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Methodological Approaches to Modeling the Pathology of the Nervous System

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Abstract

The pathology of the nervous system is of great interest to researchers in the field of medicine and physiology. However, today there is no clear understanding of the issues of experimental modeling of diseases of this system. The methods presented in this article for modeling diseases of the nervous system, in our opinion, should provide significant assistance to researchers in this area. Our article is devoted to methods of modeling experiments on animals. To study the nervous system in normal and pathological conditions, adequate animal research models are needed. These experimental models make it possible to clearly and simply demonstrate the response of the nervous system to various processes. The data obtained as a result of the experiment can serve as a fundamental basis for further research in the framework of neurophysiology, as well as serve as a basis for clinical research.

Keywords: Nervous system; Experimental; Animals

Introduction

Pathological changes in the central nervous system can cause violations of a wide variety of body functions the psyche, movements, sensitivity, blood circulation, respiration, digestion, metabolism, thermoregulation, diuresis, etc. We present disorders of motor function, sensitivity and higher nervous activity. In the same section, disorders of tissue trophism are considered, often combined with disorders of motor function and sensitivity. We begin the presentation of the pathology of functions with violations of the motor function, since "muscle contractility is the most expressive and obvious reaction on the part of the animal organism to external and internal stimuli" (N. E. Vvedensky) [1]. Examples of disorders on the part of motor function are paralysis, hyperkinesis, ataxia, on the part of sensitivity-acute brain damage, trophic disorders, atrophy, hypertrophy, and on the part of higher nervous activity-neurosis.

Aim

The aim of this work is to generalize and systematize data on the topic of animal modeling of pathologies of the nervous system, in particular disorders of motor function, sensitivity and higher nervous activity in various cases.

Motor Disorders

Violations of motor function in lesions of the nervous system are manifested in the form of paralysis and paresis, hyperkinesis and ataxia.

Parallies

There is central paralysis that occurs when the central motor neuron is damaged, and peripheral paralysis that occurs when the peripheral motor neuron is damaged [2].

Demonstration of peripheral paralysis

Peripheral paralysis occurs when the nuclei of the anterior horns of the spinal cord, anterior roots and peripheral nerves are damaged. The easiest way to show the features of peripheral paralysis is when a peripheral nerve is cut in an animal, for example, the sciatic nerve [3,4].

1) Experience is put on a dog. The operation of transection of the sciatic nerve can be performed both in advance and right there, at the lecture. In the latter case, it should be performed under local anesthesia, since general anesthesia itself impairs motor function.

After the operation, the dog immediately experiences paralysis of the muscles innervated by the part of the nerve located below the transection - the flexors of the lower leg and all the muscles of the foot and fingers. As a result, the animal's voluntary movements are disturbed. The animal cannot bend the leg at the knee joint and make any movements with the foot and fingers. When the animal moves, the lower part of the paralyzed limb is dragged along the ground. Extension of the leg in the knee joint is possible, since the extensor of the lower leg (quadriceps muscle), innervated by the femoral nerve, is not paralyzed. Therefore, the animal can lean on the limb, although there is excessive dorsiflexion of the hock (ankle) join [2,3,5].

The sciatic nerve, like most peripheral nerves, is mixed, i.e., in addition to motor, centrifugal fibers, it also contains centripetal, sensory fibers, which are also damaged during transection. Therefore, the paralyzed part of the limb (foot) loses sensitivity [5]. The animal does not respond to touching the foot, to pricking it, cooling it (with ethyl chloride), changing position - the foot can be tucked up, and the animal will continue to stand, leaning on its back surface. Impulses from the periphery in peripheral paralysis cannot reach the cells of the spinal cord, so reflex movements also become impossible. Thus, touching a hot object causes, under normal conditions, a reflex withdrawal of the limb [6].

The division of movements into voluntary and reflex ones is conditional. Strictly speaking, voluntary movements, as I. M. Sechenov pointed out, also arise under the influence of any impulses from the outside, i.e., in essence, they are also reflex before a burning sensation occurs. With peripheral paralysis caused by transection of the sciatic nerve, it is possible to burn the foot (for example, with an alcohol flame) and the animal does not withdraw it. Thus, with peripheral paralysis, both reflex and so-called voluntary movements are disturbed [2,3]. Since muscle tone is also a reflex to proprioceptive impulses, then with peripheral paralysis, the tone of paralyzed muscles decreases - with passive flexion and extension of the foot, the researcher does not feel any resistance, the foot "dangles".

Simultaneously with a decrease in muscle tone, tendon reflexes disappear. Under normal conditions, a blow to the knee tendon causes a stretch of the quadriceps femoris muscle attached to it. In response to this stretch, accompanied by stimulation of the spinal centers by proprioceptive impulses, the muscle reflexively contracts, extending the lower leg [5]. When hitting the Achilles tendon, the gastrocnemius muscle reflexively contracts, which leads to plantar flexion of the foot. These reflexes are also possible during anesthesia of the tendon, which indicates their independence from the sensations that arise during impact. After transection of the sciatic nerve, the reflex from the Achilles tendon disappears, since impulses from the stretching gastrocnemius muscle cannot reach the spinal centers and cause its reflex contraction. The knee reflex is preserved, since the quadriceps muscle - the extensor of the lower leg, supplied by the femoral nerve, is not paralyzed when the sciatic nerve is transected. All these reflexes are demonstrated simultaneously on the healthy and paralyzed limbs of the dog.

Tendon reflexes are very fast- the interval between a blow to the tendon and the response contraction of the muscle is only 0.005 seconds. Such speed of these reflexes provides instantaneous automatic contraction of the muscle with any unexpected stretching of it. Otherwise, the tendons, which in themselves do not have contractility, would overstretch and tear at the slightest unexpected movement of the body in space. With atrophy, muscle fibers decrease in volume, and connective tissue grows between them [5]. In animals in which transection of the sciatic nerve led to the disappearance of the reflex from the Achilles tendon, hyperextensions and small tears appear, and the electrical excitability of the muscles also changes. In the initial stage, during the first week after transection, the electrical excitability of the muscles is increased: they contract at a lower current strength [2].

