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Serotonin: biological properties and its receptors

In the last decade, much attention has been paid to the study of the serotonergic system. The molecular and cellular mechanisms of the synthesis of serotonin, its metabolism and receptor interaction are well studied. The wide range of serotonin effects is explained by the presence of a wide variety of serotonin receptors. The serotonin (5-hydroxytryptamine, 5-HT) is the main mediator of the serotonergic system. In human the role of 5-HT in the central nervous system (CNS) is best characterized, where the amine remain in force as a neurotransmitter in neural synapses and participates in the formation and regulation of various physiological functions of the body in normal conditions and in pathology, playing a role in maintaining homeostasis. 5-HT is a neurohormone that has a morphogenetic and regulatory effect on target organs, including the heart and blood vessels. The serotonergic system is a link in the pathogenesis of atherosclerosis, arterial and pulmonary hypertension, coronary heart disease, atrial fibrillation and heart failure. In patients with coronary heart disease an increase serotonin concentration in the blood was found. The effect of the serotonergic system on the cardiovascular system has been studied quite thoroughly in animals. Serotonin has been shown to have a positive inotropic effect on the myocardium of the atria and ventricles of various mammals. Also, the neurotransmitter serotonin plays an important role in the formation of the brain. Low levels of serotonin in the initial stages of development will lead to the fact that the adult brain will inadequately process sensory signals. The review covers the significance and a wide range of biological effects of serotonin in the central nervous system and outside the central nervous system, which is explained by the diversity of the 5-HT receptor family.

Keywords: serotonin, adrenaline, heart, myocardium, receptor, neurotransmitter, blood vessels, ventricles of the heart, rat.

Serotonin (5-hydroxytryptamine; 5-HT) is a phylogenetically ancient indoleamine found in plants, invertebrates and vertebrates [1, 2]. In 1947, a substance with vasoconstrictor properties was discovered, it was also called mitogen of arterial smooth muscle. This thing was given the name serotonin. It is known that serotonin acts like a monoaminergic neurotransmitter in the brain and gastrointestinal tract and is also involved in various functions, such as storing and urinating urine, regulating sleep, mood and body temperature, intestinal motility and food intake [3–6]. Together with histamine, serotonin can participate in the formation of a painful reaction when you stimulate sensory receptors. In mammals, the two primary sources of serotonin are the nucleus of the dorsal suture (DRN) in the brainstem and enterochromaffin cells. They are widely distributed in the gastrointestinal tract (that is especially in the large intestine, small intestine and rectum). Serotonin is synthesized and secreted into the bloodstream by enterochromaffin cells, which are located in the gastrointestinal tract. It is also quickly absorbed and stored in dense small granules in platelets. In human about 90 % of serotonin in the body is found in the intestine, and the rest is present mainly in platelets (8–9 %) and in the central nervous system (1–2 %). DRN neurons provide dense innervation in all areas of the brain and especially store and secrete serotonin [7]. Serotonin in a living organism is involved in many vital physiological and brain processes, such as cardiovascular, respiratory and gastrointestinal functions, mood regulation, circadian rhythm, appetite, aggression and sexual behavior [8]. Serotonin (5-hydroxytryptamine) plays an important role in maintaining homeostasis. It functions as a neurotransmitter and tissue hormone, participates in the formation and regulation of various physiological parameters of the body in normal conditions and in pathology. An interesting fact is that the first contraction of the heart in an embryo is caused by serotonin. This is due to intracellular mechanisms. The morphogenetic effect of serotonin on the heart occurs when the 5-HT_{2B} receptor is activated [8, 9].

Serotonergic system is involved in the rhythm of personal biological functions in the brain, especially because of the wide representation of receptors in various areas of the central nervous system. In many ways, this affects food and sexual behavior, learning and memory, and the emotional state of the body. Thus, a large distribution of serotonin receptors in the brain in men and women is different. Increased expression of 5-HT_{2C} receptors may cause an increase in body weight. But the use of their selective antagonist (ketanserin), on the contrary, causes loss of appetite. Serotonin can cause anxiety, depression, and various phobias, which

may indicate a decrease in its level in the brain. These anxieties can be eliminated using serotonin reuptake inhibitors (tricyclic antidepressants) [10].

