Resetting the Memory: Will Scientists Erase Our Traumas?

Scientists are developing methods to change our memories so that terrifying recollections are either forgotten, altered or neutralized so that they no longer cause fear. This is meant to help victims of post-traumatic stress disorder (PTSD), and the latest experiments with humans and animals are very promising.

Will Scientists Erase Our Traumas?

For many people, memories of a traffic accident, abuse or war can be nightmarish. A loud sound or a bright light could be enough to revive a strong fear. But scientists are working on treatments in the form of cognitive therapy, medication or brain intervention that will allow terrible memories to be forgotten — or processed and stored in new ways with much less horrible effects.

Researchers have focused thus far on helping victims of post-traumatic stress disorder (PTSD) with therapy, by forcing them to recall painful memories while in safe surroundings, and teaching them to do one of three things: Replace these thoughts with less stressful ones, desensitize themselves by thinking of the fear repeatedly, or focus on stimuli, such as hand taps or particular sounds, that can be used to later distract themselves when something triggers the memory. The therapies, however, aren't always effective. Instead of erasing memories, the treatments only bury them, creating the potential for a time bomb in the memory. Sooner or later, the uncontrollable fear often returns.

MEMORIES CHANGE CONSTANTLY

In 2010, neurologist Elizabeth Phelps and her colleagues from New York University changed the procedure for PTSD therapy subtly; the breakthrough has to do with the way long-term memory works.

When people experience and learn something, it is immediately stored as short-term memory — typically these are superficial, quickly forgotten memories.

Consequently, the brain must assess very quickly whether the new knowledge is worth keeping. If so, it is redirected to the long-term memory, which is almost permanent but which takes a long time to store the information. In a process called consolidation, the nerve paths of the brain must literally be strengthened and reinforced in order to be able to store the new information.

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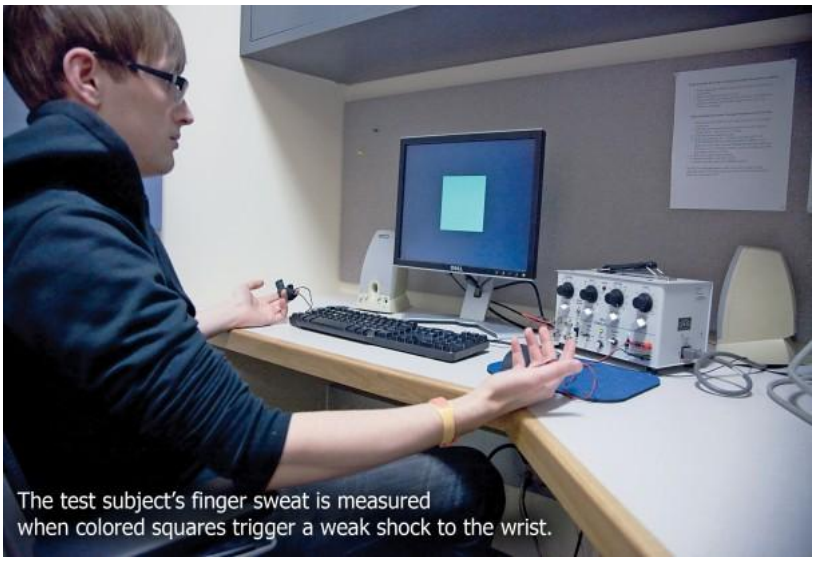


Research of recent years demonstrates that every time a recollection is retrieved from long-term memory, it has to be consolidated again in order to stay in the memory. That gives the brain a chance to process the memory and update it with new information, but it also means that what we remember is not necessarily what we originally experienced. If we tell somebody about something that happened in our youth and embellish it a little, it will always be the new — and not absolutely true — story that is subsequently stored in the long-term memory, replacing the memory of what really happened. This process is called reconsolidation, and it can only happen in a short, well-defined window of time after the recollection is retrieved from the long-term memory.

This bit of information turned out to be crucial in Phelps and her colleagues' experiment. The scientists first taught test subjects to fear colored squares. When colored squares appeared on a computer screen, the participants were given a weak electric shock on their wrist 38 percent of the time, whereas the control squares never provoked a shock. The test subjects quickly learned that the colored squares foretold of something unpleasant. The following day, they responded with fear, which the scientists could measure using sweat sensors on their skin. The control squares did not trigger any fear.

