Psychological pressure can make you more attentive, improving your memory and ability to learn. But too much stress can have the opposite effect

SPLINTERED BY STRESS

By Mathias V. Schmidt and Lars Schwabe

A needling twinge in the torso or a tense interaction with a boss is all you need to get your nerves on edge. The bills are piling up and—of course—your spouse is on your case about them. You feel as if an extra weight is pressing down on your mind.

The all too familiar sensation of stress can preoccupy your thoughts, narrowing attention to the sphere of your concerns. But its effects do not end there—stress also causes physical changes in the body. In a stressful situation, alarm systems in the brain trigger the release of hormones that prepare you to fight back or flee the scene. Among other results, these chemicals may boost blood pressure, speed up heart rate and make you breathe faster [*see box on page 26*]. They may also affect your ability to learn and remember things.

Think back on the tests you took in school. Even when you crammed like crazy, your performance on exams may have left something to be desired. Maybe key pieces of knowledge simply escaped you—until they came to mind, unbidden, several hours too late. One possible explanation for this phenomenon is stress: your anxiety may have impaired your recall.

That reasoning sounds simple enough, but it turns out that the effect of stress on memory is surprisingly nuanced. Studies have shown that under certain circumstances, psychological pressure may actually improve recall—but not necessarily of the facts you were

PHOTOILLUSTRATION BY AARON GOODMAN

terward, the men were asked to remember the words they had learned the day before. The result: stress reduced the number of emotionally charged words that the men were able to recall, although it did not affect their memory of neutral words.

Earlier experiments had found that administering the stress hormone cortisol can impair our ability to retrieve memories, but the Düsseldorf study was the first to show that stress itself can have this effect on humans, presumably by triggering the release of cortisol and other hormones. The finding may help explain why people who are feeling stressed—during an exam or a job interview, for example—sometimes have trouble remembering important information. The results also suggest that emotionally arousing material may be especially sensitive to the memory-altering effects of stress hormones, perhaps because these hormones activate the amygdala—a brain structure that plays a critical part in processing emotions.

Initially that experiment seemed at odds with earlier studies that had reported *improved* recall of emotionally arousing material after receiving cortisol or undergoing a stressful experience. In one study, published in 2003, Larry Cahill and his colleagues at the University of California, Irvine, asked 48 men and women to look at a series of emotionally charged or neutral images. Immediately afterward, some of the participants were asked to immerse a hand in ice water—a test that causes discomfort and elevated cortisol levels in most people. The control group got a painless lukewarm hand dunk instead. A week later both groups took a memory test, and the people who had experienced the cold water treatment were able to recall more images than the control group. In both studies, stress had an effect only on the emotionally charged material—but in opposite ways.

Convergence in Time and Space

How can stress facilitate memory in some experiments but impair it in others? In 2006 a research team led by Marian Joëls of the University of Amsterdam in the Netherlands came up with a "unifying theory" to resolve the conflicting reports. Joëls and her colleagues proposed that stress facilitates memory only when it is experienced at about the same time as the event that needs to be remembered and when stress hormones activate the same biological systems as those activated by the event. In brief, they theorized that stress only aids memory "when convergence in time and space takes place."

Convergence in time, as the researchers explained, is when the stress hormones are released during or immediately after

Mice subjected to chronic stress in early life do not perform well on memory tests in later life.

PAUL FLEET Alamy

the event to be remembered. Immersing your hand in ice water right after studying a series of images, for example, seems to make those images more memorable later. But stress hormones have the opposite effect when they are released before the event or a considerable time afterward—as in the study where the young men took a stress test 24 hours after studying a word list.

The other requirement proposed by Joëls's team—convergence in space—occurs when the hormones released in response to stress activate the same neuronal circuits as does the information to be processed and stored. These conditions only enhance memory, however, if the stress is short-lived. The beneficial effect disappears if the stress is chronic or repetitive.

Joëls and her colleagues also proposed a mechanism for how stress exerts these opposing effects on memory. The body's response to stress comes in two phases. At first, stress launches hormones and neurotransmitters that promote attention and help form new memories by strengthening the connections between brain cells. But just as a rocket fires a second stage once it is high in the sky, the hormone cortisol initiates a second process within an hour or so of the stressful event, and instead of promoting attention, cortisol now works to consolidate memories. The hormone suppresses the processing of any information not associated with the stressful event.

