THE SCIENCE OF ANXIETY

WHY DO WE WORRY OURSELVES SICK? BECAUSE THE BRAIN IS HARDWIRED FOR FEAR, AND SOMETIMES IT SHORT-CIRCUITS

By CHRISTINE GORMAN

IT'S 4 A.M., AND YOU'RE WIDE AWAKE—PALMS SWEATY, HEART racing. You're worried about your kids. Your aging parents. Your 401(k). Your health. Your sex life. Breathing evenly beside you, your spouse is oblivious. Doesn't he—or she—see the dangers that lurk in every shadow? He must not. Otherwise, how could he, with all that's going on in the world, have talked so calmly at dinner last night about flying to Florida for a vacation?

How is it that two people facing the same circumstances can react so differently? Why are some folks buffeted by the vicissitudes of life while others glide through them with grace and calm? Are some of us just born more nervous than others? And if you're one of them, is there anything you can do about it?

The key to these questions is the emotional response we call anxiety. Unlike hunger or thirst, which build and dissipate in the immediate present, anxiety is the sort of feeling that sneaks up on you from the day after tomorrow. It's supposed to keep you from feeling too safe. Without it, few of us would survive.

All animals, especially the small, scurrying kind, appear to feel anxiety. Humans have felt it since the days they shared the planet with saber-toothed tigers. (Notice which species is still around to tell the tale.) But we live in a particularly anxious age. The initial shock of Sept. 11 has worn off, and the fear has lifted, but millions of Americans continue to share a kind of generalized mass anxiety. A recent TIME/CNN poll found that eight months after the event, nearly two-thirds of Americans think about the terror attacks at least several times a week. And it doesn't take much for all the old fears to come rushing back. What was surprising about the recent drumbeat of terror warnings was how quickly it triggered the anxiety so many of us thought we had put behind us.

This is one of the mysteries of anxiety. While it is a normal response to physical danger—and can be a useful tool for focusing the mind when there's a deadline looming—anxiety becomes a problem when it persists too long beyond the immediate threat. Sometimes there's an obvious cause, as with the shell-shocked soldiers of World War I or the terror-scarred civilians of the World Trade Center collapse. Other times, we don't know why we can't stop worrying.

GLOSSARY

STRESS Any external stimulus, from threatening words to the sound of a gunshot, that the brain interprets as dangerous

FEAR The short-term physiological response produced by both the brain and the body in response to stress

ANXIETY A sense of apprehension that shares many of the same symptoms as fear but builds more slowly and lingers longer

DEPRESSION Prolonged sadness that results in a blunting of emotions and a sense of futility; often more serious when accompanied by anxiety disorder

There is certainly a lot of anxiety going around. Anxiety disorder—which is what health experts call any anxiety that persists to the point that it interferes with one's life—is the most common mental illness in the U.S. In its various forms, ranging from very specific phobias to generalized anxiety disorder, it afflicts 19 million Americans (*see* "Are You Too Anxious?").

And yet, according to a survey published last January by researchers from UCLA, less than 25% of Americans with anxiety disorders receive any kind of treatment for their condition. "If mental health is the stepchild of the health-care system," says Jerilyn Ross, president of the Anxiety Disorders Association of America, "then anxiety is the stepchild of the stepchild."

Sigmund Freud was fascinated with anxiety and recognized early on that there is more than one kind. He identified two major forms of anxiety: one more biological in nature and the other more dependent on psychological factors. Unfortunately, his followers were so obsessed with his ideas about sex drives and unresolved conflicts that studies of the physical basis of anxiety languished.

In recent years, however, researchers have made significant progress in nailing down the underlying science of anxiety. In just the past decade, they have come to appreciate that whatever the factors that trigger anxiety, it grows out of a response that is hardwired in our brains. They have learned, among other things:

ARE YOU TOO ANXIOUS?

