T. VYLEGZHANINA, T. OSTROVSKAYA

NERVOUS TISSUE AND THE NERVOUS SYSTEM

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КАФЕДРА ГИСТОЛОГИИ, ЦИТОЛОГИИ И ЭМБРИОЛОГИИ

Т. А. ВЫЛЕГЖАНИНА, Т. И. ОСТРОВСКАЯ

НЕРВНАЯ ТКАНЬ И НЕРВНАЯ СИСТЕМА

NERVOUS TISSUE AND NERVOUS SYSTEM

Учебно-методическое пособие

Минск БГМУ 2014

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NERVOUS TISSUE

Nerve tissue is distributed throughout the body as an integrated communication network. Structurally, nerve tissue consists of two principal types of cells:

– **nerve cells** or **neurons**;
– **glial** or **supporting cells**.

The neuron is the structural and functional unit of the nervous system.

Neurons are grouped as circuits. It is famous, that the human nervous system is formed by a network of more than 100 million nerve cells, assisted by many more glial cells. Each neuron has at least 1000 interconnections with other neurons, forming a very complex system for communication.

Neurons react promptly to stimuli with a modification of electrical potential that may be restricted to the place that received the stimulus or may be spread throughout the neuron by the plasma membrane. This propagation, called the action potential, or nerve impulse, is capable of traveling for long distances; it transmits information to other neurons, muscles, and glands.

Supporting cells or glial cells are nonconducting cells that are in intimate physical contact with neurons. Their functions include structural and nutritional support of neurons, electrical insulation, and enhancement of impulse conduction velocity.

EMBRYONIC DEVELOPMENT OF NERVOUS TISSUE

There are three sources of development of nerve tissue:

– **neural tube**;
– **neural crest**;
– **neural placodes**.

Nerve tissues develop from embryonic ectoderm induced to differentiate by the underlying notochord. First, a neural plate forms; then the edges of the plate thicken, forming the neural groove. The edges of the groove grow toward each other and ultimately fuse, forming the **neural tube**. This structure gives rise to the entire central nervous system, including neurons, glial cells, ependymal cells, and the epithelial cells of the choroids plexus.

Cells lateral to the neural groove form the **neural crest**. These cells undergo extensive migrations and contribute to the formation of the peripheral nervous system, as well as a number of other structures. Neural crest derivatives include: chromaffin cells of the adrenal medulla, melanocytes of skin and subcutaneous tissues, odontoblasts, cells of the pia mater and the arachnoid, sensory neurons of cranial and spinal sensory ganglia, postganglionic neurons of sympathetic and parasympathetic ganglia, Schwann cells of peripheral axons, and satellite cells of peripheral ganglia.

Neural placodes are focal regions of thickened ectoderm in the head of embryos that give rise to a wide variety of cell types, including elements of the paired sense organs (nose, eyes, ears) and neurons in cranial sensory ganglia.

NEURONS

All neurons have a cell body and processes that are named axon and dendrites. The cell body of the neuron contains the nucleus and those organelles that maintain the nerve cell. The processes extending from the cell body constitute a structural characteristic common for all neurons. Most neurons have only one *axon*, usually the longest process extending from the cell. A neuron has many *dendrites*, which are shorter and thicker than axon (fig. 1).

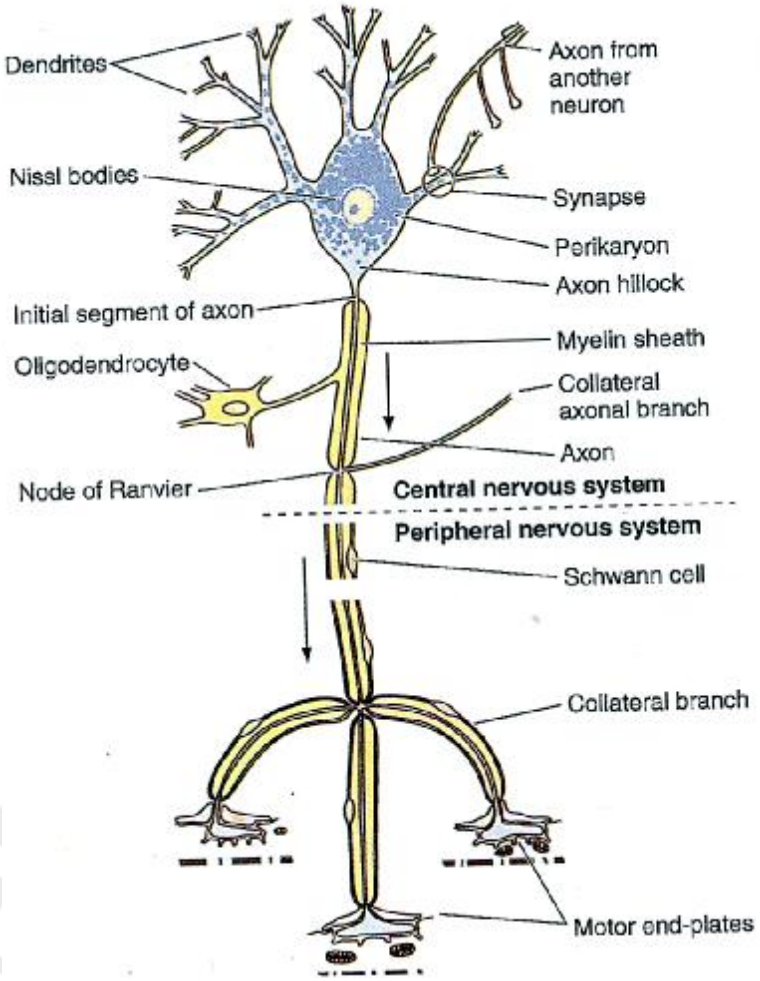


Fig. 1. Diagram of a motor neuron [7]

Dendrites are specialized in receiving stimuli from the environment, sensory epithelial cells or other neurons. Dendrites are usually short and divide

like the branches of a tree. Most nerve cells have numerous dendrites, which considerably increase the receptive area of the cell. Bipolar neurons, with only one dendrite, are uncommon and are found only in special sites. Dendrites become thinner as they subdivide into branches. The cytoplasmic composition of the dendrite base close to the neuron body is similar to that of the perikaryon but is devoid of Golgi complexes. Much of dendritic surface may be covered with synaptic contacts, and some have sharp projections, termed **dendritic spines**. Dendritic spines participate in the plastic changes that underlie adaptation, learning and memory. They are dynamic structures with a morphological plasticity based on the cytoskeletal protein actin.

Axons are neuronal processes that carry impulses away from the soma to other neurons or to effector's cells. Most neurons have only one axon; very few have no axon at all. An axon is a cylindrical process that varies in length and diameter according to the type of neurons. Although some neurons have short axons, axons are usually very long processes. Its length may be up to 100–150 cm. An axon is divisible into several regions. The **axon hillock** is the part of the soma leading into the axon. It lacks Nissl bodies. The portion of the axon between the axon hillock and the point at which myelination begins is called the **initial segment**. The initial segment is the site at which an action potential is generated in the axon. The axon diameter tends to be constant along its entire length. Axonal cytoplasm (axoplasm) possesses mitochondria, microtubules, neurofilaments, and some cistern of smooth endoplasmic reticulum. The absence of polyribosomes and rough endoplasmic reticulum emphasizes the dependence of the axon on the perikaryon for its maintenance.

Some axons have branches, termed collaterals that may contact with other neurons or even return to the soma of origin to modulate their own subsequent depolarization. Many axons undergo branching (arborization) near their terminations. The degree of terminal arborization depends on axon size and function. Each terminal branch ends in an enlargement called a terminal end-bulb or terminal bouton. Each bouton contains many mitochondria and neurosecretory vesicles.

Neurons and their processes are extremely variable in size and shape. Cell bodies can be pyramidal, spherical, ovoid, angular, fusiform, stellate, basket; some are very large, measuring up to 150 μm in diameter. Other nerve cells are among the smallest cells in the body, for example, the cell bodies of granule cells of the cerebellum are only 4-5 μm in the diameter.

There are some classifications of neurons.

I. Morphological (neurons are classified according to the amount of their processes):

– *multipolar neurons*, which have more than two cell processes, one — the axon, the others — dendrites;

– *bipolar neurons*, with one dendrite and one axon;

– *pseudounipolar neurons*, which have a single process, that is close to the perikaryon and divides into two branches.

Most neurons of the body are multipolar. Bipolar neurons are found in the cochlear and vestibular ganglia as well as in the retina and the olfactory mucosa. Pseudounipolar neurons are found in the spinal ganglia and in most cranial ganglia.

II. Functional (neurons are classified according to their function and location):

– *sensory (afferent) neurons* (receive stimuli from environment and conduct them to the CNS for processing and analysis);

– *motor or secretory (efferent) neurons* (conduct impulses from the CNS to muscles or glands);

– *interneurons* (connect sensory and motor neurons).

In the human body nerve impulses convey from one neuron to another or to the working organ indirectly, throw the chemical messenger — mediator (transmitter).

III. According of the chemical nature of the mediator the neurons classified as:

– *cholinergic* (mediator — acetylcholine);

– *aminergic* (mediator — biogenic amines: serotonin, noradrenalin, dopamine, histamine);

– *GABA-ergic* (mediator — gamma-oxybutric acid);

– *peptidergic* (mediator — peptides);

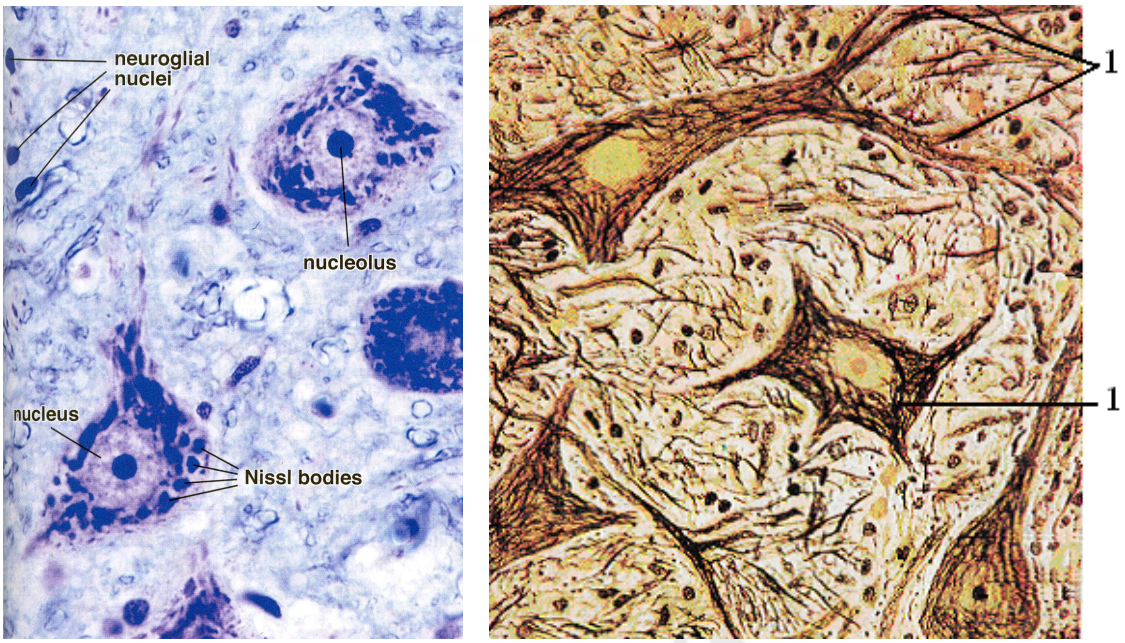
– *purinergic* (mediators — purine nucleotides adenosine).

CELL BODY

The cell body or perikaryon is the part of the neuron that contains the nucleus and surrounding cytoplasm exclusive of the cell processes. It is primarily a trophic and synthetic center, although it has receptive capabilities. The perikaryon of most neurons receives a great number of nerve endings that convey excitatory or inhibitory stimuli generated in other nerve cells.

