Medication may stop drug and alcohol addiction

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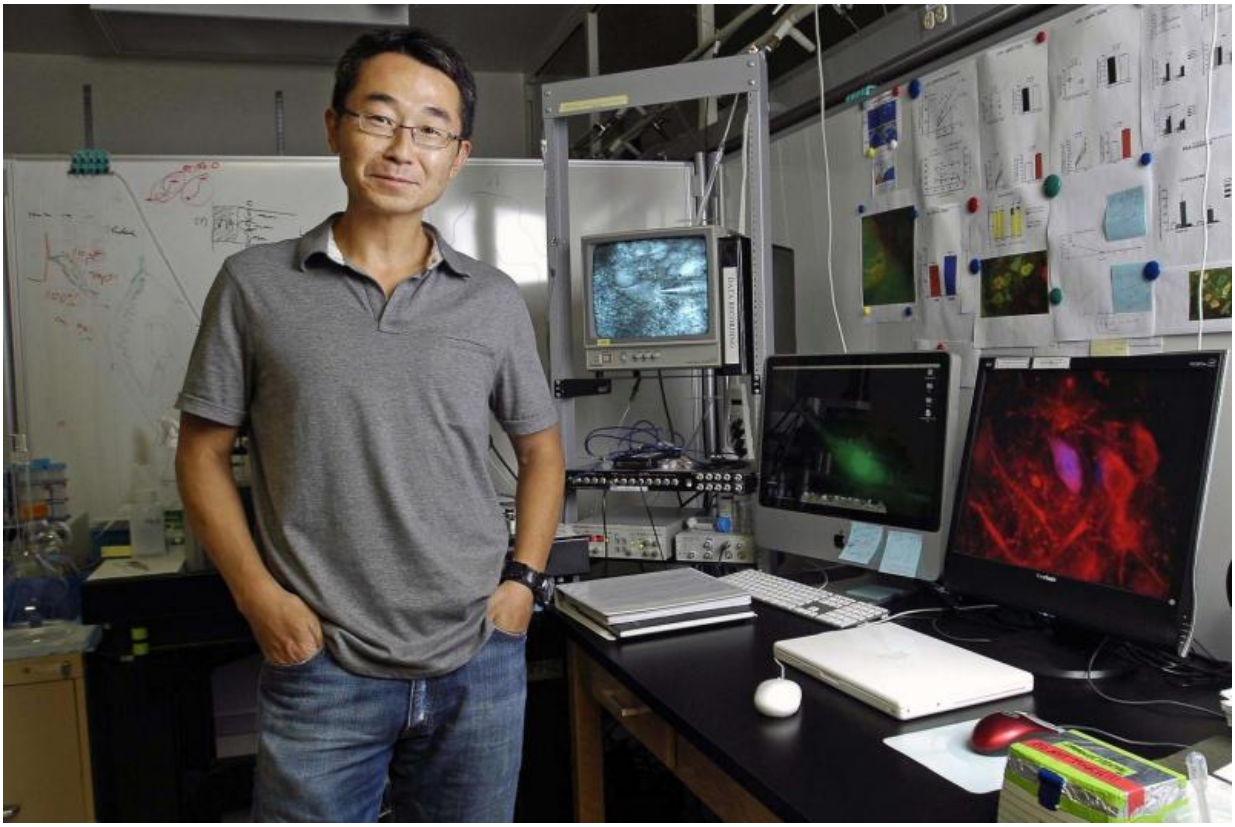

Hitoshi Morikawa and his team have discovered that an FDA-approved antihypertensive drug can stop cocaine or alcohol addiction in rats. Credit: University of Texas at Austin

Researchers at The University of Texas at Austin have successfully

stopped cocaine and alcohol addiction in experiments using a drug already approved by the U.S. Food and Drug Administration (FDA) to treat high blood pressure. If the treatment is proven effective in humans, it would be the first of its kind—one that could help prevent relapses by erasing the unconscious memories that underlie addiction.

The research is published this week in the journal *Molecular Psychiatry*.

Scientists once believed that drug addiction was simply a physical craving: Drug addicts who became sober and then later relapsed merely lacked willpower. But that view has gradually shifted since the 1970s.

Today, most experts acknowledge that environmental cues—the people, places, sights and sounds an addict experiences leading up to drug use—are among the primary triggers of relapses. It was an environmental cue (a ringing bell) that caused the dogs in Ivan Pavlov's famous experiments to salivate, even when they couldn't see or smell food.

Led by Hitoshi Morikawa, associate professor of neuroscience at The University of Texas at Austin, a team of researchers trained rats to associate either a black or white room with the use of a drug. Subsequently, when the addicted rats were offered the choice of going into either room, they nearly always chose the room they associated with their addiction.

Then one day, the researchers gave the addicted rats a high dose of an antihypertensive drug called isradipine before the rats made their choices. Although rats still preferred the room they associated with their addiction on that day, they no longer showed a preference for it on subsequent days. In fact, the lack of preference persisted in the isradipine-treated group in ways that couldn't be found in a control group—suggesting the addiction memories were not just suppressed but

had gone away entirely.

"The isradipine erased memories that led them to associate a certain room with cocaine or alcohol," said Morikawa.

Addictive drugs are thought to rewire brain circuits involved in reward learning, forming powerful memories of drug-related cues. Antihypertensive drugs all block a particular type of ion channel, which is expressed not only in heart and blood vessels but also in certain brain cells. The researchers found that blocking these ion channels in brain cells, using isradipine, appears to reverse the rewiring that underlies memories of addiction-associated places.

There are already medications that have been shown to prevent people from feeling euphoria when they take an addictive drug and that might prevent them from developing an addiction. A treatment based on this latest research, however, would be much more effective, said Morikawa, targeting the associations an addict has with the experience leading up to taking a drug.

"Addicts show up to the rehab center already addicted," he said. "Many addicts want to quit, but their brains are already conditioned. This drug might help the addicted brain become de-addicted."

Morikawa noted that because isradipine is already labeled as safe for human use by the FDA, clinical trials could potentially be carried out much more quickly than with nonapproved drugs.

One challenge with using isradipine in high doses to treat addiction is that it lowers blood pressure. So it might be necessary to pair it with other treatments that prevent blood pressure from falling too low.

More information: "L-type Ca2+ channel blockade with

antihypertensive medication disrupts VTA synaptic plasticity and drug-associated contextual memory," *Molecular Psychiatry* (June 23, 2015): nature.com/doifinder/10.1038/MP.2015.84

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