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EVOLUTIONARY DEVELOPMENT AND FUNCTIONAL STATE OF THE HYPOTHALAMIC-PITITUITARY SYSTEM (LITERATURE REVIEW)

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ABSTRACT

The hypothalamic-pituitary system of the human body is a complex neurosecretory complex that coordinates the endocrine regulation of metabolism with the work of the autonomic nervous system and the integral emotional and behavioral regulation of the limbic system. This review presents an analysis of the literature data, which indicates the entire path of development of the hypothalamic-pituitary system, nervous and humoral regulation of the body, the biological effect of hormones of the hypothalamus and pituitary gland, the physiology of the hypothalamic-pituitary system and diseases associated with a deficiency or excess of these hormones.

Key words: hypothalamus, pituitary gland, nervous regulation, humoral regulation.

INTRODUCTION

The human organism is associated with the most complex system in nature, where each cell performs only its specific role. This system, in the course of its evolutionary development, has been refined and complicated over time. This explains its predominant role in the biochain. As a result of this process, the human organism has undergone as many serious changes as possible.

The human organism functions due to closely related regulatory systems - humoral (endocrine), nervous and immune, which constitute a single holistic system. Thanks to this trio, the body adapts to environmental factors [32,33,34]

Initially, the human body was under the control of humoral regulation, which was carried out by biologically active substances through the liquid media of the body (blood, lymph, tissue fluid, saliva) [36]. However, this type of regulation of the organism could not fully fulfill the tasks that would sufficiently regulate all processes of vital activity of living organisms. There was an urgent need to transfer information between cells with the fastest possible speed for the efficiency of response to those threats that came from the environment.

The communication of the living organism and the environment is carried out in tandem by nervous and humoral regulation, which are unified and form a single system to control all organs and cells in the body. The deficiencies of one type of regulation are made up for by the superiority of the other type. Products of metabolism acting on effector organs, nerve centers, chemoreceptors located at the ends of sensitive nerves, trigger chemical reactions in the body in a humoral or reflex way. Humoral transmission of nerve impulses in the central and peripheral nervous system is carried out by mediators. Humoral regulation in the body is carried out not only by hormones, but also by products of intermediate metabolism, metabolites [36].

At the same time, the nervous regulation of the organism is much better studied than the humoral regulation, as it can be registered by various instrumental methods of research. Despite the fact that humoral regulation is evolutionarily earlier and well proven, its study is difficult due to the presence of a large number of tissues that need regulation at the cellular and organ level [25].

The immune system, which unites the organs and tissues that protect the body from various diseases, was studied later than anyone else. It detects and destroys cancer cells, is able to distinguish a pathological cell from the cells of its own body. Destruction of potentially dangerous microorganisms and toxins is carried out precisely by such cells of the immune system as lymphocytes. The system of acquired immunity first appeared in vertebrates and is represented by T-lymphocytes and antibodies produced by B-lymphocytes.

In order to understand the whole essence of the mechanisms of organism regulation, it is necessary to delve deeper into the evolutionary development of brain structures. This evolutionary process is very complex. Initially, this process begins with aquatic multicellular organisms that existed without nerves. These organisms, thanks to a simple network of nerves, only collected information from the external environment, but could not process it, but simply existed with the received information. Thus, aquatic multicellulars had a diffuse network of nerves. Further, in mollusks, flatworms and crustaceans, a nodal nervous system appears. In this form, the connection of nerve cells, namely, their excitation passes through clearly defined pathways. This type of organization of the nervous system becomes relatively vulnerable, as any damage to one of the nodes leads to a change in the functions of the whole organism. Despite this, this form of nervous system is qualitatively fast and accurate. For chordate organisms, a mixed form of nervous system is specific. The nervous system of higher animals has taken all the best. It is unambiguously high reliability of diffuse type, accuracy, precision, precision and rapidity of organization of reactions of nodal type.

The embryonic development of the brain is represented as follows. At the beginning it consisted of the telencephalon, diencaphalon, mesensaphalon and rhombencephalon, which were subsequently transformed into parts of the brain. From the rhombencephalon the hindbrain and medulla oblongata are formed. From the hindbrain the cerebral pontine and cerebellum are subsequently formed. For example, from the telencephalon (terminal brain) the cerebral hemispheres are formed, from the diencephalon (intermediate brain) - the thalamus, hypothalamus, epithalamus.

