Ministry of Health of Ukraine

Ukrainian Medical Stomatological Academy

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PHYSIOLOGY

MODULE 1: "GENERAL PHYSIOLOGY AND HIGH INTEGRATED FUNCTIONS"

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SECOND EDITION

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"УКРАЇНСЬКА МЕДИЧНА СТОМАТОЛОГІЧНА АКАДЕМІЯ"

Кафедра фізіології

Т.М.Запорожець, М.В.Рудь, Т.А.Сухомлин

ФІЗІОЛОГІЯ

МОДУЛЬ 1: "ЗАГАЛЬНА ФІЗІОЛОГІЯ ТА ВИЩІ ІНТЕГРАТИВНІ ФУНКЦІЇ"

НАВЧАЛЬНИЙ ПОСІБНИК ДЛЯ СТУДЕНТІВ ВИЩИХ МЕДИЧНИХ НАВЧАЛЬНИХ ЗАКЛАДІВ

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Навчальний посібник для студентів стоматологічних та медичних факультетів вищих медичних навчальних закладів. Основне призначення навчального посібника - вивчення фізіології збудливих тканин, нервової регуляції функцій організму, ролі ЦНС у регуляції рухових функцій, фізіології сенсорних систем, автономної та гуморальної регуляції та фізіології ВНД студентами-іноземцями з англомовною формою навчання.

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The tutorial book is addressed to English-speaking students in medical and dental faculties of High Medical Educational Establishment of Ukraine. The manual contains theoretical material and material for practical classes, questions for students' self-preparing in such content modules as excitable tissues physiology, organism functions nervous regulation, CNS role in motor functions regulation, sensory systems physiology, autonomic nervous system and endocrine glands role in visceral functions regulation.

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Approved by the Academic Council of the Ukrainian Medical Dental Academy, the journal №10 from 20.06.2018.

Contents

MODULE 1. General physiology, CNS physiology, higher integrative functions.

Content module 1: Introduction in physiology.

Lesson 1. Physiology subject and tasks. Physiological investigations methods. Excitability. Excitation. Irritation laws.

Before performing this lesson, you should study the introductory material presented here.

1. Lecture course.
2. Moroz V.M., Shandra O.A. Physiology. - 2011. Unit 1, Chapter 1.
3. Guyton A.C., Hall J.E. Textbook of Medical Physiology. - 2006. Unit 1

Relevance of the topic.

Human and animals' organism has the highest ability to adapt to the constantly varying conditions of external and internal medium. In the basis of adaptive organism reactions lies the universal property of alive tissue - irritability.

1. Objectives:

To know: excitable tissues physiological investigative methods; excitable tissues main features and activity laws; electrical current usage advantages.

To be able to: make nervous-muscular preparation, use electrical stimulation and contraction registration.

2. Topic content.

Irritability - the ability to respond to the irritating factors action by metabolism change. The irritability is evolutionarily the ancient form of tissues reaction. During evolution gradual differentiation of tissues participating in adaptive organism activity has taken place. The irritability in these tissues has reached the best expression and has received the name an excitability.

The **excitability** is an ability of a tissue to respond to an irritation specialized, single mindedly and with the biological maximal velocity.

Excitation – is a complex (complicated) process expressing by response reaction to an irritation.

A nervous, muscular, epithelial secretory tissue **(excitable tissues)** have an excitability. The specialized form of response reaction is an excitation process physiological display. A contraction will be a response reaction in any muscular tissue. At a nervous tissue it will be an impulse conduction. At a secretory tissue it will be a synthesis and allocation of biologically active substance.

The excitability of tissues is various. A measure of an excitability is the **threshold** of stimulation – minimal stimulus force, capable to cause excitation. The **stimuli** with a size that is less than a threshold one, are called **subliminal** ones. The stimuli, on force exceeding a threshold of stimulation are called **suprathreshold** ones.

All stimuli can be divided into three groups: physical, chemical and physico-chemical.

Physical stimuli - mechanical, temperature, light, sound and electrical ones.

Chemical stimuli - acid, alkalis, medicines.

Physical-chemical stimuli –osmotic pressure, pH, ion structure changing.

Besides, they distinguish **biological** stimuli - hormones, vitamins and other biologically active substances. They allocate also a group of **social** stimuli - a word.

All stimuli divide on adequate and inadequate on biological value.

Adequate stimuli are such stimuli, acting to the given biological structure under natural conditions and to perception of which it is adjusted specially (e.g., for eye retina photoreceptors the seen part of light is an adequate stimulus).

Non-adequate stimuli are such, to perception of which the given structure is not adjusted specially (e.g., for a skeletal muscle the adequate stimulus is the nervous impulse, but it can contracts at a mechanical impact too).

Between the irritation character and the answer-back reaction of an alive tissue there are close mutual relations, which find expression in the irritation laws.

Irritation force law: the more force of an irritation, the more strong is answer-back reaction (up to known limits). The further stimulus force augmentation any more does not lead to the answer-back reaction increasing, and even can cause return reaction, down to its disappearance. It is explained by the fact that each functional unit of tissues (for example, muscular) has its exaltation threshold. That's why while working the threshold stimulus, those fibers, for which this stimulus is of a such size are only involved in the answer. Others do not react.

At stimulus force augmentation the new fibers are involved, for which the given stimulus is a threshold etc. Further, when the stimulus force will exceed the opportunities of all fibers of the given tissue, its answer-back reaction to the force augmentation will not change (the resources are settled!). Such stimuli, which cause the maximal answer-back reaction, are named in physiology maximal or optimal. At the even greater stimulus force augmentation the answer-back reaction even will

decrease, as at such a stimulus force the separate functional fibers of excitable tissues even can be injured. In a result, the answer-back reaction decreases and this phenomenon in physiology is named pessimum, and the stimuli causing it - pessimal.

The law "nothing" or "everything" ("all" or "none") is shown, first of all, at the cardiac muscle work analysis. According to this law, subliminal stimuli, acting to a cardiac muscle, do not cause an answer in it (it is "nothing"), and threshold and suprathreshold stimuli cause answer-back reaction of the same size (it is named "everything"). Under the same law the functional unit of any excitable tissue works. Let's take, for example, a muscular fiber and we shall imagine, that threshold stimulus at it is 2V (electrical current strain or voltage). If we act the stimulus of 1V to it, we naturally shall not receive any reaction ("nothing"), and if we take the stimulus of 4V, the muscle will give the same answer-back reaction, as well as on 2V ("all"). Naturally, "nothing" and "everything" are relative concepts, as at the subliminal stimulus action there is a local answer (local potential), therefore it already cannot be treated as "anything".

The law of force-time – with of a stimulus force it is required less time of its influence to tissue for answer-back reaction reception. The relation between the duration and force can be expressed by the augmentation hyperbolic curve, the both branches of which go at any stage in parallel to axes of coordinates. This last circumstance forms the basis that the stimuli of a very small size (less than the threshold) cannot cause the answer-back reaction.

The excitability curve demonstrates the exact relationship between the strength and the duration of a stimulus. So, it is also called the strength—duration curve (Fig. 1).

Characteristic Features of the Curve

The shape of the curve is similar in almost all excitable tissues. Following are some of the important points to be studied in the excitability curve:

- Rheobase: This is the least possible, i.e. minimum, strength (voltage) of stimulus which can excite the tissue. The voltage below this cannot excite the tissue, whatever may be the duration of stimulus.
- Useful time: It is the minimum time required for a rheobase strength (threshold strength) to excite the tissue (1).
- Chronaxie: It is the minimum time, at which a stimulus with the double rheobase (2) strength (voltage) can excite the tissue (3).

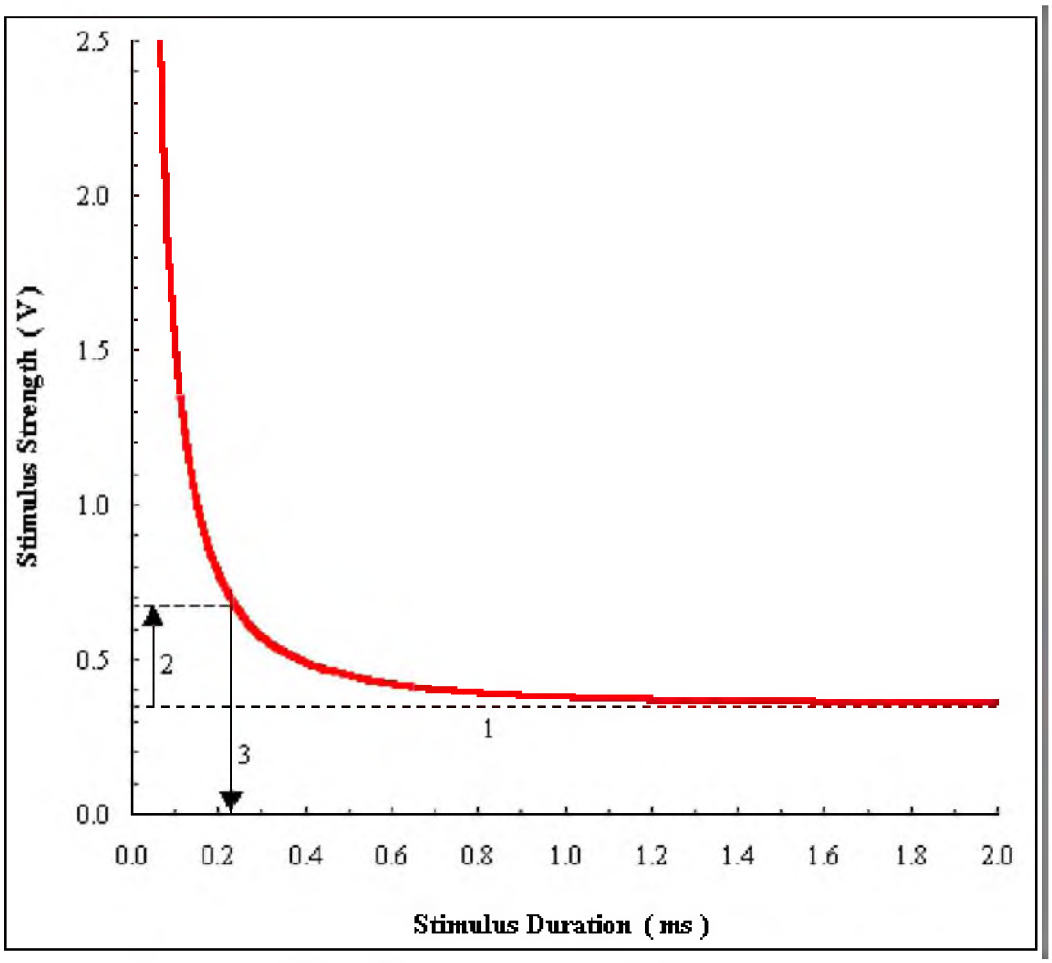


Fig.1. Strength—duration curve.

Importance of Chronaxie

The value of chronaxie is used to compare the excitability in different tissues. The measurement of chronaxie determines the excitability of tissue. Longer the chronaxie, lesser is the excitability. Chronaxie in human skeletal muscles varies from 0.08 milliseconds to 0.32 milliseconds. In frog's skeletal muscle, it is about 3 milliseconds.

Chronaxie is 10 times more in skeletal muscles of infants than in the skeletal muscles of adults.

Chronaxie is shortened by increased temperature and prolonged in cold temperature. It is shorter in homoiothermic animals than in poikilothermic animals. Chronaxie is shorter in red muscles than in white muscles.

3. Materials for auditory self-work.

Materials and methods: vertical myograph, stimulator, irritating electrods, kymograph, universal stand, preparating instruments set, pipette, gauze napkin, Ringer's solution.

Investigation object: frog.

Task 1. Acquaintance with devices for the work performing.

Electrofeeding source - has the function of voltage creating (till 0 to 40 V).

Kimograph – has the aim of graphic registration of mechanical transitions through the paper tape.

Universal stand – is for fixing the investigation object and registrating devices on it. It allows to rotate the subjects vertically and horizontally.

Myograph – is situated on universal stand. The aim of its usage is the registration of muscular contraction on kimograph drum. The main part of it are:

- Engelman's lever with the writing device at the long arm end.
- Hook for muscle fixating on the short arm.

One should fix another muscular end in a squeeze.

Myogram – the record of muscular contractions the altitude of which are increased.

Task 2. To prepare nervous-muscular preparation.

Frog is taken in a left hand (Fig.2.). Her abdomen must be orientated to the investigator's palm. He must incline frog's head forward with his thumb. One should find small deepening behind occipital bone and take in the preparation needle in suboccipital opening on depth of 1-2 mm. Having performed several transverse movements with the needle end it's necessary to separate brain from spinal cord. After that one must turn the needle toward the trunk. They take the needle in spinal canal while destroying spinal cord.

After that taking the animal by his posterior legs one cut spine (vertebral column) by the distance of 2 cm in front of spine articulation with pelvis bones. One should remove all anterior body surface cutting the skin and visceral organs. Legs posterior with pelvis and spine residue are raised up and urostyle is cutted. Urostyle is the bone formed by tail vertebras articulation. The investigator tightens the skin from posterior legs.Then one seperates legs one from another cutting carefully in the middle line the vertebral column residue and the pelvis in mons articulation. One of the legs is preparated, another one is put in Ringer's solution.

One should bring the glass stick to lumbo-sacral plexus and separate pelvis bone from spinal with scissors. The plexus should be connected with spine. One should preparate lumbo-sacral plexus to the hip joint.

One should move apart biceps brachii and musculus semimembranosus at femur dorsal surface. Then the investigator must find sciatic nerve and preparate it through all the distance carefully cutting its branches. The investigator must remove all the tissues above the hip joint. They receive the preparation "sciatic nerve-legs muscles".

For the muscular contraction registration by means of kymograph one should use the preparation "sciatic nerve-gastrocnemius muscle". For its receiving on the preparation " sciatic nerve-legs muscles" one should separate gastrocnemius muscle together with the tendon from bones and other tibia muscles alongside with the preservation of femur bone residue (1 cm). Then they remove tibia below hip joint. Gastrocnemius muscle with hip joint and sciatic nerve remain as a result. The hip joint is used for the preparation fixating in myograph.

The preparation must be often damped (moisted) with Ringer's solution for drying prevention.

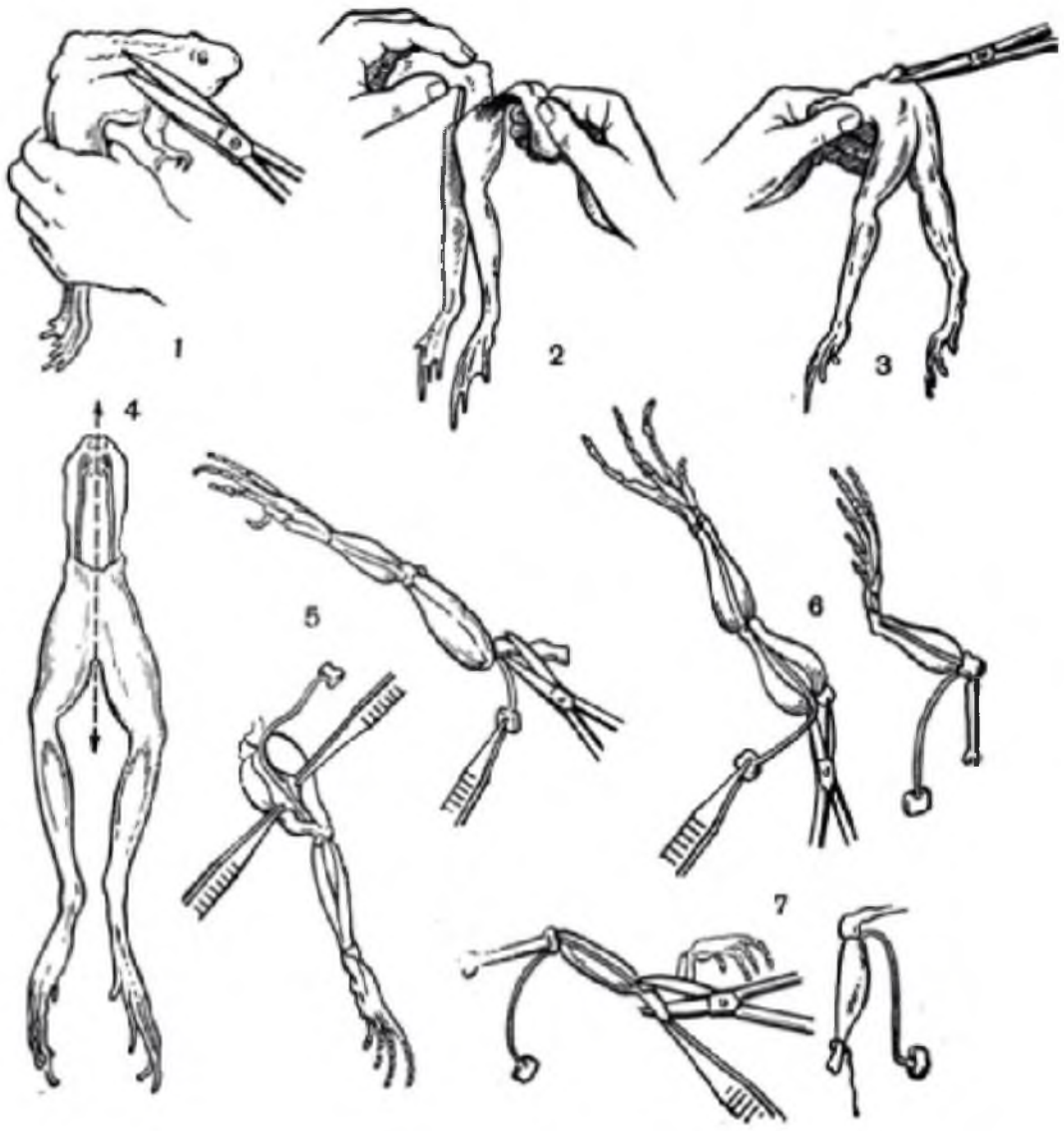


Fig.2. Nervous-muscular preparation.

Task 3. Nerve and muscle excitability measurement.

The investigation is performed on the preparation "sciatic nerve-legs muscles". The investigator put the preparation on the plate. The scientist puts sciatic nerve to the electrods. Then he slowly increases the voltage till the level at which the muscle will have minimal

answer. The founded minimal irritation force is called the irritation threshold. Then one should determine the muscle irritation threshold at its direct irritation by electrical current. For this gaim the investigator brings up the electrode to one of tibia muscles. Then he finds minimal irritation force causing muscular contraction.Compare irritation and excitability threshold at direct muscular irritation and nerve irritation (indirect irritation). Make the final conclusion.

Task 4. Draw and analyze the curve "force-time".

To mark "rheobase", "useful time", "chronaxy" on your graphic. Make the conclusions.

4. Materials for self-control:

Control questions:

1. Irritability and irritation as they are.
2. Stimuli, definition and classification.
3. Excitability.
4. Call excitable tissues.
5. Law "everything or nothing".
6. Muscular contraction force dependence on irritation force.
7. Stimulus threshold force dependence on its duration.
8. Excitability measures.
9. Lability as one of the excitable tissues features.
10. Excitability changes in course of excitation.

CONTENT MODULE 2: EXCITABLE TISSUES PHYSIOLOGY.

Lesson 2. Membrane potentials. Resting and action potentials. Excitability changes during action potential.

Before performing this lesson, you should study the introductory material presented here.

1. Lecture course.
2. Moroz V.M., Shandra O.A. Physiology. - 2011. Unit 1, Chapter 1.
3. Guyton A.C., Hall J.E. Textbook of Medical Physiology. - 2006. Unit 1, Chapter 5.

Relevance of the topic.

One can use potentials leads from body surface in clinical practice. The records received are called correspondingly to the potentials origin: electrocardiogram (ECG), electroencephalogram (EEG), electromyogram (MG) and so on.

1. Objectives:

To know: resting and action potentials physical and physiological characteristics, registrative methods, ionic mechanisms.

To be able to: draw action and resting potentials developmental schemes during time; resting potential changings during membrane de-, re- and hyperpolarization as well as scheme of excitability changes during action potential development.

2. Topic content.

Ionic basis of electrical events

The development and maintenance of resting membrane potential in a muscle fiber or a neuron are carried out by some mechanisms, which produce ionic imbalance across the cell membrane. This results in the development of more positivity outside and more negativity inside the cell. The ionic imbalance is produced mainly by two transport mechanisms in the cell membrane: sodium-potassium pump and selective permeability of cell membrane

Resting membrane potential

The potential difference between inside and outside of the cell under resting condition is known as resting membrane potential.(Fig.3.)

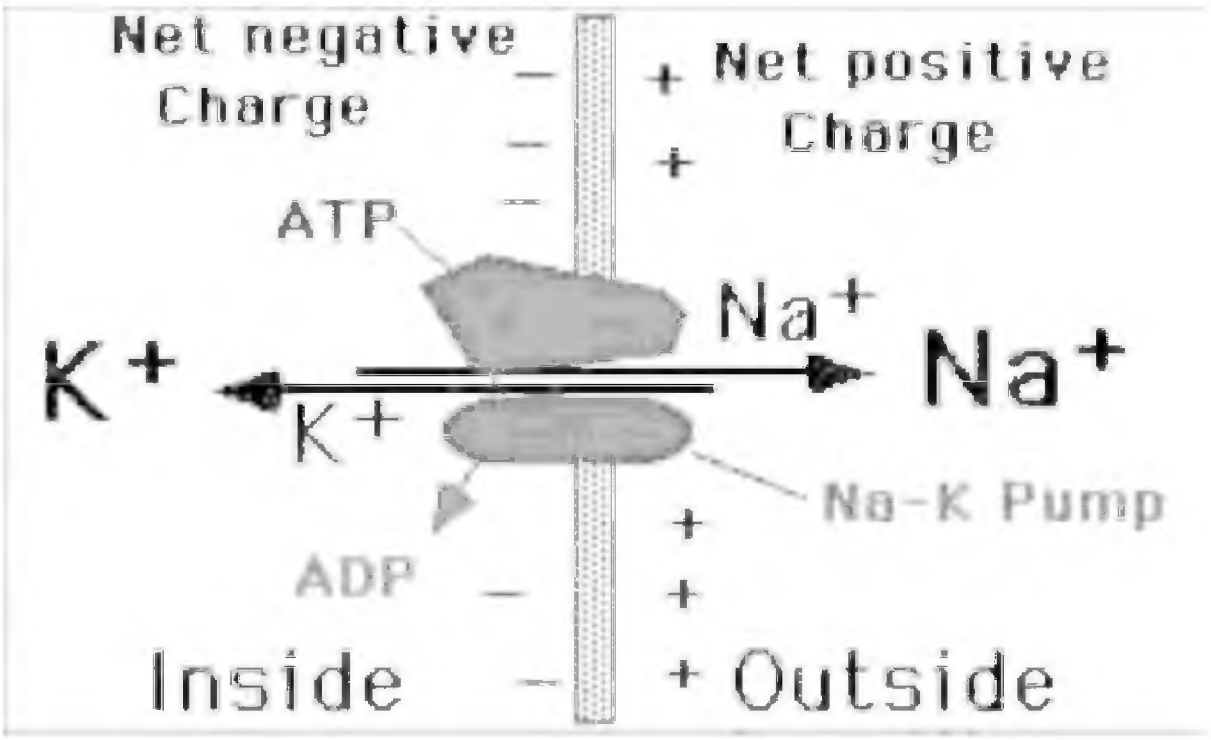


Fig.3. Resting membrane potential.

When two electrodes are connected to a cathode ray oscilloscope through a suitable amplifier and placed over the surface of the muscle fiber, there is no potential difference. There is zero potential difference. But, if one of the electrodes is inserted into the interior of the muscle fiber, potential difference is observed across the sarcolemma (cell membrane). There is negativity inside the muscle fiber in relation to the outside. This potential difference is constant and is called resting membrane potential. The condition of the muscle during resting membrane potential is called polarized state. In human skeletal muscle, the resting membrane potential is -90 mV.

Selective Permeability of Cell Membrane

The permeability of cell membrane depends largely on the transport channels. The transport channels are selective for the movement of some specific ions. Their

permeability to these ions also varies. Most of the channels are gated channels and the specific ions can move across the membrane only when these gated channels are opened.

Channels for major anions like proteins: however, the channels for some of the negatively charged large substances such as proteins and negatively charged organic phosphate compounds and sulfate compounds are absent or closed. Such substances remain inside the cell and play a major role in the development of resting membrane potential.

Leak channels: In addition, the channels for three important ions — sodium, chloride and potassium — also play an important role in maintaining the resting membrane potential.

Since, the Cl- channels are mostly closed in resting conditions, these ions are retained outside the cell. Thus, only the positive ions, Na^+ and K^+ can move across the cell membrane. The Na ions are actively transported (against the concentration gradient) out of the cell and K^+ is actively transported (against the concentration gradient) inside the cell. However, because of concentration gradient Na^+ diffuses back into the cell through Na^+ leak channels. And, K^+ diffuses out of the cell through K^+ leak channels.

In resting conditions, almost all the K^+ leak channels are opened but most of the Na^+ leak channels are closed. Because of this, K^+ ions transported actively into the cell and can diffuse back out of the cell in an attempt to maintain the concentration equilibrium. But only very little amount of Na^+ ions transported actively out of the cell can diffuse back into the cell. That means in resting conditions, the passive K^+ efflux is much greater than the passive Na^+ influx. This results in resting membrane potential with negativity inside compared to outside.

After establishment of the resting membrane potential (i.e. inside negativity and outside positivity), the efflux of K^+ ions stops in spite of concentration gradient. This is because of two reasons.

1. The positivity outside the cell repels the positive K^+ ions and prevents the further efflux of these ions.

2. The negativity inside the cell attracts the positive K^+ ions and prevents further leakage of these ions outside.

Sodium-potassium pump

Sodium and potassium ions are actively transported in opposite directions across the cell membrane by means of an electrogenic pump called sodium-potassium pump This moves three sodium ions out of the cell and two potassium ions inside the cell by using energy from ATP. Since more positive ions are pumped outside than inside, a net deficit of positive ions occurs inside the cell. This leads to negativity inside and positivity outside the cell.

Importance of intracellular potassium ions: The concentration of K^+ ions inside the cell is about 140 mmol/l, which is almost equal to that of Na^+ ions outside. The high concentration of K^+ inside the cell is essential to check the negativity. Normally, the negativity (resting membrane potential) inside the muscle fiber is -90 mV and in a

nerve fiber, it is -70 mV. Suppose if the K^+ ions are not present or decreased, the negativity increases beyond -120 mV, which is called hyperpolarization. At this stage, the development of action potential is not possible.

Action potential

When the muscle is stimulated, a series of changes occur in the membrane potential, which is called action potential. The action potential occurs in two phases.

- **Depolarization**

When the impulse reaches the muscle, the polarized condition (-90 mV) is altered, i.e. the resting membrane potential is abolished. The interior of the muscle becomes positive and outside becomes negative. This condition is called depolarization. With other words, depolarisation is membrane potentials difference decreasing.

- **Repolarization**

Within a short time, the muscle obtains the resting membrane potential once again. Interior of the muscle becomes negative and outside becomes positive. So, the polarized state of the muscle is re-established. This process is called repolarization. So, it is potentials difference restoration.

The voltage gated Na^+ channels and the voltage gated K^+ channels play important role in the development of action potential.

During the onset of depolarization, there is slow influx of Na+ ions. When depolarization reaches 7 to 10 mV, the voltage gated Na+ channels start opening at a faster rate. This is called Na+ channel activation. When the firing level is reached, the influx of Na+ ions is very great and the overshoot occurs.

But the Na+ transport is short-lived. This is because of rapid inactivation of Na+ channels. Thus, the Na+ channels open and close quickly. The Na+ channels remain in this inactivated state for some time before returning to resting condition. At the same time, the K+ channels start opening. This leads to efflux of K+ ions out of the cell, causing repolarization thereby.

Unlike the Na+ channels, the K+ channels remain open for longer duration. These channels remain opened for few more milliseconds after completion of repolarization. This causes efflux of more number of K+ ions producing more negativity inside. This is the cause for hyperpolarization.

Action potential curve (Fig.4.)

Resting Membrane Potential

The resting membrane potential is recorded as a straight baseline at -90 mV .

Stimulus Artifact (local potential)

When a stimulus is applied, there is a slight irregular deflection of baseline for a very short period. This is called stimulus artifact.

Latent Period

The stimulus artifact is followed by a short period without any change. This period is called latent period, which is about 0.5 to 1 millisecond.

Firing Level or Critical Depolarization Level

Depolarization starts after the latent period. Initially, it is very slow. After the initial slow depolarization up to -15 mV, the rate of depolarization increases suddenly. The point at which, the rate of depolarization increases is called firing level.

Overshoot

From firing level, the curve reaches the isoelectric potential (zero potential) rapidly and then overshoots the zero line up to +55 mV.

After Depolarization or Negative after Potential

The rapid fall in spike potential is followed by a slow repolarization process. This is called after-depolarization, trace depolarisation or negative after potential. The duration of this is 2 to 4 milliseconds.

After Hyperpolarization or Positive after Potential

After reaching the resting level (-90 mV) it becomes little more negative than resting level. This is called after hyperpolarization, trace hyperpolarization or positive after potential. This lasts for more than 50 milliseconds. After this, the normal resting membrane potential is restored.

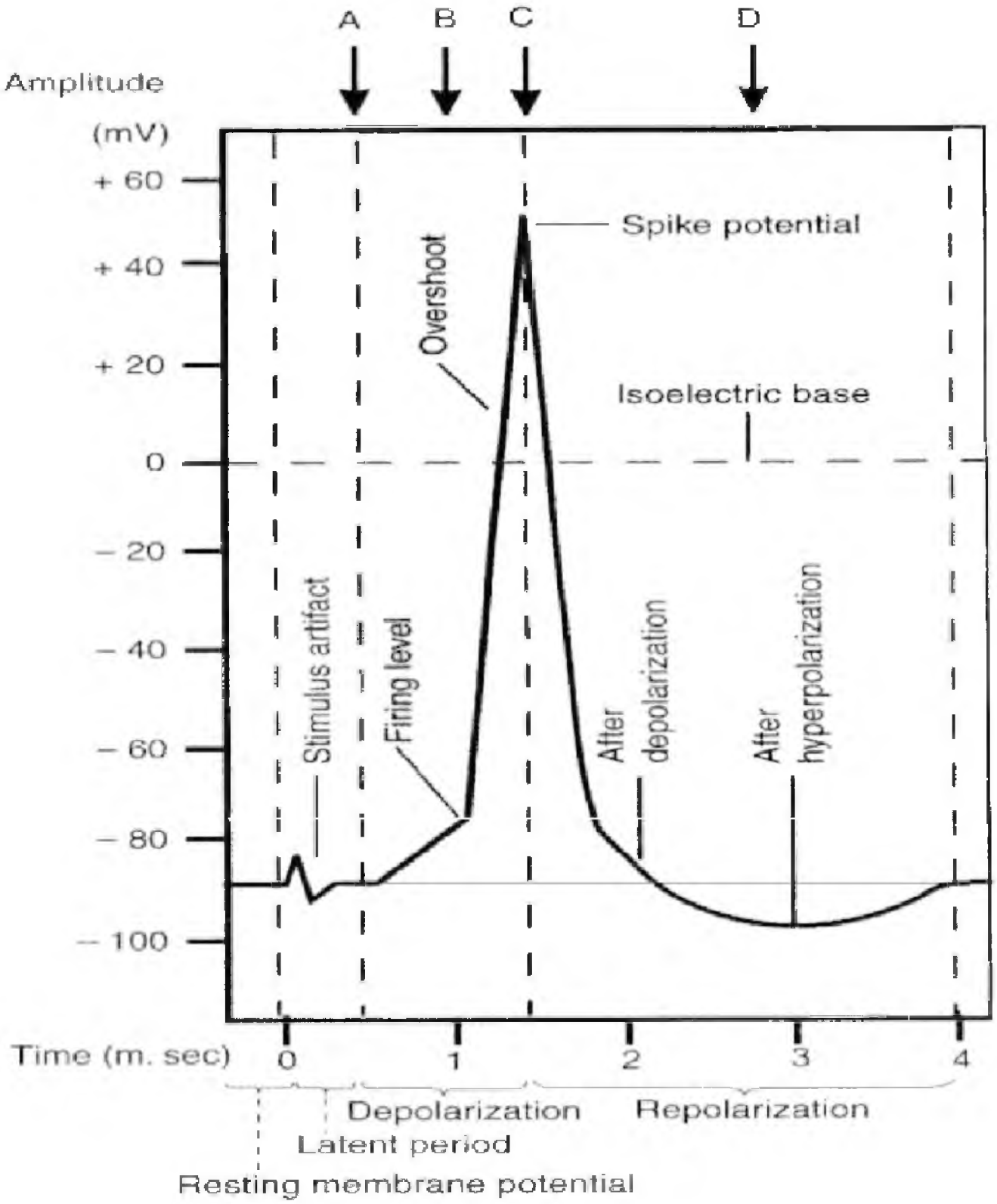

A
B
C
D
Amplitude
(mV)
+ 60
+ 40
+ 20
0
– 20
– 40
– 60
– 80
– 100
Spike potential
Overshoot
Isoelectric base
Stimulus artifact
Firing level
After depolarization
After hyperpolarization
Time (m. sec)
0
1
2
3
4
Depolarization
Repolarization
Latent period
Resting membrane potential

Fig. 4. Action potential in a skeletal muscle.

Refractory period

Refractory period is the period at which the muscle does not show any response to a stimulus (Fig.5.).

Types of refractory period.

- Absolute refractory period is the period during which the muscle does not show any response at all, whatever maybe the strength of stimulus.
- Relative refractory period. This is the period, during which the muscle shows some response if the strength of stimulus is increased to maximum.

Refractory Period in Skeletal Muscle

In skeletal muscle, the absolute refractory period falls during first half of latent period (0,005 sec). And, relative refractory period extends during second half of latent period (0,005 sec). Totally, it is 0,01 sec.

In dental practice tooth solid tissues electrical features determining is performed for acute and chronic pulpitis diagnostics. This methodics is rather complicated. It requires measurements taking into account individual peculiarities of teeth morphological shape and geometric sizes as well as obligatory following the mot possible stimulus parameters.

Nowadays one uses also possibility of oral mucosa biopotentials measurement for its functional state assessment. There was detected summary biopotentials age dynamics as well as their level change at parodontosis, oral mucosa diseases which is of important diagnostic value.

Dentist can touch with potentials occurrence between similar metals (for instance, amalgame) of different content or between crowns made from the same metal if there is metal filling under them. Appearing microcurrents can be the reason of such a phenomenon named as galvanism. Sometimes pathological process is developed in

years after denturing. It depends on the patient individual reactivity. Galvanism clinical symptoms are rather different. They can be divided into two big groups: subjective complaints which occur directly right after metallic fillings and crowns fixation in oral cavity. "Metallic taste" and some others belong to them. They are usually stopped in several days. Complaints which are appeared in prolonged time (sometimes in several years) belong to other group: metallic taste, pain. Oral mucosa inflammation can be developed: reddish color, tongue papillas swelling, erosions and ulcers appearance.

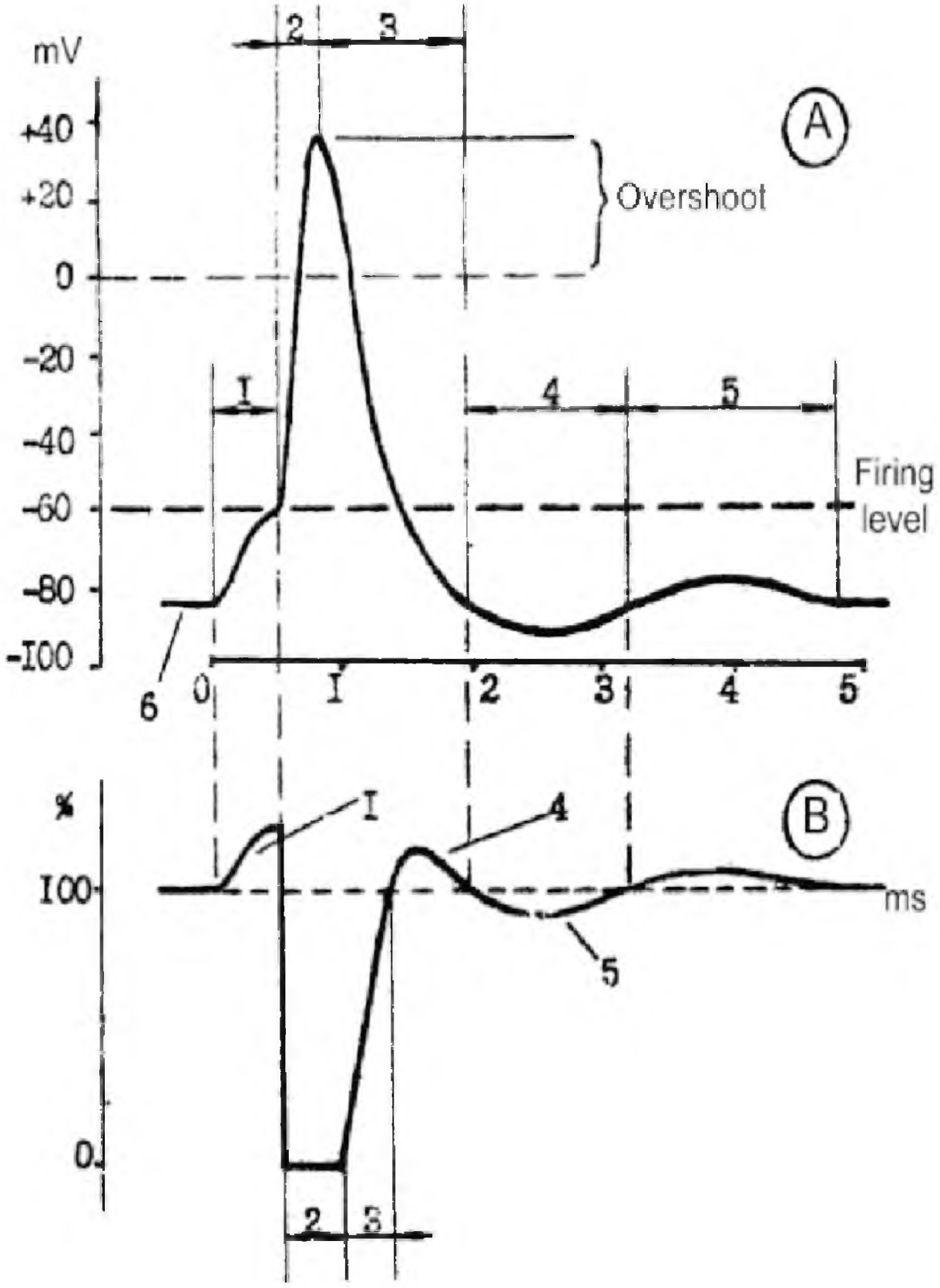


Fig.5. Action potential and changes of cell membrane excitability.

