

Endocrinological Mechanisms of Depressive Disorders and Ill Health

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Stress is common, but reactions to stress vary greatly from person to person. Acute stresses are common and are a part of daily life. Mild, short-term acute stresses are adaptive and are also part of day-to-day life. Whereas, intense (severe, pathogenic) acute stresses that are associated with life-threatening situations, real or perceived, could lead to persistent behavioral and psychological abnormalities. Stress-induced symptomatology can be mistaken for other diseases. If the intensity of the stressor exceeds adaptive capabilities of the individual, such stresses, can also result in stress-related disorders including anxiety and depression, as well as severe traumatic stress leading to post-traumatic stress disorder (PTSD). Unmanaged stress causes physical and mental strain, poor performance and lack of productivity, and can lead to harmful health outcomes, including obesity, type 2 diabetes and myocardial infarction. Approximately half of people with PTSD also suffer from major depressive disorder. Overt mental strain also can lead to depression, inability to perform, difficulties in interpersonal relationships and PTSD. Accumulating evidence supports hormone-dependent mechanisms in many of these stress-related disorders. While the latter seems to be a general phenomenon including depression (which probably is the largest group of psychological disorders), this editorial focuses on PTSD as an example to illustrate the underlying endocrine abnormalities associated with severe stress.

What is stress?

Both acute and chronic stresses can be expressed as physical, emotional or psychological. Based on their duration, stresses can be classified as acute or chronic, but based on nature of the stressor these can be categorized into physical, psychoemotional, and so forth. Over-intensive psychoemotional stresses are commonly designated as 'traumatic'; PTSD comes under this category. Unmanaged pathological stresses induces a cascade of sustained abnormalities, as in the case with PTSD. Not only the coping abilities vary from person to person, but also stress is highly individual, and its effects vary depending on genetics, upbringing, experience, ethnicity and culture. Previous experience and exposure, such as intrauterine (mal)nutrition and the environment, school or workplace bullying, discrimination, abuse and neglect, and upbringing, influence how one handles and reacts to stressful situations. Although many of these situations are beyond an individual's control, learning to handle and minimize stress is essential for balancing life. Unmanaged chronic stress can also lead to many other diseases, including eating disorders, smoking, alcohol and drug abuse, behavioral issues and addiction.

Chronic stress and ill health

In evolutionary terms, the neurohormonal changes that occur during acute stress are expected to last only for a short period. However, intense acute stress or frequent sustained stresses over a long period cause the negative biochemical and neurohormonal changes to become persistent, these escalating stresses would lead to ‘restructuring’ of brain centers related to reasoning and behavior. The adverse health issues of unmanaged stress and inappropriate or pathological responsiveness of the stress system affect and disrupt many bodily systems, including endocrine system; digestive system (stomachache, slow gastric emptying, enhanced colonic peristalsis leading to abdominal cramps and diarrhea); impairment of the immune system (frequent infections; chronic fatigue syndrome); changes in appetite and alteration of metabolism (weight gain or loss); cardiovascular dysfunction (hypertension, tachycardia, hyperlipidemia and hyperglycemia); nervous system manifestations (anxiety, depression, insomnia, lack of interest); and impaired memory.

Neurohormonal responses to stress

The most familiar acute stress response is the ‘fight or flight’ reaction. The stress response causes immediate release of the stress hormones cortisol and adrenalin, which intensify mental concentration and enhance rapid reactions; survival mechanisms. The associated neurohormonal secretions cause tachycardia and hypertension, and enhance immune responses and memory. These physiological systems have evolved to cope with day-to-day, short-term stresses and provide self-protection; however, the system is designed to return to baseline rapidly, after cessation of stress. Human bodily systems are not designed to cope with chronic stresses. Whether stress is acute or chronic, the body responds through allostasis, achieving stability and homeostasis through physiological or behavioral changes. Intense acute stresses or chronic stresses could lead to sustained excess (or under) production of stress hormones, which poses physiologic challenges. Persistent neurohormonal, biochemical and physiological abnormalities cause undesirable structural brain changes and several adverse health outcomes.

