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Novel compound halts cocaine addiction and relapse behaviors

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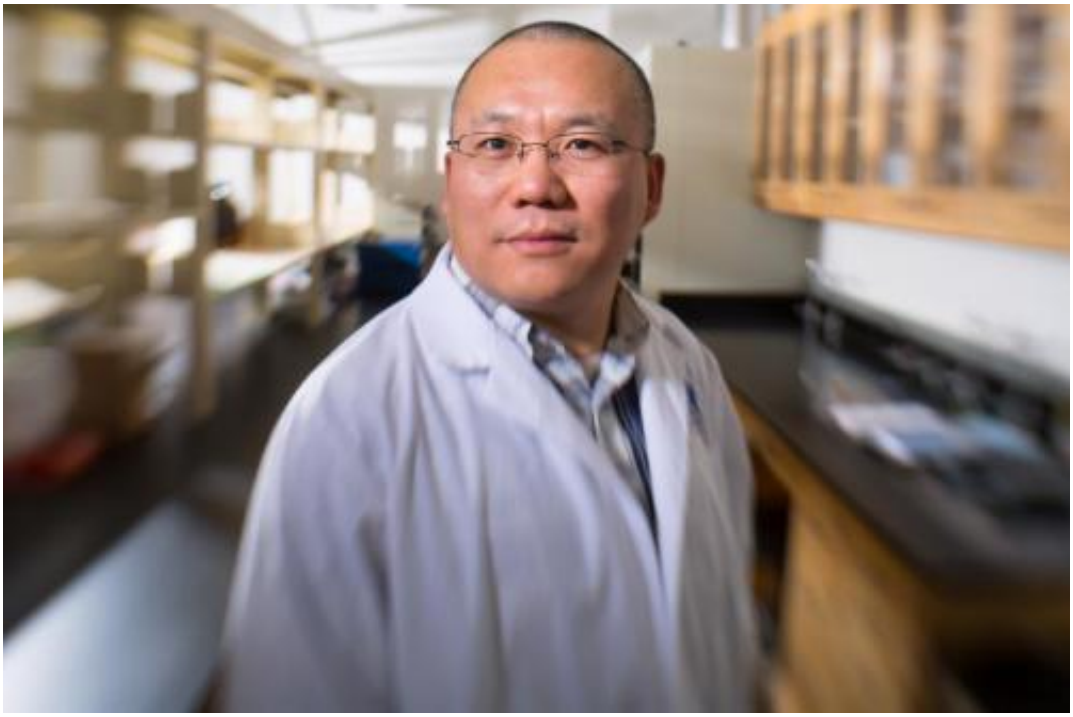

New research published by Jun-Xu Li in the UB Department of Pharmacology and Toxicology and his colleagues demonstrates that a novel compound dramatically blocked cocaine's rewarding effects and markedly blunted cocaine relapse in animals. Credit: Douglas Levere, University at Buffalo

A novel compound that targets an important brain receptor has a dramatic effect against a host of cocaine addiction behaviors, including relapse behavior, a University at Buffalo animal study has found.

The research provides strong evidence that this may be a novel lead compound for treating cocaine addiction, for which no effective medications exist.

The UB research was published as an online preview article in *Neuropsychopharmacology* last week.

In the study, the compound, RO5263397, severely blunted a broad range of cocaine addiction behaviors.

"This is the first systematic study to convincingly show that RO5263397 has the potential to treat cocaine addiction," said Jun-Xu Li, MD, PhD, senior author and assistant professor of pharmacology and toxicology in the UB School of Medicine and Biomedical Sciences.

"Our research shows that trace amine associated receptor 1—TAAR 1—holds great promise as a novel drug target for the development of novel medications for cocaine addiction," he said.

TAAR 1 is a novel receptor in the brain that is activated by minute amounts of brain chemicals called trace amines.

The findings are especially important, Li added, since despite many years of research, there are no effective medications for treating cocaine addiction.

The compound targets TAAR 1, which is expressed in key drug reward and addiction regions of the brain. "Because TAAR 1 anatomically and neurochemically is closely related to dopamine—one of the key molecules in the brain that contributes to cocaine addiction—and is thought to be a 'brake' on dopamine activity, drugs that stimulate TAAR 1 may be able to counteract cocaine addiction," Li explained.

The UB research tested this hypothesis by using a newly developed TAAR 1 agonist RO5263397, a drug that stimulates TAAR 1 receptors, in animal models of human cocaine abuse.

One of the ways that researchers test the rewarding effects of cocaine in animals is called conditioned place preference. In this type of test, the animal's persistence in returning to, or staying at, a physical location where the drug was given, is interpreted as indicating that the drug has rewarding effects.

In the UB study, RO5263397 dramatically blocked cocaine's rewarding effects.

"When we give the rats RO5263397, they no longer perceive cocaine rewarding, suggesting that the primary effect that drives cocaine addiction in humans has been blunted," said Li.

The compound also markedly blunted cocaine relapse in the animals.

"Cocaine users often stay clean for some time, but may relapse when they re-experience cocaine or hang out in the old cocaine use environments," said Li. "We found that RO5263397 markedly blocked the effect of cocaine or cocaine-related cues for priming relapse behavior.

"Also, when we measured how hard the animals are willing to work to get an injection of cocaine, RO5263397 reduced the animals' motivation to get cocaine," said Li. "This compound makes rats less willing to work for cocaine, which led to decreased cocaine use."

The UB researchers plan to continue studying RO5263397, especially its effectiveness and mechanisms in curbing relapse to cocaine addiction.