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PATHOGENETIC AND PROTECTIVE ASPECTS OF IMMOBILIZATION STRESS

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ABSTRACT

The study of the protective and pathogenetic aspects of immobilization stress remains an important area of modern clinical physiology and pathophysiology. At the current stage of development of experimental and clinical medicine, stress and its accompanying comorbid pathologies are the foundation for a number of psychosomatic diseases. Such disorders are a widespread maladaptive phenomenon. To fully restore central nervous system function after stressful exposure, it was necessary to investigate the mechanisms of post-stress complications and the interrelationships between changes in brain function and metabolism, thereby providing a comprehensive and integrated approach to unraveling the pathogenesis of stress complications. The aim of this study is to comparatively analyze the effects of acute and chronic immobilization stress on tissue-specific changes in central neuronal structures. The results of the study showed that an increase in cortisol, accompanied by a decrease in catecholamines and serotonin, reflects a depleted stress response, while an increase in autoantibodies to proteins and receptors indicates the development of neuroimmune aggression. Analysis of the obtained data confirms that the ELIN test, in combination with hormonal profiling, is a sensitive tool for the early detection of stress-induced disorders and can be used to predict neurodegenerative and psychoemotional disorders associated with chronic stress.

Introduction

Throughout life, people are constantly exposed to physical, emotional, and psychological factors that trigger stress reactions. These stress reactions can lead to a decrease in the body's immune system, thereby increasing the risk of developing infectious, allergic, and neoplastic diseases. It is known that under the influence of stress (trauma, surgery, excessive psychoemotional stress,

etc.), the course of acute and chronic diseases differs from their classic manifestations [1, 2]. Therefore, the search for pathogenetic mechanisms that underlie disease development during stress is a pressing and necessary task for modern science [3].

Chronic immobilization stress negatively impacts the central nervous system, causing structural and functional changes such as decreased gray matter volume, impaired neuroplasticity, disruptions in neurotransmitter systems (especially glutamate and GABA), and neuronal death. This leads to cognitive impairments, such as memory and attention problems, and also increases the risk of developing neurodegenerative diseases. Prolonged immobilization stress is accompanied by changes in plasma metabolism in rats: activation of catabolic reactions (decreased levels of glycosaminoglycans and hexosamines, inhibition of hexosamine synthetase activity), followed by a predominance of anabolic processes. The nature of changes in biopolymer metabolism in connective tissue correlates with blood glucocorticoid hormone levels: an increase in their levels leads to a decrease in anabolic processes. A significant depletion of phospholipids in the prefrontal cortex of rats was observed under prolonged immobilization.

Immobilization stress has a dual effect on the body: on the one hand, it triggers protective and adaptive mechanisms, while on the other, excessive and chronic activation leads to the development of pathogenic processes. The most pronounced changes develop in the central nervous system, cardiovascular system, respiratory system, and kidneys [4, 5, 6].

Damage to barrier structures, endothelial dysfunction, oxidative stress, and shifts in neurohumoral regulation form the basis for the development of neurological and psychiatric disorders, as well as cardiovascular, respiratory, and nephrological diseases.

The study of the protective and pathogenetic aspects of immobilization stress remains an important area of modern clinical physiology and pathophysiology. At the current stage of development of experimental and clinical medicine, stress and its accompanying comorbid pathologies are the foundation for a number of psychosomatic diseases. Such disorders are a widespread maladaptive phenomenon. To fully restore central nervous system function after stress, it was necessary to investigate the mechanisms of post-stress complications and the interrelationships between changes in brain function and metabolism, thereby providing a comprehensive, integrated approach to unraveling the pathogenesis of stress

complications. This integrated approach is an important tool for assessing changes in various systems and processes and combines multiple indicators into a single indicator that provides a complete picture of the dynamics and quality of ongoing changes. The above allows us to conclude that the topic under study is relevant in both theoretical and practical terms.