Most nerve cells have a spherical unusually large, euchromatic (pale staining) nucleus with a prominent nucleolus. Binuclear nerve cells are seen in sympathetic and sensory ganglia. The chromatin is finely dispersed, reflecting the intense synthetic activity of these cells.

The cell body contains a highly developed rough endoplasmic reticulum organized into aggregates of parallel cisternae. In the cytoplasm between the cisternae there are numerous polyribosomes, suggesting that these cells synthesize both structural proteins and proteins for transport. When appropriate stains are used, rough endoplasmic reticulum and free ribosomes appear under the light microscope as basophilic granular areas called *Nissl bodies* or *basophilic substance* (fig. 2, *a*).



a ***b***

Fig. 2. Neurons:
a — photomicrograph of motor neurons, stained with toluidine blue. The cytoplasm contains a great number of Nissl bodies [7]; *b* — drawings of motor neurons with abundant of neurofibrils (1) in cytoplasm [11]

The amount of Nissl bodies varies according to the neuronal type and functional state. The Golgi complex is located only in the cell body and consists of multiple paralell arrays of smooth cisternae arranged around the nucleus. The perikaryon also contains numerous mitochondria, lyzosomes, inclusions and centrioles. Nissl bodies, free ribosomes, and the Golgi complex extend into the dendrites but not into the axon. This helps to distinguish between axons or dendrites.

Neurofilaments (intermediate filaments with a diameter of 10 nm) are abundant in perikaryon and cell processes. Neurofilaments bundle together as a result of the action of certain fixatives. When impregnated with silver, they form neurofibrils (0.5–3 μm) that are visible with the light microscope (fig. 2, *b*). The neurons also contain microtubules (d = 25 nm) which consist of protein tubulin.

Because the synthetic activity of the neuron is concentrated in the nerve cell body, axonal transport is required to convey newly synthesized material to the processes. Axonal transport is a bidirectional mechanism. It serves as a mode of intracellular communication, carrying molecules and information along the microtubules and intermediate filaments from the axon terminal to the nerve cell body and from the nerve cell body to the axon terminal.

Axonal transport is described as:

– *anterograde transport* carries material from the nerve cell body to the periphery. Kinesin, a microtubule-associated motor protein that uses ATP, is involved in anterograde transport;

– *retrograde transport* carries material from the axon terminal and the dendrites to the nerve cell body. This transport is mediated by another motor protein, dynein.

The transport systems may also be distinguished by the rate at which substances are transported:

– fast anterograde transport system (1–5 m/day);
– fast retrograde transport system (1–2 m/day);
– slow anterograde transport system (0.2–4 mm/day).

Dendritic transport appears to have the same characteristics and to serve the same functions for the dendrite as axonal transport does for the axon.

NEUROGLIA OR SUPPORTING CELLS

There are two types of neuroglia:

– **macroglia**;
– **microglia** (glial macrophages).

This classification is based on the origin of cells. Macroglia originates from neuroectoderm and microglia — from mesenchyme (blood stem cells).

Macroglial cells are divided into three types:

– *astrocytes*;
– *oligodendrocytes*;
– *ependimocytes*.

Only the nuclei of glial cells are seen in routine histological preparations of the nervous system. It is necessary to use special staining to distinguish the entire glial cells. Glial cells are typically smaller than neurons. Their processes are abundant and extensive.

Glial cells are 10 times more abundant in the mammalian brain than neurons; they surround both cell bodies and their axonal and dendrites processes that occupy the interneuron spaces. Glial cells furnish a microenvironment suitable for neuronal activity.

Astrocytes are star-shaped cells with multiple radiating processes. These cells have bundles of intermediate filaments made of glial fibrillary acid protein that reinforce their structure. Astrocytes bind neurons to capillaries and the pia mater. Astrocytes with long, thin and less branched processes are called ***fibrous astrocytes*** and are located in the white matter. Silver stains reveal fibrous material in their cytoplasm. *Protoplasmic astrocytes*, with many short, thick, highly branched processes, are found in the gray matter (fig. 3, ***a***). Intermediate forms between fibrous and protoplasmic astrocytes are also present.

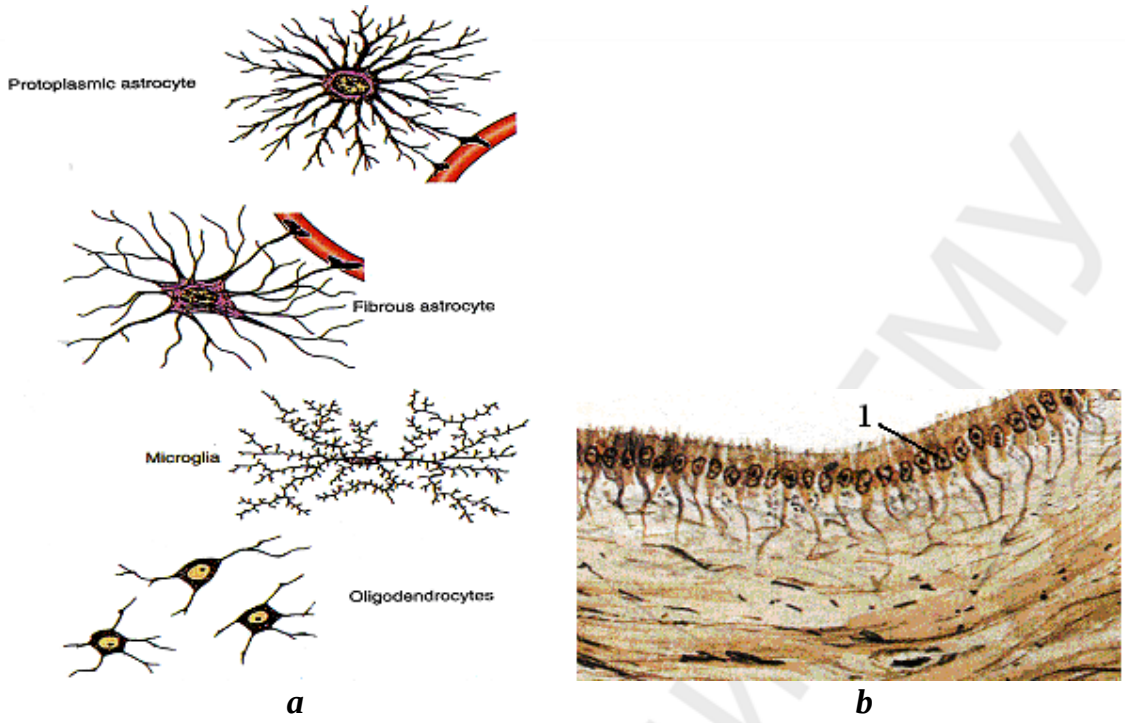


Fig. 3. Neuroglia:
a — drawings of neuroglial cells [4]; *b* — ependymal cells (1), silver-stained. Medium magnification [10]

Astrocytes are by far the most numerous glial cells and exhibit an exceptional morphological and functional diversity. The ends of their processes form end feet that may cover a large area of the outer surface of a blood vessels forming together with endothelial cells and its basal lamina **the blood-brain barrier**, they transfer molecules and ions from the blood to the neuron.

Astrocytes participate in controlling the ionic and chemical environment of neurons. Astrocytes can influence neuronal survival and activity through their ability to regulate constituents of the extracellular environment, absorb local excess of neurotransmitters, and release metabolic and neuroactive molecules.

When the central nervous system is damaged, astrocytes proliferate to form cellular scar tissue.

Oligodendrocytes, the most numerous glial cells, occur in both gray and white matter. These cells have rounded or pear-shaped bodies with relatively few processes (fig. 3, *a*).

There are two types of this kind of glia: those, which covering the processes (axons and dendrites) (Schwann cells) and those covering the bodies of the neurons (satellite cells).

Oligodendrocytes produce the myelin sheath that provides the electrical insulation of neurons in the central nervous system.

Schwann cells have the same function as oligodendrocytes but are located around axons in the peripheral nervous system.

Satellite cells surround the neuronal cell bodies in the ganglion of the peripheral nervous system. They protect neurons and control the environment around the neuronal body.

Oligodendrocytes have the ability to renew and provide regeneration of nerve fibers in PNS.

Ependymal cells form the epithelium-like lining of the fluid-filled cavities of the CNS. They form a single layer of cuboidal-to-columnar cells that have the morphologic and physiologic characteristics of fluid-transporting cells (fig. 3, *b*). The apical surface of the cell possesses cilia and microvilli. The latter are involved in absorbing cerebrospinal fluid. The basal part of these cells has processes extending deep into the gray matter.

Within the system of the brain ventricles, this epithelium-like lining is further modified to produce the cerebrospinal fluid by transport and secretion of materials derived from adjacent capillary loops. These cells, called choroidal epithelium, take part in forming the **blood-liquor barrier**.

Microglia are small elongated cells with short irregular processes found in both gray and white matter (fig. 3, *a*). Microglial cells may derive from mesenchyme, or they may be cells of neuroectoderm origin. Some microglia are components of the mononuclear phagocyte system and have phagocytic capabilities. They are involved with inflammation and repair in the adult central nervous system, and they produce and release neutral proteases and oxidative radicals. When activated, microglia retracts their processes and assumes the morphological characteristics of macrophages, becoming phagocytic and acting as antigen-presenting cells. Microglia also secretes a number of immunoregulatory cytokines.

NERVE FIBERS

Nerve fibers are the processes of neurons covered by glial sheaths. The nerve fibers may be: 1) **myelinated**; 2) **unmyelinated**.

In peripheral nerve fibers, the sheath cells are the Schwann cells, and in central nerve fibers it is the oligodendrocytes. Axons and dendrites of small diameter are usually unmyelinated nerve fibers. Progressively thicker axons are generally sheathed by increasingly numerous concentric wrappings of the enveloping cell, forming the myelin sheaths. These fibers are known as myelinated nerve fibers.

In PNS the unmyelinated processes are enveloped by Schwann cells and their basal lamina. The Schwann cells are elongated in parallel to the long axis of the processes, and the processes fit into grooves on the surface of the cell (fig. 4, *A*, *B*). The lips of the groove form a mesaxon.