Consequences of the inability to cope with stress

Feeling anxious, nervous, distracted and pressured are common when experiencing stress, but these feelings usually are transient. Additional signs and symptoms of stress include depression, fatigue, irritability, withdrawal, antisocial behavior, chest pain, dizziness, breathlessness, menstrual irregularities, erectile dysfunction and loss of libido. Although the majority of these are nonspecific, many including depression have an underlying etiology of disruption of endocrine system.

Physiological ways we cope with stress

In most instances, stress-associated symptomatology is minor, transient, appropriate for the situation. These are relieved through previously learned coping skills, such as avoidance or methods used to diffuse stress, such as engaging in leisure activities, reading, exercising, music, relaxation or meditation. However, stresses that are severe may lead to pathological status with various clinical manifestations that requires psychological or medical assistance. Regular, moderate exercises improve physical and psychological health and brain function, including memory. The long-term effects of chronic stress can be reduced by minimizing oxidative stresses, such as eating a healthy diet and avoiding smoking and drinking too much alcohol. Most people need to be educated on how to cope with stresses rather than becoming dependent on prescription medications. Relaxation tools, such as meditation, exercise, Pilates, Tai Chi and yoga, should be used as complementary methods for overcoming stress. Offering well-organized therapeutic plans to stressed individuals empower the “stressed” individuals, and enable them to overcome chronic stress and reverse the endocrinological abnormalities that impair their lifestyle and productivity. Proceeding sections examine the neurohormonal abnormalities in PTSD, as an example of a severe stress-related disorder.

Post-traumatic stress disorder

PTSD is defined as a severe anxiety disorder that develops after exposure to a stressful event with actual or perceived threat or danger to the physical integrity of oneself or another person. PTSD is a serious psychological abnormality that can affect military and civilian personnel. Depending on an individual's personality and resilience, PTSD can occur after exceedingly stressful incidents or seemingly minor ones. PTSD is a multisystem disorder with endocrine abnormalities. Combined and targeted treatments using conventional antipsychotic agents, hormone and analogs, and non-traditional methods such as meditation improve symptoms and can cure PTSD. Multiple factors, including genetic susceptibility; past experiences; cultural, spiritual and personal beliefs; experiencing discrimination, bullying, and harassment; and lack of social support, increase the risks for the development of PTSD and its relapses

Conclusions

Data support that neuroendocrine abnormalities attributed to PTSD include HPA hyper-reactivity and desensitized glucocorticoid feedback.] Resulting inconsistent hormonal pattern represents a key pathological maladaptation to stress. These abnormal hormonal, metabolic responses and mitochondrial, biochemical, and neurohormonal abnormalities lead to structural brain vicissitudes occurring in the amygdala and hippocampus, locus coeruleus, and autonomic norepinephrine centers in the brainstem, which further alters behavioral responses. The development of the symptoms of PTSD can be explained by disturbances of parallel distributed processing of neural pathways. Moreover, the disturbances of noradrenergic neurons in PTSD are likely to manifest as a dysfunctional modulation of working memory and involuntary traumatic recollection and flashback] Meanwhile, comorbidity in major depressive disorders and PTSD reflects not only overlapping symptoms in the two disorders, but also the co-occurrence of biological correlates and trauma-related phenotypes] While there are some similarities of presentation and biochemical abnormalities of depression and PTSD, the neuroendocrine abnormalities observed are much different, and thus, different modes and targeted treatments are necessary. In those with unmanaged stresses, it is essential to (1) make an accurate diagnosis earliest possible, (2) establish a network of support and (3) provide focused multimodal, individualized treatments to maximize the recovery process and prevent relapses. However, because of the underlying hormonal abnormalities, psychotherapy and psychiatric medications alone may not be adequate to cure PTSD. Thus, adjunct therapy, with treatments based on understanding the pathobiology and alterations of the neurohormonal systems, together with non-traditional approaches such as mindful meditation methods, as cost-effective. Evidence indicates PTSD is not only a psychological disorder but also a chronic medical illness resulting from endocrine pathology

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