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CHRONIC STRESS AND CORTISOL – MECHANISM OF ACTION AND IMPACT ON THE HUMAN BODY. A REVIEW ARTICLE

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ABSTRACT

Introduction and objective: In recent years, the negative impact of chronic stress on health and proper functioning of the human body has been increasingly discussed. This phenomenon is a growing problem that affects an increasingly larger part of society. The body's response to stress is the release of cortisol – a glucocorticoid hormone produced in the adrenal cortex, commonly referred to as the "stress hormone." The aim of this article is to analyze the impact of elevated cortisol levels on human organs and systems, as well as to discuss possible preventive measures aimed at reducing chronic stress levels, based on current literature data.
State of knowledge: Cortisol is a glucocorticoid hormone produced by the adrenal glands, which plays a crucial role in various physiological processes of the body. Its release is regulated by the hypothalamic-pituitary-adrenal (HPA) axis, a neuroendocrine system responsible for the body's response to stress and maintaining homeostasis. Chronic stress leads to disruptions in the proper regulation of cortisol secretion, which is associated with negative health consequences, such as metabolic disorders, obesity, progression of neurodegenerative diseases, increased risk of cardiovascular diseases, and weakened immune response. Research also indicates a link between elevated cortisol levels and the occurrence of mood disorders, including anxiety and depression.
Materials and methodology: Materials and methodology: The review is based on a thorough analysis of materials obtained from scientific databases "PubMed" and "Google Scholar," which serve as verified sources of information.
Conclusion: In order to reduce excessive cortisol secretion and its negative effects on the body, it is important to effectively counteract chronic stress. Achieving this goal requires implementing effective coping strategies and lifestyle modifications that can help reduce the frequency of stress in daily functioning.

KEYWORDS

Chronic Stress, Cortisol, HPA Axis, Impact on Health, Prevention

CITATION

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Introduction

It has long been known that chronic stress has a significant negative impact on human health, helping to accelerate the development of many chronic diseases. Numerous studies also point to a link between chronic stress and the severity of chronic pain, as well as its role in the development of psychiatric disorders such as anxiety, depression and a tendency to abuse psychoactive substances[1]. In response to a stressor, the hypothalamic-pituitary-adrenal (HPA) axis is activated, resulting in the secretion of cortisol. The highest concentration of this hormone is usually observed 20-40 minutes after the onset of a stressful situation[2]. Also important in regulating the stress response is the ability to anticipate stressful situations, which can reduce the intensity of the body's physiological response. The purpose of this article is to discuss the impact of chronic stress on the functioning of various organs and systems, the course of selected diseases, as well as to present possible preventive measures and coping mechanisms to reduce the negative impact of stress, based on the current literature.

State of knowledge

Mechanism of action of the hypothalamic-pituitary-adrenal (HPA) axis

The hypothalamic-pituitary-adrenal (HPA) axis is a key neurohormonal system essential for the normal functioning of the human body. It is responsible for regulating the secretion of glucocorticoid hormones through signal transduction and feedback mechanisms to maintain the body's physiological response to stimuli and maintain homeostasis[3]. Activation of the HPA axis in response to a stress factor begins with increased corticoliberin (CRH) production in the hypothalamus. CRH stimulates the pituitary gland to secrete

adrenocorticotropic hormone (ACTH), which then stimulates the adrenal cortex to synthesize and release glucocorticoids (GCs), including cortisol[4]. HPA axis activity is closely linked to the regulation of metabolic processes, inflammation, cognitive function and the body's response to stress. Although activation of the HPA axis is essential for the body to respond appropriately to stress, this response must be completed in a timely manner to avoid potential negative effects resulting from excessive hormone secretion.

Termination of the stress response is made possible by rapid negative feedback inhibition mechanisms at the level of CRH-secreting neurons, as well as by sustained inhibition of the HPA axis by brain structures such as the prefrontal cortex, hippocampus and amygdala. These structures play a key role in extinguishing HPA axis activation and restoring neuroendocrine balance[5].

Cortisol

Cortisol is the main glucocorticoid secreted by the adrenal cortex, commonly referred to as the "stress hormone." Its secretion is the body's classic endocrine response to stressful stimuli[6]. The hormone has diverse effects on physiological processes, including metabolism, immune system function and stress coping mechanisms.

