

# Memory 'trick' relieves drug cravings

Altering memories of drug use could stop ex-addicts from relapsing.

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Researchers have come up with a way to help prevent recovering drug addicts from relapsing — without using other pharmaceuticals to help. The approach involves modifying addicts' behaviour by weakening their memory of drug taking, which relieves their cravings and might help to prevent relapse.

Addicts tend to associate a drug's effects with drug-taking equipment and a certain environment, which can make them vulnerable to relapse if they encounter those conditions. The technique, studied by Lin Lu of the National Institute of Drug Dependence at Peking University in Beijing and his colleagues, aims to break that link by briefly reactivating the memory of drug taking and following it with an 'extinction session' of repeated exposure to the same memory cues.

The short reminder of drug-taking seems to take the memory out of storage and make it easier to overwrite.

Existing therapies try to help addicts to unlearn their habit by, for example, showing them videos of people injecting, and having them handle syringes while not under the influence of the drug. This reduces cravings in the clinic, but not when addicts return to their usual surroundings. Other approaches tested in rats involved using memory-blocking drugs to change memories of past drug use, but these are not approved for use in humans.

To boost the technique's effectiveness, Lu and his team combined the approach with a process called memory reconsolidation. During reconsolidation, information is retrieved from long-term storage and reactivated to strengthen the memory. After retrieval, however, the information becomes temporarily unstable and thus prone to alteration. Their work is published today in *Science*<sup>1</sup>.

## A cure for craving?

To use reconsolidation to wipe out drug memories, Lu and his team first taught rats to self-administer cocaine and heroin, so that they learnt to associate a particular environment with a drug high. The researchers then put the rats in the same environment, but without the drug being available.

Rats showed the least drug-seeking behaviour if they were put in the drug-taking environment for 15 minutes, removed from it for 10 minutes and then returned for 3 hours.

Next, the researchers applied the procedure to humans. They showed heroin addicts a 5-minute video of images of heroin use and drug paraphernalia, either 10 minutes or 6 hours before an hour-long extinction session, in which they were repeatedly exposed to the same images.

Addicts who were shown the video 10 minutes before the extinction session showed decreased drug cravings both during the session and up to six months later, says Lu. There was no noticeable effect on cravings in those who watched the video 6 hours before the session.

Neuroscientists think that the brief exposure beforehand reactivates the memory of drug taking, making it easier to erase the link between the cues of drug taking and getting high, and to replace it with a memory in which no such link is formed.

Participants were hospitalized throughout the study. Whether the procedure would prevent relapse for addicts in their usual environment remains to be tested.



Marianne Williams Photography/GETTY IMAGES

Seeing drug-taking equipment can prompt memories of a drug's effects and tempt ex-addicts to relapse.

## A distant memory

"It's a fantastic and fascinating study, involving very well controlled experiments in both rats and humans, and they got such dramatic results," says neuroscientist Liz Phelps of New York University, who was not involved in the work.

In 2010, Phelps and her colleagues showed that memory reconsolidation could be used to extinguish fearful memories[2]. In their experiment, participants were repeatedly shown a blue square while receiving mild electric shocks on the wrist, and learned to associate the two stimuli, so that afterwards they responded to the square with fear.

The participants were then shown the square again without receiving shocks. Some were briefly shown the square 10 minutes before this second phase. This triggered reconsolidation, which interfered with and weakened the fearful memories. Again, the procedure only worked if there was a relatively brief interval between the two stages.

"I wasn't convinced that the technique would be effective in a clinical setting or in complex, real-life situations," says Phelps, adding that she was "pleasantly surprised" by Lu's results.

Lu says that repeating the procedure regularly might prevent addicts from relapsing in the long term. He and his team would like to investigate the underlying neural mechanisms, and to see if the approach is applicable to other drugs such as alcohol and nicotine.

The procedure may also be effective for treating conditions such as post-traumatic stress disorder, but must be tested for potential side effects before it can be approved for wider use.

It would be simple to combine the new technique with existing therapies, says Phelps. "It's a very subtle manipulation that could have a big impact."

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## References

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1. Xue, Y.-X. *et al. Science* **336**, 241–245 (2012).
2. Schiller, D. *et al. Nature* **463**, 49–53 (2010).