Amygdala Dysregulation in Alcohol Dependence

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Behavioral and cellular studies indicate that brain stress-related peptides, such as corticotropin releasing factor (CRF), are recruited during the development of alcohol dependence. The GABAergic system in the central amygdala (CeA) is an important mediator of the anxiety associated with stress and drug dependence. Accumulating evidence indicates that alcohol abuse and dependence induce neuroadaptations in the CeA stress system, and these functional and circuit alterations are in part responsible for some of the behavioral and physiological phenotypes associated with alcohol dependence.

CRF release in the CeA is increased in alcohol-dependent animals during withdrawal and it contributes to withdrawal-induced anxiety and alcohol consumption. Notably, CRF strongly modulates GABAergic synapses in the CeA. I will present our work on these neuropetidergic-GABA interactions, the intracellular mechanisms underlying these interactions, and the CeA cell-type and circuit-specific adaptive changes that occur during alcohol dependence. I will also discuss similarities in CeA neuroadaptations observed with other drugs of abuse and across species.

Lastly, I will show how anti-stress peptides that are implicated in regulating voluntary ethanol intake also exert marked antagonist effects on the CRF system in the CeA. Understanding the cellular mechanisms of neuropeptides and their role in modulating amygdalar GABAergic signaling will uncover key neuroadaptive sites and provide insight into the transition to addiction and anxiety disorders, as well as into possible treatment.

Supported by grants from NIAAA (AA015566, AA06420, AA016985, AA017447, AA021491 and AA013498) and from the Pearson Center for Alcoholism and Addiction Research.

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