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Research Article

Journal of Infectious Diseases and Viruses Research

Morphofunctional Organization of The Hypothalamus and The Principles of Constructing Stereotaxic Atlases

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Submitted: 13 Dec 2022 **Accepted:** 20 Dec 2022 **Published:** 23 Dec 2022

Citation: *Dremza J.K., Maksimovich N.Ye. Bon E.I., Portonenko A.M. (2022) Morphofunctional Organization of The Hypothalamus and The Principles of Constructing Stereotaxic Atlases, J Infec Dise and Vir Res, 1(1),01-10*

Abstract
The study of the morphological features of the hypothalamus is of great interest to researchers in the field of medicine, physiology, and pathophysiology.The hypothalamus is an evolutionarily ancient formation of the central nervous system, functionally related to the regulation of the vegetative. It performs many important functions in the body, which will be described in the article. Our work reflects the principles of constructing stereotaxic atlases, which are important for determining the position of various brain structures (in particular, the hypothalamus) in stereotaxic coordinates, which is of great practical importance.

Keywords: hypothalamus, experimental, stereotaxic atlas.

Introduction

The hypothalamus is an evolutionarily ancient formation of the central nervous system, functionally related to the regulation of the vegetative. Tonkikh defined this area of the brain as the "center of the autonomic integration of the body", since the hypothalamus has a corrective effect on various processes in the visceral sphere and regulates not only the reactions of individual organs, but also the autonomic support of various activities [1,2].

In the history of studying the functions of the hypothalamus, there are three stages: 1) elucidation of the role of the hypothalamus in the regulation of vegetative processes in the body of humans and animals; 2) the study of the localization of functions within the hypothalamus, the creation of an idea of the existence of sympathetic and parasympathetic zones in the hypothalamus, which was a significant step in the study of the functions of the hypothalamus, but later it was rejected; 3) study of the mechanisms of activity of various departments of the hypothalamus [1-3].

Consideration of the physiology of the hypothalamus from the standpoint of modern biology and medicine is adequate in several aspects, among which the following can be distinguished:

1) the functions of the hypothalamus as a regulator of autonomic processes, the activity of the pituitary gland and others endocrine glands; its role in the formation of motivations and emotions, the state of sleep and wakefulness; 2) participation of the hypothalamus in the formation of ascending and descending influences on other departments brain; 3) electrophysiology of the hypothalamus; 4) biochemical organization of the hypothalamus; 5) dysfunction of the hypothalamus as a way to study the functional significance of the human hypothalamus[3-5].

Knowledge of the pathology and physiology of the hypothalamus formed the basis for the use of stereotaxic surgery of the hypothalamus and the treatment of diseases of this area of the brain with targeted, biochemical drugs [6].

Aim

The purpose of the work is to summarize the literature data on the morphofunctional organization of the hypothalamus and provide information on the principles of constructing stereotaxic atlases.

About the Physiology of The Hypothalamus

The multifunctionality of the hypothalamus should be emphasized. In this small section of the CNS, neuronal structures are concentrated that are related to the regulation and correction of various processes that occur mainly in the vegetative sphere of the human and animal body. In this respect, the hypothalamus is a unique region. Consideration of the functions of the hypothalamus as such, without its connections with other areas of the brain, of course, is conditional, since the hypothalamus is morphologically and functionally closely connected with other brain structures, including limbic structures, the cerebral cortex, etc., and in a situation of dissociation (for example, during operational isolation), its activity is significantly disrupted [4,5].

The medial part of the posterior hypothalamus topographically represents a continuation of the reticular formation of the midbrain and performs the functions characteristic of this formation

- it has a nonspecific activating effect on other parts of the brain. Pavlov, considering the hypothalamus as a zone of the brain in which irritations coming from the "inner world" are collected, emphasized the importance of this afferentation for maintaining the tone of the cerebral cortex, and Orbeli, on the basis of numerous studies, determined the role of the hypothalamus as a regulator of the adaptive-trophic functions of the higher parts of the brain . The importance of the hypothalamus in providing complex forms of behavior is also shown [4-7].

Afferent inflow to the hypothalamus is carried out through numerous pathways that provide the opportunity for information to flow to the hypothalamic neurons, which, apparently, is a morphofunctional basis that provides the ability to analyze and integrate stimuli of a different nature and form signals that control or correlate the course of reactions in the vegetative sphere [4,5].

Neurons of the hypothalamus respond to afferent stimuli - light, sound, tactile. The hypothalamus is characterized by representation of visceral afferentation, as well as the ability of some of its neurons to respond to changes in the chemical and physical properties of blood - its composition, temperature, osmotic pressure, etc. This ability is also preserved in operationally isolated areas of the hypothalamus, which indicates its perception by cells incoming humoral chemical and physical stimuli and significantly distinguishes this area from other brain structures [5,7,8].

Features of the blood supply to the hypothalamus and the relatively high permeability of the blood-brain barrier in this area of the brain determine the possibility of receiving signals about changes in the physicochemical properties of the blood. Thus, the hypothalamus is a collector, which receives information about the state of the internal and external environment through the nervous and humoral pathways [5,9].

