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Impact of Stress on the Brain: Neurobiological Mechanisms and Long-Term Consequences for Mental Health

Dmytro Kuiavets
PhD Candidate at Pavlo Tychyna Uman State Pedagogical University, Kyiv, Ukraine, dmytro.kuiavets@gmail.com, https://orcid.org/0009-0006-0986-3648

Olena Boiarchuk
Candidate of Biological Sciences, Associate Professor, Associate Professor of the Department of Health Care and Rehabilitation, Luhansk Taras Shevchenko National University, Poltava region, Lubny, Ukraine, boiarchuk.helen@gmail.com, https://orcid.org/0000-0002-4388-6011

Nataliia Levchuk
Candidate of Pedagogic Sciences, Associate Professor,Associate Professor of the Department of Biology, Vinnytsia Mekhailo Kotsiubynskyi State Pedagogical University, Vinnytsia, Ukraine, levchuknatalia@gmail.com, https://orcid.org/0000-0003-0782-8903

Tetiana Dziuba
Ph.D. Candidate of Psychological Sciences, Associate Professor, Department of Crisis Psychology, V. G. Korolenko Poltava National Pedagogical University, Poltava, Ukraine, tatjanadzuba@gmail.com, https://orcid.org/0000-0002-5950-7741

Abstract: *The article examines the concept of 'stress', highlighting both its negative and positive effects on a person's mental and physical state. The aim of the study is to clarify the concept of 'stress', review scientific sources regarding the neurobiological mechanisms of the stress response, and identify the consequences that chronic stress may have on cognitive and emotional brain functions, as well as to explore methods of rehabilitation for such conditions. Research methods: Critical analysis of scientific literature, comparison of scientific theories on the classification of stress and its types, and generalisation of neurobiological data on the effects of prolonged stress on brain structures, including the hippocampus, amygdala, and prefrontal cortex. Research results demonstrate that prolonged stress can transition into chronic stress, which in turn increases the activity of the hypothalamic-pituitary-adrenal axis, leading to the release of stress hormones: adrenaline, cortisol, and noradrenaline. As a result, individuals may experience depression, cognitive impairments, and heightened anxiety. Attention is also drawn to the interconnection between stress, the immune system, and the underlying epigenetic mechanisms. Scientific novelty lies in the holistic approach to analysing stress as a neuropsychobiological phenomenon, encompassing all levels from molecular processes to behavioural manifestations. A conceptual framework is proposed for using psychotechnologies of adaptive self-regulation as a tool for strengthening stress resilience and preventing mental disorders.*

Keywords: *stress; brain; neurobiology; cortisol; cognitive functions; depression; PTSD; neuroinflammation; self-regulation.*

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Olexiy Granovski
Ph.D. Associate Professor of the Department of Health Care and Rehabilitation, Luhansk Taras Shevchenko National University, Poltava region, Lubny, Ukraine, granovskyalexey77@gmail.com, https://orcid.org/0009-0001-5220-7420

Iryna Chorna
Candidate of Psychological Sciences, Associate Professor, Associate Professor of the Department of Psychology, Ternopil Ivan Pulyuy National Technical University, Ternopil, Ukraine, irynachorna-@ukr.net, https://orcid.org/0000-0001-6947-1140

1. Introduction

Stress is an integral part of modern life, but its chronic impact can have serious consequences for brain functioning and mental health.

Relevance of the topic. In the modern world, stress has transformed from an episodic adaptive reaction into a permanent state of human life activity. This problem becomes particularly acute in the context of global crises — the consequences of the COVID-19 pandemic and prolonged military conflicts, which generate an unprecedented level of chronic and traumatic stress. Despite the significant number of studies, the mechanisms of how stress transforms from a physiological norm into a destructive neurobiological process that damages brain structures (the hippocampus and the prefrontal cortex) and provokes neuroinflammation require deeper synthesis. Understanding the molecular and epigenetic aspects of this stress response is critically important for the development of effective rehabilitation strategies and for the prevention of depressive disorders, PTSD, and cognitive deficits, which is of strategic importance for preserving the mental health of the nation.