A. Phases of action potential: 1 – slow depolarization, 2 – quick depolarization, 3 – repolarization, 4 – hyperpolarization, 5 – negative afterpotential, 6 – rest potential.

B. Changes of excitability: 1, 4 – supernormal period, 2 – absolute refractory period, 3 – relative refractory period, 5 – subnormal period.

3. Materials for auditory self-work.

Materials and methods: scissors, anatomic tweezers, preparation needle, dielectric plate, bimetallic "balcony", plastic twezers, current source.

Investigatioin obiect: frog.

Task 1. Galwani's first experiment.

The investigator must destroy frog's spine with preparation needle, destroying body in 2 cm in front of articulation place of spine and pelvis bones(Fig.6.). It's necessary to remove frontal body part and abdomen wall with visceral organs, to remove skin from posterior legs. Copper hook of "balcony" is bought to lumbo-sacral plexus radixes (rootlets, radicles). For this aim the investigator must hang the preparation on it. Then one should touch the legs muscles with "balcony" zinc plate. In the touching moment all legs are contracted.

Draw the experiment scheme in your copy-book. Explain the reason of bimetallic "balcony" irritative action.

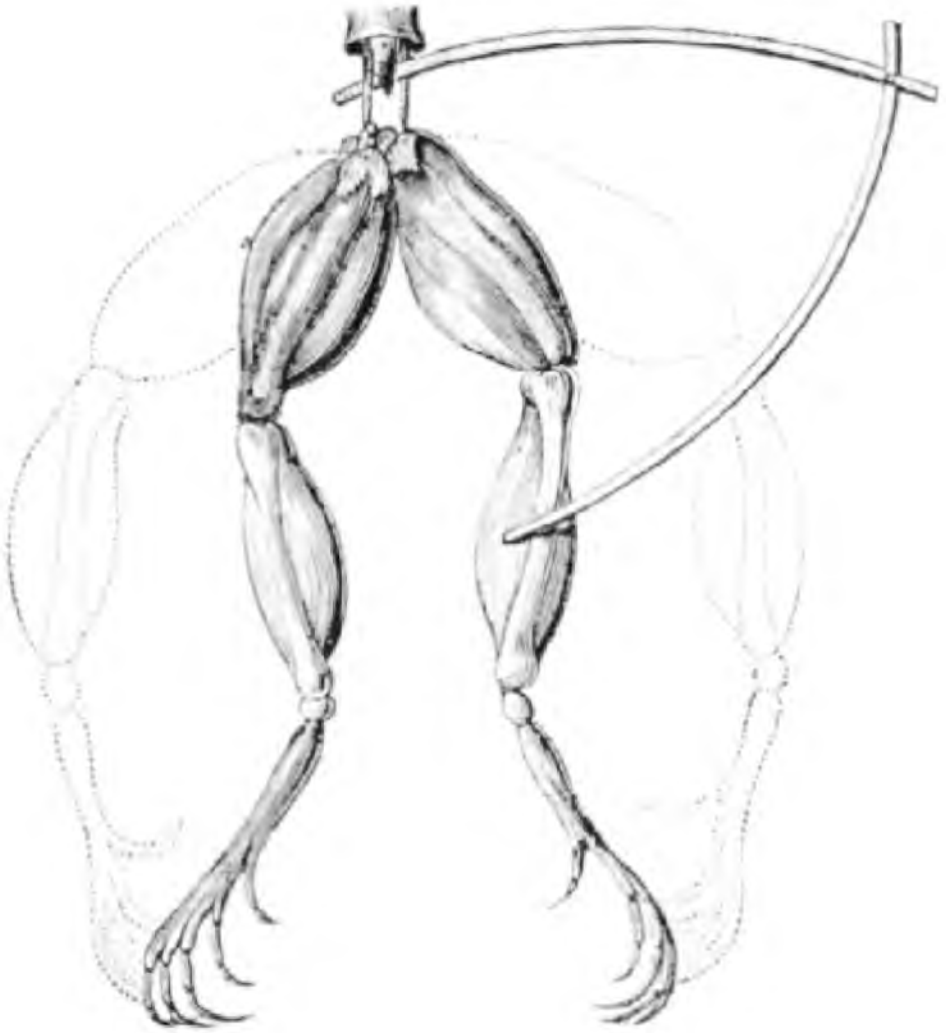


Fig.6. Galwani's first experiment.

Task 2. Galwani's second experiment (contraction without metal).

To prepare the preparation "sciatic nerve-legs muscles". To catch the spine residue with plastic tweezers, not touching the nerve (Fig.7). On femur muscles resting after the preparation one must make transversal cutting and throw on the nerve on it for the nerve's touching to the injured electronegative and non-injured electropositive muscle locuses. The experiment must be carried out some times while observing under the preparation muscles. It's very important to take the nerve possessing high excitability.

Draw the experiment scheme in your copy-books using the next figure.

Second Galwani`s experiment scheme.

Explain the reason of preparation muscles contraction.

Fig.7. Galwani's second experiment.

Task 3. K.Matteuchi's experiment.

To prepare 2 nervo-muscular preparations "sciatic nerve-legs muscles" (Fig.8.). Put them to the dry dielectric plate so that the first preparation nerve were touching to the current source electrodes and the second preparation nerve must be lied longitudinally to the first preparation muscles. After that one should act to the first preparation sciatic nerve with unconstant current in course of some seconds. The result of the current action: both legs musclular contractions. The second legs muscular contractions (the nerve of which are located on the first preparation muscle) are called secondary.

Draw the experiment's scheme in your copy-book.

They say traditionally that the second preparation nerve irritation reason is the first preparation skeletal muscle action currents.

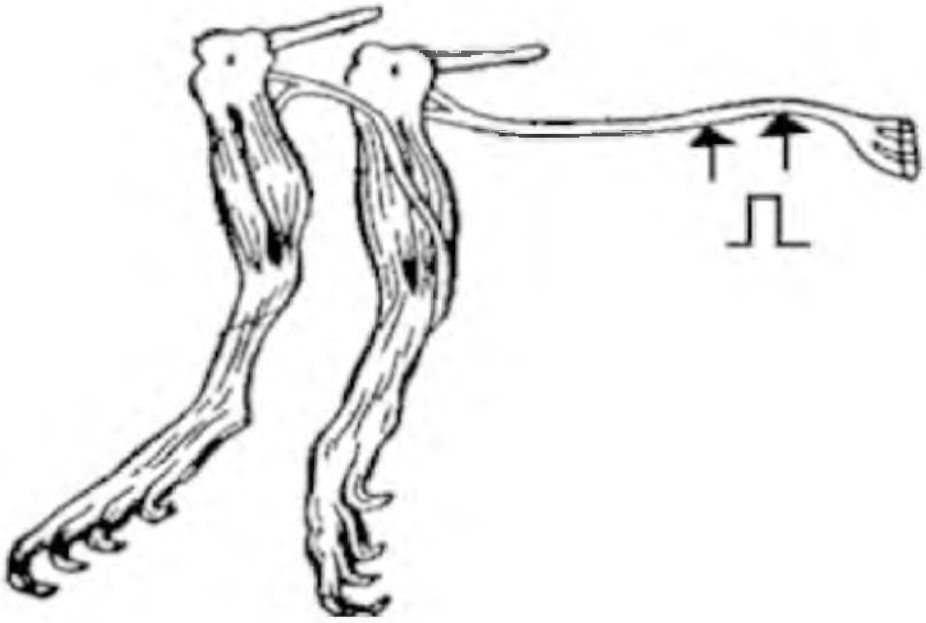


Fig.8. K.Matteuchi's experiment.

4. Materials for self-control:

1. Bioelectrical phenomena investigation methods.
2. Resting potential:
   a) Appearence reasons and ion gradients levels. Potassium-sodium pump.
   b) Plasmatic membrane permeability for different ions.
   c) Membrane potential appearence mechanisms. Membrane potential level.
3. Action potential:
   a) Action potential appearence conditions and reasons. Local answer. Depolarization critical level.
   b) Action potential altitude and duration. Rule "everything or nothing".
   c) Action potential appearence and development mechanism. Action potential phases.

4. Bioelectrical phenomena registration practical significance.

Lesson 3

Skeletal muscles contraction mechanisms investigation

Before performing this lesson, you should study the introductory material presented here.

1. Lecture course.
2. Moroz V.M., Shandra O.A. Physiology. - 2011. Unit 1, Chapter 2.
3. Guyton A.C., Hall J.E. Textbook of Medical Physiology. - 2006. Unit 1, Chapter 7.

Relevance of the topic.

Doctors meet patients with skeletal muscles disorders at different pathological conditions. Myopathies (both innate and acquired) are widely-spread nowadays. Gnatodynamometry, myoartrography belong to widely-spread diagnostic methods in dentistry.

1. Objectives:

To know: skeletal muscle excitation changings during its contraction; contractive regimes and types; contraction and relaxation molecular mechanisms.

To be able to: draw singular and tetanic (grouped) contractions.

2. Topic content.

Muscles are classified by three different methods based on different factors.

I. Depending upon strations

Depending upon presence or absence of cross striations, the muscles are divided into two groups namely:

- Striated muscle: under light microscope, in each muscle cell, a large number of cross striations (transverse lines) are seen at regular interval. These muscles, having the cross striations are called striated muscles.

Skeletal muscle and cardiac muscle belong to this category.

- Non-striated muscle: the muscles without cross striations are called non-striated muscles. These muscles are also known as plain muscles or smooth muscles.

II. Depending upon the control

Depending upon control, the muscles are classified into two types namely:

- Voluntary muscle: the activities of these muscles can be controlled voluntarily (at will). Skeletal muscles are the voluntary muscles. These muscles are innervated by somatic nerves.

- Involuntary muscle: the activities of these muscles cannot be controlled at will. Cardiac muscle and smooth muscle are involuntary muscles. These muscles are innervated by autonomic nerves.

III. Depending upon function

The muscles are classified into three types depending upon function (Tab.1):

- Skeletal muscle;
- Cardiac muscle;
- Smooth muscle.

Tab.1 Muscles types.

Striations, control and nerve supply of muscles

Muscle	Striations	Control	Nerve supply
Skeletal muscle	Present	Voluntary	Somatic nerves
Cardiac muscle	Present	Involuntary	Autonomic nerves

Smooth muscle	Absent	Involuntary	Autonomic nerves

Skeletal Muscle

Skeletal muscles are in association with bones forming the skeletal system. These muscles form from 40 to 50% of body mass. In human beings, about 600 muscles are identified. Myofibrils or myofibrillars are fine parallel filaments present in sarcoplasm of the muscle cell. Myofibrils run through the entire length of the muscle fiber. In cross section of a muscle fiber, the myofibrils are separated from one another by sarcoplasm. In some muscle fibers, some of the myofibrils are arranged in groups. These groups of myofibrils are called Cohnheim's areas or fields. The diameter of the myofibril is 0,2 to 2,0 microns. And, the length of a myofibril varies between 1,0 to 4,0 cm depending on length of the muscle fiber.

Microscopic structure of myofibril

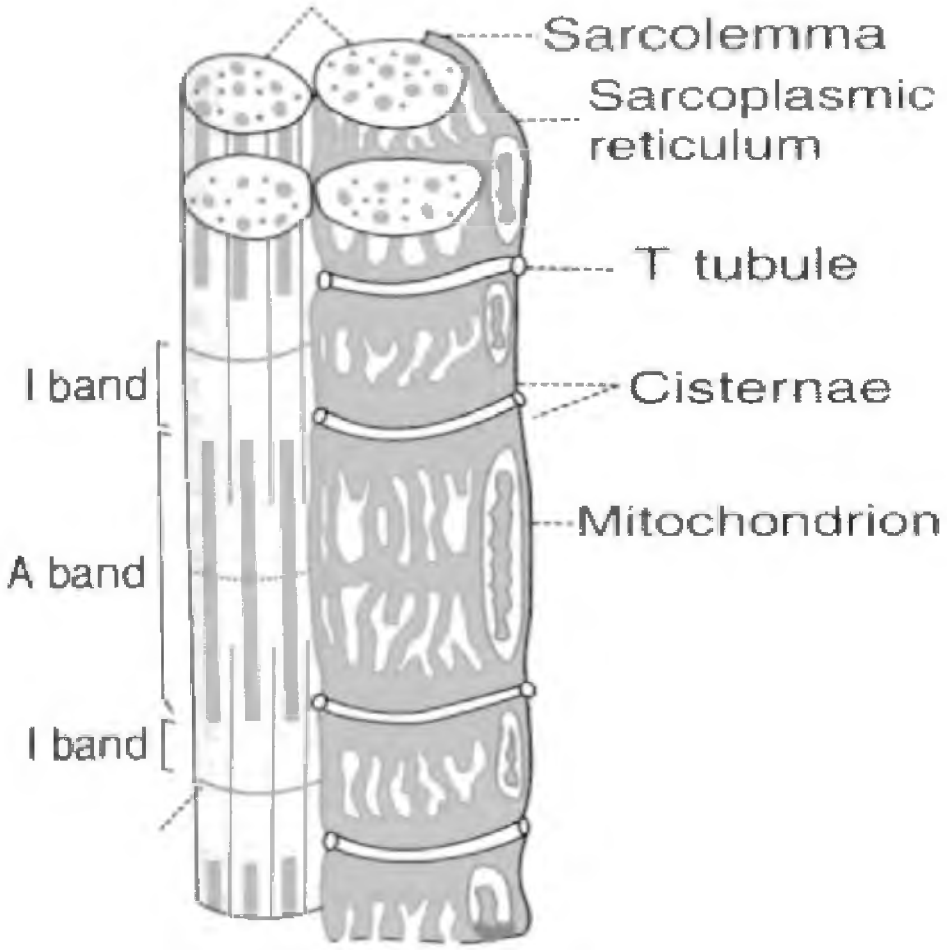
Light microscopic studies show that, each myofibril consists of a number of alternating light and dark bands. These bands are otherwise called the sections, segments or discs (Fig.9.).

Dark band is called "A" band. "A" band is anisotropic. If polarized light is passed through the muscle fiber at this area, the light rays are refracted at different directions (An = not; iso = it; trops = turning). Light band is isotropic. Rays of polarized light, passed through the muscle fiber at this area, are refracted at the sail angle. So, this band is called "I" band.

The light band is otherwise called J band and the dark bands called Q disc (Querscheibe = cross disc).

In an intact muscle fiber, "I" band and "A" band of adjacent myofibrils are placed side by side. This gives the appearance of characteristic cross striations in muscular fiber.

A narrow lighter area called "H" zone (H = hell = light-in German, "H" = Henson - discoverer) is seen at the middle of "A" band. "I" band is divided into two by a narrow line called "Z" line (in German Zwischenscheibe = between discs). The portion of myofibril in between two "Z" lines is called sarcomere.


Sarcolemma
Sarcoplasmic reticulum
T tubule
Cisternae
Mitochondrion
I band
A band
I band

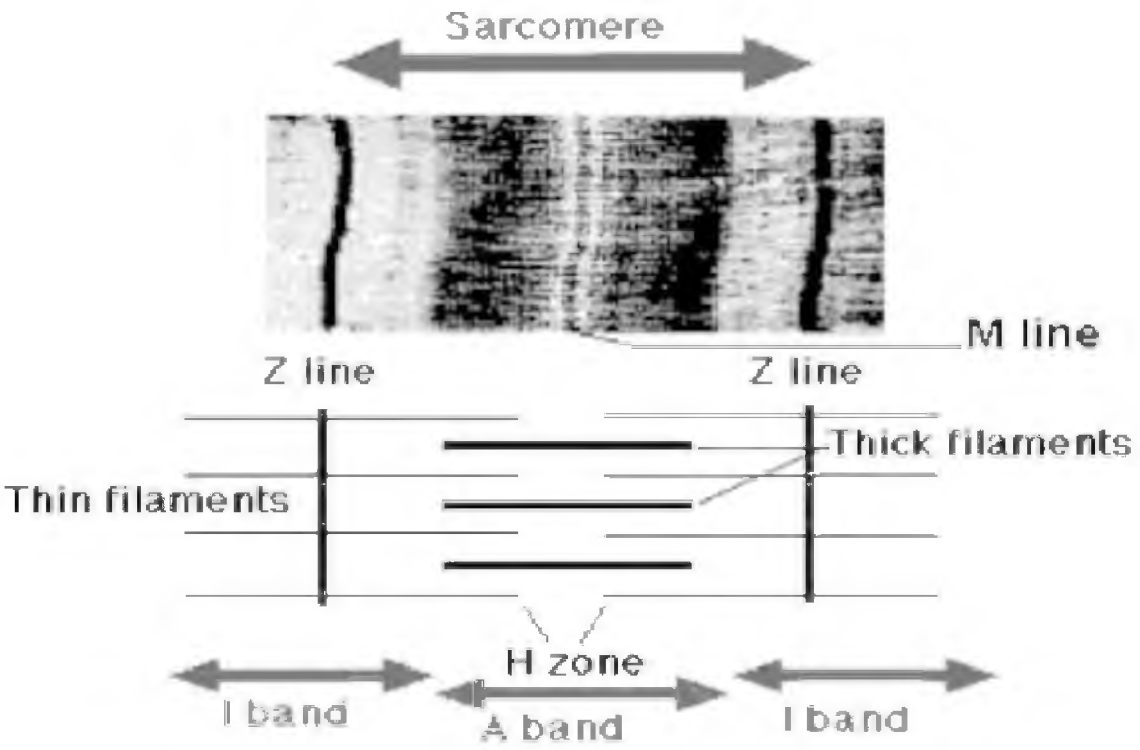


Fig.9. Structure of skeletal muscle.

Composition of muscle

Skeletal muscle is formed by 75% of water, 20% of proteins and 5% of organic substances other than proteins and some inorganic substances.

Following are the proteins present in the muscle: myosin, actin, tropomyosin, troponin, actinin, titin, desmin, myogen and myoglobin.

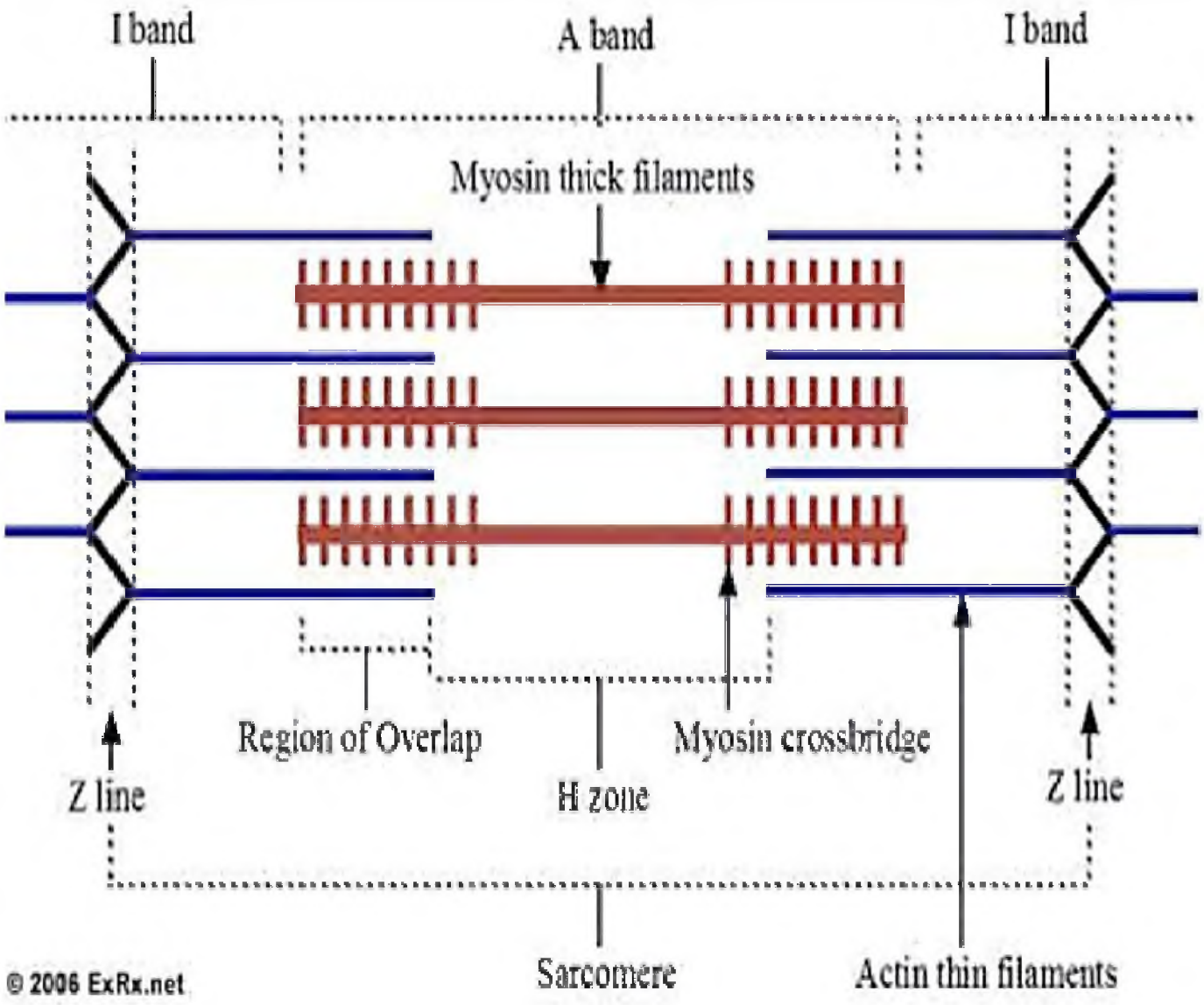


Fig.10. Sarcomere's structure (by ExRx.net., 2006)

Simple muscle contraction or twitch

The contractile property of muscle is studied by using the frog's gastrocnemius-sciatic preparation. This is also called muscle-nerve preparation.

When the stimulus with threshold strength is applied, the muscle contracts and then relaxes. These activities can be recorded graphically by using suitable

instruments. The contraction is recorded as upward deflection from the baseline. And relaxation is recorded as downward deflection back to the base line (Fig.11).

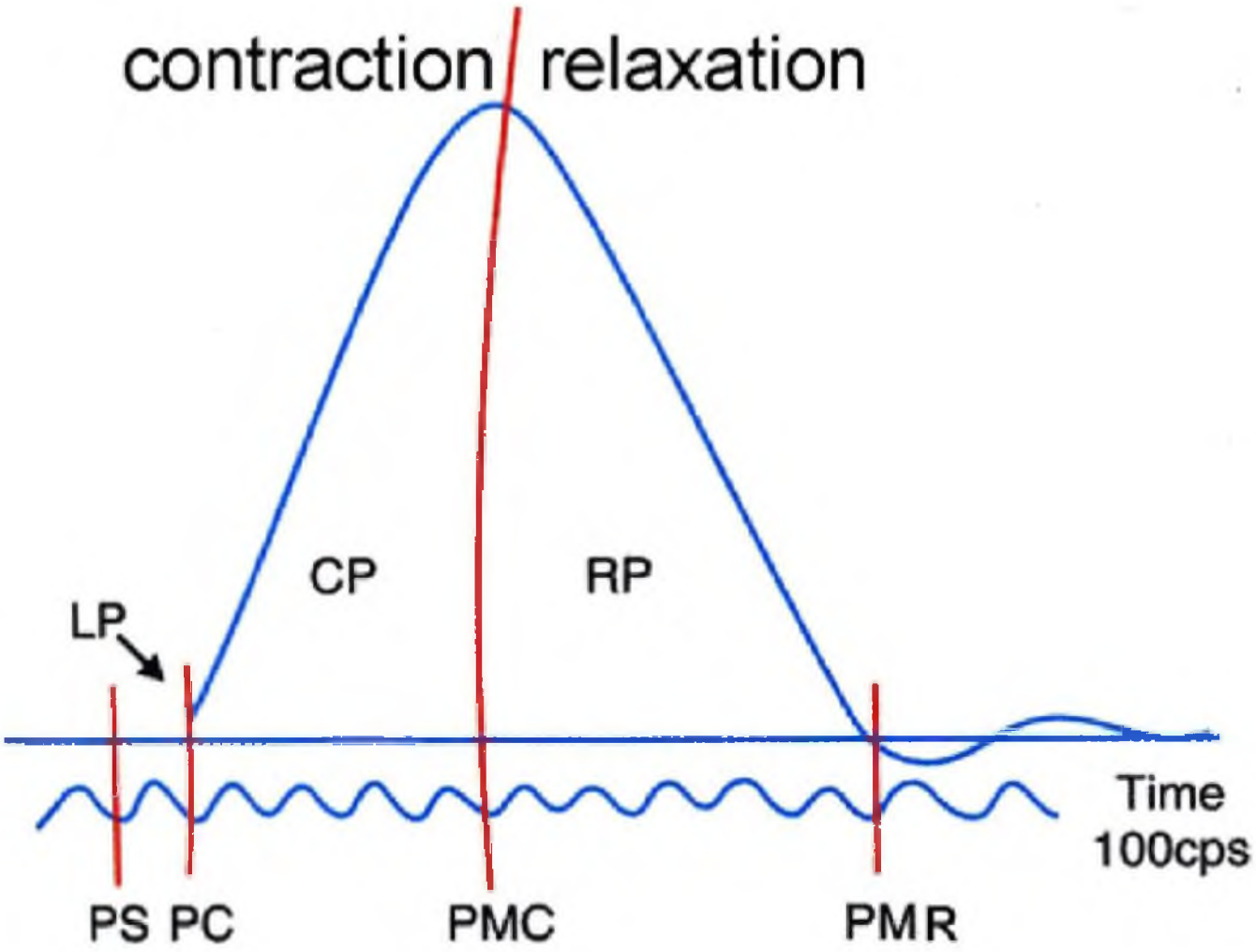


Fig.11. Isotonic simple muscle curve.

PS = Point of stimulus. PC = Point of contraction. PMC = Point of maximum contraction. PMR = Point of maximum relaxation. LP = Latent period (0.01 sec). CP = Contraction period (0.04 sec). RP = Relaxation period (0.05 sec).

Simple contraction is called simple muscle twitch and graphical recording of this is called simple muscle curve. Four points are to be noted in this curve.

1. Point of stimulus (PS): This denotes the time when the stimulus is applied.

2. Point of contraction (PC): This indicates the time when muscle begins to contract.
3. Point of maximum contraction (PMC): The muscle is contracting up to this point. This point also indicates the beginning of relaxation of the muscle.
4. Point of maximum relaxation (PMR): This point indicates complete relaxation of the muscle.

All these four points divide entire simple muscle curve into 3 periods.

1. Latent period (LP) is time interval between point of stimulus and point of contraction. There is no mechanical activity in the muscle during this period.
2. Contraction period (CP) is interval between point of contraction and point of maximum contraction. The muscle contracts during this period.
3. Relaxation period (RP) is the interval between point of maximum contraction and point of maximum relaxation. Relaxation of the muscle occurs during this period.

Duration of different periods in a typical simple muscle curve is as follows:
Latent period: 0,01 second
Contraction period: 0,04 second
Relaxation period: 0,05 second
Total twitch (contraction) period: 0,10 second

Contraction period is always shorter than relaxation period. This is because the contraction is active process and relaxation is passive process.

Tetanic or summarized contraction

In reply to a rhythmic irritation (namely such one our muscles are received) the muscle is reduced lengthly (for a long time). Such a contraction has received the name tetanic or summarized (Fig.12). If each subsequent stimulus approaches to a muscle in the period, when it began to be relaxed, there is an infused, dentate or incomplete tetanus. Impulsations rate is 30 in 1 min. It can be expressed under experimental conditions. Fits also are dentate tetanus example. So, it is not physiological. It requires much energy.

If the interval between irritations decreases so, that each subsequent stimulus comes to a muscle at that moment when it is in a contraction phase, there is a smooth or complete tetanus. Impulsations frequency is 60 in 1 min. Smooth tetanus is more physiologic. It requires less energy for its performance. Neck movements to the both sides can be example of such tetanus.

Contraction time

Contraction time or total twitch period in simple muscle varies from species to species. It is less in warm-blooded (homoiothermic) animals than in cold-blooded (poikilothermic) animals. In the same animal, it varies in different groups of muscles.

Based on contraction time, skeletal muscles are classified into two types, the red muscles and white muscles. Similarly, depending upon contraction time and myosin ATPase activity the muscle fibers are also divided into two types, type I and type II fibers. Type I fibers (slow fibers or slow twitch fibers) have small diameter. Type II fibers (fast fibers or fast twitch fibers) have large diameter. Most of skeletal muscles in human beings contain both types of fibers.

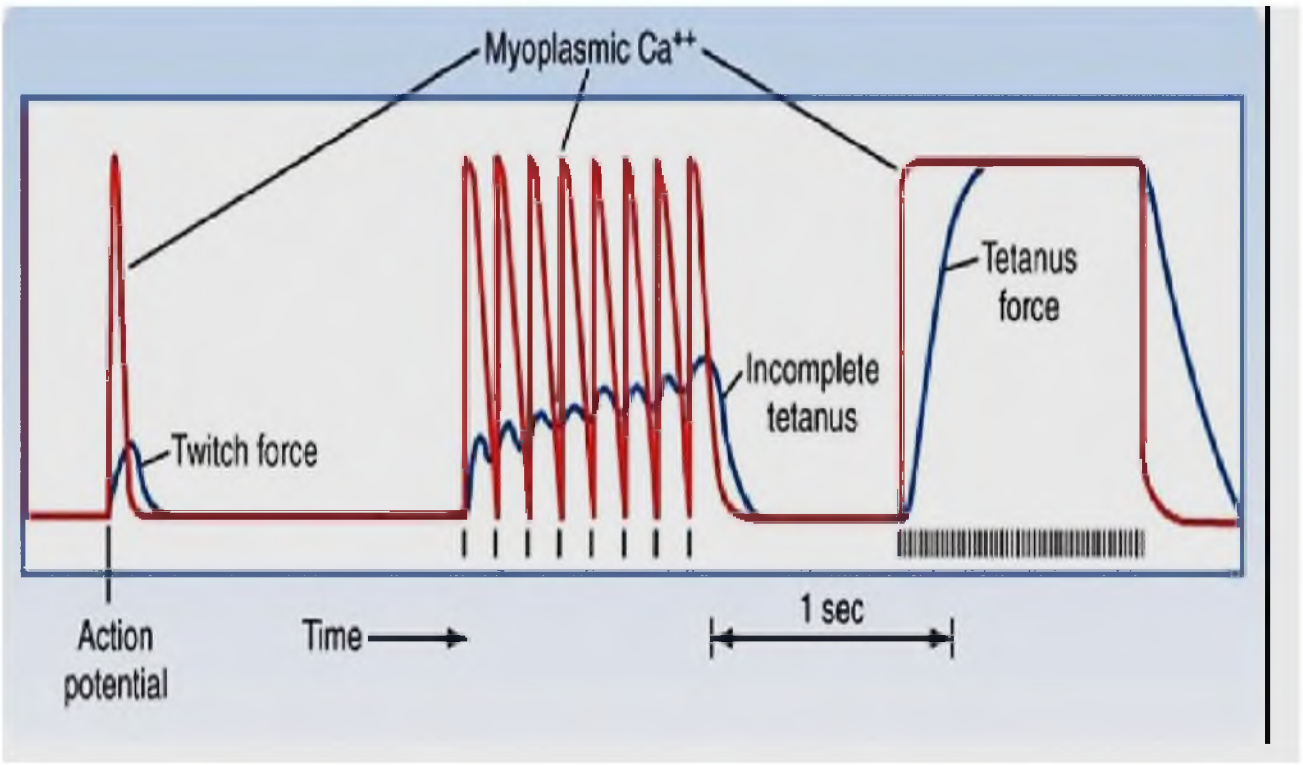


Fig.12. Tetanic or summarized contraction.

Red Muscles

Muscles containing large number of type I fibers are called red muscles, slow muscles or slow twitch muscles. These muscles have longer contraction time. Back muscles and gastrocnemius muscles are red muscles.

White Muscles

Muscles containing large number of type II fibers are called white muscles, pale muscles, fast muscles or fast twitch muscles. These muscles have shorter contraction time. Hand muscles and ocular muscles are white muscles.

The characteristic features of red and white muscles are given in table below. (Tab.2)

Tab.2 Features of red and white muscles.

Red (slow) muscle	***Pale (fast) muscle***
1. Myoglobin content is more.	Myoglobin content is less

2. Sarcoplasmic reticulum is less extensive	Sarcoplasmic reticulum is more extensive
3. Blood vessels are more extensive	Blood vessels are less extensive
4. Mitochondria are more in number	Mitochondria are less in number
5. Response is slow with long latent period	Response is rapid with short latent period
6. Contraction is less powerful	Contraction is more powerful
7. This muscle is involved in prolonged and continued activity	This muscle is not involved in prolonged and continued activity
8. Fatigue occurs slowly	Fatigue occurs quickly
9. Depends on cellular respiration for ATP production	Depends on glycolysis for ATP production

Skeletal muscles can differentiate the following types of muscular contraction according to the shortness size:

- isotonic is the muscular contraction, at which its fibers are shortened at a constant external load (under real conditions such type is practically absent);
- isometric is a muscular activation type, at which it develops a strain (tension) without the length change, it underlies the static work;
- auxotonic is a regimen, in which the muscles develop a tension and are shortened, such reductions are the characteristic of walking, run, sailing, tongue contractions. This regimen is the mostly widely-spread in human organism.

Tongue, lips muscles and masticatory muscles contractive types and regimes at conversation. During mastication mandible displacement takes place due to masticatory muscles contractions occurring in tetanic regimen (mainly incomplete). Contraction type – auxotonic (accompanied by muscle length and tension changings). Lips participate in sounds formation; one can see isometric, isotonic and auxotonic (or auxometric) contractions. Regimen – tetanus.

Masticatory muscles physiological properties. Masticatory muscles force and work. As it is well-known, maxillary-facial region muscles are divided into 2 main groups: masticatory and mimic. They belong to skeletal muscles and possess the same features. Masticatory muscles contract mainly in auxotonic regimen i.e. with parallel tension and length changing. Masticatory muscles contracture can be developed due to masticatory muscles fatigue. Contracture means muscles retarded relaxation.

Masticatory musculature belongs to force muscles. It means that they develop mainly force comparatively to other skeletal muscles which develop velocity. In course of masticatory musculature contraction force is developed. Such force is necessary for mechanical action to the food piece, its crush, wearing down and grinding. Skeletal muscle with square in 1 cm^2 can develop muscular force in 10 kg. Transversal section sum for masticatory muscles ascending mandible on 1 side of face is equal to 19,5 cm^2, from the both sides – 39,0 cm^2. Thus, masticatory muscles absolute force is equal to 390 kg. At the same time, separate teeth parodont durability is weak. That is why, pain occurs in parodont during jaws enforced closure and pressure further increasing reflectory stoppage is observed though muscular force has not exhausted yet.

Dental row masticatory center is dental-mandibular system region where food mechanical processing is performed maximally. In healthy people such center are small and large molars of another side from the one on which mastication takes place. During mastication left and right masticatory centers act in turns. As both masticatory centers functions losing crushing function is transferred to the first teeth which are adapted badly for this function performance under physiological conditions. That is why food crushing becomes bad and its processing by saliva becomes non-complete.

Masticatory pressure – is a force which is developed by masticatory muscles on mechanical food processing side. This pressure is caused by masticatory muscles

contraction and tension in periodontal tissues: the more it is the closer to the attaching place of masticatory muscles and mandible the tooth is.

Masticatory musculature work takes place when muscles are contracted; thus, it is dynamic one.

Muscular work effectiveness – or coefficient of useful action – is up to 30 per cent for masticatory musculature. The work which is in fact is performed during mastication is known as mastication effectiveness. It depends on:

- mastication intensity;
- masticatory pressure force;
- saliva qualities;
- bite character;
- tongue movement during food piece formation.

Dentists should remember about such physiological methods widely used in practice. Gnathodynamometry is used for determining the tooth supporting tissues resistance to pressure. It is performed by means of gnathodynamometer. They have special plates for teeth. Teeth transmit definite pressure to the spring during mouth closure. This pressure is recorded on the scale. It is established that frontal teeth durability is equal to 60 kg while the one for masticatory one is 180 kg. Parodont durability depends on masticatory musculature and parodont individual development, their age- and sex-dependent functional state.

Masticatory muscles injury due to their inflammation or trigeminal nerve disease can be mandible contracture reason. Reason is dealt with changes occurring in temporomandibular joint. That is why myoartrography is of clinical importance. This method allows to registrate simultaneously masticatory muscles contractions and articulatory heads movements.

3. Materials for auditory self-work.

Materials and methods: vertical myograph, stimulator, irritating electrodes, kymograph, strand, preparation instruments set, gauze napkins, Ringer's solution.

Investigation object: frog.

Task 1. Skeletal muscle contractions curves registration

- To prepare nervous-muscular preparation, to fix it in myograph and to bring the electrodes from constant current electrofeeding source. To irritate the muscle with separate key blow and to registrate (write) separate muscular contraction curve. The

velocity of kymograph drum must be maximal. Mark the separate muscular contraction phases and their duration.

- Infused (incomplete) tetanus. Right after the separate muscular contraction curve the investigator performes 10-20 fast going one after another key closing and unclosing. As a result imperfect, incomplete summation of separate muscular contractions - infused (incomplete) tetanus – occurs.
- Smooth (complete) tetanus. For its receiving the muscle must be irritated with high frequency – 50 oscillations per second. Electrodes must be brought to the unconstant current electrical feeding and the key must be closed in course of 2-5 seconds.

To measure the altitude of single muscular contraction, infused and smooth tetanus curves received at equal stimulus force.

To glue the curves received into copy-books. To make the conclusions.

Task 2. Dynamometry

The investigated person is asked to sit on the chair and to stretch his arms forward and to pressure dynamometer maximally with a hand (Fig.13). Every hand muscular force should be estimated 3 times.

The results should be written in a copy-book.