The structures of the hypothalamus, which have a corrective effect on most processes in the vegetative sphere, are characterized by the regulation of complex functions, the provision of which requires the participation of various components [5,8]. This role of the hypothalamus can apparently be defined as the regulation of homeostasis in its various manifestations (temperature, salt, immune, etc.). The meaning and peculiarity of the functioning of this area of the brain lies in the fact that it regulates the activity of physiological systems as a whole, influencing the activity of various components of the system. For example, during the act of eating, the blood supply to the gastrointestinal tract, the excretion of saliva, gastric juice, the functioning of the liver, pancreas, motor activity of the stomach and intestines, etc. change. All this occurs in a certain sequence in time and intensity, which is regulated hypothalamus [5,9,10]

The hypothalamus is involved in the regulation of temperature homeostasis. The nerve elements of the anterior hypothalamus (medial preoptic region) have the ability to respond to temperature changes, integrate temperature and non-temperature input signals from various areas of the body, influence the effector mechanisms of thermoregulation, and change behavioral reactions [4,7,11].

Under conditions of pathology (when bacteria and their metabolic or decay products act on the body), the thermal and cold sensitivity of this area of the brain changes in opposite directions, which leads to an increase in body temperature - fever. The medial preoptic region of the anterior hypothalamus is also highly sensitive to local administration of microdoses of pyrogenic agents. An analysis of the impulse activity of individual neurons under the action of pyrogens gives reason to believe that thermosensitive nerve cells in this area also have chemoreceptor properties [6,24].

Thus, in the anterior hypothalamus (medial preoptic region), neurons are concentrated that perceive temperature changes and respond to certain pyrogens. The effector part of the thermoregulatory system of the hypothalamus has been studied less clearly. It is known that the impact on the medial parts of the hypothalamus of a thermal injection causes a temperature reaction. Some researchers tend to believe that the central efferent link of thermoregulation is located in the posteromedial structures of the hypothalamus [3,4].

The same principle of functional organization is also characteristic of the hypothalamic structures that regulate osmotic pressure in the blood and tissues, blood sugar levels, and eating behavior. In the hypothalamus, the reception of blood glucose levels and other nutrients occurs in the "hunger center" - the ventrolateral nucleus and the "satiation center" - the ventromedial nucleus [4,7,10].

The neurons of the supraoptic and paraventricular nuclei were found to be sensitive to changes in the osmotic blood pressure. Those zones are involved in the management of water-salt metabolism, the secretion of a factor that stimulates the release of antidiuretic hormone by the pituitary gland. Resolution of the supraoptic nucleus entails the development of diabetes insipidus, and irritation of the anterior nuclei leads to thirst and hyperhydration [4,6,12].

The hypothalamus is also involved in the regulation of the body's immune homeostasis. With massive and local damage to the structures of the hypothalamus, suppression of the immunogenesis process is observed, and most authors associate this function with the mediocaudal part of the hypothalamus (posterior hypothalamic field) [5,10,13].

Neurophysiological analysis suggests that other structures of the hypothalamus are also related to the provision of body reactions to antigenic effects (AHP, HVM, SPM, ML) [10,13].

The role of the hypothalamus in the regulation of fat metabolism is known. When the hypothalamus is damaged, patients develop obesity, or cachexia, which some authors attribute to damage to the mamillary bodies and mediobasal nuclei of the hypothalamus. But, since various processes may lie in the genesis of obesity - an increase in appetite (“wolf hunger”), a decrease in metabolism (for example, with hypothyroidism) and a violation of fat metabolism, the presence of obesity cannot serve as sufficient evidence for judging the role of the hypothalamus in the regulation of fat metabolism [13,14].

A special place in the physiology of the hypothalamus is occupied by studies devoted to the study of its role in the regulation of the functions of the pituitary gland and, thus, all those processes that are regulated by pituitary hormones [14].

According to the data, the hypothalamus contains neurons that respond to reflex and humoral signals by releasing so-called releasing factors that increase the secretory activity of the pituitary gland, whose hormones affect the intensity of the endocrine glands. An excess of hormones in the blood, in turn, reduces the activity of cells that produce releasing factors (by the type of negative feedback). Lack of hormones reflexively or humorally stimulates the secretion of the same factors. This type of organization is typical for the regulation of the work of various endocrine glands: the thyroid, gonads, adrenal cortex. In addition, the neurosecretory function of the cells of some nuclei of the hypothalamus is known. So, in the supraoptic and paraventricular nuclei, antidiuretic hormone, vasopressin, oxytocin are formed, which, apparently, through the fibers of the hypothalamic-pituitary pathway enter the posterior pituitary gland. It is now believed that some other nuclei of the hypothalamus also have a neurosecretory function [3,6,5,15].

