Unraveling the Stress Within
“Hurry up!” snaps Pam Bosch.

I’m sitting in front of a computer trying to multiply 67 by 4 in my head before the screen changes and a new problem pops up. “Faster! Before it beeps!” chimes in Tinna Traustadottir, making me forget whether I’m carrying a 2 or a 3. I can feel my muscles tense up. My heart is pounding. I stifle the urge to scream “Shut up!” at the two thugs—as I’ve come to see them—distracting me from the problem at hand. Bosch and Traustadottir are not really thugs, although they play the role in their laboratory. They are Arizona State University doctoral students working in the Neuroendocrinology Lab. They study the effects of stress on the body. In order to better study stress, the researchers first have to create it. And I’m learning just how good they are at the job.

The timed math problems are part of the Matt Stress Response Protocol (MSRP). The MSRP was designed by Kathy Matt, an ASU professor of neuroendocrinology and director of the ASU Stress Center. Subjects using the MSRP undergo a variety of activities designed to produce a physiological stress response—that "adrenaline rush" we all know and hate. It’s hard to believe that the pleasant, cheerful Matt spends her time devising ways to make your heart race and your palms sweat. But her intentions are all good; she studies stress in order to help us understand its role in disease development. “One of the things we have been trying to do is look at how stress response differs among individuals. We want to know how stress is affected by age, gender, ethnicity, socioeconomic status, and fitness,” Matt explains.
STRESS AFFECTS THE BODY IMMEDIATELY, AS SHOWN IN PLAIN TEXT. SOME EFFECTS APPEAR LATER OR AS A RESULT OF CHRONIC STRESS. CHRONIC STRESS EFFECTS ARE SHOWN IN ITALIC

INCREASED APPETITE FOR SWEET AND SALTY FOODS

HIGH-CALORIE FOOD INTAKE LEADS TO WEIGHT GAIN AND ABDOMINAL OBESITY

ENERGY DIVERTED FROM DIGESTIVE SYSTEM

MUSCLE CONTRACTIONS THAT MOVE FOOD ALONG THE GUT SLOW DOWN

ULCERS, IRRITABLE BOWEL SYNDROME AND OTHER DIGESTIVE DISORDERS

ENERGY DIVERTED FROM REPRODUCTIVE SYSTEM

FERTILITY PROBLEMS

HEART INCREASES OUTPUT, RAPID HEARTBEAT, RISE IN BLOOD PRESSURE

HEART DISEASE

DIABETES

ELEVATED BLOOD SUGAR (FREED UP BY CORTISOL FOR QUICK FUEL)

INFLAMMATION INHIBITED TO DELAY SWELLING AROUND INJURIES UNTIL DANGER HAS PASSED

DECREASED IMMUNE FUNCTION LEADS TO SUSCEPTIBILITY TO ILLNESS AND DISEASE

DRY MOUTH

SKIN PROBLEMS, HIVES, RASH

IMMUNE CELLS MOVE OUT OF THE BLOODSTREAM AND INTO TISSUES WHERE THEY ARE MOST NEEDED

POSSIBLE LINKS TO RHEUMATOID ARTHRITIS, AUTOIMMUNE DISEASES

ADRENALINE AND CORTISOL RELEASED BY ADRENAL GLANDS

MUSCLE BECOME TENSE IN PREPARATION FOR FIGHT OR FLIGHT

BLOOD DIVERTED FROM DIGESTIVE SYSTEM TO BODY BURNING MUSCLES FOR FUEL

FREQUENCY LOWERS TO ENSURE SUFFICIENT BLOOD SUPPLY TO MUSCLES AND MIND

MEMORY PROBLEMS DUE TO ATROPHY OF NERVE CELLS IN THE HIPPOCAMPUS REGION OF BRAIN

ENHANCED CONCENTRATION, AWARENESS AND MEMORY

DECREASED MUSCLE MASS DUE TO BODY BURNING MUSCLES FOR FUEL

SKIN PRODUCES EXTRA SWEAT

SKIN PROBLEMS, HIVES, RASH

STRESS AFFECTS THE MIND AND BODY YET TOGETHER AS ONE! THIS IS WHAT IS MEANT WHEN STRESS EFFECTS ARE REFERRED TO AS CHRONIC.
THE STRESS RESPONSE

Taken by itself, the stress response is not a bad thing. Commonly called the “fight or flight response,” stress provides our body the extra edge it needs need to escape from a burning building or to fight off an attacker. There are two parts of the stress response. Part one is the sympathetic nervous system response. Located on top of the kidneys, a pair of flattened, inch-long adrenal glands release adrenaline into the bloodstream. This hormone speeds up your heart rate, raises your blood pressure, and makes you breathe faster. All of this allows your body to move quickly for attack or escape.

Part two is the cortisol response. Cortisol is another adrenal hormone the body releases in stressful situations.