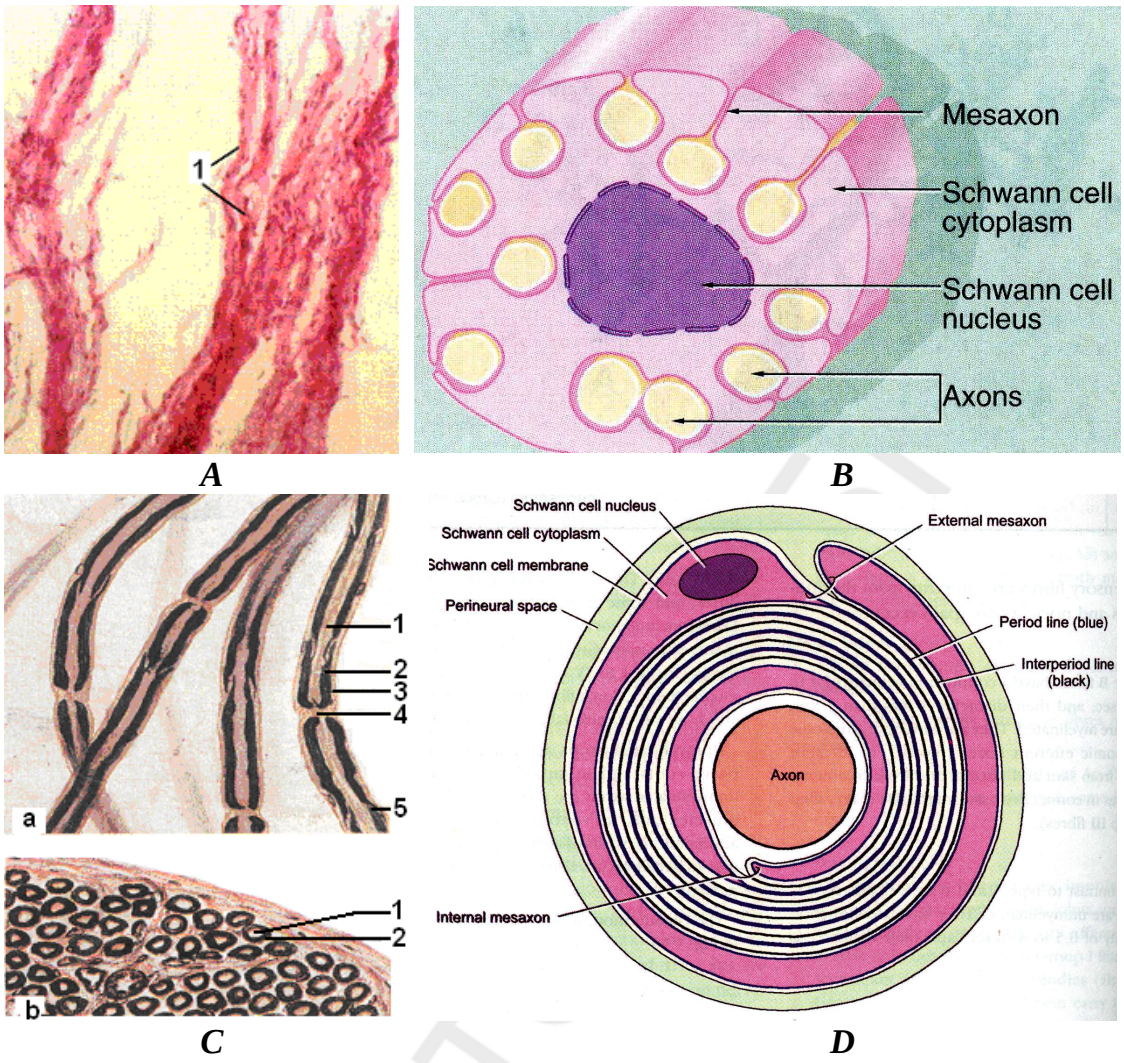


Fig. 4. Nerve fibers:
A — photomicrographs showing longitudinally sectioned of unmyelinated nerve fibers, stained by H&E. Medium magnification [12]; *B* — diagram showing a structure of unmyelinated nerve fiber [9]; C — drawings of myelinated nerve fibers as seen in slides with silver stained (a — longitudinal section; b — cross section) [11]; D — diagram showing a structure of myelinated nerve fiber [8]: *1* — axis cylinder; *2* — myelin; *3* — neurilemma; *4* — node of Ranvier; *5* — Schmidt lanterman cleft

A single axon or a group of axons may be enclosed in a single invagination of the Schwann cell surface. Large Schwann cells in the PNS may have 20 or more grooves, each containing one or more axons.

The CNS is rich in unmyelinated axons. Most autonomic nerve fibers are also unmyelinated.

In unmyelinated axons, Na^+ and K^+ channels are distributed uniformly along the length of the fiber. The nerve impulse is conducted more slowly (0.5–2.5 m/sec.).

In myelinaed fibers of the PNS, the plasmalemma of the covering Schwann cell winds and wraps around the axon, called the axis cylinder. The layers of membranes of the sheath cell unite and form myelin (fig. 4, *C*, *D*). Myelin consists of many layers of modified cell membranes. These membranes have a higher proportion of lipids. Outside the myelin sheath there is a thin layer of Schwann cell cytoplasm with nuclei. This layer of cytoplasm is called the **neurilemma**. The myelin sheath shows gaps along its path called the **nodes of Ranvier** (fig. 4, *C*); these represent the spaces between adjacent Schwann cells along the length of the axon. Interdigitating processes of Schwann cells partially cover the node.

The distance between two nodes is called an internode and consists of one Schwann cell. The length of the internode varies between 1 and 2 mm. The length of the internodes is greater in thicker fibers and shorter in thinner ones.

With the light microscope oblique clefts can often be seen in the myelin sheath. These clefts are called the **Schmidt Lanterman clefts**, and they are the areas, where adjoining layers of Schwann cell plasma membrane have failed to fuse. These spaces provide a path for passage of substances into the myelin and axon.

There are no Schwann cells in the CNS; there, the processes of the oligodendrocytes form the myelin sheath. Oligodendrocytes differ from Schwann cells in that different branches of one cell envelop segments of several axons.

Myelinated axons conduct impulses more rapidly than unmyelinated axons. Depolarization of myelinated axons occurs only at nodes of Ranvier, where insulation is reduced and Na^+ and K^+ channels are concentrated. Physiologists describe the nerve impulse as “jumping” from node to node along the myelinated axon. This process is called saltatory or discontinuous conduction. Impulse jumps from one node to the next with the speed up to 120 m/sec. The result is faster impulse conduction, less changes in ion concentration, and thus a lower energy requirement for recovery of resting potential.

REGENERATION OF NERVOUS TISSUE

It has been estimated that human neurons do not have the ability to divide, except for olfactory neurons. Dead neurons are replaced by proliferating glial cells. This process is called gliosis.

Peripheral nerve fibers can regenerate if their perikaryons are not destroyed. The next events take place in different parts of nerve fibers. Distal to injury, both the axon and myelin sheath, degenerate completely because the connection with the soma has been lost. During this Wallerian descending

degeneration, which takes about 2–3 days nearby Schwann cell proliferate giving rise to solid cellular columns. These rows of Schwann cells serve as guides to the sprouting axons formed during the reparative phase.

The proximal segment of the axon degenerates close to the injury for a short distance (retrograde ascending degeneration), but growth starts as soon as debris is removed by macrophages. Macrophages produce interleukins, thus stimulating Schwann cells to secrete substances that promote nerve growth.

The cell body also changes in response to injury. The perikaryon enlarges, chromatolysis, or dispersion of Nissl substance occurs, and the nucleus moves to an eccentric position.

During the third week after injury regeneration begins. The proximal segment of the axon grows and branches forming several filaments that progress in the direction of the columns of Schwann cells. Only fibers that penetrate these Schwann cell columns will continue to grow and reach an effectors organ. Axonal branches grow 3–4 mm/d. Growth is maintained by orthograde axoplasmic transport of material synthesized in the soma.

When there is an extensive gap between the distal and proximal segments, the newly growth nerve fibers may form a swelling called **neuroma**, that can be the source of spontaneous pain. Target organs deprived of innervation often atrophy.

The regenerative processes in the nervous system are controlled by several growth factors produced by neurons, glial cells and target cells. These growth factors form family of molecules called neurotrophins.

NERVE ENDINGS

There are three types of nerve endings:
– *afferent*;
– *efferent*;
– *interneuronal synapses*.

AFFERENT ENDINGS

Afferent (sensory) endings or receptors are specialized structures, located at the distal tips of peripheral dendrites of sensory neurons. They are able to initiate a nerve impulse in response to a stimulus.

Receptors can be classified in various ways.

I. From a functional point of view receptors can be classified on the basis of the kind of information they provide. They may be of the following types:

– *exteroceptors* react to stimuli from the external environment (touch, pain, temperature, smell, sound, etc.);

– *enteroceptors* react to stimuli from within the body (the degree of filling or stretch of the alimentary canal, bladder, and blood vessels);

– *proprioceptors* also react to stimuli from within the body, providing sensation of the body position and muscle tone and movement.

II. Receptors may be classified on the basis of the manner in which they are stimulated as follows:

– *mechanoreceptors* are stimulated by mechanical deformation, these include receptors for touch, pressure, stretch etc.;

– *chemoreceptors* are stimulated by chemical influences e. g., receptors in taste buds, or in the carotid bodies;

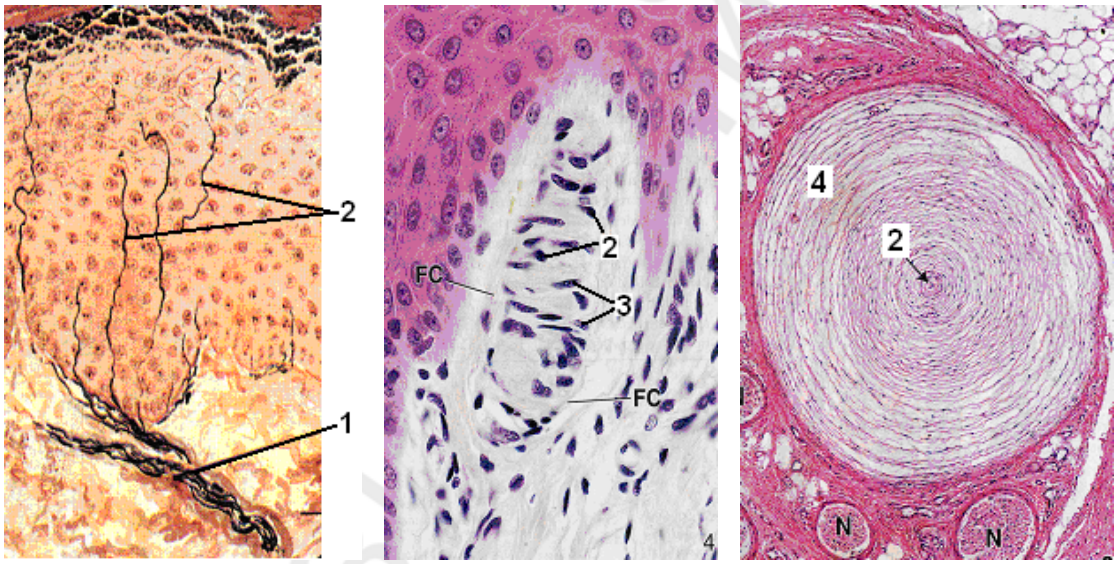
– *thermoreceptors* respond to alterations in temperature;

– *osmoreceptors* respond to changes in osmotic pressure.

Many receptors are polymodal as they may respond to more than one kind of stimulus.

III. The third way of classifying receptors is on the basis of their structure.

The simplest receptors are bare terminals of sensory nerves; they are called *free nerve endings* (fig. 5, *a*). These types of sensory endings may be mechanoreceptors, thermoreceptors, and nociceptors.



a ***b*** ***c***

Fig. 5. Afferent endings:
a — free nerve endings in the epidermis with silver stained. High magnification [11]; *b* — Meissner's corpuscle, stained with H&E. High magnification [7]; *c* — the Pacinian corpuscle, stained with H&E. Mediumh magnification [7]: *1* — nerve fiber; *2* — terminals of afferent nerve fiber; *3* — supporting (Schwann) cells; *4* — multilayered capsule; FC — fibrous capsule; N — nerves

These endings are seen in relation to the epithelial, lining of the skin, cornea, alimentary, and respiratory system. Free nerve endings in the epidermis terminate in the stratum granulosum. Such neuronal endings subserve multiple sensory modalities including fine touch, heat, and cold, without apparent

morphologic distinction. Networks of free dermal endings surround most hair follicles.

The most sensory nerve endings acquire connective tissue capsules or sheathes of varying complexity. They are called *encapsulated endings*. Structurally, they consist of a connective tissue capsule. The neural elements consist of a single or more myelinated fiber that enters the capsule, where they lost its myelin sheath and may branch (fig. 5, *b*, *c*). Many of these encapsulated endings are mechanoreceptors in the skin and joint capsules (tactile corpuscles of Meissner, Pacinian corpuscles, Ruffini endings, end bulb of Crause, Merkel discs etc).

Encapsulated sensory receptors are found in muscles (muscle spindles) and in the tendons (tendon organs), that provide information about the degree of tension in a muscle and its position.

THE EFFERENT NERVE ENDINGS

The efferent nerve endings are the contacts between the axon of an efferent neuron and target cells. There are two different types of efferent nerve endings:

– *motor endings*;
– *secretory (or secretomotor) endings*.