In the future, atrophied muscles completely lose their excitability when the nerve is irritated, responding to the action of the electrodes with sluggish, worm-like contractions [7]. The reaction to stimulation by direct current is perverted - the anode closure is accompanied by a stronger contraction, to the cathode closure, as opposed to what happens normally. The experience can be reproduced on any warm-blooded animal. The same muscle groups are paralyzed as in the dog. Arbitrary movements, reflexes and sensitivity of the foot are disturbed. In an experiment on a frog, one can clearly observe a decrease in muscle tone. The decapitated frog is suspended by the jaw. Her hanging legs do not straighten completely but remain slightly bent due to their inherent muscle tone [2]. If you cut any muscle in the middle, then the edges of the wound will diverge, like a released spring. If the frog's leg is skinned or anesthesia is administered, then the muscle tone does not disappear (anesthetize by injecting a 3% novocaine solution). When the sciatic nerve is transected, the path for proprioceptive impulses is interrupted and atony occurs - they become sluggish.

Loss of voluntary and reflex motor function, loss of tendon reflexes, atony, atrophy, changes in electrical excitability are characteristic signs of peripheral paralysis. They always appear, regardless of the location of the lesion of the peripheral neuron: the cells of the anterior horns themselves or their fibers passing in the anterior roots or in the peripheral nerves.

Demonstration of central paralysis

Central paralysis occurs when the central motor neuron (pyramidal pathway) is damaged [2]. Central paralysis is characterized by the loss of voluntary and the preservation of reflex movements. This is the main difference between central paralysis and peripheral paralysis, in which both types of movements are absent. This difference is explained by the fact that with central paralysis, the primary reflex arc is preserved, closing in the spinal cord [2]. Due to this, impulses from the periphery, closing in the lower motor neurons of the spinal cord, are able to evoke the corresponding reflex reactions. However, the so-called voluntary movements, locked in the cortex, cannot be carried out. The defeat of the central pyramidal neuron, which causes central paralysis in humans, causes only short-term paresis of the limbs in animals, which is relatively quickly restored [8]. When the brainstem is damaged, when, in addition to the pyramidal ones, the rubrospinal paths are also affected, animals and humans experience central paralysis that is very similar in external manifestations - decerebrate rigidity. This model can show signs of central paralysis. Experience put on a cat. The course of the operation is described by demonstrating dysfunction caused by inflammation [3,9]. We only recall that for the success of the operation, the animal must be healthy, strong, with good muscle tone. If rigidity develops poorly, it can be aggravated by irritation of the surface of the incision of the brainstem, pressing on the tampons located in the cranial cavity or tilting the animal's head onto its back.

After the operation, the animal has paralysis of all limbs, it cannot get up, change position [2]. Unlike peripheral paralysis, in which the peripheral reflex arc is affected, the tone of the skeletal muscles is not only not reduced, but even increased. This is explained by the fact that when the central motor neuron falls out, the peripheral reflex arc is disinhibited. When you try to bend the limb of the animal, its muscles show resistance. The limbs of the cat are unbent and stick out like sticks. At the same time, the tone also increases in other muscles, which normally counteract the force of gravity. Therefore, in a

decerebrated animal, the head is thrown back (opisthotonus), the jaws are compressed (trismus), the back is arched, the tail is raised and extended [10]. In central paralysis, in contrast to peripheral palsy, tendon reflexes are also preserved and increased. When a hammer strikes the Achilles tendon in a decerebrated animal, plantar flexion of the foot occurs [2]. When hitting the tendon of the quadriceps muscle (below the patella), the shin is unbent.

The disinhibition of the lower neurons in central paralysis leads to a distinct manifestation of combined automatic reflexes. Under normal conditions, any irritation is accompanied by a wide irradiation of impulses through the nervous system, but, despite this, the movements are strictly coordinated due to reciprocal inhibition. The animal, devoid of the inhibitory influence of higher neurons, responds to irritation with the entire set of reflexes.

1) When squeezing the foot of a normal animal, a flexion reflex of the same paw occurs. In a decerebrated animal, which is in a state of rigidity, the limb that crosses diagonally with it also bends, while in the rest the extensor tone increases, which is also observed during the normal act of walking [2,3,9].

2) If you bend down the head of an animal in a state of decerebrate rigidity, then its forelimbs automatically bend, and the hind limbs unbend. If you throw your head back, then, on the contrary, the extensors of the front and flexors of the hind limbs are strained. These combined reflexes, less pronounced, are also observed in normal animals - when the animal eats, it tilts head down and bends its front legs, and when it reaches for food, it stretches its neck and unbends its front legs.

3) The combined movements of the head and limbs are also clearly manifested when the head is turned to the side. When the head is turned to the right or to the left, the extensor tone of the limbs on the same side increases, and on the opposite side it weakens. These combined reflexes, under normal conditions, direct the movement of the entire body in the direction in which the head is turned. So, for example, when turning the head to the right, the animal leans on the right limbs, and the left ones are carried in this direction. With decerebrate rigidity, when there is no inhibitory effect of the cortex, these reflex combined movements appear more sharply (all these automatic reflexes are demonstrated simultaneously on a healthy cat) [6,11].

The same is observed with central paralysis in humans. If one half of the body is paralyzed, then the movements of a healthy limb or head may be accompanied by combined reflex movements of the paralyzed limbs [12-14]. When bending a healthy arm, the paralyzed arm automatically bends. Muscle tone can also increase as a result of additional irritation that occurs during physical work, coughing, sneezing, under the influence of mental experiences. The described reflexes arise as a result of irritation of the motor centers by proprioceptive impulses that occur during the movements of the muscles of the body. After transection of the corresponding posterior roots, through which proprioceptive impulses are sent to the central nervous system, these reflexes disappear. The automatic reflexes also include the so-called pathological reflexes, for example, the dorsal (instead of the plantar) extension of the thumb during stroke stimulation of the foot, which is observed with central paralysis in higher monkeys and humans (Babinski's reflex).

Depending on the localization of the process, central paralysis can capture various areas, but its main features remain unchanged: loss of voluntary movements, increased distortion of reflex motor reactions (muscle tone, tendon reflexes, etc.). With central paralysis, muscle atrophy does not develop or is poorly expressed, normal electrical excitability is preserved, since the primary reflex arc is preserved [2,15].

