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Review Article

Functional Organization of The Reticular Formation

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Received Date: November 05, 2024; **Accepted Date: December 16, 2024; Published Date: January 01, 2025**

Citation: Bon E. I, Maksimovich N.Ye, Zimatkin S.M, Hubarevich I.Ye, Narbutovich A.P, Otlivanchik N.I,et.al (2025), Functional Organization of The Reticular Formation, *Clinical Trials and Clinical Research*,4(1); **DOI:**10.31579/2834-5126/085

Abstract

Reticular formation can be defined as a nodal system through which a biologically important sensory signal stereotypically and simultaneously excites various sensory, integrative and motor systems of the brain and thus brings the organism into a state of reflex readiness to perform obligatory adaptive reactions.

Keywords: functional organization; reticular formation; brain

Instruction

Properties Of Reticular Neurons

During the first mircoelectrode studies, it was found that reticular neurons generate AP in the absence of any stimulation of peripheral nerves or central structures. Such spontaneous activity of reticular neurons is observed even in conditions of isolation of a part of the brain stem obtained by transections. Extracellular discharges revealed several types of spontaneous activity in the reticular formation: low-frequency irregular discharges, groups of high-frequency discharges separated by intervals of silence, and continuous regular discharges. [8,16]

With the help of intracellular leads, it was found that spontaneous hyperpolarizing and depolarizing subthreshold oscillations of the MP occur in a significant number of reticular neurons.

At the same time, it was found that in the reticular formation there are neurons with stable rhythmic activity that is completely unchanged by afferent impulsation, as well as neurons with either irregular activity or regular intervals between 11Ds, in which afferent impulsation could change the background rhythmicity. The essential difference between neurons with irregular activity and neurons with regular activity lies in the nature of the slow changes preceding the AP. [10] In neurons with irregular activity, APs develop against the background of 'synaptic noise', which is characterised by irregular appearance of ISPs and ESPs. In neurons with regular rhythmic activity, each AP is preceded by a smooth, slowly increasing depolarisation very similar to the generating potential of those neurons that are capable of generating rhythmic APs themselves. Such depolarization has been called prepotential, since it precedes the generation of APS. These slow prepotentials differ from postsynaptic potentials and represent a process of slow, steadily increasing depolarization, which precedes the transition to AP when a critical level of depolarization is reached in neurons with stable rhythmic activity. They reflect a special form of the excitatory process and are the basis of the autogenic rhythmic activity of reticular neurons.

A new class of reticular neurons, which remain silent for a long time and are activated only in response to a specific stimulus, has also been discovered in the reticular formation of the midbrain and pontine in awake cats. They form a specialized neural system, which, unlike systems of neurons with background activity, is characterized by economical discharges and is designed for phase control.

Sensory Properties of The Reticular Formation

It is proved that the reticular formation of the brain stem receives afferent information from heterogeneous sensory sources. In experiments with stimulation of sensory nerves or their receptors on neurons of the reticular formation of the medulla oblongata, bridge and midbrain, it was possible to observe the convergence of impulses of various sensory modalities and show the existence of large peripheral, often bilaterally localized fields. [11]

The degree of convergence of impulses of different sensory modalities is not the same for different regions of the reticular formation and different types of reticular neurons. Thus, neurons of the pontomedullary reticular formation and, above all, of the reticular gigantocellular nucleus are activated by various kinds of somatosensory impulses in a much greater number of cases than by impulses from the auditory and visual systems, whereas neurons of the mesencephalic reticular formation are activated predominantly by impulses from the visual and auditory systems.

However, it has recently been found that the largest number of neurons on which visual and vestibular impulses converge is concentrated in the reticular formation of the bridge at the border of its oral and caudal nuclei, the area that forms the reticulospinal pathway and also sends efferent signals to the oculomotor nuclei.[17]

Certain signs of somatotopic organization were found in the reticular formation.

Analysis of the sensory properties of neurons of the reticular formation showed the existence of a large group of reticular neurons that did not respond to sensory stimulation or responded to one, two or three forms of sensory stimulation (visual, auditory and tactile). Specialized groups of neurons were found in the pontobulbar and mesencephalic reticular formations, activated mainly by pain impulses of somatic or visceral origin. These data suggest the existence of extensive neural systems in the reticular formation, activated mainly by any one sensory modality, which is especially clearly shown for nociceptive afferent systems. In the medulla oblongata and bridge, the reticular giant cell nucleus participates in the formation of the nociceptive reticular system, and in the midbrain - the ventromedial reticular formation.

The frequency of discharges and latent periods of reactions of neurons of the reticular formation of the medulla oblongata and the bridge decrease if peripheral stimuli are repeatedly repeated with a certain frequency or sensory inputs change. Such a change in the nature of the reaction is due to a change in the "meaning" of the stimulus in the process of getting used to behavior and is its neurophysiological analogue. Integrative processes that ensure a decrease in the sensory signal in the process of behavioral addiction seem to be carried out both at the level of the reticular formation and at the level of the spinal cord spino-reticular systems.