Each skeletal muscle fiber receives its own direct innervation. The axons of motor neurons that originate in the spinal cord or brainstem, are divide into terminal branches that end on individual muscle fibers. At the site of innervation, the nerve loses its myelin sheath and its terminal portion is covered by a thin cytoplasmic layer of Schwann cells. The site where the nerve ending comes into intimate contact with the muscle fiber is a **neuromuscular junction** or the **motor end plate** (fig. 6). Each neuromuscular junction has three major components:

1. The **presynaptic (neural) component** is the terminal bouton of the axon. The bouton contains numerous mitochondria and acetylcholine-filled synaptic vesicles. The part of the bouton's plasma membrane directly facing the muscle fiber is the *presynaptic membrane*.

2. Between the presynaptic membrane (axolemma) and postsynaptic membrane (sarcolemma) there is a narrow gap about 40 nm (**synaptic cleft**) occupied by various proteins that form a basal lamina. The *primary synaptic cleft* lies directly beneath the presynaptic membrane and communicates directly with a species of *secondary synaptic clefts* created by enfolding of the postsynaptic membrane.

3. The **postsynaptic (muscular) component** includes the *postsynaptic membrane* (sarcolemma) and the sarcoplasm under the synapse. The postsynaptic membrane contains acetylcholine receptors and is thrown into numerous deep junction folds. In the sarcoplasm below the folds lie several

nuclei and numerous mitochondria, ribosomes and glycogen granules, but there aren't synaptic vesicles.

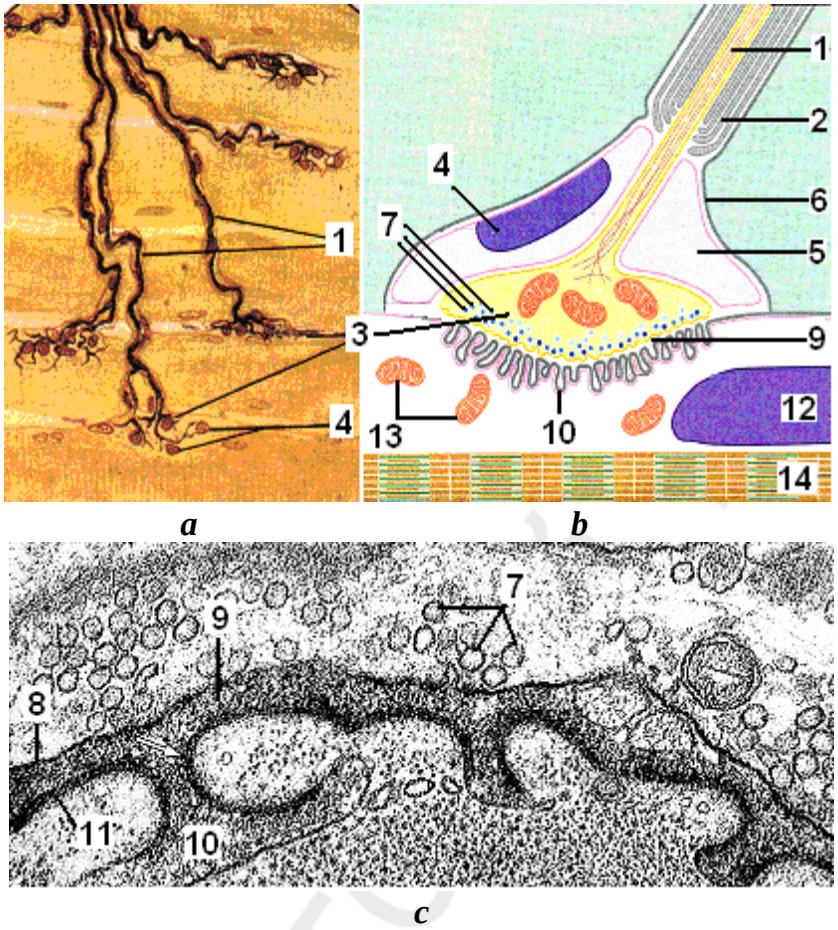


Fig. 6. Neuromuscular junction (motor end plate):
a — photomicrograph of silver stained preparation of a motor nerve and its final branches [12]; *b* — scheme of ultrastructure [9]; *c* — electron micrograph [10]: *1* — motor nerve axons; *2* — myelin sheath; *3* — terminal bouton of the axon; *4* — Schwann cell nucleus; *5* — Schwann cell cytoplasm; *6* — external lamina; *7* — synaptic vesicles; *8* — presynaptic membrane; *9* — primary synaptic cleft; *10* — secondary synaptic cleft; *11* — postsynaptic membrane; *12* — muscle cell nucleus; *13* — mitochondria; *14* — myofibril

When an action potential invades the motor end plate, acetylcholine is liberated from the axon terminal, diffuses through the cleft, and binds to acetylcholine receptors in the sarcolemma of the junction folds. Binding of the transmitter makes the sarcolemma more permeable to sodium, which results in membrane depolarization. The enzyme called acetylcholinesterase quickly breaks down the acetylcholine to prevent continued stimulation. It is necessary to avoid prolonged contact of the transmitter with receptors in the sarcolemma.

The single motor neuron may innervate from 1 to 2000 fibers. It was termed the **motor unit**. The motor nerve cell not only instructs the muscle cells to contract but also exerts a trophic influence on the muscle cells.

Smooth muscle is innervated by both sympathetic and parasympathetic nerves of the autonomic system. Its nerve fibers are usually unmyelinated. Elaborate neuromuscular junctions like those in skeletal muscle are not present in smooth muscle. Autonomic nerve axons terminate in a series of dilatations in a short distance away from the myocite surface. Terminal dilatations show the presence of vesicles with neurotransmitters and numerous mitochondria.

In sympathetic terminals the vesicles contain usually noradrenaline, in parasympathetic terminals they contain acetylcholine. Neurotransmitters released from the vesicles diffuse to the myocites, and bind to their receptors in the smooth muscle cell membrane which results in membrane depolarization. The flow of ions from neighboring cells through gap junctions can transmit the contraction stimulus from cell to cell in a wavelike pattern.

Apart from muscle effectors endings are present in relation to gland **secretary (secretomotor) endings**.

SYNAPSES

Neurons provide rapid communication between groups of serially disposed cells, permitting rapid transmission of information over long distances. Each neuron has, an average, at least a thousand interconnections with other neurons, forming a very complex system for communication. These interconnections between neurons are provided by means of **synapses**. Synapses are sites of functional contact (transmission of nerve impulses) between neurons or between neurons and effectors (target) cells (muscle and gland cells). Synapses are named according to the structures they connect, including:

- *axodendritic*, occurring between axons and dendrites;
- *axosomatic*, occurring between axons and the cell body;
- *axoaxonic*, occurring between axon and axon;
- *dendrodendritic*, occurring between dendrite and dendrite.

Most synapses transmit information by releasing chemical substances (messengers or neurotransmitters), and they are called **chemical synapses**. A chemical synapses transmits an impulse only in one direction. At some sites one cell may excite another without the release of a transmitter. At such sites adjacent cells have direct channels of communication (gap junction) through which ions can pass from one neuron to another altering their electrical status. Such synapses are called **electrical synapses**.

Electrical synapses are common in lower vertebrates and invertebrates. Few of them can be observed at some sites in the human brain. Electrical synapses transmit an impulse in two directions and without synaptic arrest.

A typical **chemical synapse** contains (fig. 7):

- *a presynaptic part (component)*;
- *synaptic cleft*;
- *a postsynaptic part (membrane).*

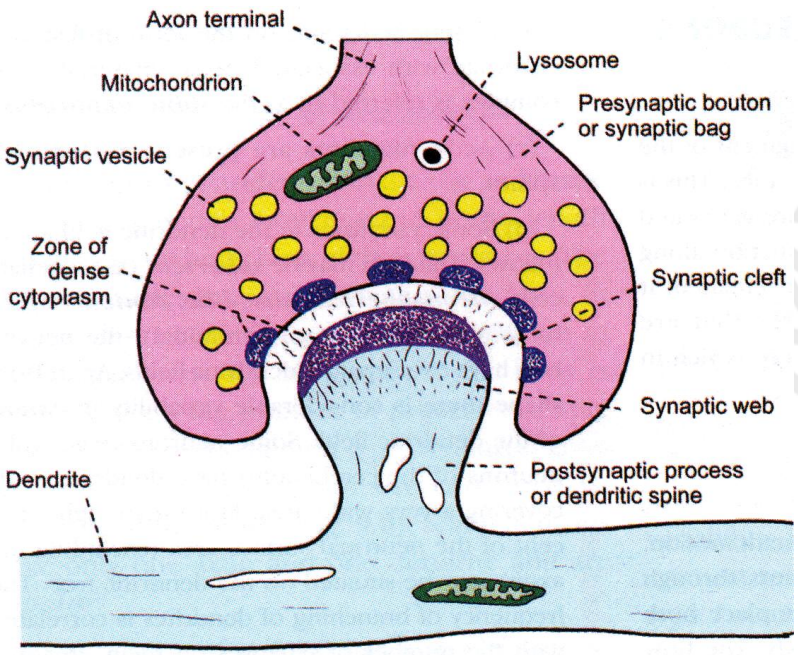


Fig. 7. Diagram showing the structure of a typical synapse as seen by EM [8]

The **presynaptic component**, the bouton terminal, is characterized by the presence of numerous synaptic membrane-limited vesicles with neurotransmitters, mitochondria and microtubules. Neurotransmitters are generally synthesized in the cell body; then they are stored in vesicles in the presynaptic region of a synaps. Some neurotransmitters are synthesized in the presynaptic compartment, using enzymes and precursors brought by axonal transport. Neurotransmitters are chemicals that, when combined with receptor protein either open or close ion channels or initiate second-messenger cascade. The most common neurotransmitters are acetylcholine, catecholamines (norepinephrine, epinephrine, dopamine and serotonin), neuroactive peptides (substance P, enkephalin, endorphin and others), and amino acids (γ-aminobutyrate, glutamate, aspartate and glycine).

Between the presynaptic and postsynaptic part there is a thin (20 to 30 nm) intercellular space called the **synaptic cleft**. This space content basal lamina material that binds the presynaptic and postsynaptic membrane together. Some clefts are traversed by dense filaments that link the membranes and perhaps guide neurotransmitters across the gap.

Postsynaptic membrane (component) contains receptors with which the messengers interact. The presynaptic and postsynaptic membranes are thicker than the membranes adjacent to the synapse. The thickened areas of membrane are active zone of a synapse. Neurotransmission takes place through this region.

Sequence of events during chemical synapse transmission. The events that take place during chemical synapse transmission are the following. Nerve

impulses that sweep rapidly (in milliseconds) along the cell membrane promote an explosive electrical activity (depolarization). This impulse briefly open, calcium channels in the presynaptic region, promoting a calcium influx that triggers the exocytose of synaptic vesicles.

The transmitter diffuses across the synaptic cleft. Receptors on postsynaptic membrane bind the neurotransmitter, causing the channels to open in that membrane, which allows ions to enter the neuron. This ion flux causes the voltage reversal (*depolarization*) in the postsynaptic membrane, thereby generating a second nerve impulse. These synapses are called **excitatory**. In some synapses the neurotransmitter-receptor interaction has an opposite effect, promoting *hyperpolarization* with no transmission of the nerve impulse. These are called **inhibitory synapses**. Thus, synapses can excite or inhibit impulse transmission and thereby regulate nerve activity.

The neurotransmitter released into the synaptic cleft acts only for a very short duration. They are removed quickly by enzymatic breakdown, diffusion, or endocytosis mediated by specific receptors on the presynaptic membrane. This removal of transmitters is functionally important because it allows the postsynaptic membrane to reestablish its resting potential and prevents an undesirable sustained stimulation of the postsynaptic neurons.

Finally, some chemical substances associated with synapses do not influence synaptic transmission directly, but influence the effects of transmitters. Such chemical substances are referred to as **neuromodulators**. These substances include vasoactive intestinal polypeptide (VIP), somatostatin, cholecystokinin and others.

