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Morphofunctional Organization of The Rat Hypothalamus

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Abstract

In the hypothalamus, it is customary to distinguish four regions: preoptic, anterior, tuberal, and mammillary. Accumulations of nerve cells in these areas form more than 30 pairs of nuclei of the hypothalamus. The data presented in the article can serve as a fundamental basis for further study of the parts of the rat brain in normal and pathological conditions with further extrapolation of the obtained data to humans.

Keywords: morphofunctional organization; rat; hypothalamus

In the hypothalamus, it is customary to distinguish four regions: preoptic, anterior, tuberal, and mammillary. Accumulations of nerve cells in these areas form more than 30 pairs of nuclei of the hypothalamus. The neurons of the nuclei of the hypothalamus have the ability to produce a neurosecretion, which, through the processes of these same cells, can be transported to the neurohypophysis or the median eminence of the hypothalamus. Such nuclei are called the neurosecretory nuclei of the hypothalamus. Each area has three zones: lateral, medial and periventricular. Each zone has a number of nuclei. Consider the preoptic region and start with the periventricular zone, it includes the following nuclei: preoptic periventricular nucleus, middle preoptic nucleus, anterioventral periventricular nucleus, suprachiasmatic preoptic nucleus. In the medial zone are: medial preoptic area, medial preoptic nucleus, anterodorsal preoptic nucleus, anteroventral preoptic nucleus, parastrial nucleus, posterior dorsal preoptic nucleus. The lateral zone includes: the lateral preoptic area and the magnocellular preoptic nucleus [1].

Consider the anterior region and its periventricular zone: the anterior periventricular nucleus, the suprachiasmatic nucleus and the paraventricular nucleus. The medial zone includes: anterior hypothalamic area, anterior hypothalamic nucleus, retrochiasmatic area, circular nucleus. The lateral zone includes: the lateral hypothalamic area and the supraoptic nucleus [1, 2].

The tuberal region of the periventricular zone includes: the tuberal periventricular nucleus and the arcuate nucleus. The medial zone includes: tuberal chasm, ventromedial nucleus and dorsomedial nucleus. The lateral zone includes: the lateral hypothalamic area and the tuberal nucleus [1].

Mammillary region-periventricular zone includes: posterior periventricular nucleus and dorsal tuberomammary nucleus. The medial zone includes: the dorsal premammary nucleus, the ventral premammary nucleus, the mammillary complex, which includes the medial mammillary nucleus, the lateral mammillary nucleus, the supramammillary nucleus, and the posterior hypothalamic region. Lateral zone: lateral hypothalamic area, magnocellular nucleus of the lateral hypothalamic area, ventral tuberomammary nucleus [1, 3].

The rostral border of the hypothalamus is formed by the optic chiasm, while the mammillary bodies define the caudal border. Between these structures, an oval protrusion from the floor of the third ventricle is the tuber cinereum, from which a median prominence protrudes and then narrows into a funnel-shaped stalk that together forms the inferior border of the hypothalamus. The medial (ventricular) surface of the brain shows other structures that direct afferent fibers to the rostral border, including the lamina terminalis and the anterior commissure. The hypothalamic sulcus is also visible on the medial surface of the brain, which is a rostral continuation of the restrictive sulcus that defines the upper border of the hypothalamus. Finally, the internal capsule, which is visible only on horizontal sections of the brain, forms the lateral border [1, 4].

The hypothalamus consists of three longitudinally oriented cell columns or zones that run along the entire rostrocaudal length of the hypothalamus. These zones can be divided into four nuclear groups or regions depending on the rostrocaudal position [1, 2, 3, 4].

Adjacent to the third ventricle, directly within the ependymal cell lining, is a thin layer of cells that make up the periventricular zone. In the periventricular zone are neurons involved in the regulation of the secretion of pituitary hormones. This zone contains several separate nuclei, but the two most prominent are the arcuate nucleus and the paraventricular nucleus, which are involved in neuroendocrine and autonomic regulation. Directly adjacent to the periventricular zone is the medial zone, which consists of several cytoarchitectonically different nuclei. The medial zone is formed by neurons included in the limbic system and forming connections with the septal area and amygdala [1].