Everybody feels a bit of anxiety from time to time, but a clinical anxiety disorder is a different matter. If you suspect you may be suffering from one, you should consult a professional for a diagnosis. The psychological diagnostic manual lists 12 anxiety conditions. Here are the signs of five of the most common ones:

PANIC DISORDER

WHAT IT IS: Recurrent, unexpected attacks of acute anxiety, peaking within 10 minutes. Such panic may occur in a familiar situation, such as a crowded elevator

WHAT IT ISN'T: Occasional episodes of extreme anxiety in response to a real threat

WHAT TO LOOK FOR: Palpitations; chest pains, sweating, chills or hot flushes; trembling; shortness of breath or choking; nausea; light-headedness or feeling of unreality; fear of losing control or dying

BOTTOM LINE: Four or more of these symptoms in at least two discrete episodes could spell trouble

SPECIFIC PHOBIA

WHAT IT IS: Consuming fear of a specific object or situation, often accompanied by extreme anxiety symptoms

WHAT IT ISN'T: Powerful aversion to certain places or things

WHAT TO LOOK FOR:

- Do you come up with elaborate ways to avoid the object or situation?
- Do you dread the next possible encounter?
- Are you aware that the fear is excessive but you are unable to control it?
- Does merely thinking about the thing you fear make you anxious?

BOTTOM LINE: Don't worry if you just plain hate, say, snakes or crowds or heights. The key is how powerful your feelings are—and how you handle them

OBSESSIVE-COMPULSIVE DISORDER

WHAT IT IS: A preoccupation with specific thoughts, images or impulses, accompanied by elaborate and sometimes bizarre rituals

WHAT IT ISN'T: Fastidious—even idiosyncratic—behavior that does not significantly interfere with your quality of life

WHAT TO LOOK FOR: Are the obsessive thoughts persistent and intrusive?

- Do you expend a lot of energy suppressing the thoughts, usually unsuccessfully?
- Are you generally aware that the thoughts are irrational?
- Is the anxiety temporarily eased by a repetitive ritual such as hand washing or a thought ritual such as praying?
- Are the rituals time consuming?

BOTTOM LINE: Some researchers question whether OCD is a genuine anxiety disorder. Whatever it is, it does respond to treatment—provided you seek help

POST-TRAUMATIC STRESS DISORDER

WHAT IT IS: Repeated, anxious reliving of a horrifying event over an extended period of time

WHAT IT ISN'T: Anxiety following a trauma that fades steadily over the course of a month or so

WHAT TO LOOK FOR: After witnessing, experiencing or hearing about an event that caused or threatened to cause serious injury, do you:

- Have recurrent recollections or dreams about the experience?
- Feel emotionally or physically as if the event were still occurring?
- Experience intense anxiety when something reminds you of the event?
- Try to avoid thoughts, feelings, activities or places associated with the event?
- Have difficulty recalling details of the event?
- Experience anxiety symptoms such as irritability, jumpiness, difficulty sleeping, feelings of detachment from others, diminished interest in things, feelings that your future is in some way limited?

BOTTOM LINE: Sometimes, PTSD will not appear until six months after the event. Seek help whenever symptoms occur

GENERALIZED ANXIETY DISORDER

WHAT IT IS: Excessive anxiety or worry, occurring more days than not for six months

WHAT IT ISN'T: Occasional serious worry that doesn't markedly diminish quality of life

WHAT TO LOOK FOR: Restlessness; difficulty concentrating or sleeping; irritability; fatigue; muscle tension

BOTTOM LINE: If you have three or more symptoms for the required six months, the diagnosis may fit

—By Jeffrey Kluger

- There is a genetic component to anxiety; some people seem to be born worriers.
- Brain scans can reveal differences in the way patients who suffer from anxiety disorders respond to danger signals.
- Due to a shortcut in our brain's information-processing system, we can respond to threats before we become aware of them.
- The root of an anxiety disorder may not be the threat that triggers it but a breakdown in the mechanism that keeps the anxiety response from careening out of control.

Before we delve into the latest research, let's define a few terms. Though we all have our own intuitive sense of what the words stress and fear mean, scientists use these words in very specific ways. For them, stress is an external stimulus that signals danger, often by causing pain. Fear is the short-term response such stresses produce in men, women or lab rats. Anxiety has a lot of the same symptoms as fear, but it's a feeling that lingers long after the stress has lifted and the threat has passed.

In general, science has a hard time pinning down emotions because they are by nature so slippery and subjective. You can't

THE ANATOMY OF ANXIETY

WHAT TRIGGERS IT...

