

Brain Facts

STRESS

THE ABILITY TO REACT in response to threatening events has been with us since the time of our ancient ancestors. In response to impending danger, muscles are primed, attention is focused, and nerves are readied for action — “fight or flight.” In today’s complex and fast-paced world, stressors are more consistently psychological or socially based, and we face them with less reprieve. The continued stimulation of the systems that respond to threat or danger may contribute to heart disease, obesity, arthritis, and depression, as well as accelerating the aging process.

Nearly two-thirds of ailments seen in doctors’ offices are adversely affected by stress; indeed, stress can both cause diseases and exacerbate existing ones. Surveys indicate that 60 percent of Americans feel they are under a great deal of stress at least once a week. Costs due to stress from absenteeism, medical expenses, and lost productivity are estimated at \$300 billion annually.

Stress is difficult to define because its effects vary with each individual. Specialists now define stress as any external stimulus that threatens homeostasis — the normal equilibrium of body function. Stress also can be induced by the belief that homeostasis might soon be disrupted. Among the most powerful stressors are psychological and psychosocial stressors that exist between members of the same species. Lack or loss of control is a particularly important feature of severe psychological stress that can have physiological consequences. Most harmful are the chronic aspects of stress.

During the past several decades, researchers have found that stress both helps and harms the body. When confronted with a crucial physical challenge, properly controlled stress responses can provide the extra strength and energy needed to cope. Moreover, the acute physiological response to stress protects the body and brain and helps to re-establish or maintain homeostasis. But stress that continues for prolonged periods can repeatedly elevate physiological stress responses or fail to shut them off when they are not needed. When this occurs, the same physiological mechanisms can badly upset the body’s biochemical balance and accelerate disease.

Scientists also believe that the individual variation in responding to stress is somewhat dependent on a person’s perception of external events. This perception ultimately shapes his or her internal physiological response. Thus, by controlling your perception of events, you can do much to avoid the harmful consequences of the sorts of mild to moderate stressors that typically afflict modern humans.

The immediate response

A stressful situation activates three major communication systems in the brain that regulate bodily functions. Scientists have come to understand these complex systems through experiments primarily with rats, mice, and nonhuman primates, such as monkeys. Scientists then verified the action of these systems in humans.

The first of these systems is the *voluntary nervous system*, which sends messages to muscles so that we may respond to sensory information. For example, the sight of a shark in the water may prompt you to run from the beach as quickly as possible.

The second communication system is the *autonomic nervous system*. It combines the *sympathetic* branch and the *parasympathetic* branch. The sympathetic nervous system gets us going in emergencies, while the parasympathetic nervous system keeps the body’s maintenance systems, such as digestion, in order and calms the body’s responses to the emergency branch.

Each of these systems has a specific task. The sympathetic branch causes arteries supplying blood to the muscles to relax in order to deliver more blood, allowing greater capacity to act. At the same time, blood flow to the skin, kidneys, and digestive tract is reduced, and supply to the muscles increases. In contrast, the parasympathetic branch helps to regulate bodily functions and soothe the body once the stressor has passed, preventing the body from remaining too long in a state of mobilization. If these functions are left mobilized and unchecked, disease can develop. Some actions of the calming branch appear to reduce the harmful effects of the emergency branch’s response to stress.

The brain’s third major communication process is the *neuroendocrine system*, which also maintains the body’s internal functioning. Various stress hormones travel through the blood and stimulate the release of other hormones, which affect bodily processes such as metabolic rate and sexual function.

The major stress hormones are *epinephrine* (also known as adrenaline) and *cortisol*. When the body is exposed to stressors, epinephrine, which combines elements of hormones and neurotransmitters, is quickly released into the bloodstream to put the body into a general state of arousal and enable it to cope with a challenge.

The adrenal glands secrete *glucocorticoids*, which are hormones that produce an array of effects in response to stress. These include mobilizing energy into the bloodstream from storage sites in the body, increasing cardiovascular tone, and delaying long-term processes in the body that are not essential during a crisis, such as

feeding, digestion, growth, and reproduction. In primates, the main glucocorticoid is cortisol (hydrocortisone), whereas in rodents, it is corticosterone. Some of the actions of glucocorticoids help to mediate the stress response, while some of the other, slower actions counteract the primary response to stress and help re-establish homeostasis. Over the short run, epinephrine mobilizes energy and delivers it to muscles for the body's response. Cortisol promotes energy replenishment and efficient cardiovascular function.

Glucocorticoids also affect food intake during the sleep-wake cycle. Cortisol levels, which vary naturally over a 24-hour period, peak in the body in the early-morning hours just before waking. This hormone acts as a wake-up signal and helps turn on appetite and physical activity. This effect of glucocorticoids may help to explain disorders such as jet lag, which results when the light-dark cycle is altered by travel over long distances, causing the body's biological clock to reset itself more slowly. Until that clock is reset, cortisol secretion and hunger, as well as sleepiness and wakefulness, occur at inappropriate times of day in the new location.

