Finding novel therapeutic targets to treat depression and drug addiction

Depression and addiction affect millions of adults in the United States; and oftentimes, there is overlap between these two dysfunctions. Yet, little is known about the underlying mechanisms.

Michelle Mazei-Robison, assistant professor of physiology, is working to understand more about these disorders.

“We know there is significant comorbidity between psychiatric mood disorders, such as depression and post-traumatic stress disorder (PTSD), and addiction. But we don't know how each is influencing the other,” Mazei-Robison said.

“We know that stress is a powerful modulator of addiction . . .”

Her group is studying how the dysfunction of dopamine neurons in the ventral tegmental area (VTA) of the brain influences mood disorders and addiction.

“We are studying this ‘pleasure center’ region of the brain at a microscopic level, looking at the neurons that make up the VTA—their shape and structure, and how they connect to other parts of the brain,” she said.

Her recent work utilizes a chronic social defeat model in mice that induces symptoms relevant to depression and PTSD.

“We’re also interested in understanding what’s happening in the VTA in response to drugs. We want to find out what makes an addict’s brain different from a person who hasn't experienced drugs—or someone who has experienced drugs but doesn't develop addiction,” Mazei-Robison said.

“We know that stress is a powerful modulator of addiction,” she continued, “so we put mice through a stress situation to see how that affects their drug intake and behavior. We then study their brains to see what these neurons look like.”

Opiate drugs change the shape of the neurons in the VTA, causing them to shrink.

“This seems to affect how they work, their output and, we believe, how pleasurable feelings are processed,” she said. “We also look at the protein and gene changes within the neurons.”

In Mazei-Robison’s study, even though all of these genetically identical mice were exposed to the same stressors, not all of them were affected in the same way; some were “resilient.”

“We know the same is true with humans. When individuals go through horribly traumatic events, some seem more able to cope,” she said.

Mazei-Robison’s study could help scientists tap into this “active coping” mechanism in the human brain. The discovery of novel therapeutic targets could lead to treatment to prevent depression and dependence on drugs.

Sophia Kaska (left), a pharmacology and toxicology graduate student, and Michelle Mazei-Robison, assistant professor, study the ventral tegmental area (VTA) of the brain—which is shown in the background illustration.

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Photographs courtesy of: Harley Seeley, Margaux Forster/The State News and the Department of Physiology.

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