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Fundamentals of Pathophysiology of Higher Nervous Activity - Literature Review

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Review Article

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Abstract

The proposed article is an experience of creating a review on the pathology of higher nervous activity. The manifestations of the functional pathology of higher nervous activity are varied, but primarily they relate to mental functions. Since the pathology of higher nervous activity is manifested not only in deviations of mental functions, but also in violations of other functions of the body (regulation of the somatovegetative sphere), the study of its mechanisms is carried out taking into account changes in the whole organism, including the humoral system. Deepening and detailing the pathogenesis of disorders of higher nervous activity will serve as a fundamental basis for the prevention and correction of diseases of the nervous system.

Keywords: Brain; Pathology; Nervous; Higher Nervous Activity

Introduction

Pathophysiology of Higher Nervous Activity

In relation to animals, the term "experimental pathophysiology of higher nervous activity" is used, which implies modeling on animals of individual symptoms and syndromes of the pathology of higher functions of the human brain and their study by objective research methods, primarily by the method of conditioned reflexes [1]. Theoretical provisions of the pathophysiology of higher nervous activity are based on the teachings of I.P. Pavlov about conditioned reflexes. However, at present, the pathophysiology of higher nervous activity widely uses modern achievements in neurophysiology and neuropathology and, accordingly, is based on experimental data established by combining the method of conditioned reflexes with electrophysiological, morphological, biochemical, and other methods of studying the higher parts of the brain. Often the concept of experimental neurosis is regarded as a synonym for experimental pathology of higher nervous activity. It would be more correct to consider experimental neuroses as a special case of the pathology of higher nervous activity and use it in relation to experimental models of individual symptoms and syndromes of neuroses or neurosis-like states in a person [2].

Manifestations of Functional

Pathology Higher Nervous Activity

The manifestations of the functional pathology of higher nervous activity are varied, but primarily they relate to mental functions. Thus, there is a weakening of the analytical and synthetic activity of the brain, a violation of long-term and short-term memory, the regulation of emotions and motivations, the regulation of the general functional state of the brain, interhemispheric relations. Usually these

disorders are manifested in eating, sexual, defensive, group behavior, which are most often studied to characterize higher nervous activity. A frequent manifestation of the pathology of higher nervous activity is a violation of the sleep-wake cycle, the regulation of autonomic and somatic functions: there is a violation of the heart rate, regulation of blood pressure, trophic supply of the skin (trophic ulcers appear, baldness occurs). Cases of myocardial infarction in animals in a state of experimental neurosis, accompanied by strong emotional arousal, have been described [3,4].

Often, the pathology of higher nervous activity is accompanied by a violation of the regulation of the digestive and excretory functions, the occurrence of stomach ulcers and other parts of the digestive system. In the pathology of higher nervous activity, hyperkinesis of the muscles of the limbs, neck, and other parts of the body may occur. The facts point to significant neurochemical changes in the blood during experimental pathology, reflecting the dysregulation of the cholinergic and catecholaminergic mediator systems of the body. Different stages of the pathology of higher nervous activity are reflected in changes in the electrical activity of the neocortex and limbic structures of the brain [5].

Since the pathology of higher nervous activity is manifested not only in deviations of mental functions, but also in violations of other functions of the body (regulation of the somatovegetative sphere, etc.), the study of its mechanisms is carried out taking into account changes in the whole organism, including the humoral system. Such a holistic approach to understanding the pathology of higher nervous activity reflects the idea of nervism and orients the search for pathophysiological mechanisms of violation of higher nervous activity at different structural and functional levels (from subcellular to organismal) of its organizations [4,5].

Mechanisms of Occurrence of Pathology of Higher Nervous Activity

All causes that can cause pathology of higher nervous activity are divided into three large groups: 1) arising in the process of interaction of the organism with the environment, including the prenatal period of life; 2) genetically determined and 3) due to a combination of the first two. The first group of causes is currently the most studied, it is extremely diverse, and therefore their systematization and identification of the main pathogenic factors among them are extremely important [6].

An external pathogenic agent reaches the brain in different ways, which significantly determine both the pathogenesis of the disease and its clinical manifestations. Therefore, in all cases of disorders of higher nervous activity, it is necessary to identify the main route of action of a pathogenic agent, starting from the primary link of its application. Given these circumstances, there are functional, post-traumatic and combined pathology of higher nervous activity [5].

Functional pathology of higher nervous activity is understood as such behavioral disorders that are caused by the influence of pathogenic stimuli on external and internal receptors. Post-traumatic pathology of higher nervous activity refers to behavioral disorders arising from the direct effect of a pathogenic agent on the brain, for example, when it is injured, hemorrhage into the brain tissue, brain tumors, etc. Combined (functional-traumatic) pathology of higher nervous activity refers to disorders arising from effects both on the receptor system of the body and directly on the brain, which occurs, for example, with radiation and thermal injuries of the head, with its mechanical damage, etc [7].