Reticulo-Bulbar Motor Systems

The reticular formation is closely related to the coordination of motor reflexes of the brain stem. The important role of its various departments in the occurrence and control of eye movements and chewing reflexes has been established.

Afferent impulses from the visual and vestibular systems, which closely interact in certain structures of the brain stem in order to preserve a clear image on the retina and maintain the balance of the head and trunk, converge not only on the vestibular nuclei, but also on the reticular formation. The main structures on which such convergence was found are the medialpic nuclei of the ponto-mesocephalic reticular formation, the giant cell reticular nucleus and the perihypoglossal nuclei, also related to the reticular ones. In turn, these structures are monosynaptically and dysynaptically connected through interneurons of oculomotor or vestibular nuclei with motor neurons of the external muscles of the eye. [4,6]

Thus, it was shown that irritation of the area between the oral and caudal reticular nuclei of the bridge causes monosynaptic EPSPs (Excitatory Postsynaptic Potential) in the motor neurons and interneurons of the ipsilateral nucleus of the abductor nerve and simultaneously dysynaptic IPSPs (Inhibitory Postsynaptic Potential) in similar groups of neurons of the contralateral nucleus of the abductor nerve.

Monosynaptic excitatory connections of the reticular formation of the bridge and okologubnoglossal nuclei with motor neurons of the nuclei of the oculomotor and oculomotor nerves were found.[1]

The paramedian region of the reticular formation of the bridge is a new premotor center, where incoming impulses are processed and information about the position of the eyes, the beginning, duration and direction of their movement is transmitted to the structures of the reticular formation and motor neurons of the oculomotor muscles. Its neurons are directly involved in the control of horizontal eye movements and control vertical eye movements through the rostral interstitial nucleus of the mesencephalic reticular formation. In this area, as well as in the reticular formation of the midbrain, a number of researchers have discovered several types of neurons whose activity is closely related and differentially correlated with various types of eye movements. Among them, the most common were neurons with uneven and paused types of activity, which coincided well with the phases of rapid eye movements.

It turned out that neurons with an uneven distribution of discharges increased their activity before and during eye movements, either with any rapid movement or when moving in a certain direction. However, their activity stopped during the period of gaze fixation or slow eye movements. Neurons of the second type — with paused activity — had continuous discharges that stopped before or during movement. Pauses occurred either during all rapid eye movements, or during rapid movements in a certain direction. [1,8] These data allowed us to assert the fact that the discharges of neurons of the reticular bridge formation are related to the parameters of eye movements or the position of gaze fixation and to establish that the parameters of eye movements are encoded by the activity of reticular neurons that precedes these movements.

It was found that neurons of the reticular bridge formation encoding the amplitude of eye movements or changes in their position transmit information to the motor neurons of the oculomotor muscles by the amount of AP. The neurons encoding the direction of movement do this by changing the frequency.

The medial reticular formation of the medulla oblongata has a monosynaptic reciprocal effect on motoneurons of antagonistic groups of masticatory muscles. It was shown that stimulation of the reticular gigantocellular nucleus area causes monosynaptic IPSPs in motoneurons of the masseter muscle and the same EPSPs in motoneurons of the biceps muscle. This reciprocal effect is accompanied by a group of nonreciprocal excitatory and inhibitory effects on both groups of motoneurons.

A study of the role of the reticular formation in the regulation of somatic motor reflexes during sleep and wakefulness has shown that impulsation from the ponto-mesencephalic reticular formation is able to modulate the monosynaptic mouth-closing reflex, leading to a significant increase in its amplitude during the slow-wave phase of sleep and wakefulness and its suppression during the fast-wave phase of sleep. With intracellular leads from these motoneurons in cats without anaesthesia, it was found that the animal's transition from the slow-wave to the fast-wave phase of sleep was accompanied by tonic hyperpolarisation of the motoneuron membrane, while stimulation of the reticular formation caused membrane depolarisation during the slow-wave phase and hyperpolarisation during the fast-wave phase of sleep. It is hypothesised that on the border between the ponto-mesencephalic reticular activating system and the medullary reticular THORMOUS system there is a section of the reticular formation with integrative properties that allows selectively connecting or disconnecting these systems and, thus, taking an active part in the animal's transition from one functional state to the opposite one.[1,5]

Studies of the neural systems of the brain stem involved in the central control of respiration have provided a number of important data on the structural and functional relationships of afferent and efferent systems of cranial nuclei and specialized areas of the reticular formation, as well as on the internal mechanisms causing periodic changes in the activity of individual groups of reticular neurons. An important contribution to solving this problem was made by Pitts, Magun and Ranson, who established by stimulating the brain stem that the nerve substrate, which can be called the "respiratory center", is symmetrically located in the reticular formation of the medulla oblongata and consists of the rostroventral region of inspiration and the dorsocaudal region of exhalation.