Cortisol increases glucose metabolism, regulates blood pressure and facilitates the body's responses in stressful situations. The hypothalamic-pituitary-adrenal (HPA) axis controls the production and secretion of cortisol in an effort to maintain physiological balance. Abnormalities in the functioning of the HPA axis can lead to the development of various conditions, such as Cushing's syndrome, associated with excessive cortisol production, and Addison's disease, resulting from cortisol deficiency.

Cortisol is synthesized from cholesterol under the influence of adrenocorticotropic hormone (ACTH), secreted by the anterior lobe of the pituitary gland. In cells, it binds to cytoplasmic receptors, initiating a biological response. Cortisol secretion follows a diurnal rhythm, reaching its highest concentrations just before waking in the morning. Stress further enhances its secretion, making cortisol a major mediator of the stress response[7]. Proper cortisol activity and an adequate response to stress are crucial for homeostasis, well-being and proper social functioning. However, excessive or chronic activity of this hormone can lead to disorders of growth and development, abnormal body composition, and promote the occurrence of numerous pathologies of a somatic and behavioral nature[8].

Effects of chronic stress and cortisol on selected systems and organs

Metabolic system

Cortisol plays an important role in regulating metabolic processes. Chronic exposure to excessive amounts of this hormone is associated with the development of insulin resistance and visceral obesity, which contributes significantly to the metabolic syndrome. This phenomenon is the result of increased release of energy stores, leading to elevated concentrations of glucose and free fatty acids in the bloodstream. [9].Moreover, it has been shown that the picture of metabolic syndrome can also occur in young and thin people who are considered potentially healthy. These individuals are referred to as metabolically obese with normal body weight (MONW). They are characterized by more visceral fat, insulin resistance, and sometimes hypercholesterolemia and hypertriglyceridemia. These changes are primarily related to excessive cortisol secretion as a result of chronic stress [10]. Abdominal obesity and also type 2 diabetes is also one of the causes of HPA axis hyperactivity induced by chronic stress. [11]. Abdominal obesity and type 2 diabetes are among the potential consequences of hypothalamic-pituitary-adrenal (HPA) axis overactivity induced by chronic stress. This leads to increased release of glucocorticoids and catecholamines, which affect glucose metabolism, increase gluconeogenesis in the liver, inhibit glucose uptake by adipocytes, stimulate lipolysis in adipose tissue, inhibit insulin secretion, and promote chronic inflammation and insulin resistance. As a result of these disorders, neuroendocrine changes occur, which are an important mechanism for the development of type 2 diabetes[12]. **I**n light of the presented data, it can be unequivocally stated that chronic activation of the hypothalamic-pituitary-adrenal (HPA) axis, leading to elevated cortisol levels, exerts a significant and multifaceted adverse effect on human metabolism. Prolonged exposure to stress, resulting in a sustained hyperactivation of this axis, contributes to the development of a range of metabolic disturbances, including insulin resistance, visceral obesity, dyslipidemia, low-grade chronic inflammation, and subsequently metabolic syndrome and type 2 diabetes mellitus.

Particularly concerning is the observation that these metabolic abnormalities may also develop in individuals who do not exhibit classical risk factors — namely, young, lean, and ostensibly healthy persons. In such cases, the phenomenon is described as metabolically obese normal weight (MONW), where chronic

stress and the associated excessive hormonal activity play a central role in the pathogenesis of metabolic dysfunction. This population poses diagnostic challenges, as conventional indicators such as body mass index (BMI) fail to accurately reflect the true metabolic status of these individuals.

Physiologically, cortisol serves an adaptive function by mobilizing energy reserves in response to stress, enhancing gluconeogenesis, stimulating lipolysis, and inhibiting insulin action. However, under conditions of chronic excess, these mechanisms become maladaptive. This leads to disturbances in glucose and lipid metabolism, concomitant impairment of immune function, and elevation of inflammatory markers. Consequently, the risk increases not only for diabetes but also for atherosclerosis, cardiovascular diseases, hypertension, and other chronic complications.

Importantly, accumulating evidence highlights a direct link between prolonged stress and structural as well as functional alterations within the brain, including the hypothalamus and pituitary gland, which may further perpetuate HPA axis dysregulation and exacerbate metabolic disorders. Thus, a vicious cycle emerges, wherein stress acts both as a cause and consequence of metabolic disturbances.

Therefore, approaches to the prevention and treatment of metabolic diseases should be expanded to include strategies aimed at normalizing HPA axis function. In addition to standard dietary and pharmacological therapies, incorporation of stress reduction techniques, improvement of sleep quality, psychological support, and moderate-intensity physical activity—demonstrated to beneficially regulate cortisol levels—is warranted.

