

# Research Journal of Pharmaceutical, Biological and Chemical Sciences

# Fundamentals Of The Functioning Of The Nervous And Humoral Regulation Of The Heart And Blood Vessels.

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#### ABSTRACT

The autonomic nervous system has a rather important modulating effect on the contractile activity of the myocardium and regulates the vascular tone. Efferent innervation of the heart is carried out with the participation of both parts of the autonomic nervous system (sympathetic and parasympathetic). Humoral regulation of the heart and blood vessels is carried out by hormones and ions of the intercellular fluid. Stimulate cardiac activity: catecholamines (adrenaline and norepinephrine). They increase the strength and rhythm of contractions. Adrenaline interacts with  $\beta$ -receptors, which activates adenylate cyclase, synthesis of cyclic adenosine monophosphate, transfers inactive phosphorylase to the active. Adrenaline increases the permeability of membranes for Ca2 +, which is involved in the reduction of cardiomyocytes. The high efficiency of the heart is due to the strict rhythm of his activity. The intensity of the heart changes under the influence of nerve impulses of the nervous system and biologically active substances. The cardiovascular system through the supragmentary parts of the autonomic nervous system - the thalamus, the hypothalamus, the cerebral cortex is integrated into the behavioral, somatic, vegetative reactions of the body. The effect of the cerebral cortex (motor and premotor zones) on the center of the circulatory system of the medulla oblongata lies at the heart of conditioned reflex cardiovascular reactions. The activation of the central nervous system is accompanied by a change in the heart rate and fluctuations in blood pressure. Keywords: heart, physiology, blood vessels, nervous regulation, humoral regulation.



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#### INTRODUCTION

Various different factors can influence the properties of the cardiac muscle (excitability, conductivity, contractility, automatism, tone) and, consequently, the main parameters of the heart - the frequency and force of contractions [1,2].

It is accepted to distinguish several forms of regulation of the heart: autoregulation (represented by its two types - myogenic and neurogenic) and extracardiac regulation (nervous, humoral, reflex) [3,4]. As is known, regulation of the heart rhythm is carried out by the vegetative and central nervous system, with the help of a number of humoral and reflex effects. Parasympathetic and sympathetic nervous systems are in a certain interaction [5].

In the body, depending on the changes in external and internal factors, the heart rate must change. These changes and the work of the heart as a whole are regulated by two mechanisms (like the work of other organs and the whole organism) - the nervous and humoral. With this adjustment, homeostasis is realized. Nervous regulation is carried out vegetatively, the nervous system is divided into parasympathetic and sympathetic [6].

Parasympathetic - in the vagus nerve pass the fibers of the nervous system - slow down, slow down the heart rate. Sympathetic - in the spinal cord - in the cervical and thoracic areas - accelerate the frequency of cardiac contraction. The work of the heart is affected by impulses coming from the vessels - in the vessels - the receptors from which excitement to the central nervous system - the change in parasympathetic and sympathetic influences - the norm of pressure in the vessels. Change in cardiac activity can occur with pain, strong emotions. Usually the heartbeat with strong emotions becomes more frequent. This affects the role of the cerebral cortex [7]. Also of great importance in the work of the heart is its humoral regulation, which is carried out by a number of substances entering the blood from the glands into the heart and other organs and tissues. It becomes clear that despite autonomic reflexes, autoregulatory mechanisms of adaptation of cardiac activity to loads play a big role in the body, since there are many effects in which the vegetative tone does not change (change in body position, blood transfusion, primary effect of changes in peripheral resistance, etc.) [8].

**Purpose:** to generalize the most physiologically significant information about the effect of extracardiac neural regulation on the cardiovascular system of a person.

## Vegetative regulation of the cardiovascular system

A higher level of adaptation of the activity of the cardiovascular system, which is performed with the participation of centers localized in the brain and spinal cord [9], as well as the activity of the autonomic nervous system [10].

The autonomic nervous system is a department of the nervous system that regulates the activity of internal organs, glands of external and internal secretion, blood and lymphatic vessels [11].

The autonomic nervous system has a rather important modulating effect on the contractile activity of the myocardium and the regulation of the tone of the heart vessels. Efferent innervation of the heart is carried out with the participation of both parts of the autonomic nervous system (sympathetic and parasympathetic).

The effect on the heart of the sympathetic nerves was first studied by the brothers Zion (1867), and then by I.P. Pavlov. I.F. Zion and M.F. Zion first described the increase in cardiac activity with irritation of the sympathetic nerves of the heart (positive chronotropic effect). I.P. Pavlov (1887) discovered nerve fibers that enhance cardiac contractions without a noticeable increase in the rhythm of the heart (positive inotropic effect). The influence on the heart of the vagus nerves was first studied by the Weber brothers (1845) who established that the irritation of these nerves inhibits the work of the heart until it completely stops during diastole.



