ClinicSearch
Clinical Research and Clinical Reports
Elizaveta I Bon *
Open Access
Review Article

Structure and Functional Organization of the Limbic System

Bon E. I *, Maksimovich N. Ye, Otlivanchik N.I, Kazakevich S.D

Riggs Pharmaceuticals, Department of Pharmacy University of Karachi Pakistan.

***Correspondence Author:** Elizaveta I Bon, Candidate of biological science, Assistant professor of pathophysiology department named D. A. Maslakov, Grodno State Medical University; Grodno State Medical University, 80 Gorky St,230009, Grodno, Belarus.

Received Date: June 03, 2025 **Accepted Date**: June 26, 2025 **Published Date**: July 30, 2025.

Citation: Bon E. I, Maksimovich N. Ye, Otlivanchik N.I, Kazakevich S.D, (2025), Structure and Functional Organization of the Limbic System, *Clinical Research and Clinical Reports,* 8(2); **DOI:**10.31579/2835-8325/179

Abstract

The limbic system includes extensive structures of the brain that are of primary importance, on the one hand, in the implementation of motivational-emotional reactions of animals, and on the other hand, in the organization of learning and memory processes. Scientific views on the structural and functional organization of the limbic system were formed under the influence of classical works, which revealed some aspects of the role of the forebrain in the regulation of behavior. However, experimental studies and theoretical works were still of decisive importance, becoming a turning point in the study of neurophysiological correlates of motivational-emotional reactions.

Key words: structure; functional organization; limbic system

Introduction

The limbic system includes extensive structures of the brain that are of primary importance, on the one hand, in the implementation of motivational-emotional reactions of animals, and on the other hand, in the organization of learning and memory processes. Scientific views on the structural and functional organization of the limbic system were formed under the influence of classical works, which revealed some aspects of the role of the forebrain in the regulation of behavior [1-5]. However, experimental studies and theoretical works were still of decisive importance, becoming a turning point in the study of neurophysiological correlates of motivational-emotional reactions. Studying the effect of damage to the temporal region of the neocortex and paleocortex on lower monkeys, dramatic changes in their behavior were discovered, expressed in the fact that the monkeys became tame, hypoactive, hyperphagic and were characterized by physical blindness, emotional lethargy, loss of fear and aggression, and hypersexuality. These observations were completely new, especially against the background of the prevailing opinion among anatomists about the functions of the so-called olfactory brain, the system of which included formations of the most rostral end of the forebrain up to the mesencephalon [4]. It is all the more remarkable that it was specialists in brain anatomy who questioned the traditional concept of the highly specialized functions of the olfactory brain and suggested that a large part of this system was involved in the regulation of affective behavior, and not olfaction. Based on studies in which a large limbic lobe was isolated at the level of the cerebral cortex, a "circle" of interconnected neural structures was described, including the cingulate gyrus, hippocampus, mammillary bodies, anterior nuclei of the thalamus and again the cingulate gyrus, and ensuring the emergence and course of emotions [3]. At the same time, the existence of numerous connections between the rostral elements of the limbic system and the hypothalamus was established. Later, this theory was revised and significantly developed. It has been suggested that the limbic system (the “visceral brain”) is important not only in regulating emotional behavior, but also in correcting internal and external signals entering the brain [5-7].

Currently, the limbic system unites brain structures of various levels and structures. The tendency to expand the boundaries of the limbic system, observed recently, should not be considered incorrect, since in fact, this system functionally integrates brain structures of mesodiencephalic, subcortical and cortical origin [7-8]. The cortical structures included in the limbic system, for their part, can be divided into two groups: the "paleocortex" or "allocortex" and the "paraallocortex", which differ significantly in their structure and location. Phylogenetically more ancient paleocortical structures meet the criteria of the "cortex" and consist of at least three layers. This group includes the hippocampus (Ammon's horn and dentate gyrus), the piriform lobe (prepyriform cortex, periamygdaloid cortex, entorhinal area), olfactory bulbs and olfactory tubercle. The paraallocortical group of limbic system structures includes only those areas of the cortex that occupy an intermediate position between the phylogenetically old paleocortex and the phylogenetically new neocortex. These include the cingulate gyrus, or limbic cortex, the presubiculum, and the frontoparietal cortex [7-9]. An important group of limbic system structures are subcortical formations that are closely related to the cortical structures of the limbic system. Of these formations, the most important role in organizing motivated behavior is currently attributed to the hypothalamus, amygdala, septum pellucidum, anteromedial nuclei of the thalamus, and part of the reticular formation [9-15].