Due to its effect on smooth cell walls, serotonin is a very powerful vasoconstrictor (with the exception of the vascular system of the heart and skeletal muscles). It increases peristalsis and muscle tone in the gastrointestinal tract, but there is almost no effect on the secretion of digestive glands, the effect on urinary tract smooth muscle is poorly pronounced [8, 10].

In recent decades, the significant role of the serotonin system as the main link in the pathogenesis of atherosclerosis, ischemic heart disease has been much discussed. Serotonin and histamine are the humoral system of regulators and modulators of important physiological processes, which in conditions of pathology turn into factors contributing to the development of the disease. Membrane serotonin transporter detected on neurons, platelets, myocardium and smooth muscle cells. If the concentration of serotonin in platelets is higher, the higher the activity of the membrane carrier. This means an increase in its release into the blood plasma and its negative effect on the vascular wall and platelets. In the central mechanisms of regulation of cardiovascular activity, the key role is played by the 5-HT_{1A}, 5-HT_2 and 5-HT_3 receptor subtypes, and the peripheral effects of serotonin on the vascular the system is mediated by 5-HT_1, 5-HT_2, 5-HT_3, 5-HT_4 and 5-HT_7 receptors. Activation of 5-HT_{1A} receptors causes central depression of sympathetic influences and further bradycardia, while 5-HT_2 receptors — sympathetic, increased blood pressure, tachycardia. With the development of anaerobic processes of serotonin through receptors 5-HT_2 starts the process of apoptosis of cardiomyocytes, which leads to the development and progression of heart failure [11].

It has been proven in mice that $5HT_{2B}$ receptors are involved in the regulation of heart development in embryogenesis, which are mutants for this receptor: due to a decrease in the number and size of cardiomyocytes, cardiomyopathy with ventricular weight loss is noted. The involvement of 5-HT_4 receptors in the development of atrial fibrillation and sinus tachycardia has been proven. In turn, the use of 5-HT_4 receptor antagonists was effective in treating this rhythm disorder. So, studying the role of the serotonergic system in the development of cardiovascular diseases will allow us to reveal more new pathogenic connections with arterial hypertension in children. Serotonin is formed from the essential amino acid tryptophan. It is usually found in many proteins in the body. Serotonin belongs to those groups of natural products that have a basic amine group (separated from the aromatic nucleus by an aliphatic chain), which consist of two carbon oxides [8].

Chemical structure of serotonin belongs to biogenic amines, tryptamine class. The starting component for the synthesis of serotonin is needed tryptophan of an indispensable acid, which is eaten [10]. Serotonin (5-hydroxytryptamine; 5-HT) is a neurotransmitter, synthesized from tryptophan amino acid (TRP) and transported across the blood-brain barrier by a specific carrier, then hydroxylated by tryptophan hydroxylase. This hydroxylation is the stage that limits the rate of serotonin biosynthesis. Elevated plasma of free tryptophan affects the increase in the concentration of tryptophan in the central nervous system (CNS), and therefore, every condition that increases the content of this amino acid in the plasma will cause an increase in the concentration in the central nervous system and central serotonin biosynthesis [10, 12–14].

The main part for the synthesis of serotonin is the replacement of tryptophan with an indispensable acid, which enters the body with food. Further, its intersection of the blood-brain barrier, that is, penetration into the brain tissue, is due to easy transport. The conveyor does not have high specificity. It is able to carry other neutral amino acids — methionine, phenylalanine, lysine and leucine, acting as competitive inhibitors for the synthesis of serotonin. Admission to the neurons is also under the control of a non-specific carrier for neutral amino acids [15].

Serotonin is transferred to synaptic vesicles using a transporter for all monoamines structurally and functionally similar to acetylcholine. Inactivation of serotonin in the synaptic cleft occurs due to the reuptake of the Na^+/Cl^- dependent serotonin cotransporter, consisting of 12 transmembrane domains. N- and C-terminals of several cells were found in the cytosol and glycosylation sites were found in the extracellular regions. Also, there is a mechanism of serotonin cleavage with the participation of monoamine oxidase A to 5-hydroxyindole-acetaldehyde. Then there is its subsequent oxidation with the participation of aldehyde dehydrogenase to 5-hydroxyindole-3-acetic acid, which is excreted in the urine [10].

