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# How Much of Your Memory Is True?

New research shows that memories are constantly being re-written by our minds.

By Kat McGowan | Monday, August 03, 2009

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Rita Magil was driving down a Montreal boulevard one sunny morning in 2002 when a car came blasting through a red light straight toward her. "I slammed the brakes, but I knew it was too late," she says. "I thought I was going to die." The oncoming car smashed into hers, pushing her off the road and into a building with large cement pillars in front. A pillar tore through the car, stopping only about a foot from her face. She was trapped in the crumpled vehicle, but to her shock, she was still alive.

The accident left Magil with two broken ribs and a broken collarbone. It also left her with post-traumatic stress disorder (PTSD) and a desperate wish to forget. Long after her bones healed, Magil was plagued by the memory of the cement barriers looming toward her. "I would be doing regular things—cooking something, shopping, whatever—and the image would just come into my mind from nowhere," she says. Her heart would pound; she would start to sweat and feel jumpy all over. It felt visceral and real, like something that was happening at that very moment.

Most people who survive accidents or attacks never develop PTSD. But for some, the event forges a memory that is pathologically potent, erupting into consciousness again and again. "PTSD really can be characterized as a disorder of memory," says McGill University psychologist Alain Brunet, who studies and treats psychological trauma. "It's about what you wish to forget and what you cannot forget." This kind of memory is not misty and watercolored. It is relentless.

More than a year after her accident, Magil saw Brunet's ad for an experimental treatment for PTSD, and she volunteered. She took a low dose of a common blood-pressure drug, propranolol, that reduces activity in the amygdala, a part of the brain that processes emotions. Then she listened to a taped re-creation of her car accident. She had relived that day in her mind a thousand times. The difference this time was that the drug broke the link between her factual memory and her emotional memory. Propranolol blocks the action of adrenaline, so it prevented her from tensing up and getting anxious. By having Magil think about the accident while the drug was in her body, Brunet hoped to permanently change how she remembered the crash. It worked. She did not forget the accident but was actively able to reshape her memory of the event, stripping away the terror while leaving the facts behind.

Brunet's experiment emerges from one of the most exciting and controversial recent findings in neuroscience: that we alter our memories just by remembering them. Karim Nader of McGill—the scientist who made this discovery—hopes it means that people with PTSD can cure themselves by editing their memories. Altering remembered thoughts might also liberate people imprisoned by anxiety, obsessive-compulsive disorder, even addiction. "There is no such thing as a pharmacological cure in psychiatry," Brunet says. "But we may be on the verge of changing that."

These recent insights into memory are part of a larger about-face in neuroscience research. Until recently, long-term memories were thought to be physically etched into our brain, permanent and unchanging. Now it is becoming clear that memories are surprisingly vulnerable and highly dynamic. In the lab they can be flicked on or dimmed with a simple dose of drugs. "For a hundred years, people thought memory was wired into the brain," Nader says. "Instead, we find it can be rewired—you can add false information to it, make it stronger, make it weaker, and possibly even make it disappear." Nader and Brunet are not the only ones to make this observation. Other scientists probing different parts of the brain's memory machinery are similarly finding that memory is inherently flexible.

Someday this new science of memory could cure PTSD and other mental traumas. Already it corrodes our trust in what we know and how we know it. It pokes holes in eyewitness testimony, in memoirs, in our most intimate records of truth. Every time we remember, it seems, we add new details, shade the facts, prune and tweak. Without realizing it, we continually rewrite the stories of our lives. Memory, it turns out, has a surprising amount in common with imagination, conjuring worlds that never existed until they were forged by our minds.

**On the Trail of the Memory Meme**

Neuroscientists have long viewed memory as a kind of neural architecture, a literal physical reshaping of the microstructure of the brain. In the 19th century, the pioneering neuroanatomist Santiago Ramón y Cajal theorized that information was processed in our heads each time an electrical impulse traveled across a synapse, the gap between one nerve cell and the next. Memories were made or altered, he proposed, when structures near the synapse changed.

More than a century later, the textbook description of episodic memory (conscious knowledge of an event) is a more sophisticated version of that same basic idea. Memory formation requires an elaborate chemical choreography of more than a hundred proteins, but the upshot is that sensory information, coded as electrical pulses, zips through neural networks of the brain. The impulses cause glutamate (one of the brain's main neurotransmitters) to pop out of one nerve cell and travel across the synapse to activate the next by binding to its receptors, chemically active signaling stations on the cell surface. Ultimately the electrical and chemical signals reach the centers of memory, the almond-size amygdala and the banana-shaped hippocampus, adjacent structures buried on either side of the brain.