In summary, chronic stress and the resulting HPA axis hyperactivity constitute critical yet often underrecognized risk factors in the development of metabolic syndrome and type 2 diabetes, even among individuals with normal body weight. Contemporary medicine should thus consider not only classical metabolic parameters but also the influence of psychological and neuroendocrine factors on patient health. A holistic approach that integrates both physical and mental health is essential for the effective prevention of chronic diseases in increasingly younger and ostensibly healthy populations.

The digestive system

Chronic stress, and the resulting increased secretion of cortisol, also has a negative impact on the gastrointestinal system. The neuroendocrine axis is responsible for maintaining the proper balance between the brain and gut, often referred to as the “gut-brain axis.” Maintaining proper correlation between these systems is essential for proper gastrointestinal function, stress response and maintenance of overall body homeostasis.

Studies indicate that dysregulation of the gut-brain axis and increased cortisol secretion affect the proper functioning of the gastrointestinal tract, leading to disorders and increased gastrointestinal symptoms. In this context, stress and emotional factors play an important role, which can contribute to the increase in the complaints of irritable bowel syndrome (IBS) [13]. Stress also adversely affects the course of inflammatory bowel disease (IBD). The brain transmits signals to the gastrointestinal tract through neural, circulatory and endocrine mechanisms via the gut-brain axis. This process initiates changes in the secretion of corticotropin-releasing hormone (CRH), increases mast cell activity, affects neurotransmission in the autonomic nervous system and the function of the intestinal barrier, all of which exacerbate the inflammatory response in IBD.

In addition to activating the HPA axis and increasing cortisol levels, stress also leads to activation of the autonomic nervous system and the secretion of pro-inflammatory cytokines such as interleukin-8, interleukin-1β, interleukin-6 and tumor necrosis factor α. As a result, there is an increase in the permeability of the intestinal barrier and translocation of bacteria into the intestinal wall, which promotes the release of cytokines and has a negative impact on the course of IBD[14]. Another example of the impact of chronic stress on the digestive system is Crohn's disease, which is a chronic inflammation of the digestive tract. The etiology of this disease includes genetic, psychological, immunological and inflammatory factors. Studies have shown that overactivity of the hypothalamic-pituitary-adrenal (HPA) axis modulates the inflammatory response through the action of glucocorticoids[15]. Based on the examples discussed above, it is evident that chronic stress exerts a detrimental impact on the course of gastrointestinal diseases, promoting their progression. The underlying mechanisms include disruption of the gut–brain axis, increased intestinal barrier permeability, and enhancement of inflammatory responses, all of which play a key role in the pathogenesis of disorders such as irritable bowel syndrome (IBS) and inflammatory bowel diseases (IBD), including Crohn’s disease. As our understanding of the complex interplay between the nervous, endocrine, and immune systems deepens, there is growing recognition of the significance of psychological and emotional factors in the etiopathogenesis of gastrointestinal disorders.

These disturbances are not merely the result of physiological stress responses but stem from the chronic nature of stress exposure, which induces long-lasting alterations in the functioning of the hypothalamic–pituitary–adrenal (HPA) axis and in gut–brain communication systems. Prolonged activation of these pathways leads to dysregulation of the inflammatory response and impairment of the intestinal mucosal barrier's protective function, thereby creating conditions conducive to the development and exacerbation of chronic inflammatory diseases.

Moreover, an increasing body of research highlights the pivotal role of the gut microbiota, whose composition and function are also adversely affected by chronic stress. Dysbiosis—a state of microbial imbalance—may aggravate clinical symptoms, compromise intestinal permeability, and amplify immune responses, thereby perpetuating a vicious cycle of disease pathogenesis.

Circulatory system

Chronic stress has significant adverse effects on the cardiovascular system, increasing the risk of developing cardiovascular disease. Studies show that in adults with increased atherosclerotic plaque burden, stress is a significant contributor to the onset of these conditions. Moreover, in patients already diagnosed with cardiovascular or cerebrovascular disease, chronic stress worsens prognosis and is associated with poorer treatment outcomes[16]. In recent years, there has been particular interest in the determination of hair cortisol levels as a biomarker of chronic stress in cardiovascular disease (CVD). This method allows quantitative assessment of the body's total exposure to cortisol over an extended period, making it a reliable diagnostic tool. The results of the study indicate that elevated hair cortisol levels correlate with both a higher incidence of cardiovascular disease and poorer recovery in patients[17]. Elevated cortisol levels have also been linked to the risk of developing hypertension. Although high blood pressure is a classic symptom of Cushing's syndrome, recent research suggests that cortisol may also play a role in the development of other forms of hypertension. Increasing evidence suggests that excess of the hormone may contribute to the development of primary hypertension[18]. Cardiovascular disease is one of the leading causes of morbidity and mortality in Cushing's syndrome, with the risk persisting even in properly treated patients. Excessive cortisol levels can lead, among other things, to elevated blood pressure[19]. In addition, studies involving people of similar age, same gender and from the same geographic region, regardless of their socioeconomic status and lifestyle, have shown that chronic stress significantly increases the risk of stroke, cardiovascular disease and worsens the prognosis of patients[20].