Demonstration of disorders of motor function in case of damage to the motor analyzer of the cerebral cortex

Half an hour before the demonstration, a rabbit under local anesthesia makes a trepan hole in the bones of the parietal region on the right or left, no closer than 0.5cm to the midline, with a diameter of about 2-3cm. At the lecture, the dura mater is opened crosswise and the middle part of the upper surface of the hemispheres corresponding to the location of the motor analyzer is removed with a sharp spoon or scalpel with 1-2 movements. Removal of the brain itself is painless and does not require general anesthesia. Bleeding is stopped with a tampon [8,16]. The animal uses all its limbs immediately after the operation -it does not have paralysis. Only paresis is noted when making sharp turns, jumping or throwing a rabbit over the table- it is noticeable that the paws on the side opposite to the operation lag behind in movement and spread out to the sides.

After a while, not only the usual automatic movements are restored, but new movements can also be assimilated, despite the removal of the corresponding cortical zones [8,17]. Thus, damage to the central end of the motor analyzer in animals affects only the accuracy and fitness of individual movements, whereas in humans, paralysis of the corresponding part of the body occurs. Even with the complete removal of the entire brain anteriorly from the visual bumps, dogs, cats and rabbits maintain normal muscle tone and the usual reflex postures and movements are carried out normally. The relatively large ability to compensate for the defect in animals is explained by the fact that their movements are mainly of an unconditionally reflex nature and are closed mainly in the lower parts of the central nervous system. Due to this, it is possible for animals to develop conditioned motor reflexes after removing the main core of the motor analyzer. In humans, most motor reflexes are conditioned reflex reactions and are more subordinate to the cerebral cortex [12,18].

Demonstration of disorders of motor function in spinal cord injury

When the spinal cord is destroyed, peripheral paralysis occurs in the lower lumbar and sacral segments, since the nuclei of the anterior horns of those segments of the spinal cord that innervate the hind limbs are destroyed. With a higher cut of the spinal cord, central paralysis of the hind limbs occurs, since the reflex arcs of the lower parts remain intact.

Technique of Spinal Cord Cutting Surgery

1) The animal is placed on its stomach, a wa-face is placed under the hypochondrium. They operate on the left. Incision of the skin and subcutaneous tissue to aponeurosis, semi-oval, with a bulge to the left, from IX to XII thoracic vertebra. Then a longitudinal incision of the aponeurosis is made, the muscles are separated from the bones with a scalpel. The lateral surface of the spinous processes of the IX, X and XI vertebrae is cleaned subcostally with a chisel. The muscles are pushed back, the gutter is tamponed. The same is done on the right [8,16]. They push the muscles apart with hooks. The supraspinous and inter-spinous ligaments are dissected between the VIII-XII processes. The spinous processes of the IX, X and XI vertebrae are bitten off at the very base. Forceps remove the arch of the X vertebra, and if this is not enough, then another arch (for example, the IX vertebra). A hole is formed with a size of 0.5-2cm. The epidural fat is torn with tweezers. The dura mater is cut longitudinally with eye scissors strictly along the midline, trying not to injure the spider web. Then the spider shell protruding into the hole is dissected. Cerebrospinal fluid spurts from the incision. The left edge of the shells is lifted with tweezers, one branch of the eye scissors is inserted and the shells are longitudinally dissected, as far as possible, upwards. The right edge of the shells is lifted. Anesthesia is deepened. A single-toothed blunt hook is carried out

between the shells and the brain, it is wound up on the right under the brain as carefully as possible so as not to crumple the brain. The brain is also raised at the level of the X thoracic vertebra, immediately caudal to the hook, carefully cut, trying not to touch the anterior spinal arteries. If this happens, the bleeding stops by itself as soon as the brain is lowered into place. Check the completeness of the intersection. Lay both segments so that the cross-section surfaces fit well together. The edges of the incision of the shells are straightened, but not sewn. The muscles are sewn up, then the skin. A gauze roller is placed on the skin for 24 hours. The skin sutures are removed on the 5th-6th day [10,14].

2) For an acute experience, the operation of cutting the spinal cord can be greatly simplified and carried out at the lecture itself. To do this, under local anesthesia, cut the skin directly under the place of departure of the last rib, at the level of the first lumbar vertebrae for 5-6cm, push the muscles in a blunt way and, exposing the spine, bite it with bone forceps together with the spinal cord contained in it. The bleeding is stopped with tampons. Such a simplified technique of the operation allows it to be carried out in 3-5 minutes, without prior preparation [10,13,14,17]. Immediately after cutting at the level of the upper lumbar vertebrae of the spinal cord, the central paralysis of the hind limbs-paraplegia - occurs in the animal. Such an animal can neither lean on its hind limbs, nor move them when walking. Moving, it pulls up the entire back of the trunk, dragging it behind it. If the spinal cord is cut in the same way at the level of the cervical vertebrae, then paralysis of all four limbs occurs-tetraplegia (The experiment can be performed on the same rabbit on which paraplegia was demonstrated [10]). Immediately after cutting the spinal cord of the animal, all reflexes disappear (spinal shock), but after a while, sometimes already at a lecture, an increase in flexor reflexes is detected. In response to the injection of the foot, the limb bends sharply. A few days later, the flexion reflex of one limb is accompanied by the extension of the symmetrical (cross-extension reflex), which can be shown in one of the following lectures. The tone of the muscles of the extremities remains sluggish for a long time. When cutting half (right or left) of the spinal cord in an animal experiment, unlike what is observed in humans when half of the spinal cord is affected, there is not paralysis, but paresis of the limb on the same side. Paresis disappears after a while. If, after that, the second half of the spinal cord is cut (above the site of the primary injury), then this also turns out to be insufficient for a persistent violation of the functions of the limbs in the animal.

3) The experiment can be put on a frog. The frog's spine, along with the spinal cord, is cut below the shoulder girdle with ordinary scissors. To demonstrate the increased reflex excitability that occurs with spinal paralysis, the spinal cord is cut 3-4 days before the lecture. If you put such a frog on a table and hit it, then it will develop an attack of convulsions in paralyzed limbs. If this frog is injected with strychnine (1ml of a 1: 1,000 solution), then convulsions initially develop in the posterior half of the body. Reflex excitability of paralyzed limbs increases due to disinhibition of the peripheral reflex arc.