Different effects of serotonin are mediated by a variety of its receptors distributed throughout the body [15, 16]. Signaling of serotonin occurs through the plasma membrane receptor system. Currently, it has at least 15 related receptors, divided into 7 families. All but one of them are the superfamily of G-protein coupled receptors (5-HT recipes are in accordance with the nomenclature of the International Society for Fundamental and Clinical Pharmacology (IUPHAR) (Table 1) [16].

Table 1

Families of serotonin (5-HT) receptors

Family	Potential	Type	Mechanism of action
5-HT_1	Inhibitory	G_i/G_0-protein coupled	Decreasing intracellular concentration of cAMP
5-HT_2	Excitatory	G_{q11}-protein coupled	Increasing intracellular concentration of IP3 and DAG
5-HT_3	Excitatory	Ligand-gated Na^+/K^+ channel	Depolarization of cell plasma membrane
5-HT_4	Excitatory	G_s-protein coupled	Increasing intracellular concentration of cAMP
5-HT_5	Excitatory	G_i/G_0-protein coupled	Decreasing intracellular concentration of cAMP
5-HT_6	Excitatory	G_s-protein coupled	Increasing intracellular concentration of cAMP
5-HT_7	Excitatory	G_s-protein coupled	Increasing intracellular concentration of cAMP

Many members of the fourth G-protein coupled receptor (GPCR) family. They have the ability to form homo-or hetero-oligomers with biochemical and functional characteristics, including receptor pharmacology, signaling, and regulation, and are unique to these oligomeric conformations. These GPCR oligomers are not only found in the GPCR type, they are also found in different families and subtypes. G-protein coupled receptors are also known as serpentine receptors or hemi receptors, which can form a huge family of transmembrane receptors. Receptors of this family are found only in plant, animal cells and choanoflagellates. About 80 % of primary messengers (neurotransmitters, hormones, neuromodulators) interact with specific receptors that are associated with effectors of G-proteins [17–19].

Five receptors belong to the 5-HT_1 class (5-HT_{1A}, 5-HT_{1B}, 5-HT_{1D}, 5-HT_{1E}, 5-HT_{1F}), all of which are associated with G_i/G_0 and negatively regulate the function of alternating current. Human 5-HT_{1A} and 5-HT_{1D} receptors, which are located mainly on the body and dendrites of serotonergic neurons belong to autoreceptors (in rats, these are subtypes 5-HT_{1A} and 5-HT_{1B}) [10].

Of the serotonin receptors, the most widely distributed torus is 5-HT_{1A}. In the central nervous system, 5-HT_{1A} receptors are present in large volumes in the cerebral cortex, hippocampus, amygdala and suture nucleus, septum, but in small quantities they have also been proven in the thalamus and basal ganglia [13]. Also, they are located in the micellar plexus and gastrointestinal tract. In the brain, 5-HT_{1A} receptors act as autoreceptors and postsynaptic receptors. They are involved in suppressing the «release» of neurons, regulating the production of ACTH (adrenocorticotropic hormone) (but not prolactin), regulating behavior and eating [13, 20]. 5-HT_{1B} and 5-HT_{1D} receptors are involved in the pathophysiology of migraine. 5-$HT_{1B/1D}$ receptor agonists (triptans) have anti-migraine effects. They contribute through 5-HT_{1B} receptors to the intracranial arteries (vasoconstriction), while the effects, through the 5-HT_{1D} receptors, are thought to be neuronal. Due to the lack of selective pharmacological agents, specific antibodies, and animal models in permissive models, the function of the 5-HT_{1E} receptor is unknown [20].

There is no polymorphism in the 5-HT_{1E} receptor gene among people. This indicates a high degree of evolutionary conservation of the genetic sequence. Thereby, showing that the 5-HT_{1E} receptor plays an important physiological role in humans. It is assumed that in humans, due to the large number of receptors in the frontal cortex, hippocampus and olfactory bulb (which are brain regions essential for memory regulation), 5-HT_{1E} receptor is involved in memory regulation [13, 21].