These two distinct stages of the stress response explain why stress can have such contrary effects on memory. Initially stress enhances perception and learning, but later, stress obstructs the processing of new information. According to this model, recalling an event such as being late to an exam should be easy because the stress occurs during the experience. But remembering information during the test is more difficult because the stress of taking the exam occurs hours or days after learning the information.

Stress not only affects how much information we retain in memory but also what type. Our memory is not like one big drawer into which we toss everything that we experience and

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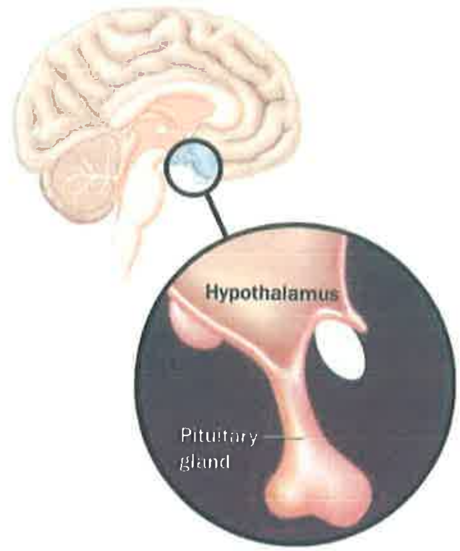
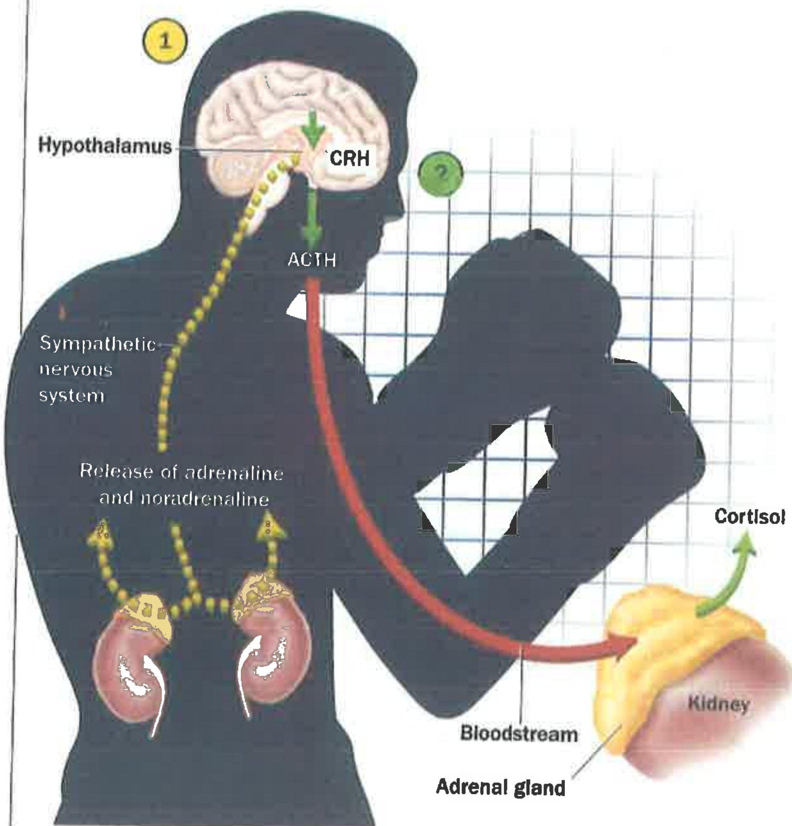
Defense Mechanisms

When we find ourselves in situations that seem threatening, the hypothalamus—a structure that lies deep in the brain—sends out an alarm. This triggers two cascades of activity: a rapid response that releases one set of hormones and a more delayed one that releases a different set of hormones. Together these two lines of defense not only enable us to cope with acutely stressful situations but also prepare us for similar future situations by strengthening our memory of what we have just been through. *—M.V.S. and L.S.*



(1) Rapid Response

The hypothalamus sends a signal along fibers of the sympathetic nervous system to the adrenal medulla, located in the core of the adrenal gland just above the kidney. The adrenal medulla then releases the stress hormones adrenaline and noradrenaline, which prepare the body for a rapid fight-or-flight response. Energy reserves are mobilized; blood pressure and heart rate increase to better supply nutrients to the muscles; respiration increases so that more oxygen reaches the brain; natural painkillers are released preventively; and platelets are activated to minimize blood loss in case of injury.