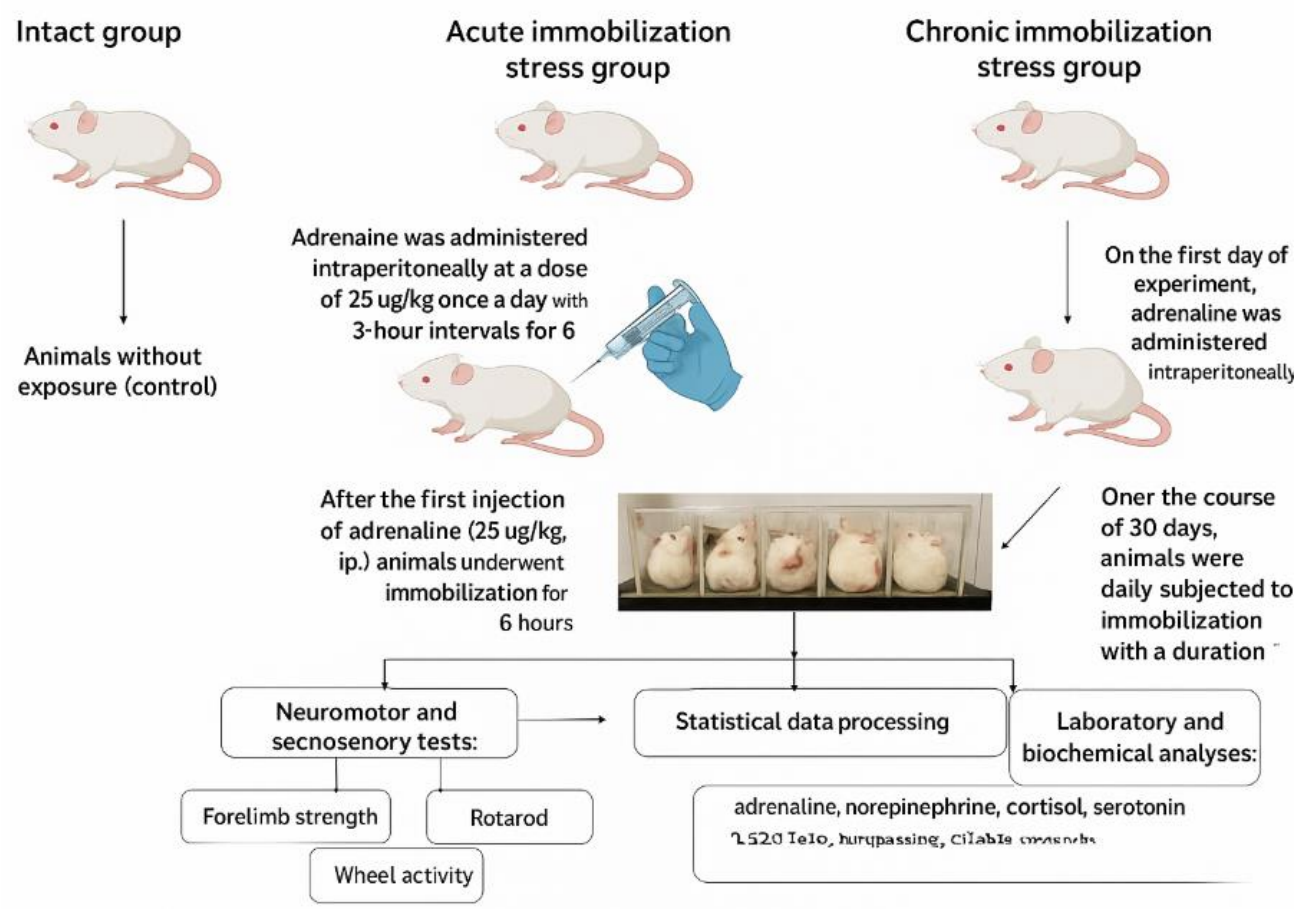
The aim of this study is a comparative analysis of the effects of acute and chronic immobilization stress on tissue-specific changes in central neuronal structures.

Materials and Methods

The experiment will involve 60 albino male rats, weighing 200-220 grams initially, divided into three groups. The first group will include intact animals; the second group will consist of animals with acute immobilization stress. The third group is rats with a chronic immobilization stress model. To model acute emotional-immobilization stress in the experiment, after fixing the animal, adrenaline is administered intraperitoneally twice with an interval of 3 hours at a dose of 25 μg/kg with a duration of immobilization after the first administration of adrenaline of 6 hours, with daily exposure to the stressor for 6 days. The chronic immobilization stress model is reproduced by fixing the animal in a metabolic chamber for a duration of 3 hours for 30 days. The method will be modified by a single administration of adrenaline at a dose of 10 μg/kg. Using the enzyme immunoassay method and standard test systems of the ELI-Neuro-Test group (Immunculus Medical Research Center, Moscow, Russia), it is planned to study the serum content of neurotropic IgG antibodies directed to the following proteins of the nervous tissue: neurofilament protein-200 (NF-200), glial fibrillary acidic protein (GFAP), S-100 protein, myelin basic protein (MBP), voltage-dependent Ca-channel (V-dependent Ca-channel), glutamate receptors (Glu-R), dopamine receptors (DA-R), GABA receptors (GABA-R), serotonin receptors (Ser-R), cholinergic receptors (Chol-R), DNA, β2 glycoprotein (B2GP). Free radical oxidation activity was determined by measuring malondialdehyde (MDA) and diene conjugate (DC) levels, as well as superoxide dismutase (SOD) and catalase activity using standard spectrophotometric methods. The test used to assess motor-coordination impairments was conducted using the Rotarod+ hardware and software system (Neurobotix LLC, Russia).