Among the hypothalamic factors that regulate the activity of the pituitary gland, there are stimulating - releasing factors (RF) and inhibitory - inhibiting factors (IF), which affect the intensity of the work of certain cells of the anterior pituitary gland, although with the exclusion of these influences, some, so-called basal, level of secretion triple hormones persists[2,10,7]. Aleshin [3,6] cites the following triple pituitary hormones, as well as factors activating and inhibiting them, found in the hypothalamus:

Hormone	activating factor	depressing factor
Somatotropic Hormone (STH)	SRF	SIF
Adrenocorticotropic Hormone (ACTH)	CRF	CIF (?)
Thyroid Stimulating Hormone (TSH)	TRF	
Follicle stimulating hormone (FSH)	FRF	
Luteinizing Hormone (LH)	LRF	LIF
Lactotropic hormone, or prolactin (LTH)	PRF (?)	PIF
Melanin cytostimulating hormone (MSH)	MSH-2F	MIF

The localization of these functions in the hypothalamus has been studied by many authors, but at present it is fair to speak only of a greater or lesser concentration of neurons that have a particular function in a particular zone. The complexity of this issue is determined by two circumstances: 1) cellular elements producing IF and RF, most concentrated in a certain zone, are also scattered and in other, adjacent departments of the hypothalamus; 2) in the hypothalamus, apparently, there are neurons that do not release RF, but affect the activity of their release by other cells of the hypothalamus; these neurons are also not concentrated in the form of a rigidly defined center[2,3,6,10].

According to Sentagothai and co-authors, both possible types of localization exist in the hypothalamus - “mosaic” and “general model”, i.e., individual processes and complex functions or activities, with the second variant of organization predominating [3].

As an example, the role of the hypothalamus in the regulation of sexual function can be considered. The hypothalamus regulates the generative and endocrine functions of the sex glands through the pituitary gland, and the gonadotropic hormones of the anterior lobe of the latter - follicle-stimulating and luteinizing - can be represented as transmitters that transmit the influence of the hypothalamus to the sex glands. It has been experimentally established that the cyclicity or continuity of the secretion of these hormones by the pituitary gland, i.e. secretion according to the female or male type, is determined by the hypothalamus, and male sex hormones, influencing the hypothalamus, change the female type of secretion that initially occurs in ontogenesis to a continuous, male one. The regulation of gonadotropic functions is carried out by two structures of the hypothalamus: the "lower center" - the arcuate and ventromedial nuclei and the "higher center" located in the preoptic region of the mediobasal hypothalamus. Influences coming from the arcuate and ventromedial nuclei cause basal secretion of pituitary hormones, which occurs continuously, but the amount of luteinizing hormone (LH) released in this case is not enough to cause ovulation. The "higher center" stimulates the work of the "lower" one, and as a result of this activation, there is a massive release of LH by the pituitary gland (the so-called ovulation quota). Thus, the preoptic region controls the cyclicity of luteinizing hormone secretion [2,5,7].

Regulatory influences of the hypothalamus reach the pituitary humorally through the portal vascular system. Therefore, we are talking about the release in the hypothalamus of a biologically active and strictly specific substance - RF. Initially, the factor that activates the secretion of follicle-stimulating hormone (FRF) and luteinizing hormone (LRF) was separated. However, recently data have appeared that allow us to consider that they are identical, and the factor that activates the regulation of gonadotropic functions was named Gn RF, the amount of which is reflected in the quantitative and qualitative characteristics of the pituitary gland, i.e., the secretion of FSH and LH [2,6-9].

The work of the hypothalamic centers depends on the level of sex hormones in the blood and neurogenic influences. There was a point of view linking the secretion of Gn RF with the activity of the supraoptic and paraventricular nuclei, however, at present, researchers are inclined to the above opinion regarding the role of the small-cell mediobasal part of the anterior hypothalamus, including the paraventricular gray matter bordering the lower half of the third ventricle and the area of the gray tubercle. At the same time, the secrets of the large cell nuclei of the hypothalamus - supraoptic and, possibly, paraventricular (vasopressin, oxytocin) - affect the activity of the structures of the hypothalamus that regulate the gonadotropic activity of the pituitary gland [2].

In addition, dopamine- and serotonergic axons terminate on small neurons of the anterior mediobasal hypothalamus and their terminals, the neurons of which are located in other parts of the brain, in particular, in the hypothalamus. The signals coming through these axons affect the secretion of Gn RF: dopamine enhances its return, and serotonin inhibits it [2].

The preoptic area (suprachiasmatic nucleus) in females is characterized by an increased content of serotonin, a periodic decrease in the amount of which leads to an increase in the activity of the “higher center”, stimulating the “lower center” and thus enhancing the release of Gn RF into the blood of the portal system of the hypothalamus [16].

Consideration of the role of the hypothalamus as a regulator of the function of the sex glands shows the complexity of organizing this process at the hypothalamic level and, demonstrating on a specific example the principles of regulation of endocrine functions that were outlined above, reflects the main patterns of hypothalamic regulation of the work and other endocrine glands [2,16,7].

