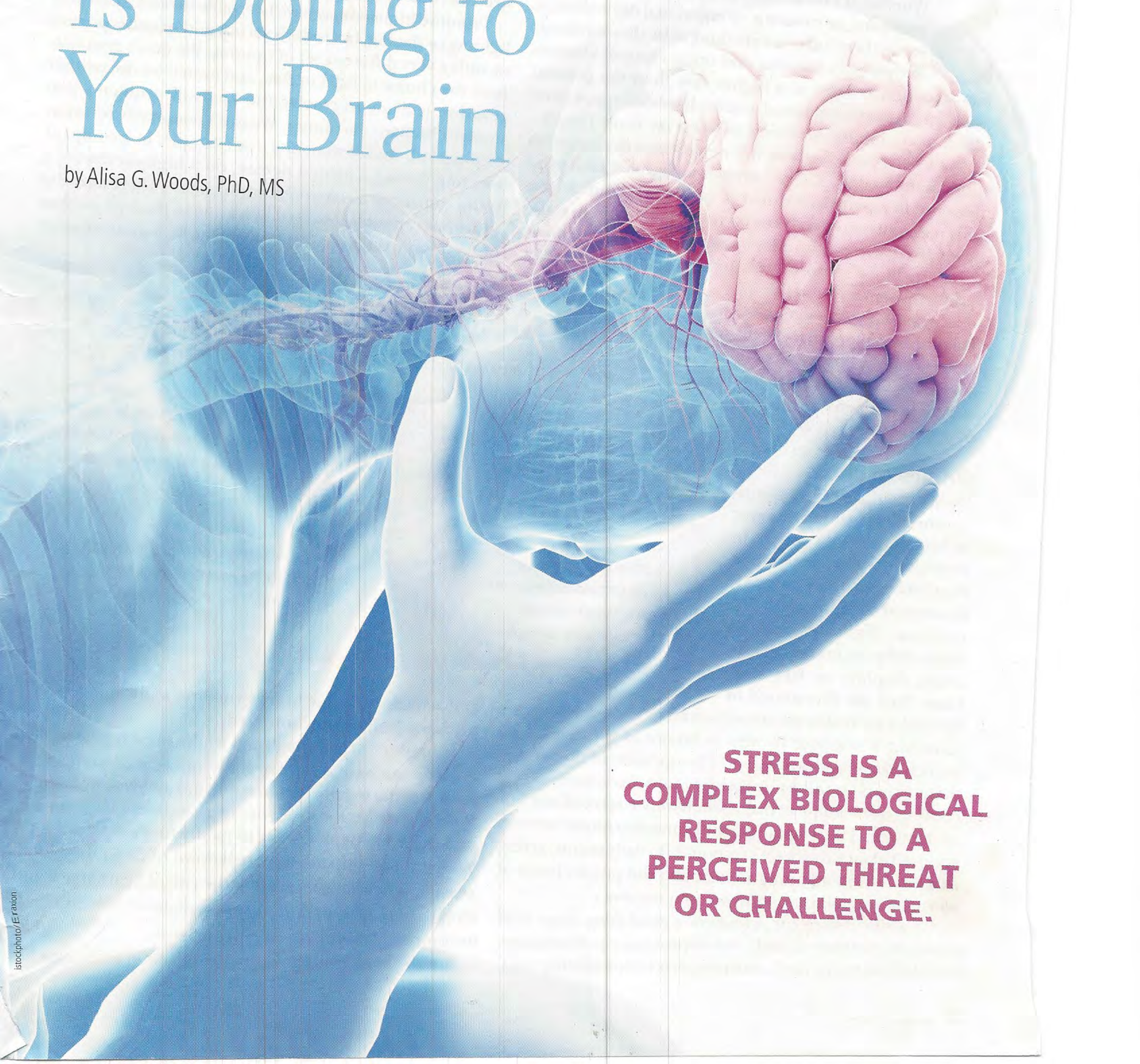
What STRESS Is Doing to Your Brain

by Alisa G. Woods, PhD, MS



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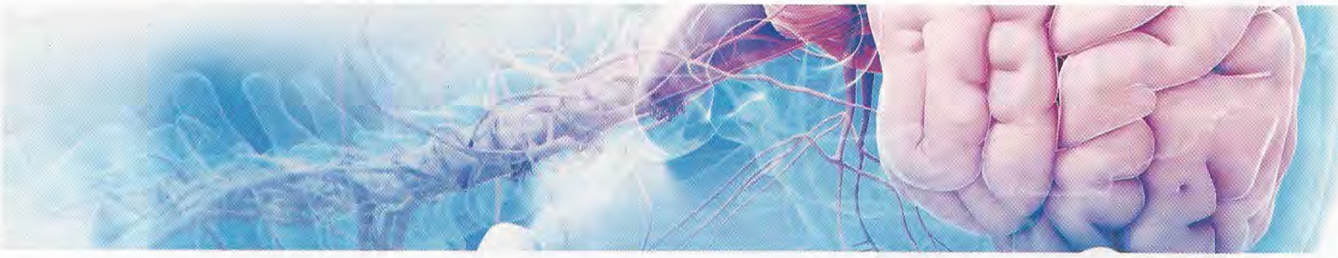
STRESS IS A COMPLEX BIOLOGICAL RESPONSE TO A PERCEIVED THREAT OR CHALLENGE.



Stress, it seems, is an unavoidable part of modern life. Whether it's on account of a job, family, economic pressures, or romantic or emotional difficulties, it seems there's always something to be stressed about. People with diabetes and other chronic illnesses may experience stress at a higher rate than the general population; managing blood glucose levels, diet, and exercise can be a significant source of worry for many people.

But what exactly is stress? It is not just an emotion or an unpleasant feeling. Rather, stress is a complex biological response to a perceived threat or challenge. Studies have shown that stress not only results from, but may help cause or worsen diabetes: Chronic elevated stress has been shown to elevate blood glucose levels and has been implicated in insulin resistance, a chief characteristic of Type 2 diabetes. This article explores the effects of stress on one important part of your body—your brain—and examines ways to reduce its negative impact.

Origins of stress

Human beings evolved in environments in which danger lurked around every corner. In response to this environment, humans and other animals developed a "fight or flight" response. Typically, animals either fight (or make a threatening display) or run away when they are threatened in the wild. Our brains are actually wired to act in this context, activating a response by what is known as the *sympathetic* branch of the nervous system. The opposite of the sympathetic branch is the *parasympathetic* nervous system, which controls our bodies normally, when we are relaxed and not under stress. The sympathetic and parasympathetic nervous systems balance the body's responses to daily events, acting as a kind of yin and yang to maintain the proper levels of alertness and relaxation throughout the day.