Neuroscientists believe that memory forms when neurons in these key brain structures are simultaneously activated by glutamate and an electrical pulse, a result of everyday sensory experience. The experience triggers a biochemical riot, causing a specialized glutamate receptor, called NMDA, to spring open and allow calcium ions to flood the cells. The ions stimulate dozens of enzymes that reshape the cells by opening up additional receptors and by prompting the formation of more synapses and new protrusions that contain still more receptors and synapses. In aggregate, these changes make neurons more sensitive to each other and put the anatomical scaffold of a memory in place.

Enacting all these changes takes time, and for up to a few hours the memory is like wet concrete—solidifying but not quite set, still open to interference. Once the process is over, though, the memory is said to be "consolidated." In the textbook description, neuroscientists talk of memory the way geoscientists describe mountains—built through a dynamic process, but once established almost impossible to reshape quickly except by extraordinary means. By the late 1990s, this explanation of memory was so widely accepted by neuroscientists that its major author, Columbia University neuroscientist Eric Kandel, was awarded the Nobel Prize. It seemed that the most important questions about memory had been answered.

No wonder, then, that Nader—at the time a young postdoc studying the neurobiology of fear at New York University—was electrified when he attended one of Kandel's lectures. "It was so beautiful and so convincing," Nader says. But he began to wonder: What actually happens when we recall the past? Does the very act of remembering undo what happened? Does a memory have to go through the consolidation process again? Nader asked his adviser, the noted fear researcher Joseph LeDoux, if he could study these questions. LeDoux says his initial response was "Don't waste our time and money," but Nader talked him into it, little suspecting just how far this line of research would go.

Meanwhile, doubts about the standard theory of memory were piling up in the world outside the neuroscience lab +

the early 1990s many people began reporting what seemed to be long-buried memories of childhood sexual abuse. These traumatic recollections frequently surfaced with the help of recovered-memory therapy techniques like hypnosis and guided imagery, in which patients are encouraged to visualize terrible experiences. Cognitive scientists suspected that some of these memories were bogus, the unwitting product of suggestion by the therapist. In support of this view, psychologist Elizabeth Loftus, then of the University of Washington, proved how easy it is to implant a false memory, especially one that is plausible. In a famous experiment, she gave volunteers a booklet narrating three true stories of events from their own childhood along with an invented tale that described their getting lost in the mall at age 5. When prompted later to write down all they could remember about the events, 25 percent were sure that all four events had actually happened to them.

Spurred on by the controversy over recovered memory, other cognitive scientists found that false memory is a normal phenomenon. David Rubin, who studies autobiographical memory at Duke University, observed that adult twins often disagree over who experienced something in childhood. Each might believe, for example, that he was the one to get pushed off his bike by a neighbor at age 8. Apparently, even the most basic facts about a past event (such as who experienced it) could be lost.

Even harrowing memories—the so-called flashbulb memories that feel as if they have been permanently seared into the brain—are not as accurate as we think. Less than a year after a cargo plane crashed into an Amsterdam apartment building in 1992, 55 percent of the Dutch population said they had watched the plane hit the building on TV. Many of them recalled specifics of the crash, such as the angle of descent, and could report whether or not the plane was on fire before it hit. But the event had not been caught on video. The “memory” shared by the majority was a hallucination, a convincing fiction pieced together out of descriptions and pictures of the event.

By the late 1990s, hundreds of psychology experiments suggested that the description of memory as a neurally encoded recapitulation of the past was so oversimplified as to completely miss the point. Instead of being a perfect movie of the past, psychologists found, memory is more like a shifting collage, a narrative spun out of scraps and constructed anew whenever recollection takes place. The science of memory was conflicted, with the neurobiological and psychological versions at odds. If a memory is wired into brain cells—a literal engraving of information—then why is it so easy to alter many years after the fact? It took an outsider to connect the dots.

**Rewriting the Past**

In the hierarchy of memory science, Karim Nader hardly ranked—a lowly postdoc, only 33 years old, and not even a memory researcher. But in 1999, inspired by Kandel’s talk, he set out to satisfy his big questions about how we recall and forget through a simple experiment. Nader tweaked a standard method used in fear research, in which rats are trained to associate a tone with an electric shock to the foot. The animals quickly learn that the sound is bad news. If they hear it weeks later, they freeze in fear. It is an easy way for the experimenter to know that they remember what took place.

