The Neurobiology of Stress and Emotions

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We often hear the term "stress" associated with functional gastrointestinal (GI) disorders, such as irritable bowel syndrome (IBS). Many patients experience a worsening of symptoms during times of severely stressful life events. But what is stress? How often does it occur? How does our body respond to stress? This article explores the mechanisms that link stress and emotions to responses that have evolved to ensure survival and that, in the modern world, affect health – including gastrointestinal function.

Introduction

Stress is an adaptive response that is not unusual or unique to only certain individuals. In humans and animals, internal mechanisms have developed throughout evolution, which allow the individual to maximize their chances of survival when confronted with a stressor. A stressor in this context is any situation that represents an actual or perceived threat to the balance (homeostasis) of the organism. In a wide variety of real, life-threatening situations – such as an actual physical assault or a natural disaster – stress induces a coordinated biological, behavioral, and psychological response.

In many ways, the stress response of an organism can be understood in analogy to the response of a nation confronted with an actual or perceived threat to its stability. As we are all too familiar, such a threat will result in the activation of a series of preprogrammed civilian (economic, security) and military measures, optimizing the chances of the nation to overcome or avoid the threatening situation. On the one hand, the readiness to quickly mount such a response is paramount to the long-term survival of the nation; on the other hand, the longer this response has to be maintained, the greater the toll will be on other functions of the society. We will return to this analogy later.

The organism's stress response often, but not necessarily, includes subjective emotional feelings like fear and/or anger. However, similar responses can also be observed in situations that are perceived as threats but which do not represent actual life-threatening situations, such as public speaking or the memory of a natural disaster. The associated subjective emotion associated with such non-life threatening stressors is frequently referred to as anxiety.

Emotions, stress, and conscious feelings

One environmental situation that triggers a distinct emotional response of the body is a real or perceived threat to the organism. The stressor is the event that triggers this particular response; fear and/or anger is the emotional feeling that may be associated with the bodily response. However, stress and fear are not the only emotions that our organism is programmed to respond to. Emotions are stereotypic patterns of the body, which are triggered by the central nervous system in response to distinct external environmental situations or to the recollection of memories related to such situations. In evolution, the basic mechanisms generating an emotional response of the body evolved long before the conscious feeling of emotions evolved in humans and in non-human primates. The reason for this is simple: Emotional responses are essential for the survival of all living organisms. For example, the emotion of fear and/or anger, and the associated fight or flight response is essential to avoiding harm from an aggressor; the emotion of love (attachment) is essential for bonding between individuals; the emotion of disgust may have evolved initially as food aversion to avoid ingestion of harmful materials.

In these different situations, the body consistently responds in an automatic, stressor-specific way, at times without our being aware of the response. Conscious emotional feelings may or may not be associated when the body responds to a stressful situation. It is important to realize that the frequently associated conscious feelings of emotions, such as fear, anger, sadness, disgust, or love, are not essential to the understanding of the basic biological mechanisms underlying the emotions. As expressed in a concise

way by Joseph E. LeDoux of the NYU Center for Neural Science: From the perspective of the lover, the conscious feeling of love is the only thing that is relevant. For the scientist who wants to understand the biological mechanism underlying the emotion of love, the biological responses of the organism are the only relevant aspects.

Basic biological mechanisms by which stressors are translated into distinct bodily responses

Whenever an emotion is triggered, a network of brain regions (traditionally referred to as the "limbic system") generates a pattern of stereotypic outputs, which ultimately induce a biological response of the body. The circuits within the brain that generate the emotional responses can be referred to as the emotional motor system (EMS). Via parallel outputs of the autonomic nervous and neuroendocrine systems, the EMS plays out an emotional response in the "theater of the body." For example, every human being produces similar facial expressions associated with specific emotions. Facial expressions of fear, anger, and sadness are so universal that a primal tribe member living in the Amazonian jungle has the identical pattern as a broker at the New York stock exchange. Specific circuits of the emotional motor system have evolved to both generate this stereotypic emotional facial response, as well as instantaneously recognize it when it occurs in somebody else. Other examples of musculoskeletal responses associated with emotions include tightening of muscles or changes in posture.