In all three cases, the impact of a pathogenic agent causes primary damage to the brain, its primary disease; therefore, the resulting disorders of higher nervous activity are primary. Violations of higher nervous activity caused by other factors or developing as a result of pathology of the body, such as an infectious disease, tumors of non-brain localization, cardiovascular disease, etc., are secondary. Most often, a secondary pathology of higher nervous activity is the result of asthenization of the nervous system, a decrease in its resistance to psychogenic or other influences [4,6].

Functional Pathology of Higher Nervous Activity

This pathology occurs for two main reasons: 1) the pathogenic agent directly affects the receptors by an unconditioned reflex mechanism; 2) a pathogenic agent has a signal value and acts through receptors on the brain according to a conditioned reflex mechanism. In addition, in humans, due to the presence of a second signaling system, the functional pathology of higher nervous activity can be caused by verbal influence, i.e., a pathogenic agent can affect the higher parts of the brain through the second (speech) signaling system [1].

The mechanisms of the functional pathology of higher nervous activity, which are due to the action of conditioned reflex stimuli, have been studied in the most detail. According to the classical ideas of I. P. Pavlov, the mechanism of such pathology consists in an overvoltage of excitation, inhibition, or their mobility. Whatever external causes the experimental neuroses depended on, they were explained by the weakening of the process of internal inhibition, leading to the predominance of the excitatory process or to disturbances in the normal mobility of excitation and inhibition and, as a result, to their pathological liability or inertia [1,2].

An imbalance between inhibition and excitation contributes to the irradiation of inhibition through the cortex, and then through subcortical structures, and the emergence of phase states. In the early stages of the development of these processes, inhibition has a protective function; it occurs after the nerve cells reach the limit of their normal operation, and therefore was called Trans limiting inhibition. But after the protective function of inhibition is exhausted, pathology of higher nervous activity begins to form [2].

These ideas of I. P. Pavlov about the mechanisms of the occurrence of pathology of higher nervous activity played an important role in the development of some methods of treating such pathology, for example, in substantiating and developing a method of sleep therapy. Sleep was considered as a case of inhibition diffused over the cortex and sub cortex, and, consequently, as a factor protecting nerve cells from pathological influences. However, at present, the presented ideas about the mechanisms of pathology have been revised, refined, and partly developed [1,6].

Thus, neurophysiological studies do not confirm the ability of inhibition to irradiate through the brain in the sense in which it was originally thought. Further, the concept of sleep as a state of diffuse inhibition throughout the cortex and subcortical structures has been significantly revised on the basis of data indicating that sleep has a complex structure and consists of several phases that replace each other in a certain sequence. One of these phases – it was called paradoxical – is characterized by increased brain activity and is accompanied by strong emotional reactions and experiences. In this phase, dreams most often appear [8].

Modern ideas about the mechanisms of the pathology of higher nervous activity are based on taking into account the role of emotions and memory, as well as humoral factors in the occurrence of pathology.

The Role of Negative Emotions

They arise under the influence of pathogenic stimuli and can take a long-term, stagnant character. This is facilitated by a long delay in the external detection of negative emotions (the so-called "unreacted emotions"), accompanied by hormonal and other chemical changes in the blood. These circumstances reduce the resistance of the nervous system to a pathogenic agent and, thus, a self-reinforcing pathological system ("vicious circle") is formed, disorganizing the activity of other systems as well. However, such a pathogenic effect of negative emotions occurs during their long-term stable course: at the early stages of their occurrence, negative emotions often play a biologically positive role, acting as a factor in the emergency mobilization of the whole organism in order to counteract the pathogenic agent [9].

The Role of Memory

The mechanism of the long-term course of pathological higher nervous activity is complex and is determined by several factors. Thus, it is believed that pathological conditioned reflexes can be formed as a result of the fixation in long-term memory of those states that arise in the brain under the influence of a pathogenic agent. These states can be reproduced to the appropriate conditioned stimulus or in the appropriate situation (situational pathological reactions) or be ubiquitous in the form of a stable pathological condition. The latter is also formed with the participation of long-term memory [7].

Another mechanism for the emergence and retention of pathological higher nervous activity may be the formation of a pathological temporal connection. Such temporary connections are especially easily formed when the general functional state of the brain is low; they can arise according to the conditioned reflex principle or another principle of learning (imprinting, figurative behavior), be situational or generalized in nature [10].