Nader trained some rats, then played the tone again 14 days later, prompting them to remember. He also simultaneously injected them with a protein-synthesis inhibitor, which prevents new memory from forming by prohibiting alteration at the synapses. According to the standard model of memory, the chemical should have no effect since the memory of the tone has already consolidated. In reality, the treated rats’ memory disappeared. When Nader sounded the tone again later, the animals did not freeze. LeDoux was won over by this simple but powerful demonstration. In 2000 Nader’s paper on reconsolidation sparked a commotion in the world of memory research. He showed that reactivating a memory destabilizes it, putting it back into a flexible, vulnerable state.

Immediately reconsolidation became a fighting word. The gossip Nader heard terrified him; some of the biggest bigwigs of memory research thought he had made a ludicrous mistake. “I had no idea how much of a backlash there was going to be,” he says. Even so, Nader kept at his experiments, and in the fall of 2001, he was scheduled to

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present his research at a huge Society for Neuroscience meeting. It would be his moment of truth, his one chance to persuade the field to take his finding seriously. "I knew the old guard was saying, 'This sucks; it's all crap,'?" he says. "I knew if I didn't hit a grand slam, this thing was dead." The talk drew an overflow crowd of more than a thousand, including the legend himself, Eric Kandel. ("I really wanted to die," Nader says.)

That day, by addressing the major criticisms of his research, Nader managed to convince his colleagues that memory reconsolidation was at least worth a serious look. Various labs took on the challenge, soon repeating his findings and discovering that many types of memory in many different species reconsolidate. Other groups began teasing out the reconsolidation process molecule by molecule. Nader's group found that the NMDA glutamate receptor—which solidifies memory—also is involved in destabilizing it. A group led by Sue-Hyun Lee at Seoul National University demonstrated that proteins must be actively dismantled to destabilize a memory, more evidence that the old memory is actually changed as it is recalled.

Brain researchers are still grappling with the implications of this idea, trying to figure out exactly how malleable memory really is. "People are willing to say we have to go back to the drawing board," says LeDoux, whose group has also continued to study reconsolidation. At the 2008 Society for Neuroscience meeting in Washington, D.C., 43 presentations focused on reconsolidation, and Nader was besieged by students and young researchers eager to talk.

With this new understanding of memory has come the even more startling possibility of new ways to control it: The era of memory treatment has arrived. For Rita Magil, who got just two doses of propranolol over the course of a single day, the results were encouraging. Her heart rate and muscle tension eased while the drug was in her body. She sensed the difference too. "I felt more detached from it," she says. "I felt that I was relating a narrative rather than describing something right in front of me right now." After the study was over, the flashbacks returned, though with less intensity. For her, the only real cure was time.

Six-session treatments with a total of 12 doses of propranolol have shown better results. Collaborating with Harvard psychiatrist Roger Pitman, who was the first to try propranolol for post-traumatic stress, the McGill group has treated about 45 PTSD patients, ranging from soldiers to rape victims. Most had been suffering for years. But after the longer treatment, their symptoms declined by half and stayed that way even six months afterward. They still remember what happened, but it is less disturbing. "They say: 'I'm not thinking about it as much. It just doesn't bother me as much anymore,'?" Brunet says. As a group, they are considered to be in remission.

The researchers must still prove that the improvement will last. If it does, it could offer rare hope to millions of people with PTSD, a disorder from which only a third completely recover.

Brunet hopes that similar treatments can address other psychiatric problems, too. Anxiety, acquired phobias, and addiction are increasingly described as disorders of emotional memory. An overly powerful fear memory, for example, can crystallize into a phobia, in which a relatively safe experience like flying in a plane is inextricably linked to a feeling of extreme danger. No matter how the phobic person tries, his emotional memory refuses to update itself to incorporate reassuring information. A treatment that restores his emotional memory to a flexible state could help him cope.

Addiction is another kind of pathological remembering, but in this case the memory is pleasurable. Just as adrenaline sears emotional memories into the brain with the help of the amygdala, drugs of abuse enlist the amygdala and the brain's reward centers to forge unforgettable memories of pleasure. Anything connected to the bliss reawakens the memory, in the form of craving. "When you see someone with a beer and a smoke and you get a craving, you are suffering from reminiscence, from an emotional memory," Brunet says. Adapting experimental methods of forgetting to addiction might make it easier to quit.

