Scientists have discovered a radical new way to treat our most traumatic memories.

BY BEN CRAIR
A pill of propranolol, which doctors have prescribed for decades to treat heart disease. Now it may be put to a very different use.
KARIN KLAVER WOKE in the darkness and searched the nightstand for her iPhone. It was 2 a.m. Her husband slept quietly beside her. They had arrived in Johannesburg early that morning on the red-eye from Amsterdam and spent the day window shopping and people watching in the city. “This is nice,” Klaver had thought to herself as she and her husband relaxed on the outdoor terrace of a shopping mall.

That evening, they retired to a bed-and-breakfast with garden rooms and enthusiastic online reviews. The couple were on their way to Port Elizabeth, where they own a house and spend several weeks each year. But this was the first time they had stayed overnight in South Africa’s biggest city.

In the blackness of the room, Klaver sensed a presence at her bedside. A man was standing there with a gun in his hand, and he raised it to her head. Terrified, Klaver rolled onto her stomach. If she was to be shot, she thought to herself, better to be shot in the back. Her movement woke her husband, and the intruder demanded their cash and valuables. Then he slipped away into the night, leaving them unharmed but shaken.

Back in Holland, Klaver, 56, struggled to resume her normal life. What had once been comfortable and familiar now felt like an iron maiden. “Everything would remind me of what happened in Johannesburg,” she said. She was nervous around unfamiliar men, and her house became a racket of threatening noises. The wind rustling in the curtains could keep her awake for hours. Nothing could dispel the dread that had overwhelmed her in that hotel room, when she was sure that she would die. “It was always there,” she recalled recently. “It felt like a balloon inside.”

Klaver found it difficult to talk about her anxiety, even with her husband. Thinking back to the robbery left her feeling even more isolated and vulnerable. “The first seconds, you feel so very, very lonely,” she said. She resisted the idea of psychotherapy, with its long sessions devoted to reliving and processing the trauma.

A year and a half later, in 2013, Klaver read an item in the newspaper about Merel Kindt, a professor of clinical psychology at the University of Amsterdam. Kindt had developed a revolutionary treatment that could “neutralize” fear memories with a single pill. This treatment was a scientific breakthrough, building on decades of psychological research. It was also deceptively simple. “It was quick and dirty, and that’s what I like,” Klaver said. She wrote an email to Kindt introducing herself, and Kindt invited her to the university for a screening.

In the lab, one of Kindt’s assistants asked Klaver a series of questions. What did she remember about the robbery? How did she feel when she remembered it? Kindt reviewed Klaver’s answers and recognized the intrusive memories, avoidance behaviors, and other hallmarks of post-traumatic stress disorder. Klaver would indeed be a good candidate for the treatment, Kindt decided.

Three weeks later, Kindt, a striking woman with sharp features, crisp blue eyes, and stylishly tousled blonde hair, ushered Klaver into a small, plain room with a table and two chairs. Klaver, who has shoulder-length silver hair, wore black to the session. Normally, a patient who had suffered a traumatic experience might expect a therapist to proceed slowly and gently, offering comfort and support. Instead, Kindt dived straight in, pushing Klaver to relive the night of the robbery and focus on the source of her fear. “There is no escape,” Kindt told her, as Klaver wept into her hands. “Nobody can help you.” After 15 minutes, Klaver seemed shattered by her memories, and Kindt abruptly stopped the interrogation. She gave Klaver a round, white pill, which she swallowed with a sip of water. “I was totally broken,” Klaver said.

Klaver went to bed early that night and slept for twelve hours. When she woke the next morning, she found that her memory was transformed. She recalled the details of what had happened in that bedroom in Johannesburg: She could still see the man’s dirty cap, oversized jeans, and cheap plastic shoes. Yet she was able for the first time to think about the experience without anxiety or panic. “It felt like there was not that much weight on my shoulders,” she said.

When she returned to see Kindt a week later, she wore white, as though to telegraph her mood reversal. “It’s really gone,” Klaver said. “It is quite special, isn’t it?” Kindt smiled and leaned forward in her chair. “Yes,” she agreed. “Very special.”