When the senses pick up a threat—a loud noise, a scary sight, a creepy feeling—the information takes two different routes through the brain

.... AND HOW THE BODY RESPONDS

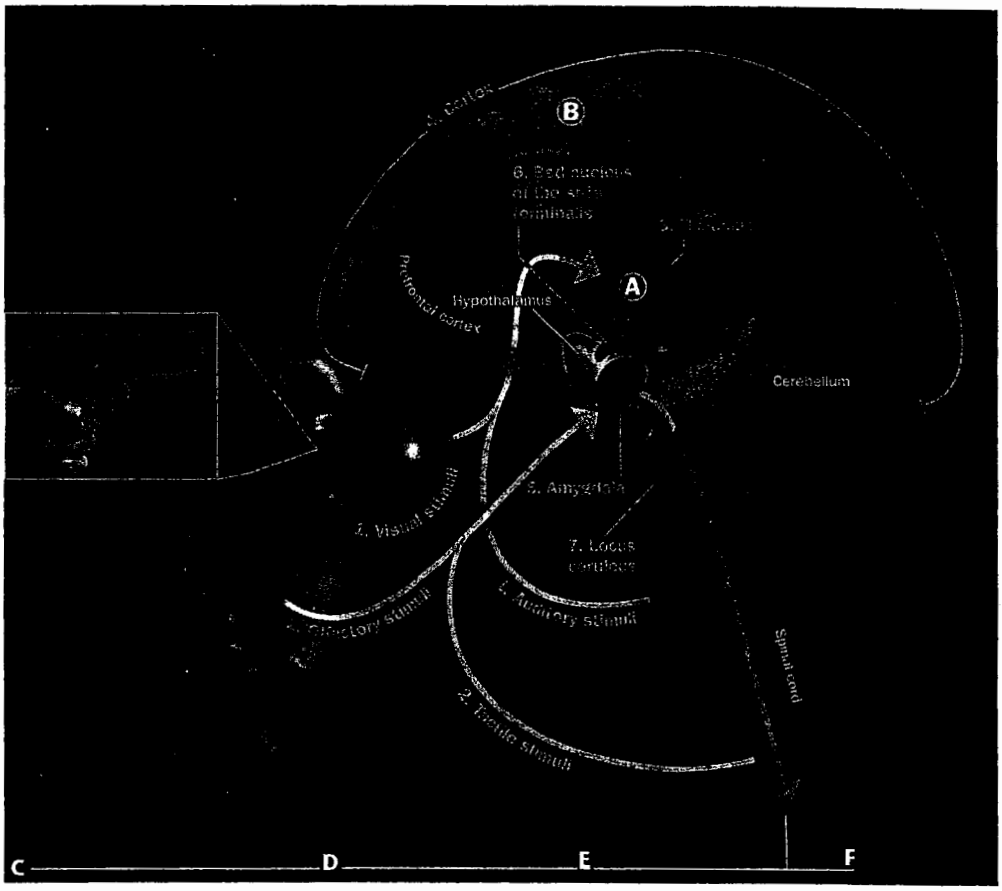
By putting the brain on alert, the amygdala triggers a series of changes in brain chemicals and hormones that puts the entire body in anxiety mode

A THE SHORTCUT

When startled, the brain automatically engages an emergecy hot line to its fear center, the amygdala. Once activated, the amygdala sends the equivalent of an all-points bulletin that alerts other brain structures. The result is the classic fear response: sweaty palms, rapid heartbeat, increased blood pressure and a burst of adrenaline. All this happens before the mind is conscious of having smelled or touched anything. Before you know why you're afraid, you are

B THE HIGH ROAD

Only after the fear response is activated does the conscious mind kick into gear. Some sensory information, rather than traveling directly to the amygdala, takes a more circuitous route, stopping first at the thalamus—the processing hub for sensory cues—and then the cortex—the outer layer of brain cells. The cortex analyzes the raw data streaming in through the senses and decides whether they require a fear response. If they do, the cortex signals the amygdala, and the body stays on alert



C Stress-Hormone Boost

Responding to signals from the hypothalamus and pituitary gland, the adrenal glands pump out high levels of the stress hormone cortisol. Too much cortisol shortcircuits the cells in the hippocampus, making it difficult to organize the memory of a trauma or stressful experience. Memories lose their context and become fragmented

D Racing Heartbeat

The body's sympathetic nervous system, responsible for heart rate and breathing, shifts into overdrive. The heart beats faster, blood pressure rises and the lungs hyperventilate. sweat increases, and even the nerve endings on the skin tingle into action, creating goose bumps