This general principle of the functional organization of the hypothalamus provides the possibility of perceiving various information coming through the nervous and humoral pathways and realizing the effect at different speeds. In addition, the foundations are being created for compensating impaired functions, i.e., the reliability of the regulatory system at the hypothalamic level is ensured in various parameters [7].

The significance of the hypothalamus in the formation of emotional behavior, noted by Bekhterev, attracted the attention of many researchers, whose efforts revealed some mechanisms of the participation of the hypothalamus in emotional reactions [2,5].

The discovery of three closed systems of the brain (especially the creation of the concept of the limbic system), linking its various structures that are involved in the regulation of emotional reactions and other complex forms of body activity, led to the emergence of a dominant point of view on the hypothalamus as a central relay station in the integration of biological motivations and emotional reactions of the body[2,4,17].

Along with other parts of the brain, the hypothalamus is involved in the regulation of the state of sleep and wakefulness, and, although there are diametrically opposed points of view regarding the localization of the mechanisms that regulate these states, at present, most researchers associate these processes with the function of the medial parts of the hypothalamus[2,14].

The system of regulation of eating behavior was also studied, the role of the lateral field (“hunger center”) and the ventromedial nucleus (“saturation center”) and their interaction in the mechanism of food saturation was shown [2,3].

The study of the electrophysiological features of the hypothalamus, which began with the study of the electroencephalographic characteristics of its various structures, made it possible to detect the polymorphism of the electrical activity of this area of the brain [7].

Connections of the anterior hypothalamus with deep layers (II–III) of the periform cortex and the dorsal hippocampus were found, although the latter are characterized by long-latency reactions, which indicates polysynaptic transmission of afferent signals from the anterior hypothalamus to this zone of the hippocampus. Upon stimulation of the posterior hypothalamus, evoked potentials, including short-latency ones, can be detected in various layers of the dorsal and ventral hippocampus, the motor cortex (sigmoid gyrus), which indicates a close connection between these brain regions [7].

Researchers have found that hypothalamic neurons are characterized by the same types of activity as neurons in other areas of the brain: impulses can be single, regular, batch, group and mixed. An essential feature is the polymodality of the cells of the hypothalamus — the irritation of various receptor devices affects the work of the same neuron (different afferent flows can converge on one neuron) [3,2,13,18].

The average frequency of spontaneous discharges of hypothalamic neurons varies from 1 to 10 imp./sec. According to Klimenko, it is 7.22 imp./sec. The structures of the hypothalamus differ somewhat in the average frequency of activity inherent in their neurons: for example, for the dorsomedial nucleus 5.8 pulses/sec., for the ventromedial — 8.2 [3,6]. However, the main indicator of the functional state of neurons is not the average frequency of pulsation, which can remain constant even under conditions of activation of functions, but the nature of the distribution of inter-pulse intervals.

The combination of electrophysiological, mathematical and machine analysis methods made it possible to describe the "mode of operation" of various structures of the hypothalamus based on the characteristics of the periodicity of the impulses of the neurons entering them. This study made obvious the existence of a limited number of variants of hypotonic neuronal impulses: 52 types of activity were detected and it was shown that, although the identification of other types of activity is fundamentally possible, the probability of their occurrence decreases exponentially [2,3,6,7,18].

Based on the identified types of "spontaneous" neuronal activity, it was possible to show the "modes of operation" characteristic of various nuclei and fields of the hypothalamus and demonstrate two main components of functional restructuring: a change in the "mode of operation" of the structure in relation to the background and a change in its interaction with other structures of the hypothalamus during activity [3].

Since during the implementation of various types of activity of the body, a functional restructuring of a number of formations of the hypothalamus occurs, which regulate the vegetative components of all processes, difficulties in determining the localization of functions in the hypothalamus are understandable. The multitude of connections, the integrative nature of regulatory influences, the need to include various systems in the implementation of the regulatory signal create the need for a dual approach to the issue of localization of functions in the hypothalamus. Recognizing the possibility of a certain concentration of functionally defined (one-digit) neurons, however, it is impossible to underestimate the importance of the participation of a complex of hypothalamic structures in the regulation of homeostatic reactions and complex forms of activity of the organism [3].

One of the main mechanisms of operation of any neurons is the transmission of signals from the ends of axons to a neuron and from a nerve cell through its processes to other neurons [9,21]. This transmission is carried out with the participation of various mediator mechanisms — cholinergic, adrenergic, serotonergic and others.

The hypothalamus is especially rich in mediators, indicating the importance of adrenergic and serotonergic mechanisms in the work of the hypothalamus. However, choline and dopamine reactive systems are also represented in it [2,4,7,11].

Along with this, serotonin was detected in the medial eminence, the role of serotonin-reactive and serotonergic mechanisms in the work of the hypothalamus was shown.