As is well known, neuroscientists have demonstrated that prolonged stress alters the very structure of brain regions, particularly the hippocampus, amygdala, and prefrontal cortex, which undergo functional changes (McEwen et al., 2016). These negative changes increase the risk of anxiety, mental disorders, and depression.

This article examines the key mechanisms of stress impact on the brain and the long-term consequences for an individual's psycho-emotional state.

The aim of the article is to clarify the concept of 'stress', review publications on the effects of stress on the brain, identify neurobiological mechanisms, determine the long-term consequences for mental health, and propose rehabilitation methods for affected individuals.

So, let us clarify the meaning of the term 'stress'. The Dictionary defines stress as "a state of the organism manifested in the form of tension or specific adaptive reactions in response to adverse external or internal factors" (Bilodid, 1970–1980).

The World Health Organisation defines the term as: "stress is a nonspecific (the same for different stimuli) reaction of the organism to any demand made upon it" (Nauholnyk, 2015).

Among the causes of stress, scientists include "any strong emotion, most often fear, anger, resentment, and even excessive joy. The causes of stress also include psychophysiological states such as fatigue, tension, anxiety, and monotony" (Rozov, 2005, p. 11).

Hans Selye, a Canadian physiologist, introduced the concept of 'stress' into scientific research as early as 1936, publishing his work in the journal *Nature* (Selye, 1936). In that article, he referred to stress as harmful factors affecting the body ('injury', 'intoxication', 'destructive agent'), viewing stress solely as a negative phenomenon. Later, in 1950, Selye published a comprehensive article, *The Physiology and Pathology of Stress*, in which he emphasised that stress should not be treated, but rather prevented or managed through the ability to live with it.

His approach laid the foundation for a new field of science, although many ideas have since been revised. Like Freud's psychoanalysis, Selye's theory spurred deeper research. The world-renowned scientist stated: "We should not avoid stress. But we can use it and enjoy it. If we better understand its mechanism, we will develop an appropriate philosophy of life" (Nauholnyk, 2015).

A distinctive feature of this review is the synthesis of fundamental neurobiological knowledge with the analysis of specific contemporary stress factors, such as the COVID-19 pandemic and military actions. This makes it possible not only to describe a theoretical model of stress but also to adapt it to the real conditions of 'multifactorial distress' in which the modern population exists, making the work practically oriented toward the development of neurorehabilitation strategies.

2. Stress Mechanisms of the Brain: Adaptation, Damage, and Consequences for Mental Health

The concept of stress as a biological phenomenon emerged more than a century ago. The well-known American psychophysiologist Walter Cannon was the first to highlight in his works how rapidly the autonomic nervous system responds to threats to the body (Aki & Nestler, 2023).

It is worth noting the significant work by Cannon and De La Paz (1911), in which the authors emphasised that the autonomic nervous system is the primary system in the body, as it constantly maintains balance and ensures internal equilibrium (homeostasis). The researcher demonstrated that it is precisely homeostasis that immediately triggers mechanisms aimed at restoring stability whenever there is any deviation from the state of balance.

Cannon and De La Paz (1911) integrated his theory of emotions with the concept of homeostasis, expanding understanding of human responses - from physiological states to psychological stress. In the second edition of his work *The Wisdom of the Body* (Cannon, 1963), he emphasised that the release of adrenaline into the bloodstream serves numerous adaptive functions. These functions prepare the body for danger - either by mobilising internal resources or by facilitating escape from threats. Adrenaline generally affects different body systems in various ways, yet simultaneously helps maintain internal stability. It is noteworthy that at that time Cannon did not use the term ‘stress’, but his publications were entirely focused on studying the body’s powerful reactions in extreme situations.

Later, Hans Selye (Aki & Nestler, 2023) studied the effects of prolonged stress and described them as the general adaptation syndrome, which is associated with activation of the pituitary gland and adrenal glands. By the mid-20th century, the development of neuroendocrinology made it possible to establish that the brain plays a leading role in regulating stress responses. Since then, the mechanisms of the hypothalamic-pituitar-adrenal (HPA) axis, which is the main pathway for forming the body’s stress response, have been studied in detail.