Demonstration of disorders of motor function in lesions of the extrapyramidal system

When the subcortical nuclei (striopallidar system) are affected, due to a sharp increase in plastic tone, the muscles freeze for a long time in the position given to them, movements are slowed down, constrained. An increase in plastic tone can be shown in the following experiment [5]. A guinea pig or rat is poisoned with Carbon Monoxide (CO) by placing it under a bell, into which a lamp gas is supplied or simply put a smoldering rag. Carbon monoxide, along with other changes in the body, causes lesions of the subcortical ganglia. When the animal's coordination of movements is disrupted and it falls on its side, it is taken out and an increase in plastic tone is shown-the limbs freeze for a long time in the uncomfortable position given to them [11,19]. Poisoning of an animal (dog, rat) with bulbocapnine (2% solution at the rate of 20mg per 1kg of weight) leads to the same consequences.

Hyperkinesis

Involuntary, violent movements in humans are extremely diverse (seizures, athetosis, chorea, etc.). In animals, it is most easy to reproduce seizures in experimental epilepsy.

Demonstrations of an epileptic seizure

1) Insert one needle of the electrode into the mucous membrane of the dog's mouth, the other — under the skin of the base of the skull. Turn on the current (from the city network) for 2-3 seconds. The dog develops an epileptic seizure [3,19]. Initially, tonic convulsions of the limbs and respiratory muscles appear a sharp tension of the skeletal muscles: the limbs are straightened, the head is thrown back, the jaws are compressed. Then tonic convulsions are replaced by clonic ones alternating flexion and extension of the limbs, trunk and head. Finally, only isolated twitching of the limbs is visible. Similar convulsions when passing an electric current occur in a decortized dog. This suggests that both tonic and clonic seizures in epilepsy are formed in subcortical formations. The lesion in the cortex in epilepsy serves only as a source of irritation of subcortical formations (A.D. Speransky) [4]. Due to the spread of irritation to other parts of the central nervous system (not only to the motor zone), during seizures, disorders of a number of autonomic functions are observed (salivation, increased blood pressure, increased heart rate, urination, defecation).

2) Seizures occur especially easily when the cerebral cortex is irritated in guinea pigs. Trepanation of the skull in pigs is performed by cracking the bone with ordinary scissors (in the center of the parietal bone), to the right or left of the midline, so as not to damage the venous sinus. The exposed surface of the brain is irritated by the touch of a finger or a spatula. As a result of irradiation of arousal, an epileptic seizure occurs in the animal, consisting of tonic and clonic convulsions [20,21]. An attack of seizures can also be reproduced by severe bleeding, suffocation of an animal, various poisoning (camphor, cardiazole, nicotine), overheating, the introduction of large doses of insulin [3,12].

Demonstration of reflex epilepsy

A chronic focus of irritation on the periphery can lead to reflex epilepsy. 1-2 weeks before the lecture, the sciatic nerve is cut in a guinea pig. As a result of irritation from the cutting site, a focus of persistent arousal occurs in the central nervous system. Light hammering of a guinea pig on the head provokes a convulsive attack [19]. Convulsive phenomena can also be the result of irritation emanating from internal organs (with pneumonia, intestinal colic) [16]. Almost all types of seizures are intensified with strong emotions, various external stimuli, arbitrary movements, etc. Therefore, the pathological focus; which is the cause of seizures, reacts to irritation according to the dominant principle. The excitement that occurs with a variety of body irritations and does not normally cause seizures, in the presence of a pathological focus in the brain, flows to it and provokes or intensifies an attack of seizures [11,19]. Seizures can also be associated with some kind of conditioned stimulus (for example, the environment in which they occurred) and occur conditionally- reflexively [19].

Ataxia

Demonstration of ataxia in violation of afferent impulses

The violation of coordination of movements is most easily reproduced by injecting 40-50ml of 0.5% novocaine solution into the muscles of the lower leg and thigh of the dog. After 10-15 minutes, ataxia develops. Voluntary movements are preserved, but they are uneven, inaccurate, and the sequence of muscle contractions is disrupted [22]. Deprived of proprioceptive sensitivity, the limb rises too high, and when it descends, it hits the ground with force. Her movements become erratic-she leans back in all possible directions. If the anaesthetized limb is lifted or given an uncomfortable position, then this position persists for a long time. Ataxia can also be reproduced by cut-

ting the posterior roots or the posterior pillars of the spinal cord, i.e. the pathways conducting impulses from the muscles [23]. The absence of impulses from the periphery can lead to a complete shutdown of the limb from function. Thus, the so-called arbitrary activity caused by impulses from the cortex becomes impossible in the complete absence of centripetal impulses. This fact once again shows that arbitrary movements are actually reflex [15,20,24].

Demonstration of labyrintho-cerebellar ataxia

A spoke is inserted into the external auditory canal of a guinea pig, the resistance of the eardrum is overcome and, by turning the spoke, the labyrinth is roughly destroyed. With a deeper introduction, the cerebellar hemisphere is destroyed at the same time. The animal immediately has violent rotational movements in the direction of injury, it loses the ability to maintain balance and fix the position of the body [15]. If the pig is put on the table and strongly turn it around the longitudinal axis of the body in the direction of damage, then it does not immediately assume a normal position and can be checked 1-2m, like a simple physical body, until the force of movement given to it by the experimenter runs out [8]. In large animals, such phenomena are not observed, since due to their significant body weight, they have greater inertia. The described disorders may be compensated for some time after the damage at the expense of other parts of the central nervous system [22-24].

Sensitivity Disorders

Demonstration of sensitivity disorders in case of peripheral nerve damage (demonstration of peripheral paralysis)

All types of sensitivity are lost in the animal-anesthesia itself occurs-loss of tactile sensitivity, analgesia-loss of pain sensitivity, thermal anesthesia-loss of temperature sensitivity, as well as loss of deep proprioceptive sensitivity. The animal does not react to touching the foot, painful tearing when it is punctured, cold when chloroethyl evaporates, high temperature when the skin is burned. Finally, the animal does not react to a change in the position of the limb-the foot can be given an uncomfortable position- bend or unbend it, and the animal retains this position for a long time. Parts of the body that have lost sensitivity are easily damaged, frostbite, burns. Animals can even gnaw off a limb that has lost sensitivity [25].

