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## **Is Every Memory Worth Keeping?**

Controversy Over Pills to Reduce Mental Trauma

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Kathleen Logue was waiting at a traffic light when two men smashed her car's side window, pointed a gun at her head and ordered her to drive. For hours, Logue fought off her attackers' attempts to rape her, and finally she escaped. But for years afterward, she was tormented by memories of that terrifying day.

So years later, after a speeding bicycle messenger knocked the Boston paralegal onto the pavement in front of oncoming traffic, Logue jumped at a chance to try something that might prevent her from being haunted by her latest ordeal.

"I didn't want to suffer years and years of cold sweats and nightmares and not being able to function again," Logue said. "I was prone to it because I had suffered post-traumatic stress from being carjacked. I didn't want to go through that again."

Logue volunteered for an experiment designed to test whether taking a pill immediately after a terrorizing experience might reduce the risk of post-traumatic stress disorder (PTSD). The study is part of a promising but controversial field of research seeking to alter, or possibly erase, the impact of painful memories -- a concept dubbed "therapeutic forgetting" by some and taken to science fiction extremes in films such as this summer's "Eternal Sunshine of the Spotless Mind."

Proponents say it could lead to pills that prevent or treat PTSD in soldiers coping with the horrors of battle, torture victims recovering from brutalization, survivors who fled the World Trade Center on Sept. 11, 2001, and other victims of severe, psychologically devastating experiences.

"Some memories can be very disruptive. They come back to you when you don't want to have them -- in a daydream or nightmare or flashbacks -- and are usually accompanied by very painful emotions," said Roger K. Pitman, a professor of psychiatry at Harvard Medical School who is studying the approach. "This could relieve a lot of that suffering."

Skeptics, however, argue that tinkering with memories treads into dangerous territory because memories are part of the very essence of a person's identity, as well as crucial threads in the fabric of society that help humanity avoid the mistakes of the past.

"All of us can think of traumatic events in our lives that were horrible at the time but made us who we are. I'm not sure we'd want to wipe those memories out," said Rebecca S. Dresser, a medical ethicist at Washington University in St. Louis who serves on the President's Council on Bioethics, which condemned the research last year. "We don't have an omniscient view of what's best for the world."

Some fear anything designed for those severely disabled by psychic damage will eventually end up being used far more casually -- to, perhaps, forget a bad date or a lousy day at work.

"You can easily imagine a scenario of 'I was embarrassed at my boss's party last night, and I want to

take something to forget it so I can have more confidence when I go into the office tomorrow,' " said David Magnus, co-director of Stanford University's Center for Biomedical Ethics. "It's not hard to imagine that it will end up being used much more broadly."

So far, only a handful of small studies have been conducted in people in the United States and France, most testing a drug called propranolol, which blocks the action of stress hormones that etch memories in the brain. The results suggest drugs may be able to prevent traumatic memories from being stored with such disturbing intensity in the first place, or perhaps deaden effects of old memories if taken shortly after they have been reawakened. The results have been promising enough that researchers are planning larger studies in several countries, including the United States, Canada, France and Israel, testing propranolol and other drugs, including the active components of marijuana.

"You always have the ability to misuse science," said Joseph E. LeDoux, a New York University memory researcher planning one of the studies. "But this isn't going to be radical surgery on memory. All we'd like to do is help people have better control of memories they want or prevent intrusive memories from coming into their minds when they don't want them."

The ability to manipulate memory has long been the stuff of science fiction, inspiring fears of government mind control and films such as the 1962 classic "The Manchurian Candidate." No one is anywhere near having the power to extract the memory of a love affair or implant complex new memories, as depicted in "Eternal Sunshine" and a 2004 "Manchurian Candidate" remake.

But scientists have started taking the first tentative steps toward developing treatments based on new insights into why emotionally charged events -- whether it be President John F. Kennedy's assassination, Sept. 11 or a first kiss -- create such indelible memories.