Class 5-HT_{2A} has three subtypes — 5-HT_{2A}, 5-HT_{2B} and 5-HT_{2C}, being 46–50 % structural homology. It is associated with Gq11 protein and increases the hydrolysis of inositol triphosphate and the intracellular concentration of Ca^{2+}. The 5-HT_{2A} receptor is the major excitatory receptor subtype among G-protein coupled receptors. It can also have an inhibitory effect on certain areas, such as the visual cortex and orbitofrontal cortex. The 5-HT_{2A} receptor is expressed in most central and peripheral tissues. 5-HT_{2A} receptors contribute to smooth muscle contraction. In addition, increased platelet aggregation and increased capillary permeability have been shown after exposure to serotonin (probably due to the activation of this receptor subtype). In the CNS, 5-HT_{2A} receptors are present mainly in the cortex, basal ganglia, and claustrum. 5-HT_{2A} stimulates the secretion of ACTH (adrenocorticotropic hormone), oxytocin, renin and prolactin, corticosterone. If 5-HT_{2A} receptor is inhibited, the behavior changes. 5-HT_{2A} antagonists such as olanzapine, seroquel, risperidone, ritanserin, and others are used and developed for the treatment of schizophrenia [13]. The 5-HT_{2A} receptors are the first of the three (A, B, and C) subtypes from the 5-HT_2 receptor family. There are many in the forebrain, especially in the cortical layer (peripheral cortex of the brain) [22], pyramidal and interneurons neurons, also the dentate gyrus of the hippocampus, parahippocampal gyrus, olfactory bulb and

the posterior horns of the spinal cord. In addition, a high density of receptors is located outside the central nervous system: Schwann cells, in the sciatic nerve, coronary arteries, atria, platelets, and brain vessels [20].

The 5-HT_{2A}-activated receptors, the major postreceptor cascades, are A_2-dependent phospholipase and phospholipase C. The secondary cascade, through the Gi/Go protein, represents the acetylate cyclase pathway. Some cell culture studies have shown that the same 5-HT_{2A} agonists, under the same cultivation conditions, have different activations and, thus, one of these cascades prevails. One of the features of the 5-HT_{2A} receptor is the relatively low affinity of the endogenous serotonin ligand with the value of the basic dissociation constant of the micromolar path compared with members of other families. The main physiological effects of 5-HT_{2A} receptors are associated with the regulation of platelet function, the cardiovascular and central nervous systems. Activation of 5-HT_{2A} receptors in platelets leads to a high increase in free intracellular calcium and proagregantny action. Such a secondary signaling mechanism leads to an increase in the contractile activity of smooth myocytes in the coronary vessels, vessels of the brain. It was revealed that the 5-HT_{2A} receptor affects the enhancement of the contractile activity of the heart [19, 20].

5-HT_{2A} receptors in the central nervous system are involved in the formation of cognitive processes, behavioral responses and memory. Twenty-three effects of 5-HT_{2A} receptors on the development of fear, anxiety, seizures, and panic were noted. In some data it can be seen that the activation of 5-HT_{2A} receptors due to the increased excitability of cortical neurons can lead to the development of visual hallucinations, a psychostimulating effect. History has shown that D-receptor studies (the old name for the 5-HT_{2A} receptor) are associated with identifying the hallucinogenic effect of bromine, dimethoxyphenylpropanamine ion (DOI), lysergic acid diethylamide (LSD), which are not selective 5-HT_2 agonists. At present, it is assumed that such psychotic effects from LSD, DOI may be the result of sensitization in the areas of ligand recognition of dopamine receptors. They promote the formation of active heteroreceptor complexes D2/5. Observing the content of inter- and intracellular serotonins, the appearance of serotonin hypotheses of schizophrenia was suggested. There have been many studies on the serotonin system in schizophrenia. In these patients, serotonin levels in platelets were analyzed. It became known that the functional state of the serotonergic system in patients with schizophrenia is much different from the control group (oscillation boundaries were much wider than in other mental disorders) [14, 19, 23].

When 5-HT_{2A} receptors are stimulated, there is a significant change in calcium levels at the intracellular level of post-receptors. This is associated not only with the activation of protein kinase C, but also Rho-kinase, which is an extracellular regulatory signal of kinase and tyrosine kinase [19].

The 5-HT_{2A} receptor affects the enhancement of the contractile activity of the heart. In a mouse model of pulmonary hypertension, it was shown that serotonin, by stimulating 5-HT_{2B} receptors, regulates the cell cycle along with platelet growth factor. Serotonin receptors such as 5-HT_{2A} and 5-HT_2B play an important role in the functioning of the lungs, thereby controlling vasoreactivity and bronchial reactivity [8, 19].