Demonstration of sensitivity disorders in spinal cord injury

The same loss of all types of sensitivity occurs in the underlying parts of the trunk when the spinal cord is cut. With a half-cut of the spinal cord (right or left), a peculiar violation of motor function and sensitivity occurs (Brown-Sekara syndrome) [25]. On the side of the lesion, paresis and a disorder of proprioceptive sensitivity occur (the conductors of which go up the same half of the spinal cord). On the opposite side, pain and temperature sensitivity drop out, since their conductors cross immediately upon entering the spinal cord. This can also be shown on a frog. Produce a half (right or left) cut of the spinal cord in a frog. After 10-15 minutes, when the spinal shock passes, both paws are lowered into 1% sulfuric acid. The flexion reflex occurs only on the side of the lesion, and the other foot remains motionless.

Demonstration of pain sensitivity of internal organs

In a rabbit, the abdominal cavity is opened along the midline under local anesthesia. The internal organs are touched and their parenchyma is cut without any reactions from the animal. A sharp pain reaction occurs only when the internal organs (liver, gastrointestinal tract) are pulled away from the mesentery attaching them [5,7]. In diseases of internal organs, pain usually also occurs when their serous membranes are affected the peritoneum, pleura, or when they are stretched during severe contractions of the stomach or intestines. The same can be shown on the brain: the animal does not react to its incisions, but gives a violent reaction to the tension of the meninges [7].

Acute Brain Injury

Acute brain damage (trauma, hemorrhage, etc.), in addition to the changes described above (paralysis, hyperkinesis, ataxia, sensitivity disorders, etc.), causes a number of general disorders; loss of consciousness, inhibition of reflex activity, disorders of autonomic functions-slowing of cardiac activity, respiration, vomiting, hyperthermia, hyperglycemia, glucosuria, etc. [15,26]. These disorders can be reproduced with brain injury in dogs, cats and other animals. Some of these disorders can also be shown in frogs with brain damage at the level of the visual halls [15]. Here we limit ourselves to demonstrating the inhibition of motor reflexes arising from this damage. Disorders of autonomic functions arising from brain damage are demonstrated in the relevant sections (pathology of blood circulation, respiration, etc.).

Demonstration of diffuse inhibition of the central nervous system in brain injury (I. M. Sechenov's experience)

The frog's skull is opened 5-10 minutes before the demonstration to do this, make a transverse incision of the skin behind the nasal openings, then cut the skin laterally on both sides by 1.5-2cm from behind so that the cranial bones are clearly visible. The skin is cut off. To open the skull, insert the tip of a narrow scalpel or a branch of thin scissors into the skull cavity above the right eye socket and hold it forward along the lateral suture of the bone, sliding along the edge of the eye socket and pointing the blade forward and upward (so as not to injure the brain). The frog's head is tightly held with the left hand. Make a transverse incision of the end of the bone and, lifting it with tweezers, separate it from the left side, passing a scalpel from front to back. The posterior part of the bone is cut off at such a level that the visual lobes are clearly visible [15].

Carefully stop the bleeding with cotton swabs. A cross-section of the brain is made at the level of the visual halls. They hang the frog by the jaw to a tripod. Immediately after cutting the brain, the time of the acid reflex is determined by lowering the frog's foot into a glass of pic with a weak solution (0.5-1%) of hydrochloric acid. The reflex appears no earlier than 20-30 seconds. After 10-15 minutes, the reflex time is checked again. By this time, it usually recovers to normal numbers 2-3 seconds. Obviously, the brain injury caused inhibition that radiated to the spinal centers, which led to the inhibition of acid reflexion. They repeatedly cause extreme irritation of the surface of the incision of the brain, this time not by trauma, but by a chemical irritant a salt crystal. The reflex time is immediately determined it increases greatly the acid reflex is inhibited again.

The salt crystal should be applied for no more than 1 minute, otherwise seizures may develop. Before applying salt, the surface of the incision is thoroughly dried with a filter paper. Inhibition of reflexes after applying a salt crystal lasts 8-10 minutes [5,15]. In numerous experiments, I. P. Pavlov showed that surgical intervention on the brain inhibits not only unconditional, but also conditioned reflexes. Obviously, the inhibition caused by pathological irritation during surgery extends to the cerebral cortex [8,13]. In humans, inhibition of reflexes in acute brain damage is much more pronounced and lasts longer. Loss of consciousness, deep inhibition of reflexes can last up to a week or more.

Trophic Disorders

Trophic disorders in the clinic include pathological changes of the skin, mucous membranes, cornea of the eye (acute bedsores, perforated ulcers, keratitis), striated musculature (atrophy, hypertrophy), joints (arthropathy), bones (osteoporosis) that occur when the nervous system is affected [27]. Systematic experimental studies by A. D. Speransky and his collaborators have shown that with lesions of the brain (mainly the hypothalamic region) and peripheral nerves (sciatic, trigeminal, etc.), trophic disorders appear not only in the formations listed above, but also in internal organs the heart, lungs, gastrointes-

tinal tract, etc [3,4,11]. These trophic disorders manifest themselves in the form of the most common pathological processes necrosis, inflammation, atrophy, dystrophy, hemorrhages, etc. This allows us to assert that the basis of pathological processes is nervous dystrophy (A.D. Speransky) [13].

Demonstration of trophic disorders when applying a ball to the hypothalamus (the experience of A.D. Speransky)

Surgery technique: it is advisable to take at least 2-3 dogs, young, small, smooth-haired, for the operation. Under general anesthesia, an incision is made of the skin and underlying tissues along the midline of the head to the spinous process of the II cervical vertebra. On the left, the skin and platysma are dissected to the level of the zygomatic arch. Then the blood vessels feeding the temporal muscle (m. temporalis) are bandaged, it is removed along the edge of the zygomatic arch and stored in a gauze napkin in case possible bleeding stops. Clamps are applied, and then ligatures are applied to all the bleeding vessels on the incision of the muscle. A rasp cleans the cranial bone and makes a hole in it with a trepan [12]. Before enlarging the hole, it is necessary to extract the cerebrospinal fluid (3-5ml) in the above way. This technique reduces bleeding from the bones, reduces the volume of the cerebral hemispheres, which after that not only do not stick out beyond the edges of the bone defect, but lag behind them, like the kernel of a nut from the shell. After fluid extraction, the dura mater is separated from the bones in all directions, especially down to the base of the brain (here one should be afraid of damage to the venous sinuses). Following this, the covering bones of the skull are removed with forceps downwards from the line connecting the outer upper corner of the eye socket with the middle of the ridge length. Melted wax is rubbed into the bleeding areas of the bones with a finger.