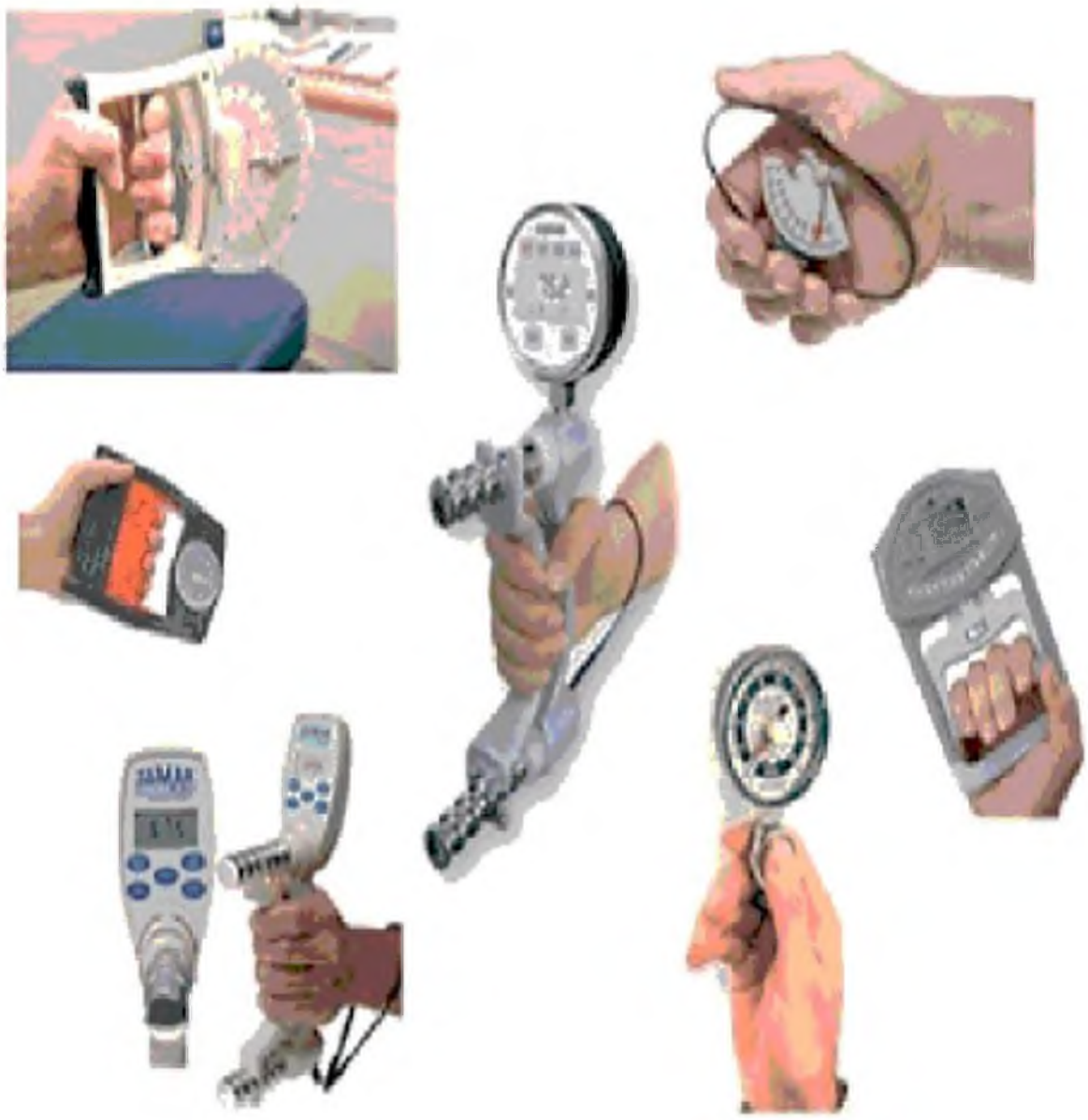


Fig.13. Dynamometry.

Electromyogram

This functional method has the most spread usage in neurology and dentistry. EMG can show not only peripheral neuron damage but also big brain (brain cortex) structures pathological changings. (Fig.14-16).

EMG can be performed at different muscles states:

- at their relaxation;
- at reflectory tonus changes (during other muscles tension, under emotional reactions, at deep inspiration);
- during arbitrary contractions.

EMG allows to study structure and function of neuromotor apparatus consisting of functional elements named as motor units (MU). MU is an integrity of motoneuron and muscular fibers group innervated by it. On EMG potentials oscillations in neuro-muscular endings (motor plates) occurring under impulses action from medulla oblongata and spine motors are fixated. EMG-record is performed at paper and tape movement velocity equal to 4-5 cm/sec and 20 cm/sec for oscillations quantity estimation.

The curve receiving at this method usage is named electromyogram. It is the result of interference of multiply action potential that appear asynchronously in different muscular fibers and is registered by means of intracellular electrodes.

There are 3 main electromyogram kinds:

- interferential – muscular biopotentials are taken off from large surface while applying the electrodes on skin;
- local – separate motor units activity is registered by means of needle electrodes;
- stimulatory – the registration of electrical muscle answer to the stimulation of nerve innervating it.

At EMG analysis one should takes into account:

- altitudes level;
- potentials oscillations frequency;
- common oscillograms structure (osclillations monotony or division into volleys, volleys form, duration and frequency).

Parameters of motor units are different because non-equal amount of muscular fibers are included in motor unit. That is why for taking information about state of motor unit of a given muscle it is essential to registrate not less than 20 action potentials. Action potential duration is 5-13 msec. Under norma in a resting state (at local bringing out with needle electrodes) the bioelectrical potentials oscillations don't increase (at summary EMG one can see low-altituded weak oscillations up to 10-15 mcV). Reflectory tonus increasing is accompanied by insignificant rising up of electrical activity (up to 50-100 mcV). At arbitrary tension frequent high oscillations

(1000-2000 mcV) are occured. In healthy people summary EMG dependently on muscular force has altitude up to 400 mcV and frequency up to 400 fluctuations per 1 second.

EMG have different picture at movement disorders that are connected with anomalies of central and peripheral nervous system and muscular apparatus as itself. The muscular bioelectrical activity changes are delt with pathological process topics, severity and course stages. EMG helps at diagnostics of central, segmentary, neuropathic and myopathic motor disturbances, it helps to determine typical disorders at early disease stage under conditions of low-expressed symptoms. It also gives the opportunity to observe process dynamics and treatment effectiveness.

EMG application in dentistry different branches

Local electromyography is used in surgical dentistry at masticatory (chewing) muscles dystrophies and hypertrophies; in stomatoneurology – at traumatic and infectious injuries of nerves of maxillofacial region; in dentistry of children – for determining the soft palate muscles bioelectrical activity in children under normal and congenital developmental anomalies.

Stimulatory electromyography is used in stomatoneurology and surgical dentistry at face nerve injuries for its conduction and impulses spreading velocity through the nerve determining as well as for the assessment of expression muscles paresis degree.

Interferential electromyography has the biggest spreading in various dentistry branches. For example, it is used in therapeutic dentistry for the registration of masticatory muscles contraction force regulation at parodontitis because there are functional-dynamic disturbances of masticatory apparatus at this disease. It is usually performed in parallel with gnathodynamometry for the assessment of mandibular (lower jaw) force during chewing.

Task 1.
Acquaintance with EMG qualitative analysis

Qualitative EMG analysis – EMG character describing:

- saturated;
- non-saturated;
- EMG rounding curve character – activity slow or sharp increasing and decreasing;
- activity phases number.

Task 2
Acquaintance with EMG quantitative analysis

This analysis includes:

- activity and rest phases duration;
- temporary intervals between activity beginning in different muscles;
- common electrical muscular activity level (the most important parameter) – is determined by EMG oscillations altitudes measurement and by means of special devices. Moda (the most common oscillations numeral, number that are repeated the most often in variation row) is usually taken as the level of summary EMG oscillations altitude. It's necessary to measure all main oscillations during definite time period (for example, for 0,5 sec) and to determine the altitude meaning the most often meets from peak to peak. Second way of summary oscillations altitude assessment is to measure 10 most expressed oscillations at definite time period with farther estimation of their middle meaning. Then the altitude of this section must be compared with proper meaning of calibrating signal and EMG altitude received must be expressed in mcV. Received EMG summary altitude is a conditional quantity but very important because it's a proportional to (it's correlated to) isometric muscular contraction intensity at any assessment way.
- Oscillations frequency – under norma is great (100 oscillations per second) and isn't connected with muscular contraction force. Thus, EMG looks like saturated one. In such cases EMG is not analysed.

Fig.14. Masticatory muscles EMG (usual one-sided mastication).

Fig.15. Scheme of EMG summary amplitude estimation. Horizontal lines run on peaks of most frequent amplitudes; vertical line is summary amplitude.

Fig.16. Non-saturated EMG (it is possible to estimate frequency and altitude on it).

4. Materials for self-control:

Control questions:

1. Call and characterize main muscles types according to structure and function peculiarities.

2. Describe the gliding (sliding) fibers theory, explaining muscular contraction.

3. Call contractile proteins (effector, regulatory) and tell about their role in course of muscular contraction.
4. Give the definition of: sarcomere; sarcoplasmic reticulum; A-disc (anisotropic); I-disc (isotropic); Z-line.
5. What muscles are arbitrary (voluntary) and what are involuntary ones? What do these terms mean?

6. Where and in what organs are there skeletal muscles?
7. Give the definition of isotonic and isometric contractions.
8. What is the trigger mechanism of skeletal muscles action potential?
9. Why tetanic contraction level is bigger than single contraction level?

10. Draw the curves of skeletal muscle excitability change in course of its exaltation.

- Electromyogram as diagnostic method.
- Principles of EMG qualitative and quantitative analysis.
- EMG clinical application (in neurology, traumatology, surgery, pediatry, surgical, therapeutical, children and orthopedic dentistry particularly).

Lesson 4
Skeletal and smooth muscles comparative characteristics

Before performing this lesson, you should study the introductory material presented here.

1.Lecture course.
2.Moroz V.M., Shandra O.A. Physiology. - 2011. Unit 2.
3.Guyton A.C., Hall J.E. Textbook of Medical Physiology. - 2006.

Relevance of the topic.

Smooth muscles are in inner organs composition. They provide motor function (alimentary tract, urinary-sexual system, blood vessels and others) due to their contraction.

1.Objectives:

To know: excitation changing peculiarities in smooth muscles during contraction, contraction peculiarities; smooth muscles features; automatism mechanism; contraction and relaxation distinguishing features.

To be able to: draw the scheme explaining smooth muscle excitability changes during its contraction; to make the table on skeletal and smooth muscles physiological features comparative characteristics.

2. Topic content.

Distribution

Smooth muscles are non-striated (plain) and involuntary muscles. These muscles form the major contractile tissues of various organs.

Muscles, which are in association with viscera, are called smooth muscles or visceral muscles. These muscles are supplied by sympathetic and parasympathetic division of autonomic nervous system. Smooth muscles form the main contractile units of wall of the various visceral organs and are present in the following structures:

a. Wall of organs like esophagus, stomach and intestine in gastrointestinal tract
b. Ducts of digestive glands
c. Trachea, bronchial tube and alveolar ducts of respiratory tract
d. Ureter, urinary bladder and urethra in excretory system
e. Wall of blood vessels in circulatory system
f. Errector pilorum of skin

g. Mammary glands, uterus, genital ducts, prostate gland and scrotum in reproductive system

h. Iris and ciliary body of the eye.

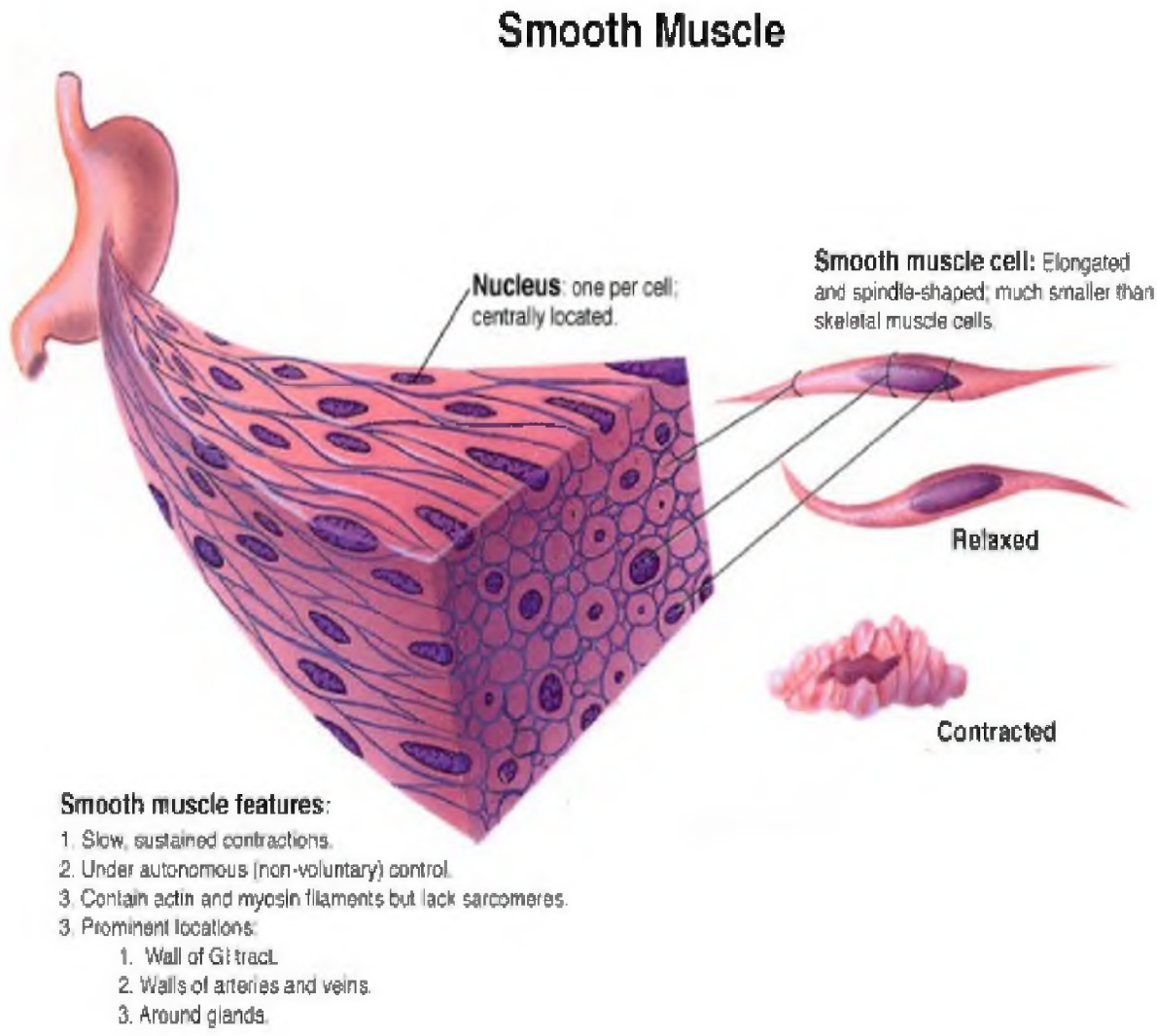


Fig.17. Smooth muscles structure.

Structure

Smooth muscle fibers are fusiform or elongated cells of different length. (Fig.17)

Smooth muscle fibers are generally very small, measuring 2 to 5 microns in diameter and 50 to 200 microns in length. Each muscle fiber contains myofibrils. The myofibrils are made up of muscle proteins. But, there are no dark and light alternated bands. This is the cause for non striated appearance of the smooth muscle.

Smooth muscle fiber contains actin, myosin and tropomyosin components. But troponin or troponin like substance is not present. For the initiation of contraction in skeletal muscle, the calcium ions released from cisternae of sarcoplasmic reticulum,

combine with troponin. But in smooth muscle, in addition to the absence of troponin, the sarcoplasmic reticulum is also poorly developed.

Electron microscopic studies reveal that some dense bodies are attached to the cell membrane and scattered all over the body of the fibers. Actin filaments are attached to these dense bodies. In between actin filaments, the thick myosin filaments are situated. There are cross bridges between actin and myosin filaments. The cross bridges help in the sliding mechanism of muscle contraction.

Contractive process in smooth muscle

In smooth muscle, latent period is long and contraction process is slow. The relaxation is also slow. Thus, the total twitch period is about 1 to 3 seconds. Stimulation of ATPase activity of myosin in smooth muscle is different from that in the skeletal muscle. In smooth muscle, the myosin has to be phosphorylated for the activation of myosin ATPase. The phosphorylation of myosin occurs in the following manner. Calcium entering the sarcoplasm from the extracellular fluid combines with calmodulin forming calcium-calmodulin complex. This activates an enzyme called calmodulin-dependent myosin light chain kinase. This enzyme in turn causes phosphorylation of myosin followed by activation of myosin ATPase. Now, the sliding of actin filaments starts.

Phosphorylated myosin gets attached to the actin molecule for longer period. It is called latch bridge mechanism and it is responsible for sustained contraction of the muscle with expenditure of little energy.

Relaxation of muscle may occur due to the dissociation of calcium-calmodulin complex.

Hormones influence on smooth muscle - some hormones of the body cause the contraction of smooth muscle and some hormones inhibit the contraction. Action of the hormone depends upon receptors present in the cell membrane. Receptors are of two types namely excitatory receptors and inhibitory receptors. Hormones binding with excitatory receptors cause contraction of muscle by producing depolarization. Hormones binding with inhibitory receptors inhibit contraction by increasing the negativity of membrane potential, which is called hyperpolarization.

Nerve supply to smooth muscle - smooth muscles are supplied by both sympathetic and parasympathetic nerves, which antagonize each other in control the activities of smooth muscles. However, nerves are not responsible for the initiation of any activity in smooth muscle. Tonus of smooth muscles is independent of nervous control.

Neuromuscular junction of smooth muscle -there is no well defined neuromuscular junction in smooth muscle. The nerve fibers diffuse on to muscle fibers The chemical neurotransmitters are directly released in the interstitial fluid.

Tab.3. Skeletal and smooth muscles comparative characteristics

Skeletal muscles	Smooth muscles
They are the structural part of musculoskeletal apparatus.	They are the structural part of inner organs and vessels membranes.
They have no plastic tonus.	They have plastic tonus.
They have fast short-termed depolarization and short absolute refractory period.	They have slow depolarization and long-termed absolute refractory period.
They have no the ability for differentiation and division.	They have the feature of differentiation, division and regeneration under injury.
They are innervated by somatic nervous system.	They are innervated by vegetative nervous system and have their own innervation apparatus (metasympathetic nervous system).
They are contracted under impulses transduction through the motor nerves from spinal motoneurons (automatism absence).	They are contracted both under impulses that occur in muscles themselves (automatism existence) and impulses transduction through vegetative nerves.
They have the ability to fast phasic contractions.	They have the ability to long-termed tonic contractions.
They realize arbitrary muscular movements that are accompanied by significant energy loss.	They realize arbitrary muscular movements that are accompanied by insignificant energy loss.
They have weak sensitivity to chemical substances.	They have high sensitivity to chemical, pharmacological, endogenous and exogenous

They react to medicines in some extent.	biologically active substances. They react to medicines in large extent.

3. Materials for auditory self-work.

Materials and methods: vertical myograph, stimulator, irritating electrodes, kymograph, universal stand, preparing instruments set, pipette, gauze napkin, Ringer's solution.

Investigation object: frog.

Task 1. Frog's stomach smooth muscles contractions registration

To cut the ring 5 mm wide from the frog's stomach. One end should be fixed on motionless hook, another one – on hook connected with writing lever. Hooks are electrodes in parallel. As smooth muscles excitability is low one should use strong and long-termed current for the irritation. Kymograph must have very slow working (movement).

To registrate and to analyze smooth muscles contraction process. To compare with the frog's skeletal muscle contractions registration.

Task 2. To compare frog skeletal and smooth muscle to chemicals

To put 2-3 drops of acetylcholine solution (warmed a little) to the frog nervous-muscular preparation. To note reaction presence or absence while recording on kymograph stripe.

To repeat the same in the second experiment but with 2-3 drops of adrenaline. To note reaction presence or absence while recording on kymograph stripe.

To do the same with stomach smooth muscle.

To glue received curves in a copy-book, to compare kymographs taken. To compare skeletal and smooth muscles sensitivity to chemicals.

4.Materials for self-control:

Control questions.

1. What muscles are arbitrary (voluntary) and what are involuntary ones? What do these terms mean?
2. Where and in what organs are there skeletal and smooth muscles?
3. What are the differences between smooth and skeletal muscular contraction?
4. Give the characteristics of smooth muscles excitability, conduction and automatism.

Content module 3: Organism functions nervous regulation
Lesson 5. Investigation of the reflex arc. Receptors physiology.

Before performing this lesson, you should study the introductory material presented here.

1.Lecture course.
2.Moroz V.M., Shandra O.A. Physiology. - 2011. Unit 2.
3.Guyton A.C., Hall J.E. Textbook of Medical Physiology. - 2006.
4.Guyton – Ganong – Chatterjee. Concise Physiology /Ed. By Dr Raja Shahzad Gull: M.B.B.S., F.C.P.S., King Edward Medical College.-Lahore, 1998 (1st Edition).-P. 261-263..

Relevance of the topic.

Nervous system diseases place one of the first places as for morbidity and lethality together with heart-vascular disorders and infectious pathology. Nervous regulation mechanisms dysregulation leads to functions discoordination and organism disadaptation. That is why nervous regulation functioning mechanisms and regularities knowledge is so essential for doctor of any speciality. Oral mucosa is often injured at dental diseases. It is expressed on its sensory function.

1.Objectives:

To know: reflex theory main principles; the term "reflex"; reflexes and reflex arches types; reflex arches main parts; receptors classification, features.

To be able to: draw reflex arch and designate its main elements; to explain excitation conductance regularities (receptor and generator potentials).

2. Topic content.

Nervous and endocrine system controls all activities of body. Primarily, nervous system is divided into two parts: central nervous system, peripheral nervous system.

Central nervous system

It includes brain and spine. It is formed by neurons and supporting cells called neuroglia. The structures of brain and spinal cord are arranged in two layers namely grey matter and white matter. Grey matter is formed by nerve cell bodies and proximal parts of axons and dendrites. White matter contains nerve fibers.

Peripheral nervous system

Somatic Nervous System

It includes nerves supplying skeletal muscles. Somatic nervous system controls movements of body by acting on skeletal muscles.

Autonomic Nervous System

It is concerned with regulation of visceral or vegetative functions. So, it is called vegetative or involuntary nervous system with other words. Autonomic nervous system consists of three parts:

a) sympathetic,
b) parasympathetic and
c) metasympathetic.

Reflex action – 1) is a protective phenomenon which occurs in response to a change inside or outside of the body; 2) response resulting from passage of a nerve impulse through a reflex arc.

Reflex arc:

It is composed of 5 components i.e.(Fig.18):

- Afferent neuron: from receptor to CNS.
- Inter Neuron (interneuron) or associative neuron: which lies inside CNS.
- Synapse: which is the contact between 2 neurons.
- Efferent Neuron: which comes from CNS upto the effector organ.
- Efferent Organ: which may be:
- skeletal muscle.
- smooth muscle.
- glands.

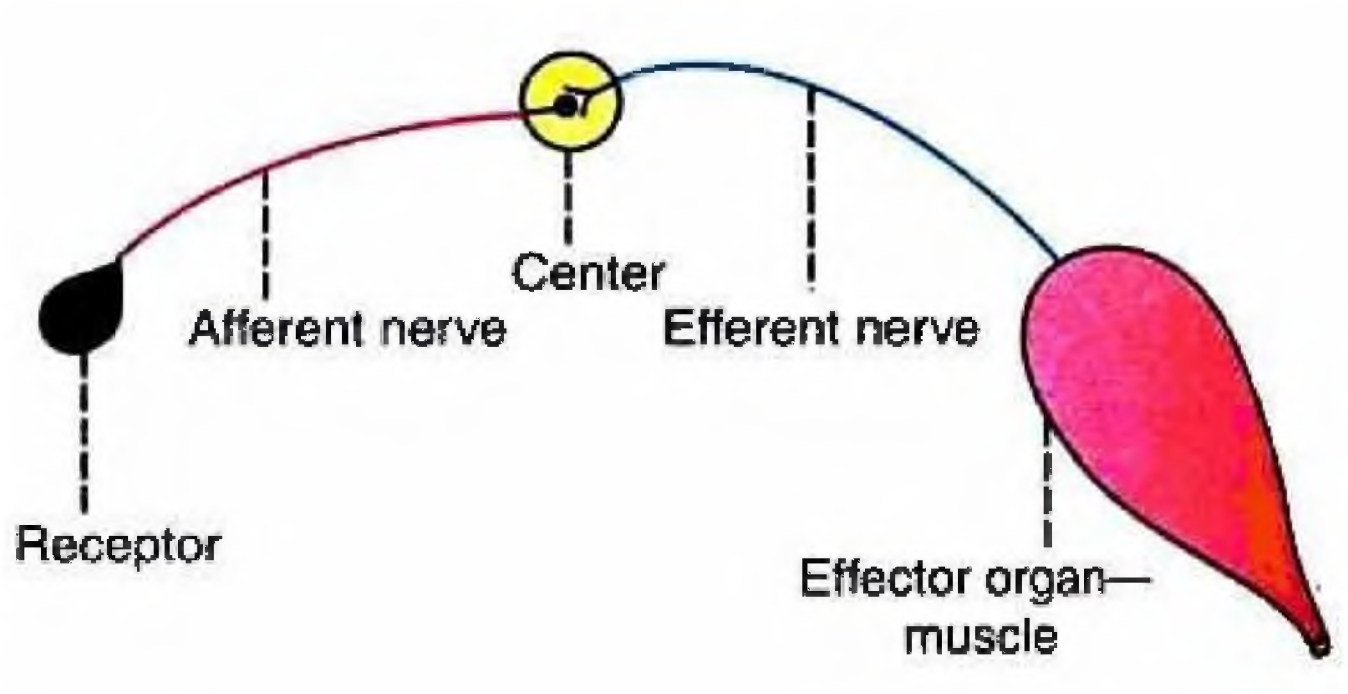


Fig.18. Reflex arc.

Reflex arc types:

1. Simple – without associative link.

Complex – with associative link.

2. Monosynaptic (little amount) (Fig.19).
   Polysynaptic: tendinous, from skin flexors et al.
3. Somatic (animalous).
   Vegetative (autonomic).

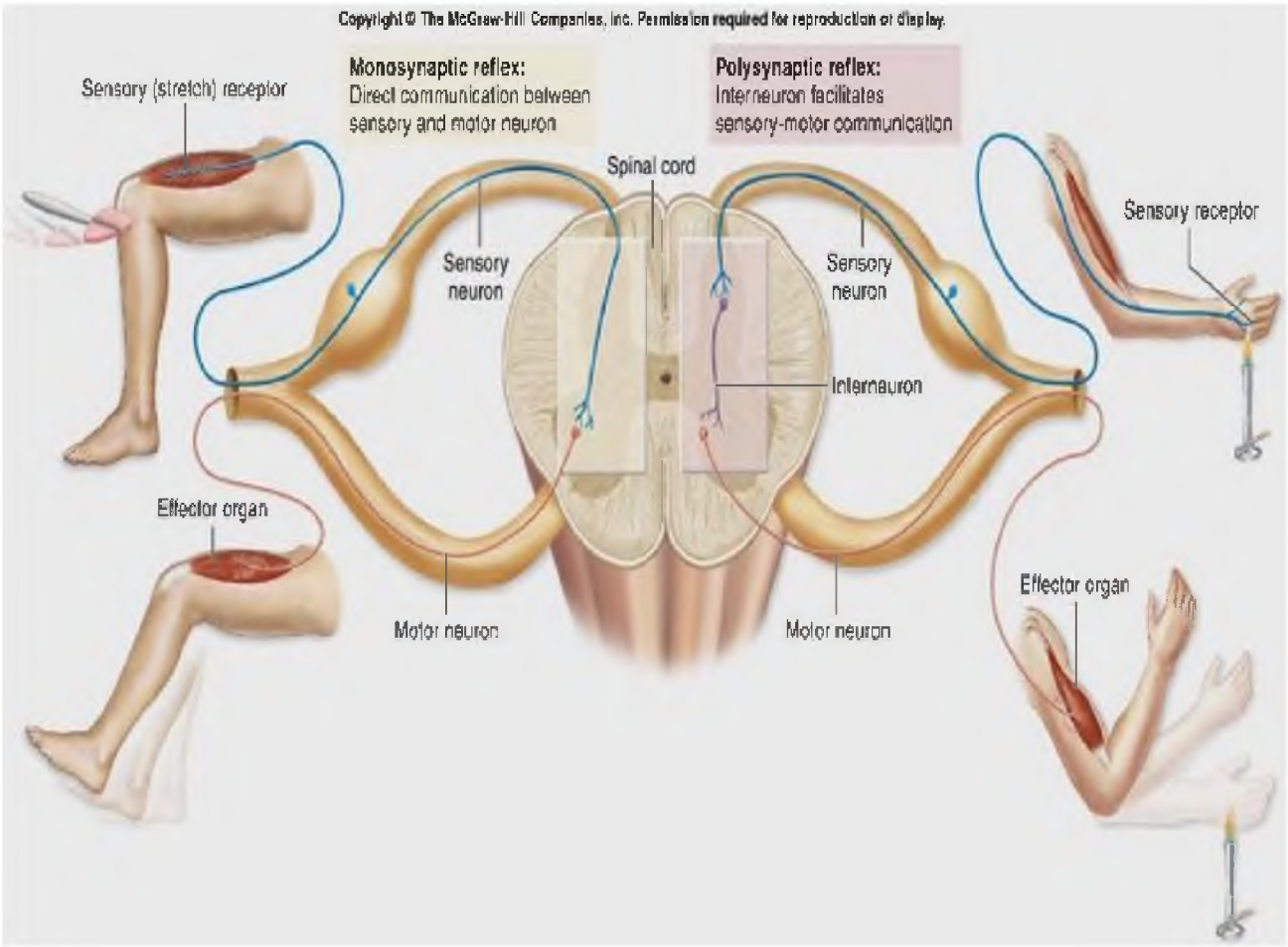


Fig.19. Reflex arc types (The McGraw-Hill Companies, Inc.).

Receptor is a specialized structure at the terminoma (end) of afferent neurons. It responds to minor changes around it, inside or outside the body.

Receptors tasks:

- giving information about stimulus nature;
- giving information about stimulus force;
- giving information about stimulus action time;
- analysis can not be realized without them.

There are several approaches to the receptors classification (and, thus, several receptors types).

Receptors classification

- According to the localization:

✓ Exteroreceptors: Skin, visual mucosas (particularly of oral cavity)
✓ Visceroreceptors: Interoreceptors – in inner organs;
✓ Proprioreceptors – in motor apparatus and vestibular apparatus.

- According to the activity character:

✓ Contact: (Fig.20) tactile (cutaneous) corpuscles for touch - Meissner's corpuscles and Merkel's discs; Pacinian corpuscles for pressure; Rouffinian bodies for vibration; temperature (free nervous terminals for heat; end bulb of Krause for cold; receptors of burning sensation); nociceptors (pain receptors); of taste.

- ✓ Distant or telereceptors - give response to stimuli arising away from the body: photoreceptors (to light); phonoreceptors (to sound); olfactory; temperature (if the irritation source is very powerful).
- ✓ Interoreceptors: presso- (baroreceptors); chemoreceptors; nociceptors; temperature; proprioceptors

Properties of receptors

1. Specificity of response - each type of receptor gives response to its own specific sensation. Stimulation of pain receptors produces pain sensation. Similarly, stimulation of touch receptors produces touch sensation. Synonym: adequacy or monomodality. Receptors order (from maximum to minimum):

- distant exteroreceptors;
- contact exteroreceptors;
- proprioreceptors;
- interoreceptors do not possess because these receptors must not react to specific stimuli but must act to any stimuli coming inside organism.

2. Polymodality is opposite to specificity. It means possibility to act to all stimuli. Receptors order (from maximum to minimum):

- interoreceptors;
- proprioreceptors;
- contact exteroreceptors;
- distant exteroreceptors (they do not have).

3. Adaptation or desensitization - when a receptor is continuously stimulated with the same strength of stimulus, after sometime the receptor stops sending impulses

through the afferent nerve. Depending upon this property, the receptors are divided into two types:

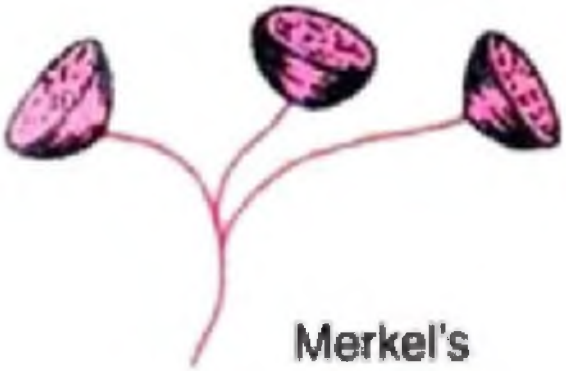
- phasic receptors, which get adapted rapidly - touch and pressure receptors;
- tonic receptors, which are adapted slowly – muscle spindle, pain receptors and cold receptors.

Maximal adaptation have exteroreceptors (more expressed – contact ones: first touching or kiss, clothes; then – distant – phono- and photoreceptors).

4. Response to increase in the strength of stimulus - during stimulation of a receptor, if response given by receptor is to be doubled, strength of stimulus must be increased 100 times. This phenomenon is called Weber-Fechner law, which states that the change in response of a receptor is directly proportional to logarithmic increase in the intensity of stimulus.

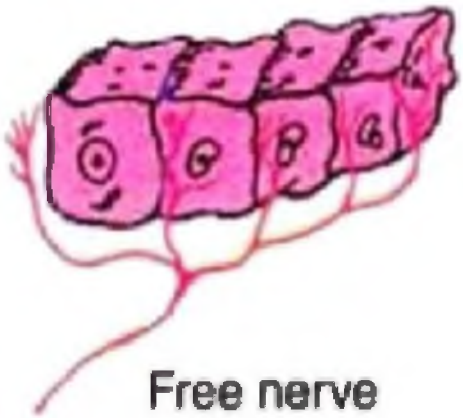
5. Electrical property - ability to generate receptor potential and generator potential.

Meissner's corpuscle (Touch)

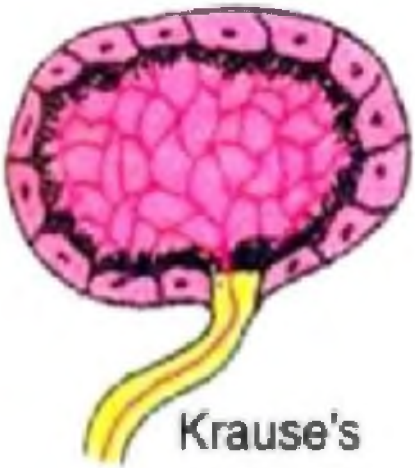


Merkel's disc (Touch)

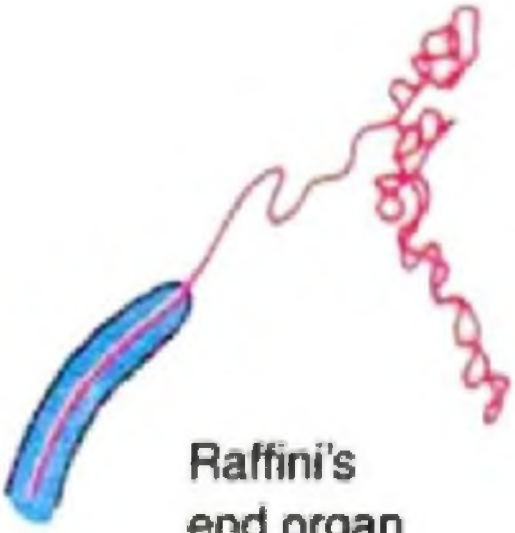
Pacinian corpuscle (Pressure)



Free nerve ending (Pain)



Krause's end bulb (Cold)



Raffini's end organ (Warmth)

Fig.20. Cutaneous receptors.

When a receptor is stimulated, a nonpropagated transmembrane potential difference is developed. This is called receptor potential. Receptor potential is not action potential. It is similar to excitatory postsynaptic potential (EPSP) in synapse, endplate potential in neuromuscular junction and electrotonic potential in the nerve fiber. Receptor potential has such important properties: it is non-propagated (local); it does not work according to the law "everything or nothing".

Receptor potential is receptor cell membrane depolarization (in complex receptor) or free nervous fiber (in simple receptor) at irritator action to the receptor. Receptor potential is local one. It coincides generator potential in simple receptor. But it differs from it in complex receptor. Generator potential is depolarization of free nervous fiber membrane at mediator portion action. Mediator releasing is caused by receptor formation generation. Generator potential is an action potential. It is equal to action potential and works according to law "everything or nothing" (receptor potential undergoes law of force correlation).

When the receptor potential is sufficiently strong (when the magnitude is about 10 mV), it causes development of action potential in the sensory nerve.

Mechanism of Development of Receptor Potential and Generation of Action Potential in the Nerve Fiber

The deformation of the nerve fiber causes opening of sodium channels. So, positively charged sodium ions enter interior of nerve fiber and a mild depolarization, i.e. the receptor potential occurs (Fig.21). This receptor potential spreads along the non-myelinated part of the nerve fiber.

When this current reaches the first node of Ranvier within the corpuscle, it cause development of action potential in the nerve fiber.

- Sensory transduction – the process, which helps the receptor to give response to a stimulus is called sensory transduction (transduction = conversion of one form of energy into another). Sensory transduction depends on type of receptor. For example, chemoreceptor converts chemical energy into action potential in sensory nerve fiber. Touch receptor converts mechanical energy into action potential in sensory nerve fiber.
- After-action - receptor action continuation after stimulus action stoppage; it is connected with rhythmical activity.

- Rhythmical activity – receptor is working despite mediator down-releasing and stimulus absence.
- Ability to transform force in frequency – receptor is increasing transformer because the more is stimulus action the bigger is generator potential duration
- (synapse is decreasing transformer because 3-5 EPSP give only 1 action potential).
- Higher excitability comparatively to neurons and nervous fibers.
- Excitability fluctuation in one and the same receptor – it is fluctuated from high level to low excitability and finally its absence because of receptor rest.
- Similar-grouped receptors have non-equal excitability because of different threshold. It allows to rest to one receptors.