NERVOUS SYSTEMS

OVERVIEW OF THE NERVOUS SYSTEM

Nervous system **(NS)** is the system of organs which consists of nervous tissue: nerve cells, with their processes, glial cells. All the organs of nervous system are parenchymal. Stoma contains blood vessels.

The main function:

– the NS enables the body to respond to continuous changes in its external and internal environments;

– it controls and regulates the functional activities of the organs and systems;

– it integrates the organs and organs system in the whole;

– it is a base for thinking.

Anatomically, the nervous system is divided into the following.

The central nervous system (CNS) consists of the brain and the spinal cord**,** located in the cranial cavity and spinal canal, respectively.

The peripheral nervous system (PNS) consists of:

– cranial, spinal and peripheral nerves that conduct impulses from or to CNS;

– spinal ganglion-collections of nerve cell bodies outside the CNS;

– specialized nerve endings.

Functionally, the nervous system is divided into the following.

The somatic nervous system (SNS) consists of somatic parts of the CNS and PNS. It provides sensory and motor innervations to all parts of the body except viscera, smooth muscle and glands.

The autonomic nervous system (ANS*)* consists of autonomic parts of the CNS and PNS. It provides efferent involuntary motor innervations to smooth muscle, the heart muscle and glands. Contraction of smooth muscle modifies the diameter or shape of tubular or hollow viscera. The ANS regulates the synthesis, composition and release of secretions. It also provides afferent sensory innervations from the viscera (pain and autonomic reflexes). The autonomic nerve system is subdivided into — sympathetic, parasympathetic and enteric.

MAIN PRINCIPALES OF THE ORGANIZATION OF NERVOUS SYSTEM

The neuron theory is a basis of the nervous system organization. The neuron theory, proposed in the latter part of the 19th century in opposition to the then prevailing view that nerve cells form a continuous reticulum or syncytium.

Statements of neuron theory.

The morphological basis:

– neuron is a structural, functional, genetic, trophic unit of the nervous system;

– anatomically neurons are separated from each other. Neurons interact with each other with help of synapses;

– neurons are the basis for pathology reactions.

The physiological basis:

– neuron is polar. Dendrites conduct the impulses to the cell body; axon conducts the impulses away from the cell body;

– neurons may be in the state of inhibition or excitation;

– interaction between neurons is **neuron integration**. Neuron integration occurs on basis of such processes as: *divergence* — when one neuron transmits impulses to several neurons; *convergence* — when one neuron receives impulses from several neurons. Neuron integration proposes the forming *nerve center*. The nerve center is structural and functional union of neurons. ***Synaptic transmission*** takes place here.

The nerve centers are divided into the nuclear nerve centers and the screen nerve centers.

The nuclear nerve center:

– neurons form a compact group;

– there are predominant processes of convergence from the afferent system;

– there is one type of neurons.

The nuclear nerve center is called ganglion in the PNS, and nuclear in the CNS.

The screen nerve center:

– neurons are situated regularly, by layers;

– there are predominant processes of divergence;

– there are functionally different types of neurons.

The main substrate of the nervous system is reflex arc. Several neurons connected by synapses form reflex arc.

The reflex arc is the chain of neurons and consists of:

1) receptor (dendrite of afferent neuron);
2) afferent neuron;
3) associative neuron;
4) efferent neuron;
5) efferent nerve ending (motor end plate).

The reflex arcs may be simple or complex. The simple arc consists of only two neurons. The complex contains three and more neurons. The reflex arcs may be somatic and autonomic (sympathetic and parasympathetic).

PERIPHERAL NERVE SYSTEM

SPINAL GANGLIA

The spinal ganglia are swellings on the dorsal roots of the spinal nerves situated in the intervertebral foramina. These ganglia contain the cell bodies of primary sensory neurons. The ganglion is covered on the outside by a connective tissue capsule. The neurons of sensory ganglion arrange in groups chiefly at the periphery of the ganglion. The groups of cells are separated by groups of *myelinated nerve* fibers. The neurons in this ganglion are of the pseudounipolar type. The spherical cell bodies vary from 20 to 100 μm. Their cytoplasm contains basophilic Nissl bodies that are dispersed. Their central nucleus is large and pale staining, and it commonly contains a single prominent nucleolus (fig. 8).

These ganglia are aggregations of many cell bodies of afferent somatic nerves, and afferent viscera nerves of the peripheral nerves system (PNS). The large neurons are for proprioception and discriminative touch; those of intermediate size are concerned with light touch, pressure; the smallest neurons transmit impulses for pain and temperature.

The cell body of each neuron is surrounded by a layer of flattened capsular cells or satellite cells (oligodendrocyte). Outside the satellite cells there is

a layer of delicate connective tissue. The peripheral process of each neuron forms an afferent fiber of peripheral nerves and terminates in sensory endings. The central process enters the spinal cord or brain through dorsal roots. The nerve impulse passes directly from peripheral to the central process, thereby bypassing the cell body. ***There is no nuclear center, therefore there is no synaptic station.***

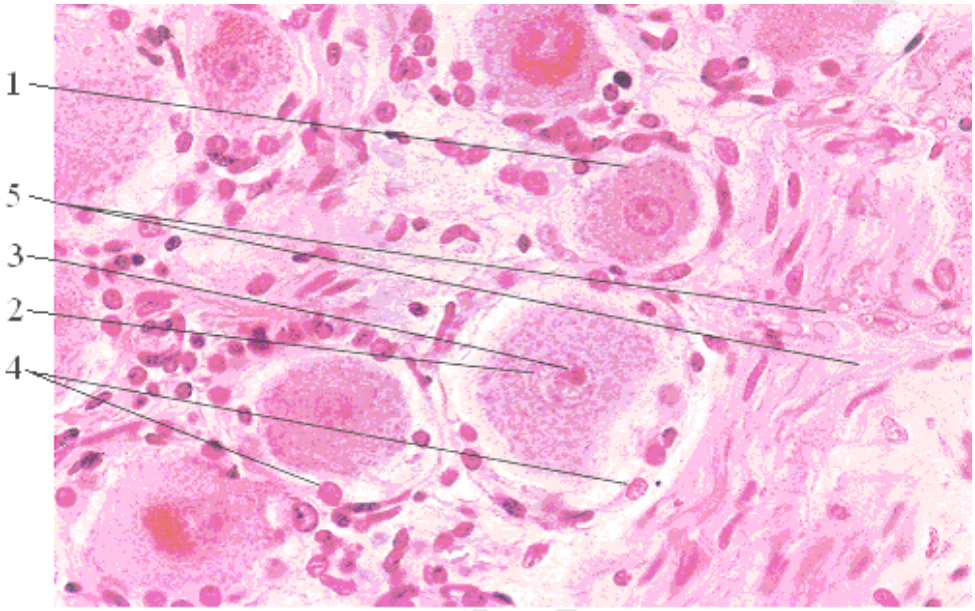


Fig. 8. Microphotograph of spinal ganglion stained by H&E, medium magnification [1]: *1* — pseudounipolar neurons; *2* — nucleus; *3* — nucleolus; *4* — satellite cells; *5* — nerve fibers

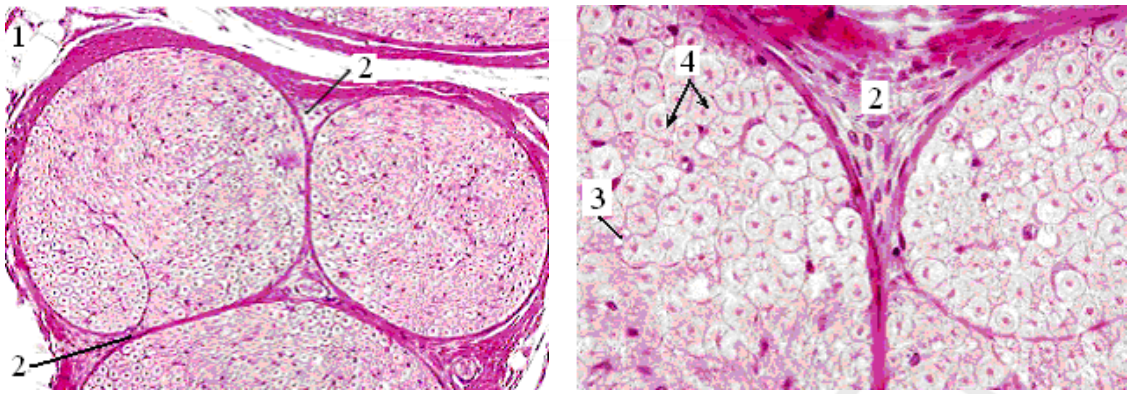
PERIPHERAL NERVES

Peripheral nerve is a bundle of nerve fibers held together by connective tissue. The nerves of the PNS are made up of many nerve fibers that carry sensory and motor (effector) information between the organs and tissues of the body and the brain and spinal cord. The nerve fiber may be formed by axon or dendrite with all of its coverings (myelin and Schwann cell). The cell bodies of peripheral nerves may be located within the CNS or outside the CNS in peripheral ganglia.

The constituent fibers of all but the smallest peripheral nerves are arranged in bundles or fascicules and three connective tissue sheaths are recognized (fig. 9).

The endoneurium includes loose connective tissue surrounding each individual nerve fiber.

The perineurium is the specialized connective tissue surrounding a nerve fascicle. The perineurium serves as a metabolically active diffusion barrier that contributes to the formation of a *blood-nerve barrier.*



a ***b***

Fig. 9. Microphotograph of peripheral nerve, cross-section, stained by H&E [**7**]:
a — medium magnification; *b* — high magnification: *1* — epineurium; *2* — perineurium;
3 — endoneurium; *4* — nerve fiber

The epineurium consists of dense irregular connective tissue that surrounds and binds nerve fascicles into a common bundle. Adipose tissue is often associated with the epineurium in larger nerve.

The nerves have their blood vessels in the epineurium and the perineurium. The endoneurium is poorly vascularized, metabolic exchange of substrates and wastes in this tissue depends on diffusion from and to the blood vessels through the perineural sheath.

AUTONOMIC NERVOUS SYSTEM

The autonomic nervous system is that portion of the NS that controls and regulates the body's internal environment. The ANS contains the central and peripheral parts. Peripheral part consists of peripheral nerves, peripheral ganglion (sympathetic and parasympathetic). Central part includes the nuclears in the gray matter of the spinal cord and the brain stem. Visceral innervation is accomplished by the afferent and efferent fibers of the ANS.

Sensory (afferent) fibers leave the organs to convey impulses to the CNS.

Visceral afferent neurons have the same arrangement as other sensory neurons and locate in the spinal ganglion.

The visceral efferent chain has two neurons: *preganglion and ganglion.* The visceral efferent fibers are divided into sympathetic and parasympathetic divisions of the ANS

Both division are composed of: a) efferent preganglionic fibers running from CNS to ganglion; b) ganglia; c) postganglionic efferent fibers from a ganglion to an innervated organ (fig. 10).

The smooth muscle and secretory cells of viscera as well as cardiac muscle, come under the dual influence of sympathetic and parasympathetic divisions of the autonomic nervous system. In some organs they are

functionally antagonistic to one another, and a delicate balance between them maintains a more or less constant level of visceral activity under conditions that usually prevail.