However, studies of the "respiratory" center" conducted by other authors using the method of brain stem stimulation have yielded contradictory results.

The detection of neurons in the brain stem that generated AP synchronously with the phases of respiratory movements allowed us to identify two main populations — inspiratory and expiratory neurons, which were further divided into subtypes in accordance with the detailed characteristics of their discharges and the time of their occurrence relative to the beginning of the phase of respiratory movements. Respiratory neurons belong to different anatomical groups. They include bulbo-spinal respiratory neurons, innervating motor neurons of the diaphragm and abdominal muscles, propriobulbar respiratory neurons connecting respiratory neurons inside the medulla oblongata, bulbo-pontine and ponto-bulbar neurons connecting the rostrocaudal systems of respiratory neurons. Obviously, this group should also include the motor neurons of the vagus nerve, which directly innervate the laryngeal muscles and generate AP synchronously with the phases of respiration.

To transmit the signal integrated in the respiratory center to the spinal respiratory mechanisms, as well as to the structures regulating blood circulation, motor activity and activity of the vegetative centers.

The topography of respiratory neurons is not limited by clear anatomical boundaries, but several areas of their maximum concentration have been found. In the reticular formation of the medulla oblongata, the lateral or ventral respiratory nucleus, which includes a part and the dorsal respiratory nucleus, localised near the solitary tract, are distinguished. The dorsal respiratory nucleus concentrates predominantly inspiratory neurons. At the level of the bridge, respiratory neurons form a pneumotactic centre capable of modifying the basic respiratory cycle.[18]

A three-dimensional reconstruction of the distribution of inspiratory and expiratory neurons in the medulla oblongata, performed using a computer, showed that respiratory neurons are combined into two symmetrical pillars extending from the caudal part of the medulla oblongata to the pneumotactic center.

The main cluster of inspiratory neurons is localised in the caudal third and dorsolateral part of the bulbo-pontine area, whereas the middle third of the ventromedial area is occupied by a population of expiratory neurons. It is also shown that respiratory neuron populations are concentrated in the columns in several high-density overlapping foci; in addition, such neurons infiltrate or surround the sensory and motor nuclei and the intracerebral part of the cranial nerve roots. A similar conclusion about the continuous rostrocaudal distribution of respiratory neurons in the brain stem was also obtained with submaximal stimulation of the brain stem structures of cats.[16]

Bulbo-spinal neurons of the lateral region of the caudal part of the medulla oblongata project predominantly to the contralateral side of the spinal cord, their axons have a conduction velocity of 55+1.25 m/s; the axons of somatic efferent neurons of the vagus nerve projecting ipsilaterally have approximately the same velocity (53 + ±19.6 m/s).

There are three mechanisms by which respiratory rhythm generation is possible: reciprocal innervation, re-excitable nerve networks, and adaptation.[19]

The hypothesis of reciprocal innervation (separate existence of interconnected centres of inhalation and exhalation) was proposed by Pitts, Magoon and Ranson, who succeeded in inducing a particular phase of respiration by stimulating the medulla oblongata. Further studies found that the probability of discharges of inspiratory neurons increased when the discharge frequency of expiratory neurons decreased. Intracellular leads from respiratory neurons revealed periodic hyperpolarising potentials in the silent phases of expiratory neurons, as well as TPSPs in inspiratory neurons during antidromic stimulation in the spinal cord axon of an expiratory neuron. The explanation of these facts by the existence of reciprocal innervation does not exclude the possibility of triggering respiratory neurons from tonically active structures of the reticular formation.

Proponents of the hypothesis of tonic activation of respiratory neurons of the medulla oblongata believe that reticular structures of the bridge form a ‘pneumotactic centre’ regulating the depth and rhythm of respiration depending on the C02 tension in the blood.

They also believe that the cause of periodic rhythmicity of respiratory neurons is the properties of their membrane. It has been shown that progressive increase in the discharge frequency of respiratory neurons can lead to membrane inactivation due to excessive depolarisation and, consequently, to cessation of AP generation. Special studies have found that the adequacy and accommodation properties of respiratory neurons cannot exert a significant role on synchronous rhythm oscillations in a whole population of respiratory neurons and that the respiratory rhythm is apparently due to the pacing activity of the ‘pneumotactic centre’.

In the caudal part of the medial reticular formation of the rabbit medulla oblongata, neurons sensitive to temperature changes in the medulla oblongata or on the skin (within 3 °C towards cooling or heating) were also found. Some of these neurons have been identified as respiratory. All of them were characterized by a linear dependence of the discharge frequency on temperature changes.