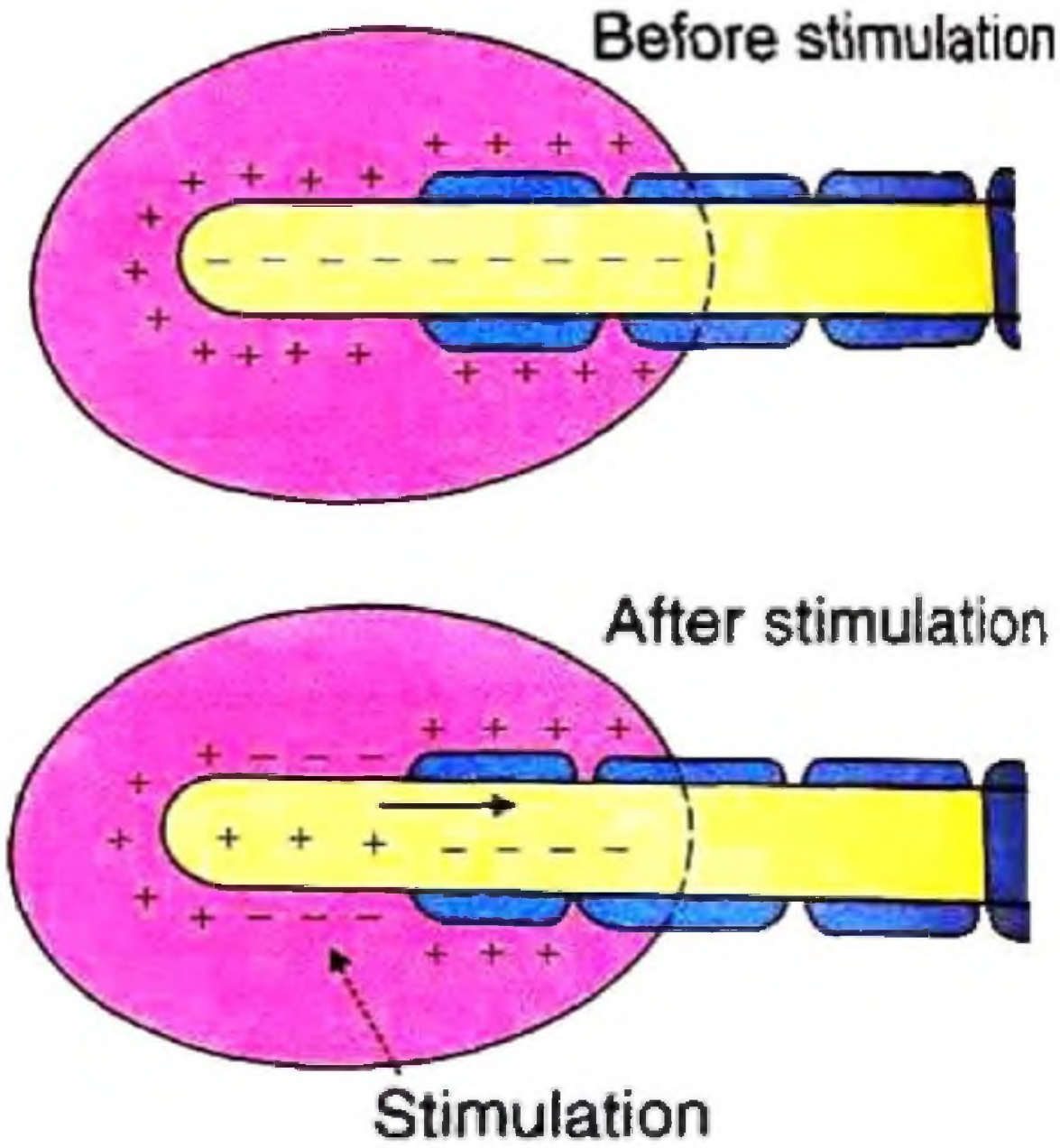


Fig.21. Development of receptor potential in Pacinian corpuscle.

3. Materials for auditory self-work.

Materials and methods: istruments preparation set, metronom, stand, acids set (sulfuric acid 0,1%, 0,3%, 0,5%, 1,0% solutions), Ringer's solution; glass, threads, novocain solution.

Investigation object: frog.

Task 1. Receptive field definition.

Every reflex has its own reflex field, i.e. body locus at irritation of which this reflex occurs. Response answer character at reflex field irritation depends not only on its localization on body surface but also on irritation force and duration.

Frog's brain must be removed. After that you receive spinal frog's preparation it's necessary to wait 2-3 minutes for spinal shock phenomena disappearance. Then the investigators must hang the frog by his inferior jaw on the hook fixated in a stand. They wash filter paper piece in 0,1% sulfuric acid solution and put it on inferior leg tibia external skin surface. To observe flexory reaction of corresponding leg. To wash the leg from acid by means of leg's plunging into water. To realize the irritation of the same leg with 0,3%, then with 0,5% of acid solutions. To choose those concentration at which one can see

maximal flexory reflex. Paper with sulfuric acid of this concentration put on lateral abdomen surface. After some minutes you can observe defensive reflex: frog takes the paper off with the nearest leg. To put the paper to the external surface of anterior leg, on the abdomen near to the thoracic part, between superior and inferior legs. You must registrate answer reaction every time. The intervals between irritations must be at least 2-3 min. After each irritation you should put the frog to the glass with water and wash the animal from acid residues.

In second experiment you should put your attention to the correlation of reflex time to stimulus force (students must perform the experiments with all solutions (time must be fixed with metronom or watch with second pointer).

Task 2. Analysis of the reflex arc.

To prepare spinal frog (Fig.22) and to hang it with inferior jaw on a stand. To put one of her legs in 0,5% of sulfuric acid.

Convince in reflex existence. To perform round skin incision below knee jerk and to release the leg from its skin. To irritate this leg tibia again. To observe the reaction.

To cut other posterior (inferior) leg hip skin of the same frog and to prepare sciatic nerve over the distance of 1,5-2,0 cm. To bring the thread under the nerve but not to tie it. To call flexion reflex by means of taking this leg fingers ends into acid. Then to tighten the nerve carefully by the thread and put the cotton wool washing into novocain solution under it for excitation transduction blocking into sciatic nerve fibers. To check the reflex existence.

To check the reflexes existence on superior legs.

To destroy the spine and to observe all reflexes disappearance.

On the base of investigations performed make the conclusion about reflex arc structure. Designate its links.

Task 3. Gustatory receptors functional mobility determining (before and after eating).

To be convinced of eating leading to demobilization i.e. actively functioning gustatory receptors number decreasing.

The work must be performed on an empty stomach or at least after 3-4 hours after eating. The experienced person tongue must be dried with filter paper. Gustatory stimulus (sugar solution: 8 grams of sugar for 20 ml of dist water) must be taken on separate tongue fungiform papillas with pipette. 4 papillas becomes differentiated at this that give sweet taste sensation. It is one probe. Students must perform 5 probes with intervals 1-2 minutes between them. One must rinse mouth out after every probe. You should investigate the same papillas. The gustatory sensation appearance is marked in protocol with sign "+", the disappearance- "-". You should count positive answers common number and express mobilization level in per cents. The investigations must be repeated after eating (sweet tea glass with white bread).

4.Materials for self-control:

Control questions.

1. The term "reflex".
2. Reflex receptor zone.
3. Reflex arc and its structure.
4. Reflex time.
5. Reflexes classification.
6. Reflex arches types.
7. Receptors distinguishing features.
8. Receptor and generator potential.
9. Receptors classification.

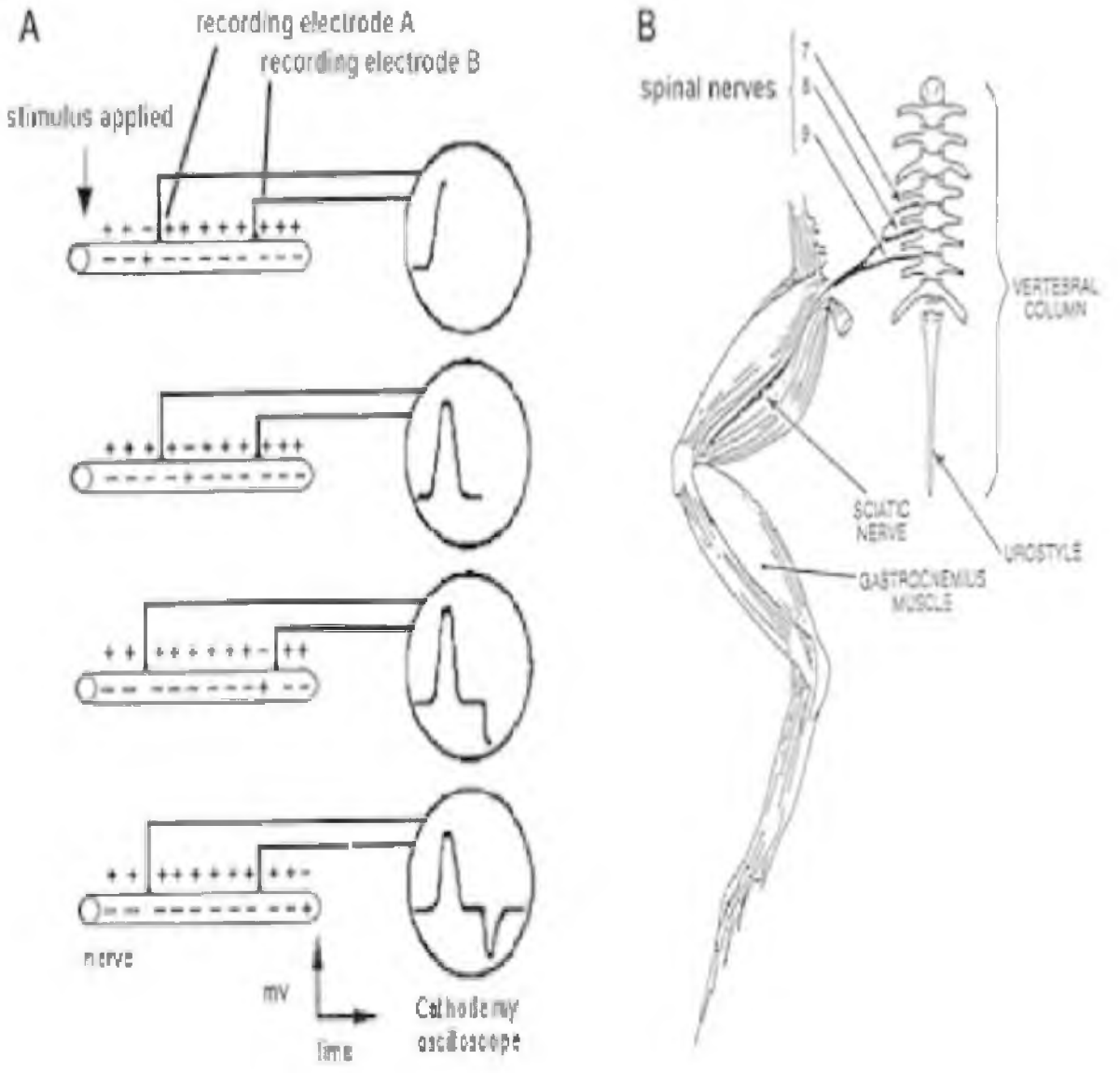


Fig.22. Analysis of the reflex arc.

Lesson 6

Excitation transmission investigation through nervous fibres.

Before performing this lesson, you should study the introductory material presented here.

1.Lecture course.
2.Moroz V.M., Shandra O.A. Physiology. - 2011. Unit 1, Chapter 2
3.Guyton A.C., Hall J.E. Textbook of Medical Physiology. - 2006. Unit 1.
4.Ganong W.F. Review of Medical Physiology.-21st ed.-2003.-Section II.

Relevance of the topic.

Doctor often meets excitation conductance disorders in nervous-muscular synapses and nervous fibers. He must influence on them well single mindedly with impulses conductance enforcement or weakening. So, he should know excitation conductance mechanisms and regularities. Nervous fiber is reflex arc afferent or efferent part. Reflex disappears at nervous impulse conductance disturbance. Different nervous fibers possess various excitability and excitation conductance different speed. It should be taken into account while medicines dosage prescription. Nervous fibers conductance laws are used in neurology and anaesthesiology.

1.Objectives:

To know: excitation developmental mechanisms in myelin and myelin-free nervous fibers; main factors determining conductance velocity; synapses main types; excitation regularities in chemical and electrical synapses.

To be able to: interpret conductivity disorders reasons, excitation nervous-muscular conductance blockade mechanisms; to draw schematically conductance mechanism in myelin and myelin-free fibers as well as through nervous-muscular synapse.

2.Topic content.

Local anesthesia physiological basement in dentistry.

Significance of excitation conductance laws (through nervous fibers) in dentistry.

Nervous fibre physiological integrity law is used in dental practice for local anesthesia performance: nervous impulse conductance through nervous fibre is possible only at its physiological integrity; narcotic substance, cooling action, ligature or weak electrical current influence lead to nervous fibre structures functioning stoppage and prevent excitation distribution.

Conductive anaesthesia - analgetic (novocaine) introduction - and excitation in pharmacological blockade zone is not distributed.

Electroanalgesia – anode (positive electrode) putting from current origin blockates receptory cells membranes depolarization; that is why nociceptive impulses do not occur.

Electrical magnetical waves application – analgesia is the result of neurons membranes depolarization prevention.

Neurons Classification (Fig.23)

Depending on number of poles:

a) Unipolar neurons – are present only in embryonic stage in human beings, from the single pole, both the processes - axon and dendrite arise;

b) Pseudounipolar – they have one axon and one dendrite but both come from one neuron body pole; example – spinal ganglia;

c) Bipolar neurons - have two poles, one for axon and another for dendrite; example – retina, cochlea spiral ganglion;

d) Multipolar neurons - have many poles, one of which gives rise to the axon and all the other poles give rise to dendrites; biggest neurons number belong to this group.

Depending on function:

a) Motor or efferent neurons - carry the motor impulses from central nervous system to the peripheral effector organs like muscles, glands, blood vessels, etc.:

- neurons of autonomic nervous system;
- alpha motor neurons – innervate extrafusal muscle fibers (out of muscular spindles);
- gamma motor neurons – innervate intrafusal muscular fibers (inside muscular spindles);

b) Sensory or afferent neurons - neurons carry the sensory impulses from periphery to the central nervous system;
c) Associative (99,8% of all) – they bind different-typed neurons.

P.S. Muscular spindles – are muscles receptors percepting muscle length and its contraction speed.

Depending on length of axon:

a) Golgi Type I Neurons - have long axons, the cell body of these neurons is in central nervous system and their axons reach remote (far) peripheral organs;

b) Golgi Type II Neurons - have short axons, are present in cerebral cortex and spinal cord, cerebellar Purkin'e cells belong to them.

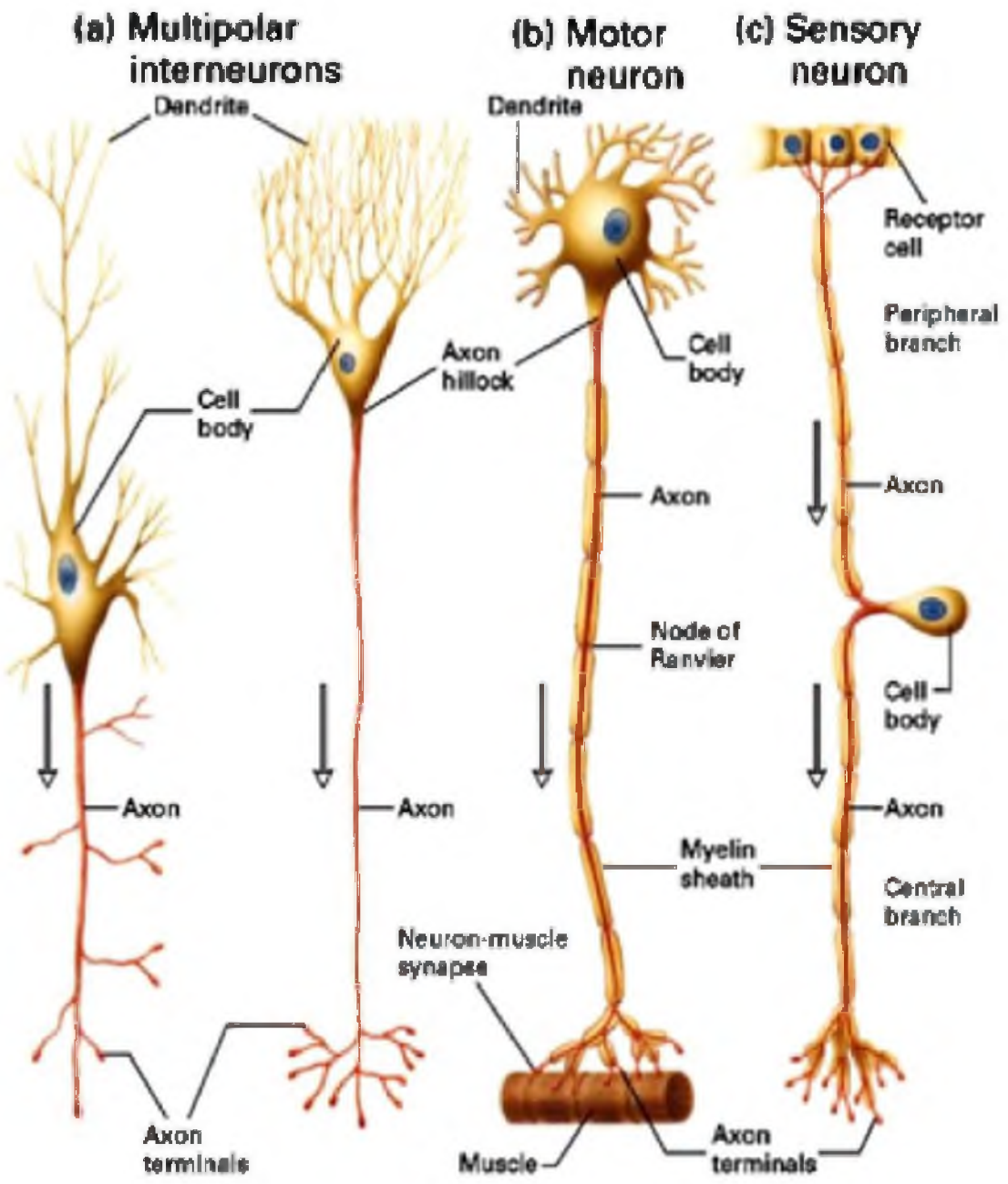


Fig.23. Neurons classification.

Nervous fibers physiology

Structure of Myelinated Nerve Fiber (Fig.24)

Axis cylinder of nerve fiber is covered by a membrane called neurilemma.

In myelinated nerve fiber, axis cylinder is covered by a thick sheath called myelin sheath. Myelin sheath in turn is covered by neurilemma.

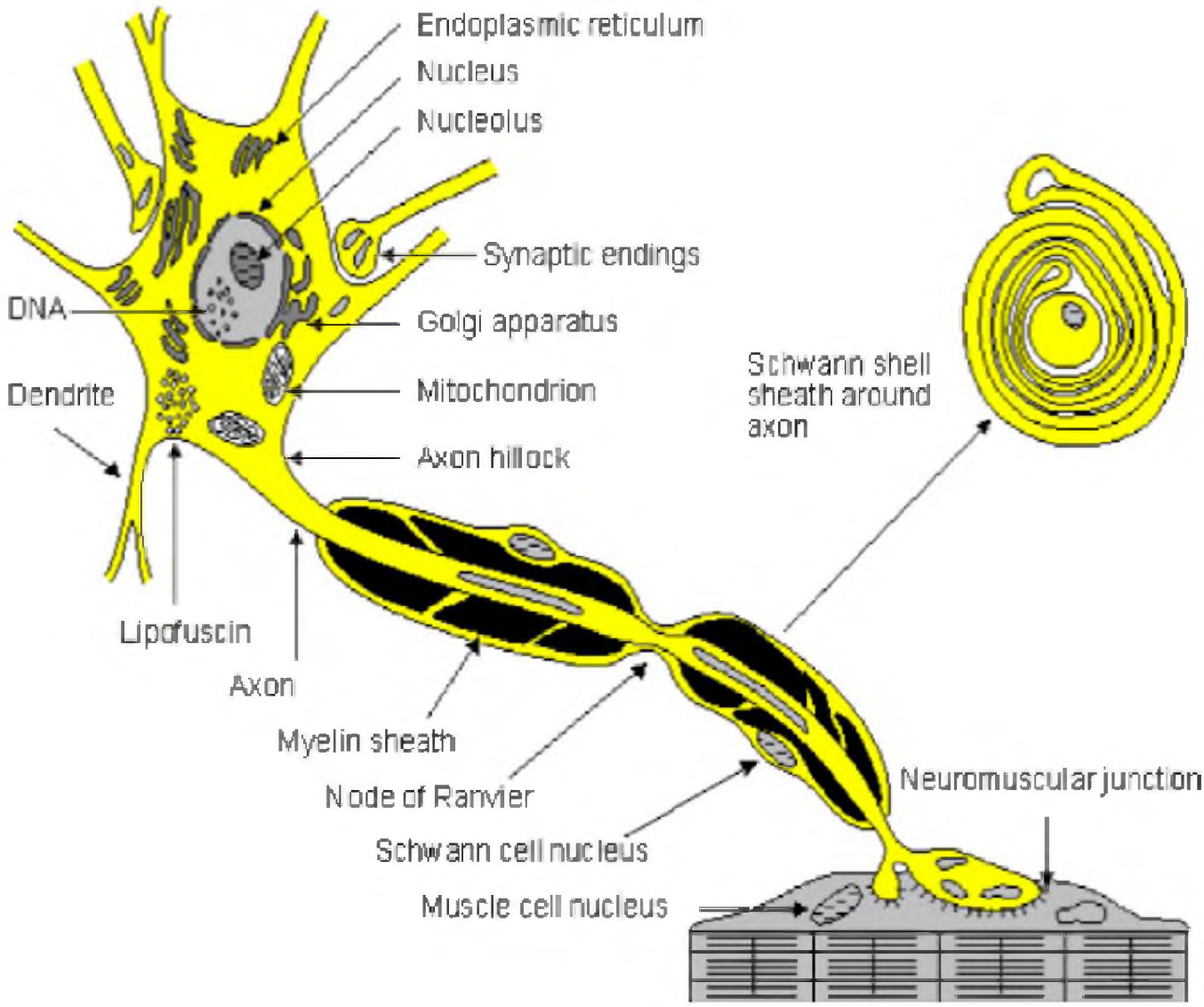


Fig.24. Myelinated nerve fiber

Myelin sheath

In a myelinated nerve fiber, axis cylinder is covered by a thick tubular sheath called myelin sheath. Myelin sheath does not form a continuous sheath and is absent at regular intervals. The area where the myelin sheath is absent is called node of Ranvier. The segment of nerve fiber between two nodes is called internode. Myelin sheath is responsible for white colour of nerve fibers. Myelin is lipoprotein.

Functions of Myelin Sheath

- Myelin sheath is responsible for faster conduction of impulse through nerve fibers. In these nerve fibers, impulses jump from one node to another.

Transmission of impulses from one node to another is by means of saltatory conduction.

- Myelin sheath also has a high insulating capacity. Because of this, myelin sheath restricts nerve impulse within single nerve fiber, and prevents stimulation of neighboring nerve fibers.

Neurilemma

Surrounding myelin sheath, there is a thin membrane called neurilemmal sheath. This is also called neurilemma or sheath of Schwann. It contains Schwann cells. Cytoplasm is thin and modified to form the thin sheath of neurilemma enclosing the myelin sheath. At node of Ranvier (where myelin sheath is absent), the neurilemma invaginates and runs up to axolemma in form of a finger-like process. Neurilemma is necessary for formation of myelin sheath (myelinogenesis). Neurilemma is absent in central nervous system.

In non-myelinated nerve fiber, the neurilemma continuously surrounds axolemma.

Nervous impulses conduction

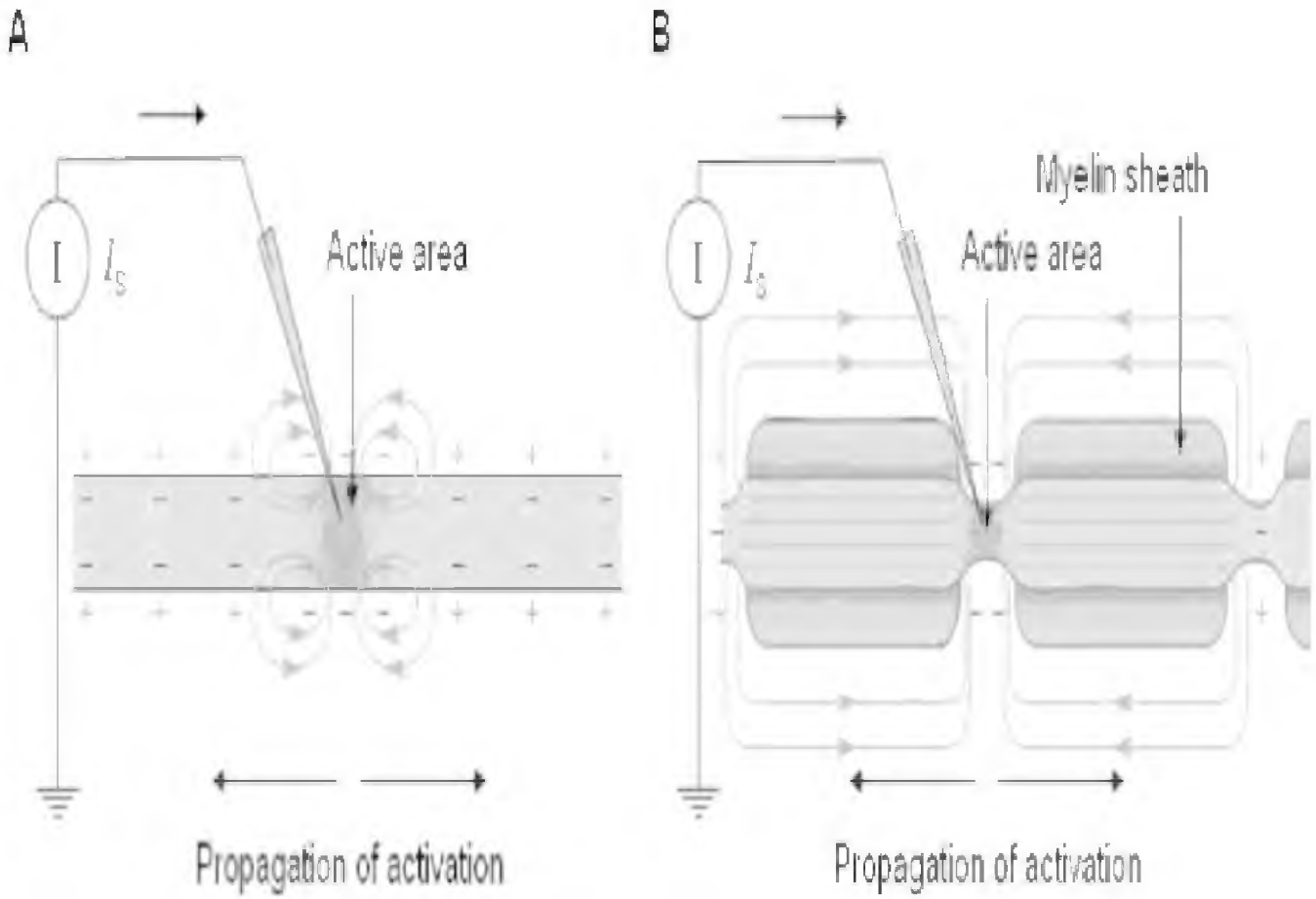


Fig.25. Mode of conduction through nerve fibers.

A. Non-myelinated nerve fiber — Continuous conduction.
B. Myelinated nerve fiber — Saltatory conduction: impulse jumps from node to node. AP = action potential.

Conduction through myelinated nerve fiber - saltatory conduction

Conduction of impulse through a myelinated nerve fiber is about 150 times faster than through a non-myelinated fiber (Fig.25). This is because, myelin sheath forms an effective insulator and flow of current through this sheath is negligible. But action potential jumps from one node to another node of Ranvier. So, velocity of conduction is faster. This type of jumping of action potential from one node to another is called saltatory conduction.

Mechanism of Saltatory Conduction

The myelin sheath is not permeable to ions. So, entry of sodium from extracellular fluid into nerve fiber occurs only in the node of Ranvier, where myelin sheath is absent. This causes depolarization in the node, and not in the internode. Thus, depolarization occurs at successive nodes. So, action potential jumps from one node to another. Hence, this is called saltatory conduction (saltare = jumping).

Tab.4. Nervous fibers classification.

Fibers type	Fibers diameter (mcm)	Transduction velocity (m/sec)	Main function
A_α Type I	13-22	70-120	skeletal muscles efferent fibers; receptors (muscular spindles) afferent fibers
A_β Type II	8-13	40-70	afferents from pressure and touching receptors
A_γ	4-8	15-40	receptors (muscular spindles) efferent fibers;

			part of afferents from pressure and touching receptors
A_δ Type III	1-4	5-15	afferents from skin temperature and pain receptors, partially pressure
B	1-3	3-14	autonomic nervous system preganglionar efferents
C Type IV	0,5-1,5	0,5-2	autonomic nervous system postganglionar efferents; pain and warmth skin receptors afferents

Velocity of impulse through a nerve fiber is directly proportional to thickness of fibers (Tab.4). Except C type of fibers, all nerve fibers are myelinated, B type is partially myelinated.

Nervous fibers properties

Excitability - nerve fibers have lower threshold for excitation than other cells. Resting membrane potential in nerve fiber is-70 mV. Firing level (critical depolarization level) is at-55 mV. Depolarization ends at +35 mV.

Conductivity - normally in body action potential is transmitted through nerve fiber in only one direction. However, in experimental conditions when the nerve is stimulated or damaged (tumor, anaesthesia, inflammation) action potential travels through the nerve fiber in both direction.

Refractory period

Summation. When one subliminal stimulus is applied, it does not produce any response in the nerve fiber. However, if two or more subliminal stimuli are applied within a short interval of about 0.5 m sec, the response is produced. This is because the subliminal stimuli are summed up together. This is known as summation.

Adaptation. While stimulating a nerve fiber continuously, excitability of nerve fiber is maximum at the beginning. Later - response decreases slowly and finally

nerve fiber does not show any response at all. This phenomenon is known as adaptation or accommodation.

Tirelessness. A nerve fiber cannot be fatigued, even if it is stimulated continuously for a long time. The reason for this is that nerve fiber can conduct only one action potential at a time. At that time, it is completely refractory and does not conduct another action potential.

Law "Everything or nothing".

Excitation conductance through nervous fibers obeyes definite laws.

1) Physiological integrity law - tells that excitation conductance through nervous fibre is possible only in a case of its non-interrupted anatomical structure and physiological features.

2) Excitation conductance two-sided law - at irritation application on nervous fibre the excitation is diverged through it in both sides from irritation place (at tooth nerve irritation pain is stretched not only on local tissues but also irradiates in other body parts).

3) Excitation isolated conductance law - excitation through nervous fibers being in a composition of mixed nerves (for example, vagus) is diverged separately, i.e. it doesn't transmit through one nervous fibre to another.

3. Materials for auditory self-work.

Materials and methods: vertical myograph, stimulator, irritating electrodes, kymograph, universal stand, preparating instruments set, pipette, gauze napkin, Ringer's solution.

Investigation object: frog.

Task 1. Isolated impulse conducting law (through nervous fibers).

The students must prepare the preparation of frog's lower extremities with skin taking off and with 3 lower vertebras saving. You should ligatured each of nervous fibers at the place of sciatic nerve exit from the spine and to separate from the spine. Students must irritate every fibre of sciatic nerve one after another with weak electrical current, while observing different irritation phenomena at it.

Task 2. Two-sized conduction law.

Students must make frog's extremity and preparated sciatic nerve so that not to hurt branchlets passing to the musculus quadriceps femoris and gastrocnemius muscle. One should irritate the nerve by electrical current near gastrocnemius muscle and observe the contraction both musculus quadriceps femoris and gastrocnemius muscle.

Task 3. Physiological integrity law.

Put the preparation on glass plate. To irritate the preparation nerve by electrical current. Frog's leg is bended. To put the ligature on sciatic nerve. To irritate the nerve by electrical current again. The muscle doesn't contract. If you attach the electrodes so that the ligature is between 2 electrodes the leg will be contracted. To repeat the examination but to use cotton wool tampon washed in novocain solution despite ligature.

Lesson 7.
Excitation transmission investigation through synapses.

Before performing this lesson, you should study the introductory material presented here.

1.Lecture course.
2.Moroz V.M., Shandra O.A. Physiology. - 2011. Unit 2
3.Guyton A.C., Hall J.E. Textbook of Medical Physiology. - 2006.

Relevance of the topic.

The term "synapse" was introduced by English physiologist Charles Sherrington in 1897 who predisposed existence of special structural-functional formations providing contacts between neural cells.

1.Objectives:

To know: main factors determining conductance velocity; synapses main types; excitation regularities in chemical and electrical synapses.

To be able to: interpret conductivity disorders reasons, excitation nervous-muscular conductance blockade mechanisms; to draw schematically conductance mechanism in myelin and myelin-free fibers as well as through nervous-muscular synapse.

2.Topic content.

Synapses physiology

A synapse is a functional point of contact between 2 neurons, neuron and myocyte or neuron as well as neuron and secretory cell that transmits impulse from first to the second cell providing excitation (inhibition) transmittance as well as nervous impulses transformation.

Classification

1.According to communication basis (Fig.26):

a) Central:

- Axo-somatic.
- Axo-dendritic.
- Axo-axonic.
- Dendro-somatic.
- Dendro-dendritic.
- Soma-somatic.

b) Peripheral:

- Neuromuscular.
- Neurosecretory.

2. According to nature (Fig.27):

- Electrical synapses (ephapses).
- Chemical synapse.

3. According to mediators – only chemical synapses.
4. According to ending effect:

- Stimulating – both electrical and chemical ones.
- Inhibition- only chemical ones.

5. Main mediators groups:

1) Acetylholine
2) Amines: Dopamine, Norepinephrine, Epinephrine, Serotonin, Histamine.
3) Excitatory amino acids: Glutamate, Aspartate.
4) Inhibitory amino acids: Glycine, Gamma-aminobutyrate (GABA).
5) Polypeptides: Substance P, other tachykinins, Vasopressin, Oxytocin, Somatostatin, Enkephalins, Cholecystokinin (CCK) octapeptide, Vasoactive intestinal polypeptide (VIP), Angiotensin II, Atrial natriuretic peptide (ANP).
6) Purines: Adenosine, ATP.
7) Gases: NO, CO.
8) Lipids: Arachidonic acid and derivatives

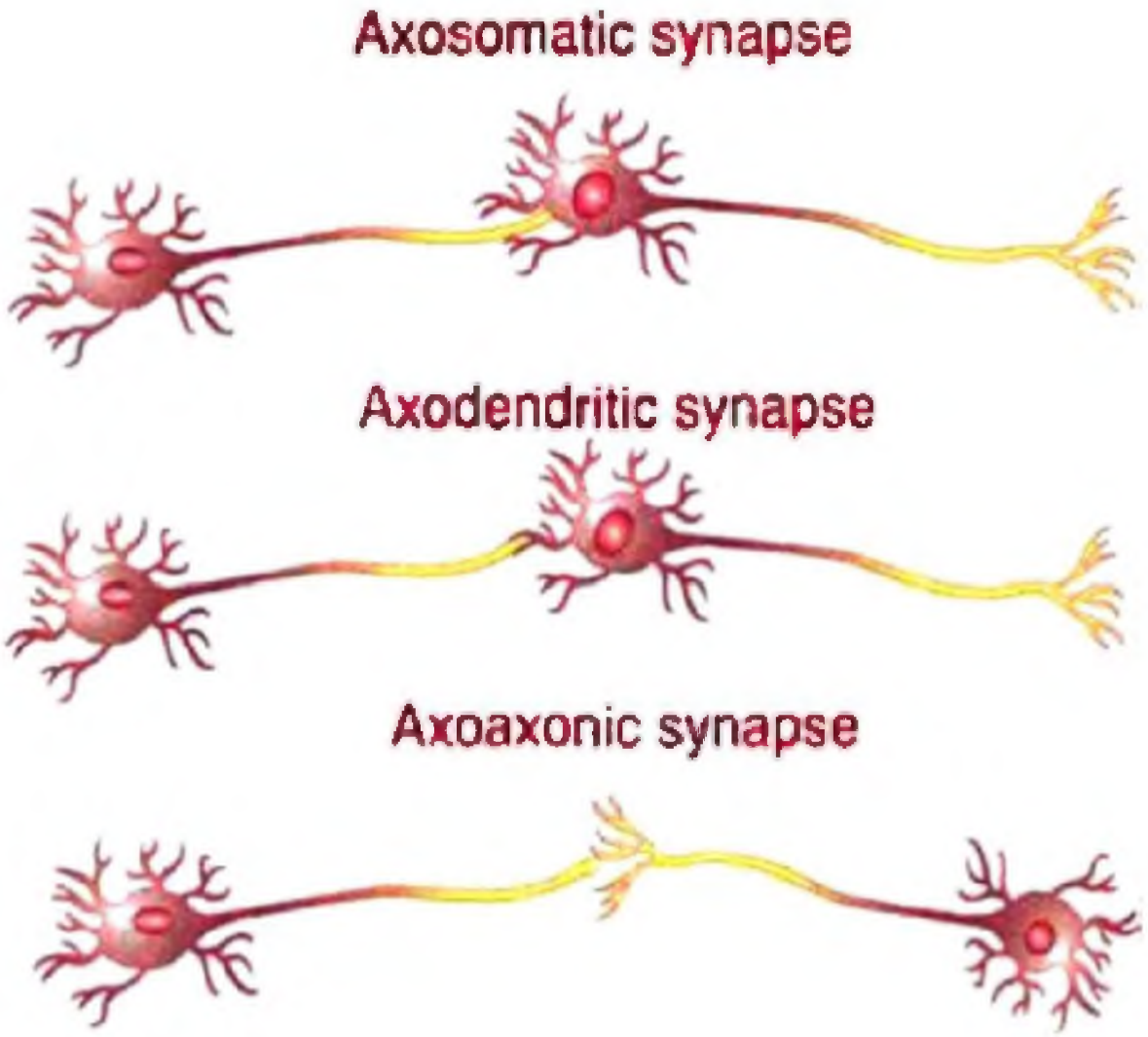


Fig.26. Classification according to communicational basis.

Synapse structure

1. Presynaptic terminal or part – usually is presynaptic axon ending.
2. Synaptic cleft – is a space dividing membranes of contacting cells.
3. Post-synaptic part – is cell locus to which presynaptic ending comes

Synaptic binding is interneuronal interaction main mechanism. It provides all major expressions of nervous system activity. It is one of the most essential structural-functional brain elements.

Neuron from which axon arises is called presynaptic neuron and neuron on which axon ends is called postsynaptic neuron. Axon of presynaptic neuron divides into many small branches before forming the synapse. These branches are known as presynaptic axon terminals. The slightly expanded presynaptic terminal has a definite intact membrane known as presynaptic membrane.

Presynaptic terminal has two important structures:

- mitochondria, which help in the synthesis of chemical neurotransmitter substances;
- synaptic vesicles, which store neurotransmitter substances.

Membrane of postsynaptic neuron is called postsynaptic membrane. It contains some receptor proteins. Small space in between presynaptic membrane and postsynaptic membrane is called synaptic cleft. Basal lamina of this cleft contains cholinesterase, which destroys acetylcholine.