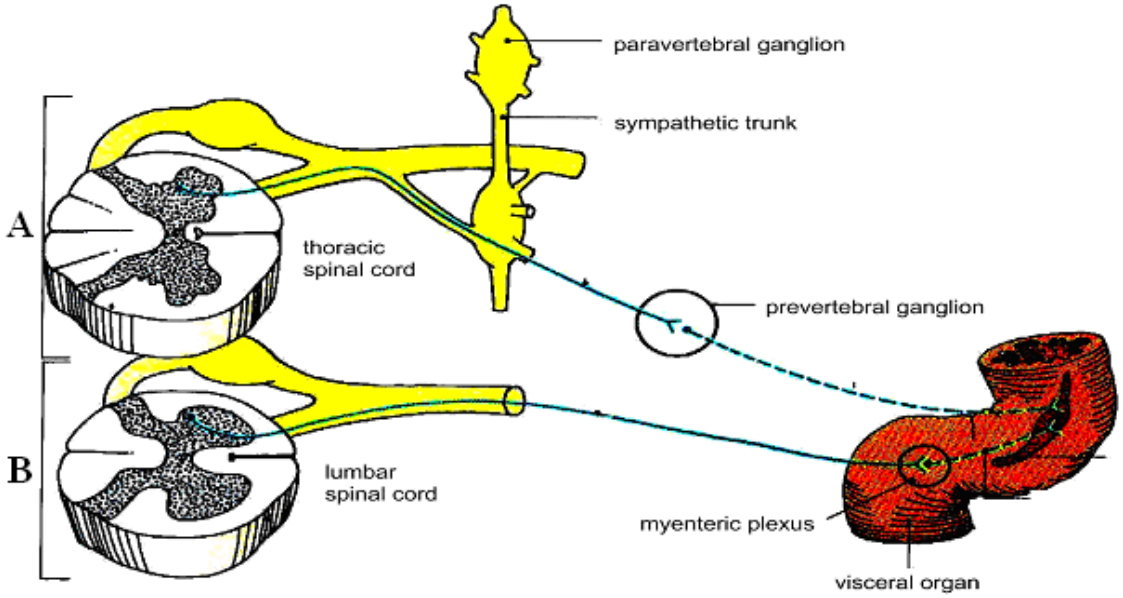


Fig. 10. Diagram of the autonomic reflex arcs — visceral efferent pathway [3]:
A — sympathetic reflex arc; *B* — parasympathetic reflex arc

Anatomical differences between sympathetic and parasympathetic reflex arcs are: 1) localization of preganglionic neurons; 2) position of the ganglion.

***Sympathetic reflex arcs*:**

1. Central sympathetic neurons (preganglionic neurons) are located in the *thoracic* and upper *lumbar* portions of the spinal cord (intermediolateral cell column).The preganglionic neurons are cholinergic.

2. This neurons send axons (preganglionic fibers) to the vertebral and paravertebral ganglia.

3. The ganglia in the paravertebral and vertebral sympathetic trunk contain the cell bodies of the effector neurons.

4. Axons of these neurons are the postganglionic efferent fibers and go to an innervated organ.

5. The preganglionic efferent fibers are short, the postganglionic efferent fibers are long.

6. Most of the principle neurons of sympathetic ganglion are *noradrenergic* at their peripheral synapses.

***Parasympathetic arcs*:**

1. The central parasympathetic neurons (presynaptic) are located in the brain stem (3, 7, 9, 10 nucleus of cranial nerves), in the sacral portion of the spinal cord. The preganglionic neurons are cholinergic as in sympathetic system.

2. They send axons (preganglionic fibers) to the ganglia in or near the wall of abdominal and pelvic organs.

3. This ganglion contains the cell bodies of the postsynaptic effector neurons.

4. Axons of these neurons are the postganglionic efferent fibers from ganglion to an innervated organ

5. The preganglionic efferent fibers are long; the postganglionic efferent fibers are short.

6. The chemical mediator at the synapses between postganglionic terminals and effector cells is *acetylcholine.*

AUTONOMIC GANGLIA

The autonomic ganglia are nuclear nerve center outside the CNS, where a presynaptic neuron makes contact with postsynaptic neurons.

The sympathetic autonomic ganglia are situated along vertebral column (paravertebral ganglion) or in the thorax, abdominal cavity (prevertebral ganglion). Each ganglion is surrounded by a dense, irregular collagenous connective tissue capsule with vascularized septa extending into its inferior. The parasympathetic ganglia (*terminal, intramural*) are located within or close to the structure they innervate

The multipolar nerve cells of autonomic ganglia are 20 to 45 μm in the diameter. The cytoplasm may contain some pigment granules, granular Nissl, eccentrically placed nucleus. The cell body is surrounded by satellite cells. The dendrites of neurons are several and are in synaptic contacts with terminal of preganglionic fibers. Each presynaptic neuron synapses with several postsynaptic neurons. The thin unmyelinated axon (group C fibers) takes the most convenient route to smooth muscle and gland cells in some viscera, to the heart, to the enteric plexus, to blood vessels, to sweat glands. The principal cells are all cholinergic in parasympathetic ganglia, but only a small proportion of them are cholinergic in sympathetic ganglia. Most of the principal cells of sympathetic ganglia are noradrenergic. All the neurons in autonomic ganglia also contain two or more peptides, which may serve as an additional neurotransmitter or as neuromodulator.

In addition to their principal cells, autonomic ganglia contain interneurons, small intensive fluorescent cells (SIF cells) with no axons. These cells of ganglia contain dopamine which they use as a transmitter.

THE ENTERIC NERVOUS SYSTEM

At the beginning of 19-th century Langley recognized the enteric nervous system, consisting of neurons contained within the walls of the alimentary canal, distinct from sympathetic and parasympathetic divisions. It was realized that well-coordinated peristaltic and related movements could occur **in the absence of any extrinsic innervation**.

From the esophagus to the rectum the walls of the human alimentary canal contain some 10^8 neurons, a population comparable to the number of neurons in the spinal cord. The cell bodies occur in two zones — the *myenteric plexus* (of Auerbach) lies between the longitudinal and circular muscle layers, and the *submucous* plexus (of Meissner) lies in the connective tissue between the circular muscle layer and the muscularis mucosa.

Each plexus consists of small groups of neurons with the groups joined to one another by thin nerves in which most of the axons are unmyelinated

Similar nerves connect the two plexuses across the circular muscle layer and carry branches from the plexuses into the smooth muscle and into the lamina propria of the mucosa (fig. 11).

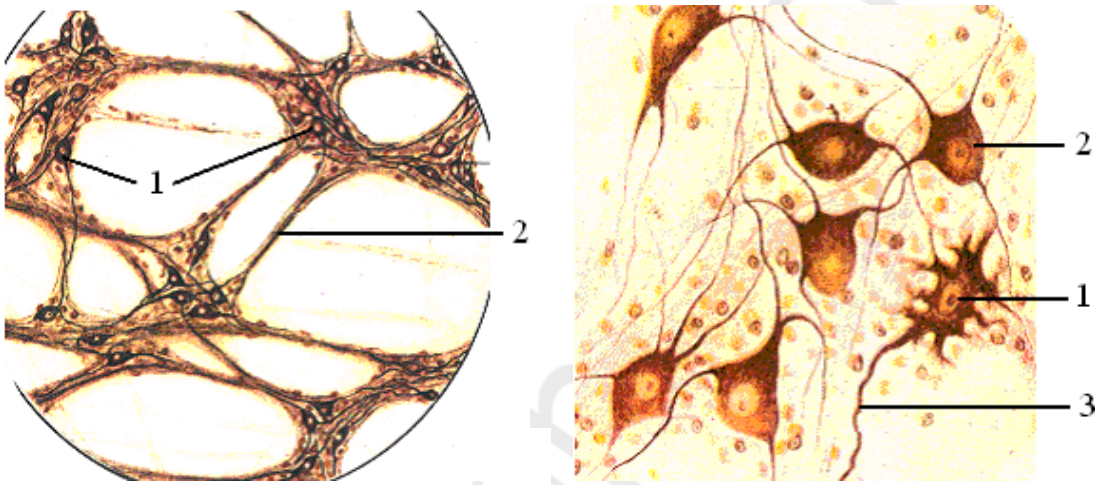


Fig. 11. Myenteric plexus, silver impregnation [11]:
a — low magnification: *1* — multipolar nerve cells; *2* — nerve fibers;
b — high magnification: *1* — efferent neuron ((I type Dogel); *2* — afferent neurons (II type Dogel); *3* — axon of efferent neurons

Most of neurons are multipolar, but there also many bipolar and unipolar ones. Multipolar neurons are efferent (I type Dogel). The bipolars are presumed to have sensory functions in initiating the peristaltic reflex. There are afferent neurons (II type Dogel). There are also interneurons within the plexuses (III type Dogel). The intrinsic neurons of the gut receive input from the sympathetic ganglia as well as from preganglionic parasympathetic neurons. The most enteric neurons contain acetylcholine and many different peptides. At least some of these substances serve as neurotransmitters.

CENTRAL NERVE SYSTEM

DEVELOPMENT OF THE CENTRAL NERVOUS SYSTEM

The central nervous system consists of the brain and spinal cord and develops from neural tube. Growth and differentiation occur to the greatest extent in the rostral portion of the neural tube, from which the large and complex brain develops. Three primary brain vesicles appear at the end of the fourth week: the *prosencephalon, mesencephalon, rhombencephalon***.** During the fifth week each of the first and third vesicles changes into five secondary brain vesicles (table 1).

Table 1

Development of the mature brain from the brain vesicles

Primary brain vesicles	Secondary brain vesicles	Mature brain
Prosencephalon	Diencephalon	Thalamus, epithalamus, hypothalamus, subthalamus
	Telencephalon	Cerebral hemispheres, consisting of the olfactory system, corpus striatum, cortex medullary center
Mesencephalon	Mesencephalon	Midbrain
Romboncephalon	Myelencephalon	Medulla oblongata
	Metencephalon	Pons and cerebellum

Tne central nervous system consists of gray matter and white matter. **Gray matter** contains the cell bodies of neurons, embedded in a neuropil made up of neuronal and glial processes. **White** matter consists mainly of long processes of neurons, the majority being surrounded by myelin sheaths. Both the gray and white matter contains large numbers of neuroglial cells and network of blood capillaries.

In some parts of the central nervous system, notify the brain stem (medulla, pons, midbrain) there are regions that contain both nerve cell bodies and numerous myelinated fibers. These regions are therefore an admixture of gray matter and white matter.

The CNS is protected by the skull and vertebrae and is surrounded by three connective tissue membranes called *meninges* — dura mater, arachnoid layer, pia matter. The dura mater is the outermoust layer and is formed by thick sheet of dense connective tissue. The arachnoid is a delicate sheet of connective tissue adjacent to the inner surface of the dura. The pia matter lies directly on the surface of brain and spinal cord. It is also a delicate connective tissue layer and is continuous with the perivascular connective tissue sheath of the blood vessels of the brain and spinal cord. Both surfaces of the arachnoid, the inner surface of the pia matter are coved with a thin squamous epithelial layer.

SPINAL CORD

The spinal cord is a flattened cylindrical structure that is directly continuous with the brain. As seen in transverse section the spinal cord has a gray and white matter.

The spinal cord is developed from the caudal cylindrical part of neural tube. The wall of the tube is subdivided into the matrix cell or ependymal layer, the mantle layer, the marginal layer (fig. 12).

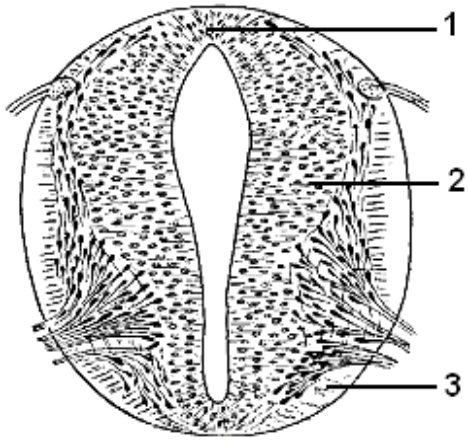


Fig. 12. Scheme of development spinal cord [3]:
1 — ependymal layer; *2* — mantle layer; *3* — marginal layer

The ependymal layer also called matrix cell layer gives rise to nerve cells, to neuroglia cells and germinal cells. There are ependymal cells in adult.

The mantle layer contains the developing nerve cells and neuroglia in embryogenesis. In adult the mantle layer forms the gray matter.