For the 5-HT_{2C} receptor, there are no selective ligands. Therefore, his actions remain almost unknown [12]. Because of the antagonism of agomelatine 5-HT_2 receptors, it acts as an effective anti-depressant. At the same time causing an increase in the level of norepinephrine and dopamine in certain areas of the brain. Serotonin is involved in the pathogenesis of acute myocardial infarction, acting through 5-HT_{2A} receptors in areas of coronary atherosclerosis. Cardioprotective effect of ketanserin (5-HT_2 receptor blocker) was noted — improvement of perfusion of myocardial ischemic zones and shortening of ischemia periods in patients with stenotic atherosclerosis of the coronary aorta. Serotonin is capable of activating myocardial cells, enhancing rhythm disturbances, causing necrosis, modulating myocardial damage. Drugs that inhibit the action of serotonin, can be used in the treatment of coronary heart disease in humans [13, 23].

The third type of serotonin receptor belongs to the superfamily of cis-loop ion-activated ion channels. They include nicotine cholinergic receptors, zinc-activated channels and strychnine-sensitive glycine receptors. The 5-HT_3 receptor consists of five subunits. Around the ion-conducting pores are organized as a homopentamer or heteropentamer. The first identified subunit was 5-HT_{3A}. It is the only subunit that forms functional homopentamers. The remaining subunits function as heteropentamers with 5-HT_{3A}, which have been identified to date (5-HT_{3B}-5-HT_E). The main function of the 5-HT_3 receptor ligand-dependent cation channel is the rapid depolarization of the cell membrane when it is excited by the influx of external Na^+ and Ca^{2+} and as a result their concentration in the cytosol increases, as well as the release of K^+ ions from the cell. In vitro evidence it was also obtained that for lithium, cesium, rubidium and magnesium ions. This leads to the formation of final central or peripheral effects. Central 5-HT_3 is involved in the release mechanisms of various neurotransmitters. When this type of receptor is activated, the secretion of serotonin from the frontal lobe, individual sections of the hypothalamus and hippocampus in guinea pigs and rats is facilitated. It may

cause decreased release of norepinephrine. This, in turn, leads to the development of depressive symptoms [14].

Activation of 5-HT_3 receptors leads to an increase in dopamine release in vitro (in rats, in the substantia nigra and striatum cells) and in vivo (in rats, in the adjacent nucleus). These effects may be due to exposure to dopamine carriers or to the participation of cholecystokinin in a process that is released when 5-HT_3 receptors are activated. Central 5-HT_3 receptors are involved in vomiting, regulation of sympathetic and parasympathetic influences, in the conduct of antinociceptive and nociceptive signals, in the perception of pain. Peripheral 5-HT_3 receptors are involved in nociception. This is confirmed by experimental studies on the reduction of 5-HT_3 pain sensitivity blockers in rats and mice with acute and chronic inflammation. It is also shown in clinical studies, with a reduction in neuropathic pain, fibromyalgia, and the adoption of 5-HT_3 antagonists [24].

5-HT_3 receptors are found in the central and peripheral nervous system and thus provide rapid depolarization. 5-HT_3 antagonists are widely used in the clinic to treat nausea and vomiting in cancer patients. In response to intraperitoneal administration of 5-HT in the heart, it has been shown that 5-HT_3 receptors cause reflex bradycardia and hypotension. This can lead to the appearance of Bezold-Jarisch reflex. It is a reflex inhibition of breathing, lowering blood pressure and bradycardia [11, 24].