The general functional state of the brain changes under the influence of many factors; it, for example, decreases as a result of prolonged restriction of the flow of visual, auditory, tactile, proprioceptive and other stimuli into the brain, which occurs when changing geographical zones (long stay in polar winter conditions), with prolonged physical inactivity, etc. As a result, it decreases and the resistance of higher nervous activity to pathogenic factors, and the resulting pathological reactions are particularly severe [11]. The question of the intimate mechanisms of the functional pathology of higher nervous activity, that is, the question of its reflection at the level of basic processes, has received significant development in recent years, which is largely determined by the emergence of new morphological and biochemical approaches to the study of the brain. Thus, using electron microscopy, it has been established that experimental neuroses are accompanied by destructive changes in the neuronal and glial elements of the neocortex, as well as its conductive apparatus, while in parallel with the destructive processes, reparative processes occur that provide one or another degree of compensation for impaired functions [10,12].

Biochemical studies of the neocortex in animals in a state of experimental neurosis revealed both reversible and irreversible disorders of the neurotransmitter system, which is of particular interest from the point of view of the possibility of creating new pharmacotherapy agents. These morphological and biochemical data are also of great methodological significance: for a long time, the opinion of neurosis as a functional disease dominated. This meant the absence of structural changes in the brain, which, as was

believed, are characteristic of other forms of pathology of higher nervous activity. The detection of ultra-structural and neurochemical changes in the brain in animals in a state of experimental neurosis suggests that neuroses also have a structural basis, which confirms the only correct conclusion that any pathology is characterized by structural changes that can be detected by adequate methods of its study [12].

Types of Higher Nervous Activity

The pathophysiology of higher nervous activity includes, as one of its most important tasks, the study of the type of higher nervous activity: as observations have shown, the rate of onset of pathology, its manifestation, and the degree of activation of protective mechanisms are largely determined by the individual characteristics of the nervous system. I.P. Pavlov understood the innate properties of the nervous system as a subtype. The type, he emphasized, is an inborn, constitutional form of manifestation of the nervous system, the genotype. But since the animal from the day of birth is exposed to the most diverse influences of the environment, an alloy is ultimately formed from innate traits (type) and traits that form in the process of individual life. This "fusion" is referred to as the phenotype, or character [13]. Since type is an innate property of the nervous system, it is reflected in such innate characteristics of the nervous system as strength, balance and mobility of nervous processes. Taking into account the various possible and most common combinations of these indicators, I.P. Pavlov identified the following main types of the nervous system: 1) strong, but unbalanced, which is characterized by a predominance of excitation over inhibition; 2) strong, balanced, with great mobility of nervous processes; 3) strong, balanced, with low mobility of nervous processes; 4) weak, characterized by a very weak development of both excitation and inhibition [14].

Most often, the pathology of the higher nervous system occurs in animals with a weak type of nervous system, therefore such animals are called "suppliers of neuroses." Nevertheless, the nature of the response of the nervous system to a pathogenic agent is determined not only by the type, but also by those features that are acquired in the process of individual life. This implies the need to take into account the "alloy" of the type and individually acquired characteristics of the nervous system. Therefore, it is now customary to characterize the nervous system by behavioral reactions, in particular, by the indicator of emotionality, by the features of regulation of the general functional state of the brain [13,14]. For example, consider one of the forms of functional pathology of higher nervous activity (behavior), called informational.

Information pathology of higher nervous activity (IP HNA) refers to disturbances in the course of higher functions of the nervous system, as well as disturbances in the vital activity of other body systems mediated by it, which occur during prolonged exposure of the brain to an unfavorable combination of the following factors: 1) a certain amount of information to be processed for making an important decision; 2) the factor of time allotted for such work of the brain; 3) the level of motivation, which determines the significance of information and the need for its processing [15].

The combination of these three factors can be unfavorable if, firstly, it is necessary to process a large amount of information (including decision making) with a long deficit of time allotted for such brain work and a high level of behavioral motivation, and if, secondly, there is a deficit information for a long time, and the motivation of behavior (for example, the need to make a decision) is very high.

So, in both cases, a triad of factors influences and unfavorably combines: 1) the amount of information (in the first case excessive, in the second it is less than necessary); 2) time (in the first case it is not enough, in the second case it is excessively large) and 3) motivation, which in both cases is very high. If the clinical picture of the disease corresponds to a neurosis, then one speaks of informational neurosis, but if it corresponds to other diseases, then it is advisable to talk about the informational pathology of the corresponding nosology [16].

Within the framework of the concept of IP HNA, the mentioned triad of factors is combined into an independent group, which emphasizes its pathogenic significance in modern conditions of human life. So, the informational pathology of HNA develops as a result of the presence of humans and animals in an unfavorable combination of the three factors discussed above, constantly affecting the brain [15].

Animal and human studies have shown that in this form of pathology there are disturbances in short-term and long-term memory, emotions, signal analysis functions, sexual, eating behavior and other instincts, there is a violation of the regulation of cardiovascular function, respiration, digestion and a number of other systems. Characteristic for this form of pathology is (in the early stages) a certain dynamics, i.e. the sequence of involvement in the pathology of different systems of the body, and at deep stages – a wide coverage of different systems, i.e., a stable violation of the functions of many systems of the body [6,10].