The marginal layer contains no nerve cells. It consists of a reticulum formed by protoplasmic processes of developing neuroglial cells. In adult there is white matter.

The white matter contains only nerve fibers traveling to and from other parts of the spinal cord and to and from brain. The white matter consists of three funiculus – dorsal, lateral and ventral. Each funiculus contains tracts of ascending and descending fibers. Functionally related bundles of axons in the white matter are called ***tracts***.

The gray matter has a roughly H-shape or butterfly outline. The gray matter contains neuronal cell bodies and their dendrites, along with axons and neuroglia.

It has been found that cells of the same type are usually clustered together into groups. Functionally related groups of nerve cell bodies in the gray matter are called ***nucleus***. Synapses occur only in the gray matter because the architecture of the spinal gray matter is essentially the same along the length of the cord, the populations of similar neurons occur in long

columns. When viewed in transverse sections of the cord many of the cell columns appear as layers, especially within the dorsal horn. Ten layers of neurons are recognized, and known as the *lamina of Rexed.*

There are three main categories neurons in the spinal gray matter.

1. The smallest cells involved in local circuitry are the ***interneurons.***

2. ***Motor cells*** of the ventral horn supply the skeletal musculature and consist of alpha and gamma motor neurons. The cells of the lateral horn and the sacral autonomic nucleus are preganglionic neurons of sympathetic and parasympathetic of the autonomic system.

3. The cell bodies of the ***tract cells***, whose axons constitute the ascending fascicules of the white matter, are located mainly in the dorsal horn.

The gray matter on each side consists of dorsal (posterior) and ventral (anterior) horns and lateral horns (intermediated zone).

Anterior horns are usually short and broad. Cell bodies of somatic efferent neurons are located here. They are multipolar, large, star-shaped, have a prominent central vesicular nucleus. There are alpha motor neurons and smaller gamma motor neurons. The alpha motor neurons supply the ordinary fibers of striated skeletal muscles. The gamma motor neurons are less numerous; they supply the intrafusal fibers of the neuromuscular spindles. The axons of the efferent neurons form the ventral root, becomes a component of the spinal nerve of that segment. The surface of both motor neurons types are densely covered with presynaptic boutons, which release either excitatory or inhibitory transmitter substances.

Posterior horns are long, narrow. They contain fibers, nerve cell bodies and neuroglia cells. The horns receive direct endings of somatic and visceral afferent fibers coming from the dorsal roots of the spinal nerves. These nerve fibers may synapse directly with motor neurons in the anterior columns or with interneurons, which then synapse with motor neurons. Axons of this neuron also may form the ascending fascicules of the white matter.

Lateral horns are present in the lower cervical, thoracic, and upper lumbar regions of the spinal cord. They contain nerve cell bodies of the visceral efferent neurons of sympathetic division of the ANS. The nerve cell bodies are smaller than the somatic motor neurons. The myelinated axons (preganglionic fibers) of these neurons leave the ventral root and enter the sympathetic ganglia.

BRAIN CORTEX

This region of the brain is concerned with memory, consciousness, intelligence, interpretation of sensatation, thinking.

Each cerebral hemisphere has a mantle of gray matter, the cortex, with a characteristic structure that consists of nerve cells and nerve fibers arranged in layers.

The cerebral cortex varies in hystological structure and thickness, depending on the region of the hemisphere.The square of the brain cortex is 2200 cm^2, the total volume of the brain is 300 cm^3. The number of cortical neurons is enormous $2{,}6 \times 10^9$–14×10^9.

All neurons of the cortex are multipolar. They are divided into two groups: **pyramidal and no-pyramidal**.

Pyramidal cells range in height from 10 to 50 μm for most cells. The other is giant pyramidal cells also known as Betz cells with cell bodies up to 100 μm high.

The cell body is triangular, with its apex directed to the surface of the cerebral cortex. The basophilic cytoplasm contains prominent Nissl substance and large round vesicular nucleus. A large apical dendrite extends from the apex of the cell and branches as it approaches the upper cortical level. Several lateral dendrites extend horizontally from the lower portion of the cell body and usually branch immediately. The axon arises from the base of the cell and may terminate in the deep cerebral cortex or extend into medulla.

The pyramidal cells are present in II, III, IV, V layers (fig. 13).

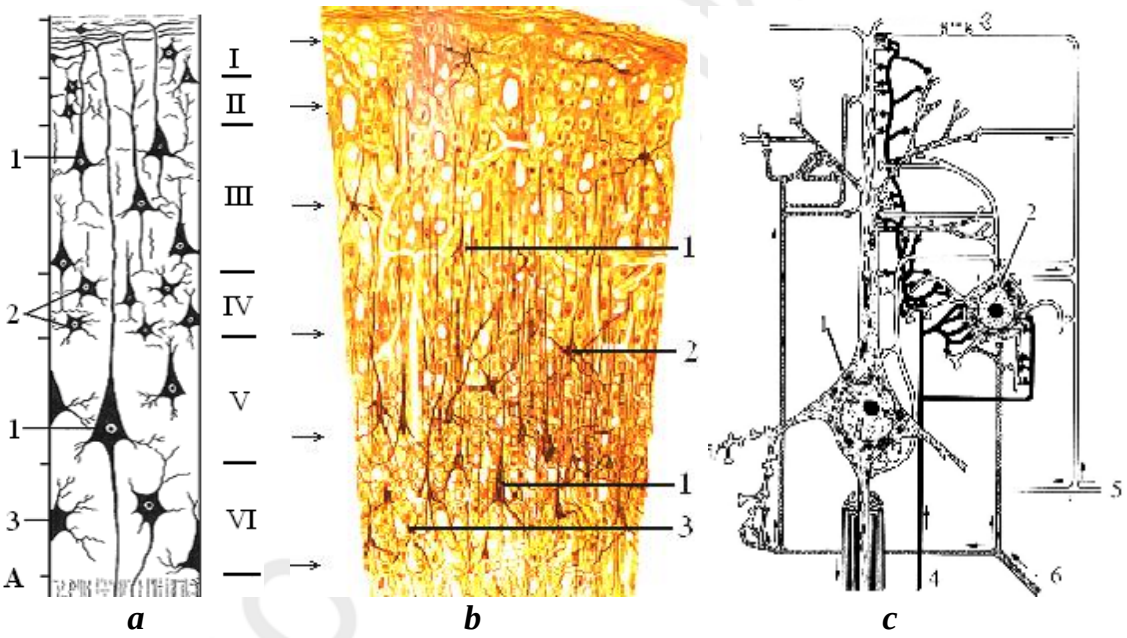


Fig. 13. Cerebral cortex:
a — schematic drawing of cortical layers; *b* — microphotograph , silver impregnation; *c* — schematic drawing of afferent fibers of cortex [10];
I — molecular layer; II — external granular layer; III — external pyramidal layer; IV — internal granular layer; V — internal pyramidal layer; VI — multiform layer;
1 — pyramidal neuron, *2* — stellate cell, *3* — fusiform cell, *4* — projection fiber; *5* — association fiber, *6* — commissural fiber

No-pyramidal cells are found in all layers of the cerebral cortex.

Stellate cells also known as granule cells are the most numerous. *Fusiform* cells are located in the deepest layer of the cortex. The identifying feature of the cell *Martinotti* is that the axon is directed toward the surface of the cortex. *Horizontal cells of Cajal* are restricted to the most superficial layer.

The pyramidal and fusiform are principal cells with widely spreading dendrites and long axon. The other types are interneurons.

The cortex is nervous center of plane (screen) type, that's why all structures are located in different layers (fig. 13). The specifity of neurons pericarions organisation calls **cytoarchitecture.**

Brain cortex has 6 horizontal layers. The layers, starting at the surface and ommitting regional differences for the present are as follows.

1. Molecular layer contains many neuroglia cells, few neurons of the granular and horizontal cells of Cajal. This layer consists predominantly of delicate neuronal processes — dendrites and axons. Most of dendritic branches come from pyramidal cells. The axons originate in cortex elsewhere in the same hemisphere, in that of the opposite hemisphere and in the thalamus.

The molecular layer is essentially a synaptic field of the cortex.

2. External granular layer contains a great many small pyramidal cells and stellate cells. The dendrites of these cells extend into the molecular layer; most of the axons terminate in deeper layers. The external granular layer makes an important contribution to the complexity of intracortical circuits.

3. External pyramidal layer contains mainly medium and large sized pyramidal cells**,** some Martinotti, granule cells. Apical dendrites extend into the layer 1; axons of pyramidal cells enter the white matter as projection, association or commissural fibers

4. Internal granular layer contains small granule cells, some small pyramidal cells. The fibers originating in the thalamus form the synapses on this type of cells. Many myelinated fibers occur in this region.

5. Internal pyramidal layer contains mainly large pyramidal cells (Betz cells), some granule cells, some Martinotti cells. The axons of the pyramidal enter the medulla as projection and association fibers.

In the motor cortex, the axons of the giant pyramydal cells form some of the fibers in the corticospinal tract.

6. Multiform layer contains fusiform cells, some small granule cells, some large granule cells. Axons of fusiform cells are included among the projection, commissural and association fibers in the white matter of the hemisphere.

The granule layers (II and IV) are predominent in the visual area, auditory and general sensory areas. This type of cortex is called ***granular cortex***.

Layers III, V and VI are predominent in the primary motor and premotor areas of the frontal lobe. This type of cortex is called ***agranular cortex***.

The cerebral cortex is divided into cytoarchitectural areas based on differences in the thickness of individual layer, neuronal morphology in the layers and the details of nerve fiber lamination. The few investigators hoped to established bases for structural and functional correlation. Brodmann's map, which was published in 1909 and consists of 52 areas, remains the most widely used map of cortical cytoarchitectural areas.

Mieloarchithecture is the specifity of nerve fibers organization. Nerve fibers within the neocortex are seen to accumulate in radial bundles and tangential bands. The radial bundles are close together; they include axons of pyramidal and fusiform cells leaving the cortex. The tangential bands consist largely of collateral and branches of afferent fibers. The most prominent tangential bands are the *outer and inner lines of Baillarger,* located in layer 4 and in the deep portion of layer 5 respectively. They run parallel to the surface for some distance and making synaptic contacts with large numbers of cortical neurons. Tangential bands consist largely of collateral and terminal branches of afferent fibers.

Cortical neurons are connected with other neurons in three ways (fig. 13, *c*).

Association fibers establish connection with cortical nerve cells in the same hemisphere.

Projection fibers (thalamo-cortical fibers) connect brain cortex with nuclei of underlying brain regions, such as the corpus striatum, thalamus, brain stem or spinal cord.

Commissural fibers connect both brain hemispheres.

The functional and structural unit of brain cortex is ***module*** or ***column***. It is organized functionally as minute vertical units that include nerve cells of all layers. All neurons in the units are activated selectively *by the same peripheral stimulus.* Each unit is 300 μm in diameter, whose height is the thickness of the cortex.

The module consists of 3 parts. *Entrance* is afferent fibers lying in the center of column. Afferent fibers originate in the same or opposite hemisphere or come from thalamus, making synapses on interneurons.

Zone of information processing includes several hundred neurons of all cortex layers.

Exit is composed by axons of pyramidal cells or fusiform cells (cortical efferent fibers) which going to the nearby cortex regions (association fibers), to another brain hemispheres cortex (commissural fibers) and than to the other parts of the brain.

CEREBELLUM

The functions of this structure are the coordination of motor movement, the maintenance of equilibration.

Anatomically the cerebellum is divided into two lateral hemispheres by a medium vermis.

The paired inferior, middle and superior cerebellar peduncles, composed of nerve fibers, connect the cerebellum with the medulla, pons, midbrain, respectively.

The cerebellum consists of:

1) a cortex or surface layer, of gray matter containing in transverse folds or folia;

2) a medullary center of white matter;

3) four pairs of central nuclei imbedded in the medullary center.