“You need energy to fuel the sympathetic nervous system response,” explains Matt. “Cortisol raises glucose levels in the blood. Glucose in turn provides fast fuel for your muscles. This response makes a lot of sense for a physical stress, like the classic lion attack,” says Matt.

Modern Americans rarely have to fend off lions. Our stresses tend to be more psychological, not physical. The body does not need a burst of strength or stamina to handle a nagging spouse or a demanding boss. But the body can’t distinguish between physical and psychological stressors.

“Nowadays it’s mostly psychological stress causing the response. The stress is often of our own making. There isn’t the metabolic demand on the body,” says Traustadottir. “That’s where the health risks start occurring, especially when there’s not a lot of time to recover in between. This response is very beneficial in the short term, but not over the long term.”

In fact, the stress response is very damaging over the long term. Cortisol is the primary culprit. “Cortisol is the hormone you always read about,” says Matt. “It destroys your memory and destroys your waistline.”

Cortisol provides a burst of fuel by freeing up glucose as an energy source. It temporarily shuts down areas such as the reproductive and immune systems. Energy used by these systems is diverted for more immediate use by the brain, heart, and muscles.

“All of these things on an acute basis are really helpful. But maintaining a stress response over a long period of time is unhealthy,” Matt says. Under chronic psychological stress, the body releases cortisol repeatedly, but does not use the fuel it provides. This leads to many health problems over time.

Medical researchers have linked chronic stress to some of the leading causes of death and illness among humans, including heart disease, diabetes, and neurological diseases. Between 75 and 90 percent of all visits to a physician are for stress-related complaints, says Matt.

**His and Her Stress** Women and men respond to stress differently. Women show a higher heart rate under stress than men. Men tend to produce more cortisol.

Matt studies these gender-based responses in animals. Her team stressed out Siberian dwarf hamsters by restraining them in mesh bags (the hamsters were not harmed by the restraint). The researchers took blood samples before and after the restraint. As predicted, the males showed a higher cortisol response, just like humans.

Siberian dwarf hamsters form lasting pair bonds. Periods of separation from their mates are very stressful. Matt found that when hamsters were allowed to form bonds, then were separated, they showed increases in levels of cortisol, decreases in levels of adrenaline, and decreases in levels of other brain chemicals called neurotransmitters. The hamsters also gained weight. ate more, and decreased their activity.

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“Think of a football player who injures his knee in the second quarter and gets carried off the field. After halftime he comes back and plays the rest of the game. Most likely they gave him a cortisol injection to reduce the inflammation.”

Kathryn Matt
"They became couch potatoes," she says. Their responses bear an uncanny resemblance to those of a human who’s just been dumped by a girlfriend or boyfriend.

Interestingly, while both sexes showed this response, it was more pronounced in males. This could be a result of the males’ higher cortisol levels. Matt cautions that it could also be related to variations in the female hamster’s reproductive cycle.

Gender differences in the stress response may be linked to gender-related disease risk. For example, although heart disease is the leading cause of death for both women and men in the United States, it presents itself differently in the two sexes.

In women, heart attacks tend to occur after menopause, and they come on very suddenly. The symptoms are different, too. Many women never feel the classic arm pain or chest crushing that men do during heart attacks. Matt wonders if male heart attacks may in part result from chronic high cortisol levels, while women’s might develop from the strong sympathetic stress response.

"Data is accumulating about the long-term effects of cortisol, but less is understood about the long-term effects of the sympathetic nervous system response," she says. The ASU scientist plans to study this part of the stress response more thoroughly.

**Autoimmune Disease**

Matt is also interested in the relationship between stress and autoimmune disease, which shows major differences between the sexes. She focuses her attention on rheumatoid arthritis (RA).

"Autoimmune diseases are three times more prevalent in women than men. We want to find out why," Matt says. She thinks that stress, especially cortisol, plays a key role. "When you talk to people with rheumatoid arthritis they will tell you that stress makes it worse. So RA should give us clues as to how stress is translated through our bodies, and its effects on the immune response," says Matt.

Bosch works with Matt to understand the stress-arthritis connection. She compares women with RA to a group of women without the disease, the healthy controls. She found that women with RA have higher resting cortisol levels and higher resting heart rates than healthy women. They seem to have a constant, though slight, stress response.

However, women with RA are less responsive to stress than healthy women. In other words, their cortisol and heart rates do not increase as much when they are stressed out using the MSRP. "We speculate that the systems are more active than they should be, and there’s a ceiling effect where there’s no more room for response," Bosch says.

She notes that RA patients tend to have higher stress levels overall, but the reason is unknown. "It’s either part of the pathology of the disease, or stress created by the illness itself."

Matt also compared RA patients to women with osteoarthritis (OA). OA presents similar symptoms to RA, but it is a wear-and-tear disease, not an autoimmune disease. Therefore, she thinks it is unlikely to be strongly linked to stress.

