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ALK in the ventral tegmental area regulates binge-like ethanol consumption and dopamine receptor sensitivity in mice

ALK is a receptor tyrosine kinase expressed in the nervous system that we previously found to regulate behavioral responses to ethanol in mice. To further characterize the ability of ALK to control ethanol consumption, we treated mice systemically with the ALK inhibitor, TAE684, and tested them for binge-like drinking using the drinking in the dark (DID) protocol. Mice treated with TAE684 drank less ethanol than controls, indicating that ALK activity in adult mice promotes binge-like drinking. Since the ventral tegmental area (VTA) is a key brain region involved in the rewarding and reinforcing effects of ethanol, we examined whether *Alk* expression in the VTA might be important for ethanol consumption. A lentiviral-delivered short hairpin RNA (shRNA) targeting *Alk* or a non-targeting control shRNA was delivered into the VTA. Mice expressing *Alk* shRNA in the VTA drank less ethanol in the DID test compared to mice expressing a control shRNA. We characterized the expression of ALK in the VTA using immunohistochemistry and found that ALK is expressed on dopamine neurons, suggesting that ALK might regulate the firing properties of these neurons. Extracellular recordings of putative dopaminergic (pDA) neurons in VTA slices treated with TAE684 showed that there was no difference in the ability of dopamine to inhibit firing of pDA neurons. However, TAE684 prevented the D2 receptor desensitization of pDA neurons induced by prolonged exposure to moderate concentrations of dopamine. Together, these data suggest that ALK activity in the VTA regulates binge-like ethanol consumption and desensitization of dopamine receptors.

Biography

Amy W Lasek received her PhD from Cornell University and completed a postdoctoral fellowship at the University of California, Berkeley. She was an Associate Investigator at the Ernest Gallo Clinic and Research Center at the University of California, San Francisco. She is currently an Assistant Professor of Psychiatry and Anatomy and Cell Biology at the University of Illinois at Chicago. She is also a PI on the NIH funded projects "Mechanisms of estrogen action in enhancing behavioral responses to cocaine", "Regulation of excessive alcohol consumption by the LMO-ALK axis", and "RNA interference core".

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