A little bit of stress can actually be a good thing, since mild stress can motivate us and even improve our performance in certain activities, such as team sports or completing tasks by a deadline. Low levels of stress may even enhance our ability to remember. Problems can arise, however, when stress becomes chronic, constant, and inescapable.

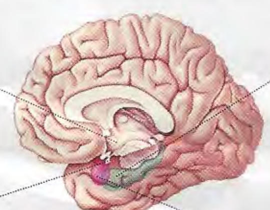
Primitive humans may have been able to react to stress by fighting or fleeing, but today's society and stressors present us with a very different set of options. We don't generally have the choice to fight or flee, and even if we do, neither reaction is likely to resolve the kinds of problems that modern humans encounter. We can't reasonably run away or physically attack someone, for example, in a company meeting during a heated debate, on a highway during a traffic jam, or in a classroom during a test. These stressful situations cannot be resolved by leaving or through displays of aggression, yet they provoke the same biological response and activate the same brain structures as the dangers that primitive humans encountered.

So most of us just sit still and let the stress build up. This buildup can have several negative physical consequences, such as reducing the immune system's ability to fight infections, increasing the incidence of gastrointestinal problems, and heightening sensitivity to pain. Stress can raise blood pressure and impede the breakdown of fat in the bloodstream, potentially increasing the risk of heart attack and stroke. And, of course, it can make diabetes more difficult to control by raising blood glucose levels.

