Chronic cocaine use triggers changes in brain's neuron structure

May 9 2012

The research, led by UB's Dietz, suggests a potential new target for development of a treatment for cocaine addiction. Credit: Douglas Levere, UB Communications

Chronic exposure to cocaine reduces the expression of a protein known to regulate brain plasticity, according to new, in vivo research on the molecular basis of cocaine addiction. That reduction drives structural changes in the brain, which produce greater sensitivity to the rewarding effects of cocaine.

The finding suggests a potential new target for development of a treatment for cocaine addiction. It was published last month in Nature Neuroscience by researchers at the University at Buffalo and Mount Sinai School of Medicine.

"We found that chronic cocaine exposure in mice led to a decrease in this protein's signaling," says David Dietz, PhD, assistant professor of pharmacology and toxicology in the School of Medicine and Biomedical Sciences, who did the work while at Mt. Sinai. "The reduction of the expression of the protein, called Rac1, then set in motion a cascade of events involved in structural plasticity of the brain -- the shape and growth of neuronal processes in the brain. Among the most important of these events is the large increase in the number of physical protrusions or spines that grow out from the neurons in the reward center of the brain.

"This suggests that Rac1 may control how exposure to drugs of abuse, like cocaine, may rewire the brain in a way that makes an individual more susceptible to the addicted state," says Dietz.

The presence of the spines demonstrates the spike in the reward effect that the individual obtains from exposure to cocaine. By changing the level of expression of Rac1, Dietz and his colleagues were able to control whether or not the mice became addicted, by preventing enhancement of the brain's reward center due to cocaine exposure.

To do the experiment, Dietz and his colleagues used a novel tool, which allowed for light activation to control Rac1 expression, the first time that a light-activated protein has been used to modulate brain plasticity.

"We can now understand how proteins function in a very temporal pattern, so we could look at how regulating genes at a specific time point could affect behavior, such as drug addiction, or a disease state," says Dietz.

In his UB lab, Dietz is continuing his research on the relationship between behavior and brain plasticity, looking, for example, at how plasticity might determine how much of a drug an animal takes and how persistent the animal is in trying to get the drug.

Provided by University at Buffalo