Thus, the limbic system unites structures that are very different in their cytoarchitecture. Subtle neuromorphological methods have revealed the most important connections between individual structures of the limbic system, on the one hand, and between the limbic system and other brain systems (with the reticular formation, basal ganglia and neocortex), on the other. In terms of elucidating the neural mechanisms of motivated behavior, the greatest interest is aroused by the connections of the hippocampus and amygdala with mesodiencephalic structures. Despite the fact that the hippocampus and amygdala differ from each other cytoarchitectonically, their projections with diencephalic structures are strikingly similar [11-15].

The hippocampus, as a cortical structure, is organized according to the screen principle. The cytoarchitectonic division of the hippocampus occurs based on the arrangement of pyramidal cells. The hippocampus is divided into two main areas: the upper and lower. The upper area differs from the lower by a more compact arrangement of pyramidal neurons. Having studied the cytoarchitectonic structure of the hippocampus in detail, four fields are distinguished: CAX, CA2, CA3, CA4. The CAX field corresponds to the upper area, its pyramidal neurons are located very densely and form two layers. The CA3 field corresponds to the lower area, the pyramidal neurons of this field are larger than in the CAX field and are located less compactly. The CA2 field lies between the CA4 and CA3 fields and consists of large pyramidal cells. Modified pyramids are presented in the CA4 field, located in a less organized manner. This field is located in the hilus and is considered part of the dentate fascia [15-17].

The hippocampus has a clearly organized structure in cross-section as well. Seven layers can be distinguished in it: 1) stratum moleculare, 2) stratum lacunosum, 3) stratum radiatum, 4) stratum pyramidale, 5) stratum oriens, 6) alveus and 7) epithelial zone. It is characteristic that in all these layers a certain organization of afferents is outlined. In the first layer, located on the border of the hippocampus and the dentate fascia, there is a bundle of axons entering the hippocampus from the subiculum, and in the second layer there is a powerful bundle of axons originating from the upper part of the hippocampus and directed to the subiculum. In the second layer of the CA4 field there are also Schaffer collaterals connecting the cells of the CA3 and CA4 fields with the apical dendrites of the pyramidal cells of the CA1 field. In the CA3 and CA4 fields, an additional layer, stratum lucidum, is distinguished, where the mossy fibers of the dentate fascia end. In the third layer, axons of various origins end on the trunks of apical dendrites. The fourth layer, i.e., the layer of pyramidal cells, has a peculiar structure; their dendrites are directed both toward the stratum moleculare and toward the alveus, which is why they are often called "double pyramids." [16-18]

The axons of the pyramidal cells go towards the alveus. Some of them have collaterals in the stratum oriens that terminate in the same layer of other fields. The main trunks of the axons go along the brainstem and, entering the fornix system, reach various parts of the forebrain and diencephalon [15-20].

The pyramidal layer is followed by the stratum oriens, which contains polymorphic cells, including basket cells. Below it is the sixth layer (alveus), which is white matter and contains myelinated fibers of pyramidal cells of all fields of the hippocampus. The seventh layer, i.e., the epithelial zone, is essentially the wall of the lateral ventricle, and it can be omitted from the neuronal organization of the hippocampus [14-20].

The hippocamps of the right and left hemispheres are connected to each other by fibers that form the hippocampal commissure - the psalterium. The clear topographic localization of afferent endings on the pyramidal cells of the hippocampus creates a good opportunity for the use of electrophysiological methods to clarify the functional properties of synaptic contacts [21-26].