According to available data, chronic stress and elevated cortisol levels have negative effects on the cardiovascular system. They promote the elevation of blood pressure, the development of atherosclerosis and increase the risk of cardiovascular disease, and worsen the prognosis of patients. The use of cortisol as a biomarker may in the future provide a valuable tool in assessing the risk of these diseases.

Nervous system

The response to stress varies from person to person, as everyone copes with stressful situations in an individual way. The problem arises when, instead of undertaking effective coping strategies, an individual succumbs to the stressor, leading to a cascading response, referred to as "disease behavior".

Research shows that acute stress triggers adaptive responses, while chronic stress promotes chronic inflammation and leukocytosis, which can manifest as depressive symptoms[21]. Many long-standing studies confirm that stress hormones have a significant effect on the human brain. Glucocorticoid receptors are present in the hippocampus, amygdala and frontal cortex - structures responsible for emotion and memory. As a result of severe stress or its chronic effects, there is a reduction in the volume of the hippocampus, modulation of the volume of the amygdala and frontal cortex, due to the neurotoxic effects of stress hormones[22]. Chronic stress also causes functional and structural changes in the brain, especially in the hippocampus. Many years of research have shown that long-term stress impairs cognitive function by affecting the hippocampus. It is worth noting, however, that once the stress subsides, memory deficits often recover partially or completely[23]. In addition, chronic stress is an important factor in the development of neurodegenerative diseases. Skillful stress management plays a key role in maintaining quality of life and the ability to improve cognitive and emotional functioning. Alzheimer's disease results in cognitive and motor dysfunction, which in itself can be a source of stress and lead to further dysfunction within the nervous system. Disruption of normal neural circuits can result in aggressive or destructive behavior[24]. As we can see, the relationship between chronic stress, cortisol secretion and nervous system function highlights the significant impact mental factors can have on brain health. Changes in the structure and function of the central nervous system can not only impair cognitive abilities, but

also increase susceptibility to the development of neurodegenerative diseases, as exemplified by Alzheimer's disease. Learning about these relationships opens up new opportunities for early diagnosis and preventive measures aimed at neurological health.

Strategies for reducing chronic stress

Psychological techniques

Chronic stress wreaks havoc on the body, as has been confirmed by many studies. It negatively affects the functioning of all systems and organs, so it is important to implement various psychological techniques that can help reduce its effects. Stress-reducing psychological interventions, such as guided relaxation, biofeedback-assisted relaxation, mindfulness training or hypnosis, can contribute to reducing subjective feelings of stress and alleviating pain[25]. One publication evaluated the effectiveness of sixteen Behavioral Stress Reduction Programs (BSRPs) in multiple studies. BSRPs have been shown to have the potential not only to increase the effectiveness of medical therapies, but also to halt or reverse the progression of diseases[26]. In addition, research indicates that cognitive and behavioral techniques can be supported by mindfulness-based practices. Mindfulness-Based Interventions (MBIs) have shown effectiveness in reducing the severity of anxiety and depressive symptoms in a large number of people. Importantly, MBIs are superior in their effectiveness to non-evidence-based treatments, as well as classic relaxation techniques[27]. In summary, psychological stress reduction techniques, including behavioral interventions and mindfulness-based practices, represent effective tools for mitigating the adverse effects of chronic stress. A substantial body of evidence confirms that methods such as guided relaxation, biofeedback, mindfulness training, and hypnosis can significantly reduce subjective stress perception and alleviate pain. Consequently, these interventions improve patients' quality of life and support the treatment process across various medical conditions.

An illustrative example of the efficacy of this approach is the evaluation of sixteen Behavioral Stress Reduction Programs (BSRPs), which demonstrated not only an enhancement of medical therapy effectiveness but also the capacity to halt or reverse disease progression. These programs, integrating cognitive-behavioral and relaxation techniques, provide patients with practical strategies to manage stress, thereby leading to improved therapeutic outcomes.