Kindt, 48, has devoted her career to understanding human fear and memory. She has built her own laboratory, published in the most prestigious scientific journals, and developed a simple treatment she hopes might one day help millions of people who suffer from PTSD, phobias, and other anxiety disorders. In her clinic, she has seen it work in hundreds of cases, and yet she still marvels every time she sees a patient disencumbered of fear and trauma after such a short procedure. In those moments, she told me recently, her work doesn’t feel like science or medicine at all. “It still feels,” she said, “a bit like magic.”

The sober-minded scientific community shares Kindt’s awe. “Cure” is a word not often encountered in psychiatry,” Roger Pitman, a psychiatrist at Harvard Medical School, wrote in December in the journal Biological Psychiatry, in response to a study in which Kindt had successfully treated a group of people who were afraid of spiders. But a cure is exactly what Kindt appears to have found.

Not all fear needs to be cured, of course. A healthy amount of fear is essential to survival. When we encounter danger, the brain activates the sympathetic nervous system. Adrenaline floods our veins, our hearts race, and our fight-or-flight response kicks into gear. The more quickly we can recognize a threat, the better our ability to avoid it in the future. In this way, our fears are lessons we have drawn from our experiences in the world. “Fear is a very adaptive emotion,” Kindt said. “Because of fear, we anticipate and plan.”

For millions of people, however, fear can be debilitating. Twenty-nine percent of people will suffer from an anxiety disorder at some point in their lives. The most common are specific phobias, in which people develop an irrational fear of a situation or an object, such as heights or spiders. Some
Merel Kindt in her laboratory at the University of Amsterdam.
people will take extreme measures to avoid the things that trigger their fears—a height-phobic person, for instance, might drive hours out of his way just to avoid crossing a bridge. Other anxiety disorders, such as panic disorder and PTSD, can be even more difficult to manage.

Kindt has been contacted by people seeking help for all kinds of fears and anxieties. There was a police officer who suffered panic attacks whenever he left the country, and a woman who had been unable to cope with her mother’s suicide. Others had the familiar phobias of snakes, dogs, heights, and spiders, as well as some stranger varieties. Recently, she heard from two people who were deathly afraid of ladybugs. A third person was terrified of balloons.

At other clinics, these patients would have undergone “exposure therapy.” A therapist would have taught them coping mechanisms and presented them with their triggers so that, over time, they could hopefully learn to tolerate them. For decades, exposure therapy has been the best method for fighting anxiety disorders. But the treatment is slow and emotionally draining, and patients often relapse after apparently successful interventions. In cases of PTSD, exposure therapy works only about half the time.

Kindt’s research, by contrast, holds out the promise of a simple treatment—maybe even a permanent cure—that doesn’t require prolonged therapy sessions or antidepressant medications. Richard Friedman, the director of the psychopharmacology clinic at Weill Cornell Medicine, recently lauded Kindt’s work in The New York Times. “These studies,” he wrote, “suggest that someday, a single dose of a drug, combined with exposure to your fear at the right moment, could free you of that fear forever.”

Indeed, Kindt’s treatment is so effective that the sudden transformation can be disorienting. A former patient named Erik, who asked to be identified only by his first name, visited Kindt’s lab last year to overcome his fear of snakes. “The next morning, I was afraid it didn’t work,” he told me recently. “The only way to find out was to expose yourself again.”

He returned to the lab and found himself able to touch a snake, first with gloves and then without them. Next he visited a reptile center. Even surrounded by snakes, he felt no fear or panic. Over the past few months, he has visited forests he had been afraid to explore, and he told me he looked forward to traveling to countries he would previously have avoided. Ireland, he said, was the only country in Europe without snakes. “It was really hard to go on vacation.”

In a culture that encourages people to conquer their fears, as though they are Mount Everest, Erik’s main qualm about his experience was that it was almost too effective. “I thought that if I overcame this, it would be a great victory in my life, but that isn’t the case,” he said. “I don’t have the feeling that I did it myself.”