The hypothalamus, as the main organ involved in the regulation of the body, consists of a large number of cells that allow it to perform complex functions. The hypothalamus develops from different cells very similar to each other (neurons, astrocytes, tanycytes, neural crest cells and endothelial cells) Each of these cell types, such as hypothalamic neurons, simultaneously differ from each other in function, substances they synthesize. All of these cells are formed from precursor stem cells called progenitors, which differentiate into a specific cell type. These cells already have persistent biomarkers that allow them and their progeny to be distinguished from other cell types. Progenitor stem cells express different genes. Cell expression is the process by which hereditary information from a stretch of DNA is converted into RNA or protein. Expression is what accounts for cell diversity. Different gene expressions result in anterior hypothalamic and tubular progenitor cells forming hypothalamic nuclei. For example, neurons form from anterior progenitor cells to form supraoptic and paraventricular nuclei. At the same time, other hypothalamic cells migrate from various parts of the neural tube to the hypothalamic region (e.g., gonadoliberin-producing neurons migrate from the olfactory mucosa-the olfactory part of the nasal cavity-to the hypothalamus [29].

Neuronal cells are formed from some and glial cells from others. Neurons are important basic structural and functional elements of the CNS and peripheral nervous system. They generate and transmit electrical impulses. These cells are different in shape and size and form 2 types of outgrowths: axons and dendrites.

Glial cells outnumber neurons and make up the majority of the central nervous system. However, glia cells are unable to generate an action potential.

Neuroglial cells differ in their origin and structure. They provide differential, support, trophic, secretory and protective functions [36].

The humoral, immune and nervous systems are three interrelated systems that complement each other. The nervous system is activated first. It begins to be activated by pain receptors. Impulses through the ganglia go to the posterior horns of the spinal cord, then go to the thalamus, where electrical impulses trigger immune and humoral regulation. Different types of immunity are activated and at the end the humoral system corrects and completely eliminates "malfunctions" in the body.

In humoral regulation, all information enters the central nervous system and excites the hypothalamus, which produces releasing hormones (liberins or statins) that subsequently control the production and synthesis of pituitary tropic hormones, which ultimately affect the peripheral endocrine gland. Thus, several intermediate effectors are involved in the process of humoral regulation. This explains the slower speed of this type of regulation in contrast to nervous regulation [2,30,35].

The hypothalamic-pituitary neurosecretory complex is the highest neuroendocrine transducer of the human body, which coordinates the endocrine regulation of metabolism with the work of the autonomic nervous system and integral emotional-behavioral regulation of the limbic system [3,37].

A great role is assigned to a huge number of hormones, which directly affect the functional capabilities of a person. Hormones inhibit or activate the action of the nervous system on the course of physiological processes, as well as act independently. Hormonal effects in reacting cells develop with a longer latency period, proceed more slowly and last longer than nervous regulatory influences. In relation to each other, hormones either play an auxiliary role, or inhibit the action of another hormone in target cells, or block or stimulate the secretion of another hormone [11].

Individuals of different ages have different genetic programs due to their different reactivity due to asynchrony in expression and repression. The endocrine system and its sensitivity to endocrinopathies is different. It depends, for example, on age. Thus, the resistance of the hypothalamic-pituitary neurosecretory complex to chronic stress is lower in adolescents than in adult individuals. In ontogenesis of puberty, corticoliberin and luliberin activity of hypothalamus sharply increase, folliliberin activity remains significantly lower compared to adult individuals, somatostatin production decreases, synthesis of antidiuretic hormone, maximum in early childhood, slightly decreases, and oxytocin production increases.

The hypothalamus is a complex brain structure, the highest neuroendocrine organ, which due to its anatomy in all members of the vertebrate class, plays an important role in regulating the main points of physiology of homeostasis and behavior, visceral and somatic functions [1,5]. It is located in the forebrain and has inseparable links of functioning with the pituitary gland, which further keeps under control the entire process of synthesis and production of both its hormones and hormones of pituitary-dependent endocrine glands [7,8,11,28,41]. The hormones of the pituitary gland and pituitary-dependent endocrine glands (adrenal cortex, thyroid and sex glands) are responsible for maintaining homeostasis, the body's response to any stress factor, the process of reproduction and growth. In addition, the hypothalamus, as the main organ of the endocrine system, determining neural connections through the autonomic nervous system regulates many physiological processes in the body. It contains the center of thirst, the center of thermoregulation, the center of hunger and satiety. The hypothalamus modifies the cycle of sleep and wakefulness through information (the amount of melatonin - the sleep hormone), which comes from the retina in the form of signals in response to the amount of light in the environment. In addition, the hypothalamus by controlling the production of sex hormones affects menstrual function, spermatogenesis. Through the hormone oxytocin, it controls a woman's fertility, pregnancy, childbirth, and lactation [9, 13, 17, 19, 26, 41]. Thus, the hypothalamus and responds to the physiology of the body through hormonal and nerve impulses. And hence, hypothalamic dysfunction can lead to various health consequences for individuals such as energy imbalance, development of diabetes insipidus and sleep disturbance [15, 31,41].