Further, it turned out that the latent period of the development of such pathology, i.e., the time from the beginning of the impact on the brain of the above triad of factors to the formation of a stable pathology, varies greatly

in different people and different animals, both of one and several species. In addition, this period is characterized by various changes in behavior, the biological significance of which can in no way be understood as pathological. There are two types of global factors influencing the development and formation of information pathology: 1) factors that reduce the resistance of the nervous system to the information triad, they can be called risk factors for the occurrence of IP; 2) protective factors preventing the development of pathology, raising the resistance of the nervous system to IP [15].

The most frequent and significant risk factors for the occurrence of IP HNA include prolonged physical inactivity, i.e. reduced, limited motor activity, violation of intraspecific relationships between individuals, for example, a deficit or distortion of mutual influence between individuals, especially in the early stages of ontogenesis, some genetically predetermined properties of the nervous system , forming the type of HNA, some brain injuries, disorders of the nervous system caused by factors that do not correspond to the definition of the information triad. All of them reduce the resistance of the nervous system to the pathogenic influence of the information triad. When listing the conditions that contribute to the emergence of IP HNA, it should be borne in mind that muscle hypodynamia occupies the first place among them in terms of the frequency of prevalence, which is largely due to the growth of professions of predominantly mental work, requiring, as a rule, a sedentary lifestyle [8,15,16].

The biological significance of the second group of factors that significantly affect the development of IP HNA is to protect the body from the onset of pathology or (if it occurs) to activate compensatory mechanisms aimed at limiting and suppressing developing pathological processes.

Any disease from the standpoint of dialectical monism is the life of a damaged organism with the participation of processes that fight the damaging agent and pathological phenomena in the body. Such a unity of forms of life activity that are opposite in their biological significance appears clearly in the study of IP behavior. Since the considered form of pathology arises gradually (as a result of prolonged exposure to the factors of the information triad on the brain), it is possible, under conditions extended in time, to trace not only the sequence of development of those processes that lead to the formation of a stable pathology and their external manifestations, but also behavioral manifestations and central processes that in the first case eliminate the external causes of the pathology, and in the second – oppose the central pathological processes [16]. The whole set of protective activity of the body according to the theory of IP HNA is considered in the following aspects:

Self-regulation of behavior aimed at avoiding the pathogenic influence of information triad factors. Below are observations that made it possible to establish the property of the brain of animals to self-regulate their behavior in order to eliminate the pathogenic effect on HNA and other body systems of an unfavorable combination of factors of the information triad, i.e., the amount of information to be processed and assimilated, the time factor allotted for such work of the brain, and level of motivation. In addition, studies are presented that have discovered the property of some limbic structures of the brain to increase the resistance of HNA to its informational pathology [16].

Let us consider specific behavioral manifestations of HNA self-regulation aimed at eliminating external pathogenic conditions. Conditioned motor-food reflexes are developed in dogs: in response to conditioned signals, the animals ran to one of the three feeders located on the floor of the experimental room, where they received a piece of meat. Each conditioned stimulus was associated with one of the feeders, and reinforcement was produced only if the animal solved the problem by running to the feeder corresponding to the signal value of the stimulus. Usually, after eating meat, the animal immediately returned to the starting place, since the next conditioned stimulus was turned on only when the animal was at the starting place [17].

A different picture of behavior is observed after pathogenic conditions arise, caused by a violation of the ratio of the information triad. In the example under consideration, this ratio was violated by reducing the time of the entire experiment by reducing the intervals between individual signals. At the same time, the level of motivation did not change (which was high, since the animal was hungry) and the amount of information load did not change – the animals were presented with the same number of conditioned stimuli. Thus, the animals carried out the same amount of analytical and synthetic activity, but under the conditions of a shortage of time. Already after several presentations of signal stimuli under these conditions, the following behavioral changes were observed: when the conditioned signal was turned on, the animal immediately left the starting place and ran to the corresponding feeder, but the time to return to the starting place increased, and the greater was the shortage of time allotted for solving the entire volume of the task, the slower the animal returned to the starting place. Thus, the animal itself increased the interval between the conditioned signals, and hence the time of the entire experiment, i.e. itself eliminated the shortage of time and brought to the optimal ratio for the given animal of the factors of the information triad–the volume of analytical and synthetic activity with the factors of time allotted for such work of the brain, and the level of motivation of behavior. Such behavior significantly increased the period of formation of pathological reactions,

i.e. period of pre-neurosis, and in some cases prevented the development of neurosis [18].