Vasomotor Centre

For a long time it was believed that the integration of cardiovascular reflexes was carried out in the vasomotor centre – a diffuse network of neurons of the bulbar reticular formation that excites or inhibits spinal sympathetic neurons. Based on the data obtained in experiments with brainstem stimulation (Fig. 2.4), the vasomotor centre was subdivided into a vasopressor - cardiac excellerator area localised in the dorsomedial and ventromedial regions of the rostral medulla oblongata, and a vasodepressor - cardioinhibitor area lying in the medial region of the caudal medulla oblongata.

The study of the regions of vaso- and cardio-regulatory fibre afferent endings showed that in the nucleus of the solitary tract and in the reticular formation lying ventral and ventrolateral to this nucleus, a large number of neurons were found that were activated or inhibited mono- and polysynaptically in response to an increase in pressure inside the common carotid artery, to the introduction of solutions containing C02 into it, as well as to electrical stimulation of the nerve of the carotid sinus.[19]

The nucleus of the solitary tract is an important integrative link in the system of cardiovascular reflexes; its neurons are responsible for both switching of primary afferents of the sinus nerve and convergence of afferent fibres of different sensory modalities. This nucleus forms a descending tract to the cervical spinal cord and is closely connected with the structures of the reticular formation, which exercise central control of respiration.

The lateral reticular nucleus is also assigned an important role in cardiovascular regulation. It has been shown that this nucleus is the site of integration of hypothalamic cardiovascular and somatic afferent signals and is involved in mediating cardiovascular reactions that occur during activation of the somatomotor system.

Recently, a number of reports have emerged that are inconsistent with the generally accepted concept of the organisation of central mechanisms, which states that afferent and supramedullary activity is integrated in the medulla oblongata and then transmitted to the spinal cord via common excitatory and inhibitory pathways. In contrast, detailed studies by Henry and Calaresu have shown that cardioaxillatory neurons of the intermediolateral nucleus of the medulla receive excitatory inputs from two medullary structures, the parvicellular and lateral reticular nuclei, and inhibitory inputs from three medullary structures, the suture nuclei, the paramedian nucleus, and the ventral subnucleus of the central nucleus of the medulla oblongata. In combination with other observations showing that under certain physiological conditions the nuclei of the reticular formation can participate independently of each other in separate components of cardiovascular reflexes, it is possible to think that a certain degree of integration required for The existence of vascular centres in the spinal cord with considerable autonomy and emphasising the independent role of the spinal cord in the reflex regulation of blood circulation is indicated by recent work. The existence of vascular centres in the spinal cord with considerable autonomy and emphasizing the independent role of the spinal cord in the reflex regulation of blood circulation is indicated by the works of recent years.[9]

At present, a number of facts have been accumulated indicating the existence of chemosensitive zones on the ventrolateral surface of the medulla oblongata. Changes in the concentration of hydrogen ions in the cerebrospinal fluid, as well as electrical stimulation or local applications of a number of chemicals to these zones caused distinct respiratory and vascular reflex reactions.

Histological studies have shown that the morphological substrate providing such distinct chemosensitive reactions during respiration and blood circulation is an extensive group of large multipolar neurons located in close proximity to the surface of the brain; a certain part of these neurons sends axons to the intermediate-lateral columns of the thoracic segments of the spinal cord. [1] There are close functional relationships between individual groups of chemosensitive neurons of the medulla oblongata, which, apparently, indicates integrative processes in this brain structure. It remains unclear whether these neurons are primary chemoreceptive neurons or whether structures that are still unknown to us perform this function.

Ascending Reticular System

The experiments of Moruzzi and Magun, which have now become classic, have aroused great interest in the concept of an ascending brain system originating in the reticular formation of the brain stem. According to this concept, impulses from peripheral afferents through the system of lateral cord cords of the spinal cord reach the medial reticular formation of the medulla oblongata and the bridge, where, after synaptic switching, they enter the ascending reticular system, through which they reach the nonspecific nuclei of the thalamus and cortex, taking an active part in the processes of sleep and awakening, wakefulness and attention.[16]

There are two parts in the ascending reticular system: the caudal, formed by the medial reticular formation of the medulla oblongata and the bridge, and the rostral, formed by the mesencephalic reticular formation. The reason for this division was the difference in the effects of stimulation of these areas in relation to the electroencephalogram. It is generally believed that the caudal part of the ascending reticular system has a synchronizing effect on the EEG, whereas the rostral part causes EEG desynchronization.

Despite extensive research, some aspects of the morphofunctional organization of the ascending reticular system of the brain are not yet clear. According to numerous electrophysiological studies, the localization of reticular neurons producing axons in the rostral direction coincides to a certain extent with the results of morphological experiments in which neurons with ascending axons were found in all areas of the reticular formation with the exception of the most caudal part. However, in experiments with antidromic identification, it was shown that the bodies of neurons of the ascending reticular system are concentrated mainly in the rostral rhombencephalic region where the largest reticular neurons lie. This type of neurons is also found caudal to the lower olive and in the reticular formation of the midbrain.