"Whatever is being learned at the time of emotional arousal is learned much more strongly," said James L. McGaugh of the University of California at Irvine. McGaugh demonstrated that strong emotions -- fear, love, hate, panic -- trigger stress hormones such as adrenalin and cortisol, which activate a part of the brain called the amygdala, creating unusually vivid, emotionally charged memories. "Any strong emotion will have that effect. It could be winning a Nobel Prize. It could be a very faint whisper in the ear, 'I love you,' at the right time."

Propranolol, widely used for heart patients, blocks the action of stress hormones on the amygdala, which led researchers to start testing whether it could prevent PTSD. The study Logue was in, along with a similar one in France, found that people who took propranolol immediately after a traffic accident or some other traumatic experience had fewer physical symptoms of PTSD months later.

"I really think it helped," said Logue, 35. "It helped not bring back my earlier bout with post-traumatic stress and made it easier to cope with this new incident. I look both ways before I cross a one-way street now, but I'm not in a panic."

So far, the research has suggested only that the emotional effects of memories may be blunted, not that the memories themselves are erased.

"I think it's an unfortunate misconception that it's blotting out memories," said Charles R. Marmar of the San Francisco Veterans Affairs Medical Center, who helped conduct the French study. "What it does is help people manage the memories so they can tolerate them."

But other researchers are trying to go further, possibly deadening or even obliterating any effects of old memories.

"People had thought that once a memory was stored or consolidated it stays that way. People thought, it's there for life -- it's fixed," said Karim Nader, a neuroscientist at McGill University in Montreal. "We showed that wasn't the case."

Laboratory rats trained to fear a tone completely lost that fear when scientists injected into their brains a drug that blocked formation of proteins necessary for memory storage while the animals were prompted to reexperience fear and store the memory again.

"When you activate a memory, it comes back up in a dynamic state and has to be restabilized using the same mechanisms that stored it in the first place. You can interfere with that," Nader said.

A small preliminary study being presented next week at a Society for Neuroscience meeting in San Diego tested for the first time whether propranolol can affect old memories in people.

"We have no idea whether it's erasing memory or putting a fence around the memory," LeDoux said. "But from the point of view of the PTSD patient, it doesn't matter as long as the effects are gone."

But some ethicists question this whole line of research.

"Our experiences and our memories in a lot of ways define us and define who we are," Magnus said. "And so that's a scary step to go down. We should be very careful about going down a path that could lead to a serious alteration of the core essence of our identities."

Beyond the personal impact, ethicists also worry about the societal implications.

"Consider the case of a person who has suffered or witnessed atrocities that occasion unbearable memories: for example, those with firsthand experience of the Holocaust," the President's Council on Bioethics wrote. "The life of that individual might well be served by dulling such bitter memories, but such a humanitarian intervention, if widely practiced, would seem deeply troubling: Would the community as a whole -- would the human race -- be served by such a mass numbing of this terrible but indispensable memory?"

The researchers acknowledge the prickly ethical questions but argue that the research should go forward because of its potential to alleviate suffering.

"I approach it from a medical standpoint -- that PTSD is as much a medical disorder as a broken leg," Pitman said. "I don't say they don't have legitimate concerns, but it's hard to argue we shouldn't pursue this just because of ethical speculations."

Psychiatrists at the University of California at San Diego are finishing a follow-up pilot study on accident victims. Pitman and the French team are starting bigger studies to confirm their initial emergency room findings. And Nader and colleagues in Montreal, and LeDoux and his colleagues in New York, are beginning studies in PTSD patients who will take propranolol immediately after reliving their traumatic memories to see if it can affect memory re-storage, known as "reconsolidation." Researchers at Hebrew University in Jerusalem are planning a similar study involving the active ingredient in marijuana.

Marmar and Pitman are working on identifying those most prone to PTSD, with the idea that they could receive propranolol immediately after a terrorist attack or some other traumatizing disaster.

"If this is safe and effective, it's one of the few tools we'd have in the case of a mass disaster," Marmar said. "What are you going to do if there's a dirty bomb? You'll have widespread panic. Do you want these poor people to be haunted by this searing memory?"

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