Acute stress also enhances memory of threatening situations and events, increases activity of the immune system, and helps protect the body from pathogens. Cortisol and epinephrine facilitate the movement of immune cells from the bloodstream and storage organs such as the spleen into tissue where they are needed to defend against infection.

Glucocorticoids do more than help the body respond to stress. In fact, they are an integral part of daily life and the adaptation to environmental change. The adrenal glands help protect us from stress and are essential for survival.

Chronic stress

When glucocorticoids or epinephrine are secreted in response to the prolonged psychological stress commonly encountered by modern humans, the results are not ideal. Normally, bodily systems gear up under stress and release hormones to improve memory, increase immune function, enhance muscular activity, and restore homeostasis. If you are not fighting or fleeing but standing frustrated in a supermarket checkout line or sitting in a traffic jam, you are not engaging in muscular exercise. Yet these systems continue to be stimulated, and when they are stimulated chronically, the consequences are different: Memory is impaired, immune function is suppressed, and energy is stored as fat.

Overexposure to cortisol also can lead to weakened muscles and can chip away at the mechanisms that keep our body systems in a healthy balance. Elevated epinephrine release increases blood pressure. Together, elevated cortisol and epinephrine can contribute to chronic hypertension (high blood pressure), abdominal obesity,

and atherosclerosis (hardening of the arteries). Epinephrine also increases the activity of body chemicals that contribute to inflammation, and these chemicals add to the burden of chronic stress, potentially leading to arthritis and possibly aging of the brain.

Stress also can contribute to sleep loss. Elevated levels of glucocorticoids can delay the onset of sleep, and sleep deprivation raises glucocorticoid levels, setting off a vicious cycle.

Scientists have identified a variety of stress-related disorders, including colitis, high blood pressure, clogged arteries, impotency and loss of sex drive in males, irregular menstrual cycles in females, and adult-onset diabetes. Aging rats show impairment of neuronal function in the hippocampus — an area of the brain important for learning, memory, and emotion — as a result of glucocorticoid secretion throughout their lifetimes.

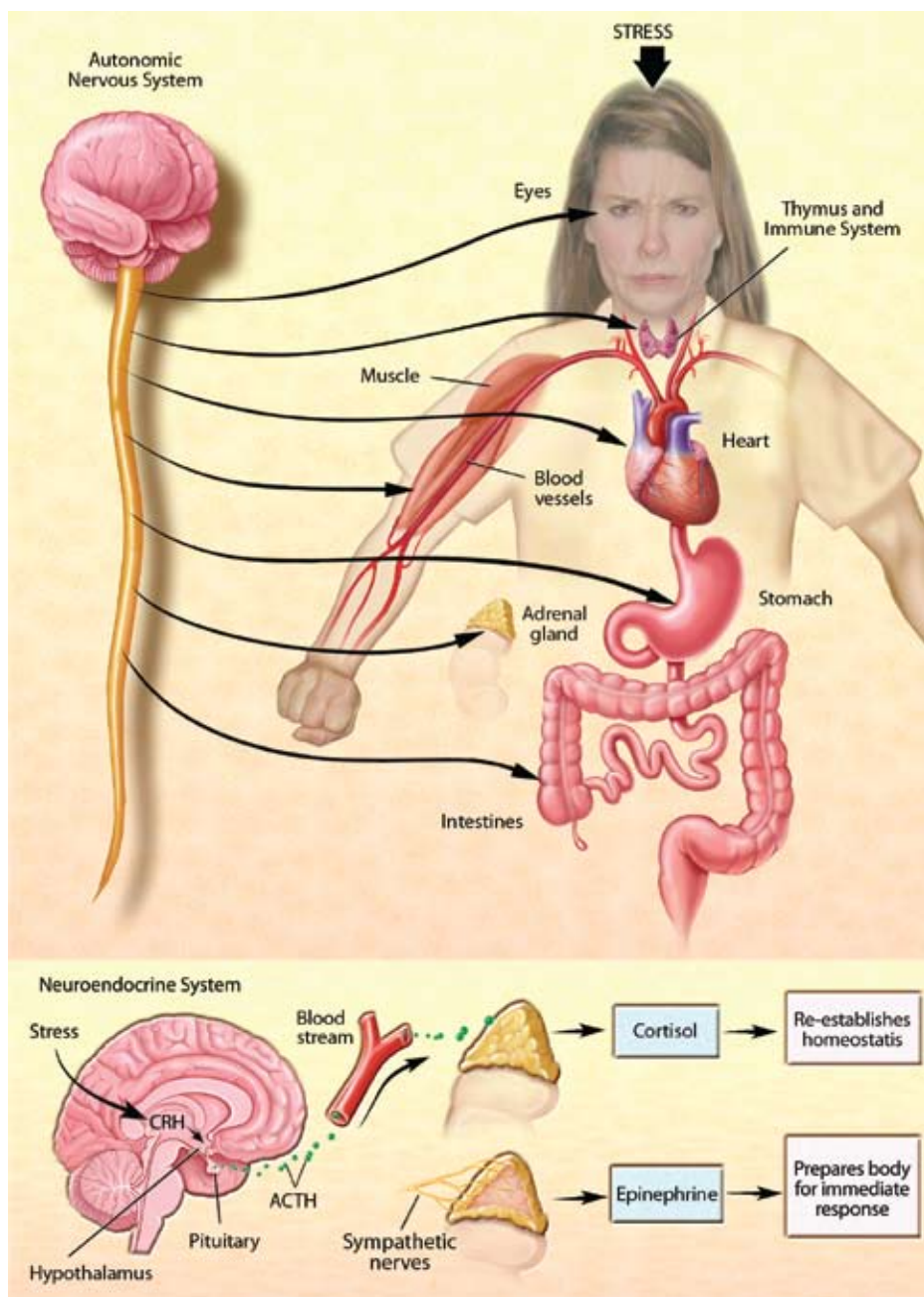
Overexposure to glucocorticoids also increases the number of neurons damaged by stroke. Moreover, prolonged exposure before or immediately after birth can cause a decrease in the normal number of brain neurons and smaller brain size.