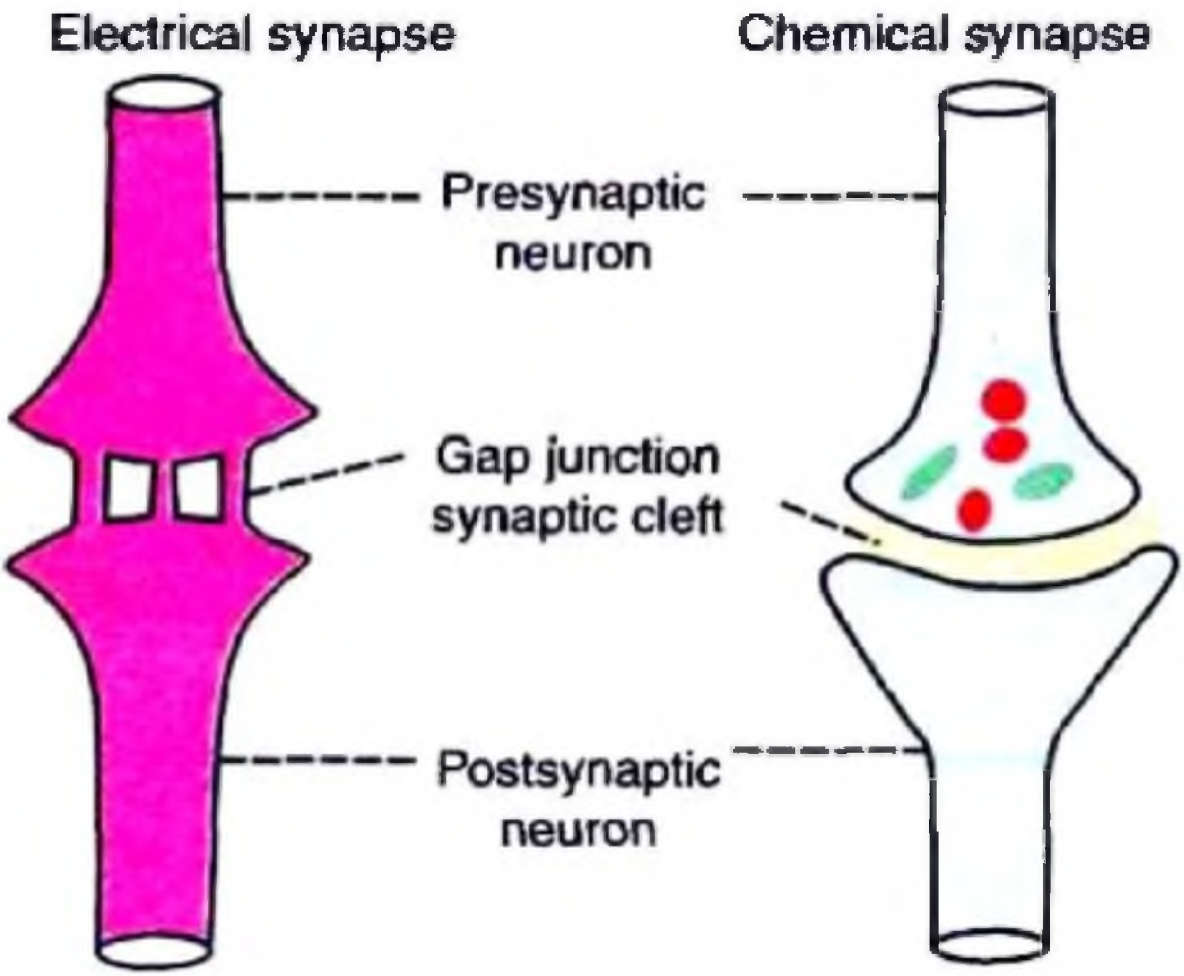


Fig.27. Classification according to nature

Function of synapse

Main function of synapse is to transmit impulses, i.e. action potential from one neuron to another. However, some of synapses inhibit these impulses and so impulses are not transmitted to the postsynaptic neuron. Thus, synapses are of two types.

- Excitatory synapses, which transmit the impulses-excitatory function and
- Inhibitory synapses, which inhibit transmission of impulses—inhibitory function.

Electrical Synapse or Ephapse

In electrical synapse, there is continuity between presynaptic and postsynaptic neurons. Continuity is provided by gap junction between two neurons. So, there is direct exchange of ions between two neurons. Because of this, action potential

reaching presynaptic terminal produces potential change in postsynaptic neuron. Important feature of electrical synapse is that synaptic delay is minimum or even absent because of direct flow of current. If in ephapse fissure between pre- and postsynaptic elements is 2 nm, in chemical ones –50-300 nm. Thus, quicker impulse distribution is in ephapse. Moreover, unlike chemical synapse, impulse can be transmitted in either direction through the electrical synapse thus in 2 directions. They are considered to be only excitatory (due to depolarization development) comparatively to chemical synapses.

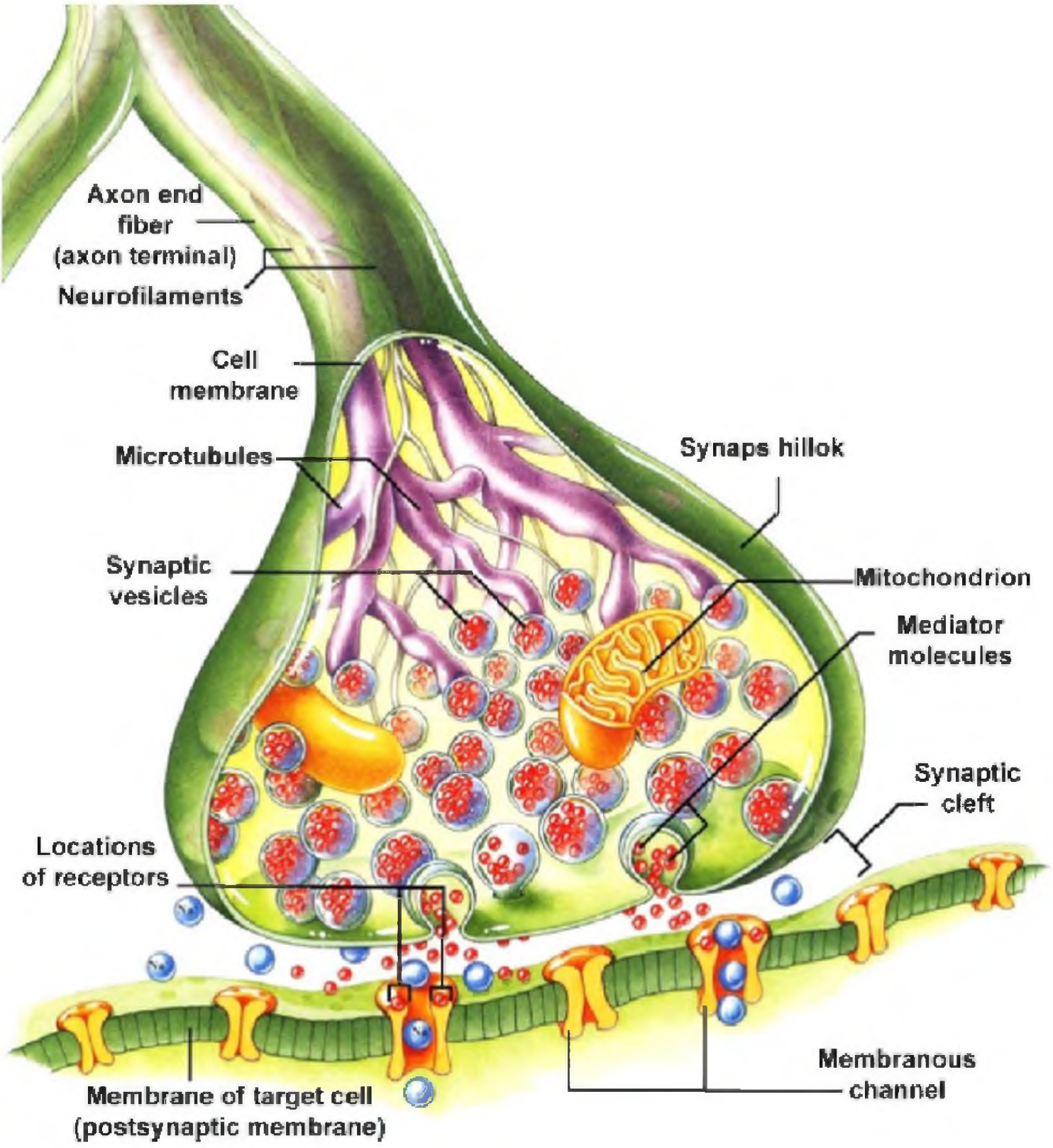


Fig.28. Chemical synapse structure.

Chemical Synapse

Chemical synapse is the junction between a nerve fiber and a muscle fiber or between two nerve fibers, through which signals are transmitted by release of chemical transmitter (Fig.28). In chemical synapse, there is no continuity between presynaptic and postsynaptic neurons because of presence of a space called synaptic cleft between two neurons. Action potential reaching presynaptic terminal causes release of neurotransmitter from vesicles of terminal. Neurotransmitter reaches postsynaptic neuron through synaptic cleft and causes production of potential change. The structure and functions of the chemical synapse are given below.

Excitatory function

When action potential reaches presynaptic axon terminal, voltage gated calcium channels at presynaptic membrane are opened. Now calcium ions enter axon terminal from extracellular fluid (Fig.29).

Calcium ions cause fusion of synaptic vesicles with cell membrane and release of neurotransmitter substance from vesicles by means of exocytosis.

Presynaptic neuron	Arrive of action potential in axon terminal
	Opening of calcium channels in presynaptic membrane
	Influx of calcium ions from ECF into the axon terminal
	Opening of vesicles and release of Ach

Passage of Ach through synaptic cleft	
Postsynaptic neuron	Formation of Ach-receptop complex
	Development of EPSP
	Opening of sodium channels and influx of sodium ions from ECF
	Opening of sodium channels in initial segment of axon
	Influx of sodium ions from ECF and development of action potential
	Spread of action potential through axon of postsynaptic neuron

Fig.29. Sequence of events during synaptic transmission.

Ach = Acetylcholine. ECF = Extracellular fluid. EPSP = Excitatory postsynaptic potential

Neurotransmitter, which is excitatory in function (excitatory neurotransmitter) passes through presynaptic membrane and synaptic cleft and reaches postsynaptic membrane. Now, the neurotransmitter binds with the receptor protein present in the postsynaptic membrane to form the neurotransmitter receptor complex. Neurotransmitter receptor complex causes production of non propagative electrical

potential called excitatory postsynaptic potential (EPSP). The most common excitatory neurotransmitter in a synapse is acetylcholine.

Mechanism of Development of EPSP

The neurotransmitter receptor complex causes opening of ligand gated sodium channels. Now, sodium ions from extracellular fluid enter the synapse, i.e. soma. As sodium ions are positively charged, resting membrane potential inside soma is altered and mild depolarization develops. This mild depolarization is called EPSP. It is a local response in the synapse.

EPSP is confined only to synapse. It differs from action potential and is similar to receptor potential and endplate potential. EPSP has such properties:

1. it is non propagated (local);
2. it does not work according to law "everything or nothing".

Significance of EPSP

EPSP is not transmitted into axon of postsynaptic neuron. It causes development of action potential in axon because of opening of voltage gated sodium channels in initial segment of axon. Now due to entrance of sodium ions, depolarization occurs in initial segment of axon and thus, action potential develops. From here action potential spreads to other segment of axon.

Properties of Synapse

1. One way conduction (Bell-Magendie law)

According to Bell-Magendie law, impulses are transmitted only in one direction in synapse, i.e. from presynaptic neuron to postsynaptic neuron.

2. Synaptic delay

During transmission of impulses via the synapse, there is a little delay in the transmission. This is called synaptic delay. This is due to the time taken for:

- Release of neurotransmitter
- Movement of neurotransmitter from axon terminal to postsynaptic membrane for mediator interaction with receptor:
    - Action of the neurotransmitter to open the ionic channels in postsynaptic membrane
    - Mediator restoration.

The synaptic delay is one of the causes for the latent period of the reflex activity.

3. Fatigue

The fatigue at the synapse is due to neurotransmitter substance, acetylcholine, level decreasing and mediator exhausting. After producing the action, this neurotransmitter is destroyed by acetylcholinesterase. Synapse is the mostly-fatigable structure in nervous system (compare: nervous fiber is practically non-fatigable).

4. Summation

When many presynaptic excitatory terminals are stimulated simultaneously or when single presynaptic terminal is stimulated repeatedly, there is summation in postsynaptic neuron. This is called summation. Summation is of two types.

- Spatial Summation

This occurs when many presynaptic terminals are stimulated simultaneously (for example, in central synapses).

- Temporal Summation

It occurs when one presynaptic terminal is stimulated repeatedly. Also subliminal stimuli summation (3-5) to form EPSP can be proper example.

Thus, both spatial summation and temporal summation play an important role in the facilitation of response.

5. Electrical properties

The electrical properties of the synapse are the EPSP and IPSP.

6. Decreasing transformation of rhythm into frequency. 3-5 subliminal stimuli on entrance will give 1 action potential on exit.

3.Materials for auditory self-work.

Materials and methods: vertical myograph, stimulator, irritating electrodes, kymograph, universal stand, preparating instruments set, pipette, gauze napkin, Ringer's solution.

Investigation object: frog.

Task 1. To study fatigue (tiredness) ability in synapse.

To prepare nervous-muscular preparation and to fix it into myograph. To irritate this preparation nerve with optimal frequency and force (voltage 1-5 V, frequency 50-100 Herz), to registrate myogram till tiredness becoming; to move electrodes to the muscle having increased the irritation force till optimum for tired muscle (10-20 V) and to continue to registrate myogram. The contraction altitude must get increased at it.

In conclusion: students must underline main synapses tiredness reasons and to mark that synapse is the most highly-tired structure in a whole central nervous system.

4. Materials for self-control:

Control questions:

1. Nervous fibre structure.
2. Nervous fibers 2 kinds and their peculiarities.
3. Nervous fibre action potential.
4. Excitation conducting laws through nervous fibre.
5. Excitation conducting ways (mechanisms) through nervous fibers of different types.
6. Conductance laws possibilities and prospects of application in dentistry.
7. Synapses structure peculiarities and classification.
8. Chemical synapses and electrical synapses functional features.
9. Ion mechanisms of exciting postsynaptic potential (EPSP).
10. Synaptic lack and its physiological role.

Lesson 8

Excitation processes investigation in CNS. Inhibition processes investigation in CNS.

Before performing this lesson, you should study the introductory material presented here.

1.Lecture course.
2.Moroz V.M., Shandra O.A. Physiology. - 2011. Unit 1.
3.Guyton A.C., Hall J.E. Textbook of Medical Physiology. - 2006. Unit 1.
4.Kapit W., Macey R.I., Meisami E. The Physiology Colouring Book: Harpers Collins Publishers, 1987.-P.16, 82.
5.Guyton A.C. Textbook of Medical Physiology.-NY, 1992.-P. 562-571.

Relevance of the topic.

Synapse is nervous system morphological unit while nervous center is a functional one.

1. Objectives:

To know: information conductance mechanisms in central synapses, neuromediators and neuromodulators role; excitation development and summation mechanisms and their role in CNS integrative function; excitation conductance peculiarities through central synapses; different inhibition types developmental mechanisms and these processes role in CNS integrative function.

To be able to: draw schematically excitation conductance mechanisms through central synapse as well mechanisms of EPSP temporary and spatial summation; to draw schematically pre- and postsynaptic inhibition as well as recurrent inhibition neuronal mechanisms.

2.Topic content.

Nervous centers physiology

Organism reflectory activity is defined by general features of nervous centres in more extent. In narrow context, nervous centre is synapse as itself and in wider aspect it is neurons complex located at different floors of CNS (this term is not anatomical, but physiological one). So, nervous center is multi-leveled structure. Main function of any nervous center is definite reflectory acts performance or managing one of organism functions.

Principle of dynamic functions localization - functional nervous centre may be localized into different anatomical (morphological) structure. For instance, respiratory center:

- medulla oblongata – working part;
- diaphragmal nerves center (C2-C4 spine segments);
- hypothalamus – respiration changing during emotional reactions (for instance, breathing acceleration at lovely person touching, kissing et al.);

- cortex – respiration adaptation to separate conditions (in singers, in highlands, in sea depth and so on).

Nervous centres hierarchy – separate sides of one organism function are managed by nervous centres localized at different levels of nervous system.

Nervous centres common features are the following:

- **One-sided impulse (excitation) conduction.**("Bell-magendie law")

During any reflex activity, the impulses are transmitted in only one direction through the reflex arc as per Bell - Magendie law. The impulses pass from receptors to the center and then from center to effector organ. It is caused by synapse structure: mediator is released only in presynaptic ending.

- **Excitation transduction lack**. Excitation transmission retardation depends on synapses and associative neurons quantity.
- **Summation** is accumulation (summing) effects of subliminal stimuli; one subliminal stimulus does not give any answer reaction because presynaptic ending releases too few mediator. It has been first described by Russian physiologist Ivan Sechenov in 1863.

There are two main summation types:

a) temporary (consequent) - when one nerve fiber is stimulated repeatedly with subliminal stimuli frequently, these stimuli are summed up to give response in the muscle; as a summation result sufficient mediator quantity is released and answer reflectory reaction occurs; example: sneezing reflex occurs at stimulus prolonged action to nasal mucosa receptors;

b) spatial - when two afferent nerve fibers supplying a muscle are stimulated separately with subliminal stimulus, there is no response; but, if both the nerve fibers are stimulated together with stimulus of same strength, the muscle contracts - this is called spatial summation; with other words, space summation occurs at simultaneous irritation of different sensory nerves conducting excitation in one and the same nervous center; its role is in fatigue liquidating (activity type changing); example: semitendineal muscle contraction reflectory contraction at simultaneous tibular and fibular nerves subliminal irritation because subliminal irritation of one nerves from them does not cause any contraction.

- **Excitation rhythm transformation**. Nervous centers are able to transform frequency and rhythm of coming impulses 2 main types:

a) reducing -

- in synapses – 3-5 EPSP (exciting post-synaptic potentials) will give just 1 action potential;
- if impulses come in nervous center with a frequency which is bigger than this nervous center lability than this nervous center will answer with rate corresponding to its abilities id est with more rare impulsation;

b) increasing –

- space summation is in the base of it;

- nervous center can answer with a series of impulses to a singular irritation coming outside.
- **Automatism**. It is a distinguishing feature of vital nervous centers.
- **Reflectory afteraction** is expressed in following: answer reflectory reaction is present during some time after stimulus action stoppage. Afteraction duration can be more than stimulus duration in many times. There exists direct dependence: the stronger and more durable irritation acts to the receptor, the more durable is afteraction. This feature reasons are in following: trace depolarization, nervous impulses circulation (ring connection existence between neurons of a given center).
- **Fatigueability**– they belong to the structures with the biggest tiredness among all nervous system parts. It is determined by nervous center low lability. It is expressed in reflectory answer gradual decreasing and further stoppage in a case of prolonged stimulus action. It is a result of synaptic transmission disorder.

Inhibition in CNS

Russian physiologist Ivan Sechenov discovered central inhibition – chemical irritation of thalamus inhibits simple spine non-conditioned reactions. He was the first who underlined that inhibition is active process. Inhibition has been considered only as passive process coming after overexcitation before Sechenov.

Inhibition is a special nervous process expressed externally in answer reaction weakening or complete disappearance. It is characterized by definite intensiveness and duration. Inhibition is an innate process which is improved in course of human onthogenesis.

Primary – it is not connected with excitation process and occurs with inhibitory cells (Ranshow cells) participation.

Secondary – appears without inhibitory neurons. It is nervous system overexcitation result.

Postsynaptic – EPSP formation. It is urgent but particular one.

Presynaptic or protective (Fig.29) - it is developed the mostly often in axo-axonal synapses in brain stem and spine. Essence: presynaptic membrane hyperpolarization. Mediator – glycine. It protects from pathological, excessive, unnecessary information. It is non-urgent but more complete comparatively to the previous one.

Inhibitory Function

Inhibition of synaptic transmission is classified into three types: postsynaptic inhibition, presynaptic inhibition and renshaw cell inhibition.

1. Postsynaptic Inhibition

This is also called direct inhibition. This occurs due to release of an inhibitory neurotransmitter from presynaptic terminal instead of excitatory neurotransmitter substance. The most important inhibitory neurotransmitter is gamma-amino butyric acid (GABA).

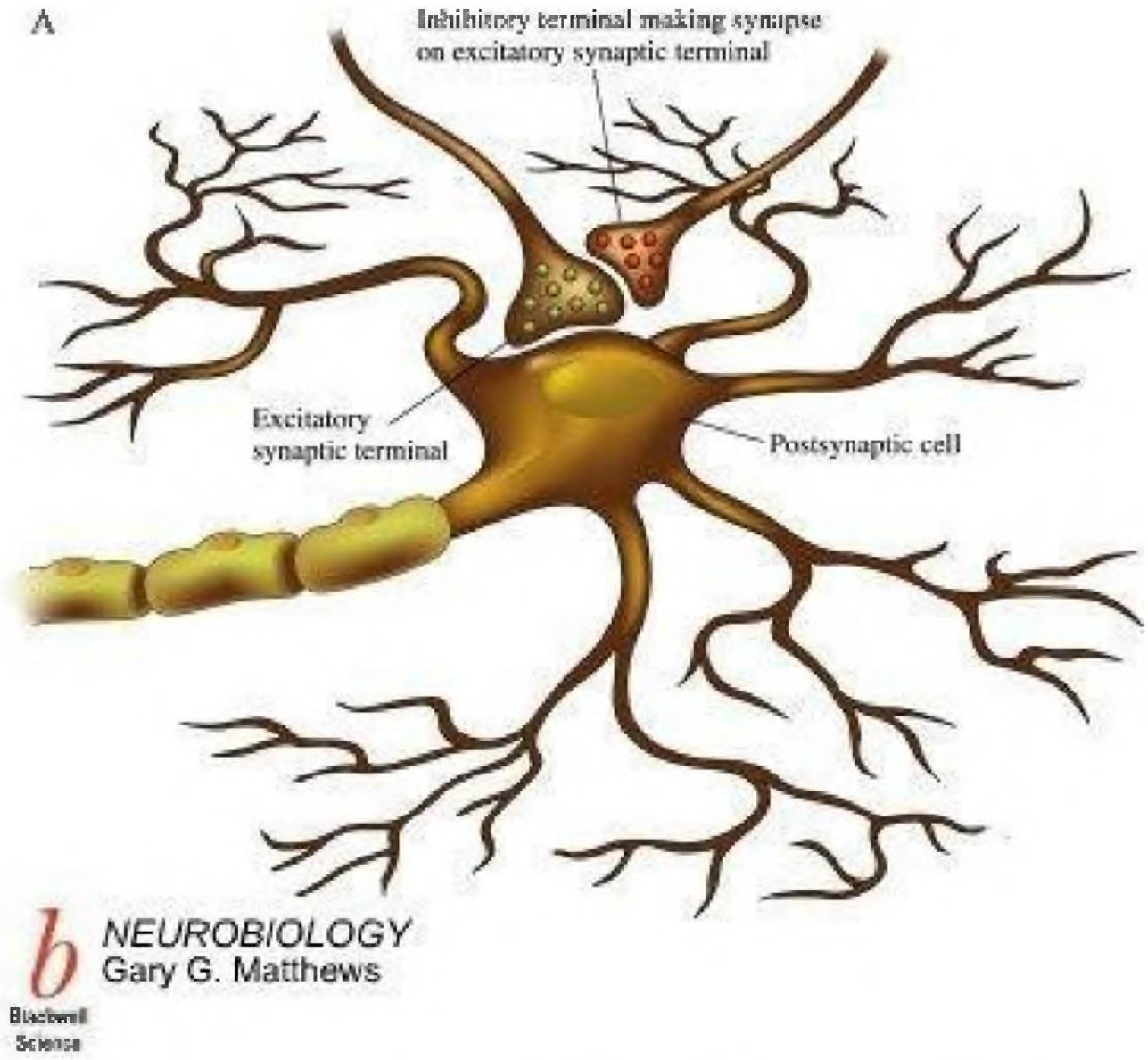


Fig.29. Presynaptic or protective inhibition (by Neurobiology Gary G. Matthews)

Action of GABA—IPSP

Inhibitory neurotransmitter substance acts on postsynaptic membrane by binding with receptor. Transmitter receptor complex opens ligand gated potassium channels instead of opening sodium channels. Now, potassium ions pass out of synapse into extracellular fluid. Chloride channels also open followed by influx of chloride ions inside. Exit of potassium ions and influx of chloride ions cause more negativity inside, leading to hyperpolarization. This is called inhibitory postsynaptic potential (IPSP). With other words, IPSP is numeral to which postsynaptic membrane membrane potential is increased (hyperpolarization) at mediator action to it.

2. Presynaptic Inhibition

This is also known as indirect inhibition and it occurs because of failure of presynaptic axon terminal to release excitatory neurotransmitter substance. Inhibitory neurotransmitter substance is glycine.

3. Renshaw Cell Inhibition

This occurs in spinal cord. Anterior nerve root consists of nerve fibers leaving spinal cord. These nerve fibers arise from alpha motor neurons in anterior grey horn of spinal cord and reach effector organ, muscles. Some of fibers called collaterals end in Renshaw cells instead of leaving spinal cord. Renshaw cells are situated in between motor neurons.

When motor neurons send motor impulses, some of impulses reach the Renshaw cell by passing via collaterals. Now the Renshaw cell is stimulated. In turn, it sends inhibitory impulses to alpha motor neurons so that the discharge from motor neurons is reduced.

Significance of Synaptic Inhibition: It helps to select exact number of impulses and to block the excess ones.

Pessimal - It is central inhibition type. It appears at irritation high frequency. High rate of answer excitation occurs at first moment. Then stimulated central neuron comes in inhibition state while working in such a regimen.

Recurrent – it is primary inhibition example. Essence: neuron activity inhibition caused by recurrent axon collateral of this neuron.

Reciprocal –It belongs to postsynaptic inhibition. This inhibition can be belonged to nervous center co-ordination principles (see materials of next lesson). Expiration and inspiration centers are inhibited reciprocally in medulla oblongata, pressor and depressor cardiac-vascular centers. It is rather distinct at spine level at highly co-ordinated acts performance (walking, running, scretching et al.). At spinal segments the excitation of motoneurons causing muscles-flexors contraction is accompanied by reciprocal inhibition of other motoneurons group leading to extensors relaxation. So, shortly, flexors excitation and parallel extensors inhibition (and on the contrary) occurs. There are two explanation of *spinal reciprocal inhibition*:

- impulses multiplication mechanism is switched on on the way from afferent fiber to muscle extensor motoneurons at muscle flexor motoneurons excitation; as a result – extensors motoneurons are receiving highly-rated impulsation leading to their pessimum state – so, inhibition;
- inhibitory associative neurons synthesizing inhibitory mediator are switched on on the way to extensors motoneurons.

Lateral – activity neurons or receptors located near to excited neurons or receptors are interrupted. Lateral inhibition mechanism provides sensory systems discriminative ability. So, it provides sounds rate determining in auditory sensory system; in visual one – increases significantly contrast of percepted image; in tactile one – encourages differentiating 2 points of touching. Lateral inhibition is connected significantly with recurrent inhibition mechanisms. It is also postsynaptic inhibition.

3. Materials for auditory self-work.

Materials and methods: current source, electrodes, preparating plank, glass plate, kymograph, current source, metronom, cotton wool, napkin, sodium chloridum, 0,5% solution of sulfuric acid.

Investigation object: frog.

Task 1. Temporary excitation summation.

The experiment must be performed on thalamic frog. For this aim it's necessary to cut frog's head behind her eyes. Then students should put the animal to the operation table. You should fix the electrodes on one of posterior legs. The electrodes must be connected with the stimulator. The electrodes must be put above and below knee joint over the distance at least 0,5 cm between each other. One should find threshold irritation force. Then one must observe the reaction at irritation with the frequency of 1 Herz, 20 Herz.

Task 2. Excitation summation.

Thalamic frog must be hanged by her inferior jaw on hook. You must put cork at the end of the hook till the end of the animal's movements. Spatial summation can be observed while flexing reflex. You must wash frog's posterior leg fingers ends in threshold concentration acid and determine reflex time having counted seconds number from the beginning of fingers sinking till the leg's jerking back moment. Then after leg's washing in the glass of water you must determine reflex time at foot sinking in acid.

5. Materials for self-control:

Control questions:

1. Nervous center and its part.
2. Exciting post-synaptic potential. EPSP ionic mechanisms.
3. How to explain nervous centers fatigue?
4. Temporal and spatial excitation summation.
5. Excitation rhythm transformation (decreasing and increasing).
6. Excitation afteraction and its significance.
7. Inhibitory neurons and their functions. Inhibitory mediators.
8. Presynaptic inhibition developmental mechanisms.
9. Postsynaptic inhibition developmental mechanisms.

Lesson 9.

Reflectory activity coordination mechanisms investigation.

Before performing this lesson, you should study the introductory material presented here.

1. Lecture course.
2. Moroz V.M., Shandra O.A. Physiology. - 2011. Unit 1.
3. Guyton A.C., Hall J.E. Textbook of Medical Physiology. - 2006. Unit 1.

Relevance of the topic.

CNS belongs to highly-regulated and at the same time to quite sensitive (vulnerable) systems. As it was mentioned above, CNS pathology nowadays takes one of dominant places in diseases, morbidity and lethality spectra.

1. Objectives:

To know: reflexes co-ordination principles with corresponding neuronal chains participation in organism adaptive reaction providing; irradiation, concentration, divergence, convergence, occlusion, dominanta, general ending ways mechanisms.

To be able to: mark schematically CNS neuronal links different types structure; draw several co-ordination principles (divergence, convergence, ending general way).

2.Topic content.

These principles make one's reflectory activity urgent, well-singleminded, accompanied by less energy consumption and so more comfortable for performance by organism. Main of them are:

Convergency (convergence) - is many afferent ways gathering to one neuron (associative or efferent one); with other words – it is so when many presynaptic neurons terminate on singular postsynaptic neuron.

Divergency (divergence) – is an ability to form polysynaptic bonds (it lies on the base of irradiation); with other words – it is so when one presynaptic neuron terminates on many postsynaptic neurons; this principle is opposite to convergence. Irradiation – (from Latin word "irradiare" – "shine, beam") – excitation distribution through CNS. 2 main types:

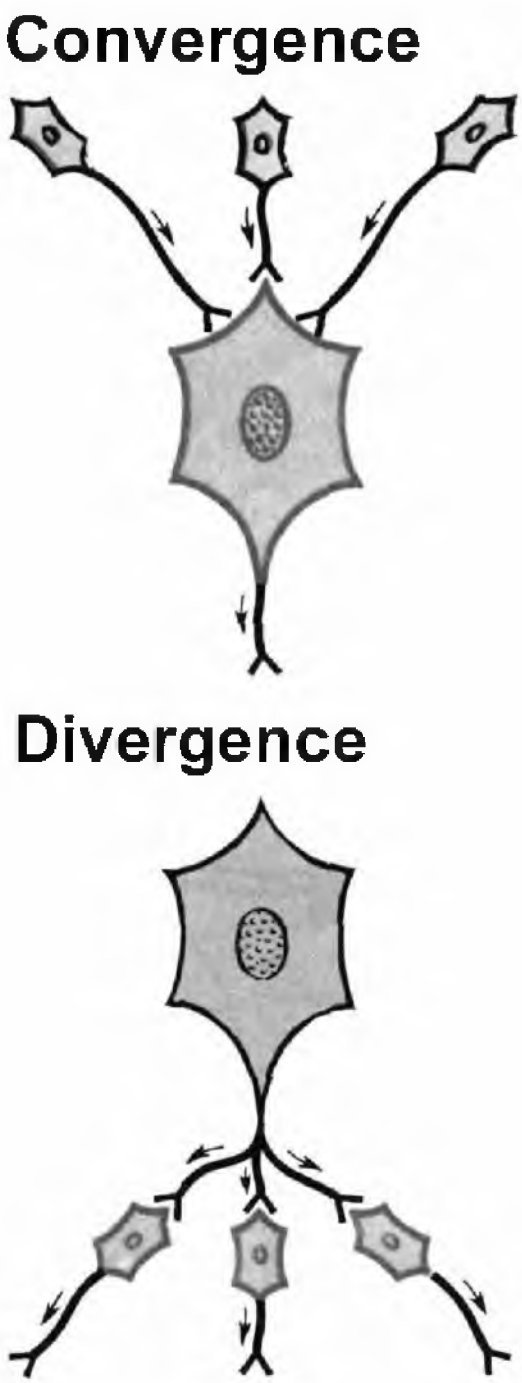


Fig.30. Convergency and divergency scheme.

a) elective – it is physiological one – impulses are distributed through definite ways involving just essential organs and muscles in the reaction; if one needs to wake up more rapidly and to have better mental abilities he can make following procedure in the morning right after standing up: washing face with cold water (at the biggest degree – "drinking through nose") will activate trigeminal nerve, reticular formation and finally cortex. It is so-called activation reaction lying on the base of human consciousness. Use this during exam – and you will see that your mental abilities will be great;

b) diffused (generalized) – other muscles get involved into the reaction, disturbing the movement and making it constrained (bound). Examples: "start fever" in sportsmen, epilepsy. This type of irradiation is physiological one for lower animals such as amphibians (their subcortex is developed more than cortex).

Total ending way principle (discovered by Charles Sherrington in 1906). Essence: impulses from many receptors of different body parts come to one motoneuron (convergence is on its base). Information through afferents come to associative neurons, efferents and finally to axon of 1 motoneuron. This axon represents total ending way. Such a principle realizing is possible because afferents number is bigger than efferents in 5 times. This principle second name is watering-can principle. Role: only several, the mostly important and essential at the moment impulses (of all coming through all different ways) will give answer reaction.

Occlusion is nervous centers interference. Final result of such an interference is less, quicker. This principle is known from dentistry (occlusion of jaws mean denturing).

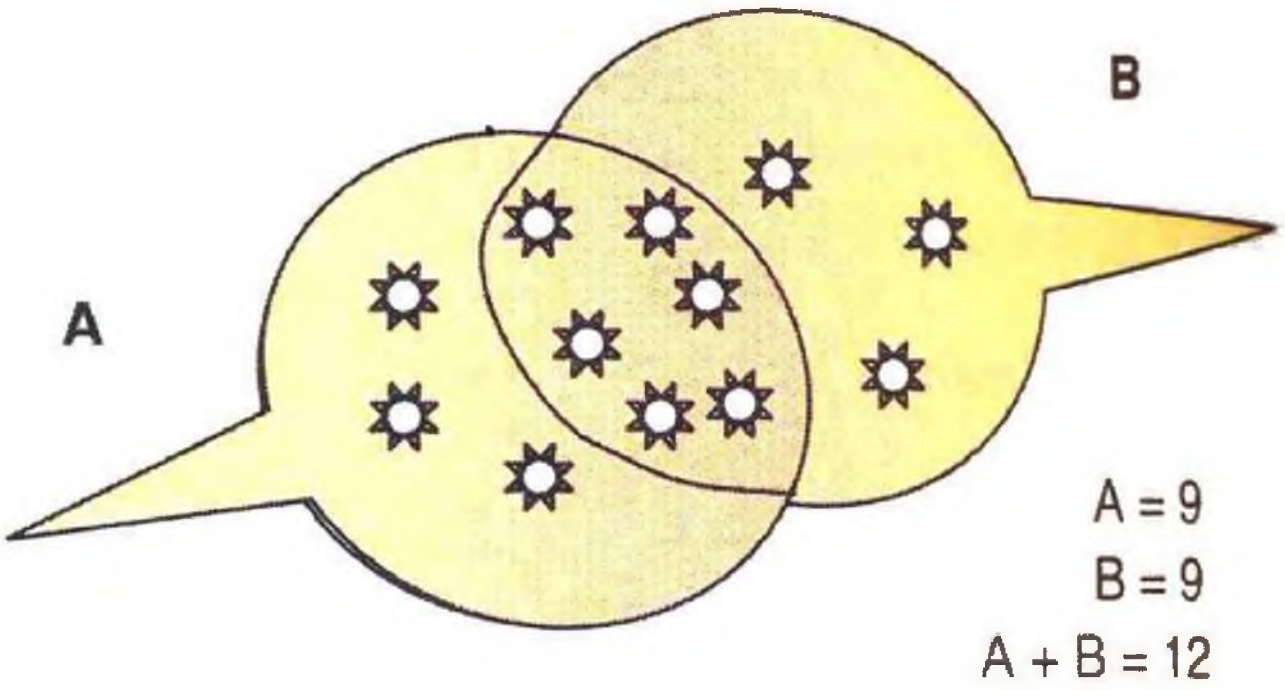


Fig.31. Occlusion.

Dominanta (Alexei Uhtomsky, 1904) – temporally prevailing excitation focus determining answer reactions character to all external and internal stimuli. External expression of dominanta is a definite activity or organism working posture (pose) supported by different stimuli and excluding other activities and poses for a given moment. Reasons: leading motivation, impulsation increasing to the excitation locus from effector, biologically-active substances (hormones and others) level increasing in blood. Examples: sexual (hormones increasing), dominanta of urinary vesicle or stomach (increased impulsation from urinary vesicle and from stomach).

Dominant focus 5 main characteristics:

- increased excitability;

- excitation stability;
- increased ability to excitation summation;
- inertia – ability to preserve excitation for long after stimulus action stoppage;
- ability to cause conjugated inhibition in neighboring nervous centers.

Feed-back reaction or **opposite afferentation principle** – afferentation from effector about action final result.

Induction of excitation and inhibition. Excitation and inhibition interact. Big hemispheres cortex definite locuses excitation causes inhibition in other cortex parts and, on the contrary, inhibition in one cortical points causes excitation in others. This phenomenon is performed by law of mutual excitation and inhibition. One differentiates 2 induction types.

a) Positive – inhibition in separate cortical point causes excitation in other locuses. Organism activity is realized by direction of this excitation, attention to the current activity is enforced.

b) Negative – excitation in one cortical focus causes inhibition in those parts which have been active before. Negative induction acts at inclination from main (dominant) activity and it is concentrated on occasional stimuli, which inhibit excitation from main stimulus. Result: coming out of the activity performed.

3.Materials for auditory self-work.

Materials and methods: current source, electrodes, preparating plank, glass plate, kymograph, current source, metronome, cotton wool, napkin, sodium chloridum, 0,5% solution of sulfuric acid.

Investigation object: frog.

Task 1. Excitation irradiation in central nervous system.

The experiment should be performed in spinal frog. Chemical or mechanical stimulus is performed for irritation. The students must irritate spinal frog's leg by nipping with tweezers or sulfuric acid solution. The animal must jerk only one of his leg back (the stimulus must be weak). Then it's necessary to increase the irritation force.

To compare the answer reactions. To make the conclusion.

4.Materials for self-control:

Control questions:

1.Interaction between excitation and inhibition processes as a base of reflexes co-ordination.
2. Irradiation (elective, diffused) and divergence.
3. General ending way principle.
4 .Convergence and concentration.
5 .Dominanta. Dominant locus features.
6. Feed-back binding or reverse afferentation principle.

7. Synergic and antagonistic reflexes.

Lesson 10.
Practical skills on the content modules 1,2,3. Situational tasks solving on the content modules 1,2,3.