Acetylcholinergic neurons are concentrated in the anterior parts of the hypothalamus, and norepinephrine, adrenaline, and dopaminergic neurons are concentrated in the posterior parts. Since we are talking about the ergicity of hypothalamic neurons (i.e. on the mechanisms of transmission of excitation from one neuron to another) and it is shown that all types of mediation are represented in the neurons of the hypothalamus, it is possible to identify only the mechanism of mediation in one or another of its areas.Neurons of various ergicity are involved in the system of nervous or neurohumoral control of functions, therefore, physiological or pharmacological methods of analysis can reveal only the specific significance of a particular form of mediation in the regulation of a particular function. The most tangible successes in this regard have been brought by histochemical methods of analysis, the results of which can enrich us with biochemical maps of the hypothalamus [2,3,7].

A large section of works concerning the physiology and pathology of the diencephalic region of the brain consists of clinical studies. We emphasize only two provisions that are justified in these studies.

1) All therapeutic diseases described by neurologists and endocrinologists that have arisen as a result of damage to the hypothalamus are manifested in violation of one, and more often several functions regulated by this area of the brain, and in most cases the disease is manifested not so much by the loss of a certain regulatory function as by an imbalance in the activity of components of regulated systems. The study of the complex of information obtained in the clinic is one of the most important ways to study the physiology of the hypothalamus and the peculiarities of its activity in humans; it was the work of the clinical plan that initiated the development of research on the physiology of the hypothalamus.

2) Despite the intensive study of the physiology of various parts of the hypothalamus, the therapy of diseases of this part of the brain (even with functional forms of pathology) is difficult [3,8,9].

This necessitates an in-depth study of the morphology, physiology, biochemistry of the hypothalamus and the search for pharmacological approaches to the correction of its activity.

The hypothalamus is a department of the central nervous system, where numerous mechanisms of regulation of vital functions are concentrated in a relatively small volume [2,3,7,14]. This is the only brain structure among the cells of which neurosecretory elements have been found. This particular part of the brain is responsible for regulating the activity of the endocrine system of the human body and animals. An essential feature of the hypothalamus is also the integrative nature of its activity, i.e. regulation of complex functions and processes that require the inclusion of many components to form a holistic response, such as maintaining temperature, immune, salt homeostasis; participation in the regulation of emotions, sleep and wakefulness, eating behavior, reproductive function[3-5,7,11,17].

The progress of cognition of the physiology of the hypothalamus is associated with the study of its biochemical, topographic, cytological characteristics, as well as with the development of stereotaxy of the hypothalamus [17,19].

MORPHOLOGY OF THE HYPOTHALAMUS AND CLASSIFICATION OF ITS FIELDS AND NUCLEI

ANATOMY

The hypothalamus is part of the intermediate brain (diencephalon) and is located in its basal parts. Dorsally, it borders on the thalamus (thalamus), the rostral border is a plane passing through the terminal plate (lamina terminalis), and the caudal one is a conditional plane drawn posteriorly from the mamillary bodies (corpora mamillaria) [4,11,8,7].

Macroscopically, the hypothalamus is divided into 3 parts: the first section, located above the visual cross, is called the anterior or optical, the second one begins behind the chiasm and stretches to the mamillary bodies - this is a gray hillock, which is often called the tuberal or middle part of the hypothalamus. From the gray hillock begins a funnel (infundibulum), which stretches to the pituitary gland (hypophisis). The third section is located caudally from the gray hillock, and two protrusions are distinguished in it — mastoid, or mamillary, bodies. The part of the hypothalamus that is located in the region of the mammillary bodies is called the posterior hypothalamus [11,4,2,8,7].

Cytoarchitectonics

Since 1896, when Kelliker defined the boundaries of the hypothalamic region and identified clusters of large neurons in it, calling them nuclei (supraoptic and paraventricular), intensive study of the "central gray matter" and the allocation of cell groups in it has been going on. Morphological features served as the basis for the selection of neuronal clusters: limitation from surrounding formations and similarity of the cytological structure of neurons within the group[3,2,7].

The term "nucleus" or hypothalamic fields or areas (area) is most often used to refer to the cellular thickenings of the hypothalamus.The only criterion for naming a particular group of neurons as a field or nucleus is the degree of its restriction from other parts of the hypothalamic region. Therefore, it is not surprising that researchers are not unanimous on this issue [6,4,15].

The complexity of the microscopic structure of the hypothalamus determines the inconsistency of opinions on the number of cell groups that can be isolated in the hypothalamus. Suffice it to say that some authors identify 15-16 nuclei; others — 32, and Brockhaus described 48 hypothalamic nuclei [3,6].

Classification Of Fields And Nuclei Of The Hypothalamus

Usually a single principle is taken as the basis of classification. The basis for the separation of the hypothalamus was:
1) macroscopic structure in the rostrocaudal direction,
2) microscopic structure in the mediolateral direction,
3) cytoarchitectonic principle,
4) the ratio of the nuclei of the hypothalamus to the pituitary gland,
5) fibrous structure,
6) the functional significance of its various parts,
7) phylogenetic principle [3,6].