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**The Reconsolidated Life**

While neuroscientists were skeptical of Nader's findings, cognitive scientists were immediately fascinated that memory might be constantly revamped. It certainly seemed to explain their observations: The home run you hit in Little League? Your first kiss? As you replay these memories, you reawaken and reconsolidate them hundreds of times. Each time, you replace the original with a slightly modified version. Eventually you are not really remembering what happened; you are remembering your story about it. "Reconsolidation suggests that when you use a memory, the one you had originally is no longer valid or maybe no longer accessible," LeDoux says. "If you take it to the extreme, your memory is only as good as your last memory. The fewer times you use it, the more pristine it is. The more you use it, the more you change it." We've all had the experience of repeating a dramatic story so many times that the events seem dead, as if they came from a novel rather than real life. This might be reconsolidation at work.

Reconsolidation research has helped foster a growing sense that the flexibility of memory might be functional—an advantage rather than a bug in the brain. Reconsolidation might be how we update our store of knowledge, by making old memories malleable in response to new information. "When you encounter a familiar experience, you are remembering the original memory at the same time, and ?the new experience somehow gets blended in," says Jonathan Lee of the University of Birmingham in England, who recently found evidence for this effect in animals. "That is essentially what reconsolidation is." The evident purpose of episodic memory, after all, is to store facts in the hope of anticipating what might happen next. From the perspective of survival, constructive memory is an asset. It allows you to pull together scraps of information to simulate the future on the fly.

"The brain knows there is a future," says neuroscientist Yadin Dudai, head of the department of neurobiology at the Weizmann Institute of Science in Israel, who collaborates with Nader and LeDoux. Facing something new, we want to link the novel information with memories to better interpret the situation. If the side effect is a few mistakes, that is probably a small price to pay. "Having a memory that is too accurate is not always good," he says.

Put another way, memory and imagination are two sides of the same coin. Like memory, imagination allows you to put yourself in a time and place other than the one we actually occupy. This isn't just a clever analogy: In recent neuroimaging studies, Harvard psychologist Daniel Schacter has shown that remembering and imagining mobilize many of the same brain circuits. "When people are instructed to imagine events that might happen in their personal future and then to remember actual events in the past, we find extensive and very striking overlap in areas of brain activation," he says. Other researchers have found that people with severe amnesia lose their ability to imagine. Without memory, they can barely picture the future at all.

**The Spotless Mind**

Reconsolidation modifies old memories, but other new research points the way toward erasing them wholesale. One technique for blanking out the past, developed by Joe Tsien at the Medical College of Georgia, flows from his studies of memory formation. When calcium floods a neuron as a memory is formed, it turns on an enzyme called CaMKII (calcium/calmodulin-dependent protein kinase). Among many other things, the enzyme responds to signals from NMDA receptors, leading to more receptor activity and stronger signaling throughout the network of cells.

You would think, therefore, that the more CaMKII, the more robust a memory would be. But in experiments with mice, Tsien has found there is a limit. If he drives CaMKII above the normal limit while the animal is actively remembering an experience, the memory simply vaporizes, as the connections between the cells suddenly weaken. The effect happens within minutes, and it is permanent and selective, affecting the recalled memory while leaving the others unchanged. Indeed, when Tsien trained a mouse to fear both an unfamiliar cage and a particular tone, then pumped up CaMKII while the mouse was in the cage, it forgot the cage-fear memory but not the tone-fear memory. "At the time the memory was retrieved, it disappeared," he says. "It erases the memory being recalled. It is feasible that by manipulating specific molecules, we can selectively alter memories in the brain."

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Todd Sacktor, a professor of physiology, pharmacology, and neurology at the State University of New York Downstate Medical Center in Brooklyn, has found a blunter but more powerful technique that can eradicate whole categories of memory. He studies protein kinase M-zeta (PKMzeta), which is involved in memory maintenance. As calcium rushes into a memory neuron, PKMzeta is synthesized, linking up with spare glutamate receptors and dragging them to the synapse, where memory construction occurs. With more receptors at the synapse, signals are boosted and amplified and the memory persists.