E Fight, Flight or Fright

The senses become hyperalert, drinking in every detail of the surroundings and looking for potential new threats. Adrenaline shoots to the muscles, preparing the body to fight or flee

F Digestion shutdown

The brain stops thinking about things that bring pleasure, shifting its focus instead to identifying potential dangers. To ensure that no energy is wasted on digestion, the body will sometimes respond by emptying the digestive tract through involuntary vomiting, urination or defecation

(Continued on following page)

Source: Dennis S. Charney, M.D., National Institute of Mental Health. TIME Diagram by Joe Lertola. Text by Alice Park

THE ANATOMY OF ANXIETY

continued

1. Auditory and visual stimuli
Sights and sounds are processed first by the thalamus, which filters the incoming cues and shunts them either directly to the amygdala or to the appropriate parts of the cortex

2. Olfactory and tactile stimuli
Smells and touch sensations bypass the thalamus altogether, taking a shortcut directly to the amygdala. Smells, therefore, often evoke stronger memories or feelings than do sights or sounds

3. Thalamus
The hub for sights and sounds, the thalamus breaks down incoming visual cues by size, shape and color, and auditory cues by volume and dissonance, and then signals the appropriate parts of the cortex

4. Cortex
It gives raw sights and sounds meaning, enabling the brain to become conscious of what it is seeing or hearing. One region, the prefrontal cortex, may be vital to turning off the anxiety response once a threat has passed

5. Amygdala
The emotional core of the brain, the amygdala has the primary role of triggering the fear response. Information that passes through the amygdala is tagged with emotional significance

6. Bed nucleus of the stria terminalis
Unlike the amygdala, which sets off an immediate burst of fear, the BNST perpetuates the fear response, causing the longer-term unease typical of anxiety

7. Locus ceruleus
It receives signals from the amygdala and is responsible for initiating many of the classic anxiety responses: rapid heartbeat, increased blood pressure, sweating and pupil dilation

8. Hippocampus
This is the memory center, vital to storing the raw information coming in from the senses, along with the emotional baggage attached to the data during their trip through the amygdala

ask a rat if it's anxious or depressed. Even most people are as clueless about why they have certain feelings as they are about how their lungs work. But fear is the one aspect of anxiety that's easy to recognize. Rats freeze in place. Humans break out in a cold sweat. Heartbeats race, and blood pressure rises. That gives scientists something they can control and measure. "You can bring on a sensory stimulus that makes an animal—or human—fearful and study its effects," says Dr. Wayne Drevets of the National Institute of Mental Health (NIMH). "Then you can take the stimulus away and see how the animal calms down."

Indeed, a lot of what researchers have learned about the biology of anxiety comes from scaring rats and then cutting them open. Just as the Russian physiologist Ivan Pavlov showed 100 years ago that you could condition a dog to salivate at the sound of a bell, scientists today have taught rats to fear all kinds of things—from buzzers to lights—by giving them electrical shocks when they hear the buzzer or see the light. The animals quickly learn to fear the stimulus even in the absence of a shock. Then researchers destroy small portions of the rats' brains to see what effect that has on their reactions (an experiment that would be impossible to conduct in humans). By painstakingly matching the damaged areas with changes in behavior, scientists have, bit by bit, created a road map of fear as it travels through the rat's brain.

The journey begins when a rat (we'll get to humans later) feels the stress, in this case an electric shock. The rat's senses immediately send a message to the central portion of its brain, where the stimulus activates two neural pathways. One of these pathways is a relatively long, circuitous route through the cortex, where the brain does its most elaborate and accurate processing of information. The other route is a kind of emergency shortcut that quickly reaches an almond-shaped cluster of cells called the amygdala.

What's special about the amygdala is that it can quickly activate just about every system in the body to fight like the devil or run like crazy. It's not designed to be accurate, just fast. If you have ever gone hiking and been startled by a snake that turned out to be a stick, you can thank your amygdala. Joseph LeDoux, a neuroscientist at New York University, calls it "the hub in a wheel of fear."

But while the amygdala is busy telling the body what to do, it also fires up a nearby curved cluster of neurons called the hippocampus. (A 16th century anatomist named it after the Greek word for seahorse.) The job of the hippocampus is to help the brain learn and form new memories. And not just any memories. The hippocampus allows a rat to remember where it was when it got shocked and what was going on around it at the time. Such contextual learning helps the poor rodent avoid dangerous places in the future. It probably also helps it recognize what situations are likely to be relatively safe.

