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Addiction: Nature or Nurture?

Peer pressure, an unstable home environment and other emotional issues are often blamed for adolescent addiction. From the viewpoint of biopsychology and neuroscience, these factors combine with dysfunctions in neural pathways leading to addictive behaviors.

Dr. Susan Ferguson, a new principal investigator in the Center for Integrative Brain Research, focuses her research on understanding the neural circuitry underlying addictive behavior.

“There is a particular brain circuit that is thought to be responsible for addiction,” says Susan. “The basal ganglia system and its major relay station – the striatum – are thought to mediate reward, motivation, decision making, impulsivity and compulsivity; both positive and negative types of behaviors.”

She continues, “This circuitry becomes disrupted in addictive individuals who assign abnormally high value to the pursuit of their addictions. Therefore, addiction is truly a brain disease in that the affected individual really can’t control him or herself.”

The breakthrough of an animal model

The core of Susan’s research looks at two cell populations in the striatum. The direct pathway cells with dopamine D1 receptors motivate the circuit to proceed with a behavior, while the indirect pathway cells with dopamine D2 receptors act as a brake to stop that behavior.

During her post-doctoral studies, she worked with Dr. John Neumaier, an expert in viral-mediated gene transfer at the University of Washington and collaborated with Dr. Bryan Roth of the University of North Carolina at Chapel Hill. During this collaboration, Susan placed an artificial receptor into the two main cell types of the striatum of animals. She administered drugs that bind to these receptors to temporarily shut down part of the striatal circuitry and observed how this change influenced the development of behaviors associated with addiction in the animals.

“That was quite a breakthrough as it had never been done before in an animal model,” Susan recalls.

At Seattle Children’s, Susan continues to pursue this avenue of research using more complex animal models. One example is a drug self-administration model where rats press a lever to administer their own drugs. Susan will examine how shutting down parts of the basal ganglia circuit affect this behavior.

Additionally, Susan received funding to investigate behavioral inhibition, a task that involves training animals to withhold a behavior so they can receive a reward.
In behavioral inhibition, the animal subject learns to press one lever, then a second lever very rapidly to get a food pellet. Next, it is trained that if a tone accompanies the pressing of the first lever, it will get a food pellet only if it does not press the second lever. This can be difficult since the animal is used to pressing the second lever to receive the food pellet.

“Addicts do not withhold responses well,” says Susan. “You tell them not to do something; they have a hard time following that instruction. Through this model, we can hopefully probe more about impulsivity.”

**Not just an adult disease anymore**

With all the news about adolescent drug and alcohol use, Susan believes that “we need to look at addiction as not just an adult disease.”

In a 2009 *Morbidity and Mortality Weekly Report* by the Center for Disease Control and Prevention, a Youth Risk Behavior Surveillance study showed that 41.8% of American high school students consume alcohol and 20.8% use marijuana. Susan’s research data will provide scientific insight into this alarming issue.

The circuit of Susan’s research interest is also implicated for Attention Deficit Hyperactivity Disorder (ADHD).

“Striatal circuitry is changed in children with ADHD,” she says. “They have issues with impulsivity. Looking at the behavioral inhibition model also helps us understand how impulsivity is working in these kids.”

**A researcher and a ‘soccer mom’**

Susan was drawn to Children’s because of the diverse interests of the researchers.

“With my background in behavioral research and developing animal models to try to understand diseases, I am excited about the potential opportunities to collaborate with other researchers,” she says.

Outside of work, Susan is a true “soccer mom.”

“My kids and our 1-year-old Golden Mountain Dog keep me very busy,” says Susan. She and her husband, a pediatric radiologist at Children’s, enjoy all the outdoor activities the Pacific Northwest has to offer.

—Richard Chan
from *Interaction Research News*