Statistical processing of the results was performed using the STATISTICA 6.0 software package in a Windows environment. The significance of differences was assessed using parametric and nonparametric criteria: Student's t-test (for normal distribution) and

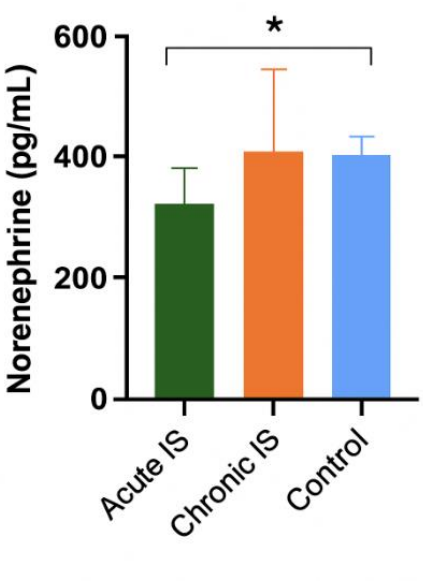
Mann-Whitney U-test with Bonferroni correction (for non-normal distribution).

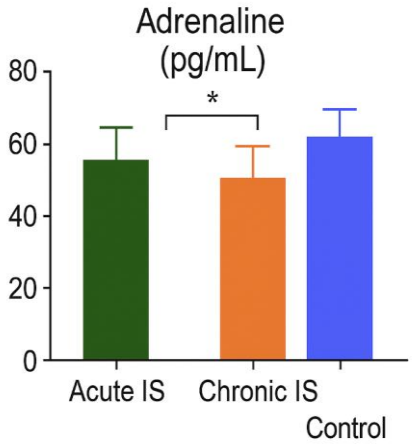


Results and Discussion

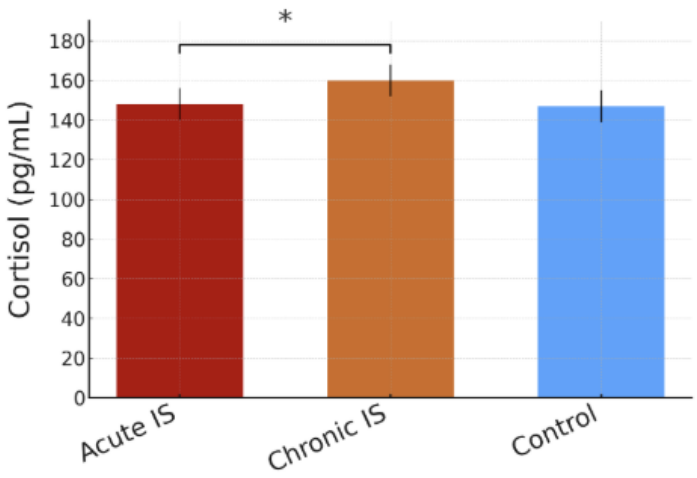
Acute stress reduces NA levels, whereas chronic stress returns them to control. This indicates the activation of the body's adaptive mechanisms via the catecholamine system.

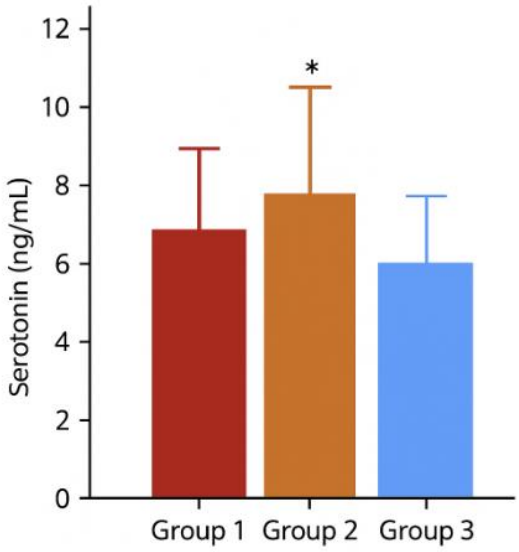
During acute immobilization stress, adrenaline levels increase as a rapid adaptive response. However, chronic stress results in a decrease, reflecting depletion of the catecholamine system and a weakening of the stress response.