The main elements of this mechanism are: Corticotropin-releasing factor (CRF) – a substance released by the hypothalamus that triggers the hormonal response; Adrenocorticotropic hormone (ACTH) – produced in the pituitary gland, released into the bloodstream, and stimulates the adrenal glands to synthesise glucocorticoids (in humans, this is cortisol, and in animals, corticosterone); Glucocorticoids act on the body’s cells through two types of receptors: glucocorticoid receptor (GR) and mineralocorticoid receptor (MR). They regulate energy use, glucose metabolism, and the general physiological stress response. In the brain, particularly in the hippocampus, there is a high concentration of these receptors. They regulate neuronal activity through both genomic and non-genomic mechanisms.

GR activation in the brain (particularly in the hippocampus and cortex) signals excess stress hormones and triggers negative feedback to halt further endocrine activation.

These substances cause the onset of depression and other psychological disorders. For example, in one of Binder’s studies (Binder, 2009), the relationship between GR activity, genetic mechanisms, and stressful situations-targeted for the development of new medications-was presented. Scientists generally distinguish four types of stress: physical, metabolic, physiological, and psychosocial. Responses to them depend on personal characteristics, prior experiences, and the context in which stress occurs. However, all ultimately activate the HPA axis, initiating a common physiological response.

In the article by Krupa et al. (2025), the authors emphasise that prolonged chronic stress, caused by environmental, social, or personal factors, activates major physiological systems: the hypothalamic-pituitary-adrenal (HPA) axis and the autonomic nervous system. This leads to increased production of cortisol and other hormones. While this mechanism supports adaptation in the short term, its prolonged activation can damage key brain regions, particularly the hippocampus, amygdala, and prefrontal cortex. Dysfunction in these structures results in difficulties with emotion regulation, memory, decision-making, and reduces overall stress resilience.

Attention should also be given to the theoretical study by McEwen et al. (2015), which highlights that the brain is the central organ determining perception and adaptation to social and physical stressors. These processes occur through a wide range of interacting mechanisms - from membrane receptors and cytoskeletal elements to epigenetic regulation and non-genomic pathways. The response to stress involves structural remodeling of neural networks, which may indicate effective adaptation. However, if such changes persist after the stressor is removed, this may reflect insufficient resilience of the neural architecture. Central to these processes are excitatory amino acids and glucocorticoids, along with an expanding range of both extracellular and intracellular mediators, including endocannabinoids and brain-derived neurotrophic factor (BDNF). The result of these interactions is dynamic gene expression changes, regulated by epigenetic mechanisms such as histone modifications, methylation and hydroxymethylation of CpG islands, and the activity of retrotransposons capable of affecting genomic stability.

The study of mechanisms that determine brain plasticity and vulnerability forms the basis for developing new therapeutic approaches in the treatment of anxiety and depressive disorders, as well as cognitive impairments associated with aging. In the work by McEwen (2006), both protective and potentially harmful effects of stress mediators are analysed, with the brain occupying a central role in these processes. It is the brain that determines what is perceived as stress and shapes physiological and behavioural responses, interacting with the cardiovascular, immune, and other body systems. Stressors - whether large-scale events or daily challenges - can trigger processes leading to allostatic load, that is, the exhaustion of the body due to constant strain on regulatory systems. Combined with genetic predispositions, behavioural patterns, and social conditions, this may contribute to the development of various diseases.

Although stress hormones temporarily protect and help in adaptation, chronic stress negatively affects the brain, especially the hippocampus, amygdala, and prefrontal cortex, altering their structure and functions. In addition to pharmacological treatment, lifestyle changes and support measures at the socio-political level make a significant contribution to reducing stress levels.

Caradonna et al. (2022) emphasise that the multifactorial nature of stress-related disorders requires an in-depth study of molecular mechanisms in preclinical models. For this purpose, researchers consider different types of stressors, from environmental factors to genetic predispositions, which shape the patterns of hormonal regulation. Using RNA sequencing, they analysed genomic changes in the ventral hippocampus of mice exposed to chronic oral corticosterone (CORT) and chronic social defeat stress (CSDS).