Like most members of the 5-HT group, serotonin receptors of the fourth type (5-HT_4) belong to the conjugated G-protein and are encoded by one genetic site [24]. Many splice variants are also described for it, which form at least ten isoforms of receptors — 5-$HT_{4(ag)}$, 5-$HT_{4(hb)}$, 5-$HT_{4(i)}$, 5-$HT_{4(n)}$. Their alternative compound is in the extracellular region between the IV and V transmembrane domains or C-termini. When the receptor is active, the fundamental difference between these options lies in the intracellular organization and interaction with the cell's substructures (but not in the affinity of the site responsible for binding to the ligands). 5-HT_4 receptors and β1-, β2-, β4-adrenoreceptors have a common mechanism of intracellular regulation. Agonists bind to these receptors and lead to the activation of the Gs protein and the subsequent activation of adenylate cyclase, which forms cAMP from ATP. cAMP binds to the regulatory subunit of the protokinase A (PKA) and causes its dissociation with the catalytic subunits, i.e. leads to activation of PKA. PKA, as well as PKS, phosphorylates various cellular proteins, including intranuclear ones. PKA, as well as PKS, phosphorylates various cellular proteins, including intranuclear ones. PKA causes an increase in the intracellular concentration of Ca^{2+} by activating the L-type Ca^{2+} channels. Presynaptic 5-HT_{1D} receptors inhibit the release of norepinephrine, while 5-HT_4 receptors, on the contrary, increase its release [16]. It is assumed that 5-HT_4 receptors are involved in learning and memory. Many studies have noted that 5-HT_4 receptors can improve the cognitive functions of animals when stimulated within different behavioral paradigms. The effect of 5-HT_4 receptors in the CNS may be associated with the release of acetylcholine [25].

In the CNS, preferential localization of receptors on postsynaptic membranes is noted in the basal ganglia, including the substantia nigra, the caudate nucleus, the pale nucleus, the membrane, the nucleus accumbens, the hippocampus, and in the motor cortex the red nucleus and ventral horns of the spinal cord [26]. The expression of all isoforms is noted in the urinary bladder and urinary tract and the human colon [27, 28]. The 5-HT_4 receptors are preferentially linked to Gs protein and promote the formation of cyclic adenosine monophosphate. 5-HT_4 receptors are widely distributed in the brain and on the periphery. In the brain, 5-HT_4 receptors are associated with functions such as memory and cognitive function. When signaling receptor is disturbed, pathologies such as Alzheimer's disease, eating disorders (for example, anorexia nervosa) and depression may occur [29]. When the 5-HT_4 receptor is activated, acetylcholine is released in the ileum and the esophagus and colon in pigs shrink. He is also involved in the modulation of gastrointestinal motility and secretory responses of the intestinal mucosa [30].

The 5-HT_5, 5-HT_6, 5-HT_7 receptors are metabotropic, which control the adenylate cyclase system by means of the G-protein [10]. The least studied of all types of serotonin receptors is 5-HT_5. This class includes two receptors, namely the receptor 5-HT_{5A} and 5-HT_{5B}. Both 5-HT_{5A} and 5-HT_{5B} are expressed in mice and rats, and the 5-HT_{5A} receptor functions only in humans. The 5-HT_{5B} receptor is present as a pseudogen. However, early-stop codons interrupt the expression of the functional protein. 5-HT_{5A} receptors have been shown to bind to Gi/Go and inhibit forskolin-induced (activator AC) AC activity in HEK 293 cells (human embryonic kidney). These receptors are expressed in several areas of the brain, but to date no evidence of 5-HT_5 receptor expression in the cardiovascular system is known. Three variants of 5-HT_7 receptor splicing were found in both humans (5-HT_{7A}, 5-HT_{7B}, 5-HT_{7D}) and rats (5-HT_{7A}, 5-$HT_{7B,}$ 5-HT_{7C}, 5-HT_{7E}) [31].

In conclusion, describing a wide range of biological effects of serotonin, it should be noted that it modulates the processes of higher nervous activity, causes a reduction in the smooth muscles of the bronchi,

intestines, vessels, has a pronounced effect on the myocardium and other organs and systems of the body. In the process of ontogenesis, simultaneously with the synthesis of serotonin in tissues, the number of serotonin receptors increases. They interact, leading to the initial contraction of smooth muscles, the primary manifestations of the electrical activity of the central nervous system and the heart. In other words, without serotonin and serotonin receptors, it is impossible to initiate and maintain the most important functions of the body, which makes it possible to consider serotonin-reactive structures as «receptors of life», and serotonin as an unified trigger for the central nervous system, heart and smooth muscles in various species of living beings.

