eNpHR3.0) carrying viruses into BLA, followed by medial NAc shell targeted microinjections of CNO or placement of optic fibers. We tested the function of this pathway using the Sucrose Preference, sex-reward seeking behavior (Scent of a Mouse) and Palatable Food tasks.

Results: Viral genetic tracing identified a novel CRH+ projection from the BLA to the medial NAc shell. Activation of the projection using chemo- and optogenetic excitation reduced preference for sucrose, palatable food, and the scent of a female mouse. Compared with control mice, male mice that experienced ELA had reduced preference for sucrose, palatable food and for the scent of a female mouse. In adult ELA mice, chemo- and optogenetic inhibition of the CRH-specific BLA-NAc projection rescued all three reward-seeking behaviors.

Conclusions: We identify a novel CRH+ BLA-NAc projection and establish its role in mediating the effects of ELA on reward-seeking behaviors. These discoveries provide new, important information about the mechanisms of reward-seeking behaviors and provide potential selective targets for prevention and intervention in the disruption of such behavior that accompanies several psychopathologies.

Disclosure: Nothing to disclose.