Dopamine is a neurotransmitter, important in many functions, including learning, movement, attention and reward. Robinson is focused on the key role of dopamine in the association between cues and drug experience. Addiction links cues and drug experiences leading to cues, e.g. seeing an alcohol advertisement or establishment prompts hunger for the reward, e.g. craving for drug. Psychologists have found that addicted individuals respond to cues that they learned were rewarding when first experimenting with drugs, even after they stop being rewarding, e.g. continued drug seeking in the absence of reward (and likely presence of negative consequences). The psychological shifts from goal-directed behavior to automatic habitual behavior are thought to be based on changes in dopamine neurotransmission.

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Data from this study will provide important information on how the brain differentially encodes goal-directed versus habitual alcohol drinking. Robinson thinks that these studies could potentially identify novel mechanisms that would be of crucial importance to understand the development and treatment of alcohol abuse and alcoholism.

Wilhelmsen Awarded Five-Year R01 Grant

Bowers Center for Alcohol Studies Researcher Donita Robinson, Ph.D., recently received her first Research Project Grant (R01) from the National Institutes of Health’s National Institute on Alcohol Abuse and Alcoholism. Totaling just over a million dollars, the five-year project will examine dopamine release and neural activity in rat models of habitual alcohol drinking and cue-induced relapse.

The project, titled “Habits and cues in alcohol drinking: Dynamic striatal activity,” will look at the major factors that contribute to habitual alcohol drinking, such as the learning processes underlying habit formation and the degrees to which habits versus goal-directed behaviors may influence the susceptibility to relapse.

“Alcoholism is a chronic disorder that typically spans several decades and may be perpetuated by learned, habitual behavior. Studies in rats can model the contribution of habit to alcohol drinking and allow direct measurement of brain function during these behaviors,” said Robinson.

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The genetics of alcoholism is one of the great challenges of 21st century medicine. We know that alcoholism is associated with families. Genetics are important, although family association likely includes both genetic and environmental factors, since alcohol exposure differs in families with alcoholism. Both protective and risk genes are likely very important in the genetics of alcoholism. We know that metabolize alcohol play a role in the genetics of alcoholism. Individuals who have very fast alcohol dehydrogenase and/or slow aldehyde dehydrogenase gene alleles have an endogenous Antabuse-like reaction to alcohol that protects them from becoming alcoholic. The endogenous Antabuse-like reaction makes them sick when they drink alcohol, yet these metabolic alleles do not protect all from becoming alcoholic.

Many factors, including animal genetic models of alcoholism, suggest genes that regulate brain function may be important in alcoholism. Family history and risk for alcoholism are genetically linked to a low sedative response to alcohol. We don’t know how many factors in the regulatory network contribute to alcoholism.

The endogenous Antabuse-like reaction to alcohol is controlled by at least two genetic variants in humans. One variant, DRD2, is associated with alcoholism and other disorders. Another variant, DRD4, is associated with the expression of the gene and the clinical condition of alcoholism.

The increasingly sophisticated genetic analyses that identify risk factors in specific populations. By a systematic approach to identifying genetic variation in alcoholism, we can increase our understanding of how genes influence the development of alcoholism. The genetics of alcoholism can include differences in tolerance, withdrawal, compulsive drive, impulsive actions promoting negative consequences, and social and family factors that contribute to the diagnosis of alcohol dependence. Another part of the complexity is that other mental diseases, such as depression and anxiety, are often diagnosed as co-morbid when combined with alcohol dependence. All of these factors make it very difficult for geneticists to find which alleles of genes associate with alcoholism.

What is exciting about Kirk Wilhelmsen’s work is the use of novel combinations of genes, unique environmental factors, and specific phenotypic aspects of the diagnosis that associates individuals with similar symptoms and allelic genotypes. This novel and interesting new direction requires incredible computing and mathematics but may unravel the complexity and allow us to understand the genetics of alcoholism.

Dr. Linda P. Spear
Received the 2008 Bowles Lectureship Award
This annual award honors distinguished researchers that have made significant contributions to our understanding of the causes, prevention and/or treatment of alcoholism and alcohol abuse.