By this point, the other half of the stress signal has reached the cortex, which confirms that there's a danger present and figures out that it's causing pain. Once the shock has warn off, a part of the brain called the prefrontal cortex sends out an all-clear message and lets the amygdala know that it's O.K. to stand down. At least it's supposed to. It seems that it's harder to turn off a stress response than to turn it on. This makes sense, in terms of survival. After all, it's better to panic unnecessarily than to be too relaxed in the face of life-threatening danger.

Discovering this basic neural circuitry turned out to be a key breakthrough in understanding anxiety. It showed that the anx-

WHAT CAN YOU DO

There are as many ways to relieve anxiety as there are things that make us anxious. The key is to find the way that works for you—and use it

BEHAVIORAL THERAPY

When the brain sets anxiety alarms ringing, our first inclination is to find the off switch. Behavioral scientists take the opposite approach. They want you to get so accustomed to the noise that you don't hear it anymore. The standard behavioral treatment for such anxiety conditions as phobias, obsessive-compulsive disorder (OCD) and panic disorder is to expose patients to a tiny bit of the very thing that causes them anxiety, ratcheting up the exposure over a number of sessions until the brain habituates to the fear. A patient suffering from a blood phobia, for example, might first be shown a picture of a scalpel or syringe, then a real syringe, then a vial of blood and so on up the anxiety ladder until there are no more rungs to climb. There is a risk that if treatment is cut short (before the patient has become inured to the anxiety triggers), the anxious feelings could be exacerbated. But done right, behavioral therapy can bring relief from specific phobias in as little as two or three sessions. Social anxiety takes somewhat longer, and OCD may take a good deal longer still.

COGNITIVE THERAPY

Rather than expect patients to embrace anxiety, cognitive therapists encourage them to use the power of the mind to reason through it. First popularized in the 1980s, cognitive therapy teaches people who are anxious or depressed to reconfigure their view of the world and develop a more realistic perspective on the risks or obstacles they face. Patients suffering from social-anxiety disorder, for example, might see a group of people whispering at a party and assume the gossip is about them. A cognitive therapist would teach them to rethink that assumption. Some behavioral therapists question cognitive techniques, arguing—not without some justification—that a brain that was so receptive to reason wouldn't be all that anxious in the first place. Cognitive therapists dispute that idea, though some have begun incorporating behavior-modification techniques into their treatment.

ANTIDEPRESSANTS

When talk therapy doesn't work—or needs a boost—drugs can help, especially the class of antidepressants called selective serotonin reuptake inhibitors: Prozac is the best known of these drugs, which work by preventing the brain from reabsorbing too much of the neurotransmitter serotonin, leaving more in nerve synapses and thus helping to improve mood. Another SSRI, Paxil, was recently approved by the Food and Drug Administration specifically for the treatment of social-anxiety disorder, though the others seem to work as well. A third, Zoloft, has been approved for OCD and panic disorder. Each formulation of SSRI is subtly different—targeting specific subclasses of serotonin. And side effects—which can include dry mouth, fatigue and sexual dysfunction—will vary from person to person. A new group of antidepressants, known as serotonin-norepinephrine reuptake inhibitors, may be even more effective in treating anxiety disorders than the SSRIs are. As the name implies, SNRIs target a second neurotransmitter called norepinephrine, which is secreted by the adrenal fight-or-flight response—thus actually increasing anxiety symptoms in many situations. However, norepinephrine also helps control emotion and stabilize mood, and, properly manipulated along with serotonin, may be able to do just that for the anxious person.

MINOR TRANQUILIZERS

If the antidepressants have a flaw, it's that they sometimes don't start working for weeks—a lifetime for the acutely anxious. For this reason, many doctors recommend judicious doses of fast-acting relaxants such as the benzodiazepines Xanax, Valium or Klonopin to serve as a temporary bridge until the SSRIs have a chance to kick in. The downside of such drugs is that they can be highly addictive and may merely mask symptoms. For this reason, doctors will prescribe them very carefully and strictly limit refills.