The projection pathways of the hippocampus have long attracted the attention of researchers. The fornix system was described in detail long ago, being considered its only hippocampal output. Later, other pathways were identified, but the fornix is still considered the main formation through which the hippocampus is connected with various mesodiencephalic structures. The fibers of the fornix at the level of the septum are divided into two main bundles: the compact column of the fornix and the more diffuse precommissural fornix [20-24], which contains fibers coming from the CA3 and CA4 layers of the hippocampus and ending mainly in the nuclei of the septum. Most of the fibers are interrupted in the lateral nucleus, and the other, passing further, gives endings on the cells of the lateral preoptic area and the lateral hypothalamus. From these formations, the descending part of the medial forebrain bundle begins, forming a powerful system of connections of the forebrain with non-specific structures of the midbrain and pons. The compact column of the fornix passes behind the anterior commissure and is directed to the mamillary bodies. However, some of the fibers, before reaching the mamillary bodies, depart from the column and are directed to the anterior nuclei of the thalamus, as well as to its rostral intralaminar and medial regions. Most of the fibers of the column of the fornix terminate in the mamillary body, and some bypass it and, passing in the dorsal direction, contact the cells of the rostral part of the central gray matter of the midbrain. The mamillary tract, composed of axons of the cells of the mamillary bodies, is divided into two bundles: the mammillothalamic tract, going to the nuclei of the anterior thalamus, as well as to its nonspecific nuclei, and the mammillotegmental tract, going to the tegmental nuclei. In addition to indirect connections via the mammillary bodies, the hippocampus is connected to the anterior nuclei of the thalamus and the direct pathway. The anterior nuclei of the thalamus, which belong to the limbic system, project to the limbic cortex [14-20].

The limbic cortex is considered the highest section of the entire system and consists of the cingulate gyrus and the entorhinal cortex. The cingulate gyrus, located above the corpus callosum, on the medial wall of the hemisphere, is an intermediate formation between the paleocortex and neocortex; in its complex cellular composition and six layers, it is similar to the neocortical formation. The entorhinal region lies on the mediobasal surface of the hemisphere and through a number of complex links (parasubiculum and subiculum) passes into the hippocampus. The limbic cortex receives afferent connections from the neocortex, mainly from the secondary and associative zones of the posterior part of the hemispheres and the frontal-premotor zones [9-12].

The cingulate gyrus sends projections to the entorhinal region, which in turn is the main source of cortical afferents of the hippocampus. Thus, the main limbic circle is closed. Bilateral connections between individual links of this circle are apparently necessary not only for normal functioning, but also for its structural existence. This is indicated by transneuronal degeneration in various limbic structures when the cingulate gyrus is removed [15].

It is now well known that both archipalaeocortical and neocortical formations are structurally and functionally connected with such subcortical links of the limbic system as the hypothalamus and amygdala, as well as the reticular formation, a significant part of which belongs to the limbic system. The main input of the hippocampus through the septum is made up of projections from the reticular formation and hypothalamus, and the septum, an important formation of the limbic system, is located precisely on the path between the hippocampus and the reticulohypothalamic structures [15]. Fibers directed from the mesodiencephalic structures mainly switch in the medial nucleus, which occupies a central place in the septum and in the ventral direction passes into the nucleus of the diagonal fasciculus. In the medial nucleus, medium and large multipolar and spindle-shaped neurons are located in the form of separate clusters. The lateral nucleus of the septum consists of uniform, rounded or multipolar cells of medium size. Ascending projections from the medial septum go to the hippocampus. No projections to the hippocampus are traced from the lateral nucleus. The lateral nucleus sends fibers to the medial septum. However, the hippocampal descending pathways project to the lateral nucleus of the septum and through it switch to the medial nucleus, due to which the cyclic connection is closed between both the hippocampus and the septum [18].

The most important subcortical structure of the limbic system, closely connected with the hypothalamus, is the amygdala. Unlike other structures of the limbic system, it is closely connected with the basal ganglia. The amygdala is a symmetrical structure located in the ventromedial part of the rostral pole of the temporal lobe. In the phylogenetic series, the presence of the amygdala is observed already in cyclostomes, and it reaches full development in mammals. In the amygdala, two parts can be distinguished: the more ancient cortico-medial part and the younger basolateral part. The cortico-medial part is located medially and consists of the cortical, medial and central nuclei. The basolateral part consists of the lateral and basal nuclei []4-11.