Among stress reduction techniques, mindfulness-based interventions (MBIs) have gained increasing recognition in recent years. Research shows that MBIs effectively reduce the severity of anxiety and depressive symptoms while improving overall emotional functioning. Importantly, MBIs have demonstrated superior efficacy compared to traditional relaxation techniques and non-evidence-based methods, as confirmed by numerous meta-analyses and controlled trials. Due to their flexibility and relative ease of integration into daily life, mindfulness and other psychological techniques can be readily adopted by patients, enhancing both their effectiveness and the durability of therapeutic benefits.

In light of these findings, the implementation of psychological techniques in the management of chronic stress is not only justified but essential. Integrating these methods with conventional therapeutic strategies can significantly enhance patients' quality of life and treatment efficacy. The inclusion of standardized stress reduction programs into clinical practice should be considered an integral component of modern medicine, particularly in diseases where psychological factors play a significant role

Lifestyle

Lifestyle plays an important role in reducing chronic stress. Studies indicate that regular physical activity significantly reduces the level of perceived stress. People who undertake regular exercise show lower concentrations of cortisol, which translates into less negative effects of this hormone on the human body[28]. Another study evaluated the effects of meditation on mental stress levels in women with breast cancer. The practice of meditation was shown to have significant benefits, reducing physical and emotional symptoms such as anxiety, mental stress and depression[29]. Also, lifestyle, including proper sleep hygiene, plays an important role in reducing symptoms of anxiety, depression and lowering stress levels. Findings from studies involving a large group of people suggest that a health-promoting lifestyle can be a beneficial, cost-effective alternative to traditional treatments, with multidimensional mental health benefits[30]. A healthy lifestyle encompassing regular physical activity, relaxation techniques such as meditation, proper sleep hygiene, and other health-promoting habits constitutes a key element in reducing chronic stress and its detrimental effects on the body. The implementation of these healthy behaviors can effectively lower cortisol levels—one of the primary stress hormones—and mitigate its harmful impact on the nervous, hormonal, and immune systems. Consequently,

mental health improves, providing essential support in the prevention and treatment of chronic stress and its associated disorders.

Moreover, lifestyle factors can serve as important adjuncts to psychological and medical therapies. Incorporating healthy habits into daily routines enhances the effectiveness of interventions such as behavioral stress reduction techniques and mindfulness-based practices. This holistic approach addresses both physical and psychological aspects of health, leading to better therapeutic outcomes and an improved quality of life for patients.

In light of numerous studies, promoting a healthy lifestyle should be an integral part of strategies aimed at combating chronic stress at both individual and systemic levels. Health education and preventive programs focusing on increased physical activity, improved sleep quality, and relaxation training may serve as effective tools to reduce societal stress burden. Such initiatives benefit not only individuals but also have the potential to decrease healthcare costs associated with treating stress-related disorders.

To conclude, the prevention and management of chronic stress require a multidimensional approach in which a healthy lifestyle plays a role as significant as psychological interventions. Integrating these elements into clinical practice and patients' everyday lives may yield lasting health benefits, enhance mental functioning, and reduce the risk of developing numerous chronic somatic and psychiatric conditions.

Conclusions

Chronic stress and the associated increase in cortisol have multifaceted effects on the functioning of the human body, with particular emphasis on the metabolic, digestive and cardiovascular systems. Mechanisms of cortisol action include modulation of carbohydrate, lipid and protein metabolism, which in the long term leads to the development of insulin resistance, dyslipidemia and obesity - factors that predispose to the development of metabolic syndrome and type 2 diabetes.

In addition, the chronic effects of cortisol affect the integrity and function of the gastrointestinal tract through impaired gastrointestinal motility, increased susceptibility to inflammation and intestinal dysbiosis, which translates into impaired digestion and absorption of nutrients. At the same time, chronic stress and elevated levels of cortisol promote cardiovascular dysfunction, manifested by hypertension, increased activation of the sympathetic nervous system and increased atherosclerotic processes, which significantly increases the risk of cardiovascular incidents.

In light of accumulated evidence, chronic stress and hyperactivation of the hypothalamic-pituitary-adrenal axis are important pathogenetic factors in the development of numerous chronic conditions. Understanding these mechanisms is essential for the development of effective preventive and therapeutic strategies that can contribute to improving the health of the population and the quality of life of individuals exposed to long-term stress.

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