In these models, genes common to the stress response were identified, which are involved in the regulation of neurotransmission, cytoskeleton formation, and vascularisation processes. Among them, genes determining resistance or sensitivity to stress were found, activated both in the case of CORT and during CSDS. This allowed researchers to demonstrate the existence of shared genomic mechanisms underlying the multifactorial nature of stress-related disorders and to emphasise the need to consider hormonal, environmental, and genetic influences in such studies.

Tank and Wong (2015) emphasise that acute stress is a real threat that negatively affects the maintenance of the body’s internal balance. Such stress is caused by both physical and psychological factors. In a situation of acute stress, the body instantly activates the autonomic nervous system and neuroendocrine regulatory mechanisms. This causes physiological changes that ensure a rapid response to danger and restore balance after its removal. Under the influence of the autonomic nervous system, the adrenal glands release adrenaline, while the adrenal glands together with nerve endings release noradrenaline. These hormones interact with adrenergic receptors in various organs and tissues. Additionally, catecholamines (adrenaline and noradrenaline) are released in the brain, where they affect receptors of the central nervous system. The action of these catecholamines is short-term - lasting less than an hour - and includes increased cardiac activity, redistribution of the body’s energy resources, and maintenance of heightened alertness.

Over the past two decades, neurobiologists have devoted significant attention to the study of physical and psychological stress. This interest has led to the development of more precise animal models for investigating stress-related pathologies and exploring ways to treat them. These models allow for easy and effective differentiation between psychological and physical stress. To understand the behavioural changes underlying major depression, molecular and cellular studies are necessary. If the balance of a person's internal state is disrupted, the likelihood of developing psychological disorders arises. Neurobiologists first identify the type of stress and then assess its impact through neuromediators. In addition, the factors that caused the stress are determined, and only then is a plan for pharmacological or non-pharmacological treatment developed. In India and the Western world, the use of herbal remedies for stress treatment is becoming widespread, creating a large market for anti-stress products. Non-pharmacological methods, such as meditation and yoga, are gaining increasing popularity due to their effectiveness and lack of side effects.

The article summarises the changes caused by stress. In addition, to better study the effects of stress, animal models are selected for research. Stress is extremely common today, and, as is known, all living organisms are capable of coping with it. Prolonged stress causes negative consequences in the body and activates the neuroendocrine system, specifically the limbic system, hypothalamus, pituitary gland, and adrenal glands. Moreover, it interferes with hormonal mechanisms, including the production of corticosterone. Chronic stress can lead to mental disorders such as anxiety or depression, which are accompanied by excessive formation of free radicals and oxidative stress. Various stressors activate complex interactions of hormones and neural signals, resulting in both behavioural (e.g., anxiety, loss of appetite, reduced sexual activity, and impaired cognitive functions) and physiological responses (activation of the hypothalamic-pituitary-adrenal axis, increased levels of glucocorticoids). Such stressors induce physiological changes, such as elevated body temperature and accelerated heart rate, as well as behavioural changes.

Kocamer Şahin and Aslan (2024) believe that stress is considered to arise when the body deviates from its usual state of equilibrium due to a real or perceived threat. Stress responses are necessary to adapt to environmental changes and for an adequate reaction to a threat. However, this defense mechanism should be switched off after the threat is eliminated. If a state of anxiety persists for too long, the system becomes unstable. Prolonged stress can negatively affect brain functioning and contribute to the development of mental disorders. Chronic stress is also associated with serious diseases such as cancer, diabetes, and cardiovascular diseases. Psychological stress usually arises from emotional tension, life difficulties, and mental discomfort. The main factors leading to it include misunderstandings at work, physical injuries, frustration, betrayal, family problems, unexpected events, or unmet basic needs.

Psychological stress differs from mechanical stress (e.g., bone fractures or burns), although both can trigger inflammatory processes. However, this review examines psychological stress specifically. Traumatic stress affects cognitive functions. For example, in post-traumatic stress disorder (PTSD), problems with concentration, memory, and decision-making are observed. Inflammatory processes can worsen cognitive function. In particular, pro-inflammatory agents such as cytokines and activated microglia are involved in stress-induced brain dysfunction. This review examines the sequence: stress → subclinical inflammation → cognitive impairment (see Table 1).