The afferent pathways of the amygdala can be classified as olfactory, diencephalic, and cortical. The olfactory bulbs project first to the piriform cortex and are connected to the amygdala through it. Diencephalic afferent fibers go to the amygdala through the corticostriatal pathways and the medial association bundle. A connection has also been established between the dorsal thalamus and the amygdala. Bilateral connections between the piriform cortex and the basolateral part of the amygdala are realized through the longitudinal association bundle. The amygdala also receives fibers from the temporal and orbital cortex. In addition, the evoked potential method has shown close connections between the entire basofrontotemporooccipital cortex and the amygdala. For its part, the amygdala also actively influences other structures of the limbic system. The main efferent pathways of the amygdala can be grouped into two systems: the dorsal and ventral amygdalofugal fiber systems. The former conducts impulses mainly from the corticomedial and partly from the basolateral part of the amygdala, the latter originates from the basolateral region [13-17].

The corpus callosum is divided into commissural, postcommissural, and supracommissural parts. The postcommissural fibers terminate in the rostral hypothalamus, but some of them are associated with the medial forebrain bundle. The supracommissural component terminates in the ventromedial hypothalamus. The ventral amygdala-lofugal system terminates mainly in the lateral hypothalamus. The amygdala also projects to the thalamus [12]. There is also an amygdala-thalamo-orbitofrontal connection system through which the amygdala actively influences the frontal association area of the cortex. In discussing the significance of the efferent connections of the amygdala, it is worth paying special attention to the fact that the projection pathways of the amygdala and hippocampus have a common termination zone in the diencephalic structures and that the fiber systems originating in these areas can serve as secondary pathways along which nerve impulses originating in the hippocampus and amygdala are propagated [21-22].

The diencephalic link of the limbic system is the hypothalamus. The hypothalamic groove, located as a notch in the wall of the ventricle, is the border of the hypothalamus and thalamus. The rostral part of the hypothalamus merges with the preoptic area, which is a telencephalic structure by genesis, but due to its close connection with the anterior hypothalamus is rightfully considered its part. The posterior border of the hypothalamus is a conventional plane drawn behind the mammillary bodies. Laterally, the hypothalamus extends to the ventral part of the thalamus, the indefinite zone (zona incerta) and the nuclei of Forel's field. The hypothalamus is divided into right and left halves by the third ventricle. In the literature, there is a division of the hypothalamus into different zones and areas both in the rostrocaudal and mediolateral directions. The hypothalamus can be divided into the following zones: 1) the preoptic area with its nuclei, 2) the supraoptic area with the supraoptic, paraventricular, suprachiasmatic, and anterior hypothalamic nuclei, 3) the tuberal area with the dorsomedial, ventromedial, arcuate, lateral hypothalamic, and posterior hypothalamic nuclei, 4) the mamillary area with the medial mamillary, lateral mamillary, intercalary, premamillary, and supramamillary nuclei [14-26].

The hypothalamus receives extensive afferent fibers from various areas of the cerebral cortex, as well as from the thalamus, globus pallidus, amygdala, visual system, reticular formation, spinal cord, and other structures of the central nervous system. Because of these connections, the hypothalamus can be considered as a nodal point of an extensive neural mechanism extending from the medial wall of the hemispheres caudally to the inferior border of the midbrain. Important projections of the hippocampus and amygdala to the hypothalamus through the fornix and the ventral amygdalofugal pathway were indicated in the description of the main limbic circle. In addition, many ascending and descending fibers of the medial forebrain bundle connect the rostral structures of the limbic system with the preoptic area and the lateral hypothalamus. The corticohypothalamic ones are of great functional importance. Based on electrophysiological data, it was suggested that there are direct connections between the premotor, sensorimotor, suprasylvian and ectosylvian areas with the anterior, dorsomedial, posterior and mammillary nuclei of the hypothalamus. The frontal area of the cortex sends projections to the hypothalamus through the septum. Some other cortical projections come to the hypothalamus through the anterior nuclei of the thalamus, thereby creating cyclic connections between these formations of the limbic system. Direct mesencephalic tracts go from the midbrain to the hypothalamus [9-17].

In describing the main limbic circle, the importance of the mammillothalamic tract was pointed out, through which the hypothalamus can actively influence the limbic nuclei of the thalamus and the limbic cortex. An extensive periventricular system of fibers originates from the posterior hypothalamus, tuberal and supraoptic nuclei. Some of these fibers terminate in the midline nuclei of the thalamus, as well as in its dorsomedial nuclei. The majority terminate in the tectal and tegmental nuclei of the midbrain and pons. Commissural pathways and intrahypothalamic connections play an important role in the functional organization of various areas and nuclei of the hypothalamus. Most of the intrahypothalamic connections are formed by fibers of the ventromedial nucleus, contacting neurons of the lateral hypothalamus and dorsomedial nucleus [12-19].