A similar behavior is observed if the experimenter does not change the time of the experiment between conditioned signals, but increases the load on the analytical-synthetic activity of the brain. At the same time, after the first increase in the volume of the load on the HNA, adaptation to new conditions occurs (days 29–47), and after the second, further increase in the volume of the load on the HNA, a steady increase in the time to return to the starting place is observed. The understanding of these reactions as having biologically positive significance acquires a fundamental character: until recently, they were considered as early symptoms of pathology and, accordingly, were subjected to suppression ("treatment") instead of taking measures to strengthen them. The described reactions reflect the self-regulatory activity of the brain. Hence the great practical significance of these conclusions: it is necessary to find ways to activate and strengthen the corresponding self-regulatory forms of behavior, and in all periods of the development of the disease, but especially at the stage of pre-disease, when the self-regulatory mechanisms of the brain are well expressed and their purposeful strengthening can play a decisive role in increasing psychophysiological resistance organism [17].

Central Mechanisms of the Protective Activity of the Brain

The development of methods and principles for activating self-regulatory (in a broad sense, protective) mechanisms of the brain requires knowledge of the corresponding target – structures that play a particularly important role in organizing such a function. The theoretical background of the search for a system of brain structures that perform a protective function after exposure to a pathogenic agent is as follows. After the onset of the impact of a pathogenic agent (for example, an unfavorable combination of the informational triad) on HNA, pathological processes develop in certain brain structures that are detected by electrophysiological, biochemical and ultrastructural studies that disrupt the normal interaction between individual brain formations (new correlation relationships arise between them). After the fixation of all processes in long-term memory, stable pathological states of the brain are formed, which manifests it outwardly in various non-adaptive reactions [17].

Simultaneously with the emergence of the brain system that determines pathological reactions, brain structures are activated that prevent the development of pathological processes. One of the external manifestations of such a protective activity of the brain is the self-regulatory forms of behavior described above, aimed at the active elimination of a pathogenic situation, in our example, the elimination of an unfavorable combination of the information triad. In addition, two more types of defense reactions develop in the brain: activation of brain structures that nonspecifically increase the resistance of the nervous system to external pathogenic influences, and activation of brain structures that suppress the formation of pathological processes [19].

Let us consider experiments that make it possible to consider the stated views on the central defense mechanisms of the brain in IP HNA as justified. The most significant results were obtained in experiments using the technique of locomotor self-stimulation of the brain. To do this, irritating electrodes are first implanted into different brain formations, through which an electric current with rectangular pulses is passed, while the current is turned on by the animal itself during its movement along the floor, which is divided into sections, and each section is telemetrically connected to a certain irritating electrode, i.e. with a certain brain structure: as soon as the animal stands on one of the sections of the floor, stimulation of the corresponding brain formation is switched on. All of the above takes place in the room where, according to the previously described method, the IP HNA is produced.

It has been established that if an animal has the opportunity to choose between structures for their self-stimulation, then at the initial stages of the development of the IP HNA, it predominantly stimulates the transparent septum, i.e. instead of moving along the floor of the experimental room in different directions, it lingers for a long time (many minutes) in the area associated with irritation of the transparent septum. Such activation of this structure prevents the development of IP HNA or significantly increases the period of its occurrence. A similar effect, although less pronounced, is observed with self-stimulation of the lateral hypothalamus or medial amygdala. It is obvious that the transparent septum, the lateral hypothalamus and the medial part of the amygdala constitute a system or part of the brain system, the stimulation of which enhances its protective function and prevents the development of pathology of the HNA [7,15].

So, using a comprehensive methodological approach to the study of the behavior of animals and humans, the ability of the brain to respond with the occurrence of pathology of HNA in response to prolonged exposure to an unfavorable combination of the triad was discovered; the volume of highly significant information, the time factor and the level of motivation. Such pathology of HNA, called informational, has not only a specific etiology, but also a characteristic dynamics of the development of symptoms and syndromes. Protective (including self-regulatory) forms of behavior and central mechanisms that prevent its development were revealed at the early stages of the onset of IP HNA, i.e., the ability of

the brain to self-regulate its behavior in order to protect the body from the pathogenic influence of information triad factors in their unfavorable combination was discovered. The main risk factors for the occurrence of IP HNA have been established and etiologically and pathogenetically substantiated principles and methods for its prevention and treatment have been developed [20].

Post-Traumatic Pathology of Higher Nervous Activity

This type of pathology is expressed in violation of certain forms of behavior. The pathogenesis of violations of eating, defensive, sexual behavior, as well as the pathogenesis of violations of memory, emotions, and the sleep-wake cycle has been studied in most detail. As noted, the creation of models of post-traumatic pathology of higher nervous activity aims to reproduce various brain injuries; a person caused by a brain hemorrhage, a brain tumor, a gunshot or other traumatic injury. The creation of such models is achieved by extirpation of the brain tissue, transection of the adductor paths, electrical coagulation of individual parts of the brain, etc.