The nuclei in the medial zone are particularly involved in the regulation of the autonomic nervous system and are also involved in the regulation of the neuroendocrine system. Finally, neurons located in the lateral zone are diffusely located between the fibers of the medial forebrain bundle. The lateral zone has few nuclei or clear landmarks, but contains important pathways such as the median forebrain bundle. The lateral zone, limited by the fornix, is involved in the regulation of the autonomic nervous system [1, 4].

Each of the zones described above is further subdivided into regions based on rostrocaudal landmarks. The anterior region runs from the terminal plate to the caudal side of the optic chiasm. The part of the anterior region rostral to the optic chiasm is often also referred to as the preoptic region, however this distinction is now less emphasized. The next area that is identified when moving in the caudal direction is the tuberal area. The edges of this area include areas that are higher and include the tuber cinereum. Finally, the posterior region is defined by the region above and includes the mastoid bodies [4].

Preoptic area

The suprachiasmatic nucleus consists of small densely packed dark neurons. It is usually divided into dorsomedial and ventrolateral parts [5].

Cyto- and myeloarchitectonics. This nucleus receives afferent fibers from the retina and plays an important role in the control of circadian and circadian biorhythms. Serotonergic fibers of neurons of the midbrain suture go to the ventral part of the nucleus, as well as projections from the ventral part of the lateral geniculate nucleus containing neuropeptide Y. Efferent fibers go to the periventricular nucleus and the anterior hypothalamic nucleus. The suprachiasmatic nucleus is related to the regulation of sexual dimorphism, and pathological processes in the region of this nucleus lead to accelerated puberty and menstrual irregularities. The same nucleus is the central driver of circadian rhythms [4, 5].

The median preoptic nucleus is a dense collection of small cells in the terminal lamina that extends along the anterior border of the third ventricle from the apex of the preoptic recess of the third ventricle dorsocaudally to a small triangular area between the descending columns of the fornix. The median preoptic nucleus plays an important role in the control of the cardiovascular system. It receives afferents from the subfornical organ and the parabrachial nucleus and sends projections to the paraventricular nucleus and large cell groups, as well as to the dorsomedial nucleus of the hypothalamus [6].

The anteroventral periventricular nucleus occupies a ventral position in the periventricular zone of the preoptic region and is located directly caudal to the vascular organ of the terminal plate. This is an oval cluster of densely located neurons involved in the regulation of water and electrolyte balance, autonomic functions of gonadotropin secretion [6, 7].

Cyto- and myeloarchitectonics. Afferent fibers come from the brainstem, posterior and medial nuclei of the amygdala, and from the nuclei of the septal region. Efferent fibers go to gonadotropin-releasing-containing neurons and to dopaminergic neurons of the arcuate nucleus. The ventrally anteroventral periventricular nucleus is separated from the optic chiasm by the suprachiasmatic preoptic nucleus, which is composed of obliquely oriented fusiform cells, also known as the ventromedial preoptic nucleus. The anteroventral periventricular nucleus also receives strong signals from the ventral lateral septal nucleus, which transmits multimodal information from the hippocampal formation to the periventricular and medial hypothalamus. The nucleus is also intensively innervated by all parts of the periventricular zone of the hypothalamus, the medial preoptic nucleus and the dorsomedial nucleus of the hypothalamus. The anteroventral periventricular nucleus also receives afferent fibers from many of the same brainstem nuclei that direct afferents to the medial part of the medial preoptic nucleus. The large oval medial preoptic nucleus extends almost the entire length of the preoptic region and consists of three separate subdivisions: the sparse cell lateral part of the medial preoptic nucleus, the densely celled medial part of this nucleus, and the compact, very dense central part [4, 6, 7].

The medial preoptic nucleus receives afferent fibers from the posterior and medial nuclei of the amygdala, the main nucleus of the terminal stripe, the caudal and ventral portions of the lateral septal nucleus, and certain areas of the brainstem, including the ventral tegmental region, the nucleus of the solitary tract, and the parabrachial nucleus. It plays an important role in the regulation of cardiovascular reactions and water balance [6, 7].