1. Many authors base their classifications on the division of the hypothalamus in the rostrocaudal direction according to the anatomical principle. An example of such a separation of the hypothalamic nuclei of the rabbit brain can be the grouping of the hypothalamic nuclei of the rabbit brain, which Fifkova and Marshall adhere to in their stereotactic atlas [3,6]:

Preoptic and supraoptic zones	Medial preoptic field;
	Lateral preoptic field;
	Anterior hypothalamic field;
	Paraventricular nucleus;
	Supraoptic core;
	Suprachiasmatic nucleus.
Tuberal zone	Ventromedial hypothalamic nucleus;
	Dorsomedial hypothalamic nucleus;
	Dorsal hypothalamic nucleus;
	Posterior hypothalamic nucleus;
	Arcuate core;
	Lateral hypothalamic field.
Mamillary zone	Supramamillary core;
	Mamillary medial nucleus;
	Mamillary lateral nucleus;
	Insertion core.
Subthalamic zone	The interstitial nucleus:
	Unnamed zone;
	Lewis 's body.

2. The division of the hypothalamus in the mediolateral directions began to be carried out when it became obvious that the lateral and medial parts of the hypothalamus differ significantly from each other in the structure of neurons, connections and functions. Bogolepova, on the basis of studying the development of the human hypothalamus, distinguishes 4 departments with the following divisions [4,15,8,20,6]:

Anterior section	Preoptic area;
	Supraoptic nucleus;
	Paraventricular nucleus;
	Anterior hypothalamic field.
Middle medial section	Ventromedial nucleus;
	Dorsomedial nucleus;
	Infundibular nucleus;
	Posterior hypothalamic field.
Middle lateral section	Lateral hypothalamic field;
	Lateral hypothalamic nucleus;
	Tuberal nucleus;
	Periforal nucleus.
Posterior section	Medial mamillary nucleus;
	Lateral mamillary nucleus.

Attempts to group the hypothalamic nuclei according to the cytoarchitectonic principle have not received wide distribution. Waren proposed to single out a group of isomorphic and heteromorphic nuclei, classifying the supraoptic, suprachiasmatic, ventromedial, infundibular, lateral tuberal, periventricular, medial and lateral mamillary bodies as isomorphic, and all other nuclei of the hypothalamus as heteromorphic [3,4,6].

4. There are also few attempts to divide the hypothalamus depending on the ratio of its nuclei to the pituitary gland. Spiegel distinguishes the pituitary nuclei: supraoptic and paraventricular, and non-pituitary - all the rest [6].

5. The division of the hypothalamus, depending on the structure of its nerve fibers into myelinated and non-myelinated sections, has not become widespread, since on the basis of this principle only one area of the hypothalamus is distinguished - mamillary bodies, in which myelinated fibers are found, the rest of the hypothalamus is ungrouped [6].

6. Hess established that when the anterior part of the hypothalamus is irritated, phenomena characteristic of the parasympathetic part of the nervous system are observed, and when the posterior part is irritated, signs characteristic of the sympathetic part of the nervous system are observed. In this regard, he proposed to divide the hypothalamus into two sections - anterior and posterior [6].

7. Based on the phylogenetic origin of various structures of the hypothalamus, M. S. Tolgskaya distinguishes in it a group of phylogenetically ancient formations, which include the supraoptic and paraventricular nuclei, and a group of phylogenetically new formations, which includes the nuclei of the gray hillock and mamillary bodies [3,4,6].

The most successfully proposed by V. S. Kesarev is the division of the hypothalamus according to the topographic principle. He singled out the following zones in it, depending on their location in relation to the wall of the third ventricle and along the base of the brain in the rostrocaudal direction [3]:

Paraventricular zone	occupies the area along the wall of the III ventricle throughout the hypothalamus in the rostrocaudal direction
Basal zone	located on the base of the brain, adjacent to the paraventricular zone
Lateral zone	located between the paraventricular and basal zones
Mamillary zone	represents the location of the mamillary bodies

A cytoarchitectonic study showed that the cell groups in the rabbit hypothalamus can be isomorphic or heteromorphic [15]. The isomorphic are mainly those groups of neurons that are clearly delimited from other parts of the hypothalamus, they are usually called the hypothalamic nuclei. To heteromorphic - formations that do not have clear boundaries, they are often called hypothalamic fields. Consequently, the fields and nuclei of the hypothalamus differ from each other not only in the nature of their boundaries, but also in the different composition of neurons.

Carried out in parallel with the cytological study, the analysis of the nature of the distribution of the volumes of nerve cells in each of the studied formations of the hypothalamus showed that in all heteromorphic hypothalamic fields, the histograms of the distribution of neuronal volumes are polymodal, and in isomorphic hypothalamic nuclei they are monomodal [3,4,15,7].

Since polymodality in the statistical distribution serves as an indicator of the heterogeneity of a group of values, and monomodality characterizes a homogeneous set, the obtained quantitative estimates of the neuronal composition of the fields and nuclei of the hypothalamus confirm the above idea of heteromorphic and isomorphic formations in the hypothalamus.