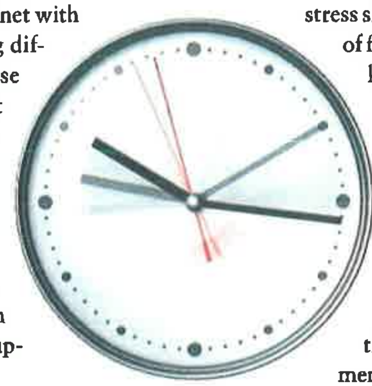
(2) Delayed Reaction

Later the body releases another set of hormones from the hypothalamus, pituitary gland and adrenal cortex in sequence. First, corticotropin-releasing hormone (CRH), which is produced in the hypothalamus, travels along a special network of capillaries to the pituitary gland, an almond-size structure located near the base of the skull. There CRH triggers the release of another hormone, adrenocorticotropic hormone (ACTH), which travels to the adrenal cortex via the bloodstream and triggers the release of cortisol—the most important human stress hormone.

Cortisol boosts the action of adrenaline and noradrenaline while at the same time preparing the body for a return to normal. It puts a damper on the body's inflammatory and immune responses and promotes the transformation of nutrients into fats and glycogen, thereby replenishing spent stores of energy.

THERESA SAKNO

learn. Rather it resembles a giant filing cabinet with many drawers and folders, each containing different types of information. Some of these files—including the episodic memory that gives us access to life experiences—are extremely sensitive to stress. Memories of practical skills such as bicycling and typing, on the other hand, are barely affected by stress. These different memory systems work in parallel and may even compete with one another, and stress plays a role in determining which memory system has the upper hand at any given moment.



stress simplifies our learning behavior at the expense of flexibility, making it harder for us to apply our knowledge to new situations. If a fire alarm goes off in a building, for example, you might find that you can remember only that you usually follow the first hallway on the left to reach the main entrance. But that knowledge is of little use if the main entrance is blocked and you need to find your way out through a side entrance.

In 2009 we confirmed the hypothesis that under stress, the brain favors rigid "habit" memory over more flexible "cognitive" memory.

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Simpleminded Learning

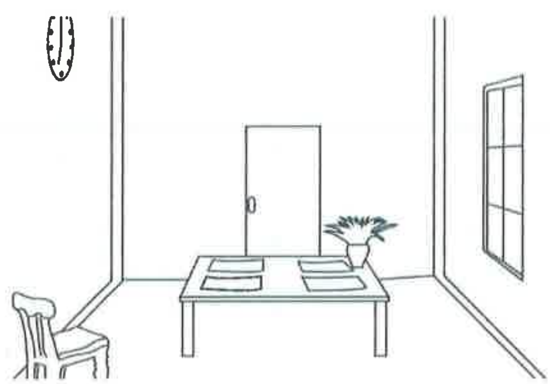
To test the effect of stress on various learning strategies, we conducted an experiment in 2007 at the University of Trier in Germany. We showed the participants a three-dimensional model of a room containing a chair, a potted plant and a table with four cards lying face down on it [*see illustration below*]. The object of the game, which every participant played 13 times, was to win 50 cents by selecting the "winning" card from among the four cards. Half the players were subjected to the Trier social stress test before playing the card game.

What none of the players was told was that the winning card was always located in the same place—in the corner next to the potted plant. At first, players picked the winning card only by chance. But as the game went on, the participants used one of two strategies. Some players oriented themselves spatially, using the relation between various objects in the room—such as the door, a window and a clock hanging on the wall—as clues to where the winning card might be located. Other players used a "stimulus response" strategy: they looked for a simple association between the winning card and another object in the room. We were easily able to test which strategy a subject was using simply by moving the plant and placing winning cards in two of the four positions—next to the plant's new location and in the corner where the winning card had previously been located. If a player selected the card that had always been in the winning corner, we concluded that he was using a spatial learning strategy. On the other hand, a player who selected the card next to the now repositioned plant was probably using a stimulus-response learning strategy.

The results revealed that participants who had not taken the stress test were much more likely to use the more flexible—but more mentally taxing—spatial learning strategy. Under stress, almost all the participants fell back on the simpler stimulus-response strategy.