The percentage of identified neurons with ascending axons was low and ranged from 5 to 17%. These neurons form two ascending tracts with a wide range of conduction velocities, the stimulation of which led to the appearance of postsynaptic responses in neurons and VP in relay and nonspecific nuclei of the thalamus.

There are reports of direct reticulocortical projections based on physiological experiments and anatomical observations, according to which they appear to be either fibers of the serotonergic system extending from the nucleus of the midbrain suture to the frontal lobes of the cortex, or fibers of the noradrenergic system starting near the reticular formation of the brain stem and also reaching the cortex.[15-17]

It has been shown that the transmission of sensory information from the sensory organs to the cortex essentially depends on the internal state of the brain and that the thalamic relay nuclei must be involved in the selection of the most important sensory information at the moment. There are extensive experimental data indicating that the thalamic relay nuclei are not a simple collector for the transmission of sensory information to the cortex, but represent a complex integrative system in which different sensory streams are processed and interact. The most interesting discovery of sensory physiology of the last decade was the discovery of the important role of the ascending reticular system in controlling the transmission of sensory information through the relay nuclei of the thalamus. It turned out that the ascending reticular pathways significantly influence the volume and quality of sensory information transmitted to the brain.

It was shown that high-frequency stimulation of the midbrain reticular formation caused desynchronisation of the EEG, which is accompanied by facilitation of transmission through thalamic relay nuclei and suppression of background activity of neurons of non-specific thalamic nuclei. Similar effects, but less pronounced, were observed with stimulation of the reticular formation of the pontine and medulla oblongata.

Control by the reticular formation of the transmission of sensory information to the thalamus is accomplished by several integrative mechanisms. The first of them is the maintenance of thalamo-cortical systems in a state of increased excitability during electrocortical and behavioural the signs of the awakening reaction compared to the state of these systems during drowsiness and sleep. This is achieved, on the one hand, by suppressing the background activity of non-specific thalamic nuclei neurons, which relieves hyperpolarisation of the thalamo-cortical membrane of relay nuclei neurons. On the other hand, impulsation from the reticular formation to the thalamic relay nuclei leads to the appearance of VG1C11 and AP in thalamo-cortical relay neurons, and when this impulsation ceases, hyperpolarisation caused by return collaterals, synchronous inhibitory waves in the thalamus and EEG synchronisation develop in thalamo-cortical relay neurons. Under these conditions, afferent impulses are apparently unable to raise the threshold of excitability of thalamic relay neurons, which is similar to the closure of sensory channels to the cortex.

It has also been shown that the ascending reticular system has its own mechanism of collateral interaction, which provides a decrease in the activity of individual groups of neurons projecting into thalamic nuclei. A possible effect of suppression of background activity in the ascending reticular system in such cases will be a decrease in the flow of reticulofugal impulses into thalamic structures and, consequently, a transition to electrophysiological correlates of drowsiness and sleep.

The reticular formation controls the transmission of sensory information to the brain at various levels of sensory systems. Thus, the level of the dorsal columns - medial lemniscus is controlled by inhibitory influences coming to the neurons of the nuclei of the dorsal columns from the medial reticular formation of the medulla oblongata. The reticular formation can also modify transmission in sensory systems at the level of primary sensory neurons. It has been shown that transmission through trigeminal mesencephalic nucleus neurons can be inhibited or facilitated by stimulation of the gigantocellular reticular nucleus of the medulla oblongata.

Reticulo-Cerebellar Systems

The reticular formation processes and transmits a significant amount of information from the spinal cord to the cerebellum through a system of specialized nuclei. The main nucleus carrying out such a connection is the lateral reticular nucleus. Its axons end in the form of moss-like fibers in the granular layer of various regions of the cerebellar cortex; their stimulation causes ERPS in the neurons of the granular layer and Golgi cells. Neurons of the paramedian nucleus and suprahypoglossal nucleus send their axons to the cerebellar cortex, as well as to the fastigial and intermediate nuclei; However, the intensity of cerebellar blood flow through these structures is low, since only 10% of the neurons of the paramedial nucleus are activated antidromally when the cerebellar cortex is stimulated.[4]

The lateral reticular nucleus is considered as an important integrative center, which is located in the chain of two feedback systems that combine the structures of the spinal cord, cerebral cortex and brainstem with the cerebellum. Impulses from the cutaneous, muscular and articular receptors of the spinal cord emanating from two spinoreticular tracts interact on neurons of the lateral reticular nucleus with monosynaptic excitatory influences from the motor cortex, the red nucleus and the fastigial nucleus. It is believed that the impulse from the lateral reticular nucleus, formed as a result of this interaction, establishes the optimal level of excitation of the output neurons of the cerebellar cortex - Purkinje cells.