The RA patients had lower resting cortisol rates than the OA patients, but higher levels of prolactin, a hormone that stimulates the immune system. The RA patients also had higher resting heart rates. When under stress, the RA subjects continued to have higher heart rates and lower cortisol levels than stressed OA patients.

"Autoimmune diseases are the result of excessive immune function. Perhaps, then, the low levels of cortisol, which normally suppresses the immune system, contributes to the disease. The rise in prolactin would further stimulate the immune system. "Of course, we don’t yet know"
A PLACE FOR STRESS

Stress is a real killer. Chronic stress is linked to several major causes of death and a majority of doctor visits. Scientists are finding that if we could manage stress better, we could save a lot of money and pain. But stress is not an easy topic to tackle. If we hope to understand and reduce chronic stress, we must address it on biological, psychological, economic and policy levels. Enter the ASU Stress Center, more formally known as the ASU Center for Study of Stress and Science. At the center, researchers from ASU and the surrounding biomedical community are joining forces to find answers. Research teams include scientists from disciplines such as psychology, biology, nursing, family studies, health care administration and policy, economics, and bioengineering. The Stress Center includes five working groups. They study stress in relation to cardiovascular diseases, metabolic disorders, mental health and sleep disorders, musculoskeletal disorders, and environment. The initial formation of this group was funded through Arizona's Proposition 301 tax revenues.

With its share of funding, the Stress Center has provided seed grants to individual researchers. These scientists are conducting pilot studies to collect data that can then be used to attract larger grants from other funding sources. For more information about the ASU Stress Center, visit http://www.asu.edu/stress.

if the low cortisol is a cause or an effect of the RA,” cautions Matt. “The women we studied have had the disease for a long time. We need to compare these results to women who are early in their diagnosis of disease.”

THE FITNESS FACTOR

Not all the factors influencing the stress response are beyond a person’s control. If you want to lower your stress levels, Matt recommends that you get moving. “We always say exercise raises your resiliency to stress. It takes more to invoke a stress response, and it is resolved much more quickly,” says Matt.

Exercise places a physical stress on the body. Not surprisingly, heart rate, respiration, and cortisol levels all rise when you work out. “If you ran for two hours you’d see an increase in cortisol. That would be helpful—the muscles need fuel. It’s a beneficial increase,” says Traustadottir.

However, fit people have a smaller stress response to exercise than unfit people. “If you exercise on a regular basis, it takes a higher work-load to get the same rise [in cortisol] as it would in an untrained person. The system adapts,” she adds.

Psychological stress creates the same hormonal stress response as physical exertion. Traustadottir wants to know if adaptations to exercise carry over to psychological stress as well. For example, will a marathon runner stay calmer in a traffic jam than a couch potato?

The ASU researcher also is interested in the effects of aging. Baseline cortisol levels increase with age, but no one is sure whether it is a natural process or the result of decreased activity levels. Traustadottir wants to know if physical fitness can help prevent this change.

To find out, she compared three groups of women: young unfit, older unfit, and older fit. She measured each individual’s baseline heart rate, blood pressure, and hormone levels. Then she asked subjects to undergo the MSRP and measured these values again. As expected, fit individuals had lower heart rates and blood pressures at baseline and throughout the trial compared to the unfit women. However, the fit subjects showed a higher—but shorter—cortisol response when stressed, possibly reflecting an enhanced capacity to respond.

Currently, Traustadottir is comparing the stress response and recovery of these groups after a treadmill exercise. She also measures variables such as bone density, insulin sensitivity, body composition, and cognition.

“All these factors have been associated with higher cortisol. What we don’t know is whether fitness will influence them,” Traustadottir says. “There’s no doubt that fitness will build muscle and increase bone density. I want to see if it occurs through the changes in the stress response. People say, ‘Of course fitness does that.’ But we need the evidence-based research results to prove it.”

The ASU scientists are now working to expand their studies to examine the effects of ethnicity and socioeconomic status on the stress response. They will also study how differences in the stress response might link to cancer, mental health, cardiovascular disease, and diabetes.

Work at the ASU Center for the Study of Stress and Science will add to our fundamental knowledge of how stress affects us, and how we can manage stress better. But Matt is quick to point out that you don’t want to eliminate the stress response entirely. “You still need it on the occasion that you need a physical boost,” she explains. When a child falls in the pool, or a mugger grabs you in the parking lot, you may just be grateful for that helpful hormone rush.

STRESS RESEARCH IN THE NEUROENDOCRINOLOGY LAB IS FUNDED THROUGH THE ARIZONA BIOMEDICAL INSTITUTE, THE ARTHRITIS FOUNDATION, THE NATIONAL INSTITUTES OF HEALTH, AND NASA. FOR MORE INFORMATION, CONTACT TRAVIS MATT, PH.D., EXERCISE AND SPORT RESEARCH INSTITUTE, 480.965.7906. SEND E-MAIL TO: KMATT@ASU.EDU

PAM BOSCH