These results and data from other studies suggest that We subjected half our subjects to the ice-water stress treatment for several minutes, whereas participants in the control group immersed their hand in lukewarm water. Afterward everyone was asked to choose between chocolate milk and orange juice by clicking on symbols on a computer screen. The participants quickly learned which symbols would deliver the drink of their choice, but then we spoiled their appetites by feeding them chocolate pudding or oranges.

When they resumed choosing drinks, the participants in the control group who had eaten chocolate pudding avoided the now devalued chocolate milk, and participants who had eaten oranges avoided orange juice. But their stressed counterparts responded differently: even though the participants reported no further interest in the food they had just eaten, they continued to click on the symbol associated with it. They



STRATEGY FOR STRESS
In this test, subjects try to pick the "winning" card from among four cards lying face down on a table. Under stress, participants fall back on a simple strategy: they look for a single clue, such as a potted plant placed next to the winning card. Unstressed participants are more likely to orient themselves in relation to features seen in the room—a more difficult but more accurate spatial learning strategy.

GETTY IMAGES (*clock*); SCIENTIFIC AMERICAN MIND; SOURCE: "STRESS MODULATES THE USE OF SPATIAL VERSUS STIMULUS-RESPONSE LEARNING STRATEGIES IN HUMANS," BY LARS SCHWABE ET AL., IN *LEARNING AND MEMORY*, VOL. 14, NO. 1–2; JANUARY 2007 (*test room*)

It may even be possible to develop drugs that enhance the positive effects of stress on memory and recall.

had become victims of habit, operating on autopilot. The evolutionary advantage of this strategy is obvious—it enables the brain to concentrate on more important things in a stressful situation.

Life in the Rat Race

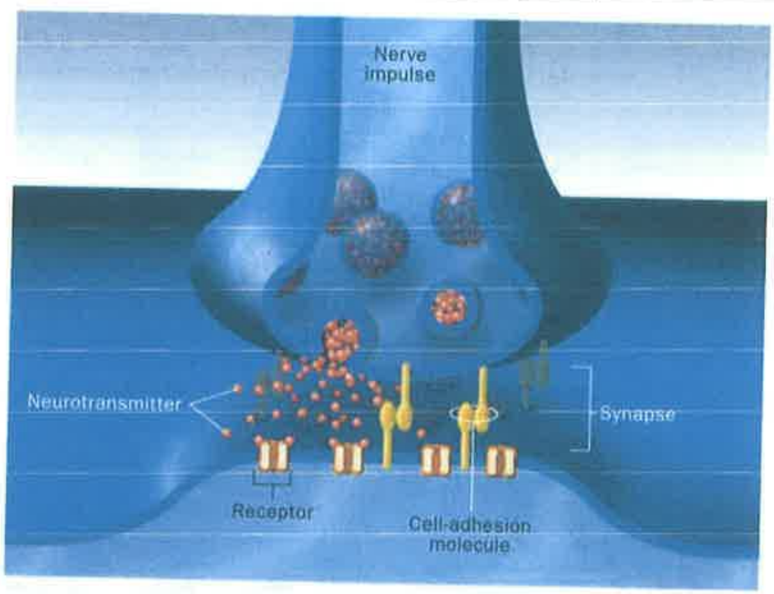
Tests on human volunteers can help reveal the effects of stress on learning and memory, but animal experiments also provide clues. Rats, mice, chicks and other vertebrates release hormones and neurotransmitters in response to stress, just as we do. And as with people, animals must remember places and events: Where did I find food yesterday? Where is my nest? Which places are dangerous and must be avoided? Reliable memories of stressful events are essential for survival.

Scientists have devised a number of methods for measuring learning and memory in animals. One frequently used approach, developed in 1984 by Richard Morris of the University of St. Andrews in Scotland, is a water maze—a large basin filled with cold water. (Unlike a conventional maze, the water "maze" does not have branching passages.) Rats placed in the basin cannot see a small platform hidden just below the water's surface, but they are highly motivated to find it: the faster they do so, the sooner they can get out of the cold water. At first, a rat placed in the water finds the platform only by chance. After repeated tests, though, the rat learns to use conspicuous markings on the walls to quickly find the platform.

Studies using the water maze have shown that stress hormones play an important part in the learning process in rats as well as humans. For example, in 1992 Melly S. Oitzl and E. Ronald de Kloet of Leiden University in the Netherlands demonstrated that in the absence of stress hormones, rats perform poorly in a water maze. After Oitzl and de Kloet removed the rats' adrenal glands, which are responsible for releasing the stress hormone corticosterone (similar to human cortisol), the animals needed much more time to locate the underwater platform. The researchers observed the same effect after they blocked corticosterone receptors in the rats' brain.