The reticular formation is also involved in the transmission of cortico-fugal impulses to the cerebellum. It has been shown that an important role in this is played by the reticular nucleus of the pontine cover, the axons of which reach the cerebellar cortex. Fibres from all cortical areas, fibres from the red nucleus and efferent cerebellar nuclei (interpository and deptate), stimulation of which causes monosynaptic ISPs, as well as fibres from the upper vestibular nucleus, which monosynaptically inhibit reticular neurons, terminate on neurons of this nucleus.

Obviously, like other specialised nuclei of the reticular formation, the reticular nucleus of the pontine cover integrates signals from various afferent and descending systems before sending them to the cerebellar cortex.

Reticulo-Spinal Systems

Reticulo-spinal neurons occupy a considerable volume in the reticular formation of the brainstem, they are concentrated mainly in the medial reticular nucleus and are divided into two groups differing in the speed of conduction in axons. The two large descending systems formed by them - lateral and ventromedial reticulo-spinal tracts - distribute their terminations at all levels of the spinal cord and play an important role in the mechanism of supraspinal motor control, causing direct monosynaptic excitation or inhibition of spinal motoneurons, influencing interneurons lying in the chains of complex motor reflexes, and controlling presynaptic sensory inputs of the spinal cord. Reticulo-spinal neurons are part of complex descending systems linking the cerebral cortex and a number of brain structures with neural elements of the spinal cord. Their properties and functional organisation are covered in detail in the literature.[2]

The neurons of reticulo-spinal systems have a wide range of possibilities for participation in a variety of integrative processes. Complex motor reactions associated with various forms of animal behaviour, such as habituation, orientation reflexes, pain and defensive reactions, pacing, eye movements, are achieved due to the extensive convergence of impulses of various modalities arriving through the afferent systems of the brainstem and spinal cord, various projections from the rostral structures of the brain and cerebellum, and powerful bilateral connections of all levels of the reticular formation. The structures of the ventromedial part of the reticular formation of the hindbrain exert a regulating effect on various links of the protective spinous-bulbospinal reflexes.

Proprioreticular Systems

The importance of knowledge about the functional interaction between the caudal and rostral regions of the reticular formation is obvious, and although extensive anatomical studies clearly show the rich intertwining of the nervous systems of both regions, the principles of this interaction remain largely unclear. It is known that the caudal reticular formation is an antagonist of the rostral reticular system, and, in turn, the reticular formation of the midbrain is able to modulate the activity of the caudal reticular formation.

Microelectrode studies have revealed that the structures of the reticular formation of the midbrain, pontine and medulla oblongata are interconnected by mono-, oligo- and polysynaptic proprioreticular pathways, through which the reticular formation of the midbrain exerts a powerful and diffuse excitatory effect on the reticular neurons of the pontine and medulla oblongata, and the nuclei of the reticular formation of the medulla oblongata also elicit excitatory, though less pronounced, postsynaptic responses in the mesencephalic reticular neurons.[7] Both of these parts of the reticular formation can also evoke TPSP, but in these cases inhibitory influences from the caudal reticular formation, stimulation of which evokes short-latency inhibitory responses in midbrain reticular neurons, are more effective. These studies indicate the existence of reciprocal influences between the caudal deactivating and rostral activating reticular systems and are a direct experimental confirmation of the previously proposed hypothesis about the presence of a feedback system of reticular homeostasis control in the reticular formation.

Functions Of Amino-Specific Systems

It is known that biogenic amines or monoamines are hormones involved both in metabolism and in the transmission of nerve impulses. In the last decade, the involvement of amine-specific systems has been revealed in various integrative processes of the brain, the ability of these systems to modulate the activity level of many neurons has been studied, and their role in controlling complex brain subsystems that carry out various behavioural reactions and maintain the state of sleep and wakefulness has been demonstrated.

Using the histofluorescence technique, two independent monoaminergic (catecholaminergic and serotoninergic) neuronal systems traced continuously from the caudal regions of the brainstem to the forebrain were detected. The neuronal bodies of these systems are localised in the brainstem, and their axons distribute their terminations to all structures of the central nervous system.

Serotonin-containing neurons (group B) are localised near the midline throughout the medulla oblongata, pontine and midbrain, whereas catecholamine-containing neurons (noradrenaline, dopamine, group A) lie in the lateral regions of the medulla oblongata and pontine, converging towards the midline in the rostral part of the midbrain.