The *immune system*, which receives messages from the nervous system, also is sensitive to many of the circulating hormones of the body, including stress hormones. Although acute elevations of stress hormones actually facilitate immune function, sustained exposure to moderate to high levels of glucocorticoids acts to suppress immune function.

While acute, stress-induced immunoenhancement can be protective against disease pathogens, glucocorticoid-induced immunosuppression also can be beneficial. Normally, the glucocorticoids help reverse the immunoenhancement brought about by stress. Without this reversal, there is an increased chance of diseases of overactive immunity and inflammation, such as *autoimmune disorders*, which occur when the body's immune defenses turn against body tissue. Synthetic glucocorticoids like hydrocortisone and prednisone suppress the immune system and therefore are used often to treat autoimmune and inflammatory diseases.

One important determinant of resistance or susceptibility to disease may be a person's sense of control as opposed to a feeling of helplessness. This phenomenon may help explain large individual variations in response to disease. Scientists are trying to identify how the perception of control or helplessness influences physiological responses to stress, including the regulation of immune function.

The cardiovascular system receives many messages from the autonomic nervous system, and stressful experiences have an immediate and direct effect on heart rate and blood pressure. In the short run, these changes help in response to stressors. But when stressors are chronic and psychological, the effect can be harmful and result in accelerated atherosclerosis and increased risk for heart attack.



THE STRESS REACTION. When stress occurs, the sympathetic nervous system is triggered. Norepinephrine is released by nerves, and epinephrine is secreted by the adrenal glands. By activating receptors in blood vessels and other structures, these substances ready the heart and working muscles for action. Acetylcholine is released in the parasympathetic nervous system, producing calming effects. The digestive tract is stimulated to digest a meal, the heart rate slows, and the pupils of the eyes become smaller. The neuroendocrine system also maintains the body's normal internal functioning. Corticotrophin-releasing hormone (CRH), a peptide formed by chains of amino acids, is released from the hypothalamus, a collection of cells at the base of the brain that acts as a control center for the neuroendocrine system. CRH travels to the pituitary gland, where it triggers the release of adrenocorticotropic hormone (ACTH). ACTH travels in the blood to the adrenal glands, where it stimulates the release of cortisol.

Research supports the idea that people holding jobs that carry high demands and low control, such as telephone operators, waiters, and cashiers, have higher rates of heart disease than people who can dictate the pace and style of their working lives.

Behavioral type affects a person's susceptibility to heart attack. People at greatest risk are hostile, irritated by trivial things, and exhibit signs of struggle against time and other challenges. Researchers found that two groups of men — one with high hostility scores and the other with low hostility scores — exhibited similar increases in blood pressure and muscle blood flow when performing a lab test. This

finding confirmed that hostility scores do not predict the biological response to simple mental tasks.

Then the researchers added harassment to the test by leading the subjects to believe that their performances were being unfairly criticized. Men with high hostility scores showed much larger increases in muscle blood flow and blood pressure and showed slower recovery than those with low hostility scores. Scientists found that harassed men with high hostility scores had larger increases in levels of stress hormones. Thus, if you have personality traits of hostility, learning to reduce or avoid anger could be important to avoid cardiovascular damage.