EXERCISE

Before turning to drugs or talk therapy, many people prefer to try to bring their anxiety under control on their own. Unlike most emotional or physical conditions, anxiety disorders respond well to such self-medication—provided you know how to administer the treatment. One of the most effective techniques is simple exercise. It's no secret that a good workout or a brisk walk can take the edge off even the most acute anxiety. Scientists once believed the effect to be due to the release of natural opiates known as endorphins, but new research has called this into question. Regardless, working out regularly—most days of the week, if possible for at least 30 minutes or so—may well help recalibrate the anxious brain.

ALTERNATIVE TREATMENTS

One of the most popular self-treatments is yoga, which is both a form of exercise and a way to quiet the mind by focusing attention on breathing. Indeed, even without yoga, breathing exercises can help quell an anxiety episode, if only by slowing a racing heart and lengthening the short, shallow breaths of a panic attack. Many anxiety sufferers have relief through meditation or massage—even just a 10-min. foot treatment. For those willing to travel a little farther from the mainstream there's aromatherapy (enthusiasts recommend rose and lavender scents), guided imager (a form of directed meditation used with some success by people recovering from cancer and open-heart surgery) and acupuncture.

LIFESTYLE CHANGES

If all else fails, go back to basics and try cleaning up your lifestyle. For starters, you can cut back or eliminate the use of sugar, caffeine, nicotine, alcohol and any recreational drugs you may be taking. Are you eating right and getting enough sleep and leisure time? Finally, if your job or the place you live is making you anxious, you might consider moving to a less stressful environment or finding a different line of work.

—By Jeffrey Kluger. With reporting by Sora Song/New York

iety response isn't necessarily caused by an external threat; rather, it may be traced to a breakdown in the mechanism that signals the brain to stop responding. Just as a car can go out of control due to either a stuck accelerator or failed brakes, it's not always clear which part of the brain is at fault. It may turn out that some anxiety disorders are caused by an overactive amygdala (the accelerator) while others are caused by an underactive prefrontal cortex (call it the brake).

It may also be that an entirely different part of the brain holds the key to understanding anxiety. Michael Davis, a behavioral neuroscientist at Emory University in Atlanta, has spent six years studying a pea-size knot of neurons located near the amygdala with an impossible name: the bed nucleus of the stria terminalis, or BNST. Rats whose BNST has been injected with stress hormones are much jumpier than those that have got a shot in their amygdala. Could the BNST be at the root of all anxiety disorders? The clues are intriguing, but as scientists are so fond of saying, more research is needed.

Of course, what you would really like to know is whether any of the work done in rats applies to humans. Clearly researchers can't go around performing brain surgery on the amygdalas of living patients to see if it affects their anxiety levels. But the fascinating case of a woman known only by her research number, SM046, suggests that when it comes to fear, rodents and hominids really aren't so different.

Owing to an unusual brain disorder, SM046 has a defective amygdala. As a result, her behavior is abnormal in a very particular way. When scientists at the University of Iowa show SM046 pictures of a series of faces, she has no trouble picking out those that are happy, sad or angry. But if the face is displaying fear, she cannot recognize the feeling. She identifies it as a face expressing some intense emotion, but that is all. Her unusual condition strongly suggests that even in *Homo sapiens*, fear takes hold in the amygdala.

But studying brain-damaged patients can teach scientists only so much. They would also like to know how anxiety works in normal, intact brains. For this, brain scans have proved invaluable.

For years, doctors have used CAT scans and MRIs to help them diagnose strokes, brain tumors and other neurological conditions. But as the technology has become more sophisticated, researchers have started to employ it to tease out some of the subtle changes associated with mental illness. "We're not yet able to use these scans in a diagnostic way," says Dr. David Silbersweig of the Weill Cornell Medical College in New York City. "But we're getting pretty specific about the areas of the brain that are implicated in a number of psychiatric disorders."

One type of brain scan helps identify structures that are the wrong size or shape. Two years ago, researchers at the University of Pittsburgh showed that the amygdalas of a group of overanxious young children were, on average, much larger than those of their unaffected peers. Perhaps they just had more fear circuits to contend with? Neuroscientists are tempted to say yes, but they admit the conclusion is pretty speculative. Another group of researchers found that patients with post-traumatic stress disorder had a smaller hippocampus than normal. Perhaps their stressful experiences had somehow interfered with the hippocampus' ability to make new memories and, just as important, forget the old ones? Again, no one knows for sure.