Cyto- and myeloarchitectonics. Afferent fibers of neurons go to the parabrachial nucleus, and efferent fibers go to the paraventricular and dorsomedial nuclei of the hypothalamus. Each of the afferent fibers into the medial preoptic nucleus is topographically distributed within its three subdivisions, with projections of the nuclei of the hypothalamus of the periventricular zone ending predominantly in the nucleus, and projections of the ventral subiculum, the caudal part of the lateral septum, and stem serotonergic neurons ending in the lateral part of the medial preoptic nucleus. The projections of this nucleus are just as extensive and include areas thought to mediate neuroendocrine, autonomic, and somatomotor responses. The medial part of the medial preoptic nucleus sends its projections to the parts of the hypothalamus involved in the regulation of hormone secretion from the anterior pituitary gland, such as the anteroventral periventricular nucleus, the arcuate nucleus, and the paraventricular nucleus. The lateral part of the medial preoptic nucleus forms connections with the projection to the lateral septum and the perifornical region of the hypothalamus, as well as projections to several nuclei of the brainstem. In addition to this nucleus, four smaller nuclei can be distinguished in the medial preoptic region, although little is known about the functional role of these nuclei. The first of these smaller groups of cells is the anteroventral preoptic nucleus, which lies at the base of the medial preoptic region between the anteroventral periventricular nucleus and the nucleus of the diagonal Broca's strip and is separated from each nucleus by clearly demarcated areas of sparse cells. The neurons of this cluster contain GABAergic and galanin-containing neurons, which form connections with the tuberomammary nucleus [4, 6, 7].

The anterodorsal preoptic nucleus lies in the dorsal part of the medial preoptic region.

In nomenclature, the anterior dorsal preoptic nucleus, together with the ventral part of the lateral septal nucleus, constitute the "septohypothalamic nucleus". However, they differ significantly in their cytoarchitectonics, neurochemistry and connections [8].

The posterior dorsal preoptic nucleus is a small cluster of large dark-stained neurons that lie at the caudal levels of the preoptic region near the posterior end of the parastrial nucleus, slightly ventrolateral to the anterior macrocellular part of the paraventricular nucleus along the medial border of the nucleus of the terminal stria bed [4, 8].

Anterior area

The main part of this area is occupied by the oval anterior hypothalamic nucleus, which lies ventrolaterally from the caudal pole of the medial preoptic nucleus. On the basis of cytoarchitectonics, this nucleus can be divided into anterior, central, and posterior components. Significant projections are directed to the anterior periventricular and paraventricular nuclei of the hypothalamus. Ventral to the third ventricle and between the optic chiasm and the arcuate nucleus of the hypothalamus lies an area designated as the retrochiasmatic area, which contains supraoptic commissure fibers and neurons projecting to the brainstem and spinal cord [8].

Tuberal region

The arcuate nucleus is divided into small-celled dorsomedial and ventrolateral parts, containing medium-sized neurons involved in the regulation of the functions of the adenohypophysis.

Cyto- and myeloarchitectonics. Afferent fibers come from the paraventricular hypothalamic nucleus and the anteroventral periventricular nucleus, the medial preoptic, dorsomedial, ventral premamillary nuclei, the medial nucleus of the amygdala, the nuclei of the septal region and the trunk. Efferent fibers are mainly limited to the periventricular zone [9].

The tuberal region of the hypothalamus contains two large and well-differentiated nuclei: the ventromedial and dorsomedial nuclei of the hypothalamus. The ventromedial nucleus is the largest group of cells in the tuberal region and consists of two distinct cell aggregations, designated the dorsomedial and ventromedial divisions. The ventromedial nucleus also receives afferent signals from all parts of the medial hypothalamus, except for the medial and lateral mastoid nuclei. In addition, the ventromedial nucleus receives signals from the lateral zone, the posterior region of the hypothalamus and the suprachiasmatic nucleus, and forms efferent connections with other nuclei of the medial zone of the hypothalamus. The ventromedial nucleus also sends extensive projections to the amygdala and to the septal nuclei, and also provides downward projections to the brainstem nuclei. In addition, the central, lateral, and medial nuclei of the amygdala receive afferents from the ventromedial nucleus [4, 9].