Studies show that stress is associated with inflammatory processes. This is confirmed by the fact that people with autoimmune and inflammatory diseases (for example, diabetes or fibromyalgia) often exhibit depressive symptoms (Sedda et al., 2025). The level of pro-inflammatory cytokines increases in post-traumatic stress disorder (PTSD), depression, and other mental disorders, prompting the study of causal relationships. Stress mobilises the body and leads to physiological changes such as increased glucose levels, blood pressure, and heart rate (American Psychological Association, 2023). This inflammatory response, occurring through activation of the nervous system and release of inflammatory cytokines, is regulated by the hypothalamic-pituitary-adrenal (HPA) axis and the hormone cortisol. Acute stress, which is mild or short-term, does not cause significant inflammation. However, prolonged stress can increase the

body's sensitivity to inflammation. Cortisol plays an important role in cognitive function and behaviour. In the case of chronic stress, such as in depression, glucocorticoid resistance may develop in the hypothalamic-pituitary-adrenal axis, allowing inflammatory processes to persist without negative feedback (Knezevic et al., 2023). This can lead to neuroinflammatory changes in the brain: high levels of cortisol stimulate microglia, resulting in the production of more pro-inflammatory substances, which negatively affect nerve cells and cognitive functions.

Table 1. Empirical Data on the Effects of Stress on the Brain and Mental Health

№	Author(s), Year	Model or Object of Study	Type of Stress	Key Findings
1	Cannon W.B., 1911, 1963	Humans, animals (physiology)	Acute stress ('fight or flight' response)	Adrenaline release → increased heart rate, energy mobilisation. Stress = adaptive response via the autonomic nervous system.
2	Selye H., 1950-ті	Rats	Chronic stress	Developed the concept of 'general adaptation syndrome'; activation of pituitary and adrenal glands, physiological exhaustion.
3	McEwen (2006) McEwen et al. (2015)	Humans, animals	Chronic psychosocial stress	Structural changes in hippocampus, prefrontal cortex, and amygdala; allostatic load occurs. Microglia activated, BDNF decreases, neuroplasticity impaired.
4	Krupa et al. (2025)	Hypothalamic–pituitary–adrenal (HPA) axis (animal model)	Chronic social and environmental stress	Reduced hippocampal volume; memory and emotional regulation impairments. Increased cortisol → neurotoxicity.
5	Caradonna et al. (2022)	Mice, CSDS and CORT models	Chronic social stress, chronic hormonal load	Shared genetic mechanisms in CSDS and CORT; changes in gene expression related to stress resilience. Genes regulating neurotransmission, cytoskeleton, and vascular function identified.
6	Kumar et al. (2012)	Rat models	Psychological and physical stress	Chronic stress → depression, cognitive impairments, decreased neurotransmitters. Studied effectiveness of herbs and non-pharmacological interventions (yoga, meditation).
7	Tank and Wong (2015)	Neurophysiological models	Acute stress	Release of adrenaline and noradrenaline → short-term activation of heart, muscles, brain. Temporary increase in attention.
8	Kocamer Şahin Ş., Aslan E. (2024)	Theoretical analysis, review	Chronic psychological stress	Chronic stress → decreased concentration, cognitive impairments. Inflammatory process occurs, microglia activated, pro-inflammatory cytokines released.
9	Aki Hl, Nestler E.J. (2023)	Review	Psychological, biological stress	Stress causes changes in gene expression related to depression. Potential targets for pharmacological intervention.
10	Binder E.B., study of GR receptors (cited in Nestler, 2023)	Humans (genetic studies)	Genetic susceptibility to stress	GR receptor polymorphism affects the risk of developing depression; stress influences the regulation of the NR3C1 gene.

3. Classification of Stress States and Psychosocial Consequences of Chronic Strain

According to Sharma (2018), stress states can be classified by their nature, duration, and impact on the body, and they can have both positive and negative consequences.

Some stress situations can be pleasant, inspiring, and motivating. This type of stress is called **eustress**. It can activate the body, improve cardiovascular function, increase endurance, sharpen

attention, and enhance cognitive abilities. Not all stress is harmful. Some stress situations can be enjoyable, stimulating, and motivating. This type of stress, known as eustress, can be beneficial by energising the body, improving heart and vascular function, increasing stamina, enhancing focus, and improving cognitive performance. This view is supported by Chu et al. (2024). Such positive stress, or eustress, energises the body, supports cardiovascular function, increases endurance, and enhances mental activity. Eustress improves concentration, promotes clarity of thought, and stimulates intrinsic motivation.

