Anxieties can become strongly etched into the brain. But don’t worry—researchers may find ways to erase them

By Rüdiger Vaas
It is a remarkable achievement that today, at least in developed countries, we seldom encounter any natural, fear-evoking situations. We are not likely to meet up with snakes or crocodiles or to find ourselves without shelter during a storm. But in our efforts to command nature and our fellow human beings, we have created new hazards: highways and greenhouse gases, machine guns and bioterrorism, and the social pressures of failure and embarrassment. That these dangers are not immediate enough to evoke real fear for most people is scarcely a blessing; the anxieties of modern life can be debilitating. “Perhaps man is the most fearful of all creatures,” comments Irenäus Eibl-Eibesfeldt, anthropologist emeritus at the Max Planck Institute of Behavioral Physiology in Seewiesen, Germany, “because along with such elementary fears as those of predators, he also suffers from an intellectually grounded fear of existence.”

More intellectual work, however, might free us from this burden. Research into how the brain transmits, sustains, and remembers fears and anxieties is providing clues about how to control or even eliminate them. Understanding the demon will help us overcome it.

Where the Nightmare Begins

Strangely, flat-out fear may be easier to handle than anxiety. We see a vicious dog running at us, our brain sounds alarms, our heart and lungs race, and we fight or flee. As scary as such an experience is, it comes to a clear end, and the body and brain return to their normal states. Anxiety is much more insidious and can be more harmful over time. Many people even enjoy playing with fear by reading ghost stories, watching horror films or participating in extreme sports. But anxiety can dampen the joy of discovery, spoil the fun of games, inhibit initiative and creativity, and, in greater doses, ruin an individual’s health.

Other than addictions, anxiety disorders are the most common of all mental problems. More than 10 percent of Americans and Europeans suffer from them. Most common are phobias—exaggerated fears of specific things such as spiders or snakes and situations such as heights or enclosed spaces. Common, too, are compulsive feelings of dread, whereby people can describe what makes them anxious but not why.

Recent studies hint that anxiety disorders and even general anxiousness have a genetic component, although a person’s environment certainly has the most influence. Identical twins—even those who grow up separately—share more fears than fraternal twins do. There is, of course, no single gene for fear; many genes are involved in interactions with neurotransmitters and their receptors. The genes that command the biological clock, which is responsible for an organism’s inner rhythms, also appear to contribute in a way we do not yet understand.

Scientists have already succeeded in breeding fearfulness and fearlessness into rats. Normally, rats will not remain long in an open area; they have an instinctive fear of places that do not offer shelter from predators. But just a few generations of inbreeding and selection can result in rats that differ markedly in the length of time they will loiter in an open field.

The neurobiological bases of anxiety and fear are now relatively well described. No single region of the brain is solely responsible for creating anxiety and awareness of it. Rather fear springs from a collaboration among many brain areas.

Imaging experiments show that parts of the temporal lobes, on the left and right sides of the brain, experience greatly increased blood flow not just during panic attacks but from everyday anxi-
Fighting off a vicious dog is scary, but the event ends and the body and brain return to normal. Anxiety is much more insidious and harmful over time.

Danger Rears Its Head

When we perceive a threat, the thalamus integrates sensory and motor information and sends it to the amygdala. The thalamus also alerts the amygdala to thoughts about danger that arise in areas of the cerebral cortex responsible for consciousness. The amygdala, in turn, sends signals back that can influence our awareness and even memory of danger. The amygdala’s closely connected central nucleus sends commands to the hypothalamus, which causes stress hormones to be released that raise blood pressure and ready the body to defend itself. The central nucleus also instructs the brain stem and central midbrain, which control the fear reaction and fear paralysis. The amygdala’s lateral and basal nuclei control behavioral changes, such as changing directions during flight.
fear of strangers begins in infants at just this time—they are incapable of experiencing this type of anxiety in their first six months.

The hypothalamus, a part of the midbrain, is also important and is currently a target for psychiatric drugs. It controls the hormone system and influences the sympathetic nervous system, which together marshal the body’s resources to respond to threats. But the same network can disable the body’s reactions. Being “paralyzed by fear” may have had evolutionary advantages, keeping prehistoric humans perfectly still so that predators did not notice them or react to their movements.

The most active region of the brain during fear and anxiety is the amygdala, just below the temporal lobe. When researchers stimulate it electrically, levels of the hormone cortisol increase, as do a subject’s physical signs of fear. The amygdala is especially active during dream sleep, a probable cause for anxiety dreams and nightmares. And when the amygdala is injured, feelings of anxiety diminish but cognitive functions remain much the same. Interestingly, patients who are born with amygdala damage cannot recognize fear in the faces of others.

**Learning Fear, then Erasing It**

Infants, for their part, do not react with fear when shown pictures of threatening faces. But while still young, they come to know that malevolent faces usually lead to malevolent words or deeds. The fact that memories of fear can work unconsciously was first recognized in the early 1900s by Edouard Claparède. He was a psychol-

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**Emotionally intense experiences may “scar” cerebral tissue in ways that produce anxiety disorders. Drugs could prevent the scars from forming.**

Using functional magnetic resonance imaging of a lower (left) and higher (right) cross section of the brain, scientists have shown that both the left and right sides of the amygdala are active when processing facial expressions of fright (green) as well as during conditioned fear (red). The information processing during both situations is quite different, however. Expressions of fright produce activity more in the left side of the upper amygdala than in the right side, whereas the response to conditioned fear is more evenly distributed.
ologist at Geneva University who later founded the Jean Jacques Rousseau Institute, which became a famous educational center for leading psychologists. Claparède was treating a woman who, because of a brain injury, could no longer process new information. He had to introduce himself to her at each appointment. One time he entered the room with a thumbtack hidden in the palm of his hand and shook hands with her. When she arrived for her next visit, she refused to shake hands, although she could not provide any reasonable explanation for why. Claparède concluded that an unconscious memory must have warned her.