The root cause of fear, and how to treat it, has been one of modern psychology’s central questions. In the early twentieth century, Sigmund Freud argued phobias were “protective structures” springing from a patient’s “repressed longing” for his mother. In 1920, however, the American psychologist John B. Watson put forward a simpler theory: People develop fears through negative experiences. To test his hypothesis, he sought to condition an infant, whom he called “Little Albert,” to fear a white rat by presenting the rat to the child and simultaneously striking a steel bar.

Indeed, the loud noise upset Little Albert, and he soon wailed not only at the sight of white rats but also other furry objects. Watson was quick to justify the child’s sufferings. “They will be worth all they cost if through them we can find a method which will help us remove fear,” he wrote.

Watson’s experiment falls far short of contemporary ethical and scientific standards, but it nevertheless established an important principle: that fear could be learned. That discovery, in turn, suggested a different treatment for anxiety disorders from Freud’s psychoanalytic method. “If a fear or a phobia is the result of a learning experience, then it also means you can somehow learn not to fear anymore,” Kindt explained.

In the second half of the twentieth century, cognitive behavioral therapy incorporated Watson’s insight into mental health care. Rather than trying to help patients by dredging up repressed memories and urges to consciousness, as Freud had done, therapists sought to modify behaviors and teach their patients positive ways of thinking. The aim was not so much to uncover the hidden source of a person’s fear, but rather to help him reduce and manage his fear when he encountered a trigger.

In 1992, Kindt began working toward her Ph.D. in clinical psychology at the University of Amsterdam. As a student, she learned that cognitive behavioral therapy—and exposure therapy, specifically—was psychology’s best tool for treating anxiety disorders. (Antidepressants can be an alternative in particularly severe cases.) If you could convince a person who is afraid of heights to stand on a balcony, for example, his fear response would eventually abate, and he would learn the balcony was harmless. In the future, he could remember this safe experience rather than his older, irrational association between balconies and danger.

Exposure therapy has its limits, however. “In fear memory, people or animals learn a rule, whereas with extinction memories they learn an exception to the rule,” Kindt explained. A height-phobic patient who learned not to fear balconies would still typically fear other high places. And long after the treatment, the old fear could return unexpectedly, and the patient would be overwhelmed with panic once again. The fear memory was like an old bomb—buried, but not defused.

“I felt like we did not really understand why exposure therapy sometimes works and sometimes doesn’t,” Kindt said. As a student, she wondered whether there might be a better treatment—a way, perhaps, to defuse fear memories altogether.

Most other scientists believed that was impossible. “The dogma was, once a memory is fixed, it’s fixed for your lifetime,” said Susan J. Sara, a professor of neuroscience at the Collège de France in Paris, who has studied how memories are formed.
In the 1960s, researchers started to pinpoint exactly how new memories are created. In one set of experiments, they gave rats a drug that inhibited protein synthesis in the brain. Then they trained the rats to fear a bell by pairing it with an electric shock. Soon, the rats froze in terror whenever the bell chimed. The following day, however, the rats no longer froze when they heard the bell. They appeared to have forgotten their learning. The drug had disrupted their long-term memory formation.

From this, the researchers concluded that long-term memories require protein synthesis—whatever new memory subtly altering the cellular structure of the brain. This process is called “consolidation,” and scientists believed it happened only once for each memory in the hours immediately after learning.

Different types of memories consolidate in different parts of the brain. Explicit memories of life events, for instance, consolidate in the hippocampus, the long, pointlike structures near the center of the brain. Emotional memories, including fear, consolidate nearby in the amygdala, which activates the fight-or-flight response when it senses danger. The subjective experience of fear often involves both of these memory systems—a person will consciously remember past experiences while also undergoing several automatic physiological responses, such as increased heart rate—but they operate independently of each other.

Anxiety disorders, these scientists proposed, are caused by fear memories that “over-consolidate” in the amygdala. They found they could enhance or impair a rat’s memory by tweaking the levels of stress hormones in the brain immediately after learning. Adrenaline, for instance, boosted rats’ ability to remember a maze, while an adrenaline-blocking drug weakened it. “Adrenaline is released when you get stressed, and you tend to remember things better if you were excited at the time of learning,” said James McGaugh, one of the authors of consolidation theory.