1. To assess resting membrane potential as well as action potential of nervous and muscular fibers.

2. To draw action potential and excitability changes during it.
3. To estimate depolarization threshold.

4. To draw muscles contraction curves (dependently on irritation rate) and excitability changing during them.

5. To explain muscles contraction and relaxation mechanisms.

6. To explain ways of excitation nervous-muscular conductance and different factors influence on these processes.

7. To interpret masticatory muscles electromyogram.

By this link you can find an additional information (situational tasks) for the preparing: **(Physiology Poltava)**
https://www.facebook.com/profile.php?id=100013316025779

CONTENT MODULE 4: "CNS ROLE IN MOTOR FUNCTIONS REGULATION"

Lesson 11

Spinal cord role investigation in motor organism functions regulation.

Before performing this lesson, you should study the introductory material presented here.

1. Lecture course.
2. Moroz V.M., Shandra O.A. Physiology. - 2011. Unit 1, Chapter 2
3. Guyton – Ganong – Chatterjee. Concise Physiology /Ed. By Dr Raja Shahzad Gull: M.B.B.S., F.C.P.S., King Edward Medical College.-Lahore, 1998 (1st Edition).-P.295-301.
4. Ganong W.F. Review of Medical Physiology.-21st ed.-2003.-Section II.

Relevance of the topic.

Spine represents main canal for afferent (cutaneous, temperature, proprioceptive and noceoceptive or pain) signalization from peripheral receptors to CNS highest parts. At afferent impulses conductance disorders through spine (at syphilitic spine injury i.e. tabes dorsalis) human being can not perform movements at closed eyes (ataxy).

1. Objectives:

To know: spine structure, reflex function, role in motor and vegetative functions regulation, activity principles, pyramidal and extrapyramidal ways; muscular tone spinal regulation mechanisms; spinal reflexes study role for spine disorders topic diagnostics; spinal shock and its developmental mechanisms.

To be able to: assess tendon reflexes existence and muscular tone in the investigated person.

2. Topic content.

+The length of the spinal cord is about 45 cm in males and about 43 cm in females.

Spinal cord is cylindrical in shape with two spindle shaped swellings—the cervical and lumbar enlargements. These two portions of spinal cord innervate upper and lower extremities respectively. Below the lumbar enlargement, the spinal cord rapidly narrows to a cone shaped termination called conus medullaris. A slender non-nervous filament called filum terminale extends from conus medullaris downward to the fundus of the dural sac at the level of second sacral vertebra. Spinal cord is made up of 31 segments.

Cervical segments = 8
Thoracic segments = 12
Lumbar segments = 5
Sacral segments = 5
Coccygeal segment = 1

Each spinal nerve is formed by an anterior (ventral) root and a posterior (dorsal) root. Both the roots on either side leave the spinal cord and pass through the corresponding intervertebral foramina. The first cervical spinal nerves pass through the foramen between occipital bone and the first vertebra called atlas. The cervical and thoracic roots are shorter whereas, the lumbar and sacral roots are longer. The long nerves descend in dural sac to reach their respective intervertebral foramina. This bundle of descending roots surrounding the filum terminale resembles the tail of horse. Hence, it is called cauda equina.

On the anterior surface of spinal cord, there is a deep furrow known as anterior median fissure. The depth of this is about 3 mm. Lateral to the anterior median fissure on either side, there is a slight depression called the anterolateral sulcus. This denotes the exit of anterior nerve root. On the posterior aspect, there is a depression called posterior median sulcus. The posterior median sulcus is continuous with a thin glial partition called the posterior median septum. It extends inside the spinal cord for about 5 mm and reaches the gray matter. On either side, lateral to the posterior median sulcus, there is posterior intermediate sulcus. It is continuous with posterior intermediate septum, which extends for about 3 mm into the spinal cord. Lateral to the posterior intermediate sulcus, is the posterolateral sulcus. This denotes the entry of posterior nerve root.

Internal structures of spinal cord

Substance of spinal cord is divided into inner gray matter and outer white matter. Gray matter is the collection of nerve cell bodies, dendrites and parts of axons. It is placed centrally in the form of wings of the butterfly and it resembles the letter H. Exactly in the center of gray matter, there is a canal called the spinal canal. White matter is the collection of myelinated and unmyelinated nerve fibers (Fig. 32).

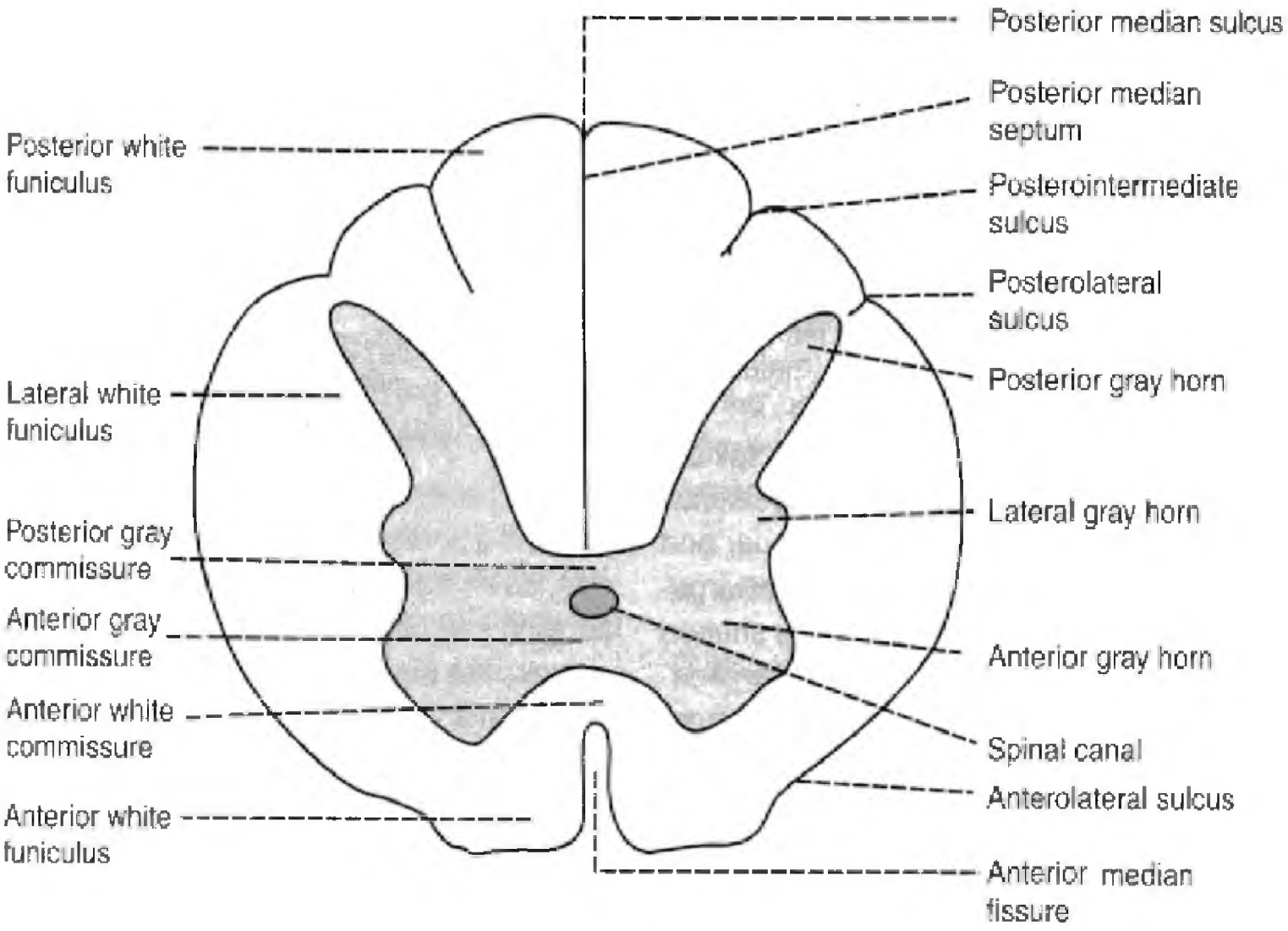


Fig.32. Section of the spinal cord — thoracic segment.

Anterior gray horn.There are three types of motor neurons located in anterior grey horn

Alpha motor neurons: Alpha motor neurons are large and multipolar cells. Axons of these neurons leave the spinal cord through the anterior root and end in groups of skeletal muscle fibers, i.e. extrafusal fibers.

Gamma motor neurons: Gamma motor neurons are smaller cells scattered among alpha motor neurons. These neurons send axons to the intrafusal fibers of the muscle spindle.

Renshaw cells - are the inhibitory neurons playing an important role in synaptic inhibition at the spinal cord.

Neurons in Lateral Gray Horn

In thoracic and upper two lumbar segments, the gray matter forms a small projection in between the anterior and posterior horns. This is called the lateral gray horn. This has cluster of nerve cells called intermediolateral horn cells. These cells give rise to sympathetic preganglionic fibers, which leave the spinal cord through the anterior nerve root.

Neurons in Posterior Gray Horn

The posterior gray horn contains the sensory neurons, which receive impulses from various receptors of the body through posterior nerve root fibers. Four groups of neurons are present in the posterior gray horn.

White matter of spinal cord

White matter of spinal cord surrounds the gray matter. It is formed by the bundles of both myelinated and unmyelinated fibers, but predominantly the myelinated fibers. The anterior median fissure and the posterior median septum divide the entire mass of white matter into two lateral halves. The band of white matter lying in front of anterior gray commissure is called the anterior white commissure.

Each half of the white matter is divided by the fibers of anterior and posterior nerve roots into three white columns or funiculi.

Spinal proper functions:

- Spinal reflexes.
- Organism motor activity coordination particularly spinal motor neurons functions.
- Vegetative reactions.
- Urination and defecation.

Pyramidal Tracts

Pyramidal tracts of spinal cord are descending tracts concerned with voluntary motor activities of the body. These tracts are otherwise known as corticospinal tracts. There are two corticospinal tracts, the anterior corticospinal tract and lateral corticospinal tract. While running from cerebral cortex towards spinal cord, the fibers of these two tracts give the appearance of a pyramid on the upper part of anterior surface of medulla oblongata. Hence, these two tracts are called pyramidal tracts.

The pyramidal tracts are concerned with voluntary motor activities and were the first tracts to be found in man (Fig. 33-34).

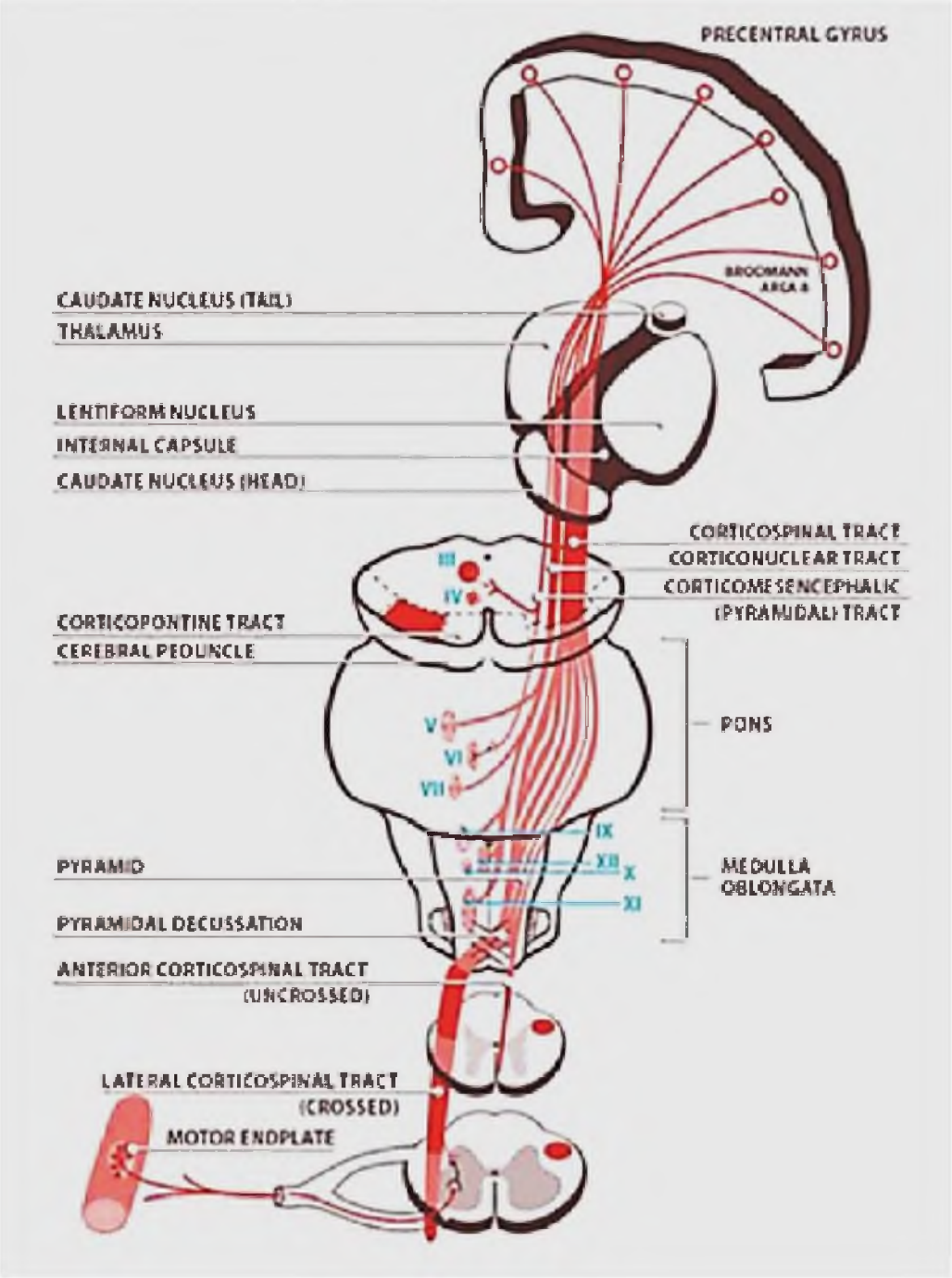


Fig.33. Corticospinal and corticonuclear tracts.

Fibers of pyramidal tracts arise from the following nerve cells **in the cerebral cortex**.

1. Giant cells or **Betz cells** or pyramidal cells in precentral gyrus of the motor cortex. The giant cells are situated in area 4 (primary motor area) of frontal lobe of the cerebral cortex.

2. Parietal lobe of cerebral cortex particularly from somatosensory areas (areas 3, 1, 2). It is believed that 30% of pyramidal fibers arise from primary motor area (area 4) and supplementary motor areas, another 30% from premotor area (area 6) and the remaining 40% of fibers arise from the parietal lobe particularly from somatosensory areas (areas 3, 1, 2). All the above fibers form the fibers of upper motor neurons of motor pathway.

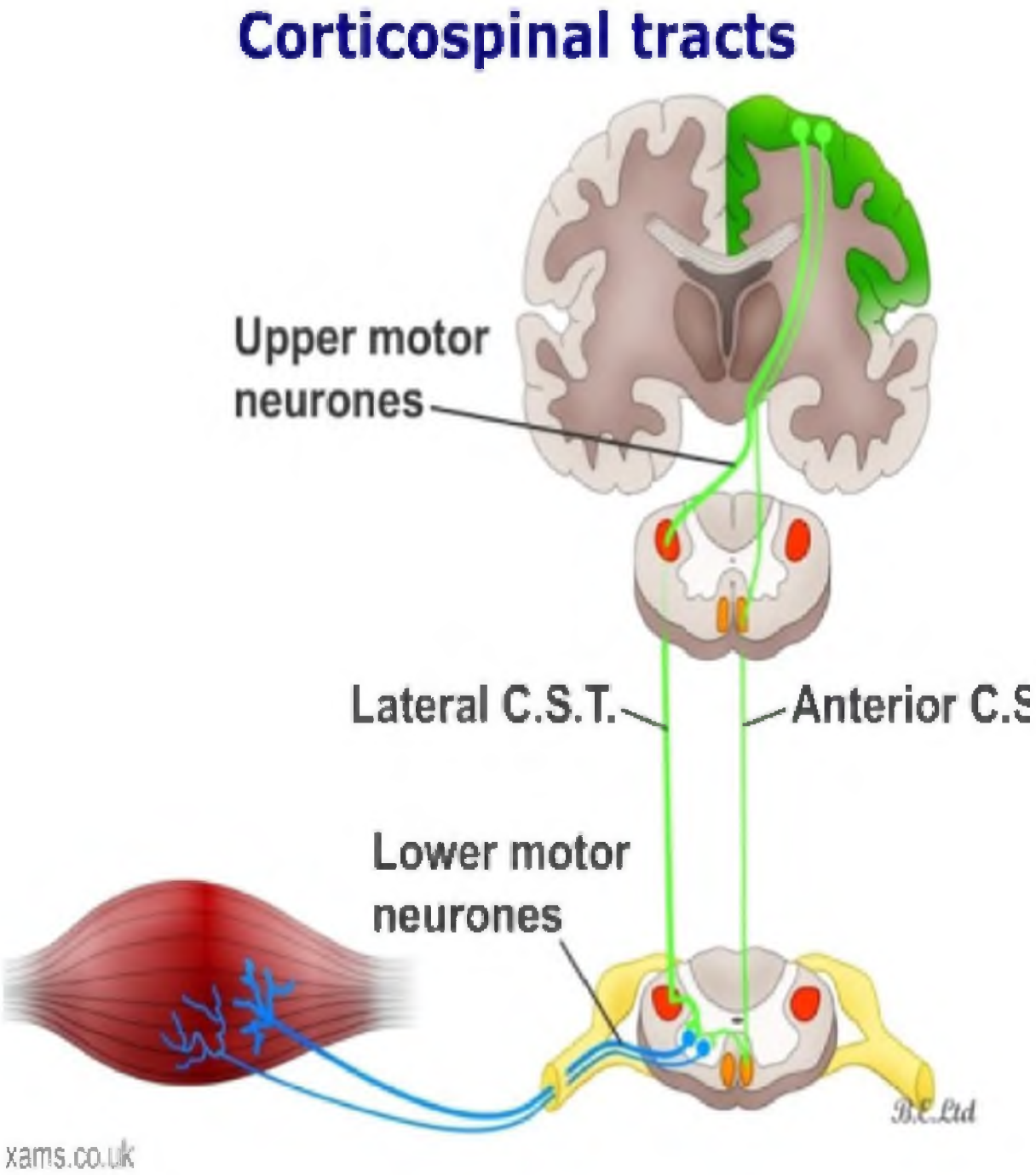


Fig. 34. Corticospinal tract. (by B.E. Ltd)

Course

After taking origin, the nerve fibers run downwards in a diffused manner through white matter of cerebral hemisphere and converge in the form of a fan like structure along with ascending fibers which project from thalamus to cerebral cortex. The fan like structure is called corona radiata. Then, the fibers descend down through internal capsule, midbrain and pons. While descending through pons, the fibers are divided into different bundles by the nuclei of pons. At the lower border of pons, the fibers are grouped once again into a compact bundle and then descend down into medulla oblongata.

This compact bundle of corticospinal fibers gives the appearance of a pyramid in the anterior surface of upper part of medulla. Because of this, the corticospinal tracts are called the pyramidal tracts.

At the lower border of medulla, the pyramidal tract on each side is divided into two bundles of unequal sizes. About 80% of fibers from each side cross to the opposite side. Thus, the fibers of both sides while crossing the midline form pyramidal decussation. After crossing and forming pyramidal decussation, the fibers descend through the posterior part of lateral white funiculus of the spinal cord. This bundle of crossed fibers is called the crossed pyramidal tract or lateral corticospinal tract or indirect corticospinal tract.

The remaining 20% of fibers do not cross to the opposite side but descend down through the anterior white funiculus of the spinal cord. This bundle of uncrossed fibers is called the uncrossed pyramidal tract or anterior corticospinal tract or direct corticospinal tract. This tract is well-marked in cervical region. Since, the fibers of this tract terminate in different segments of spinal cord, this tract usually gets thinner while descending through the successive segments of spinal cord. The fibers of this tract are absent mostly below the midle thoracic level. Before termination, majority of the fibers cross to the opposite side at different levels of spinal cord.

Termination

All the fibers of pyramidal tracts, either crossed or uncrossed, terminate in the motor neurons situated in anterior gray horn either directly or through internuncial neurons. The axons of the anterior motor neurons supply the skeletal muscles directly by passing through the anterior nerve root. The neurons giving origin to the fibers of pyramidal tract and their axons are together called the upper motor neurons. The anterior motor neurons in the spinal cord and their axons are called the lower motor neurons.

Function

The pyramidal tracts are concerned with voluntary movements of the body. Fibers of the pyramidal tracts transmit motor impulses from motor area of cerebral cortex to the anterior motor neurons of the spinal cord. These two tracts are responsible for fine, skilled movements.

Effects of Lesion

The lesion in the neurons of motor cortex and the fibers of pyramidal tracts is called the upper motor neuron lesion. The following are the symptoms:

1) Voluntary movements: Voluntary movements of the body are very much affected. Initially, there is loss of voluntary movements in the extremities. Later, it involves the other parts of the body like hip and shoulder.

2) Muscle tone. The muscle tone is increased leading to spasticity of muscles. The muscles are paralyzed. This type of paralysis of muscles is called the spastic paralysis. The spasticity is due to the failure of inhibitory impulses from cerebral cortex to reach the spinal cord.

3) Reflexes: All the superficial reflexes are lost. And the deep reflexes are exaggerated. Some pathological reflexes are positive.

Spinal shock is observed after spine cutting. All spine functions disappear rapidly at this. Spinal reflector reactions are restored quickly in lower animals (in frogs – in 10-15 min) moreover, the lower alive organism is the restoration time less is because they have developed subcortex comparatively to cortex. Cutted spine is practically not restored in human being. There are some theories of spinal shock. F.Goltz considered spinal shock as an irritation result. But Ch. Sherrington, G.Trendelenburgh also studied spinal shock at spine cooling blockade. Repeated cutting of spine lower than first cutting also does not cause spinal shock. All this indicates to the fact that spinal shock occurs due to spine separation from brain parts located above.

Microelectrode investigations demonstrated that motoneurons do not suffer at spinal shock. Associative neurons are injured due to which reactions to afferent stimuli are absent.

Spinal animals – are animals with cutted spine on the border with medulla oblongata.

Spinal animals features:

- Respiration absence.
- Low blood pressure, decreased vascular tone.
- Losing the ability to support gomoyothermic (constant body temperature).
- Disappearance of all forms of single minded activity (alimentary, sexual, protective).
- Anal and urination centers paralysis at spine cutting lower than lumbal parts.

3. Materials for auditory self-work.

Materials and methods: neurologic hammer.

Investigation object: human being.

Task 1. To investigate muscular tone in human being

Muscular tone must be determined by palpation and by passive movements in joints performance. You should determine by palpation the degree of muscular tension. Light tension is observed at normal muscular tone. The students assess the degree of resistance to passive movements by the passive movements performance.

At significant hypotony the movements volume is increased and they are performed without any resistance.

At hypertony passive movements at the first moments of flexion meet with strong (significant) resistance.

Task 2. To investigate surface (skin) reflexes on stretch

Abdominal reflexes (Fig.35):

- superior – it's caused by puncture irritation of abdomen skin in parallel of rib arc; the reflexes arc is closed at D_6-D_8 segments of spinal cord (from D – dorsal);
- intermediate – by similar irritation but at horizontal dimension at navel level; the reflexes arc is closed at D_9-D_{10};
- inferior- in parallel to groin plica; the reflexes arc is closed at D_{11}-D_{12}.

Plantar reflex - is a plantar flexion of foot toes as a response of puncture irritation of external plantar limb; the reflexes arc is closed at L5-S2 and is in sciatic nerve.

At injury of corresponding motor nerve and corresponding link of reflector arc the response reaction is decreased or disappeared (areflexy), muscular atony, atrophy are observed.

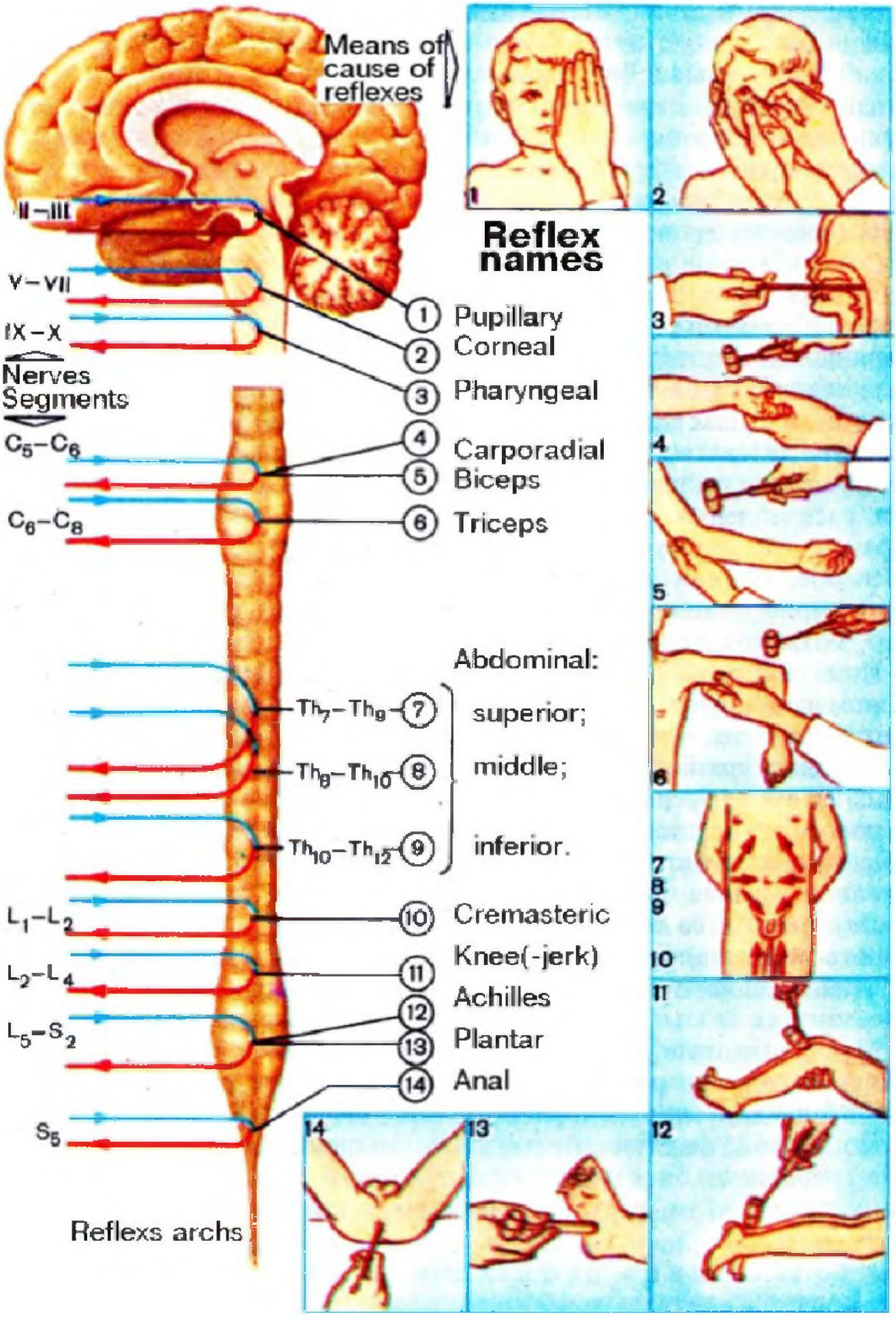

Means of cause of reflexes
II–III
V–VII
IX–X
Nerves Segments
C5–C6
C6–C8
Th7–Th9
Th9–Th10
Th10–Th12
L1–L2
L2–L4
L5–S2
S5
Reflexs archs
Reflex names
1 Pupillary
2 Corneal
3 Pharyngeal
4 Carporadial
5 Biceps
6 Triceps
Abdominal:
7 superior;
8 middle;
9 inferior.
10 Cremasteric
11 Knee(-jerk)
12 Achilles
13 Plantar
14 Anal

Fig.35. The main neurological reflexes investigation scheme

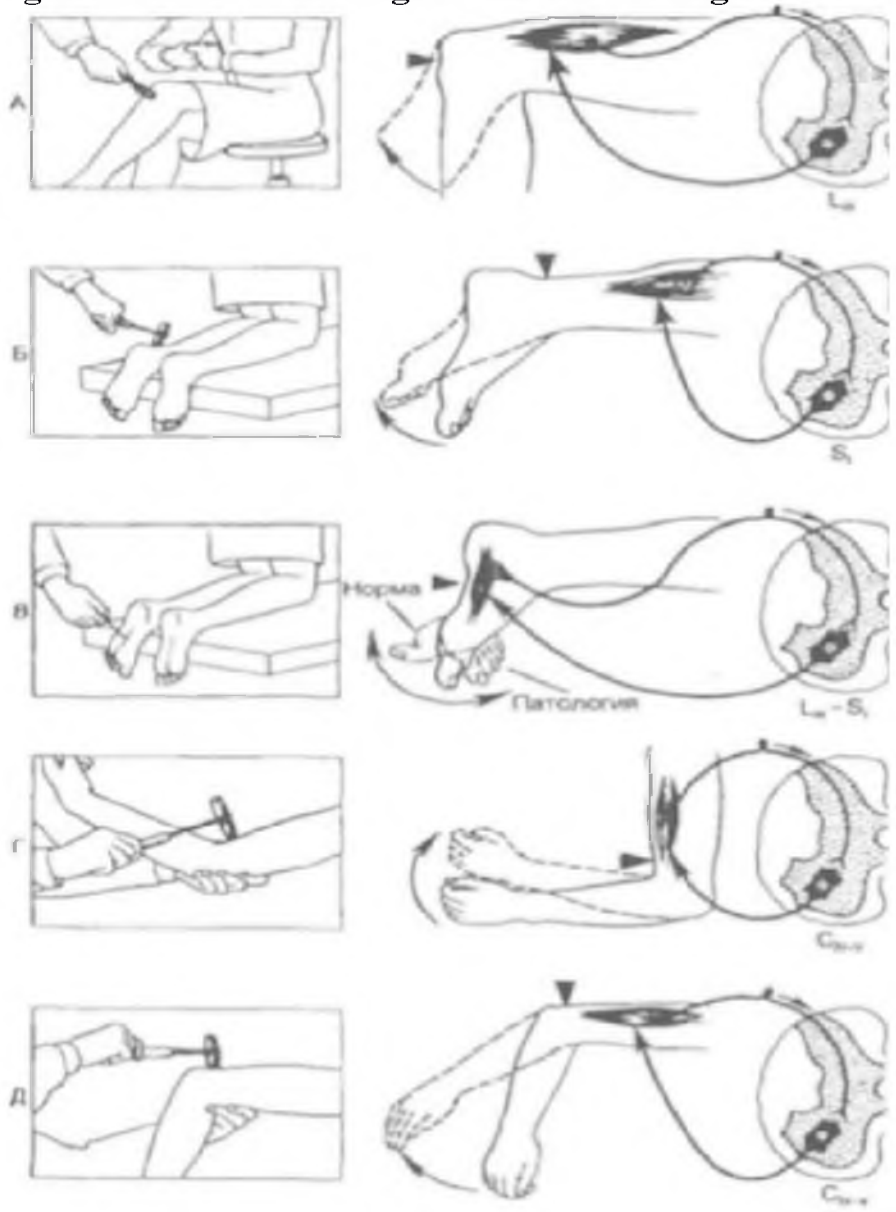


Fig.36. Deep (profound) spinal reflexes investigation

Task 3. Deep (profound) spinal reflexes investigation

Biceps-reflex – is caused by irritation of muscle tendon above cubital joint by neurologic hammer. Answer reaction – hand flexion in cubital joint. The reflexes arc is closed at C_5-C_6. Afferent and efferent fibers are in muscular-cutaneous (skin) nerve structure.

Triceps-reflex - is caused by hammer shock on triceps-muscle tendon, on 1-1,5 cm upper of posterior process of ulna. Answer reaction- muscular contraction and antebrachium (forearm) extension. The reflexes arc is closed at C_6-C_8. The fibers are in medianus, radialis and muscular-cutaneous nerves.

Brachioradialis reflex –is investigated by hummer shock onto awl-like processus of radius. Answer reaction – flexure in cubital joint and antebrachium pronation. Origin

location: investigated person hand must be bended at obtuse angle in cubital joint; person's examined hand is supported by doctor's hand at the locus between pronation and supination. The reflexes arc is closed at C_5-C_8. The fibers are in medianus, radialis and muscular-cutaneous nerves.

Knee jerk or patellar tendon reflex - is caused by light shock of hummer on musculus quadriceps femoris tendon. Answer reaction – tibia extension. The reflexes arc is closed at L_2-L_4. Sensor and motor fibers are in femoral nerve. Every doctor must know how to elicit knee jerk. Knee jerk can be elicited by tapping the patellar tendon after the knee is semiflexed by placing one knee over the other while sitting on a chair or edge of a table. Immediately after the tendon tap the quadriceps femoris muscle contracts and there is jerking forward of the leg. There can be some alterations in knee jerk.

Knee jerk is decreased or lost in:

- Lesions in afferent neuron e.g. tabes dorsalis (Neurosyphilis).
- Lesions in center, e.g. poliomyelitis.
- Lesions in efferent neuron, e.g. lower neuron i.e. nerve pathway from anterior horn cell to muscle.
- During sleep and anaesthesia.

Knee jerk is increased or exaggerated in:

- Upper motor neuron lesion.
- Tetany, where there is increased neuromuscular excitability.
- Neurotic subjects due to hyperexcitability of CNS.

Pendular knee jerk occurs in lesion of neocerebellum which is characterized by hypotonia. In this type of knee jerk:

- Contraction of quadriceps is weaker than in normal knee jerk.
- Relaxation of quadriceps is quicker than normal knee jerk leading to quick fall of the leg like a dead weight. This is followed by vibrations or swinging of the leg like a pendulum. Hence the name pendular knee jerk. Hypotonia is the cause of the pendular knee jerk.

Achilles' reflex – the investigated person kneels on a chair for free feet hanging. To shock with hummer on achilles' (calcaneus) tendon. Answer reaction – musculus gastrocnemius contraction and plantar foot flexion. The reflexory arc is closed at S_1-S_2. Sensor and motor fibers are in tibial nerve.

If profound myotatic reflexes are decreased or lost it testifies to reflector arc links disturbances. If answer reaction to the irritation is increased with significant excitation irradiation and involving other muscular groups into the answer reaction, reflector field spreading - it testifies to suprasegmental central nervous system disorder existence.

4. Materials for self-control:

Control questions:
1. Innervation segmentary character and its significance.
2. Spinal centers.
3. Spinal conductive tracts.
4. Spinal reflexes.
5. Spinal shock.

Lesson 12.

Spine conductive function investigation.

Before performing this lesson, you should study the introductory material presented here.

1.Lecture course.
2.Moroz V.M., Shandra O.A. Physiology. - 2011. Unit 3, Chapter 1.
3.Guyton A.C., Hall J.E. Textbook of Medical Physiology. - 2006.
4.Ganong W.F. Review of Medical Physiology.-21st ed.-2003.-Section II.
Kapit W., Macey R.I., Meisami E. The Physiology Colouring Book: Harpers Collins Publishers, 1987.-P. 86.

Relevance of the topic.

Irritation from nociceptors of facial skin, oral cavity, tongue mucosa, periodontal and pulpal receptors is directed through nervous fibers (maxillary and mandibular nerves) to sensory neurons in trigeminal nerve ganglion.

1. Objectives:

To know: sensory information (nociceptive, tactile, temperature and proprioceptive sensitivity) conduction ways; superficial and deep sensitivity physiological mechanisms.

To be able to: to investigate pain, temperature, tactile, deep sensitivity; to draw superficial and deep sensitivity conductive ways.

2. Topic content.

2 main sensitivity types.

Superficial:

- nociceptive (pain),
- temperature,
- tactile.

Profound or deep:

- muscular-articular sense;
- trunk and extremities location in space;
- pressure and body weight sense;
- vibration sense.

Distribution of superficial and deep sensitivity impulses to subcortical parts is performed through **3-neuronal pathway:**

I-st neuron for all types of sensitivity is located in spine nodes. II-nd neuron make crossing.

Superficial sensitivity pathway (Fig.37-38) – through posterior radices impulse comes in posterior corns, where ***II-nd neuron*** is located; then fibers pass through anterior comissure to opposite side, ascend obliquely on 2-3 segments higher in a consisting of spine lateral funiculus up to thalamus (visual tubercle nucleus). It is spinothalamic tract.

III-rd neuron is in thalamus ventrolateral nucleus forming thalamocortical tract. Then impulse comes to internal capsule, radiate crown and finally postcentral gyrus (Fig.38). In case of stem injury at any segment level superficial sensitivity disappears on opposite (contralateral) side of body surface on 2-3 segments lower than the injury level.

Deep sensitivity pathway:
I-st neuron is in spinal ganglion without coming in corns passes to posterior funiculus on one-named (ipsylateral) side. Fibers from lower extremities are located medially and form Goll's fascicle; from upper extremities – forming so-called cuneate fascicle of Burdach – passing to medulla oblongata to posterior funicles nuclei where ***II-nd neuron is located.***

Then the pathways perform crossing (forming medial lemniscus) and enter into thalamus forming bulbar-thalamic tract. The tract ends in thalamus ventral-lateral nucleus where the ***III-rd neuron*** is originated from. Then thalamocortical pathway is formed and passes to internal capsule and cortex postcentral gyrus.

Somatic sensory afferents differ from each other depending on sensory function (Tab.5.). Mechanoreceptor axons are the largest and fastest (proprioception – Aα, touch and pressure – Aβ), information about pain & temperature is conducted by smaller fibres (Aδ and C).

Sensory function	Receptor type	Afferent axon type[a]	Axon diameter	Conduction velocity
Proprioception	Muscle spindle	 Ia, II	13–20 µm	80–120 m/s
Touch	Merkel, Meissner, Pacinian, and Ruffini cells	 Aβ	6–12 µm	35–75 m/s
Pain, temperature	Free nerve endings	 Aδ	1–5 µm	5–30 m/s
Pain, temperature, itch	Free nerve endings	C	0.2–1.5 µm	0.5–2 m/s

Table 5. Sensory afferents.