The hypothalamus is divided into medial and lateral hypothalamus. The medial hypothalamus is involved in energy regulation and consists of the VMN (ventromedial nucleus), ARC (arcuate nucleus) and paraventricular nucleus (PVN) [3,11,18,19,39].

The ARC contains two groups of neurons. The first group of neurons produces orexigenic peptides (agouti-related protein and neuropeptide Y (NPY)). The second group is anorexigenic peptides (proopiomelanocortin (POMC) and cocaine- and amphetamine-related transcripts (CART)). POMC neurons are precursors of the anorexic peptide α-melanocyte-stimulating hormone (α-MSH), which acts on the melanocortin 4 receptor (MC4R) and reduces appetite and food intake [19,41]. The PVN expresses melanocortin receptors 3 and 4 and NPY receptors. It also produces neuropeptides such as corticotropin-releasing hormone, oxytocin and vasopressin, which have anorexigenic effects [19,22,40]. The hypothalamic anorexigenic center is also influenced by leptin, insulin, ghrelin, and peptide YY. Efferent signals from the PVN and LH, in turn, stimulate the sympathetic nervous system (SNS) or vagus nerve via the autonomic nervous system, promote the production of growth hormone, somatostatin, and thyroid hormone, which are also involved in adipose tissue metabolism and metabolic rate [11,19,38].

Speaking about the nervous and humoral regulation of the body, it is necessary to remember about the so-called "happiness" hormones. Positive emotions are impossible without the participation of hormones. Stress, depression, sadness and other negative phenomena often arise because the production of dopamine, serotonin, oxytocin and endorphins is blocked.

Dopamine inhibits prolactin production, increases blood pressure levels, increases the strength and frequency of heartbeats, increases blood flow in the kidneys and hypernatriuria, and relaxes the smooth muscles of the stomach and intestines.

As a neurotransmitter, dopamine affects the formation of motivation, feelings of pleasure, feelings of reward and desire, and emotional reactions accompanying motor activity. Its amount increases when achieving a goal and even the very anticipation of this moment, with pleasant tactile sensations, eating delicious food, rest, physical activity.

Another neurotransmitter is serotonin, which improves memory, attention, perception; speeds up and facilitates movement; lowers pain threshold; controls sex drive and reproductive function; provides adequate sleep, aids digestion; reduces allergic reactions; regulates uterine and fallopian tube contractions during labor; promotes good mood; and participates in the synthesis of pituitary hormones

Endorphins are a group of chemical compounds that are naturally produced in the neurons of the brain. They have and analgesic effect; stress tolerance; reward function: feeling of euphoria; involved in the regulation of arousal and inhibition.

Unambiguously we can say with certainty that the clear work of the hypothalamus is necessary for the normal functioning of the human body. Hence, any changes in the body that affect the hypothalamus can make it not work as it should, and this will consequently affect the regulation of many aspects of the body. This is why we say it is the "conductor", as it has the ability to balance the overall hormonal movement indirectly through another important organ, the pituitary gland.

The pituitary gland (hypophysis, glandula pituitaria) is an endocrine gland that is connected to the intermediate medulla via a funnel. It is located in the Turkish saddle and is protected by bony walls on all 3 sides [1,12]. The robust protection of the pituitary gland in the Turkish saddle reflects its exceptional role in the body. “No organ of the human body is so well protected, so centrally located, or so carefully hidden” (Cushing H.,1930).

The pituitary gland consists of three parts. The anterior part (adenohypophysis)-where tropic hormones are produced, the posterior part (neurohypophysis)-where ADH and oxytocin accumulate, which are produced in the hypothalamus, and the middle part, which produces melanocyte-stimulating hormone (MSH, melanotropin), which affects the formation of pigment (melanin) [1,5,20]. Pituitary function is regulated by hypothalamic releasing factors, hormones of peripheral endocrine glands (negative feedback principle) and para- and autocrine secretion of the pituitary gland itself [6,37]. Throughout life, pituitary cells adapt to (patho-) physiological hormonal changes. For example, during lactation (increased prolactin production), during stressful stress on the body (increased ACTH production) [27].