The proposed division of all formations of the hypothalamus into hetero- and isomorphic ones is close to what is described by Varen, but a simple association of heteromorphic fields into one group, isomorphic nuclei into another, as he does in his classification, does not help to understand the structure of the hypothalamus, therefore, probably, his the grouping of hypothalamic formations is not widely used. At the same time, the cytoarchitectonic principle underlying the classification of nuclei and fields of the hypothalamus makes it possible to distinguish groups of heteromorphic and isomorphic formations and to identify common features and differences in their neuronal structure [7,6].

The study showed that along the entire length of the hypothalamus in the rostrocaudal direction along the walls of the third ventricle there are three large groups of neurons that pass one into another without distinct boundaries and are similar to each other in a number of ways, these are the medial fields of the hypothalamus (medial preoptic, anterior hypothalamic and posterior hypothalamic field). All of them are heteromorphic formations consisting of 2-3 types of nerve cells [15,6]. Using the terminology of Nissl (nerve cells with a well-defined large perikaryon with large clumps of basophilic substance are somatochromic elements, medium nerve cells, in the perikaryon of which the basophilic substance is located in small grains, are cytochrome, and small neurons with a narrow rim of the cytoplasm with diffusely staining basophilic substance are karyochromic elements), we can conclude that all three types of nerve cells are found in the medial hypothalamic fields [17,15]. The bulk are cytochrome neurons (with an average volume of 450 µm3); karyochromic (with an average volume of 200-350 µm3) and somatochromic (with an average volume of 800-1000 µm3) are much less common, and their number and ratio in different fields, along with the topographic position, is a distinctive feature of each field [15,6].

The lateral parts of the hypothalamus are occupied by two lateral hypothalamic fields (lateral preoptic and lateral hypothalamic), which do not have a clear boundary in the rostrocaudal direction and adjoin the medial hypothalamic fields throughout the hypothalamus. Like the medial fields, they are heteromorphic formations, but in contrast to them, the bulk of these fields are somatochromic neurons (with an average volume of 800-1300 µm3), and neurons of another type are much less common, which can be attributed to the karyochromic elements of the nervous system. systems (with an average volume of 200–350 µ m3) [15,3,6].

In the basal part of the hypothalamus are the hypothalamic nuclei containing any one type of neuron [15]. Some of them consist of karyochromic elements (suprachiasmatic, arcuate, posteromedial and mamillary lateral nuclei), others - from cytochrome neurons ventromedial, supramamillary and mamillary medial nuclei) and a group of nuclei is represented by nerve cells of the somatochromic type (paraventricular, supraoptic and intercalated). An exception in its topographic position is the paraventricular nucleus, which, unlike the others, lies not at the base of the hypothalamus, but in its dorsal part among the neurons of the anterior hypothalamic field [6].

Based on the above data on the features of the neural structure of various formations of the hypothalamus, it is proposed to divide it into 3 zones:

Medial zone	located along the wall of the third ventricle, consists of three medial fields: medial preoptic, anterior hypothalamic and posterior hypothalamic
Lateral zone	occupies the lateral parts of the hypothalamus, consists of two lateral fields: lateral preoptic and lateral hypothalamic
Basal zone	located at the base of the hypothalamus, includes the supraoptic and suprachiasmatic nuclei in the region of the chiasm, the paraventricular, ventromedial, postero-medial, arcuate nuclei in the region of the gray tubercle, and the supramamillary, medial mamillary, lateral mamillary and intercalary nuclei in the region of the mamillary bodies.

The proposed division of the hypothalamus is close to the classification given by V. S. Kesarev, however, it is based not only on the topographic location of the hypothalamic zones in relation to the third ventricle, but also on the cytoarchitecture of the fields and nuclei of the hypothalamus. The advantages of such a division are that, firstly, no artificial boundaries are created, as is the case when the anterior, middle, and posterior sections of the hypothalamus are distinguished, and, secondly, the differences in its medial, lateral, and basal parts are reflected. At the same time, the division of the hypothalamus into medial, lateral and basal zones also implies its division in the rostrocaudal direction, since the fields and nuclei of the hypothalamus lying in one or another zone have a certain topographic position in relation to such clearly expressed anatomical formations as chiasma opticum, tuber cinereum, corpora mammillaria [2,3,6].

In concluding this brief review, we consider it expedient to refer to a number of existing atlases containing data on the rabbit diencephalon [17,19]. They can be subdivided into atlases without stereotaxic coordinates, in which microphotographs from the frontal sections of the brain stained according to Nissl are presented with varying degrees of detail, and atlases in stereotaxic coordinates, which mainly show diagrams from the frontal sections of the brain [17,19].

Material and Methods

Features of Stereotaxic Brain Study

In the most well-known and frequently used stereotaxic atlases of the rabbit brain, the coordinates were calculated on a brain fixed in the skull (with a mixture of 96% alcohol and 10% formalin). Although this variant of fixation is considered the most successful, nevertheless, the volume of the brain changes as a result of perfusion with this mixture, which underlies errors in operations on the living brain along the coordinates selected in the atlases. In connection with this circumstance, it was necessary to refine the stereotaxic coordinates on the unfixed brain [17,19].