In contrast, **distress** is a state that negatively affects physical and mental health. Distress is accompanied by feelings of anxiety, tension, dissatisfaction, and often reduces overall performance.

4. Acute, Episodic, and Chronic Stress

Acute stress occurs unexpectedly and is caused by a sudden, unexpected situation. A person immediately experiences emotional fluctuations such as anger, anxiety, irritation, and mood deterioration. Sometimes these changes may occur during sports or other competitive events.

Episodic acute stress is observed in individuals who frequently face a series of stressful events. It appears in highly emotional and ambitious people who often encounter multiple stressors. This type of stress arises occasionally but tends to repeat frequently.

Chronic stress results from prolonged exposure to negative factors. It is not always as intense as acute stress, but it is more destructive due to its cumulative effect. Extended stress pressure harms not only the body but also the psyche.

Chu et al. (2024) add, in the classification of stress by duration, source, and response, **traumatic stress** - which arises from exposure to intense, shocking events such as natural disasters, serious accidents, or acts of violence. These events exceed an individual's ability to cope with psychological challenges and may lead to **post-traumatic stress disorder (PTSD)**, characterised by intrusive memories, avoidance of triggers, and heightened nervous excitability.

Environmental stress occurs due to adverse external conditions, such as noise, pollution, overcrowding, or a threatening environment. These factors can cause prolonged tension, reduced well-being, and increased anxiety.

Psychological stress is usually caused by internal emotional experiences, such as fear, excessive expectations, social pressure, or low self-esteem. It manifests as constant anxiety, intrusive thoughts, tendencies toward perfectionism, or persistent self-criticism.

Physiological stress is the body's reaction to physical factors that worsen rather than improve its state. Triggers may include illnesses, physical injuries, chronic sleep deprivation, or deficiencies in essential nutrients. Initially, this stress mobilises biological defense mechanisms, but prolonged exposure leads to deterioration of the body's condition.

Lukashenko (2019) emphasises the importance of studying the psychological state of military personnel to provide timely psychological support. The researcher demonstrates that men who have participated in combat belong to a high-risk group for developing psychogenic disorders.

Psychological trauma resulting from combat falls under the classification of **post-traumatic stress disorder (PTSD)** (the term 'Post-traumatic Stress Disorder' was introduced into scientific use in 1980 by M. Horowitz and B. Dohrenwend). Consequences of combat-related stress include symptoms of **'psychological defense'** (explicit or feigned amnesia, mental inhibition, avoidance of memories or associations with traumatic events) and **'return'** (intrusive memories, fears, sleep disturbances, nightmares, overwhelming anxiety, loss of joy and calm).

During the COVID-19 pandemic, according to research by Lin and Yeh (2023), people were widely exposed to numerous stressors, such as fear for their own health and life, anxiety for loved ones, social isolation, and loss of jobs or income. This led to an increase in cases of mental disorders, including depression, anxiety, PTSD, as well as greater use of psychoactive substances. Individuals with pre-existing mental illnesses were particularly vulnerable to COVID-19, and a further rise in stress-related disorders is expected after the pandemic. The COVID-19 pandemic disproportionately affected vulnerable population groups, including low-income individuals and

members of virus-impacted communities, who already faced inequality due to systemic racism. Beyond the social impact, COVID-19 also caused serious neuropsychological complications (Narayanan et al., 2025). Patients often experienced cognitive impairments, disorientation, memory problems, sleep disturbances, anxiety, depression, and sometimes even new psychiatric symptoms.

The causes include complications of the disease itself, inflammation, thrombosis, and the direct effects of the virus on the brain. Recent studies indicate that up to 40% of patients who have recovered from COVID-19 may suffer from prolonged psychological symptoms. It has also been found that individuals with prior mental disorders have poorer prognoses if infected with the virus.