Vegetative neuropathy is characterized by damage to the motor, sensory and reflex functions of internal organs, especially cardiovascular, gastroenteric and urogenital systems, violation of vasomotor thermoregulation, trophism, vegetative control of endocrine secretion, pupillary reflex change, respiratory control [12].

Morphological changes in this disease are characterized by segmental demyelination, degeneration of axons, the appearance of large vacuoles in the cytoplasm of sympathetic ganglia, degeneration and swelling of dendrites. Changes in vegetative fibers innervating the cardiac muscle are manifested in a decrease in the density of myelin fibers, hyperergentophilia, and fragmentation of the number of fibers with a decrease in their number. Ultrastructural studies of tissues of patients with chronic autonomic neuropathy indicated the degeneration of terminal nerves, innervating, in particular, the artery of small caliber [13].

The most characteristic and severe clinical manifestations of autonomic neuropathies in the cardiovascular sphere are orthostatic hypotension, constant tachycardia at rest, a fixed heart rhythm resistant to the administration of medications, and painless myocardial infarctions [14].

Orthostatic hypotension - the most frequent sign of vegetative neuropathy - is manifested by the appearance of general weakness, dizziness, darkening in the eyes, numbness of the lips, faintness, unpleasant sensations in the epigastric region ("tight knot", "twisting", "rolling", "numbness"), sometimes - fainting at the transition from horizontal to vertical position. These phenomena develop with a sharp decrease in systolic pressure by 20 mm Hg. and more (positive orthostatic test). The frequency of this complication varies among the contingent of patients with polyneuropathies from 4 to 11%, and among patients with vegetative disorders reaches 35%.

The genesis of orthostatic hypotension in patients with cardiac autonomic neuropathy is associated with the loss of the sympathetic vasoconstrictor reflex of the splanchnic lining of the internal organs, muscles and skin as a result of afferent fibers of the vasomotor arc, changes in renin plasma concentration due to autonomic disorders of sympathetic innervation of the juxtaglomerular apparatus and a decrease in basal and stimulated standing) concentrations of noradrenaline and angiotensin II in blood plasma. An important role is also played by a decrease in the sensitivity of baroreceptors due to parasympathetic autonomic disorders, as well as violations of the central regulation of vascular tone [15].

## Humoral regulation of the cardiovascular system

Humoral regulation is carried out by hormones and ions of the intercellular fluid. Stimulate cardiac activity: catecholamines (adrenaline and norepinephrine). They increase the strength and rhythm of contractions. Adrenaline interacts with  $\beta$ -receptors, adenylate cyclase is activated, cyclic adenosine monophosphate is formed, inactive phosphorylase is converted into active, glycogen is broken down, glucose is formed and as a result of these processes energy is released. Adrenaline increases the permeability of membranes for Ca2 +, which is involved in the reduction of cardiomyocytes [16].

Oppress heart activity: acetylcholine, hypoxemia, hypercapnia, acidosis, ions K<sup>+</sup>, HCO<sup>-</sup>, H<sup>+</sup>. For normal heart activity, electrolytes are of great importance. The concentration of K<sup>+</sup> and Ca<sup>2+</sup> ions affect the automatic and contractile properties of the heart. Excess K<sup>+</sup> causes a decrease in the rhythm, contraction force, a decrease in the excitability and conductivity of the myocardium. Washing of the isolated heart of animals with a concentrated solution of K<sup>+</sup> leads to relaxation of the myocardium and cardiac arrest in the diastole. The ions of Ca<sup>2+</sup> increase the rhythm, increase the strength of the heartbeats, the excitability and conductivity of the myocardium [17].

The lack of  $Ca^{2+}$  weakens the contractions of the heart. With a gradual increase in the content of  $Ca^{2+}$  in the surrounding cardiomyocyte environment (hypercalcemia), the force of myocardial contractions increases synchronously. If the excess of  $Ca^{2+}$  becomes large, then the intensity of contraction begins to decrease (due to incomplete relaxation of the myocardium), and then the heart stops in the systole phase [18].

Humoral regulation of the heart is carried out with the help of various compounds. Thus, the excess of potassium ions in the blood leads to a decrease in the force of the heart contractions and a decrease in the excitability of the cardiac muscle. Excess calcium ions, on the contrary, increases the strength and heart rate,



increases the speed of excitation through the conduction system of the heart. Adrenaline increases the frequency and strength of heartbeats, and also improves coronary blood flow as a result of stimulation of myocardial  $\beta$ -adrenergic receptors. A similar stimulating effect has on the heart hormone thyroxine, corticosteroids, serotonin. Acetylcholine reduces the excitability of the heart muscle and the strength of its contractions, and norepinephrine stimulates cardiac activity.