After removing the bones to the level of the zygomatic arch, the dog's mouth is opened as wide as possible. At the same time, the coronal process of the lower jaw descends downwards and pulls all the muscles, vessels and nerves running from the lateral surface of the skull to the lower jaw. They pass over the bone with the handle of a scalpel, while exposing the entire lateral surface and part of the base of the skull. The opened deep part of the integumentary bones is removed as close as possible to the midline. It is necessary to make sure that the bone forceps do not capture the muscles at the bottom of the suspension pit, since there are large blood vessels accompanying the II and III branches of the trigeminal nerve [6,16]. When the bones are removed, a T-shaped incision of the dura mater is carefully made with thin scissors. The horizontal part of it goes from the corner of the eye socket back, the vertical part goes from the middle of the horizontal and down to the edge of the bone defect.

Then the operator moves to the right side of the operating table, the anesthetizer turns the animal's head to the right side, so that the brain, due to gravity, is slightly behind the base of the skull. At the same time, the entire left temporal lobe of gyrus pyriformis and the edge of tractus olfactorius are visible. When pressing with a scalpel handle or a spatula, the pituitary gland area between the carotid artery and n. oculomotorius is visible [8,16]. The assistant at this time pulls on the opposite edge of the hole.

Immediately after the pituitary gland is exposed, a pre-prepared glass ball the size of a pea is taken, which is pushed between the carotid artery and the oculomotor nerve and placed immediately behind the back of the Turkish saddle. The dog's head is turned to the usual position, while the pituitary gland falls into place, the brain sinks to the base of the skull. The operation is completed by layer-by-layer suturing of the wound. The dura mater is sewn tightly. Instead of a ball, you can use a glass half-ring with a diameter of 1-1.5cm and a thickness of 2-3mm. At the moment of lifting the brain, it is put on a funnel (infundibulum) and rotated so that its ends look forward. 1-2 weeks after applying the ball, trophic disorders begin to develop on the mucous membranes, skin and cornea. There is bleeding of the gums, loosening of them, erosion and ulcers on the mucous membranes of the mouth and tongue, teeth are destroyed. Conjunctival inflammation and corneal opacity often develop [9].

As a rule, baldness of the skin develops, especially on the head and around the eyes (in the form of glasses). Trophic ulcers on the extremities may appear a little later [3]. If the animal prepared for the lecture dies, it is necessary to open it, since trophic changes occur in the internal organs during this operation. Massive hemorrhages in the lungs, the pylorus of the stomach, the duodenum, the area of the bauginian flap and the rectum are not uncommon. When examining the intestinal mucosa, traces of old hemorrhages are also found in the form of brown or asp-gray spots and stripes, ulcers and erosion of the mucosa. Sometimes you can find papillomas [3,13,15,27]. Thus, chronic irritation of the central nervous system the brain in the region of the hypothalamus causes widespread trophic disorders in animals. As the experiments of M. K. Petrova have shown, the same trophic disorders can occur not only with organic brain damage, but also after its functional injury by the so-called "mistake".

Demonstration of trophic disorders in the defeat of the branches of the trigeminal nerve

The experiment is put on a rabbit or a dog. An incision is made over the exit site of the subglacial nerve (from the anterior edge of the arcus zygomaticus to the upper edge of the nostril) about 2cm long. They cut the muscle that raises the upper lip, find a reddish-brown soft lymph node. The suborbital nerve is located up and inside of it. It is exposed, 2-3 drops of croton oil (or bile, etc.) are injected and cut across the swelling of the nerve formed by the injected substance. The wound is not sewn up. On the 1st-2nd day, the animal develops bilateral conjunctivitis, an ulcer appears on the lip. Then keratitis often develops, ulcers on the cornea, symmetrical ulcers on the healthy lip and tongue. Trophic disorders are aggravated if, after cutting the nerve, additional irritation of the nervous system is produced by extracting cerebrospinal fluid [9,4,27].

Demonstration of trophic disorders in case of damage to the Gasser node

The experiment is put on rabbits or rats. The Gasser node can be damaged

1) under the control of the eye by opening the skull

2) by piercing through the temporal bone.

The carotid arteries are clamped, the skin on the crown is cut (under general anesthesia), a piece of parietal bones is cut out, which is left hanging on the periosteum. Cerebrospinal fluid is extracted. Having cut the dura mater, the hemisphere is lifted to the right or left, then the fold of the dura mater covering the gasser node is dissected, its crushing is performed with eye tweezers. Having lowered the hemisphere, the dura mater is straightened, the cut-out piece of bone is laid and stitches are applied to the periosteum and to the skin. The clamps are removed from the carotid arteries [12,27]. The scalpel is installed perpendicular to the temporal bone between the external auditory canal (vein) and the lateral edge of the eye (artery) above the zygomatic arch. After passing the bone, the scalpel is directed inside, down and back.

After 10-20 seconds after the lesion of the node, the pupil narrows, dimples appear on the cornea, after 15-60 minutes, corneal wrinkling develops. After a day, the cornea acquires a bluish tint, indicating a slight turbidity. After 3 days, the cornea becomes bluish-white, with purulent exudate in the center. After another 2-3 days, the crimson iris adheres tightly to the white thickened cornea, barely shining through it [3]. By the 10th day, a piercing ulcer of the eye usually appears. The iris and cornea are soldered together and protrude forward in the form of a purple-red cone sprouted by vessels. After 2-3 weeks, the reverse development of the process begins and by the end of the month the ulcer is eliminated, being replaced by an eyesore. In rats, the reverse development of ulcers begins after 5-6 days.

Demonstration of atrophy and hypertrophy

1) The experiment is set 2 weeks before the lecture. In one rabbit, the sciatic nerve is cut in the middle third of the thigh, in another rabbit (of the same weight), the Achilles tendon is cut. In both cases, the calf muscle is paralyzed. The lecture demonstrates the inactivity of the calf muscle in both rabbits. Then they are hammered, the calf muscles are extracted and weighed. Muscle atrophy after cutting the sciatic nerve is more pronounced than after cutting the Achilles tendon. This is due to the preservation of nerve connections during the cutting of the Achilles tendon. Preservation of nervous regulation of tissue nutrition prevents the rapid development of atrophy [3,4]. With immobility of the limb caused by ankylosis (joint fusion), its muscles also atrophy, but even in this case, atrophy cannot be reduced to inactivity of the organ. This atrophy has a reflex character and is caused by irritation of the nerve centers by pathological impulses emanating from the damaged joint [3,8] If, by cutting the posterior roots, interrupt the path of passage of these impulses, it is possible to slow down the development of atrophy.

