



Cocaine and the teen brain: Yale research offers insights into addiction

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Source: [Yale University](#)

When first exposed to cocaine, the adolescent brain launches a strong defensive reaction designed to minimize the drug's effects, Yale and other scientists have found. Now two new studies by a Yale team identify key genes that regulate this response and show that interfering with this reaction dramatically increases a mouse's sensitivity to cocaine.

The findings may help explain why risk of drug abuse and addiction increase so dramatically when cocaine use begins during teenage years.

The results were published in the Feb. 14 and Feb. 21 issues of the *Journal of Neuroscience*.

Researchers including those at Yale have shown that vulnerability to cocaine is much higher in adolescence, when the brain is shifting from an explosive and plastic growth phase to more settled and refined neural connections characteristic of adults. Past studies at Yale have shown that the neurons and their synaptic connections in adolescence change shape when first exposed to cocaine through molecular pathway regulated by the gene integrin beta1, which is crucial to the development of the nervous system of vertebrates.

"This suggests that these structural changes observed are probably protective of the neurocircuitry, an effort of the neuron to protect itself when first exposed to cocaine," said Anthony Koleske, professor of molecular biophysics and biochemistry and of neurobiology and senior author of both papers.

In the latest study, Yale researchers report when they knocked out this pathway, mice needed approximately three times less cocaine to induce behavioral changes than mice with an intact pathway.

The research suggests that the relative strength of the integrin beta1 pathway among individuals may explain why some cocaine users end up addicted to the drug while others escape its worst effects, Koleske theorized.

"If you were to become totally desensitized to cocaine, there is no reason to seek the drug," he said.

Koleske and Jane R. Taylor, professor of psychiatry and psychology and an author of the Feb. 14 paper, are teaming up with other Yale researchers to look for other genes that may play a role in protecting the brain from effects of cocaine and other drugs of abuse.

Shannon Gourley, now of Emory University who worked with Koleske and Taylor, is lead author on the Feb. 14 paper detailing how the structural response to cocaine protects against

cocaine sensitivity. Anastasia Oleveska and Michael S. Warren are other Yale authors on this paper. Warren and William D. Bradley of Yale are co-lead authors of the latest Neuroscience paper describing the role for integrin beta 1 in the control of adolescent synapse and dendrite refinement and stability. Yu-Chih Lin, Mark A. Simpson, Charles A. Greer are other Yale-affiliated authors.

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