In summary, prolonged stress can lead to mental disorders such as anxiety or depression, accompanied by increased production of free radicals and oxidative stress. Moreover, this type of stress may be associated with serious illnesses, including cancer, diabetes, and cardiovascular problems.

According to Rozov (2005), the use of psychotechnologies for adaptive self-regulation not only reduces stress levels but also enhances stress resilience, supports psychological well-being, and promotes overall health. This is particularly important in conditions of heightened emotional and physical load in modern life. Table 2 contains a classification of stress states and their psycholosocial consequences.

Table 2: Classification of Stress States and Their Psychosocial Consequences

Type of Stress	**Characteristics**	**Possible Consequences / Symptoms**	**Sources**
Eustress (positive stress)	Short-term, stimulating. Activates body resources.	Increased endurance, improved cognitive functions, clarity of thought.	Sharma (2018)
Distress	Causes emotional, physical, and mental strain.	Anxiety, reduced performance, emotional exhaustion	Sharma (2018)
Acute stress	Sudden, short-term, response to a specific situation.	Emotional outbursts, anger, anxiety, temporary low mood.	Sharma (2018)
Episodic acute stress	Recurrent, periodic, triggered by regular stressors.	Persistent tension, fatigue, risk of progression to chronic stress.	Sharma (2018)
Chronic stress	Prolonged exposure to stress-inducing factors.	Depression, anxiety disorders, PTSD, chronic diseases (cancer, diabetes, CVD), cognitive impairments.	Sharma (2018)
Traumatic stress	Occurs due to severe shock events.	Intrusive memories, fear, amnesia, mental inhibition, anxiety, nightmares.	Chu et al. (2024), Lukashenko. (2019)
Environmental stress	Exposure to adverse environmental conditions.	Chronic anxiety, worsened well-being, sleep disturbances.	Chu et al. (2024)
Psychological stress	Internal experiences, perceived threats.	Anxiety, perfectionism, obsessive thoughts, self-blame.	Chu et al. (2024)
Physiological stress	Physical stimuli or illness.	Weakened health, exhaustion, biochemical imbalance.	Chu et al. (2024)
COVID-19 and post-pandemic stress	Fear, isolation, economic instability.	Depression, anxiety, psychotic symptoms, cognitive impairments.	Ned (2021)

5. Conclusion

The article traces the evolution of the concept of stress from the classical works of Walter Cannon and Hans Selye to the modern models of allostasis developed by Bruce McEwen. This creates a solid foundation for understanding the subject of the study. A significant advantage of the work is the clear and logical explanation of the functioning of the hypothalamic–pituitary–adrenal (HPA) axis. Particularly valuable is the analysis of the interaction between glucocorticoid (GR) and

mineralocorticoid (MR) receptors, which is key to understanding the differentiation between adaptive stress and a pathological state.

The inclusion in the review of epigenetic processes (methylation of CpG islands, activity of retrotransposons) and the analysis of the role of brain-derived neurotrophic factor (BDNF) brings the article to the contemporary level of neurobiological research.

Prolonged stress triggers rapid physiological responses through systems such as the HPA axis and the autonomic nervous system. Over time, it also induces lasting changes in brain function, neural cells, and behaviour, which can negatively affect both physical and mental health.

Despite these risks, modern science already offers proven ways to protect against stress: self-regulation techniques, psychological support, medical interventions, and lifestyle changes that help minimise harmful consequences.

In particular, the use of adaptive self-regulation psychotechnologies, such as stress-reducing nutrition, phytotherapy, physical activity, as well as psychotherapeutic and neuropharmacological approaches, provides ways to strengthen stress resilience, prevention, and rehabilitation.

To effectively protect mental health in today's challenging conditions, it is essential to understand how stress functions in the brain and body and what consequences it entails. This knowledge enables scientists to develop effective methods for prevention and support for individuals.

Statement on the Use of Artificial Intelligence

Artificial intelligence tools were used at certain stages of the preparation of this manuscript to support language editing, translation, and improvement of textual clarity. The authors maintained full responsibility for the conceptualisation of the study, data interpretation, and the final content of the manuscript. The use of AI technologies did not influence the scientific conclusions of the research and served solely as an auxiliary instrument for improving the quality of the presentation.

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