Another type of brain scan tells scientists which brain cells are using the most oxygen or soaking up the most nutrients. The idea, explains Dr. Scott Rauch of Massachusetts General Hospital, is that any area that seems more active than usual while someone is anxious may play an important role in making the person that way. Rauch's team has spent the past eight years scanning groups of combat veterans, some with post-traumatic stress disorder and some without, to see which areas of the brain light up when they hear tapes recounting their most troubling memories. So far, the signals in the amygdala appear to be more active in those with PTSD than in those without. In addition, signals to the prefrontal cortex of PTSD subjects seem to be weaker than in those without the disorder. Perhaps this explains why the patients still feel threatened even when they are perfectly safe.

The next step, Rauch says, is to scan groups of people who are likely to be thrust into dangerous situations—fire fighters, say, or police officers. Then it may be possible to determine if any changes in their brains are the result of traumatic situations or if the changes predate them. Either is plausible. The stress of surviving a building collapse, for example, could turn a normal amygdala into an overactive one. Or an already overactive amygdala may overwhelm the brain in the wake of a disaster.

Eventually, researchers would like to learn what role our genes, as opposed to our environment, play in the development of anxiety. "It has been known for some time that these disorders run in families," says Kenneth Kendler, a psychiatric geneticist at Virginia Commonwealth University in Richmond, Va. "So the next logical question is the nature-nurture issue." In other words, are anxious people born that way, or do they become anxious as a result of their life experiences?

Kendler and his colleagues approached the question by studying groups of identical twins, who share virtually all their genes, and fraternal twins, who, like any other siblings, share only some of them. What Kendler's group found was that both identical twins were somewhat more likely than both fraternal twins to suffer from generalized anxiety disorder, phobias or panic attacks. (The researchers have not yet studied twins with post-traumatic stress disorder or obsessive-compulsive disorder.)

The correlation isn't 100%, however. "Most of the heritability is in the range of 30% to 40%," Kendler says. That's a fairly moderate genetic impact, he notes, akin to the chances that you will have the same cholesterol count as your parents. "Your genes set your general vulnerability," he concludes. "You can be a low-vulnerable, intermediate-vulnerable or a high-vulnerable person." But your upbringing and your experiences still have a major role to play. Someone with a low genetic vulnerability, for example, could easily develop a fear of flying after surviving a horrific plane crash.

There is plenty to learn about how anxiety and fear shape the brain. One of the biggest mysteries is the relationship between anxiety and depression. Researchers know that adults who suffer from depression were often very anxious as children. (It's also true that many kids outgrow their anxiety disorders to become perfectly well-adjusted adults.) Is that just a coincidence,

as many believe, or does anxiety somehow prime the brain to become depressed later in life? Brain scans show that the amygdala is very active in depressed patients, even when they are sleeping. Studies of twins suggest that many of the same genes could be involved. "There's a lot of overlap," says Dr. Dennis Charney, chief of the research program for mood and anxiety disorders at the NIMH. "Anxiety and depression have a similar underlying biology, and the genetics may be such that anxiety surfaces early in life and depression later on." Still, no one can say for sure.

Certainly antidepressants, like the serotonin reuptake inhibitors (Prozac and others) have proved very helpful in treating anxiety; some doctors think they are even more effective against anxiety than they are against depression. Although no one knows exactly why these antidepressants work, one important clue is that their effects don't show up until after a few weeks of treatment. The pathways for toning down anxiety are apparently much more resistant than those for ratcheting it up.

It's a mistake, however, to think that pills alone can soothe your neurochemistry. Remember the cortex? That's where you would expect psychotherapy to work, increasing the repertoire of calming messages that can be passed along to the amygdala. Certain desensitization techniques can also help the brain learn, through the hippocampus, to be less reactive. Of course, you have to do it right. Reliving a trauma too soon after it happened could also make the memory harder to erase.

There are no guidebooks to tell you when it's safe to venture out again. In many ways, the whole country last September was made part of an unwitting experiment in mass anxiety. Our brains are even now in the process of rewiring themselves. How successfully we navigate this delicate transition will depend a lot on our genes, our environment and any future attacks.

—Reported by Alice Park/Bethesda, Leslie Whitaker/Chicago and Dan Cray/Los Angeles

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