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The role of the lateral habenula in alcohol use disorder

Abstract:

Alcohol use disorder (AUD) affects approximately 14.1 million people in the United States, and alcohol is one of the most widely used and misused drugs globally (WHO, 2018). Ethanol has both rewarding and aversive properties, which are crucial in the development of AUD. While the rewarding property is associated with increased dopamine release in areas like the nucleus accumbens, the aversive property is less understood. The lateral habenula is described as the "aversion center" in the brain. It serves as a hub for receiving and relaying signals from the limbic system to various brainstem regions involving serotonergic, dopaminergic, and norepinephrinergic pathways. It is activated by aversive events, making it a potentially critical region in AUD. Research indicates that ethanol regulates the activities of LHb neurons through multiple mechanisms, including dopamine and Corticotropin-releasing factor signaling. This regulation contributes to ethanol-induced conditioned place aversion. Animals experiencing withdrawal from chronic ethanol consumption exhibit elevated pain sensitivity, anxiety levels, and sensitivity to stress, especially in females. This aversive state is associated with the hyperexcitability of LHb neurons, involving both presynaptic and postsynaptic mechanisms. Prolonged alcohol consumption increases proinflammatory cytokines and microglia in the brain. Interleukin-6 (IL-6) and IL-18 receptors, highly expressed in the habenula, modulate the excitatory synapses on LHb neurons. Manipulating IL6/IL18 in the LHb can regulate anxiety- and depressive-like behaviors during acute abstinence, with a more significant effect observed in females. In summary, the lateral habenula is critical in developing alcohol use disorder.

About the Speaker

Dr. Zuo, MD, Ph.D., is a physician and has earned a Ph.D. in pathophysiology. She has joined Dr. Ye's lab since 2011, working on neural mechanisms underlying drugs of abuse, particularly alcohol use disorder. In the past ten years, she has published over 47 peer-reviewed publications. She is an expert in many ex vivo and in vivo techniques, including the patch clamp, chemogenetics, molecular, and stereotaxic surgery for guide cannula microinjections, immunohistochemistry, and behavioral approaches.