Manipulating memory to treat addiction

A behavioural procedure that alters memory effectively prevents the cravings of heroin addicts

Photograph: Denis Closon/ Rex Features

A study published today in the journal Science describes a simple behavioural procedure that reduces heroin addicts' cravings and could also prevent them from relapsing after they've kicked the habit. As I explain in this news story for Nature, the procedure involves manipulating addicts' memories of past drug use, and could lead to non-pharmacological therapy for addiction, as well as psychiatric conditions such as post-traumatic stress disorder and phobia.

Preventing cravings is one of the biggest challenges in the treatment of addiction, because they often cause ex-addicts to relapse into drug use. Current treatments effectively relieve cravings in the clinic, but not when addicts return to their usual environment, because exposure to paraphernalia and other stimuli associated with the effects of the drug trigger the addict's habitual response of using the drug once again.

These responses occur because of classical conditioning, a form of associative learning discovered by the Russian physiologist Ivan Pavlov about a hundred years ago. Pavlov had built a canula-like device for measuring the amount of saliva produced by dogs in response to food. During his experiments, he noticed that his dogs began to salivate when the lab assistants who fed them entered the room, even if they weren't carrying any food.

Pavlov speculated that the dogs had learned to associate the lab assistants with being fed, and set out to test this idea. He gave the dogs food and rang a bell at the same time. After repeating this several times, the dogs learned to associate the bell with the food, so that afterwards they would salivate when they heard it. In the same way, addicts quickly associate paraphernalia and other drug-associated cues with the pleasurable effects of the drug, so that seeing these cues triggers cravings and drug-seeking behaviour.

Pavlov also noticed, however, that his dogs stopped salivating in response to the bell if they heard it several times without then receiving food, because this caused them to un-learn the association between the two. This process – called 'extinction' – forms the basis of cue exposure therapy, in which addicts are repeatedly exposed to drug-associated cues and prevented from responding to them in the usual way of using the drug. The idea is that this will weaken the learned associations between the cues and the effects of the drug.

Cue exposure therapy relieves cravings in the clinical setting, but is less effective in doing so when addicts are re-exposed to drugs and associated cues later on. The new procedure could make this therapy more effective. It combines cue exposure with manipulation of a process

called memory reconsolidation, in which information is retrieved from long-term storage and then reactivated so that it can be strengthened.

Shortly after retrieval the information is rendered temporarily unstable and prone to alteration. The new study builds on earlier research by Joe LeDoux and Liz Phelps of New York University, showing that reconsolidation can be manipulated during this early time window. In 2009, LeDoux and his colleagues published a study which demonstrated that interfering with reconsolidation can weaken fear memoríes in rats.

The following year, he collaborated with Phelps on a follow-up study which showed the same procedure can also weaken fear memories in humans. "We used a very simple classical conditioning paradigm in which a blue square was paired with a mild electric shock to the wrist," Phelps explained. This caused the participants to associate the square with the shocks, and to respond with fear when shown the square on its own.

Afterwards, all the participants underwent extinction sessions, in which they were shown the square without receiving shocks. One group was briefly shown the square 10 minutes earlier, to trigger reconsolidation of the fear memory and coincide it with the training. The others saw the square 6 hours before the training.

"We did the extinction training during reconsolidation, and what seems to have happened is that we somehow updated the old fear memory," says Phelps. "In those particular subjects we didn't see any evidence of the fear memory returning. We brought the subjects back a year later and showed that the fear did not come back in the group that got extinction during reconsolidation."

The new procedure is a variation on this, but also manipulates reconsolidation of addicts' memories of past drug use to weaken their habitual responses to paraphernalia and other drug-related stimuli. The researchers, from National Institute of Drug Dependence at Peking University, show that it effectively reduces the cravings induced by such cues for up to six months.

One series of experiments showed that the procedure effectively reduces drug-seeking behaviour in rats. The rest were performed on heroin addicts who were hospitalized throughout the study for detoxification, so it remains to be seem whether the procedure will be effective in preventing cravings outside of the clinical setting.

"These new findings are powerful confirmation of our earlier work using this procedure to diminish the return of fear in rats and humans," says LeDoux. "Hopefully they'll rekindle interest in the clinical implications of this paradigm, which can potentially improve the efficacy of extinction-based exposure therapy for many psychiatric conditions."

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