Private physiology

The serotoninergic system is formed by the suture nuclei, which are grouped into the ponto-bulbar posterior (B1-B5) and mesencephalic anterior (B6-B9) complexes. Each of the suture nuclei differs from each other in its efferent connections, but in general, the neurons of the posterior complex send axons predominantly in the caudal direction (to the ponto-bulbar reticular formation, to the sensory and motor nuclei of cranial nerves, deep nuclei and cerebellar cortex and to the spinal cord), whereas neurons of the anterior complex are connected mainly with structures of the midbrain and forebrain (substantia nigra and other mesencephalic formations, nonspecific thalamic nuclei, hypothalamus, basal ganglia, cortex). There is a certain degree of overlap between the innervation areas of the posterior and anterior complexes. The suture nuclei are closely interconnected by afferent fibres. The nuclei of the posterior complex receive a large number of afferents from the ponto-bulbar reticular formation, tegmental regions of the midbrain, vestibular nuclei, upper tubercles of the quadratochalmia, but no direct afferents from the spinal cord and cerebellum have been found. The forebrain nuclei are the place of convergence of afferents from a number of structures of the limbic system and mesencephalic reticular formation.[5]

Electrophysiological studies have found that sero-toninergic neurons in both non-narcotised animals and animals under chloralose anaesthesia have spontaneous activity with a frequency of 0.5-5 imp/s, which is suppressed in free-living animals during the transition from quiet walking to sleep. Various chemical substances, activation of pain or temperature receptors, stimulation of the reticular formation, ventromedial medulla, and habenular nucleus also suppress the spontaneous rhythmicity of most of the identified rhythms serotoninergic neurons of the anterior complex, but non-serotoninergic neurons are easily activated. The neurons of the posterior complex of the suture nuclei are also sensitive to various sensory stimuli, especially pain and temperature stimuli. In these neurons, peripheral impulses caused an increase in the frequency of background rhythmicity. The frequency of background rhythmicity of serotoninergic neurons of the suture nuclei decreased with increasing serotonin concentration in brain tissue.

Stimulation of suture nuclei has an inhibitory effect on many brain functions. Inhibition of polysynaptic bulbar and spinal reflexes, suppression of sensory impulse transmission through trigeminal sensory nuclei and thalamic nuclei, reduction of cortical EP amplitude, suppression of background rhythmicity of reticular formation neurons and neurons of other brain structures, including cortical neurons, were observed. Stimulation of the anterior complex suture nuclei produced slow-wave sleep and suppression of experimental convulsive seizures. The inhibitory effects occurred with long latency periods, which is caused by the slow rate of impulse conduction along thin unmyelinated axons of suture nuclei neurons, and lasted from several tens to several thousands of milliseconds.

The catecholaminergic system is divided into noradrenergic and dopaminergic systems. Neurons containing noradrenaline are located mainly in the lateral part of the brainstem covering (groups A1-A7), as well as in the medulla (AH-A13). Neurons containing dopamine are localised in the midbrain (compact part of the substantia nigra, the area dorsal to the nucleus interpoduiculpra, lateral mesencephalic reticular formation: groups A8-A10). Cell groups A8-A13 send their axons mainly in rostral direction to the cortex and various subcortical structures, while neurons of groups A1-A7 distribute their axons among the brainstem and spinal cord structures.

An essential place in the catecholaminergic system is occupied by the locus coeruleus, which is localised in the pontine and projects to almost all brain regions, including the cerebral cortex, cerebellum, hypothalamus, various brainstem structures and the spinal cord. Most of the neurons of the locus coeruleus are noradrenergic, but about 25% of them contain dopamine. Serotonin-containing neurons have been found within the locus coeruleus.

The neurons of the locus coeruleus receive large amounts from other areas of the catecholaminergic as well as the serotoninergic system; clear projections from the ventromedial nucleus of the hypothalamus, the peribrachial regions, the mesencephalic circumventricular substance and dorsal plexus, as well as the fastigial nucleus and cerebellar cortex, can be traced to this area. Neurons of the locus coeruleus have background activity of the bundle type, the frequency of which in unanesthetised rats is 4.2+1.1 imp/s and decreases under nembutal to 2.6+1.2 imp/s. Conduction velocity along their thin unmyelinated axons ranges from 0.3 to 1.4 m/s. Neurons of the blue nucleus are activated polysynaptically when stimulating those brain regions that receive axonal projections from the areas of the locus coeruleus. It has also been found that sensory inputs of different modalities from the trunk and limbs, as well as from the auditory and visual systems, converge onto the same neurons of the locus coeruleus. Transsynaptic and antidromic activation of the neurons of the locus coeruleus can suppress or facilitate the background rhythmicity of these neurons.

Stimulation of the locus coeruleus area causes extensive changes in the activity of somatic and visceral brain systems. In this case, inhibition of background activity of neurons of various structures, including the serotoninergic system, is observed, transmission at various levels of sensory systems is suppressed or facilitated, depressor reactions of central and peripheral origin, respiratory reactions, and micturition are differentially modulated. It is proved that the system of neurons of the blue nucleus plays an important role in the regulation of the sleep-wake cycle, learning processes, and memory.[15]

It is believed that the role of the system of neurons of the locus coeruleus is to integrate and transmit through widely branching projections to all structures of the brain information about changes in the state of various systems of the organism, which corresponds well to the modern idea of the entire noradrenergic system as a mediator and integrator of behavioural excitation and autonomous functions.