When Sacktor deactivated PKMzeta with a compound called zeta-inhibitory peptide (ZIP), he got a spectacular response: total amnesia for one type of memory. Rats that had learned a day or a month before to avoid part of a platform that was rigged with electric shock forgot everything they knew about the location generating the jolt. “You inhibit the PKMzeta and those glutamate receptors float away very, very fast,” he says. “As a result, the memory is lost—very, very fast.”

Certain types of memory are encoded in different brain areas, and depending on where Sacktor injects the inhibitor in his animals, he can zap away different categories of memory. In the hippocampus, he erases memory for spatial locations like the platform; in the amygdala, fear memories; in the insular cortex, memories of nauseating taste. Very rarely, Sacktor says, neurosurgeons remove nerve clusters to help disturbed psychiatric patients who do not respond to any other treatment. His research may eventually provide a way to erase memory without causing damage.

The implications are staggering. If stored memories were inscribed in the brain, it is hard to imagine how flipping one chemical switch could erase them so quickly. “It really is a paradigm shift in how people think about long-term memories,” Sacktor says. In the old view, erasure should cause permanent brain damage as the synapses are ripped apart. Instead, Sacktor’s rats’ brains remain intact. Once the ZIP treatment wears off, the animals behave and even learn normally again. “It’s like wiping a hard disk,” he says.

ZIP is nowhere near ready for human use. First, the compound would have to be made activity-dependent in order to target specific memories. You would also have to find a way to get it to the right spot in the brain without using a needle. People are clamoring to be test subjects anyway. When Sacktor’s study first came out in 2006, people, especially rape survivors, tracked him down, imploring him to eradicate their painful memories. “They were suffering,” he says. “They couldn’t work or have relationships. Some of them wanted everything erased.” They didn’t care that it would also vaporize all they had ever known.

**Benevolent Forgetting**

If you feel that you’ve heard this story before, there’s a reason. Moviemakers love the idea of erasing memory, and they work a consistent theme: If you try to undo the past, you pay the price. Nader’s research supposedly inspired the 2004 movie *Eternal Sunshine of the Spotless Mind*, in which Jim Carrey and Kate Winslet both pay to have memories of their painful love affair obliterated. Needless to say, it makes them both miserable. But not as miserable as Arnold Schwarzenegger’s character in *Total Recall*, from 1990, in which he learns that his real memories have been erased, that his life is a fake, and that his faux wife, played by Sharon Stone, is trying to kill him.

You don’t have to be a rape survivor or a soldier to have memories you would rather forget. For most people, though, unpleasant memories also serve as a guide. Indeed, some fear the consequences of undermining appropriately bad memories—say, allowing a murderer to forget what he did. Members of the President’s Council on Bioethics warn that altering the memory of a violent crime could unleash moral havoc by lifting the repercussions of malice. “Perhaps no one has a greater interest in blocking the painful memory of evil than the evildoer,” their report cautions.

Beyond all this, memory is the essence of who we are. *Eternal Sunshine of the Spotless Mind* is difficult to watch as Carrey’s character flails around in confusion and loss. His fear and desperation may be a realistic portrayal of what it would be like to erase your memory: basically, a waking nightmare. Memory is how you know who you are, how yc +

point yourself toward a destination. We already know that people with Alzheimer's disease do not feel liberated. They feel utterly lost.

Thankfully, Nader and Brunet's studies suggest much more benevolent possibilities. If he had received reconsolidation therapy, Carrey's character would not have forgotten Winslet's. He simply wouldn't care that much about her anymore. He would be able to look at his failed relationship as if through the wrong end of a telescope. What is on the other side is still visible, but it is tiny and far away.

That is basically what all these scientists hope to do. Nader, Brunet, and Pitman are now expanding their PTSD study with a new, $6.7 million grant from the U.S. Army, looking for drugs that go beyond propranolol. They are increasingly convinced that reconsolidation will prove to be a powerful and practical way to ease traumatic memories. Sacktor also believes that some version of the techniques they apply in the lab will eventually be used to help people. Most recently, LeDoux's lab has figured out a way to trigger reconsolidation without drugs to weaken memory, simply by carefully timing the sessions of remembering. "The protocol is ridiculously simple," LeDoux says.

None of these researchers are looking to create brain-zapped, amoral zombies—or even amnesiacs. They are just trying to take control of the messy, fragile biological process of remembering and rewriting and give it a nudge in the right direction. Brunet's patients remember everything that happened, but they feel a little less tortured by their own pathological powers of recollection. "We're turning traumatic memories into regular bad memories," Brunet says. "That's all we want to do."

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