During this "adaptation" period, subjects still reacted emotionally when the colored square appeared, even when they were not given an electric shock; the brain had paired the memory of the colored square with fear. This can be compared to a very mild form of PTSD, Phelps explains.

"The long-term memory stores the feeling of fear and the recollection of the event separately in two different parts of the brain, i.e., the amygdala and the hippocampus," she says. "With our studies, we try to alter the fear memory as it is expressed without influencing the subject's knowledge of the events that occurred."

Next, the scientists tried to disassociate the memory from the unpleasant feeling by making colored squares appear without ever provoking electric shocks. In the beginning of this "extinction" period, the colored squares made the test subjects sweat, but over the course of the session, the fear faded away. The traditional PTSD therapy — recalling unpleasant memories in safe surroundings — had apparently helped. But when the experiment was repeated the next day, the colored square caused fear and sweat again.

Consequently, the scientists changed the procedure slightly. Ten minutes before the extinction training began, one group of test subjects was shown a colored square once and given an electric shock, which immediately caused a fear response. Subsequently, subjects from this group were allowed to calm down by watching TV for 10 minutes before the proper extinction training began, in which there were no shocks. They once again learned that the colored square had become harmless. But once the effect of the treatment was tested the next day, the result was very different — they showed no reaction to the colored square at all. And one year later, this group still showed no signs of fear when seeing a colored square. Another group received extinction training six hours

after being reshocked. The extended reprieve proved useless, as these test subjects still demonstrated fear when seeing a colored square. The effect of this experimental cure — specifically, waiting just 10 minutes to administer extinction training against PTSD — appeared permanent.

Not only had the subjects who had the memory of the colored squares reactivated before the extinction training been cured of their fear, they had also become immune to fearing them. On the day following the treatment, scientists made the group experience new electric shocks every time they saw a blue square, but their memories refused to learn. Sweaty hands only appeared once they were actually given electric shocks. When they just saw a blue square, they remained calm.

The considerable difference between the results is due to the unpleasant memory being reactivated shortly before the extinction. Phelps says that the reconsolidation window is opened when the test subjects are confronted with their fear of the colored square, and so the memory can be processed. During the subsequent extinction period without shocks, a whole new memory of the colored square being harmless is created, and this new, processed memory supersedes the original pairing of colored squares and electric shocks.

Though it may seem that the extinction training should recall the memory — and thus allow it to be stored in a less unpleasant version — it seems that the window for reconsolidation can only be opened if the memory is presented together with the physical discomfort, and then only for a limited time.

"*Reconsolidation can do its magic and change a memory in an open window between 10 minutes and four hours after it has been reactivated,*" says one of the scientists, Joseph LeDoux.

MEDICATION HAS THE SAME EFFECT

This study represents the first time that scientists have managed to manipulate a memory in a way that may help people with PTSD without the use of medication. But in recent years, scientists such as Merel Kindt of the University of Amsterdam have demonstrated that drugs such as propranolol, which blocks receptors in the amygdala essential to fear-memory formation, can block the fear responses that correspond with a memory.

Stress hormones, such as norepinephrine, activate receptors in the amygdala that play a role in the reconsolidation of fear memories, locking fears into the long-term memory. Scientists had previously demonstrated in experiments with rats that propranolol blocks the stress hormones from activating these amygdala receptors, apparently disrupting reconsolidation of reactivated fear memories.

The Dutch experiment was much like Phelps' but used pictures of spiders instead of colored boxes. Instead of giving the test subjects extinction training, they were given a pill containing propranolol before the spider was shown again and the unpleasant memory was reactivated. The treatment turned out to have the same positive effect as therapeutic extinction. The next day, the test subjects who had been treated with propranolol did not respond to the spider with fear, and it was no longer possible to retrain them to fear it. But subjects who got the dummy drug or who were not given the propranolol pill responded with the same fear as before the treatment.