Violations of individual forms of behavior have some common, as well as particular manifestations, typical for each form. Common to all are the already mentioned violations of the balance of strength and mobility of the processes of internal inhibition and excitation. These changes contribute to the state of inhibition – a decrease in motor activity and the emergence of phase states that can result in a deep inhibition of the neocortex function with subsequent involvement of subcortical structures in the process. In other cases, there is an increase in the state of excitation. These changes in behavior of a general nature are largely determined by the type or individual characteristics of the nervous system [11].

Pathology of Eating Behavior

It has been described with extensive damage to the neocortex and partial damage to the frontal and orbital cortex. With damage (removal) of the frontal parts of the neocortex, animals are not able to distinguish edible objects from others, therefore they eat things that are unsuitable for food and do not differentiate between different concentrations of saline solutions. These violations are explained by damage to the mechanism of afferent synthesis of the formation of a functional system of eating behavior. When the orbital (orbital) area of the neocortex is damaged, the unconditioned reflex secretion to food irritation sharply decreases, which is explained by the presence of a cortical representation of the food center in this area. With extensive removal of the neocortex or as a result of cutting its pathways, there is a long-term decrease in unconditioned reflex food secretion and an almost complete loss of conditioned reflexes developed on the basis of food reinforcement. The degree of these disorders increases in the ascending evolutionary series of animals and indicates the increasing role of the neocortex in the regulation of feeding behavior from lower to higher animals [12,21].

A variety of deviations from normal eating behavior are observed when the limbic structures of the brain are damaged. Thus, in dogs, the destruction of the basal-lateral part of the amygdala causes a violation of food conditioned reflexes and a decrease in the unconditioned reflex reaction to food stimuli, however, these changes are also observed when other structures of the limbic brain and cannot be considered specific. Deep and characteristic eating disorders occur due to damage to the hypothalamus; Bilateral destruction of the ventromedial nucleus of the hypothalamus in rodents, carnivores, and primates causes hyperphagia, and damage to the lateral hypothalamus causes aphagia up to the death of animals from cachexia [21].

This gives reason to believe that the pathogenesis of the described changes in eating behavior is due to a violation of the regulation of hunger and satiety. Meanwhile, numerous observations convince us that different parts of the hypothalamus are related to the organization and regulation of other components of eating behavior. Thus, damage to the middle part of the lateral hypothalamus causes a violation of the initial impulse to get food, and the destruction of the more lateral part causes a violation of the regulation of food intake. So, a violation of different parts of eating behavior occurs when a number of brain structures are damaged, united in the system of regulation of eating behavior, while neocortical structures are of paramount importance in the formation of individually acquired food reactions, and hypothalamic structures play an extremely important role in the organization and regulation of unconditional reflex component of different parts of eating behavior [12].

Pathology of Defensive Behavior

Due to the extirpation of the anterior parts of the frontal region of the neocortex, in rodents, carnivores, and primates, the active-defensive reaction intensifies, which sometimes turns into aggressive behavior, worsens the course of conditioned reflex defensive reactions; the pathogenesis of these changes is associated with a weakening of the emotion of fear. The disappearance of the fear reaction is also observed due to damage to the cingulate gyrus, which is also expressed in an increase in active-defensive behavior. Characteristic changes in defensive behavior take place after damage to the amygdala – fear and aggressiveness disappear in animals, they become tame and obedient [1].

These manifestations of traumatic damage to the amygdala are called Klüver-Bucy syndrome. Due to damage to the ventromedial part of the hypothalamus, an increase in active-defensive behavior and the emergence of aggressiveness occur, while damage to the posterior part of the hypothalamus enhances the passive-defensive reaction – such animals are cowardly, their emotional reactions are sluggish. It is assumed that the pathogenesis of the described changes in the defensive reaction is of a neurochemical nature and is associated with dysregulation of the serotonergic system of the brain [22].

Pathology of Sexual Behavior

It has been established that extensive damage to the neocortex in higher vertebrates impairs the ability to mate; this reaction disappears completely due to damage to 60% of the entire area of the cerebral cortex. However, such animals retain an erection and become aroused in the presence of a female in heat. An increase in sexual activity in different animal species was found due to damage to the amygdala, on the contrary, a weakening of sexual activity is noted when even small areas of the anterior hypothalamus are damaged. Less pronounced violations of sexual behavior are observed with damage to other structures of the diencephalon and midbrain. However, from the point of view of the pathogenesis of these disorders, it is important that there are different systems of regulation of different components of sexual behavior – from preliminary game reactions to the completion of sexual intercourse [1].

Memory Pathology

Memory impairment is a common symptom of post-traumatic pathology of higher nervous activity and is observed when the brain is damaged in different locations. At the same time, a selective effect of damage to different brain structures on individual forms of memory (conditioned reflex, figurative, long-term, and short-term) and memory phases (signal perception, its fixation and reproduction) was found. In addition, there are large differences in the results of the effect of brain damage on memory in animals belonging to different stages of evolutionary development: the effect of damage to the forebrain increases significantly in the ascending series of animals [23].

