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Short Communication

Pathophysiology of Chronic Stress: Effects on Neuroendocrine Axis and Immunity

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Abstract

Although aging of the cardiovascular system is not the primary cause of organismal aging as a whole, it significantly influences its rate and manifestations. These changes reduce the body's ability to adapt and increase the risk of developing diseases. Despite the fact that these changes are regular and progressive in nature, their severity and individual features vary depending on genetic, environmental, and behavioral factors. Studying age-related changes in the heart and blood vessels helps to more accurately diagnose, treat, and prevent circulatory system diseases, as well as to distinguish natural age-related transformations from pathological ones. Understanding the processes of myocardial and vascular aging allows not only to predict the likelihood of cardiovascular complications but also to select individualized treatment for elderly people. This article reviews the main age-related changes in the cardiovascular system: structural remodeling of the vascular wall and myocardium, features of central and peripheral hemodynamics, disorders of neurohumoral regulation, as well as the nature of the cardiovascular system's response to physical exertion in elderly and senile individuals.

Key words: aging; cardiovascular system; vascular remodeling; arterial stiffness; hemodynamics; cardiac output; myocardial contractility; neurohumoral regulation; autonomic nervous system; physical exertion; exercise response; vascular tone; muscle fibers; vagus nerve

Summary

Chronic stress is a growing issue in modern society. The accelerated pace of life, social instability and occupational pressures create conditions for long-lasting stress factors. Chronic stress is seen as a key risk factor for the development of somatic and mental illnesses: cardiovascular pathologies, metabolic syndrome, depression and immunodeficiency states.

Pathophysiological mechanisms of chronic stress are associated with dysregulation of the neuroendocrine system, especially the hypothalamus-hypophyseal adrenal axis (GGS), and impairment of immune function. Interaction between the nervous, endocrine and immune systems is carried out through a network of neurotransmitters, hormones and cytokines that form a single neuroendocrine-immune system.

The aim of this work is to analyze the pathophysiological mechanisms of chronic stress, its influence on the neuroendocrine axis and immunity, as well as the clinical consequences of long-term stress exposure.

The Concept and Classification of Stress

Stress definition and types

The term "stress" was coined by the Canadian physiologist Hans Sele in 1936. Stress, by its definition, is the body's non-specific reaction to any claim. Currently, stress is understood as a set of non-specific adaptive reactions to the exposure of extreme stimuli (stressors) aimed at maintaining homeostasis.

Distinguishes between acute and chronic stress. Acute stress arises from short-term exposure to severe stress, is adaptive and contributes to resilience. Chronic stress develops with long-term exposure to stressors, accompanied by depletion of adaptive resources and a shift in protective responses to pathological ones.

Stages of stress development

G. Selje identified three phases: the reaction of anxiety, the phase of resistance and the phase of exhaustion. Stressors are factors that can disrupt homeostasis: physical (trauma, infection, hypoxia), psychological (anxiety, fear, frustration) and social (economic problems, unemployment). The significance of stress is determined by an individual's subjective assessment.

Neuroendocrine Mechanisms of Chronic Stress

The central axis of the neuroendocrine response to stress is the GGS axis. When stressed, the neurons secreting corticoliberin (CRH) and vasopressin (AVP) in the paraventaricular nuclei of the hypothalamus are activated. These neuropeptides stimulate the secretion of ACTG in adenopituitary, which reaches the cortex of the adrenal glands and activates glucose synthesis (cortisol).

Glucocorticoids are key stress hormones that provide adaptation through the modulation of metabolism, cardiovascular system and immune response. In

chronic stress there is dysregulation of the GHN axis: in early stages - hyperactivation with increased cortisol, in late stages - hypoactivity with depletion of resources.

The Little Adrenaline System

In parallel, the like-adrenaline system is activated. In response to stress, noradrenaline is released from the sympathetic nerves and adrenaline from the adrenal glands, providing rapid physiological preparation ("fight or run" reaction). Chronic activation leads to arterial hypertension, tachycardia and metabolic changes.

Other neuroendocrine changes

Chronic stress reduces growth hormone secretion, depresses the thyrotrope axis (symptoms of hypothyroidism), and suppresses reproductive function. The dysfunction of the dopamine system lies at the heart of depressive states.

The Effects of Chronic Stress on Immunity

The immunosuppressive effect of glucocorticoids

Glucocorticoids have a powerful immune suppressive effect through intracellular receptors that modulate the expression of inflammatory mediator genes. The production of provoking cytokines (IL-1, IL-6, IL-12, FNO-alpha) is reduced, and the antigenic presentation function of macrophages is suppressed. The T-cells undergo apoptosis, their proliferation and IL-2 products are reduced.

Differentiation in plasma cells and antibody synthesis (especially IgG) is reduced in B-lymphocytes, leading to decreased human immunity and increased susceptibility to infections.

Changes in cellular immunity

In chronic stress, lymphocyte redistribution occurs between the lymphoid organs and blood, followed by lymphopenia. Functional activity of NK cells is reduced, which weakens anti-tumor immune surveillance. The T-helper response is shifting towards Th2-type, which explains the exacerbation of allergic and autoimmune diseases.

Inflammatory response

Chronic stress is associated with systemic low-intensity inflammation - elevated IL-6, IL-1bit, FNO-alpha, S-reactive protein. Mechanisms include the activation of the adrenal system and the resistance of tissues to the anti-inflammatory action of glucocorticoids. Chronic inflammation is a key factor in atherosclerosis, metabolic syndrome and depression.

Clinical Consequences

Somatic diseases

Chronic stress - a significant risk factor for cardiovascular diseases: arterial hypertension, ischemic heart disease, stroke. Metabolic disorders include insulin resistance, dyslipidemia, abdominal obesity, type 2 diabetes.

Mental and immune disorders

Chronic stress is a leading risk factor for depression and anxiety disorders. Pathophysiology includes dysregulation of the serotoninary and dopaminergic systems, and neuro-inflation. The cytokine hypothesis of depression links elevated cytokines to triptophan metabolism disruption and neurotrophic factors.

Immunosuppression shows increased susceptibility to infections (respiratory, herpes simplex, HIV, tuberculosis), reduced cancer surveillance.

Conclusion

Chronic stress is a complex pathophysiological process with neuroendocrine dysregulation. Central to this is the activation of the GNS and simpato-adrenal system with overbinding hypersecretion of glucocorticoids and catecholamines.

The immune system is a primary target of stress hormones. Chronic stress causes immunosuppression with disruption of cellular and humoral immunity, decreased NK cell activity. At the same time, systemic low-intensity inflammation - the link between stress and somatic pathology - develops.

Clinical outcomes include cardiovascular disease, metabolic syndrome, type 2 diabetes, depression, and increased infectious morbidity. Understanding pathophysiological mechanisms is essential for developing strategies for the prevention and treatment of stress-associated diseases.

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