#### Characteristics of adreno- and holinoretseptorov heart

Sympathetic activation is accompanied by vasoconstriction of peripheral vessels due to the activation of  $\alpha_1$ -adrenergic receptors on smooth muscle cells, whereas the effects of the sympathetic nervous system on the heart are mediated by  $\beta_1$ -adrenergic receptors. The ratio of  $\beta_1/\beta_2$ -adrenergic receptors in left ventricular myocardium in healthy individuals is 80/20, while in patients with severe chronic heart failure - 60/40. In the sympathetic regulation of the cardiovascular system,  $\alpha_2$ -adrenergic receptors play a secondary role; at the same time, in the vascular endothelium  $\alpha_2$ -adrenoreceptors model adrenergic vasoconstriction. The sympathetic nervous system interacts with the reninangiotensin-aldosterone system and the vascular endothelium. Angiotensin II affects the release and re-uptake of norepinephrine by binding to the presynaptic receptors of postganglionic fibers, and also stimulates the sympathetic nervous system, affecting the central regulatory mechanisms. At the same time, stimulation of  $\beta_1$ -adrenergic receptors of the juxtam glomerular apparatus of the glomerulus of the kidneys leads to an increase in renin synthesis and activation of the reninangiotensin-aldosterone system, as a result of which arterial pressure rises, and sodium and water retention occurs in the body [19].

In medicine,  $\beta$ -adrenoreceptor antagonists are actively used,  $\beta$ -adrenoceptors, a group of drugs that is quite extensive in terms of the number of representatives, which are now effectively used in various diseases of the cardiovascular system: arterial hypertension, coronary heart disease, acute myocardial infarction and secondary prevention after an infarction, chronic heart failure, supraventricular and ventricular arrhythmias, hypertrophic cardiomyopathy, glycosidic intoxication, syndrome of udder lined Q-T, tetralogy of Fallot, mitral stenosis. The list of indications for the use of  $\beta$ -blockers also includes prevention of migraine, essential tremor, withdrawal syndrome, situational anxiety, thyrotoxicosis, hyperparathyroidism, glaucoma, portal hypertension and gastrointestinal bleeding.

Thus, the heart receptors are an important point of its regulation, which begins to be actively used in medicine [20,21].

#### Age changes in the regulation of the cardiovascular system

In a study in healthy people aged 36-45, there was a lack of reliable dynamics of antioxidant protection of platelets and the level of lipid peroxidation in them, which in many respects caused the preservation of low activity of the blood platelets. Intensification of lipid peroxidation in older patients was accompanied by a higher activity of platelets in them, which was maximum expressed at 60 years of age. Obviously, this is associated with an increase in the sensitivity of platelet receptors to exogenous effects on platelets, including an increase in the concentration in the blood of von Willebrand factor, a coagulant of platelet adhesion, with a simultaneous increase in the number of receptors to it (GPI) on the surface of the blood platelets. Receptor changes on the membranes of the blood plates, due to the reaction of the hemostasis system to the dynamics of the functional state of the whole organism, are undoubtedly a consequence of complex adaptive reactions and the membrane composition of platelets, which ultimately determine their adaptation to the established age-related changes in tissues and organs.

The increase in intravascular activity of platelets in individuals of second adulthood after 45 years of age also indirectly indicates an increase in the level of aggregation inducers (thrombin, adenosine diphosphate, adrenaline) in the blood with age, and an increase in the basal sensitivity of platelets to them. At the same time, a significant decrease in the amount of intact discoid form of platelets begins to develop in healthy blood vessels from the age of 45, indicating an increase in the activity of their receptors [5].

Also, the state of the parts of the autonomic nervous system undergoes significant changes throughout the life of a person. In infancy, there is a marked predominance of sympathetic nerve influences in the functional and morphological immaturity of both links of the autonomic nervous system. The



development of the sympathetic and parasympathetic parts of the autonomic nervous system after birth occurs intensively, and at the time of puberty, the density of the location of the nerve plexuses in various parts of the heart reaches its highest values. At the same time, young people are noted for the dominance of parasympathetic influences, manifested in the initial vagotonia at rest. Beginning with the 4th decade of life, involutive changes begin in the apparatus of sympathetic innervation, while maintaining the density of cholinergic nerve plexuses. Desimpatization processes lead to a decrease in sympathetic activity and a decrease in the density of the distribution of nerve plexuses on cardiomyocytes, smooth muscle cells, promoting the heterogeneity of the potential-dependent properties of the membrane in the cells of the conducting system, the working myocardium, the walls of the vessels, the hypersensitivity of the receptor apparatus to catecholamines and can serve as the basis for arrhythmias, including fatal. There are also sexual differences in the state of the vegetative nervous tone. Thus, in women of young and middle age (up to 55 years), the activity of the sympathetic nervous system was lower than in men of similar age [22].