A variety of methodological approaches are used to study the functional organization of the limbic system and its individual links. These approaches are: 1) studying the effect of damage to limbic structures on various types of behavior, 2) studying the effect of direct electrical and chemical stimulation of limbic structures, and 3) studying the dynamics of electrical activity of limbic system structures during behavioral acts. Neuropharmacological and neurochemical methods of analyzing the functional organization of the limbic system have recently been fruitfully combined with these three main methods. The complexity of the structure of the limbic system significantly limits the capabilities of these methods. In particular, it is very difficult, and sometimes impossible, to isolate a particular structure from the entire system. Extreme caution is also required when directly stimulating individual limbic structures, since there is a high probability of spreading loops of irritating electrical current, as well as diffusion of the chemical stimulant to neighboring areas of not only limbic, but also other origin. The possibilities of interpreting the results of studying the dynamics of electrical activity of limbic structures during the implementation of motivated behavior are no less limited [17-23]. Despite the above, the limbic system has such a specific relationship to the organization of motivated behavior and to the process of learning and memory that the information obtained using these methods has great scientific and cognitive value.

References

1. Bon' E.I. (2018). Structure and development of the rat hippocampus E.I. Bon', S.M. Zimatkin Journal of GrSMU. 16 (2). 132-138.
2. Bon' E.I. (2019). Structural and functional organization of the rat thalamus E.I. Bon' Orenburg Medical Bulletin. (3) 34-39.
3. Bon' E.I. (2018). Morphological characteristics of the parahippocampal region of the rat E.I. Bon', S.M. Zimatkin Tyumen Medical Journal. (4). 6-10.
4. Bon' E.I. (2020). Histological characteristics of neurons of the neocortex and hippocampus of rats in late ontogenesis E.I. Bon', T.L. Alad'eva Chrono medical Journal. (1).46-49.
5. Bon, EI (2023). Retrosplenial and cingulate cortex of the rat brain – cyto- and chemoarchitectonics / EI Bon, NY Maksimovich, S. M. Zimatkin, VA Misyuk // Clinical Genetic Research. 2(1). 1-5.
6. Bon', E.I. Cerebral ischemia. Histological characteristics of neurons in the parietal cortex and hippocampus of rats / E. I. Bon', S. M. Zimatkin, M. P. Pumpur (2023). // Spring anatomical readings: collection of articles from the Republican scientific and practical conference dedicated to the 65th anniversary of the Department of Normal Anatomy of Grodno State Medical University, 29-33.
7. Bon' E. I. (2019). Histological changes in pyramidal neurons of the parietal cortex and hippocampus of rats with total cerebral ischemia / E. I. Bon', N. V. Valko // Collection of materials from the conference of students and young scientists dedicated to the 95th anniversary of the birth of Professor Gennady Alekseevich Obukhov, April / [editorial board: V. A. Snezhitsky and others]. - Electronic text data and programs - Grodno: Grodno State Medical University, 51-52.
8. Bon' E.I. (2022). The central nervous system of the rat: a textbook for students of the second stage of higher education (master's degree) in the specialty 1-79 80 01 profiling pathological physiology and applicants in the specialty 14.03.03 - pathological physiology / E. I. Bon', N. E. Maksimovich, S. M. Zimatkin. - Grodno: GrSMU, 226