This makes sense from an evolutionary standpoint. The same adrenaline rush that causes an animal to flee a bear will before the memory consolidated. This was possible in some circumstances, such as in hospital emergency rooms. In 2002, Roger Pitman published a study in which victims of car accidents and other trauma at Massachusetts General Hospital in Boston were given either a placebo or propranolol, a beta blocker that is one of the most commonly prescribed heart medicines in the world, which also lowers adrenaline and noradrenaline levels in the brain. Three months later, almost half of the placebo patients showed signs of PTSD, like sweaty hands and higher heart rates, when recounting their trauma. None of the members of the propranolol group exhibited symptoms. Pitman’s experiment had worked.

Such a measure raised ethical concerns, however. Only 10 to 30 percent of all trauma victims develop PTSD, and there is no way to predict who will and who will not. It is normal for victims to suffer in the days and weeks immediately following their trauma, so doctors need to wait at least a month in order to make a PTSD diagnosis—long after the memory consolidation window has closed. Regarding Pitman’s study, many doctors were uncomfortable with the idea of administering a drug to patients that could alter the emotional texture of memories that most of them would otherwise integrate healthily into their lives.

In 2003, the President’s Council on Bioethics condemned the use of “memory bluters” like propranolol following trauma. “In the immediate aftermath of a painful experience, we simply cannot know either the full meaning of the experience in question or the ultimate character and future prospects of the individual who experiences it,” the council wrote. “By ‘rewriting’ memories pharmacologically we might succeed in easing real suffering at the risk of falsifying our perception of the world and undermining our true identity.”

The treatment drew comparisons to the 2004 film Eternal Sunshine of the Spotless Mind, in which scientists erase a couple’s shared memories after a painful breakup. Leon Kass, the lead author of the council’s report, called propranolol “the morning-after pill for just about anything that produces regret, remorse, pain, or guilt.”

In 2003, Kindt was working as an associate professor at Maastricht University. She lived with her husband and children in Amsterdam, and commuted two-and-half hours by train to the school several times a week. She spent the time poring over neuroscience and clinical psychology journals. On one train ride, she came across the work of a scientist named Karim Nader, then at NYU.

Nader had published an article in Nature in 2000 that sent shock waves through the scientific community. His findings built on research Susan J. Sara had conducted several years earlier. Sara had made a chance discovery in her lab in Paris: While studying the function of a specific brain receptor, she had taught rats to solve a maze, but accidentally induced amnesia in the animals a day later, after their memories had consolidated. According to consolidation theory, these old memories should have been impervious to disruption. But
apparently this was not the case. To explain the result, Sara proposed that consolidation didn’t happen just once, but over and over again. “Memory is reconsolidated, so to speak, each time it is retrieved,” she wrote in her report.

Nader tested this idea specifically with fear memories. He trained rats to fear a tone by pairing it with a shock, and let them rest for 24 hours, so the memory would consolidate. Then he played the tone once to remind the rats of the previous day’s learning, and immediately injected a drug that blocked protein synthesis into the rats’ brains. When Nader tested the rats again a day later, they no longer froze in terror when he played the tone. They had forgotten their fear, even though the fear memories had consolidated. Nader theorized that old memories were made “labile” whenever they were recalled, and required further protein synthesis in order to remain usable in future situations. In other words, under the right circumstances, our memories could be changed.

Nader’s and Sara’s findings upended previously held notions about the way memory works. “The idea that a memory trace becomes labile when it’s reactivated doesn’t fit too well with the idea of consolidation,” Sara said. Many of their peers initially resisted the idea. “It was very hard to get this work published, because it challenged the consolidation theory,” she said. But the implications were profound. “It might be possible,” Nader wrote in his Nature article, “to treat persons with post-traumatic stress disorder or other related anxiety conditions by reactivating traumatic memories under conditions that would prevent reconsolidation.”

Kindt was thrilled when she read about Nader’s work. “It was a sort of accepted idea that emotional memory is forever, that the best thing you can do is form an inhibitory memory, but the fear memory is always there and we have to live with it,” she said. “I realized this might mean we can change fear memory.”