Acute and chronic immobilization stress are accompanied by elevated cortisol levels, reflecting activation of the hypothalamic-pituitary-adrenal axis. Persistently elevated cortisol levels during chronic stress indicate depletion of adaptive reserves and impaired neuroendocrine regulation. Acute and, especially, chronic immobilization stress is accompanied by elevated serotonin levels, reflecting activation of the serotonergic system as an adaptive mechanism. Long-term maintenance of high serotonin levels may indicate the development of a neurochemical imbalance and the risk of developing depressive states [7, 8].





Acute immobilization stress causes damage to axons and glial cells, manifested by a decrease in antibodies to NF-200 and GFAP—this is the acute neurodestructive stage. Chronic stress triggers an autoimmune and inflammatory response: increased antibodies to S-100 and MBP reflect glial activation, demyelination, and emotional and behavioral disturbances. Thus, the process transitions from the destructive phase to the immune adaptation phase, characteristic of prolonged neuroinflammatory stress [9].

Acute immobilization stress is characterized by functional disturbances in

impulse transmission, whereas chronic stress leads to autoimmune restructuring of the receptor system, affecting the dopaminergic and glutamatergic systems. This reflects the immune mechanisms of neuropsychiatric and emotional disorders characteristic of prolonged stress [8, 10]. In acute stress, temporary suppression of inhibitory and serotonergic mechanisms predominates, while in chronic stress, a persistent imbalance of the GABA, serotonin, and opioid systems develops, which leads to the development of depressive, anxious, and painful conditions characteristic of prolonged stress exposure.

Parameter Group	**Marker (Protein or Receptor)**	**Acute Stress**	**Chronic Stress**	**Clinical / Physiological Significance**
Neural Tissue Proteins	NF-200	Decreased	Partially restored	Axonal damage (degeneration)
	GFAP	Sharply increased	Slightly elevated	Astrocyte damage, reactive gliosis
	S-100	Slightly elevated	Moderately elevated	Neuroglia activation, emotional disturbances
	MBP (Myelin Basic Protein)	Slightly elevated	Elevated	Demyelination of nerve fibers
Ionic & Neurotransmitter Receptors	V-Ca-channel	Decreased	Moderately elevated	Impaired neuromuscular conduction
	N-cholinoreceptor	Decreased	Decreased	Muscarine-like reactions
	Glu-R (Glutamate Receptor)	Slightly altered	Elevated	Enhanced excitatory transmission, cognitive activation

Parameter Group	Marker (Protein or Receptor)	Acute Stress	Chronic Stress	Clinical / Physiological Significance
	DA-R (Dopamine Receptor)	No significant change	Sharply elevated	Imbalance in motivational-reward processes
Neurotransmitter Systems	GABA-R (GABA Receptor)	Decreased	Decreased	Weakened inhibitory system, increased excitability
	5-HT-R (Serotonin Receptor)	Decreased	Stabilized or slightly elevated	Emotional lability (instability)
	Opioid-R	Slightly altered	Sharply decreased	Suppression of the anti-pain (opioid) system
	β-Endorphin	Decreased	Decreased	Weakening of natural anti-stress mechanisms

Immobilization stress models a universal pathogenetic cascade in which acute adaptation progresses into a chronic neuroinflammatory and neurodegenerative state. Increased cortisol levels, coupled with decreased catecholamines and serotonin, reflect a depleted stress response, while increased autoantibodies to proteins and receptors indicate the development of neuroimmune aggression. The data obtained confirm that the ELIN test, in combination with hormonal profiling, is a sensitive tool for the early detection of stress-induced disorders and can be used to predict neurodegenerative and psychoemotional disorders associated with chronic stress. The results obtained will allow for the assessment of the central and peripheral nervous system and the diagnosis of nervous system disorders before the first symptoms of the disease appear. Early diagnosis of neurodegenerative processes can slow the progression of the

pathological process and improve patients' quality of life.

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