9. Zimatkin S.M. (2017). Postnatal organellogenesis in pyramidal neurons of the rat cerebral cortex / S.M. Zimatkin, E.I. Bon // Morphology. (2) 20-24
10. Zimatkin S.M. (2017). Dark neurons of the brain / S.M. Zimatkin, E.I. Bon // Morphology. 152, (6).81-86.
11. Bon' E.I. (2018). Structural and neurotransmitter organization of various parts of the cerebral cortex / E.I. Bon', S.M. Zimatkin // Bulletin of the Smolensk State Medical Academy. 2(17).85-92.
12. Bon' E.I. (2019). Changes in the chromatophilia of the cytoplasm of large pyramidal neurons of the rat neocortex in postnatal ontogenesis / E.I. Bon', S.M. Zimatkin // Bulletin of the Smolensk State Medical Academy. (1).10-16.
13. Bon' E.I. (2019). Dynamics of morphological changes in pyramidal neurons of phylogenetically different parts of the rat cerebral cortex during total cerebral ischemia / E.I. Bon', N.E. Maksimovich. S.M. Zimatkin, N.A. Valko, V.N. Kot, O.V. Mosin, A.G. Sulzhitsky // Bulletin of the Smolensk State Medical Academy. (2). 5-13.
14. Bon' E.I. (2019). Postnatal morphogenesis of internal pyramidal neurons of the rat neocortex / E.I. Bon', S.M. Zimatkin // Tyumen Medical Journal. (1) 44-49.
15. Bon EI (2024). Synchronizing mechanisms of the thalamus / EI Bon, N.Ye. Maksimovich, A.A. Rishkel // J. Surgical Case Reports and Images. 8(2) 1-4.
16. Bon' E.I. (2019). Morphological features of neurons of the cerebral cortex of rats in the late periods of postnatal development / E.I. Bon', S.M. Zimatkin, T.L. Alad'eva // Orenburg Medical Bulletin. (4) 42-45.
17. Bon' E.I. (2020). Histological characteristics of neurons of the neocortex and hippocampus of rats in late ontogenesis / E.I. Bon', T.L. Alad'eva // Chronomedical Journal. (1) 46-49.
18. Bon' E.I. (2017). Microscopic organization of the rat isocortex / S.M. Zimatkin, E.I. Bon' // News of medical and biological sciences. (4) 80-88.
19. Bon' E.I. (2019). Postnatal morphogenesis of internal pyramidal neurons of the rat neocortex / E.I. Bon', S.M. Zimatkin // Tyumen Medical Journal. (1) 44-49.
20. Bon' E.I. (2021). Development of the rat isocortex in antenatal and postnatal ontogenesis / E.I. Bon' // Chronomedical Journal. (1) 31-34.
21. Bon' E.I. (2018). Dynamics of morphofunctional changes in the rat isocortex in postnatal ontogenesis / E.I. Bon', D.S. Kaptyukh, V.O. Ganetskaya // Proceedings of the V Republican scientific and practical conference "Modern achievements of young scientists in medicine", Grodno, November 23, 2018 / Grodno State Medical University; editorial board: V.A. Snezhitsky (editor) [et al.]. - Grodno: Grodno State Medical University, 48-51.
22. Bon' E. I. (2019). Structural reorganization of the rat neocortex in postnatal ontogenesis / E. I. Bon', D. S. Kaptyukh, V. O. Ganetskaya // Collection of materials from the conference of students and young scientists dedicated to the 95th anniversary of the birth of Professor Gennady Alekseevich Obukhov, April 25-26, 2019 / [editorial board: V. A. Snezhitsky (editor-in-chief) and others]. – Electronic text data and programs – Grodno: Grodno State Medical University. 51-52
23. Bon' E.I. (2020). Dynamics of morphological disorders of rat hippocampal neurons in stepwise subtotal cerebral ischemia / E.I. Bon', N.E. Maksimovich, S.M. Zimatkin // Orenburg Medical Bulletin. (1) 46-53.
24. Bon', E.I. (2022). Changes in the histological characteristics of pyramidal neurons of the neocortex and hippocampus of rats during cerebral ischemia in a comparative aspect / Bon' E.I., Maksimovich N.E., Lychkovskaya M.A. // Modern problems of medical biochemistry: collection of materials of the International scientific conference dedicated to the 85th anniversary of the birth of Professor V.K.Kukhta, Republic of Belarus, Minsk, January 25, 2022 / edited by A.D.Taganovich, N.N.Kovganko, V.V.Khrustalev. - Minsk: BSMU, 24-27.
25. Bon, EI (2022). Rat Hippocampus – Development and Morphological Organization / LI Bon, SM Zimatkin, AV Malykhina // Journal of Surgical Case Reports and Images. 5(2). 1-6.
26. Bon, EI (2023). Methods of simulating the pathology of the nervous system experimentally / EI Bon, N. Ye. Maksimovich, EV Moroz // Journal of Clinical Research and Clinical Trials, BRS Publishers. 2 (1) 1-7.

ClinicSearch