Operations were performed on 40 rabbits under hexenal anesthesia in a stereotaxic apparatus to clarify the stereotaxic coordinates. In the experiments we used the Horsley-Clark coordinate system most frequently used in modern research. The main requirement for the installation of the skull in this system is the exact observance of the difference in inclination between the two reference points on the skull: bregma (bregma) - the intersection of the coronary and sagittal sutures and lambda (lambda) - the intersection of the sagittal and lambdoid sutures [18,21].

Bregma should be 1.5mm above lambda. Precise positioning of the skull in this position is quite laborious, but it guarantees a constant tilt of the head in the rostrocaudal direction, which contributes to the correct hit in the selected area of the brain. Bregma is the zero point, from which the counting is carried out forward with a minus sign and backward with a plus sign. The zero frontal plane passes through the same point [19,21].

We considered it expedient to abandon the usual procedure for immersing needles into the brain to determine the zero planes, and used a more accurate, in our opinion, method of dissecting the brain in the frontal, sagittal, and horizontal planes. To do this, in a stereotaxic apparatus, using an eye scalpel sharply sharpened on both sides, brain incisions were made corresponding to: a) zero frontal plane - at the level of bregma (20 animals), horizontal plane - 10 mm down from the main horizontal plane passing through the bregma and an imaginary point lying 1.5 mm above the lambda (10 animals) [19,3,21].

A comparison of cuts made on the brains of several animals in each of the three determined planes showed that in all cases there is some variation in the levels obtained, which, apparently, depends on a number of factors, ranging from the difference in the size of the skull of experimental animals and ending with the inevitable errors of the technique used. The level of the frontal, sagittal or horizontal section, which occurred most frequently during the comparison, was taken as the zero plane. The null frontal plane obtained in this way was located 1 mm closer to the rostral pole, and the null horizontal plane was 1 mm more dorsally than indicated in the stereotaxic atlas of Fifkova and Marshall. The difference in the location of the zero planes is mainly due to the fact that, unlike the indicated authors, we determined these planes on a living unfixed brain [19,18,22,23,3].

Since we are not aware of atlases of the rabbit brain, where sagittal and horizontal sections of the brain in stereotaxic coordinates would be given, then according to the series of sections obtained in these planes, our own schemes were compiled [19,3].

Obtaining Standard Brain Sections Parallel to The Zero Frontal Plane

This procedure is constantly associated with significant difficulties, since it is practically impossible to position the brain extracted from the skull at the same inclination, under which it was during the stereotaxic examination, without a special device. For this purpose, a form was specially designed and made of paraffin, in which the rabbit brain fixed in 10% formalin was placed, so that the cerebellum was located on a flat area of the form. Two parallel sections were made with a scalpel and the area of the hypothalamus was excised. As a result of numerous tests, it was found that if the cerebellum is located 1.6 cm above the olfactory part of the brain, then the sections obtained on a freezing microtome from the block cut out in this way turn out to be parallel to the zero frontal plane. This makes it possible to compare them with the schemes in the atlas and correctly judge the relationship between individual hypothalamic formations [19,3].

Methods Used in Compiling the Atlas

Frontal, sagittal, and horizontal sections prepared from a rabbit brain fixed in 10% formalin on a freezing microtome had a thickness of 60 μm and were serially made every 0.5–1.0 mm from each other.

These unstained sections were photographed at 7:1 magnification. The schemes are made in accordance with the photographs and are given in stereotaxic coordinates in such a way that each division of the coordinate grid is 1 mm.

To study the cytoarchitectonics and neuronal composition of the fields and nuclei of the hypothalamus, a series of celloidin sections 12–20 μm thick were prepared, they were stained with thionine according to Nissl. Tables of frontal, sagittal and horizontal stained sections are given in accordance with the levels of unstained sections at a magnification of 27:1, and individual fragments at a magnification of 480:1 [19,18,23,3].

Along with the study of topographic relationships in the hypothalamus, as well as the cytoarchitectonics and cytology of its individual formations, a quantitative analysis of the neuronal composition of the nuclei and fields of the hypothalamus was carried out. Based on the measurement of mutually perpendicular diameters of neuron bodies, their volume was calculated using the ellipsoid formula:

$V=\pi a^2/b$

where a is 0.5 of the largest diameter, b is 0.5 of the smallest diameter [19,2,3].

Quantitative data obtained on the basis of measuring 100 neurons in each studied hypothalamic formation were statistically processed: histograms of the distribution of nerve cell volumes were plotted on a logarithmic scale (with a logarithm base of 1.3) and the nature of the distribution was evaluated. This made it possible to identify not the average, but the modal volumes of neurons (Mo), characteristic of various formations of the hypothalamus, and to judge the degree of homogeneity of the analyzed nuclei and fields by the sizes of their constituent nerve cells [19].

Discussion and Conclusions

So, this article summarizes and systematizes data on the morphological and functional organization of the hypothalamus, and also provides the principles for constructing stereoscopic atlases.

Thus, the data on the organization of the hypothalamus presented in the review represent a fundamental basis for further study of this system, making it possible to create a basis for clinical research.

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