The histologic structure of the pituitary gland is determined by the presence of 2 types of cells - chromophobic and chromophilic cells. Chromophilic cells include acidophilic cells (somatotrophs producing growth hormone and lactotrophs producing prolactin), which are stained with acidic dyes and basophilic cells (gonatotrophs producing FSH and LH, thyrotrophs producing TSH and corticotrophs producing ACTH), which are stained with basic dyes. Chromophobic cells are represented by undifferentiated progenitor cells and cells of early and late stages of the secretory cycle [10,20]. The middle part of the pituitary gland is poorly developed. The neurohypophysis consists of axons of neurons of large-cell hypothalamic nuclei (supraoptic and paraventricular). This part of the pituitary gland accumulates neurosecretes containing hypothalamic hormones such as oxytocin and vasopressin [4,20].

The connection between the hypothalamus and the pituitary gland was proved centuries ago by Galen in De Usu Partium, Galen's major treatise on physiology and Anatomicae Administrationes. The doctrines were continued by Andreas Vesalius in De Humani Corporis Fabrica (1543). In these the author painted the relationship of the hypothalamic hypothalamic subcutaneous tissue and the pituitary gland. The term “pituitary stalk” was introduced into literature only in 1742 by Joseph Leo, and mankind heard about the term “hypothalamus” in 1893 thanks to the works of Swiss anatomist Wilhelm Hissom. Later, many discoveries in the world, which do not stop to this day, laid the ground for the study of the leading role of the hypothalamus in the hormonal regulation of the body, the influence on all the processes taking place in the human body.

Hypothalamic-pituitary system under the influence of external and internal factors definitely gives “failure” in its work, which is manifested by dysfunction.

Dysfunction of the hypothalamic-pituitary system can be considered according to several criteria:

I. Level of damage
primary lesion - pituitary lesion
secondary lesion - hypothalamic lesion
II. Functional status
hypofunction
hyperfunction
III. Etiology
congenital
acquired
IV. By time of developing
“early” forms (before puberty)
“late” (after puberty).
V. By scale
total
partial
subtotal

Hypothalamic damage is caused by energy imbalance leading to hypothalamic obesity; development of central and idiopathic forms of diabetes insipidus; sleep disturbance; behavioral and emotional disturbance; temperature disturbance.

The causes of hypothalamic-pituitary dysfunction are cellular defects at the level of genes (mutations of hypothalamic releasing hormones, pituitary hormones, as well as enzymes involved in their synthesis) [21]. Many scientists have proved the connection between hypothalamic and pituitary dysfunction and gene polymorphism. Thus, Jeong et al., 2006 and Zhao et al., 2012 in their works on mouse models determined the connection of phenotypes in patients with septo-optic dysplasia (SOD) with the defect of hypothalamic pattern (rhythm) formation, which led to pituitary hypoplasia and absence of optic disc. Data from the works of other scientists indicate that the Wnt/β-catenin pathway also plays a clinically significant role in hypothalamic pattern formation, as SOD patients with Wnt effector variants TCF7L1 have been identified (Gaston-Massuet et al., 2016). A large number of additional genes are associated with hypothalamic developmental abnormalities leading to hypopituitarism (Mehta and Dattani, 2008), including SOX2 and SOX3.

Also hypothalamic-pituitary dysfunction may be due to direct damage to both the hypothalamus and pituitary gland by tumor, hemorrhage, or concussion; the influence of various kinds of exo- or endogenous toxic substances. These factors lead to impaired synthesis of hormones of the hypothalamus and adenohypophysis.

Dysfunction of the hypothalamic-pituitary system can manifest as either hypo- or hyperfunction.

HHS diseases due to hypofunction include diabetes insipidus (vasopressin deficiency), hypopituitarism (deficiency of tropic hormones - Sheehan's syndrome, Simmonds syndrome, conditions after cranial irradiation, chemotherapy and surgical treatment of pituitary tumors, congenital aplasia of the pituitary gland, genetic defects in differentiation of pituitary and hypothalamic cells, empty Turkish saddle syndrome, neuroinfections, hemorrhages of pituitary tissue, ischemia and necrosis of the pituitary gland after massive blood loss, pituitary dwarfism) [14,16,24]. Lack of hypothalamic hormones reduces the production of pituitary hormones. Examples include diseases such as Kallmann syndrome and hypothalamic hypothyroidism.

Hyperfunction occurs in hyperplasia and adenoma of the pituitary gland (acromegaly, gigantism, ACTH-dependent Cushing's syndrome, prolactinoma, malignant tumors of the adenohypophysis), in the syndrome of inadequate ADH production. An exception to this is increased prolactin production, which increases after such lesions that lead to loss of inhibitory hypothalamic tone (empty Turkish saddle syndrome) [21].

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