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The lateral hypothalamus to lateral habenula projection, **but not the ventral pallidum to lateral habenula projection**, regulates voluntary ethanol consumption

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Highlights:

- Lesioning the stria medullaris increases voluntary ethanol consumption
- Disconnection of the lateral hypothalamus to lateral habenula projection increases voluntary ethanol consumption.
- Disconnection of the ventral pallidum to lateral habenula projection does not alter ethanol-directed behaviors.

Abstract

The lateral habenula (LHb) is an epithalamic brain region implicated in aversive processing via negative modulation of midbrain dopamine (DA) and serotonin (5-HT) systems. Given the role of the LHb in inhibiting DA and 5-HT systems, it is thought to be involved in various psychiatric pathologies, including drug addiction. In support, it has been shown that LHb plays a critical role in cocaine- and ethanol-related behaviors, most likely by mediating drug-induced aversive conditioning. In our previous work, we showed that LHb lesions increased voluntary ethanol consumption and operant ethanol self-administration and blocked yohimbine-induced reinstatement of ethanol self-administration. **LHb lesions also attenuated ethanol-induced conditioned taste aversion suggesting that a mechanism for the increased intake of ethanol may be reduced aversion learning.** However, whether afferents to the LHb are required for mediating effects of the LHb on these behaviors remained to be investigated. Our present results show that lesioning the fiber bundle carrying afferent inputs to the LHb, the stria medullaris (SM), increases voluntary ethanol consumption, **suggesting that afferent structures projecting to the LHb are important for mediating ethanol-directed behaviors**. **We then chose two**