Profound disturbances of all types of memory are observed in higher vertebrates after extensive destruction of the neocortex; largely for this reason, conditioned reflexes are developed with great difficulty and easily disappear, i.e., are not retained. Damage to the prefrontal cortex leads to a significant disruption of delayed reactions (they are realized with the participation of short-term memory), while conditioned reflexes (they are realized with the participation of long-term memory) change insignificantly and briefly. The effect of damage to individual projection areas of the neocortex – delayed reactions and conditioned reflexes – depends on the duration of the signal application: if it is less than 100 ms, then the trace is not retained after the removal of the projection zone corresponding to the signal. Consequently, the projection zones of the neocortex not only perceive, but also retain the trace arising from a short-term (less than 100 MS) acting stimulus. Such trace retention is necessary for signal analysis, i.e., for assessing its biological significance. A significant violation of figurative memory occurs due to damage to the associative areas of the neocortex [12].

Violation of short-term memory (violation of delayed reactions) is observed with damage to other parts of the brain. Damage to various structures of the limbic brain (cingulate and piriform gyrus, amygdala) causes suppression or complete disappearance of short-term memory, however, these disorders are reversible and function is fully or partially restored within a few months. Of particular interest is the pathogenesis of memory impairment caused by damage to the hippocampus as the leading symptom known in the clinic of Korsakov's syndrome [12,22].

It has been established that damage to different parts of the hippocampus affects memory differently. Damage to the dorsal section causes deeper damage than the ventral sections. Damage to the hippocampus has a more pronounced effect on short-term than long-term memory. The impact of damage to the hippocampus on memory increases in the ascending evolutionary series of animals. It is also believed that the hippocampus is important in the function of translating short-term memory into long-term memory and plays a predominant role in the primary fixation of the trace, while the function of long-term retention of the trace is not associated with the hippocampus. Finally, and most likely, the hippocampus is thought to influence memory through its involvement in the organization of emotional responses; as a result of its damage, the regulation of the emotional reaction is disrupted, which secondarily impairs the normal organization of memory [12,22,24].

Memory impairment is also observed when other structures are damaged. The pathogenesis of memory impairment due to damage to various brain structures can be explained on the basis of the idea of the existence of two closely related systems: the brain system of memory organization and the brain system of memory regulation. In higher vertebrates, the memory organization system is determined by the activity of the forebrain – the neocortex. This is confirmed not only by data on cortical damage, but also by the results of a study of the electrical activity of individual neurons, which made it possible to detect

neurons that play a large role in maintaining an individually formed trace. These neurons are represented mainly in the neocortex, mainly in its associative areas, are combined into a system of learning neurons and are the primary elements of the formation of a developed trace reaction. All this explains such a deep memory impairment with extensive damage to the neocortex and the differentiated influence of individual areas of the neocortex on memory [24].

The second brain system related to memory function is the memory regulation system, which has a modeling effect on trace reactions. The pathogenesis of the effect of damage to the structures of this system on memory can be explained taking into account the fact that the structures of the memory regulation system are directly related to the mechanisms of organizing an emotional reaction; their influence on memory is largely mediated by a change in emotional reaction. This explains the well-known observation: the duration of retention of a trace from any stimulus depends significantly on the strength of the emotional reaction caused by this stimulus [22].

Pathology of Emotions

Refers to frequent manifestations of post-traumatic pathology of higher nervous activity. Most often, they occur when the limbic structures of the brain are damaged, but since the regulation of emotions occurs with the participation of the neocortex, pathological changes in the course of emotional reactions are also observed due to damage to the latter. These changes can be expressed in the strengthening or weakening of emotions, the distortion of the sign of emotions, when instead of a normally observed positive or negative emotion, their opposite reaction occurs [9].

With extensive removal of the neocortex, one can observe a reaction of rage, however, it cannot be considered as a true emotional (i.e., "experienced"), but reflects the activation of only effective mechanisms of this reaction. As a result of damage to the sensorimotor cortex, positive emotions are suppressed, and after damage to the proreal convolutions in dogs, the emotion of fear is initially suppressed, and then this emotion acquires an enhanced character for a long time. In the latter case, the limbic-hypothalamic mechanisms of emotion are released from the inhibitory influence of the prefrontal cortex on them.

Damage to the frontal areas in monkeys during lobectomy inhibits emotional reactions, as a result of which mimic and aggressive reactions, communication gestures lose expressiveness and vivacity. A change in the nature of the emotional reaction is observed when the hippocampus is damaged: the intensity of emotions to threatening situations decreases, which is explained by the weakening of fear reactions, while at the same time, emotional reactions to positive stimuli increase. Due to the removal of the cingulate gyrus, aggressiveness decreases, animals become affectionate [25].