In recent years, scientists have conducted thorough research into how fear-linked situations are stored in our memories. When rats, for example, hear a tone and are then given an electric shock, they soon begin to react with fear to the sound alone. The central nucleus of the amygdala seems to be key to storing fear memories.

Remarkably, the hippocampus in the temporal lobe—one of the most important regions for conscious memories of facts—plays no role in standard conditioning (for example, in tests in which rats learn to associate stimuli that are neither threatening nor desirable). But it becomes influential when the context of the stimulus matters. In experiments, if a neutral tone is accompanied by a special light, then when the light alone is shown, a reaction is set off in the hippocampus. This proves what Claparède suspected: the conscious memory for facts and the emotional memory are two different systems.

Indeed, in 1890 psychologist William James proposed that “an impression may be so exciting emotionally as almost to leave a scar upon the cerebral tissues.” Today scientists are beginning to understand how such neuronal “scars” arise and produce anxiety disorders. Perhaps they will be able to produce therapeutic drugs to prevent these traces from forming.

It may even be possible to erase the sensation of fear. Experts are increasingly convinced that the so-called long-term potentiation of neurons is crucial to emotional memory. In this mechanism, connections among neurons that are frequently used become etched or hardwired, in part by the creation of more receptor molecules on these neurons that are tailored to receive a certain chemical stimulus. When these receptors are blocked in lab tests, however, fear conditioning no longer functions, so it might be possible to design drugs that control or prevent fears from being laid down in the brain. In addition, as neurons learn fear, they synthesize particular proteins, and the process continues even after the conditioning experience stops. Scientists have determined that they can erase fear reactions in lab animals that were learned as much as two weeks earlier if they can block the synthesis of the related proteins in a part of the amygdala called the basal nucleus. There also appears to be a window of opportunity for interfering with remembered fears soon after the fear memory is reactivated. It might therefore be possible to erase traumatic memories with drugs.

Erasing debilitating fears remains a hope for the future. Right now researchers are simply trying to “turn off” conditioned responses to stimuli.

(The Author)

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Classic psychology experiments have shown that when rats are first conditioned with an electrical shock to fear a tone when it sounds, they later fear the tone even without the associated shock. Yet after they repeatedly hear the tone for some time without the shock, the learned fear reaction disappears. Researchers have determined that the reaction is not forgotten but is being actively suppressed by the nervous system, under the direction of the cerebral cortex.

What actually happens during suppression? When a fear reaction is conditioned, the neurons involved group themselves into ensembles that act in unison. These ensembles remain after suppression but do not react because they no longer propagate an activating impulse. This means that even after the reaction is curbed, the ensembles can become reactivated by a new impulse—which is probably how phobias arise.

**Drugs or Dialogue?**

Finding chemical compounds that could suppress remembered fears will be a challenge. In the meantime, researchers are trying to improve
drugs that can interfere with the chemical messengers that have been shown to arouse anxiety: the neurotransmitters.

The success of certain psychotropic drugs indicates that anxiety disorders can arise from the presence of too little GABA—gamma-aminobutyric acid, an inhibitory neurotransmitter. The benzodiazepine tranquilizers such as chlordiazepoxide (Librium) or diazepam (Valium) bind to GABA receptors and reinforce the effects of the transmitter. Animal experiments show that targeted delivery of benzodiazepines to the amygdala—which is rich in GABA receptors—lessens anxiety, whereas GABA antagonists block this effect. In addition, researchers have found a small protein in the brains of both humans and rats that can bring about anxiety, apparently by docking to the benzodiazepine binding sites of the GABA receptors.

Along with GABA, the neurotransmitter serotonin also influences anxiousness. Drugs such as fluoxetine (Prozac) affect the serotonin receptors. And irregularities in the dopamine system can also lead to some types of anxiety disorders.

Psychotherapy is the alternative to drugs for curing anxiety disorders. Doctors have developed various therapies, and great controversy exists over which are effective. Psychoanalysts, for example, seek to resolve a patient’s unconscious conflicts, from which they claim anxieties spring. Cognitive talk therapists try to get anxieties under control by helping a patient change his or her attitude toward certain stimuli.

Behaviorists, for their part, doubt the significance of unconscious memories and attempt to treat situations, which seems to be helpful with phobias. Some behaviorists try to gradually reduce a patient’s sensitivity to an anxiety-provoking stimulus by slowly getting him or her accustomed to it. Others use “exposure therapy”—bringing the patient face-to-face with the stimulus in a massive, shocking way in order to “deaden” him or her to it. Both therapies aim to induce “counterconditioning,” which supposedly causes the patient to “unlearn” the anxiety.

Regardless of their methods, therapists and drug designers face a difficult task in calming fears and anxieties. There are far fewer connections from the cortex to the amygdala than vice versa—perhaps giving rational thought little sway. The imbalance is why fears and other emotions can so easily overwhelm us and why it is so hard to voluntarily suppress such feelings. This must be the reason that therapy often goes on so long and often is only somewhat effective.

We humans also excel at creating fears. One of the most powerful and effective functions of the brain, says New York University neurobiologist Joseph E. LeDoux, is the ability to quickly fashion memories out of stimuli that are connected to hazards, then preserve them for a long time and automatically put them to use when similar situations arise in the future. Yet, he notes, this incredible luxury is expensive—we have more fears than we need. The fault, LeDoux maintains, seems to lie with our extraordinarily effective fear-conditioning system, activated by our well-developed ability to imagine fears and our inability to control them.