Cortex of cerebellum. Three layers are evident on histological section. From the surface to the white matter of the folium there is a molecular layer, the layer of Purkinje cells, the granular cell layer (fig. 14).

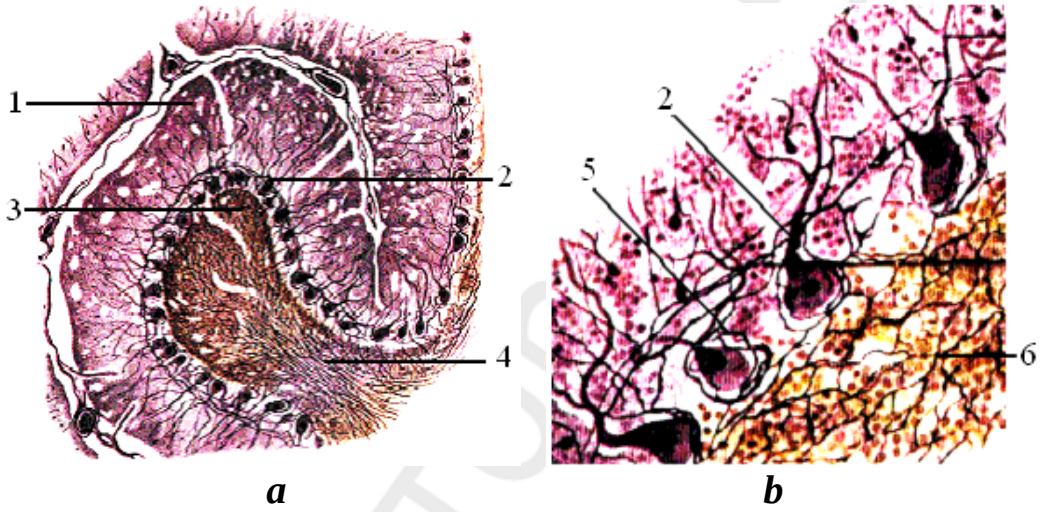


Fig. 14. Microphotograph of cerebellum, silver impregnation [10]:
a — low magnification; *b* — high magnification: *1* — molecular layer; *2* — Purkinje cell layer; *3* — granule cell layer; *4* — white matter; *5* — basket around of Purkinje cell; *6* — mossy fibers

The molecular layer contains relatively few nerve cells. *Basket* cells are scattered in the molecular layer near the bodies of Purkinje cells. *Stellate* cells are scattered in the superficial part of the molecular layer.

The dendrite of the basket cell branches in the transverse plane of the folium, receiving synaptic contacts from many granule cell axons.

The axons of the basket cell are directed across the folium and form characteristic synapses with about 250 Purkinje cells. Each collateral branch forms a basketlike arrangement around the cell body of a Purkinje cell.

Dendrites of the stellate cells are contacted by axons of granule cells. Axons of stellate cells synapse mainly with Purkinje cell dendrites.

The molecular layer is a synaptic layer made up of profusely branching dendrites of Purkinje cells and axons of granule cells in the deepest layer.

The Purkinje cell layer consists of a single row of bodies of Purkinje cells. The number of Purkinje cells is about of 15 million. These cells are easily recognized by their flask-shape cell bodies. Their dendrites enter the molecular layer and form synaptic junctions with parallel fibers. Each collateral branch of basket cell forms a basketlike arrangement around the cell body of a Purkinje cell.

The granule cell layer consists of closely packed small neurons — granule cell, from which axons extend into the molecular layer. Each cell has a spherical nucleus. The short dendrites have clawlike endings that are contacted by mossy fibers.

The unmyelinated axon of small granular cells enters the molecular layer where it bifurcates and runs parallel with the folium — *parallel fibers.* These axons also synapse with dendrites of stellate, basket and Golgi cells in the molecular layer.

The *Golgi cells* are situated in the outer portion of the granule cell layer and their dendrites extend into the molecular layer, where they are contacted by parallel fibers.

The afferent fibers to the cortex are:

– mossy fibers terminate in synaptic contact with granule cells;

– climbing fibers enter the molecular layer and wind among the dendrites of Purkinje cells.

The only fibers leaving the cortex are axons of Purkinje cells. These fibers terminate in central nuclei of the cerebellum.

Large proportion of the afferent fibers to the cerebellum are mossy fibers that terminate in synaptic relation with dendrites of granule cells.

The synaptic configuration that includes:

– the rosette of mossy fibers;

– dendrites of granule cells;

– the axon of Golgi cells.

This structure is known as a glomerulus or rosettes of the cerebellum (fig. 15).

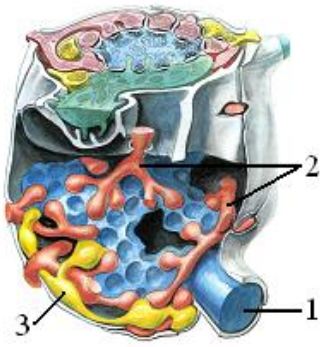


Fig. 15. Glomerulus of the cerebellum [7]:
1 — the rosette of mossy fibers; *2* — the dendrites of granule cells; *3* — the axon of Golgi cells

Intracortical circuits. The excitement pathway:

Mossy fiber → Granular cell → Its axon → Contact with dendrites of Purkinje cell → Purkinje cell body → Neurons of cerebellum nuclei. Synapses between mossy fibers and granule cells, granule cells and Purkinje cells are excitotary.

Suppressive pathway:

Mossy fiber → Granular cell → Its axon (parallel fibers) → Dendrites of stellatar and basket cell → Their bodies → Synapses of these cells on Purkinje cells → Purkinje suppression (fig. 16). Synapses between stellate, basket cells and Purkinje cells are inhibitory.

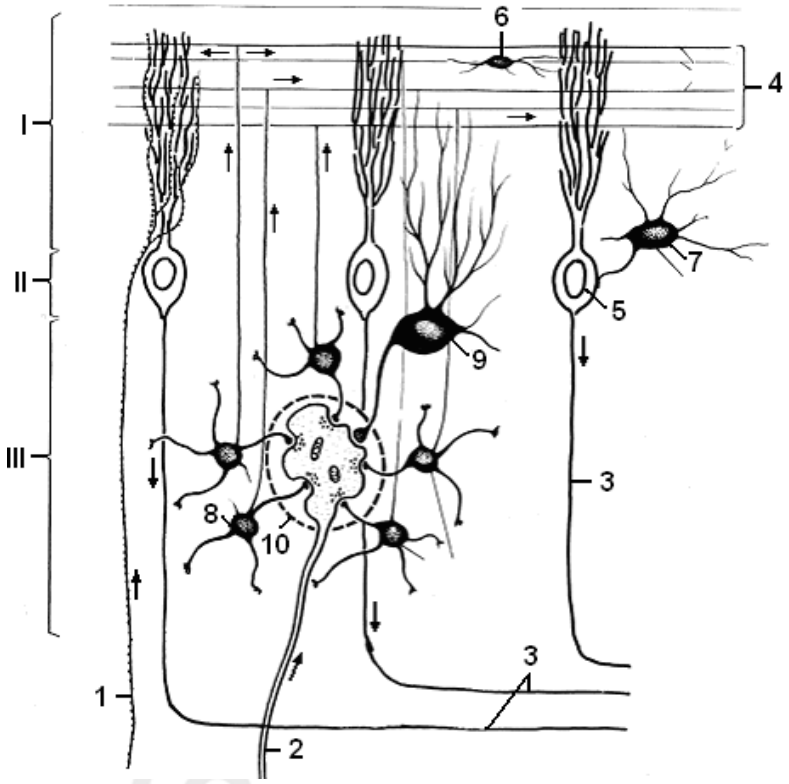


Fig. 16. Schematic drawing of the cerebellum illustrating cell and fiber arrangement and direction of nerve impulses [1]:
I — molecular layer; II — Purkinje cell layer; III — granule cell layer:
1 — climbing fiber; *2* — mossy fiber; *3* — axons of Purkinje cell; *4* — parallel fibers; *5* — Purkinje cells; *6* — stellate cells; *7* — basket cells; *8* — granule cells; *9* — large stellate cell (Golgi cell); *10* — glomerulus

The input to the cortex is excitatory. However this is modified by intracortical circuits that inhibit Purkinje cells and therefore suppress transmission from cortex to the central nuclei. Only *small granular cells are excitatory cells.* Golgi cells, basket, stellate cells and Purkinje are inhibitory cells.

TEST FOR CONTROL

1. What are the embryonic sources of nerve tissue?

a) mesenchyme;
b) ventral mesoderm;
c) neuroectoderm;
d) endoderm.

2. Call the structural components of nerve tissue:

a) neurons;
b) neuroglia;
c) ground substance;
d) collagen and elastic fibers.

3. What structures does form the basophilic substance (Nissl's bodies) of neuron's cytoplasm?

a) rough endoplasmic reticulum;
b) microtubules;
c) Golgi complex;
d) smooth endoplasmic reticulum.

4. The nerve cell has 5 processes. How many axons and dendrites it has?

a) 4 dendrites and 1 axon;
b) 3 dendrites and 2 axons;
c) 2 dendrites and 3 axons;
d) 1 dendrite and 4 axons.

5. What cells belong to the macroglia?

a) ependymal cells;
b) astrocytes;
c) oligodendrocytes;
d) big neurons of brain cortex;
e) glial microphages.

6. What structures of nervous tissue form the nerve fibers?

a) oligodendrocytes;
b) microglia;
c) fibrous astrocytes;
d) protoplasmic astrocytes;
e) processes of nerve cells.

7. What nerve endings call receptors?

a) Meisner's bodies;
b) Fater–Pachini corpuscle;
c) neuromuscle spindle;

d) neuromuscle synapses (motor plates);
e) axodendritic synapses.

8. Posterior horn of spinal cord contains:
a) motor neurons;
b) sensory neurons;
c) associative (intermediate) neurons;
d) autonomic nuclei.

9. Where do the sympathetic nerve centers localize in the spinal cord?
a) in anterior horns;
b) in white matter;
c) in lateral horns of thoracic and lumbar part of spinal cord;
d) in prevertebral ganglions.

10. Where do the sensory neurons localize?
a) in spinal ganglions;
b) in posterior horns of spinal cord;
c) in intramural ganglions;
d) in white matter.

11. Peripheral nerves are composed of:
a) nerve fibers;
b) epineurium;
c) nerve body;
d) endoneurium;
e) perineurium.

12. The cytoarchitecture of brain cortex is:
a) regular localization of neuroglia;
b) regular localization of Bets cells;
c) regular localization of nerve fibers;
d) localization of the cortex's neurons.

13. The following statements regarding the granular type of the cerebral cortex are true:
a) contains a well-developed external granular layer;
b) contains a well-developed internal granular layer;
c) is characteristic of the sensitive areas of the cortex;
d) contains a well-developed internal pyramidal layer.

14. The following statements regarding column (module) of brain cortex are true:
a) myeloarchitecture of the brain cortex;
b) structure-functional unit of brain cortex;
c) the groups of neurons of brain cortex, which worked together and localized surround the afferent nerve fiber;

d) cylinder, which include all layer of brain cortex, 300 microns in diameter.

15. What structures does the gray matter of the brain compose?

a) the bodies of neurons and glial cells;
b) nerve fibers;
c) glial cells only;
d) blood vessels.

16. What parts of the brain have "screen type" organization of neurons?

a) brain cortex;
b) cerebellum cortex;
c) brain stem;
d) hypothalamus.

17. What structures form the synapses with Purkinje neurons?

a) axons of granular neurons;
b) dendrites of stellate neurons;
c) climbing fibers;
d) mossy fibers;
e) axons of stellate neurons.

18. Each of the following statements concerning cerebellar cortex is true, except:

a) its molecular layer contains stellate and basket cells;
b) lacks blood vessels;
c) its granular layer contains granule cells and Golgi cells;
d) its middle layer contains Purkinje cells;
e) contains protoplasmic astrocytes, oligodendrocytes and microglia.

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