Immediately lateral to the ventromedial nucleus lies the **tuberal nucleus**, which consists of an oval cluster of small to medium-sized neurons embedded in the tuberal part of the lateral hypothalamus. Many neurons in the nucleus tuberal express estrogen receptor mRNA. The tuberal nucleus receives afferents from the medial preoptic nucleus, ventromedial and ventral premammary nuclei, while efferents go to the periventricular and paraventricular nuclei of the hypothalamus, the amygdala, and the midbrain. The dorsomedial hypothalamic nucleus occupies the dorsal half of the tuberal region between the anterior hypothalamic nucleus, rostrally, and the posterior hypothalamic region, caudally [10].

Cyto- and myeloarchitectonics. The dorsomedial nucleus receives afferents from other nuclei of the hypothalamus, the nucleus of the bed of the terminal plate and the ventral part of the nucleus of the lateral septum, as well as the brain stem. Descending fibers form the periaqueductal tract. The functional role of the dorsomedial nucleus remains a subject of discussion, but it is believed to be involved in the regulation of sexual and feeding behavior, circadian rhythms, and thermogenesis [4, 10].

Mammillary region

The mammillary part of the medial zone of the hypothalamus is represented by the mammillary complex, which consists of the medial and lateral mammillary (mammillary body) and supramammillary nuclei, together with the premammillary nuclei (dorsal and ventral) and the posterior hypothalamic region. The mammillary body is divided into the medial mammillary nucleus, which occupies most of the mammillary body, and the lateral mammillary nucleus, which is easily distinguished by large, dark stained neurons [3].

The medial mammillary nucleus is further subdivided into three parts: a small medial part located in the midline, a lateral part which is much larger, and a posterior part. The projection axons form two main pathways: the descending mammillotegmental pathway, containing fibers from both the medial and lateral mammillary nuclei, which terminate in the nuclei of the Gudden tegmentum, and the ascending mammillothalamic pathway, which terminates in the anterior thalamic complex. In addition, the mammillary region lacks extensive intrahypothalamic connections typical of other groups of cells in the medial zone [3, 4, 8].

The premammary nuclei lie at the level of the mastoid recess of the third ventricle, immediately caudal to the ventromedial nucleus of the hypothalamus and rostral to the mastoid body [11].

The dorsal premammary nucleus appears as a collection of hypochromic trapezoidal or rectangular neurons and is bounded laterally by the fornix and medially by a cell-poor area that separates the two nuclei. This nucleus serves as an interface between the anterior nuclei of the medial zone and the mammillary body.

The ventral premammary nucleus is a compact cluster of dark-stained neurons. The ventral premammary nucleus sends its main afferents to the posterior amygdala nucleus, the medial preoptic nucleus, the main nucleus of the terminal plate bed, and the posterior dorsal part of the medial amygdala nucleus [12].

The supramammillary nucleus lies between the mastoid body and the posterior hypothalamic region and borders dorsolaterally on the ventral tegmental region. It can be divided into a large cell lateral part and a small cell medial part containing many dopaminergic neurons. The supramammillary nucleus forms connections with the dentate gyrus, the hippocampus, and the entorhinal cortex.

The caudal hypothalamic region is bounded laterally by the mammillothalamic tract and merges in the midline at the level of the mastoid depression and includes the tuberomammillary and ventral nuclei [13].

The nuclei of the caudal region receive afferent fibers from the lateral septal nucleus and nuclei of the bed of the terminal strip, the medial preoptic nucleus, the lateral preoptic and hypothalamic regions, and the ventromedial nucleus. Efferents go to the neocortex, basal ganglia, septum, thalamus, and cerebellum.

Lateral zone

The lateral zone of the hypothalamus can be divided into the **preoptic, anterior, tuberal, and mastoid regions**. However, since clear division criteria have not emerged, it is generally considered to have only two main divisions: the **lateral preoptic** area (preoptic level) and the **lateral hypothalamic** area (anterior, tuberal, and mastoid levels) [13].