2) 1-2 weeks before the start of the lecture, the kidney and testicle are removed from one side of the rabbit. The left kidney is probed from the back, the skin and muscles are cut above it (parallel to the costal edge, retreating from it by 1-2cm) at a distance of 5-8cm, a general ligature is applied to the chyle of the kidney, pulling the vessels and ureter at the same time. Then the kidney is removed. In the same way, the testicle is probed beforehand, the scrotum is opened and after applying a ligature to the rope, the testicle is removed. The removed organs are weighed and fixed in 5% formalin. At the lecture, the rabbit is slaughtered and the remaining kidney and testicle are extracted from the corpse. The volume of the entire kidney increases by 2 times compared to the previously extirpated kidney, while the volume and weight of the testicle do not change. Hypertrophy of the remaining kidney is explained by the strengthening of its function. Already on the second day, it completely provides normal diuresis. The number of simultaneously functioning glomeruli, which normally makes up Vs of the total number, increases sharply [3,4,8,12]. Removal of one of the testicles does not cause hypertrophy of the other, since it is not subjected to the constant and continuous load that the tissues of the remaining kidney experience. Strengthening the function of the organ serves as a physiological stimulator of tissue growth. For the same reason, hypertrophy develops in the remaining parts of the liver after removal of one of its lobes (the operation is easiest to perform on a rabbit), hypertrophy of the heart with damage to its valves, with hypertension and prolonged physical work, etc.

Higher Nervous Disorders

Activities

In humans, violations of higher nervous activity manifest themselves in the form of a perversion of perception - illusions, hallucinations (auditory, visual, gustatory, etc.), in the form of thinking disorders - delusional ideas (persecution, poisoning, grandeur, etc.) and obsessive ideas (fear touch, redness, fear of squares, etc.), in the form of impaired attention, memory, dementia, disorders of the emotional sphere (depression, euphoria), consciousness, behavior (stupor, catatonia, negativism, mutism, psychomotor agitation, etc.) [28]. Reproduction of clinical psychopathology in animal experiments is possible only to a limited extent. The study of conditioned reflexes opened the way to an objective analysis of disorders of higher nervous activity in humans, made it possible to reveal the causes and mechanisms of some mental disorders, which, as IP Pavlov showed, are based on violations of conditioned reflex activity [28].

Demonstration of violations of conditioned reflexes in dogs with a remote cerebral cortex

It (similar to a deep organic disorder of higher nervous activity in humans) can be reproduced by removing the cerebral cortex in dogs. After this operation, all conditioned reflexes developed in the process of individual development disappear in the animal, and it is impossible to develop new ones. Unconditioned reflexes are preserved [20]. Surgery to remove the cerebral cortex in a dog. The technique of opening the skull is the same as during the operation of applying a ball to the hypothalamic region (see the Trophic Disorders section), with the difference that the incision of the scalp is made not along the midline, but to the right or left of it. After opening the dura mater, the cortex of one of the hemispheres is removed with a sharp spoon, trying, if possible, to capture the basal part of the cortex. Bleeding is stopped with tampons. The meninges are straightened and sewn up. Apply skin sutures. After 1-2 months after the first operation, the cortex of the second hemisphere is also removed [4,28]. After the operation, artificial feeding of the dog is provided (first, water, milk with glucose and broth are introduced through a probe, then they are fed with ordinary food, pushing it into the mouth). After 2 months the dog starts to eat by itself. In the first days after the operation, the dog is kept in a warm room in a canvas cradle with a hole for urine drainage. Then, in order to protect the animal's head from accidental injury, the dog is placed in a cage with walls lined with oilcloth with a layer of cotton wool or felt underneath. The dog is shown at a lecture 2 months after the removal of the second hemisphere, when the consequences of the injury itself are already passing and the animal does not need artificial feeding. Unconditioned reflexes to auditory stimulation in dogs with a removed cerebral cortex are preserved. The dog reacts to a sharp knock, the sound of a horn, a strong call, etc. There are no conditioned reflexes to auditory stimuli - the dog does not respond to a nickname, to the barking of other dogs, etc [6].

Unconditioned reflexes to visual stimulation are preserved. They direct the light of the lamp into the eyes of the dog, its pupils narrow, it turns its head away. There are no conditioned reflexes to visual stimuli - the dog does not respond to threatening movements. Unconditioned reflexes to irritation of the olfactory receptors are preserved - the dog turns its head away from the ether, tobacco smoke, ammonia. There are no conditioned reflexes to irritation of the olfactory receptor - the dog does not turn away from the bottle with ether or ammonia while it is closed, from the cigarette until the smoke gets into her nose, does not react to the smell of a cat seated next to her. Unconditioned food reflexes are also preserved. The dog can eat on its own, making rhythmic movements of the tongue and muscles of the head and neck. As satiation progresses, the chewing movements weaken and the dog stops eating. The taste is preserved. Moisten the meat with a solution of cinchona or mustard - the dog spits it out. Digestion of food, consisting of a complex chain of secretory and motor reflexes, is almost not disturbed. However, conditioned reflex reactions to a food stimulus are completely absent. The dog does not react to showing food, does not find meat, even if it is put on its nose. She only starts eating when food is placed in her mouth or her face is put into a bowl of food. There is no conditioned reflex separation of saliva and gastric juice by the appearance and smell of food [5].

The same patterns are found in relation to motor function and sensitivity. Unconditioned motor reflexes are preserved for a wide variety of stimuli. They cause painful irritation of the paw - the dog pulls it away. They give the paw the wrong position - the dog corrects it. Dip a paw in hot and cold water - the dog pulls it out of the water. With tactile stimulation - scratching the side - a scratching reflex occurs. These reflexes are usually excessive, not adequate to irritation, often accompanied by a violent motor reaction, screeching, growling, and the desire to bite. This depends, apparently, on hyperpathia arising in connection with irritation from postoperative scars in the brain or as a result of disinhibition of the lower parts of the central nervous system, which occurs as a result of the removal of the cortex. The dog does not have paralyses - it moves independently, however, the coordination of movements is disturbed - they are rude, awkward; turning his head to the place of painful irritation, the dog misses, does not find it. Conditioned motor reflexes are sharply disturbed. The dog is given a

bone - he cannot hold it with his front paws. The dog loses the ability to dig the ground with its front paws, to give a paw. The development of new motor conditioned reflexes (training) in such dogs is impossible [8,12,16]. Orientation in space is disturbed - having entered a narrow passage, the dog cannot either jump out of it or turn back, but continues to climb forward, onto the wall, to the point of complete exhaustion, until it accidentally steps back and comes out backwards. This can be shown by placing a tall box without top and rear walls in the way of the dog.