But the most troubling physical effects of stress may be

BRAIN STRUCTURES

Brain structures involved in the stress response include the following:



those that occur in the brain. To best understand how chronic stress affects the brain, we first need to look at the brain structures and hormones involved in a typical stress response.

The stress response

The areas of the brain active in the stress response are part of a biological system called the *hypothalamic-pituitary-adrenal axis,* or the HPA axis for short. Information regarding danger is channeled to an area of the brain known as the *hypothalamus,* which sits just forward of the center of the brain, beneath the wrinkled cerebral cortex that covers the top of the organ. The hypothalamus processes all types of sensory information, including stressful things that one sees, hears, tastes, feels, smells, or experiences in any way. The hypothalamus then emits a hormone called CRH (*corticotropin releasing hormone*), which activates the *pituitary gland,* a small structure that dangles off the bottom of the brain.

CHRONIC STRESS HAS BEEN SHOWN TO ELEVATE BLOOD GLUCOSE LEVELS AND HAS BEEN IMPLICATED IN INSULIN RESISTANCE.

The pituitary gland is a "master" hormonal gland, controlling the production of hormones in many different areas of the body. In a typical stress response, it sends a signal through the blood using a hormone called ACTH (*adrenocorticotropic hormone*). ACTH tells the *adrenal glands,* located near the kidneys, to produce adrenaline and cortisol. These two hormones ready the body for flight or flight. They do this by shutting down many bodily systems, such as the immune and digestive systems, so that the body's energy can instead be used entirely for the task at hand. These hormones also increase blood pressure and heart rate, as well as the release of glucose from the liver, to give the body energy. While this response may be a fine short-term strategy, chronic stress wreaks long-term havoc on the body, damaging tissues and increasing the incidence of disease and disorders.

Chronic stress and the brain

To understand the effects of chronic stress on the brain, we'll need to examine two more structures within this complex organ, known as the *amygdala* and the *hippocampus.* The amygdala is a pea-shaped structure near the front of the brain, and the hippocampus, which is curved like the seahorse from which it gets its name, is located behind it. These two interconnected structures are essential to processing the stress response. The amygdala is activated during fear and anger and has long been understood as an essential brain area for these emotional responses. It is now understood, however, that the amygdala may play a wider role in letting people know what is important in their environment, beyond just the extremes of anger and fear.

The hippocampus has long been understood as an important memory center of the brain, critical for converting short-term to long-term memory and for processing certain types of memories, such as where objects are located in space. More recent discoveries show that the hippocampus is also heavily involved in processing emotions. In fact, signals from the hippocampus are critical for shutting down the stress response after it is no longer needed.

There is evidence that chronic stress may damage the hippocampus, impairing its ability to help shut down the stress response. Cells in the hippocampus have what are known as *receptors* for cortisol released during the stress response. Receptors are biochemical "locks" on the surface of a cell that molecules, such as cortisol, can bind to. When cortisol binds to the surface of a neuron in the hippocampus, this sets off a biological response within the cell that has many effects, including letting more calcium into the cell. At normal levels of stress this is fine, but excessive cortisol overactivates the receptors, letting in too much calcium and harming the cells. As evidence of the potentially lethal effects of cortisol, when rats are given high doses of the hormone, cells in the hippocampus seem to die.

Because the hippocampus plays a role in shutting down the stress response, any damage to this structure may have the effect of prolonging or intensifying the stress response, which can in turn cause even more damage. The amygdala, by contrast, plays a role in supporting and maintaining the stress response. If the hippocampus becomes damaged and less active as a result of excess cortisol over time, the amygdala may become even more active. In fact, neuroimaging studies have shown that people with major depressive disorder and anxiety disorders often have a hippocampus that has shrunken in size and an amygdala that is larger than normal. While these effects may be seen over time as a result of excessive stress, having a small hippocampus or a large amygdala to begin with may predispose individuals to depression and anxiety.