As researchers replicated and expanded on Nader’s and Sara’s findings, they found evidence of reconsolidation in animals as different as crabs, fish, chickens, and snails. “It’s throughout the animal kingdom,” said Carsten Wotjak, an expert in neuronal plasticity at the Max Planck Institute. The basic theory works like this: In any given situation, the brain will retrieve old memories to inform an organism’s behavior. If the memory is relevant to the situation, the organism can act on the information; if it is not relevant, then the organism can learn from the situation and create a new memory. With reconsolidation, researchers argued, there seemed to be a brief window in between the retrieval of an old memory and the creation of a new memory in which the old memory is vulnerable to manipulation.

Kindt wanted to make the leap from studying reconsolidation in animals to humans—a huge challenge, given the complexity of the human brain. In the past, many promising lines of research had fallen flat in this transition. But Kindt looked forward to the task. “What I really liked and still like about studying emotions is that they are very difficult to grasp in an experimental setting,” she said.

In 2003, Kindt took a job as a professor at the University of Amsterdam and began to lay the groundwork for her research into reconsolidation. Four years later, she won a grant to study the theory in humans. She couldn’t simply repeat Nader’s method, however. The drug he had used on rats, anisomycin, is too toxic for people. She was aware, though, of the studies Pitman, McGaugh, and others had conducted using propranolol. If propranolol could be used to prevent new fear memories from over-consolidating, she wondered, could it also perhaps be used to keep old, traumatic memories from reconsolidating?

In 2008, Kindt and a colleague, Marieke Soeter, recruited 60 undergraduate students to come to their lab for a three-day study. The rooms were small and sterile, with little equipment except for computers and a few strange wires: an electrode to deliver shocks and nodes to measure the subjects’ reactions. On the first day, Kindt conditioned the students to fear an image of a spider shown on a slide by pairing it with an unpleasant shock. She and Soeter then divided the students into three groups. On the second day, two of the groups received propranolol while the third group received a placebo. Then one of the propranolol groups and the placebo group had their memories of the previous day’s trial “reactivated” with a single presentation of the spider slide. On the third day, Kindt and Soeter showed the subjects the image yet again, to see if they still responded fearfully.

“IT was a Saturday morning, and Marieke had analyzed the data for the whole night,” Kindt remembered. “I woke up, and the first thing I did was I opened my laptop. There was already a graph in my inbox, and there was a flat line.” The group that had received propranolol and reactivation showed almost no fear response 24 hours later. It was gone completely. “I thought, ‘This cannot be true,’” Kindt said. “But then we checked it and double-checked it. I asked someone else to check it blind with the raw data from the computer to be sure.”

Kindt and Soeter immediately replicated the study in order to shore up their confidence. Then they began to expand their research. For subjects who received propranolol, they found that the fear response was still gone even 30 days later (it had returned in the control groups). Moreover, reminder shocks, which reinstated fear in the control groups, didn’t work on those subjects who had received the drug. It was as if she and

Kindt still marvels when she sees a patient disencumbered of fear.
"It still feels," she said, "a bit like magic."
A tarantula in Kindt’s lab. After her treatment, arachnophobic patients were able to approach the spider and, even more incredibly, reach out and touch it.
Soeter had removed the red M&M from the jar. They had found a way to defuse the bomb.

As extraordinary as this discovery was, Kindt still felt it was a bit limited. It was one thing to condition people to fear a picture with a few mild shocks in a lab, but real trauma was something else entirely. Fear-conditioning studies tested fears that were only a day old, after all, while people often live with anxieties and phobias for years before seeking treatment. Kindt’s ultimate goal was to find a cure for the kind of fear that people like Karin Klaver felt. “I thought this fear is so much stronger than what we instill by the fear conditioning,” Kindt said. She was skeptical that her treatment would even work on such patients. “I could imagine that it wouldn’t happen at all,” she said.

In 2013, Kindt recruited subjects who were very afraid of spiders—one of the most common phobias, and a fear that is also relatively easy to control in a laboratory setting. She instructed the participants to approach a terrarium that held a tarantula inside. Most of the participants struggled even to look at it. After two minutes, Kindt took them to another room and gave them either propranolol or a placebo. A few days later, Kindt put them back in the room with the spider. Every single participant in the propranolol group was able to approach the tarantula and, even more incredibly, reach out and touch its hairy abdomen with a finger. A year later, the propranolol group still reported levels of spider fear so low they would not have qualified for the study in the first place.