Significant disturbances in the course of emotional reactions occur due to damage to the amygdala; these disorders are so characteristic that they are known as the "almond-shaped syndrome", which consists in increased hunger and increased sexual activity, in the suppression of the fear reaction – wild and aggressive monkeys turn into tame ones. This syndrome was originally described as a consequence of damage to the temporal cortex, but its association with damage to the amygdala is now generally accepted. At the same time, it must be borne in mind that the amygdala is a complex structural formation and damage to its different departments causes different symptoms of emotional disturbance [22].

The following example can serve as evidence that different emotional reactions have a complex representation in the brain and are regulated by different systems: destruction of the medial amygdala inhibits the manifestation of fear, and destruction of the dorsal region increases aggressiveness; destruction of the midbrain suture in males causes the manifestation of aggressiveness towards females, but does not affect the nature of the reactions that arise towards males. At the same time, there are certain species differences between animals in terms of the manifestation of influence on emotional reactions, which gives grounds for the conclusion that there is not only an individual, but also a species peculiarity of the localization of the central mechanisms of emotional reactions [11,22].

Pathology of the Sleep-Wake Cycle

It has already been noted that for a long time sleep was regarded as a passive state of the brain, opposite to wakefulness; it was believed that the main function is to restore the energy of the brain after it has been awake for many hours Even IP Pavlov opposed the understanding of sleep as a passive state. It is now known that sleep has a complex structure, consists of a number of phases and has a multifaceted function. The most common point of view is that sleep consists of two main phases – slow-wave and REM (paradoxical) sleep, each of which, in turn, is heterogeneous. For example, in the slow phase of sleep, four successive stages are distinguished [1].

Post-traumatic sleep pathology is reflected in the disruption of these phases and stages, and it is important that they have a different central organization, and, therefore, brain damage manifests itself differently in different phases and stages of sleep. Thus, damage to the anterior neocortex

causes a significant reduction in the duration of REM sleep. Damage to the anterior preoptic area of the hypothalamus causes a decrease in the duration of slow-wave sleep. A differentiated participation of brain structures in the regulation and correlation of wakefulness and sleep has been established, which explains the different effects of brain injuries on these states. Thus, damage to the anterior hypothalamus causes a sleep disorder, and damage to the posterior hypothalamus causes a wakefulness disorder. Thus, the pathogenesis of post-traumatic disorders of the sleep-wake cycle requires taking into account, firstly, the complex structure of this cycle and, secondly, the multilevel systemic organization of its central mechanisms [8].

Secondary Pathology of Higher Nervous Activity

Such pathology occurs as a result of preliminary asthenization of the nervous system by some disease that is not primarily caused by neurogenic factors (infectious, oncological, acute and chronic anemization, etc.). These factors reduce the resistance of the nervous system to a variety of pathogenic influences, which becomes the cause of the developing disease of the nervous system. In these cases, the root cause of the pathology is the state of the nervous system, which is denoted by the term "asthenization", and the stimulus that causes the pathology of higher nervous activity is a triggering factor that does not play a decisive role in the picture of the development of the pathology. In this case, in pathogenetic terms, and, consequently, from the point of view of the search for the main direction of therapy and prevention, it is much more important to identify the causes of preliminary asthenization of the nervous system. Meanwhile, it must be taken into account that the occurrence of a particular vegetative-somatic disease, especially life-threatening, such as cancer or pathology of the cardiovascular system, has a psychogenic destabilizing effect on the higher (mental) and emotional functions of the body. Such people have a feeling of fear, prolonged anxiety, and this, in turn, has a psychogenic effect on diseased organs and systems, and a "vicious circle" of mental and somatovegetative pathological relationships is again formed and launched [2].

Compensation for the Pathology of Higher Nervous Activity

From the beginning of the action of a pathogenic agent on higher nervous activity to the formation of its stable pathology, a certain time passes, during which, along with the development of pathological processes, activation of protective, including self-regulatory mechanisms of the brain takes place. Both the former and the latter have complex dynamics of development in time and space, are characterized by certain external – behavioral, vegetative, humoral, electroencephalographic and other manifestations, as well as structural and neurochemical changes in the central nervous system [5].

Since both pathological and compensatory mechanisms are activated simultaneously, the doctor faces the most important task of their differentiation, the correct determination of the diagnostic value: often early manifestations of compensatory (self-regulatory) brain activity are mistakenly taken as early symptoms of pathology and, accordingly, are eliminated for the purpose of "treatment" instead of to be maintained and strengthened. All of the above applies to both functional and post-traumatic pathology of higher nervous activity. This issue is of particular importance in the early stages of pathology – pre-pathology, that is, before pathological reactions acquire a steady course and reactions of a non-adaptive nature occur [2].

Thus, deepening and detailing the pathogenesis of disorders of higher nervous activity will serve as a fundamental basis for the prevention and correction of diseases of the nervous system.

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