Healing the hippocampus

Research has shown that cortisol-related damage to the hippocampus may be reversible. In one study, researchers at the University of California, San Francisco, looked at the hippocampi of 241 Gulf War veterans. Eight-two of the veterans had experienced, or were currently experiencing, chronic post-traumatic stress disorder (PTSD), which is considered a type of anxiety disorder. The researchers used magnetic resonance imaging (MRI) to scan the brains of all participants. The 41 veterans with current PTSD had, on average, smaller hippocampi. The good news was that this effect seemed to be reversible: The 41 veterans who had recovered from PTSD had hippocampi the same size, on average, as the 159 veterans who had never had PTSD. Other studies have shown that longer duration and greater severity of PTSD is related to the reduction of the size of the hippocampus, and that certain drugs such as antidepressants seem able to help reverse hippocampal shrinkage.

While scientists once believed that brain cells could not divide and reproduce in the adult brain, it is now understood that several brain regions, including the hippocampus, have the capability to generate new cells. Exercise and antidepressants have been shown to promote new hippocampal cell growth, and it's possible that other treatments for depression may have this effect as well. Any activity that reduces stress and increases relaxation could, in fact, counteract hippocampal cell loss and possibly promote new cell generation. A molecule known as BDNF (*brain-derived neurotrophic factor*), whose levels are increased by both exercise and antidepressants, may be one reason for this effect. Taking *opioids*—drugs related to those derived from the opium poppy, which include morphine and heroin as well as many prescription painkillers—may contribute to cell death in the hippocampus and lead to higher levels of stress, anxiety, and depression.

Other brain areas

In addition to shrinking the hippocampus, stress can affect other areas of the brain. The *prefrontal cortex*, located in the front of the head, is important for planning, logic, and higher mental functions. Chronic stress, as well as sleep loss, can lead to changes in the branches of brain cells, which are known as *dendrites*, located in this region. The small parts of these dendrites, called *spines*, can actually be lost as a result of stress. This may lead to less flexibility in one's ability to think and reason.

Stress can compromise the normal function of the blood–brain barrier. When working properly, the blood–brain barrier acts as a filter that prevents certain substances, such as toxins and large molecules, from entering the brain from the bloodstream. Stress may lead to a breakdown in this function, with molecules not normally allowed to penetrate the brain entering as a result. This gives us one more reason to monitor and regulate stress levels.

Not only are these tips good for your general physical and mental health, but they may also help prevent the reduction in hippocampal size that occurs with normal aging. Because the hippocampus is understood to process information about memories and to help regulate emotions, maintaining hippocampal health can help you preserve your memory and may help prevent emotional problems like depression and anxiety. Fortunately, the hippocampus is a changing but also resilient brain area, so promoting its health is something nearly all of us can do.

Reducing stress in your life can have wide-ranging positive effects, from lowering blood glucose levels to promoting cardiovascular health. Experiencing some stress is, of course, inevitable. But there is always something, and probably many things, you can do to make your life less stressful. If you need a motivation boost to make these changes, remember the lasting positive impact that stress reduction can have on your brain. And when a stressful situation arises, you can tell yourself that "it's all in your head," because now you know it's true. □

PROTECTING YOUR BRAIN

If you're interested in achieving better brain health, many relaxation techniques can be helpful. Here are some examples of activities and techniques that may help keep stress in check:

- Meditation
- Tai chi
- Prayer
- Biofeedback (using feedback on physical functions—such as brainwaves, heart rate, or muscle activity—to help change these functions)
- Guided imagery (mentally following a series of images described by a practitioner or recorded program)
- Psychotherapy (therapeutic interaction with a mental-health professional)
- Massage
- Labyrinth-walking
- Mindfulness
- Yoga
- Deep-breathing exercises

Other tips for better brain health include the following:

- Engage in mental exercise on a regular basis (chess, reading, discussion groups, etc.)
- Follow a healthy diet (reduce saturated fats and increase omega-3 fatty acids)
- Consume alcohol in moderation
- Get enough sleep
- Drink enough water
- Exercise at least 30 minutes a day

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