Even though most of us are completely unaware of it, similar stereotypic emotion-specific responses are also generated within our internal (visceral) organs. In a stressful situation they include responses such as stimulation of the cardiovascular system (increased blood pressure, heart rate, cardiac output) required to prepare the body for the "fight or flight" response. Of particular relevance for those with a functional GI disorder like IBS, is the fact that the emotion of fear is associated with inhibition of upper GI (stomach and duodenum) contractions and secretions, and with stimulation of lower GI (sigmoid colon and rectum) motility and secretions. The former may contribute to a sensation of fullness and lack of appetite, the latter to diarrhea and lower abdominal pain. This response pattern of the digestive tract may have evolved in order to minimize the exposure of the small and large intestine to ingested food and waste material during a time when all energy is shunted toward the skeletomotor system to maximize success of the fight and flight response. Interestingly, when the emotion shifts to anger, the pattern of upper GI activity is reversed, with stimulation of gastric contractions and acid secretion.

The beneficial and detrimental effect of the stress response

In addition to elaborate mechanisms that have evolved to activate the stress response when needed to protect the organism, equally effective mechanisms have evolved to turn it off immediately when no longer needed, or to rapidly habituate to repeated occurrences of the same stressor. Apparently these systems of activation and inactivation of the stress response, which have evolved over millions of years, have been perfected to deal with the daily threats to survival for all organisms involved in the cycle of prey and predators. However, in humans living in modern societies we are increasingly beginning to realize a phenomenon that has been referred to as the wear and tear, or the *allostatic load*, of stress. This detrimental effect of stress may manifest following a one time severe stressor (life threatening situation), following repeated smaller stressors, or following a major sustained stressor over a period of time.

Let us again take the example of a nation responding to an acute or perceived threat by mounting a massive mobilization of civilian and military resources ("fight response" or "defense reaction"). In the majority of situations, mounting the response will be sufficient to avoid the potential damage, and the country can return to its normal civilian function within a relatively short time. However, if the threat persists, or the response is maintained over a long period of time, there will be substantial costs to the society (i.e., allostatic load) such as the channeling of resources from civilian to military projects, and dealing with psychological and physical impact of military conflicts.

What is the wear and tear of severe, repeated, or sustained chronic stress in humans? The remarkable thing is that in the absence of predisposing "vulnerability" factors (e.g., genetic factors, adverse early life experiences) or in the presence of "resilience" factors (e.g., possibly genetic, strong social support system), a large number of people are remarkably resilient to this wear and tear of chronic stress. However, in the vulnerable person, it has

frequently severe consequences. For example, the acute increase in heart rate and blood pressure is an essential response to optimize the physical strength of a threatened organism, but the chronic changes developing with persistent increase in cardiovascular function lead to hypertension and coronary artery disease. An acute increase in vigilance is important to better recognize an enemy; however, persistent hypervigilance is associated with a variety of common chronic conditions such as anxiety disorders. Finally, while acute stimulation of the immune system has a beneficial effect, chronic stress can be associated with suppression of cellular immunity, and detrimental effects on health.

Men vs. women: Fight and flight vs. tend and befriend

A problem with research into the biology of stress is that the preponderance of such research has been conducted in males. Prior to 1995, females constituted only about 17% of participants in laboratory studies of physiological and neuroendocrine responses to stress, while in recent years, the gender bias has somewhat decreased.

Could it be that the majority of research studies on the stress response apply only to men, and not to women? In an article, reviewed in May 2000, by the *New York Times*, a prominent Professor of Psychology from UCLA, Shelley Taylor and colleagues, summarized published scientific evidence from behavioral and biological studies and made a strong argument for differences in the way male and female animals, and men and women, respond to stressful, threatening situations. The authors made the following theoretical assumptions about the evolution of gender-specific stress response patterns:

- Traditionally and throughout evolution, males have been selected that mount a successful behavioral response to a threat, which maximizes the survival of self by either defeating the enemy or overcoming the threat. A similar evolutionary advantage exists for males that are able to flee from a superior enemy. However, the same fight and flight response, which is advantageous for the survival of the male individual, puts defenseless and unprotected offspring at significantly greater risk of being harmed.
- The fight and flight response should result in the selection of males that maximizes biological mechanisms to assure superior fight or flight responses, such as cardiovascular performance, motor planning, and necessary neuroendocrine responses, such as activation of the sympathetic nervous system and the hypothalamic-pituitary-adrenal (HPA) axis – systems essential to self-preservation.