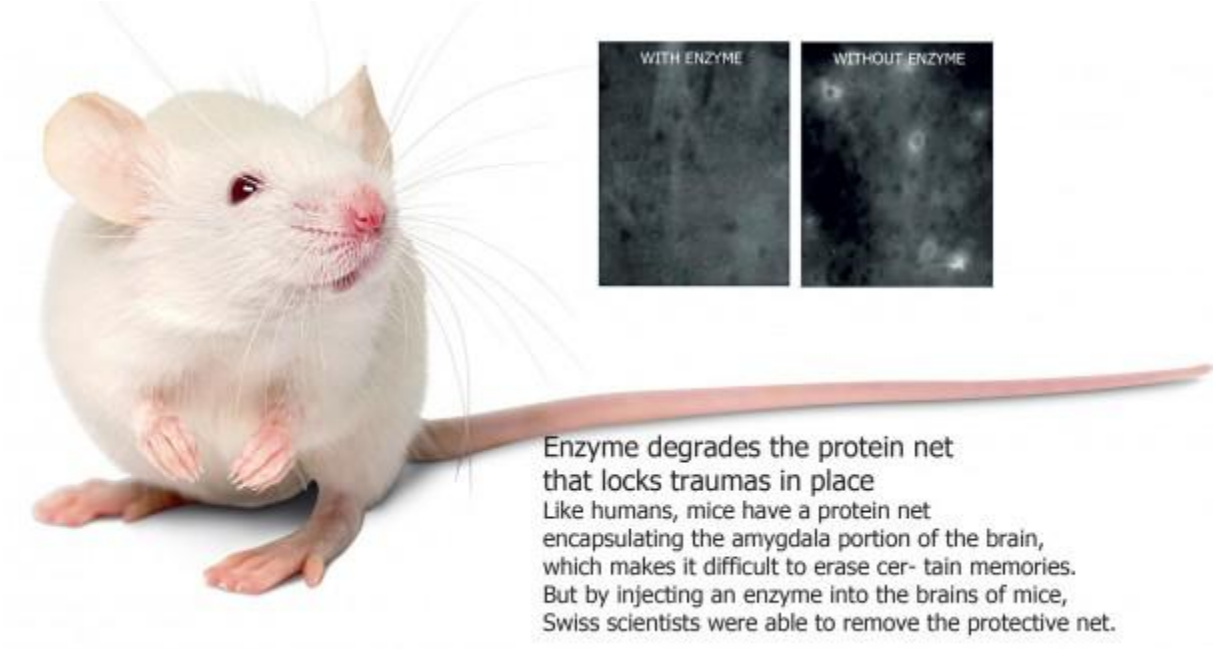
Both Kindt and Phelps have tested whether their treatment methods have any unintended side effects on the memory, but have found none so far. The propranolol treatment had no discernible effect on the test subject's ability to learn, and in Phelps' experiment, other memories were unaffected.

ENZYME MAY HELP PREVENT PTSD

Though medication and extinction therapy within the reconsolidation window both offer promise for PTSD treatment, using these methods to cure the disorder may be a long way off.

"*As of yet, we have only investigated simple associative fears in the laboratory — which is quite different from the complex, intense fear memories that are linked to PTSD,*" Phelps says of the cognitive therapy.

"From a theoretical perspective of how memory works, these results are quite exciting to us. As a realistic technique to treat PTSD, we are a long way off, and may never get there."



Another type of treatment, designed to help soldiers who suffer from horrifying memories all their lives, may be able to prevent PTSD. In 2009, Nadine Gogolla from Harvard University published findings indicating that an injection of enzymes in the brain can destroy the protective "net" that locks in the strong emotions associated with fear memories in the brain, making patients more responsive to PTSD treatment.

Gogolla and her colleagues worked with mice that were given electric shocks in their paws when they heard a certain sound, which subsequently made them freeze in fear whenever they heard the sound. The scientists examined the brains of the mice and discovered that many of the amygdala nerve cells were covered in a matrix of extracellular chondroitin sulfate proteoglycans (CSPGs), or proteins, that bind together to form a net. The brain creates this net as we grow old, which prevents formerly malleable memories from changing.

This net in the amygdala of mice indicates that the brain protects intense memories and that they cannot be forgotten by extinction training, so scientists tried to remove the net by injecting an enzyme into the mice's amygdala. Without the net in place, the unpleasant memories could be erased by simple extinction therapy during which the sound was repeated without giving the animals electric shocks.

Researchers are hopeful that they can replicate the results in humans, but one important caveat is that the enzyme must be injected before the bad memory is formed. If the treatment were to be used on soldiers, research suggests that doctors would have to inject patients before they were deployed. The net also regenerates after a while, so the enzyme treatment does not permanently destroy the ability to pair certain events and unpleasant feelings. Cyril Herry of the Friedrich Miescher Institute for Biomedical Research in Switzerland, one of the study's co-authors, is opti- mistic about future treatment options: "[Net] degradation might be useful in situations in which the probability of developing PTSD is high, such as war situations," he says. "[Net] degradation might then have a preventive effect on PTSD development."