Changes in the emotional sphere are expressed in an increase in negative emotions - the dog easily has fits of rage, it growls, tries to bite when its position changes, especially with rough, awkward movements, resists even when trying to bring it to a bowl with food. The absence of conditioned reflex reactions to stimuli from the external environment leads to the fact that the dog sleeps most of the time. She wakes up only from unconditioned irritations - touch, bright light, strong knocking, etc., or under the influence of irritations from the internal environment (hunger, urge to urinate and defecate). Demonstration of violations of conditioned reflexes during the removal of the hemispheres in birds. Hemisphere removal in birds is much easier than decortication in dogs. The resulting disturbances in conditioned reflex activity are fundamentally the same as those observed in decorticated dogs.

The technique for removing hemispheres in birds

The feathers on the back of the head are cut off with scissors, the bird is fixed on the machine with its back up. A 0.3% Novocaine solution is injected into the skin and under the skin. An incision is made in the skin and periosteum along the midline of the head above the parietal and occipital bones, 1.5-2cm long. The edges of the skin wound are pulled to the side, the periosteum is scraped off. To the right and a tear from the midline (do not touch the venous sinus!), Make windows in the skull with a diameter of 5-6 mm with trefin or small bone tweezers. Bleeding from the diploe is quickly rubbed with a piece of cotton dipped in melted wax. Thin sharp scissors open and excise the dura mater within the boundaries of the defect. Then, with a narrow flat metal plate, pieces of the brain substance are quickly scooped out, moving it forward to remove the frontal section and back to remove the occipital (carefully!). In the midline, care is also taken not to cause bleeding from the sinus. The remaining parts of the large brain are removed with a small sharp spoon. It should be noted that due to a decrease in intracranial pressure, the midbrain protrudes somewhat, accidental damage to which can cause the death of a bird [5,16].

After making sure that the removal of the large brain is complete, the wound is tamponed with cotton wool and the same is done on the other side. Tampons are left until the bleeding stops completely (for 10-15 minutes). The skin wound is sutured with one row of sutures after the final stop of bleeding. After the operation, during the day, the birds do not receive any food or drink, on the second day they are given a half portion, on the third - the usual food. In the early days, the birds cannot feed on their own, so they are fed daily as follows. The bird is wrapped in a towel, leaving the head, neck and keel of the chest free (to facilitate breathing), laid on the table, open the beak and pour a little grain into the depths of the mouth with a small scoop or spoon or push a small lump of porridge. They also provide water. The swallowing reflex is preserved, after a few days the birds begin to eat on their own, and the food is swallowed. With careful care, decerebrated birds can live for several months and even more than a year [6].

The bird is shown 3-5 days after the operation. In non-spherical birds, as in barkless dogs, conditioned reflexes disappear, unconditioned ones remain. They demonstrate the preservation of unconditional reactions to sound - with a loud knock, the sound of a horn, a strong call, the bird shudders. There are no conditioned reflex sound reactions - the bird does not respond to the usual feeding signals (knock of falling grain, beckoning). Unconditioned reflexes to visual stimuli are preserved in the bird - it blinks in bright light, avoids obstacles when walking, and lands exactly when flying from top to bottom. However, she has no conditioned reflex reactions to visual stimulation - she does not respond to threatening movements, to the presence of a dog and a cat. So, if a dog is placed nearby, a decerebrated bird makes no attempt to either escape or defend itself. Conditioned food reflexes are also absent - the bird does not look for food, does not go to it, and begins to peck only when grain is thrust into its beak. At the same time, she often misses, poorly captures food. Unconditioned motor reflexes in the bird are preserved. She has no paralysis, she walks on her own, when thrown into the air she flies to the floor, balances well on a narrow perch. There are no conditioned reflex motor reactions, so the bird sleeps almost all the time, waking up when hungry, or wanders aimlessly.

Neurosis

Under this name, functional disorders are distinguished in the clinic, for the explanation of which it is not possible to find organic changes either in the central nervous system or in peripheral tissues [20]. At the present time there is no reason to sharply oppose neuroses to organic diseases. Violations of function in organic diseases also cannot be explained only by pathoanatomical changes in organs and tissues. And here these disorders depend on reflex disturbances in the regulation of the activity of the organ under the influence of irritation from the lesion. This will be shown in numerous demonstrations throughout the course [11,29]. I.P. Pavlov's research showed that some neuroses are based on conditioned reflex mechanisms [11,20].

Demonstration of inhibition of the food reflex

To a metal bowl into which liquid food is poured, one wire is connected from the mains, and the other electrode is applied to the dog's front paw (the skin under the electrode is preliminarily shaved and moistened with saline). Touching the food, the dog closes the circuit and experiences an electric shock. After two or three attempts, the dog refuses to eat [20,29].

Demonstration of functional motor disorders with strong exteroceptive and proprioceptive stimuli

1) 1In a glass jar, in which a strong electric bell is installed, several rats are placed, marked with different colors. Include a call for 2-3 minutes. In the most excitable rats, there is a strong motor excitation, sometimes convulsions. Excitation soon gives way to inhibition. Rats fall and freeze for several minutes in a motionless state. After 10-15 minutes, rats with an excitation attack are injected subcutaneously with 0.3-0.5ml of a 10% solution of sodium bromide, and rats that did not respond to the call, 0.1-0.2ml of 1% phenamine solution. After 30-45 minutes, the bell is turned on again [17,20,29].

Discussion and Conclusions

So, this article summarizes and systematizes data on the modeling of animal pathologies of the nervous system, in particular disorders of motor function, sensitivity and higher nervous activity in various cases. Thus, the data presented in the review on modeling the pathology of the nervous system in the experiment represent a fundamental basis for further study of this system, deepening and detailing the pathogenesis of diseases, allowing you to create a basis for clinical research.

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