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М.Ж. Ахметова, Г.М. Тыкежанова, Ф.А. Миндубаева, Р.Р. Нигматуллина

Серотонин: биологиялық қасиеттері және оның рецепторлары

Соңғы он жылдарда серотонинэргиялық реттелуге көп мән беруде. Серотонин синтезінің молекулалық және жасушалық механизмдері, оның метаболизмі, рецепторлық әрекеттесуі жақсы зерттелген. Серотониннің жан-жақты әсері оның серотониндік рецепторларының көп болуымен түсіндіріледі. Серотонин (5-гидрокситриптамин; 5-hydroxytryptamine, 5-HT) — серотонинэргиялық жүйенің негізгі медиаторы. Адамда 5-HT орталық жүйке жүйесінде (ОЖЖ) ағзаның қалыпты және патологиялық физиологиялық түрлі қызметтерін реттейтін, жалпы гомеостаздың тұрақтылығын сақтап тұратын нейрондық түйіспелердегі негізгі нейромедиатор ретінде қызмет жасайды. 5-HT өзінің нысана мүшелеріне, соның ішінде жүрек және қан тамырларға морфогенетикалық және реттеуші әсер етеді. Серотонинэргиялық жүйе атеросклероз, артериялық және өкпе гипертензиясы, жүректің ишемиялық ауруы, жүрекшелердің фибрилляциясы, жүрек жеткіліксіздігі патогенезінің бастамасы болып табылады. Ишемиялық аурумен ауратын емделушілер қанында серотонин концентрациясын жоғары болып табылады. Серотонинэргиялық жүйенің жүрек-қантамыр жүйесіне әсері жануарларда жақсы зерттелген. Серотониннің түрлі сүткоректілердің жүрекшелер мен қарыншалар миокардына оң инотропты әсері байқалған. Сонымен қатар нейромедиатор серотонин бас миының қалыптасуында да маңызды рөл атқарады. Серотониннің аз деңгейінің әсерінен дамудың бастапқы кезеңдерінде ересек адамның бас миы сенсорлық дабылды бұрыс қабылдауы байқалады. Шолу мақаласында 5-HT рецепторларының көп түрлерінің болуымен түсіндірілетін, серотониннің ОЖЖ және одан тыс жерлердегі кең биологиялық маңызды әсері қарастырылған.

Кілт сөздер: серотонин, адреналин, жүрек, миокард, рецептор, нейромедиатор, қан тамырлары, жүрек қарыншылары, егеуқұйрық.

М.Ж. Ахметова, Г.М. Тыкежанова, Ф.А. Миндубаева, Р.Р. Нигматуллина

Серотонин: биологические свойства и его рецепторы

В последнее десятилетие большое внимание уделено изучению серотонинэргической системы. Достаточно хорошо изучены молекулярные и клеточные механизмы синтеза серотонина, его метаболизма, рецепторного взаимодействия. Широкий спектр эффектов серотонина объясняется наличием большого разнообразия серотониновых рецепторов. Серотонин (5-гидрокситриптамин; 5-hydroxytryptamine, 5-HT) — основной медиатор серотонинэргической системы. У человека лучше всего охарактеризована роль 5-HT в центральной нервной системе (ЦНС), где амин выступает в качестве нейромедиатора в нейронных синапсах и участвует в формировании и регуляции различных физиологических функций организма в норме и при патологии, играя важную роль в поддержании гомеостаза. 5-HT является нейрогормоном, который оказывает морфогенетическое и регуляторное действие на органы-мишени, в том числе сердце и сосуды. Серотонинэргическая система является звеном патогенеза атеросклероза, артериальной и легочной гипертензии, ишемической болезни сердца, фибрилляции предсердий, сердечной недостаточности. У пациентов с ишемической болезнью сердца выявлено повышение концентрации серотонина в крови. Влияние серотонинэргической системы на сердечно-сосудистую систему достаточно глубоко изучено на животных. Показано, что серотонин оказывает положительное инотропное действие на миокард предсердий и желудочков различных млекопитающих. Также нейромедиатор серотонин играет важную роль в формировании головного мозга. Низкий уровень серотонина на начальных стадиях развития приведёт к тому, что взрослый мозг будет неадекватно обрабатывать сенсорные сигналы. В обзоре рассмотрены значимость и широкий спектр биологиче-

ского действия серотонина в ЦНС и вне ЦНС, который объясняется разнообразием семейства 5-НТ рецепторов.

Ключевые слова: серотонин, адреналин, сердце, миокард, рецептор, нейромедиатор, кровеносные сосуды, желудочки сердца, крыса.

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