One of the patients in Kindt’s spider study, a psychology student named Sascha de Waal, told me she had feared spiders ever since she was a little girl. “You have a feeling if you have a problem for a long time, then it takes a long time to get rid of it,” she said. And yet in a day it was gone. Kindt still sometimes finds it hard to believe herself. “It is so strange to see someone who is so scared come back and start to move to the spider,” she said. “They touch it, and they say, ‘Wow, wow.’”

Since Kindt published her findings in December, her peers have similarly marveled at the results. “Kindt and her team are like magicians of reconsolidation,” said Karim Nader, who now runs a laboratory at McGill University. It is exciting for basic scientists like Nader and Sara, who focus on the mechanisms of memory, to see someone unlock the potential of this knowledge to actually improve people’s lives. “For people like us, who work in the basic sciences and are always being questioned about the relevance of their work, it’s very gratifying to see this body of work emerging from her laboratory,” Sara said. In light of Kindt’s study, Pitman wrote in his commentary, the prospects for reconsolidation-based treatments “seem more promising than ever.”

Science thrives on replication, and nearly every doctor I spoke with said they wanted their peers to replicate Kindt’s spider study before they thought about using her method in clinical practice. But there are few hurdles to widespread adoption. Propranolol, which has been used for decades to treat heart disease, is a safe, cheap, and common drug. (It earned its inventor, Sir James Black, the Nobel Prize for Medicine in 1988.) All Kindt’s method requires is a patient willing to tolerate a short exposure to their trauma and an off-label prescription. Daniela Schiller, a professor of psychiatry and neuroscience at NYU who, like Kindt, has studied reconsolidation in humans and its potential for treating anxiety, said she hoped their findings will become part of mainstream clinical practice within the next ten years.

Kindt is currently focusing her research on the specific conditions that trigger reconsolidation in people with more complicated anxiety disorders than specific phobias. She believes reconsolidation is normally initiated by what she calls a “prediction error”: The actual events that follow a trigger must be different from the outcome the patient anticipated. In the case of arachnophobic patients, this is relatively straightforward: They fear the tarantula will attack them, and it does not. Or they fear their panic will overwhelm them, but are able to remain in control. For people with PTSD, however, memory is much more complex, and it is harder for researchers like Kindt to pinpoint the external stimuli, such as a tarantula, that will trigger their fear memories. Nevertheless, Kindt’s work with these anxiety disorders so far has been very successful: It has worked 70 percent of the time with panic disorder and in ten of the twelve PTSD cases she has accepted.

Kindt is aware her work brings to mind Eternal Sunshine of the Spotless Mind. But she prefers to say her treatment “neutralizes” fear memories, instead of erasing them. Her patients are able to remember the traumatic experiences that caused their fear. But now, instead of developing an extreme anxious response, they are able to deal with those experiences normally. Kindt hopes that, for some patients, her treatment will open a door to more conventional forms of psychotherapy, rather than replacing them. By removing mental blockages and making it easier for people to think about what has hurt them, it may enable them to analyze and discuss their personal histories in ways they couldn’t previously.

“We’re not advocating that it would be a good idea to wipe a memory completely of traumatic events,” said Jonathan Lee, a psychologist specializing in reconsolidation at the University of Birmingham in the U.K. “What we’re hoping this approach might do is to essentially give the patient back some control over those unconscious urges, that avoidance, or the physiological fright.”

Perhaps it will even help people appreciate the positive role fear can play in their lives. Kindt once took a pill of propranolol herself before her daughter underwent surgery. The drug has a palliative effect—musicians often take it before big performances—and she did not want to feel anxious while her daughter was in the operating room. “During the operation, I was indeed very relaxed,” she said. Afterwards, though, she wondered whether the medication had deprived her of an important memory. The surgery wasn’t a traumatic event, after all, merely a stressful one. “My memory feels very strange,” she said, thinking back. “Normally I might have had a very emotional memory, but now it’s just an event.” Not all fears need to be neutralized. “I missed the emotion,” Kindt said. “It gives color to experience.”

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