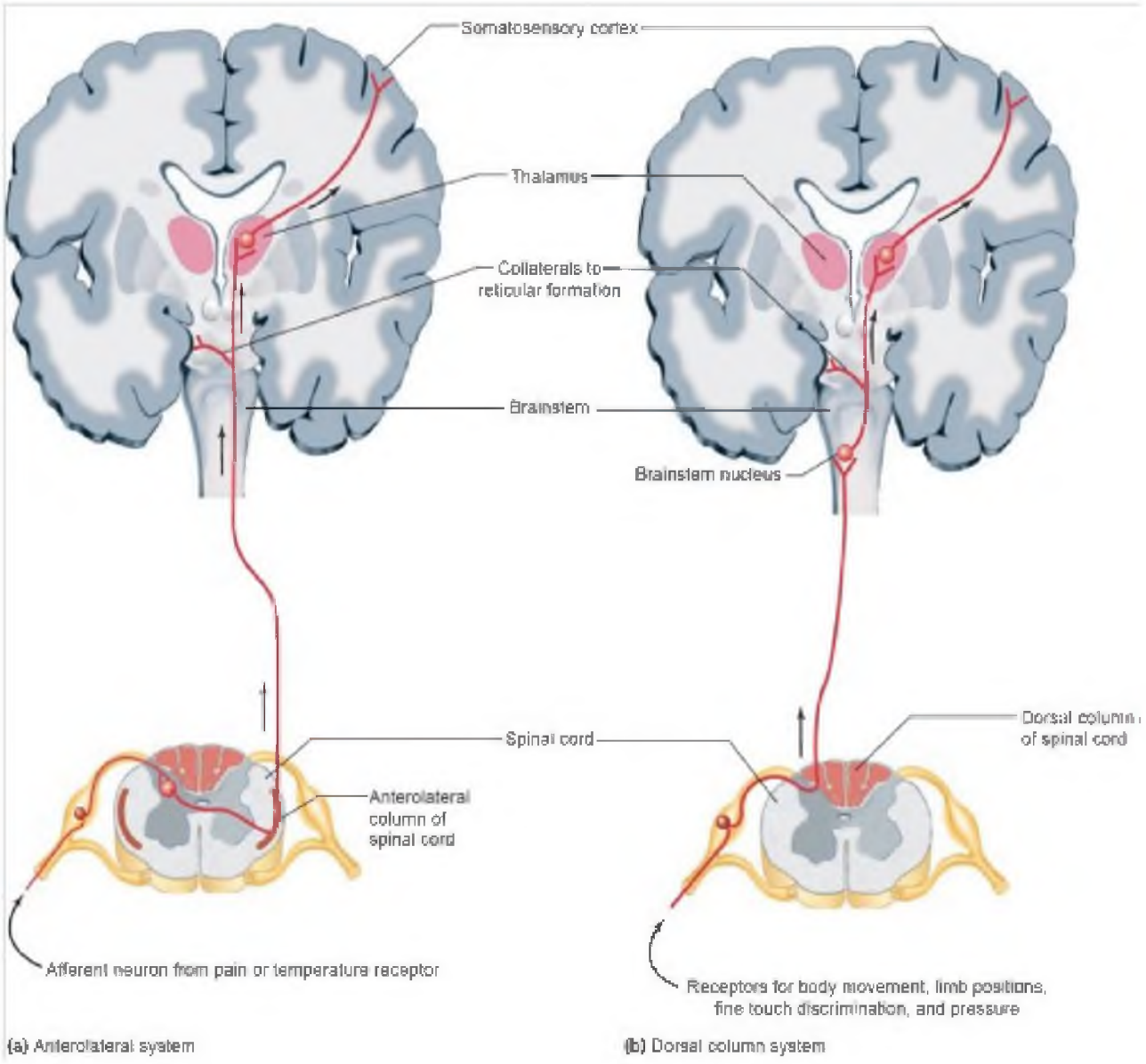


Fig.37. Ascending (sensitive) spinal tracts.

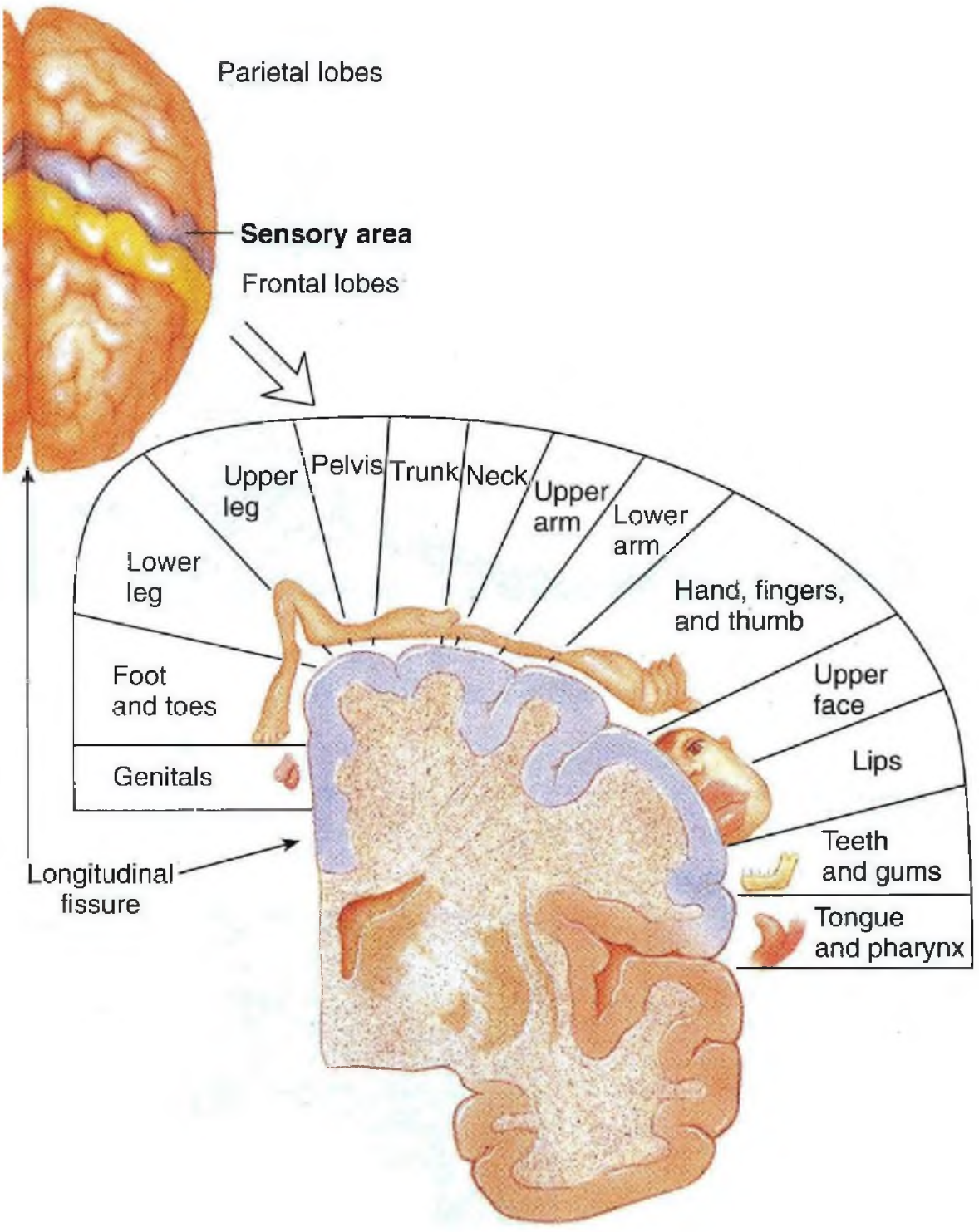


Fig.38. Cortex postcentral gyrus

Functions

The tracts of the posterior white funiculus convey impulses of following sensations:

1. Fine, i.e. epicretic tactile sensation.

2. Tactile localization: It is the ability to locate the area of skin where the tactile stimulus is applied.
3. Tactile discrimination: It is the ability to recognize the two stimuli, which are applied over the skin simultaneously.
4. Sensation of vibration: This is the ability to perceive the vibrations (from a vibrating tuning fork placed over bony prominence) conducted to deep tissues through skin.
5. Conscious kinesthetic sensation: It is the sensation (awareness) of various muscular activities in different parts of the body.
6. Stereognosis: It is the ability to recognize the known objects by touch with closed eyes.

The lesion in the fibers of these tracts or lesion in the posterior white column leads to the following symptoms. The symptoms appear on the same side below the lesion.

1. Loss of fine tactile sensation. However, crude touch sensation is normal.
2. Loss of tactile localization.
3. Loss of two point discrimination.
4. Loss of sensation of vibration.
5. Astereognosis: It is the inability to recognize known objects with closed eyes.
6. Lack of ability to differentiate the weight of different objects.
7. Loss of proprioception: There is inability to appreciate the position and movement of different parts of the body. Because of the loss of proprioception, the voluntary movements become uncoordinated, slow and clumsy. This condition is known as sensory ataxia or posterior column ataxia.

Physiological bases of pain and anesthesia.

Pain is an unpleasant sensation and emotional experience associated with or without actual tissue damage.

Pain classification:

- Fast (sharp) pain;
- Slow (chronic) pain.

By localization:

1. somatic:
   - superficial (from skin);
   - deep (from muscles, bones, joints, connective tissue);
2. visceral – from internal organs.

Classification nociceptors:

1. mechanosensitive nociceptors respond to intense or damaging mechanical stimuli;
2. mechanothermal nociceptors respond to thermal stimuli (<15°C or >45°C);
3. polymodal nociceptors respond to thermal, mechanical or chemical stimuli (histamine, bradykinin, potassium ions, serotonin, acetylcholine, acids). Prostaglandins and substance P increase the sensitivity of nociceptors.

Referred pain

When input nociceptive afferent activate interneurons, in may lead to the phenomenon of referred pain, in which the sensation of pain is experienced at a site other than the injured tissue (Fig.39-40.). For example, during a heart attack, a person often has pain in the left arm. Referred pain occurs because both visceral and somatic afferents often converge on the same neurons in the spinal cord (Fig.39.).

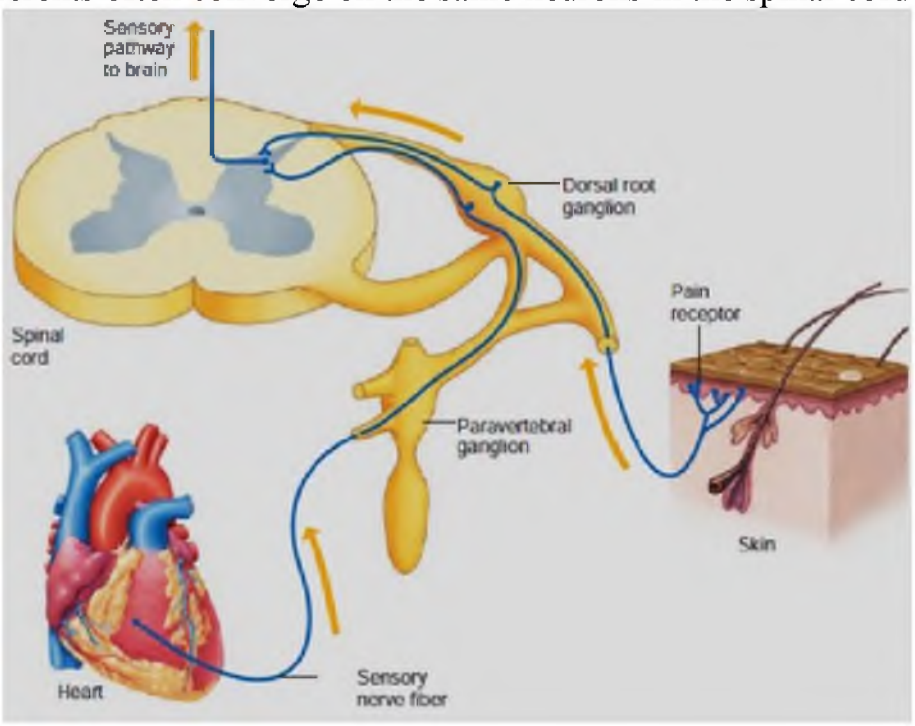


Fig.39. Convergence of visceral and somatic afferent neurons onto ascending pathways.

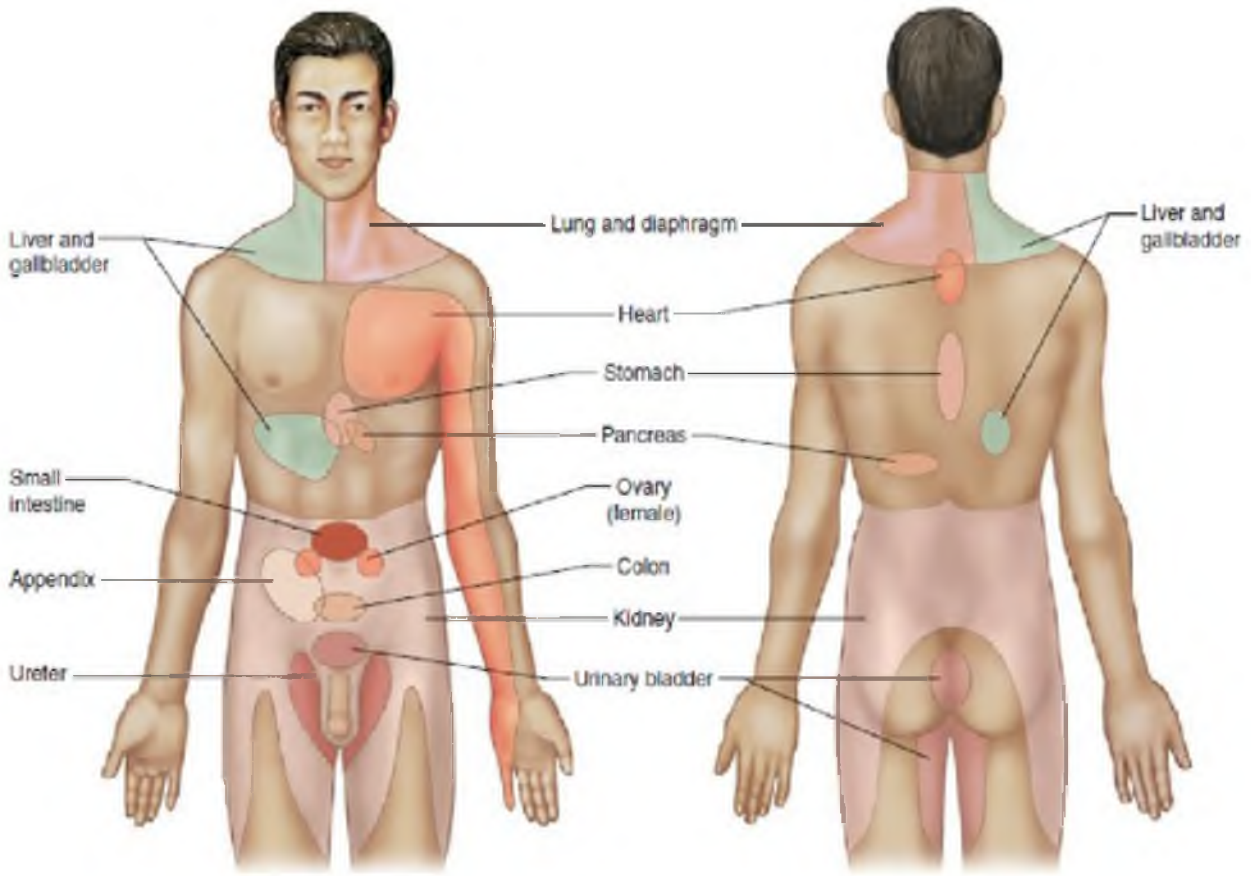


Fig.40. Regions of the body where we typically perceive referred pain.

Analgesia system

Analgesia is the absence of pain in the presence of a nociceptive stimulus. Analgesia system consists of descending systems that modulate the transmission of ascending pain signals: the periaqueductal gray (PAG); periventricular areas of the mesencephalon and upper pons surround the aqueduct of Sylvius; the raphe magnus nucleus; the nucleus reticularis paragigantocellularis.

Also, it includes gelatinose substance of the dorsal horns of the spinal cord. Activation of mechanoreceptors modulates the transmission of pain to higher centres (gate theory of pain). There are structures which produce transmitter substances: endogenic opioids (dinorphine, endorphins and encephalines); neurotensine; oxitocine; vasopressin; serotonin; epinephrine.

3. Materials for auditory self-work.

Materials and methods: neurologic hammer, needle, cotton-wool, weight set, subject (big) glass, Weber's compasses.

Investigation object: human being.

Task 1. To investigate hands and face skin pain sensitivity

There may be painful sensation in face and head region at oral cavity organs diseases. For example, at the diseases of teeth of superior jaw sensation locus is localized for incisival teeth in a region of plica fronto-nasal (it's maximal in superciliary arch at 1,5 cm from its middle); for canine teeth (fang) and premolars – in nasolabial region of corresponding side; at injury of the 1st and 2nd molars – in cheek region; the 2nd and 3rd molars – mandibular region. At pathology of teeth of

mandibular: for teeth incisivi, canine teeth and 1st premolar - chin region; for the 2nd molar – in sublingual region maximal downwards and backwards from the mandibular angle or at region of acoustic external meatus; at the diseases of the 3rd molar maximal pain is localized in front of muscle sternocleidomastoid.

One can irritate the skin of face or hand by needle. The irritation mustn't be too strong or frequent. One should first determine whether the investigated person differentiates prick or touching. For this aim it's necessary in turn but without regular order to touch to skin with blunt and acute subject. While this procedure the investigated person is proposed to find out the character of influencing (blunt or acute one). The injections must be short-termed, they mustn't cause acute pain. For clarifying of the boundaries of changed sensitivity the investigation must be performed out of healthy locus and on the contrary.

Task 2. Temperature sensitivity investigation on hand

For stimuli you must use 2 test tubes (with hot – of 40-50°C and cold 25°C or lower water). One should determine first whether the investigated person differentiates warm from cold (healthy people feel the temperature difference in 2°C). Then you must compare the temperature stimuli perception intensivity on different skin locuses of hands, face and to determine the boundaries of increased or lost temperature sensitivity.

Task 3. Muscular-articular sensitivity investigation

At muscular-articular sensitivity investigation one should check up the sense of passive movements, localization sense, skin kinesthesia, pressure and weight sense. The investigator asks the investigated person close his eyes; the first one moves the fingers of investigated person. The last (investigated person) must find out the localization of extremity. The investigated person must reproduce the localization of other extremity with his closed eyes. If he doesn't differentiate light movements their altitude must be increased. The investigator must touch to the investigated person's very easy without extra (spare) influencing onto the skin receptors.

Skin kinesthesia must be checked up by shift of plica, the investigated person must determine the direction of shift.

Task 4. Pressure and weight sense investigation (Weber-Fechner law)

The investigated person is sitting with closed eyes and puts his hand on the table. The investigator puts subject glass to the ends of investigated person's straighten fingers. The investigator puts the weight of certain mass onto the glass and the pressure sense is estimated. Then while slow increasing the weight mass the investigated person is asked when he will feel the addition in weight. The experiment must be performed several times while checking up the sensation threshold at different loading (10, 20, 50, 100 and 200 g) and the constant quantity must be estimated (K= addition size /origin weight mass).

In conclusion it's necessary to compare constants received in 5 experiments. Under norma the investigated person must tell about difference in 10% of weight mass.

Task 5. Complicated sensitivity types investigation.

Stereognostic sense - is the ability to recognize by palpation familiar subject with closed eyes (coin, key, pin, needle etc). Healthy person usually solves this task easy and successfully, he characterizes subject's features (dense, soft) correctly.

Discriminative sense – separate sensation of 2 irritations putted on the skin simultaneously. It is investigated with Weber's compasses. Compasses legs are making together up to double touchings will be percepted like one. Norma: 1,0-1,5 cm between legs should be percepted like 2 separate points.

Irritation location sensation – the investigated person must answer where the irritation is made by the investigator.

Skin plica kinesthesia-see task number 3.

5. Materials for self- control:

Control questions:

1. Total representations about pain: types, mechanisms, nociceptors, nociceptive sensitivity spinal and stem conductive ways.
2. Modern data about nociceptive system. Analgesia.
3. Explain the phenomenon of referred pains and their clinical significance.
4. Spinal and stem temperature sensitivity conductive ways.
5. Proprioceptive sensitivity ways.
6. Spinal and stem deep sensitivity conductive ways.

Lesson 13
Posterior brain role investigation in motor and sensory functions regulation

Before performing this lesson, you should study the introductory material presented here.

1. Lecture course.
2. Moroz V.M., Shandra O.A. Physiology. - 2011. Unit 3, Chapter 3.
3. Ganong W.F. Review of Medical Physiology.-21st ed.-2003.
4. Guyton A.C. Textbook of Medical Physiology.-NY, 1992.-P. 625-626.

Relevance of the topic.

Normal functioning of this brain part is vital because even the least injury of this area as a rule leads to grave vital activity disorders (respiration, heart and vessels, digestion activity disturbances).

1. Objectives:

To know: posterior brain reflectory activity; posterior brain morphological-functional peculiarities; reticular formation ascendant and descendant influence mechanism; cranial-cerebral nerves role; medulla oblongata centers.
To be able to: investigate cranial-cerebral nerves function and posture static reflexes.

2. Topic content.

Posterior brain consists of pons and medulla oblongata.

Medulla oblongata functions:

I Reflectory:

1. Defensive:

- cough;
- blinking;
- tears releasing;
- vomiting.

2. Alimentary:

- sucking;
- swallowing;
- releasing of digestive juices.

3. Cardiovascular (heart and vessels activity regulation).
4. Respiratory.
5. Control of volume of information conducting by spinal column.
6. Sound frequency, intensity and origin recognizing.

II Conductive.

Medulla oblongata is continued downwards as spinal cord. This forms main pathway for the ascending and descending tracts of spinal cord. It also has many important centers, which control the vital functions.

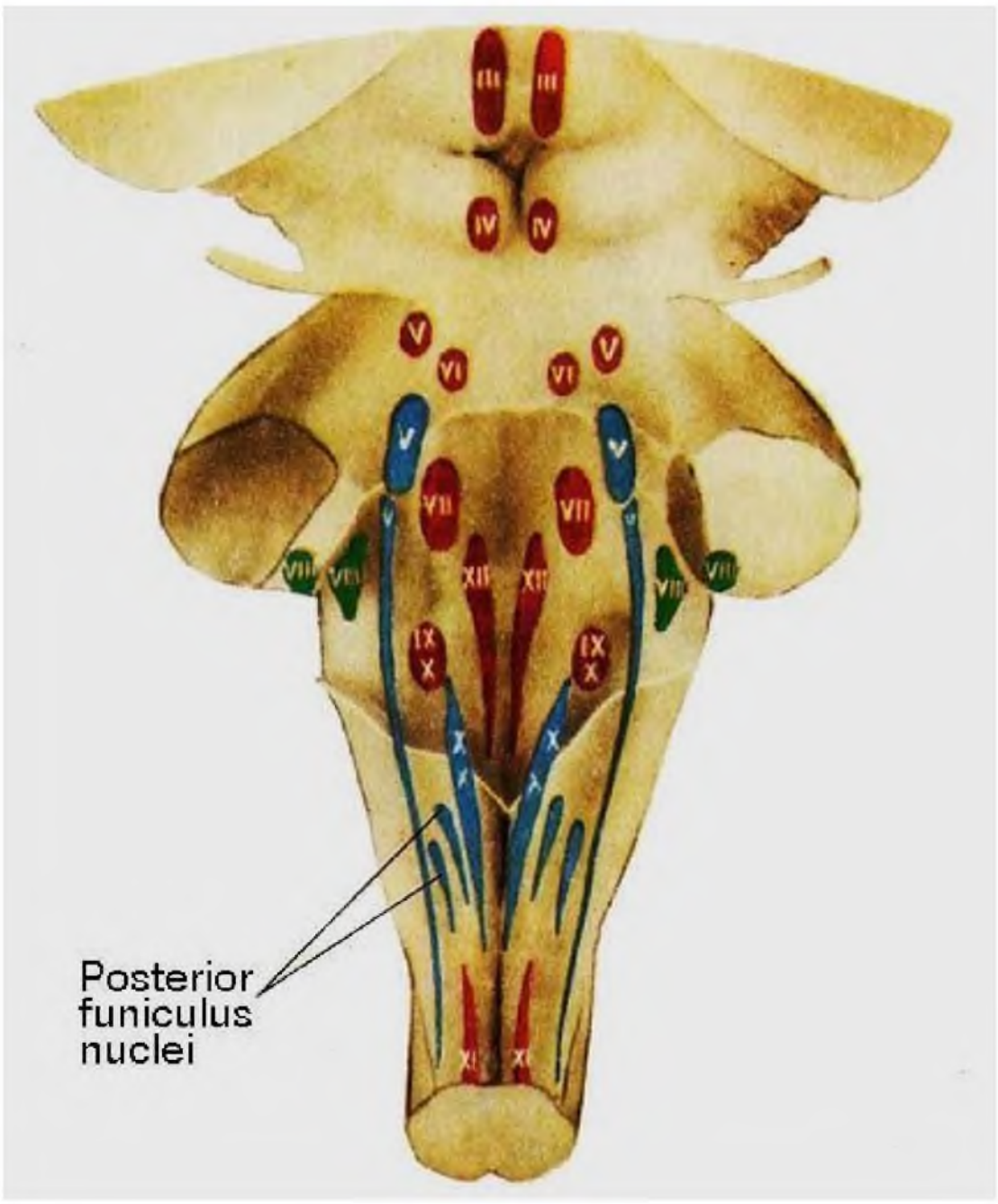


Fig.41. Localization of cranial nerve nuclei, anteroposterior projection.

Motor nerve nuclei mark *red*, *sensory nerve* nuclei mark *blue*, *vestibulocochlear nerve* nuclei mark *green*.

Respiratory centers: Inspiratory and expiratory centers are the medullary respiratory centers maintaining normal rhythmic respiration.

Vasomotor center: This center controls blood pressure and heart rate.

Deglutition center: This center regulates the pharyngeal and esophageal stages of deglutition.

Vomiting center: It induces vomiting during irritation or inflammation of GI tract.

Superior and inferior salivatory nuclei: The salivatory nuclei control the secretion of saliva.

Table 6. Cranial-cerebral nerves and their functions

Nerve	Nuclei location	Functions
I pair, olfactory nerve	Skull	Participates in olfaction (smelling)
II pair, optic	Skull	Participates in vision
III pair, oculomotor	Midbrain	Rises superior eyelid, turns eyeball up, down, inside and outside
IV pair, trochlear	Midbrain	Innervates muscles turning eyeball below and outside
V pair,	Pons	Sensory part innervates skin of face, frontal-parietal

trigeminal nerve		head parts, haired part, eyeball, nasal and oral mucosa, anterior 2/3 of tongue, facial skull bones periosteum, dura mater of anterior and middle cranial fossae, proprioreceptors of masseter muscle ocular and mimic muscles. Motor fibers innervate masseter, temporal, medial and lateral pterygoideal, mandibular-hyoideal muscle as well as muscle rising tympanal membrane
VI pair, abducent nerve	Midbrain	Innervates eye muscles abducting eyeball outside
VII pair, facial nerve	Pons	Innervates mimic and other muscles of face and head, platysmal and stylo-hyoideal muscles; sensory part provides innervation of 2/3 of tongue
VIII pair, vestibular-cochlear nerve	Medulla oblongata	2 parts: vestibular (provides static reflexes and gravitation overcoming id est regulates body orientation in space) and acoustic (comes to quadrigemina inferior collins in lateral lemnisc and thus provides orienting reflex to sound stimuli)
IX pair, glosso-pharyngeal	Medulla oblongata	Motor part innervates stylo-pharyngeal muscle rising pharynx; sensory part – posterior 1/3 of tongue (bitter taste), soft palate, pharynx, fauces, epiglottis anterior surface, acoustic tube and tympanal cavity; vegetative parasympathetic nuclei innervate parotid salivary gland (much liquid saliva releasing)

X pair, vagus	Medulla oblongata	Motor fibers innervate soft palate, pharynx, larynx, epiglottis, oesophagus superior part, vocal cords, smooth muscles in stomach, small intestine and large intestine superior part; sensory part innervates inner organs; provides voice and swallowing
XI pair, accessory	Medulla oblongata	Innervates sterno-cleido-mastoideal muscle (provides head turning in opposite side) and trapezial muscle (together with the first muscle, participates in respiration enforcement)
XII pair, hypoglossal	Medulla oblongata	Motor part provides tongue turnings

Cranial nerve nuclei: The nuclei of 12th, 11th, 10th and some nuclei of 8th and 5th cranial nerves are located in the medulla oblongata (Fig.41).

12th cranial (hypoglossal) nerve controls the movements of tongue.

11th cranial (accessory) nerve controls the movements of shoulder.

10th cranial (vagus) nerve controls almost all the vital functions in the body: cardiovascular system, respiratory system, Gl, etc.

8th cranial nerve (the cochlear division of this nerve), which has the relay in medulla oblongata is concerned with the auditory function. *Vestibular nuclei*: Vestibular nuclei contain the second order neurons of vestibular nerve. There are four vestibular nuclei situated in the rostral part of medulla and caudal part of pons namely, superior, medial, lateral and inferior vestibular nuclei (nuclei of Schwalbe, Deuters, Behterev. Vestibulospinal tract is originated from Deuters' nucleus). The medial and inferior vestibular nuclei extend into the medulla. All the medullary centers and nuclei of cranial nerves are controlled by the higher centers situated in cerebral cortex and hypothalamus.

Pons cerebrum

This forms a bridge between medulla and midbrain.

The functions of pons are:

1. The axons of pontine nuclei join to form the middle cerebellar peduncle or the brachium pons, pons forms the pathway connecting the cerebellum with the cerebral cortex.
2. The pyramidal tracts pass through the pons.
3. The medial lemniscus is joined by the fibers of 10th, 9th, 7th and 5th cranial nerves in pons.
4. The nuclei of 8th, 7th, 6th and 5th cranial nerves are located in pons (Fig.42).
5. It contains the pneumotaxic and apneustic centers for regulation of respiration.
6. Pons also contains the vestibular nuclei, which are already mentioned in medulla oblongata.

Lesion of a brainstem due to bulbar paralysis

- *The lesion of a hypoglossal nerve leads to speech disturbance which call* ***dysarthria.***
- *Two-sided lesion of IX, X nerves nuclei result in losing of pharyngeal and palatal reflexes, the swallowing is broken -* ***dysphagia*** *is observed.*
- *The paralysis of muscles of larynx results to hoarse vote. It is* ***dysphonia.***
- ***Bulbar paralysis (peripheral)*** *– at a lesion nuclei, roots, trunks of the IX, X, XII nerves an atrophy of tongue, muscles of pharynx, soft palate, fibrillar oscillations are observed; pharyngeal reflexes get decreased.*

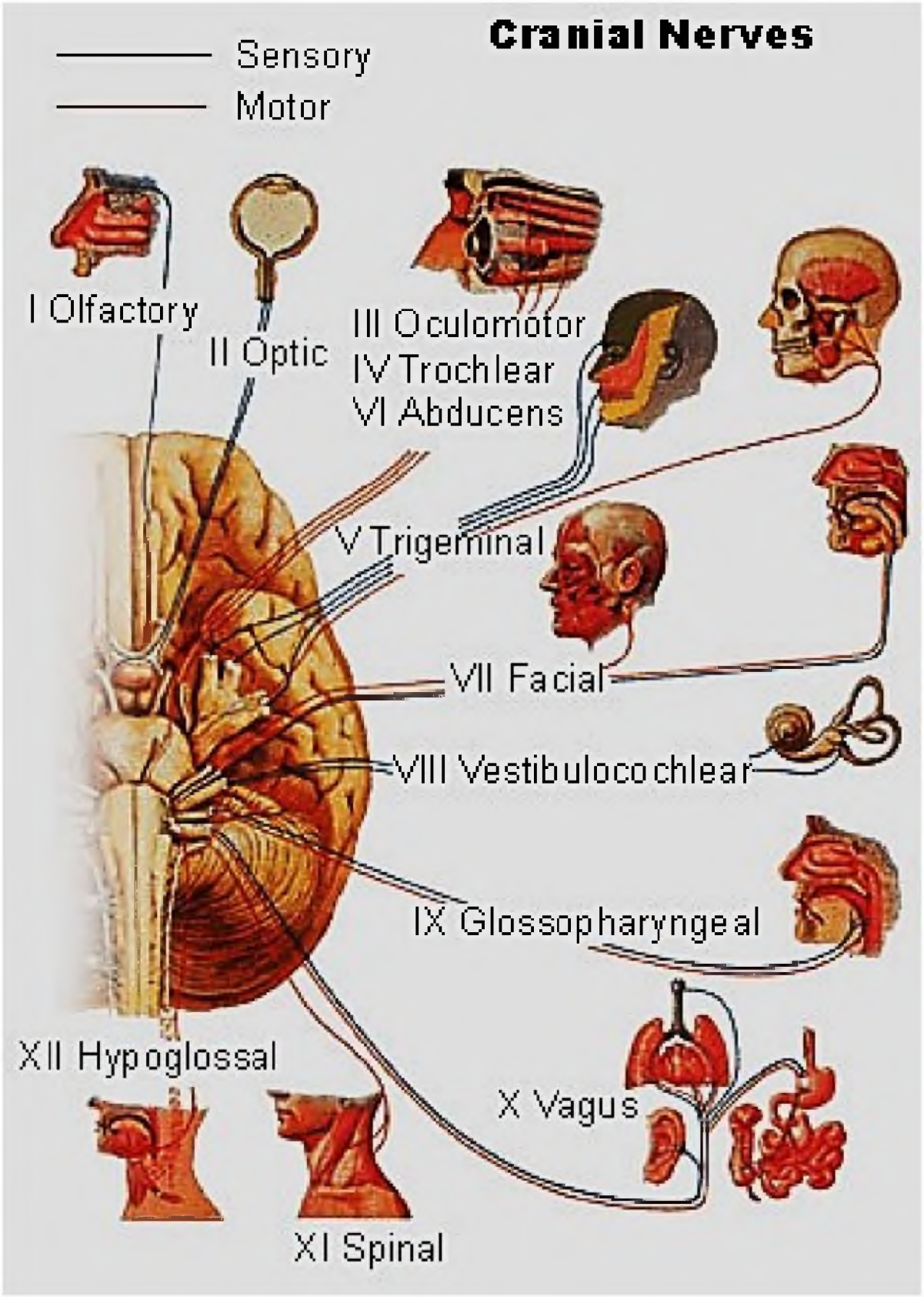


Fig.42. Cranial nerves functions

3. Materials for auditory self-work.

Materials and methods: neurologic hammer, paper strip.

Investigation object: human being.

Task 1. Trigeminal nerve (V-th pair investigation)

- Corneal reflex – the investigated person looks up and towards. The investigator touches with thin paper strip to the inferior-exterior eyeside without touching the eyelashes. The reflex arc - orbital nerve (Vth pair ramus), pons, facial nerve. Decreasing or lost of corneal reflex is found out at trigeminal nerve, facial nerve, pons injuries, at shock, in course of narcosis.
- Conjunctival reflex – is caused by touching to conjunctive. Answer reaction- eyelid close. Reflex arc – see like at corneal reflex.
- Superciliar reflex - is caused by hummer shock at superciliar arc limb. Answer reaction - eyelid closure. Reflex arc – orbital nerve, pons, facial nerve.

Mandibular reflex - the investigated person slightly opens his mouth. Masticatory muscles contraction is caused by hammer shock down on chip from one than from another side. Answer reaction – mandible lifting.

This reflex can be absent under normal conditions.

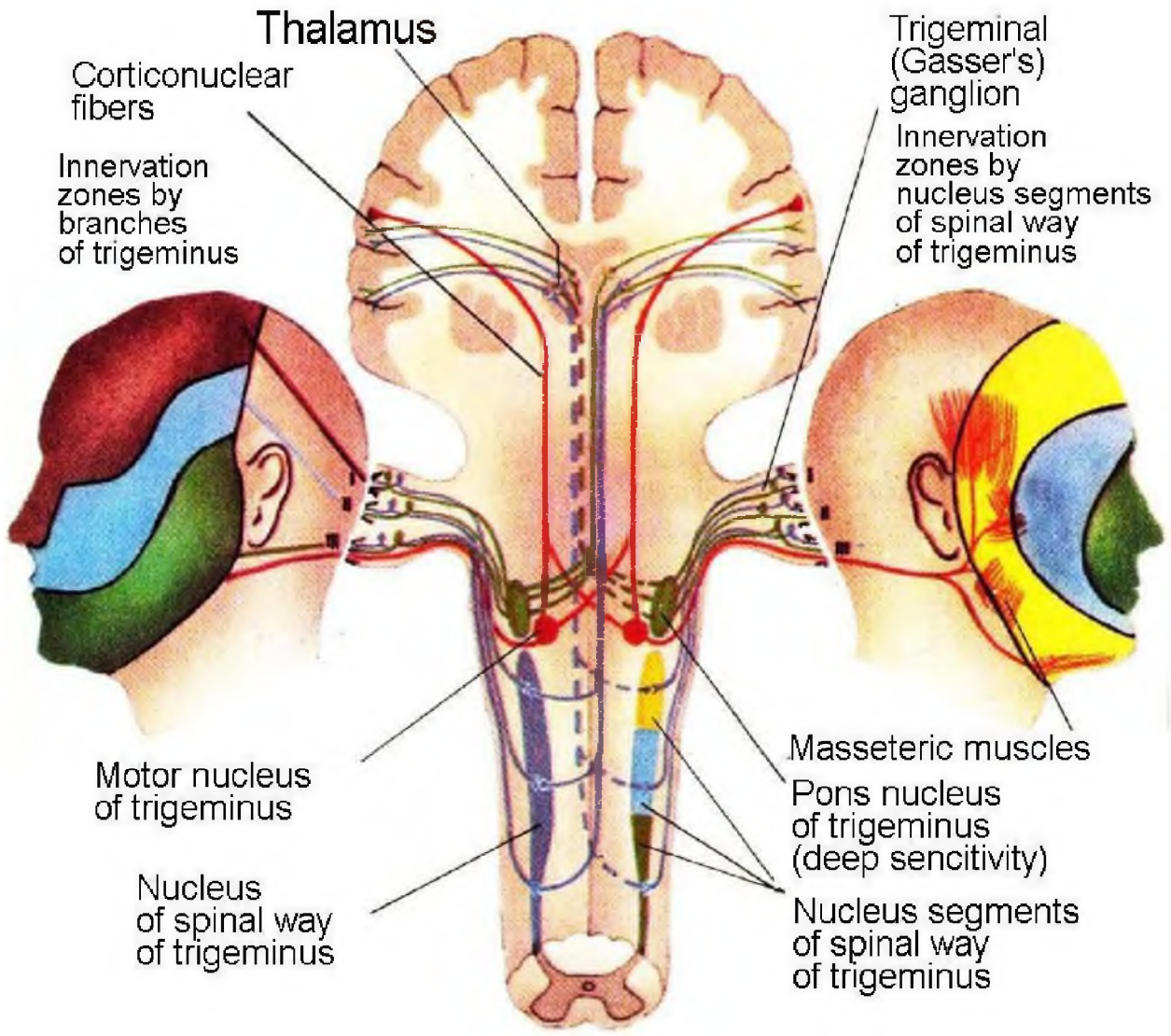


Fig.43. Functional scheme of trigeminal nerve.

Trigeminal nerve (V pair) is mixed. It conducts sensitivity information from face skin, head hairy area anterior part, nasal and oral cavity, tongue, eyeball, cerebral sheathes and realizes motor innervation of masseters.