But as with humans, timing is everything. Stress that is independent of the learning situation can impair memory, as David M. Diamond, then at the University of Colorado Health Sciences Center, and three colleagues showed in an experiment in 1996. First they trained rats to forage for food hidden in seven arms of a 14-arm radial maze. After about a month, the rats rarely visited the arms without food. Then the experiment began. As soon as the rats had eaten four of the seven treats, the rodents were removed from the maze and placed in either a familiar or a stressful environment for up to four hours. After the unstressed rats returned to the maze, they had not forgotten where to find the three remaining treats, but the stressed rats made many more errors while searching for the treats.

Persistent or intense stress may even decrease cognitive capacities over the long term. In 2009 our research team at the Max Planck Institute for Psychiatry in Munich showed that mice that were subjected to chronic stress in early life do not perform well on memory tests in later life, compared with their unstressed littermates. The reasons for the difference are buried deep in the brain.



CLOSE CONNECTION
Nerve impulses travel through the brain by jumping from one nerve cell to the next across a gap called the synapse. At every synapse, the upstream nerve cell releases a puff of neurotransmitters, chemical messengers that travel across the gap and bind to receptors on the downstream cell. Specialized cell-adhesion molecules connect the two cells across the gap, stabilizing the synapse. Recent research indicates that stress affects the production of cell-adhesion molecules, which may in turn affect long-term memory by strengthening or weakening synapses.

GETTY IMAGES (*paper wad*); GEHIRN & GEIST/ART FOR SCIENCE (*nerve*)

Animal studies suggest that stress in early life can impair memory in adulthood. The same may be true for humans.

Stronger Synapses

Memories depend on the structural connections between the brain's nerve cells—the synapses where nerve impulses jump from one cell to the next. A particular stimulus, such as a green traffic light, triggers a cascade of signals that activate what we have already learned: green means go. Step on the accelerator.

Learning strengthens these cellular connections. As a result, signals are more easily transmitted from one nerve cell to its neighbors—a process known as long-term potentiation. This process is what allows the brain to store and recall information. Synapses can grow stronger or weaker over time, depending on their level of stimulation, and memories in turn can be reinforced or forgotten.

If stress hormones are brought to bear on the nerve cells during the right window of opportunity, they can produce a long-lasting improvement in signal transmission and with it memories of that particular event or place. If the hormones are not present at the right time, however, the connections between the nerve cells are comparatively weaker—and memories of that moment are harder to access.

Specialized cell-adhesion molecules may be a key to the learning process at the cellular level. These proteins connect two nerve cells, stabilizing the synapse between them and enabling the transmission of signals from cell to cell. Cell-adhesion molecules have an important role in reestablishing contact between nerve cells. They also assist in enabling the synapses to change strength in response to increased or decreased signal transmissions.

Recent research suggests that stress affects the production of cell-adhesion molecules, thereby affecting long-term memory. A team led by Carmen Sandi of the Brain-Mind Institute of the Swiss Federal Institute of Technology in Lausanne has found that stress activates neural cell-adhesion molecules (NCAMs) in the hippocampus—a region of the brain that is essential for learning new information and consolidating it in long-term memory. Mice in which NCAM activation has been suppressed by genetic manipulation have impaired learning and memory.

With a better understanding of how stress affects memory at the cellular level, we may be able to develop new drugs to treat stress-induced cognitive disorders, perhaps even Alzheimer's disease. One example of such work is a research project sponsored by the European Union, called MemStick, which is studying the effect of cell adhesion. The project's hypothesis is simple: if cell-adhesion molecules are responsible for forming or stabilizing synapses, we should in theory be able to develop analogous substances that restore memory by simulating the function of these molecules. And in fact, researchers have already developed a mimetic peptide for NCAM—a small protein that is similar to a portion of the molecule. If rats under chronic stress are treated with this peptide, they show reduced loss of cognitive performance.

This success offers hope that someday new drugs will be able to reduce—and perhaps even reverse—the negative effects of stress on memory processes. It may even be possible to develop drugs that are able to enhance the positive effects of stress on memory and recall: imagine a pill that could help you ace an exam or job interview. That glimmer of hope is something to think about the next time you feel the pressures of life, work and love closing in on you. M

(Further Reading)

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