Lateral preoptic area

The lateral preoptic area is characterized by weakly stained (thionin by Nissl method) neurons of medium size. The only nucleus in the preoptic part of the lateral zone is the **large cell preoptic nucleus** containing large cholinergic neurons that form connections with the olfactory bulb, pontine nuclei, and isocortex.

Lateral hypothalamic region

The lateral hypothalamic region can be further divided into three rostrocaudal subregions, which correspond to the anterior, tuberal, and mammillary regions of the hypothalamus. The anterior lateral hypothalamic region is bounded medially by the anterior region of the hypothalamus and the descending columns of the fornix. Laterally, it merges with the amygdala. The lateral hypothalamic region forms connections with the nuclei of the thalamus, septum, nuclei of the solitary tract, and parabrachial nuclei [14].

The hypothalamus is the main subcortical center that regulates autonomic functions. Irritation of the anterior group of nuclei imitates the effects of the parasympathetic nervous system, its trophotropic effect on the body: increased secretion and motility of the gastrointestinal tract, pupil constriction, bradycardia, lowering blood pressure. The supraoptic and paraventricular nuclei are involved in the regulation of water and electrolyte balance by producing antidiuretic hormone (vasopressin).

Stimulation of the posterior group of nuclei has ergotropic effects, activates sympathetic effects: pupil dilation, tachycardia, increased blood pressure, inhibition of motility and secretion of the gastrointestinal tract.

The hypothalamus provides thermoregulation. The nuclei of the anterior group contain neurons responsible for heat transfer, and the posterior group – for heat production. The nuclei of the middle group are involved in the regulation of metabolism and eating behavior. In the ventromedial nuclei there is a saturation center, and in the lateral nuclei there is a center of hunger. The destruction of the ventromedial nucleus leads to hyperphagia – increased food intake and obesity, and the destruction of the lateral nuclei – to a complete refusal of food. In the same core is the center of thirst. The hypothalamus contains centers for protein, carbohydrate, and lipid metabolism, as well as centers for regulating urination and sexual behavior (the suprachiasmatic nucleus) [1, 15].

The regulation of many body functions by the hypothalamus is carried out with the help of pituitary hormones and peptide hormones: liberins, which stimulate the release of hormones from the anterior pituitary gland, and statins, which inhibit their release. Peptide hormones (thyroliberin, corticoliberin, somatostatin, etc.) through the portal vascular system of the pituitary gland reach its anterior lobe and cause a change in the production of the corresponding adenohypophysis hormone.

The supraoptic and paraventricular nuclei, in addition to participating in water-electrolyte metabolism, lactation, and uterine contractions, produce hormones of a polypeptide nature – oxytocin and antidiuretic hormone (vasopressin), which reach the neurohypophysis with the help of axonal transport, accumulate in the extensions of acons – bodies Herring, and then, as necessary, are released into the blood of the capillaries of the neurohypophysis through the axovasal synapses. These hormones affect the contraction of the pregnant uterus during childbirth and the reabsorption of water in the renal tubules, as well as vascular tone, respectively [16].

The suprachiasmatic nucleus is related to the regulation of sexual behavior, and pathological processes in the area of this nucleus lead to accelerated puberty and menstrual irregularities. The same nucleus is the central driver of circadian (circadian) rhythms of many functions in the body [17].

The hypothalamus is directly related to the regulation of the sleep-wake cycle. At the same time, the posterior hypothalamus stimulates wakefulness, and the anterior – sleep. Damage to the posterior hypothalamus can cause pathological lethargic sleep, and damage to the anterior hypothalamus can cause insomnia [17, 18].

The hypothalamus produces neuropeptides related to the antinoticeptive (pain-relieving) system, or opiates: enkephalins and endorphins [19].

The hypothalamus is part of the limbic system, which is involved in the implementation of emotional behavior.

Irritation of the anterior hypothalamus provokes a manifestation of fear, a passive-defensive reaction, and the posterior hypothalamus provokes active aggression, an attack reaction [20].

The data presented in the article can serve as a fundamental basis for further study of the parts of the rat brain in normal and pathological conditions with further extrapolation of the obtained data to humans.

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