#### Disorders in the cardiovascular system with arterial hypertension

In the Russian Federation, the main leading modifiable risk factors remains arterial hypertension, occurring in approximately 26% of the country's citizens and affecting the quality and life expectancy, is especially important for working people.

It is known that the frequency of development of arterial hypertension in women significantly increases with the onset of menopause. In perimenopausal women with menopausal syndrome, the incidence of arterial hypertension is increased to 52.4% compared with healthy women of this age group, which increases the risk of coronary heart disease by 3 times, and the stroke by 7 times [3].

Arterial hypertension is one of the most urgent problems of modern medicine, which is due to its high prevalence, progressive course with the development of various complications, including life-threatening conditions. It is established that the sources of arterial hypertension are very often in adolescence, when the formation of neurohumoral regulation of the hemodynamic system is carried out. It is shown that in 33-42% of such patients the arterial pressure remains elevated in the future, and in 17-25% of them arterial hypertension acquires a malignant course with gradual transformation into hypertensive disease. In the pathogenesis of arterial hypertension, especially at the initial stages of its development, the leading role is assigned to autonomic dysfunction, which disturbs the balance between cardiac output and vascular resistance. It is traditionally believed that arterial hypertension is associated with hypersympathicotonia. Nevertheless, as a result of a number of studies, it was established that some of the patients had an increase in the functional activity of the cholinergic system. Undoubtedly, when appointing treatment and rehabilitation measures in each specific case, it is necessary to take into account the type of autonomic regulation of the patient [13].

Thus, the combination of isolated sympathicotonia with excessive vegetative reactivity and hyperdiastolic variant of providing activity in this category of patients is associated with greater severity and duration of arterial hypertension, as well as with the formation of myocardial hypertrophy of the left ventricle. The increase in the functional activity of the parasympathetic autonomic nervous system reduces the average level of arterial pressure, restraining the processes of cardiac muscle remodeling.

#### Dysfunction in the cardiovascular system in chronic heart failure

In recent years, facts have become known that indicate the possibility of not only corrective, but also trigger effects of the nervous system on the rhythm of the heart, when the signals coming along the nerves initiate contractions of the heart.

Chronic heart failure occurs in 5% of people under the age of 65 years and in 10% of people older than 80 years [10]. According to the Framingham study, after the appearance of the clinical symptoms of chronic heart failure within 6 years, about 80% of men and 65% of women die. In recent years, diagnostics and approaches to the treatment of chronic heart failure have been improved [9,10], however, despite the efforts of modern methods of treatment, chronic heart failure continues to spread, worsening the patients' quality of life, their emotional state, and limiting their physical capabilities [25].



From the modern point of view, the main role in the activation of compensatory mechanisms (tachycardia, the Frank-Starling mechanism, the constriction of peripheral vessels) is played by the hyperactivation of local or tissue systems and neurohormones. These include sympathic-adrenal system and its effectors norepinephrine and adrenaline and renianangotensin-aldosterone system and its effectors angiotensin II and aldosterone, as well as a system of natriuretic factors.

It is believed that a violation of the pumping function of the heart in chronic heart failure and a decrease in cardiac output activates the sympathetic division of the autonomic nervous system, whose initial increase in activity in chronic heart failure is compensatory because it promotes cardiac output and redistributes the regional blood flow to the heart and skeletal muscles. In this case, renal vasoconstriction leads to a delay in sodium and water, which improves the perfusion of vital organs, but a further increase in the activity of the sympathetic department of the autonomic nervous system is characterized by a whole complex of adverse effects in the form of increased myocardial oxygen demand, increased ischemia, and cardiac arrhythmias [4].

#### CONCLUSION

In the region of the brainstem, in the reticular formation of the medulla oblongata and in the bridge, there are vasomotor stem cells. The vasomotor centers are also affected by the higher parts of the central nervous system. Regulatory influences of these stem centers are carried out, mainly, by changing the tone of the sympathetic nerves, whose tone also depends on the afferent impulses from the heart and blood vessels. The high efficiency of the heart is due to the strict rhythm of his activity. The intensity of the heart changes under the influence of nerve impulses of the nervous system and biologically active substances. The cardiovascular system through the supragmentary parts of the autonomic nervous system - the thalamus, the hypothalamus, the cerebral cortex is integrated into the behavioral, somatic, vegetative reactions of the body. The effect of the cerebral cortex (motor and premotor zones) on the center of the circulatory system of the medulla oblongata lies at the heart of conditioned reflex cardiovascular reactions. Irritation of the structures of the central nervous system changes the heart rate and blood pressure.

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