Different considerations apply to females:

- Compared to males, females make a greater investment initially in pregnancy and nursing, and typically play the primary role in bringing offspring to maturity. Therefore, behavioral responses to threats that were successfully passed on would have been those that protected offspring as well as self.
- This maternal investment should result in selection of female stress responses that do not jeopardize the health of both the female and her offspring, and maximize the likelihood that they will survive.
- This response pattern should favor the development of biological mechanisms that inhibit the fight and flight response, and shift the individual's attention to caring and tending to the young (attachment behavior) and to forming networks of females for the defense of the group.

Men and women: Biological differences in the stress responses

Based on these considerations, the authors make a convincing argument that high sympathetic nervous system activation (targeted primarily at the cardiovascular system, thereby optimizing physical performance), effective activation of pain inhibition systems (to prevent distraction of fight and flight performance from injury related pain), and high cortisol responses (that mitigate the immune response and repress inflammation) are characteristic biological components of the male stress response. These responses are related to higher male sex hormone levels.

In contrast, in females, greater activation of vagal mechanisms (associated with parasympathetic nervous system "relax and restore" responses and increased gastrointestinal activation), and greater release of oxytocin (a calming hormone amplified by estrogen) and endorphins within the brain will inhibit the underlying fight and flight response, and promote attachment behavior both to the offspring as well as to other females.

Do these differences also apply to the non-life threatening stressors of daily life, and could the differences in biological mechanisms play a role in the well known fact that men are more likely to die of chronic diseases of the cardiovascular system (hypertension, coronary artery disease), while women appear more likely to suffer from a wide range of functional disorders, such as IBS, fibromyalgia, and interstitial cystitis?

What does this have to do with IBS

Converging evidence from different laboratories and research groups are consistent with the concept of an "enhanced stress responsiveness" as a major vulnerability factor in many IBS patients. As outlined above, such an enhanced stress responsiveness may not be obvious to the affected individual, until he or she is exposed to a period of sustained threatening stress (financial or employment problems, divorce, aftermath of a major disaster with consequences on daily life), repeated mild to moderate stressors, or a one time severe (life threatening) type stressor (robbery or physical assault). Under these circumstances the mechanisms that normally turn off the stress response are overwhelmed, and attempts of the nervous system at adaptation or habituation fail. Many of the vulnerability factors for such enhanced stress responsiveness have been identified and many of them occur in a particular vulnerable period of the developing brain (before age 10). Some of the best-studied factors include loss of the primary care giver, distant mother-child relationship, emotional neglect, and physical and verbal or sexual abuse.
In order to understand how a chronically enhanced stress response can produce the cardinal symptoms of IBS (abdominal pain and discomfort associated with altered bowel habits) we have to go back to the earlier section on the emotional motor system: activation of the stress system will stimulate contractions and secretion in the sigmoid colon and rectum. Depending on the specific emotional context (fear vs. anger), the upper GI tract will be either inhibited (fear) or stimulated (anger). In addition, recent research in animals has demonstrated a phenomenon referred to as stress-induced visceral hyperalgesia. What this means is that in vulnerable animals, exposure to an acute moderate stressor will make the colon more sensitive to distension (and the perception of discomfort or pain).

Why do the symptoms go away after one stressful situation has resolved and persist in another? Amongst many factors, anxiety and fear generated by IBS symptoms themselves are sufficient in many patients to maintain the stress responsiveness in a chronically enhanced state. Some of the more common symptom related anxieties include: Am I close enough to a bathroom when my symptoms come on? Will I be OK for the rest of the day, unless I completely empty my colon in the morning before leaving the house?

Perceptions of pain, muscle tensions, and other somatic symptoms can cause stress levels to spiral upward. Self-regulation strategies that reduce unpleasant symptoms offer both physical and psychological relief.

—Rolf Sovik

What can IBS patients do to guard against the detrimental effects of allostatic load and enhanced stress responsiveness

Based on our current state of knowledge, little can be done in the affected patients to reverse vulnerability factors that have been programmed into our genes or have been hardwired into our nervous system during the first few years in life. Nevertheless, a variety of cognitive and behavioral approaches may be useful in protecting ourselves against the effects of allostatic load, or the wear and tear, of stress. These include: 1) Developing effective coping styles towards life stress and IBS symptoms; 2) Learning to activate mechanisms in the body that oppose the stress response and induce what has been referred to as the "relaxation response" through various relaxation techniques (e.g., breathing exercises, progressive relaxation, hypnosis, meditation); and 3) Moderate but sustained exercise.

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