

## **Project 7: Ethanol, Stress and Dopamine**

**Sara R. Jones, Ph.D., Principal Investigator**

Wake Forest University School of Medicine, Winston-Salem, NC

We propose to examine the impact of chronic ethanol exposure and withdrawal stress on the DA system of genetically defined mice. A repeated ethanol withdrawal paradigm developed within the INIA-Stress Consortium has been shown to increase drinking in C57Bl/6 (C57) mice, and we hypothesize that DA system function is reduced following this paradigm. Because of the central role that the DA system plays in the neurobiology of addiction, it is vital to understand the effects of ethanol exposure and withdrawal on the DA system. Our general hypothesis is that low endogenous DA function in brain predisposes mice to high alcohol preference and consumption, and further that chronic ethanol exposure and withdrawal decreases DA function. We will use microdialysis in freely moving mice and cyclic voltammetry in brain slices to examine the function and dynamics of the DA system in detail. The brain areas to be examined were chosen by the consensus of INIA investigators who will interact with this project. They include the nucleus accumbens (NAc, core and shell regions), basolateral amygdala (BLA) and ventral tegmental area (VTA). These experiments will be performed first on inbred "alcohol-preferring" C57BL/6J (C57) mice and "alcohol-avoiding" DBA/2J (DBA) mice. We will then examine mice created or characterized by INIA consortium projects and cores with targeted deletions of genes, extreme gene expression patterns related to the DA system and extreme phenotypic responses to ethanol or stress effects.

**Relevance:** The interaction of stressful events and ethanol consumption is of critical importance in human alcoholics and stress is an important factor in relapse events. Understanding the combined effects of ethanol and stress on the dopamine system, which is critical for reward processes, will aid in the understanding of the neurobiological mechanisms underlying alcoholism and may lead toward new insights into pharmacotherapies for the treatment of alcoholism.