Another, the most studied structure of the catecholaminergic system is the black substance, consisting of a larger - reticular and smaller - compact areas. The substantia nigra sends its axons to the neostriar region, as well as to the ventral medial and anterior nuclei of the thalamus, to the cortex, amygdala, midbrain covering and reticular formation of the pontine.

Electrophysiologically, it has been established that the neurons of the substantia nigra are divided into two types. The first type includes neurons characterised by low frequency (0.5-8 imp/s), unusually long (4-5 ms) APs and very low conduction velocity (0.58 m/s). These neurons form the dopaminergic pathway and lie in the compact area. The second type is formed by neurons with a higher background rhythmic frequency (0.1-60 imp/s), shorter (2-3 ms) APs and higher conduction velocity (2.8 m/s). These neurons are output non-dopaminergic neurons projecting to the thalamus, pontine and forebrain, and lie in the retinal area. The substantia nigra is thought to be involved in the regulation of motor function as well as pain sensitivity, causing a depressant effect on these systems.

There is experimental evidence of the presence in the brainstem of other neurochemical systems (cholinergic, GABAergic) closely interacting with the above systems, but their functions are still largely unclear.[12]

The Antinociceptive System

The discovery in the 1970s of endogenous opioids (enkephalins and endorphins), morphine-like substances that cause analgesia, and various types of opioid receptors on the membrane of neurons of individual CNS structures allowed us to draw an important conclusion that the brain has internal mechanisms for suppressing pain, and to approach the disclosure of their neural organization. There is now a lot of evidence that there is a powerful and relatively specific neuron system in the brain stem designed to suppress pain, which has efferent pathways to the nociceptive structures of the spinal cord. This system is activated by stimulation of afferent pathways and direct stimulation, as well as by opioids of exogenous or endogenous origin, and has endorphinergic synapses at nodal points that activate this system. The full boundaries of this system have not yet been delineated. According to a number of authors, the antinociceptive system is formed by closely interrelated structures lying on three levels: the periaqueductal gray matter of the midbrain, the large suture nucleus and the magnocellular reticular nucleus of the medulla oblongata, and neurons of the gelatinous substance of the dorsal horn of the spinal cord. Other researchers believed that the system also includes the periventricular structures of the intertidal brain.

The current hypothesis about the mechanism of action of the central antinociceptive system, based on extensive experimental material, suggests that the flow of nociceptive impulses through neurons with endorphyergic synapses activates the central (periventricular — periaqueductal) component of this system. Neurons of this system, in particular neurons of the periaqueductal gray matter, in turn activate, possibly through encephalinorgic synapses, neurons of the large suture nucleus and the reticular magnocellular nucleus. From these structures, the serotonergic spinal pathway and C. are directed to the spinal cord. In addition, neurons of the reticular magnocellular nucleus send efferent fibers to the large suture nucleus. In the spinal cord, the endings of the spinal fibers are found mainly on neurons I, II and V plates of the dorsal horn, which form the main postceptive ascending pathways. The impulses in these neurons are suppressed by the arrival of discharges along the spinal pathway. There are also enkephalinergic interneurons in these plates. Their axons are distributed on the preterminals of thin myelin and myelin-free fibers, most of which transmit post-perceptual information to the brain. The excitation of this link leads to a blockade of the nociceptive afferent input. There is evidence that the dopaminergic and noradrenergic systems also participate in the modulation of nociceptive flow at various levels of the brain.

Thus, the brainstem contains nerve structures with the help of which a number of the most important integrative mechanisms are performed, aimed at coordinating the activity of the central nervous system and all functions of the organism as a whole.

The main system of integrative control of the brainstem is the reticular formation. Occupying an important strategic position in the brainstem, this system has structural features and a peculiar functional organisation that serve as a basis for extensive spatial connections and a variety of physiological effects. The main components ensuring the integrative activity of the reticular formation are the obligatory inflow of afferent pulsation from various sensory systems and structures of the brain and spinal cord and the background rhythmic activity of reticular neurons. The interaction of these processes in the reticular formation, leading to activation or inhibition of different types of reticular neurons, allows it through its efferent systems to effectively control the processes of sensory information transmission, to regulate posture and movements, to change the activity of cardiovascular, respiratory systems and various internal organs, as well as to take part in a number of higher brain functions (sleep, wakefulness, attention, learning, emotions, memory).

In general, the reticular formation can be defined as a nodal system through which a biologically important sensory signal stereotypically and simultaneously excites various sensory, integrative and motor systems of the brain and thus brings the organism into a state of reflex readiness to perform obligatory adaptive reactions. [17-18]

Monoaminergic systems are equally important in the functioning of the brain stem. Their extremely close interaction with the most important integrative structures and, first of all, with the reticular formation, their ability to exert a very long-term, mainly inhibitory, effect on various reflex and neurochemical reactions give reason to consider them an important component of the integrative mechanisms of the brain stem.

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