Trigeminal node lays on anterior surface of a pyramid of a temporal bone.

There are ***three branches of a trigeminal nerve*:**

Ophthalmic nerve conducts signals from skin of forehead, anterior hairy of head, upper eyelid, interior angle of an eye and dorsum of nose.

Maxillary nerve conducts sensitivity from skin of inferior eyelid, external angle of an eye, top of cheeks, upper lip, maxilla and its teeth.

Mandibular nerve conducts signals from inferior lip, inferior part of cheeks

Task 2. Facial nerve (VII-th pair) investigation

For this gaim it's necessary to perform face examination (Fig.44): difficulties at mastication, muscular volume diminishing, frontal and nasolabial plicas asymmetry, whether the face become distorted (mouth angle). They ask to perform masticatory movements putting their fingers to the facial muscles. The investigator asks the investigated person to wrinkle, to frown (knit) the eyebrows, to close eyes, to billow cheeks, to show teeth, to stretch lips. Orbicular muscle force determining - the investigated person is asked to close his eyes strongly. The investigator tries to raise eyelid superior determining resistance force at this. To make the conclusion.

Task 3. Glossopharyngeal nerve (IX-th pair) investigation

The investigation must be begun from the determining of the investigated person voice timbre and sounding. At disorder of innervation of velum palatinum (if it doesn't close nasopharynx cavity completely) the voice is nasal. At vocal chords injury one can aphony and wheezing. Then the investigator must examine soft palate. The investigated person is asked to tell "A" (at one-sided injury at given side soft palate doesn't tighten).

Palatine and pharyngeal reflexes – with the paper rolling up into long strip to touch the soft palate and pharynx posterior wall mucosa. Answer reaction is swallowing and vomiting. Reflexes are realized by means of glossopharyngeal and vagus nerves. The decreasing or lost of these reflexes can be both at healthy people and at injury of IX-th and X-th pairs of cranial nerves or their nuclei in medulla oblongata (so-called bulbar syndrome).

Task 4. Accessory nerve (XI-th pair) investigation

Accessory nerve is a motor one, it innervates sternocleidomastoid and trapezius muscles (head turn in an opposite side and shrugging one's shoulders). The investigated person turns his head towards and up and restrains in such location. The investigator tries to oppose to this. For sternocleidomastoid muscle force you can tell according to resistance degree. Trapezius muscle is investigated by raising and fixating in such a situation. Shoulder girdle is lowered at paralysis.

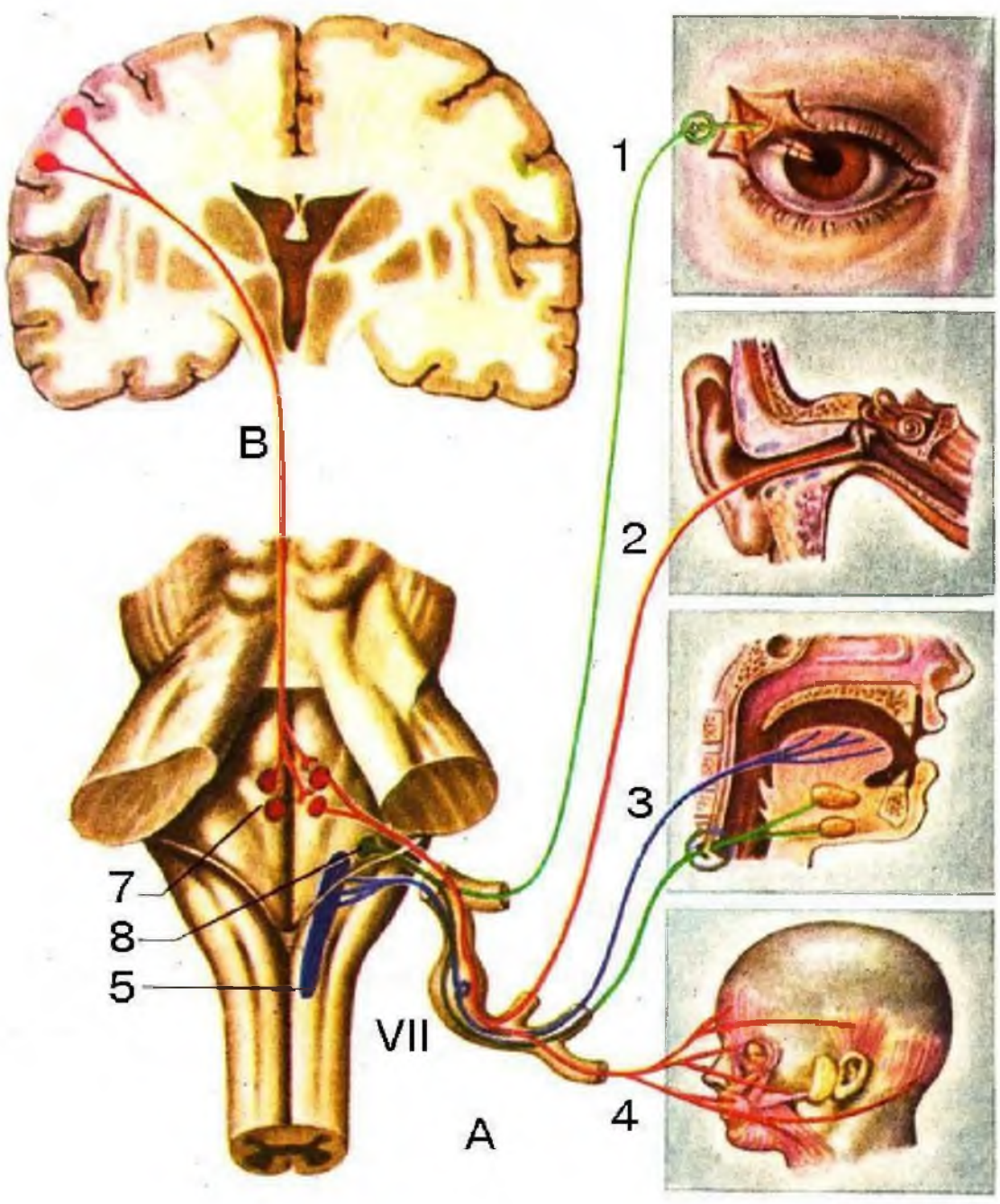


Fig.44. Functional scheme of facial nerve: 1 – greater petrosal nerve, 2 – stapedial nerve, 3 – tympani chord, 4 – facial nerve, 5 – solitary pathway nucleus (gustatory nucleus), 6 – upper salivatory nucleus, 7 – facial nerve nucleus, 8 – corticonuclear tract.

Task 5. Hypoglossal nerve (XH-th pair) investigation

This nerve innervates the tongue. One should perform the tongue investigation. It's necessary to put it forward behind the teeth line. At one-sided nerve injury – atrophy of the same tongue half, thinness, foldedness of mucosa, fibrillations. The tongue is sticked out in a sick side. At injury of two nerves – the tongue is almost immovable, the speech is disturbed as well as pushing of chilus in mouth.

The injury of V, IX, X, XIIth *pairs leads to the disorders of swallowing (dysphagia), sounding voice loss (aphony), speech nasal shade (nasolaly), anomaly of correct order of articulate sounds pronunciation (dysarthria).*

4.Materials for self- control:

Control questions:

1. Medulla oblongata centers.
2. Medulla oblongata reflectory activity.
3. Posterior brain vegetative reflexes.
4. Posterior brain conductory function.
5. Reflexes the mostly often determined in dentistry (for dentists).

Lesson 14
Midbrain role investigation in motor and sensor functions regulation

Before performing this lesson, you should study the introductory material presented here.

1.Lecture course.
2.Moroz V.M., Shandra O.A. Physiology. - 2011. Unit 3.
3. Ganong W.F. Review of Medical Physiology.-21st ed.-2003.-Section II.

4. Guyton A.C. Textbook of Medical Physiology.-NY, 1992.-P. 636-638.

Relevance of the topic.

Masticatory and mimic muscles function can be changed at this brain part injury. Particularly, black substance is responsible for coordination of movements connected with food taking.

Dentists can get in touch with patients suffering from oral cavity motor and sensor functions disorders due to midbrain pathology.

1. Objectives:

To know: midbrain morphological-functional peculiarities; midbrain reflex activity; brain stem sensory function; stem reticular formation structure, connections and role; midbrain cranial-cerebral nerves role; midbrain vegetative reflexes.

To be able to: explain mechanisms explaining muscular tone disorders in "mesencephalic" animals.

2. Topic content.

Midbrain lies between pons and diencephalon. It consists of two parts:

A. Tectum - comprising superior and inferior colliculi

B. Cerebral peduncles - consisting of basis pedunculi, substantia nigra and tegmentum, which includes red nucleus.

Superior Colliculus

It is a small structure and is an important center for reflexes. Through the tectospinal tract, the superior colliculus controls the movements of eyes, head, trunk and limbs in response to visual impulses. The efferent fibers from superior colliculus going to the nucleus of III cranial (oculomotor) nerve cause constriction of pupil during light reflex. Thus, it forms the center for light reflex. Superior colliculus also

receives afferents from optic tract, which helps in the integration of optical and postural reflexes.

Inferior Colliculus

It consists of single layer of neurons to which the lateral lemniscus (auditory fibers) synapses. The inferior colliculus is the center for auditory reflexes. Stimulation of this also produces reflex vocalization.

Cerebral peduncles

It consists of pyramidal tract fibers in the middle, temporopontine fibers laterally and frontopontine fibers medially.

Substantia Nigra

It is situated below the red nucleus. Substantia nigra is considered as one of the components of basal ganglia. Its pathology is known as parkinsonism. The distinguishing features are like at Parkinson's disease. Reason is one: dophamine deficiency.

Tegmentum

This lies dorsal to substantia nigra and is actually the upward continuation of the reticular formation in pons.

Three decussations take place in tegmentum. It also contains red nucleus.

1. Superior cerebellar peduncle: This is formed by fibers between cerebellum and other parts of central nervous system. The fibers are predominantly efferent fibers from dentate nucleus of cerebellum; and few fibers are from other cerebellar nuclei—nucleus globosus and nucleus emboliformis.
2. Forel's decussation: This is due to the crossing of rubrospinal tracts from either side.
3. Mynert's decussation: It is due to the crossing of medial longitudinal bundle formed by the efferents of 3rd, 4th and 6th cranial nerves.

Red Nucleus

Red nucleus is a large oval or round mass of gray matter extending between the superior colliculus and hypothalamus.

Red nucleus has two parts:

1) Nucleus magnocellularis, which is formed by large cells. Fibers from this form the rubrospinal and rubrobulbar tracts.

2) Nucleus parvocellularis, which is formed by smaller cells. The fibers from this form mainly the rubroreticular tract.

Connections of Red Nucleus

Afferent connections: Red nucleus receives fibers from:

1. Motor cortex (area 6) to nucleus parvocellularis—corticorubral fibers

2. The globus pallidus and subthalamic nuclei to nucleus magnocellularis—pallidorubral fibers.
3. Dentate nucleus (of opposite side) to nucleus magnocellularis - cerebellorubral or dentatorubral tract.

Efferent connections: Red nucleus sends efferent fibers to various parts of brain and spinal cord.

1. Rubrospinal tract to spinal cord
2. Rubrobulbar tract to medulla
3. Rubroreticular fibers to reticular formation
4. Rubrothalamic tract to lateral ventral nucleus of thalamus
5. Rubroolivary tract to inferior olivary nucleus
6. Fibers to nuclei of 3rd, 4th and 6th cranial nerves.

Functions of Red Nucleus

1) Control of muscle tone: Because of its connections with cerebellum, vestibular apparatus and skeletal muscle, the red nucleus plays an important role in maintaining the muscle tone.

2) Control of complex muscular movements: Red nucleus controls the complex muscular movements.

3) It plays an important role in the integration of various impulses received from many important areas of brain.

4) Control of skilled movements: Red nucleus plays an important role in controlling skilled muscular movements by its connections with spinal cord and cerebral cortex.

Decerebrative rigidity (Fig.45). Cutting at the level of Varolii pons anterior limb (rubro-spinal tract) causes in muscles extensors tone increasing in animals. Such animals do not save equilibrium and fall down. This phenomenon is known as decerebrate rigidity. It is considered that such a state is delt with cerebellum and red nuclei descendant influencing liquidating to bulbar centers.

Animals with brain cutting at anterior colliculi level are known as mesencephalic animals. Mesencephalic animals differ from spinal ones with muscular tone

regulation and body position in a space. Decerebrative rigidity is absent in them. Red nuclei in midbrain causes inhibitory influencing on vestibular nucleus of Deuters to which afferentation from auricular labirinthus and muscular proprioreceptors comes through vestibular-spinal tract. Red nuclei decomposition causes expressed decerebrative rigidity in animals. Red nuclei irritation leads to significant muscular tone decreasing – the animals become "like a sac". Decerebrative rigidity is determined also by afferentation coming to Deuters' nuclei from muscles proprioceptors and vestibular apparatus. Spine posterior radici and vestibular nerves cutting also cancels decerebrative rigidity.

If red nuclei do not give inhibitory influencing at posterior brain level, than central excitations are increased and get diffused. Thus, extensors activity is increased selectively.

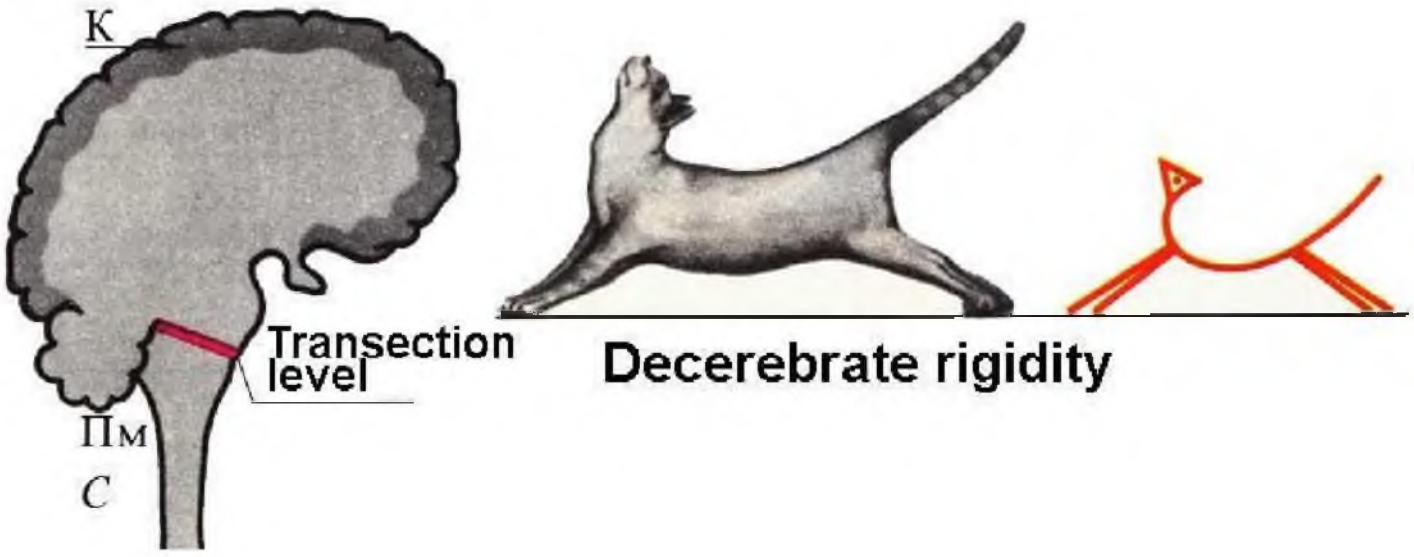


Fig.45. Decerebrative rigidity

Midbrain and basal nuclei structures participation in mastication and swallowing regulation:

They are black substance in midbrain (dopamine source regulating respiration, mastication and swallowing alternation) and caudate nucleus, shell (putamen) among basal ganglia because they inhibit substantia nigra (black substance) activity with inhibitory mediator gamma-amino-oleic acid secretion through third basal ganglion - globus pallidus.

3. Materials for auditory self-work.

Materials and methods: scale, rotating arm-chair, stall.
Investigation object: guinea pigs, the investigated person.

Task 1. To investigate nerves: oculomotor (III), trochlear (IV) and abducens (VI).

While examination of eyeballs the investigator should pay the attention to the:

- pupils' width;
- orbital fissures width,
- pupil shape,
- eyeballs localization in orbit (falling back, protrusion),
- strabismus (cross-eyedness or squint-eyedness).

Pupillary reactions – the investigated person eye should be closed by scale or hand. After this it's necessary to determine change of another pupil size. To ask to perform eyes movement on the right and on the left.

At III-rd or IV-th pairs (cranial-cerebral nerves) injury orbital fissure can be narrowed or closed – ptosis. At III-rd pair injury one can see pupil deformation, disturbance convergent eyes movement disturbance.

Task 2. Stato-kinetic human reflexes.

The investigated person must sit in rotatory arm-chair, turn his head forward and close his eyes. In such a position horizontal semicircular channels are investigated. Then it's necessary to carry out arm-chair rotation on the right or on the left with the velocity of 5 times in 10 sec (1 turn in 2 sec). Then to stop arm-chair quickly, to ask the investigated person to open his eyes and to observe eyelids movements, how long do they continue. It's also possible to carry out rotation with head turned on 90° on right or left shoulder or tossed (throwed) back on 60° behind (vertical channels are investigated). To describe investigated reactions, to call receptive fields of investigated reflexes and to indicate closure level of them in CNS.

To take another investigated person, to sit into arm-chair. To propose to turn his head on 30° forward, to perform rotation as in previous investigation, to stop arm-chair and to propose to investigated person to go after rotation directly on straight line forward. To observe movements character.

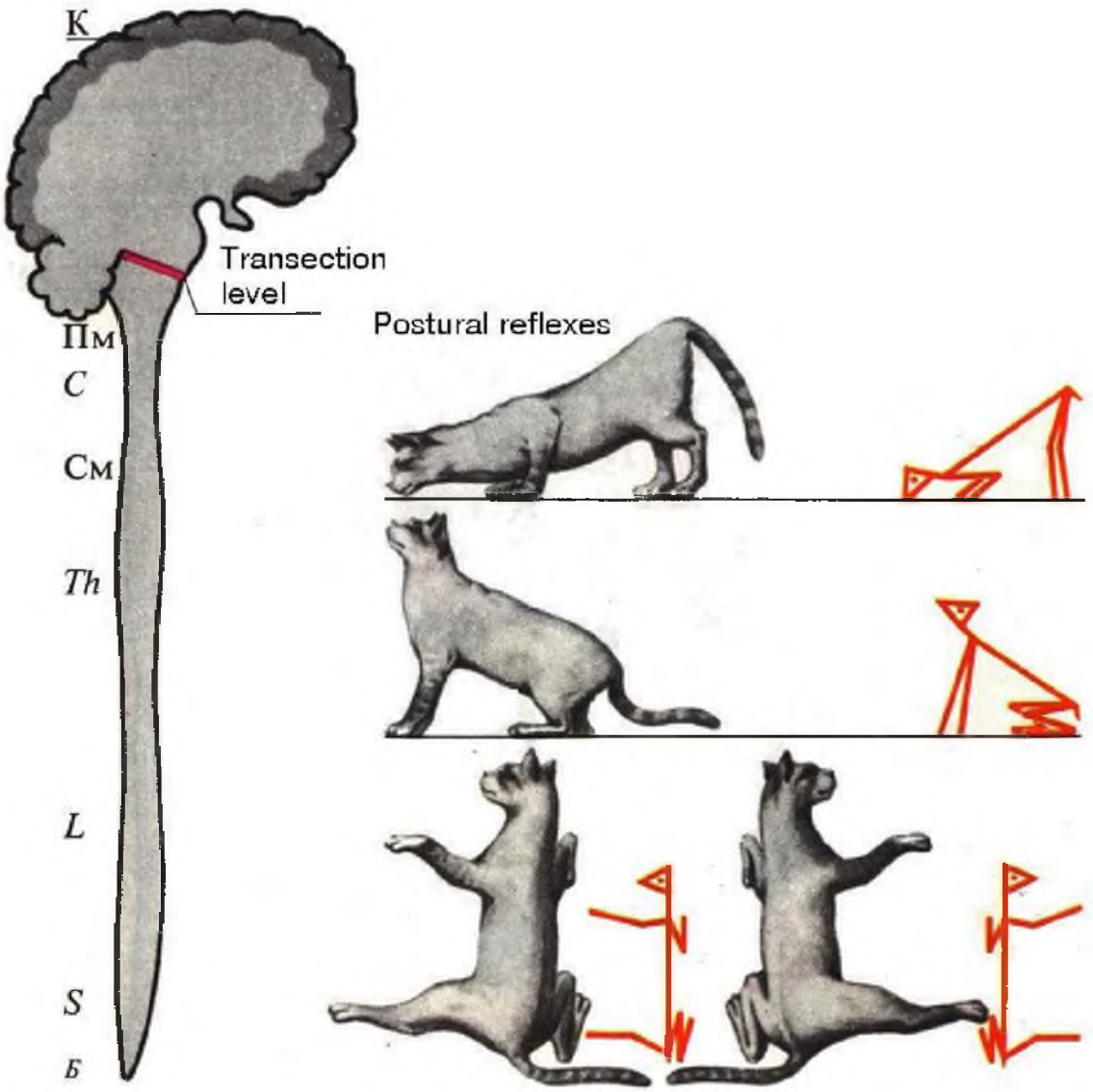


Fig.46. Postural reflexes.

Statokinetic reflexes provide maintenance of a posture during change of movement speed; they are linked to exaltation of semicircular ducts receptors. *Nystagmus* appears during body rotation in a horizontal plane.

Lifting reflexes are augmentation of tone of muscles-extensors during acceleration upwards and augmentation of tone of muscles-flexors at acceleration downwards.

Task 3. Investigate static and statokinetic reflexes in guinea pig.

To put guinea pig to the table, to pay the attention to animal's pose, head location, moving reactions. To turn over the animal on his back and to lie with his abdomen up. To pay attention to movement character, their order and definite animal pose.

To put guinea pig on board, (Fig.46) to raise and to rock the animal, in turn raising board anterior or posterior end. Pay attention to fore-limbs (anterior extremities) status and movement, head status. To put down or to raise the board very

fast, while observing anterior extremities status at the beginning and at the end of the movement, animal head status.

To put guinea pig on rotating chair, to perform rotations in horizontal plane to the right or to the left, to pay the attention to animal pose shift in course of movement, to

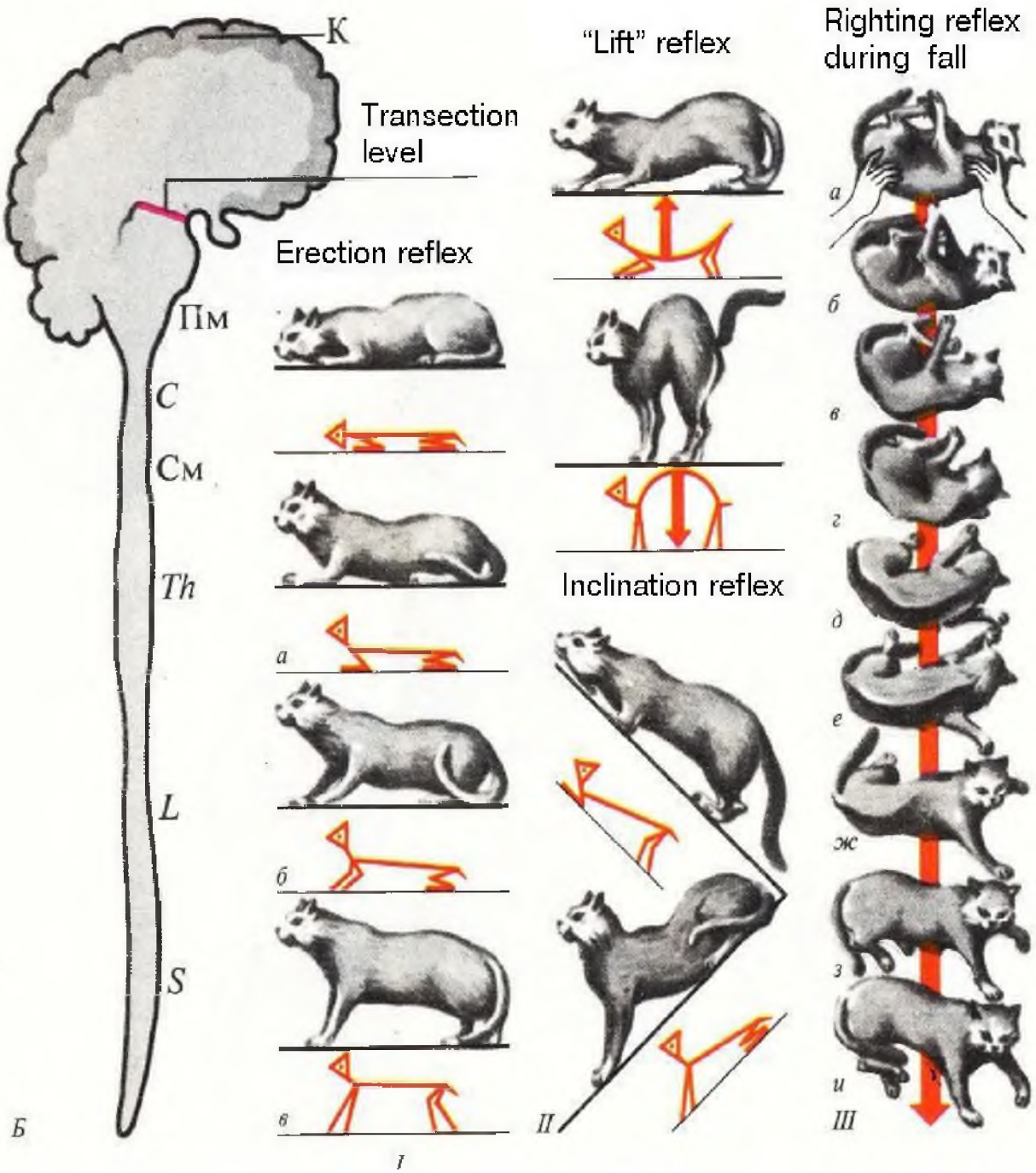


Fig.47. Static and statokinetic reflexes.

head movement in course of rotation. To indicate, what happens at the rotation beginning and at rotation stoppage.

Statokinetic reflexes (Fig. 47) provide maintenance of a posture during change of movement speed; they are linked to exaltation of semicircular ducts receptors. **Nystagmus** appears during body rotation in a horizontal plane.

Lifting reflexes are augmentation of tone of muscles-extensors during acceleration upwards and augmentation of tone of muscles-flexors at acceleration downwards.

4.Materials for self- control:

Control questions:

1. Midbrain reflex function.
2. Vestibular apparatus, irritation conditions for otholitic and ampullar vestibulary receptors.
3. Decebrative rigidity.
4. Stato- and statokinetic reflexes.
5. Midbrain vegetative reflexes.
6. Midbrain ascendant and descendant conductory ways.

Lesson15

Cerebellum, diencephalon, basal ganglia role investigation in organism motor functions regulation

Before performing this lesson, you should study the introductory material presented here.

1.Lecture course.
2.Moroz V.M., Shandra O.A. Physiology. - 2011. Unit 3.
3. Ganong W.F. Review of Medical Physiology.-21st ed.-2003.-Section II.
4. Kapit W., Macey R.I., Meisami E. The Physiology Colouring Book: Harpers Collins Publishers, 1987.-P. 101, 102.
5. Guyton – Ganong – Chatterjee. Concise Physiology /Ed. By Dr Raja Shahzad Gull: M.B.B.S., F.C.P.S., King Edward Medical College.-Lahore, 1998 (1st Edition).-P.301-305, 309-313.

Relevance of the topic.

Dentists can get in touch with such cerebellum pathological states: hyperkinesis – myoclonuses (fast fascillations of separate muscular groups) of swallowing musculature, soft palate and pharynx wall; speech disorder - scanding- accents are not on necessary syllable but is divided with equal intervals; at circulation disorder in cerebellum (at arteria closure – Vallenberg-Zaharchenko syndrome) – sensitivity is disordered on face, soft palate and vocal cord are paralyzed.

Structural organization of a cerebellum.

It is located above medulla oblongata and pons cerebrum. It consists of two hemispheres, vermis and three peduncles pairs (nervous fibers). (Fig.48)

The hemispheres are divided into anterior and posterior lobes. They consist of cortex of a cerebellum and nuclei (nervous cells). There are nuclei in white matter of hemisphere and vermis of cerebellum: fastigial, globosus, emboliformis, dentatus nuclei.

Upper peduncles connect it with midbrain, medium peduncles – with the pons, inferior peduncles – with medulla oblongata.

Neuronal structure of cerebellar cortex

The cortex consists of three layers:

- 1-st – molecular: dendrites of Purkinje cells, piriform cells (Purkinje's cells), bodies of basket cells, stellate cells.
- 2-nd – ganglionic: bodies of piriform cells;
- 3-rd – granular: bodies of association [intercalary, internuncial] neurons.

Two types of afferent fibers (climbing and mossy) come to cortex.

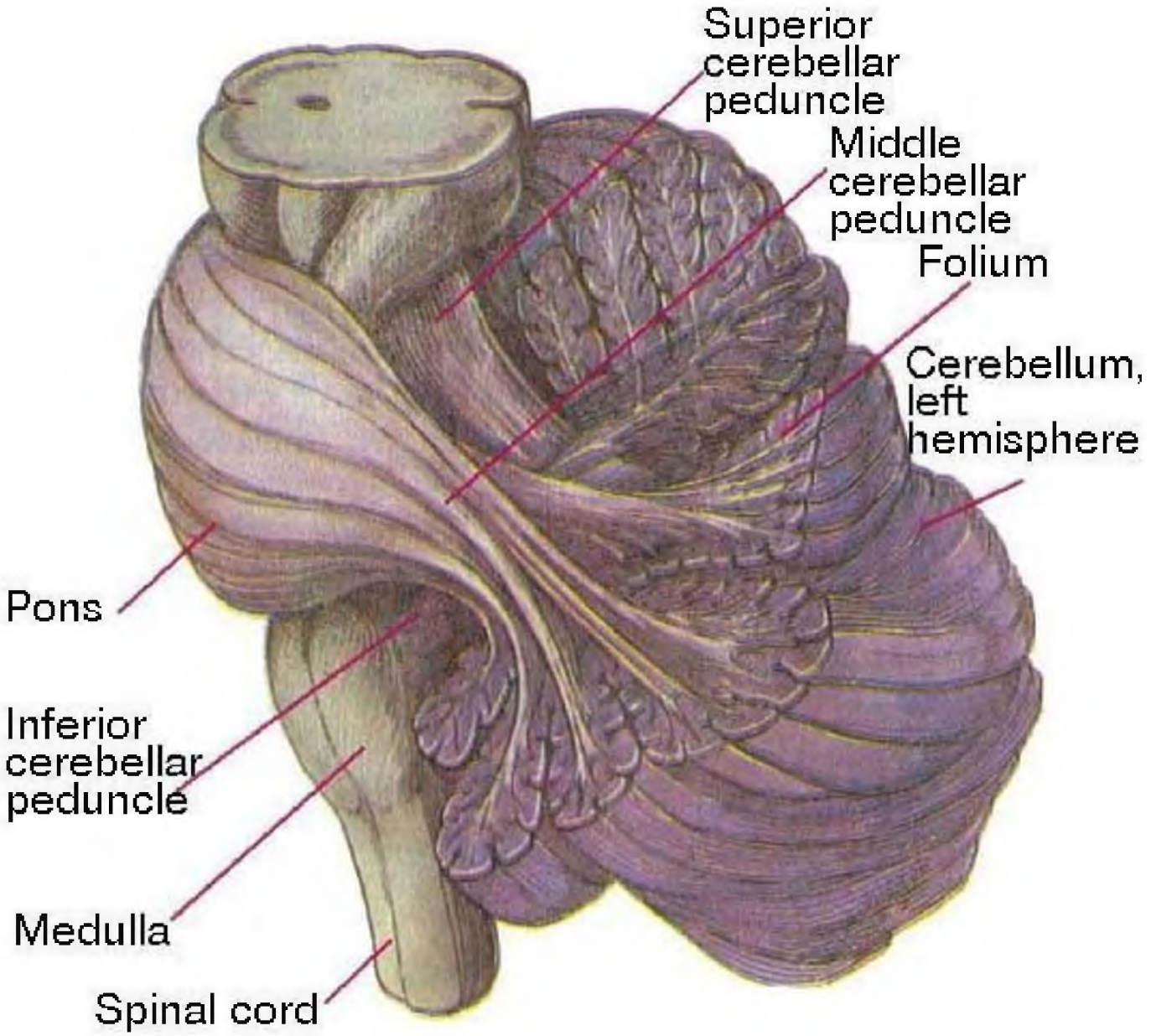


Fig.48. Cerebellum anatomical location

Somatotopic projection (Fig.49) in a cortex of vermis and hemispheres of a cerebellum.

Collector of afferent impulses in cerebellum is fastigial nucleus, which sends them to piriform neurones (Purkinje cells) of cerebellar cortex according to the somatic

projection. Upper extremities are represented in anterior departments of hemispheres, inferior ones are represented in posterior departments, head and neck are represented in anterior parts of vermis cortex and trunk is represented in posterior part. The proximal parts of extremities are projected more medially, distal parts – more laterally, hemispheres are responsible for coordination of movements of extremities, vermis – of trunk.

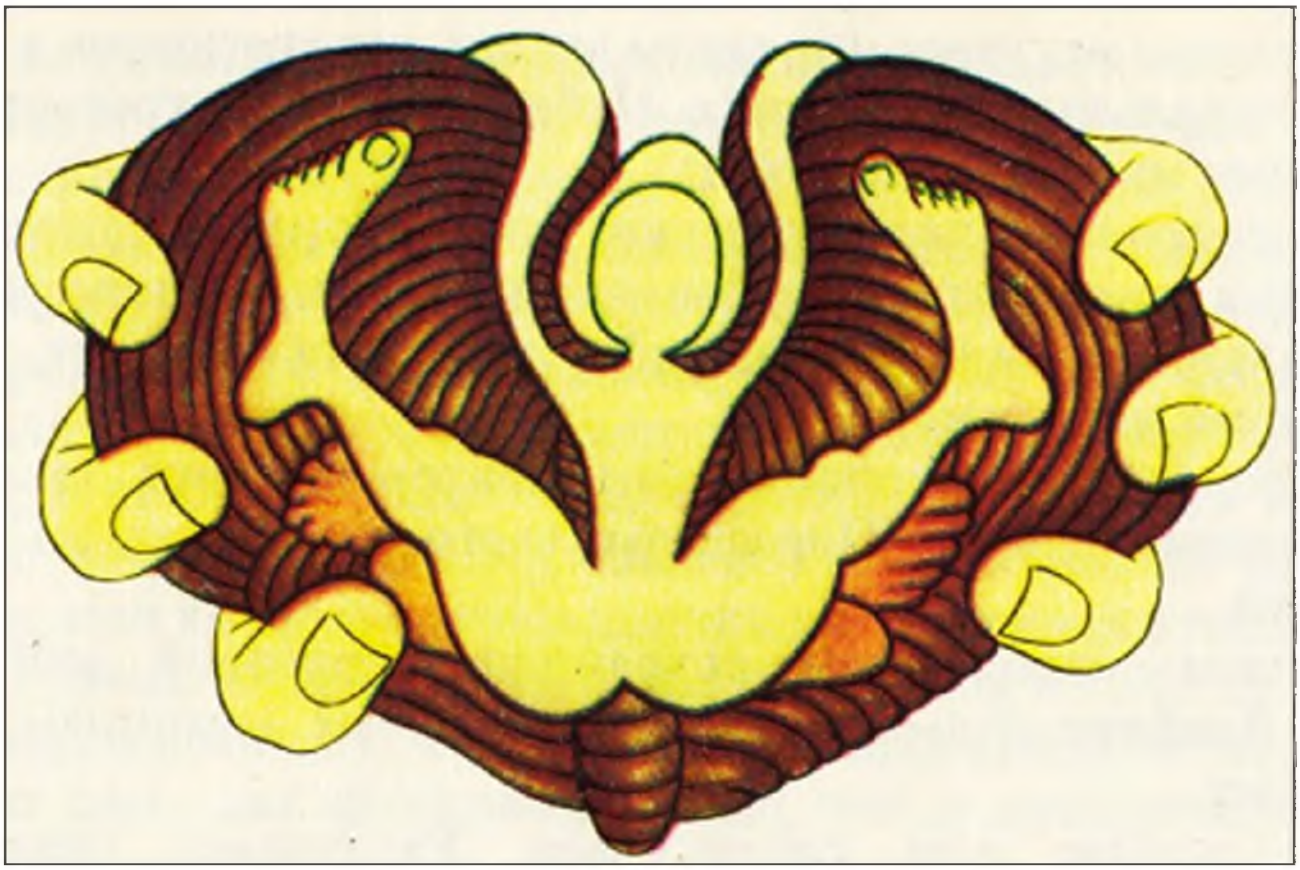


Fig.49. Somatotopic projection in cortex of cerebellum (vermis and hemispheres)

Tab.7. Functions of cerebellum

Functions		Division of cerebellum involved
1. Regulation of tone,	By receiving impulses from vestibular	Vestibulocerebellum

posture and equilibrium	apparatus	
	By receiving impulses from proprioceptors in muscles, tendons and joints, tactile receptors, visual receptors and auditory receptors	Spinocerebellum
2. Regulation of coordinated movements	1. Damping action 2. Control of ballistic movements 3. Timing and programming the movements 4. Servomechanism 5. Comparator function	Corticocerebellum (Neocerebellum)

Cerebellum and its connections

Cerebellum receives afferent impulses from all receptors stimulating during locomotion (from proprioceptors, vestibular, visual, and acoustical). Cerebellum influences onto red nucleus and reticular formation of brainstem, which send impulses to spinal cord gamma motor neurons regulating muscle tone.

Cerebellum lesion (Fig.50)

Static ataxia – it is infringement of statics in rest (shaking).

Dynamic ataxia – it is locomotion coordination disorder at performance of targeted movements. A tremor of extremities – so-called intentional tremor – is observed. Walking is shaky, "drunk".

Cause of cerebellar ataxia is the disturbance of conjugative work of muscles – agonists and antagonists, disproportion of locomotion – dysmetria. Rapid change of one locomotion by others, inverse ones – ***adiadohokinesis*** (pronation and supination) is impeded.

Asynergia – it is disturbance of mutual conjugated movements.

Atony – it is loss of muscle tone (anterior part of cerebellar posterior lobe is responsible).

Astasia – it show up in ability of muscles to realize oscillating motions (tremor, shaking) and in disabilities to conjoint tetanic contraction.

Tremor – it is oscillating motions in various body segments.

The excision of cerebellum does not cause disappearance of reflectory responses; tonic reflexes of brainstem are non-changed.

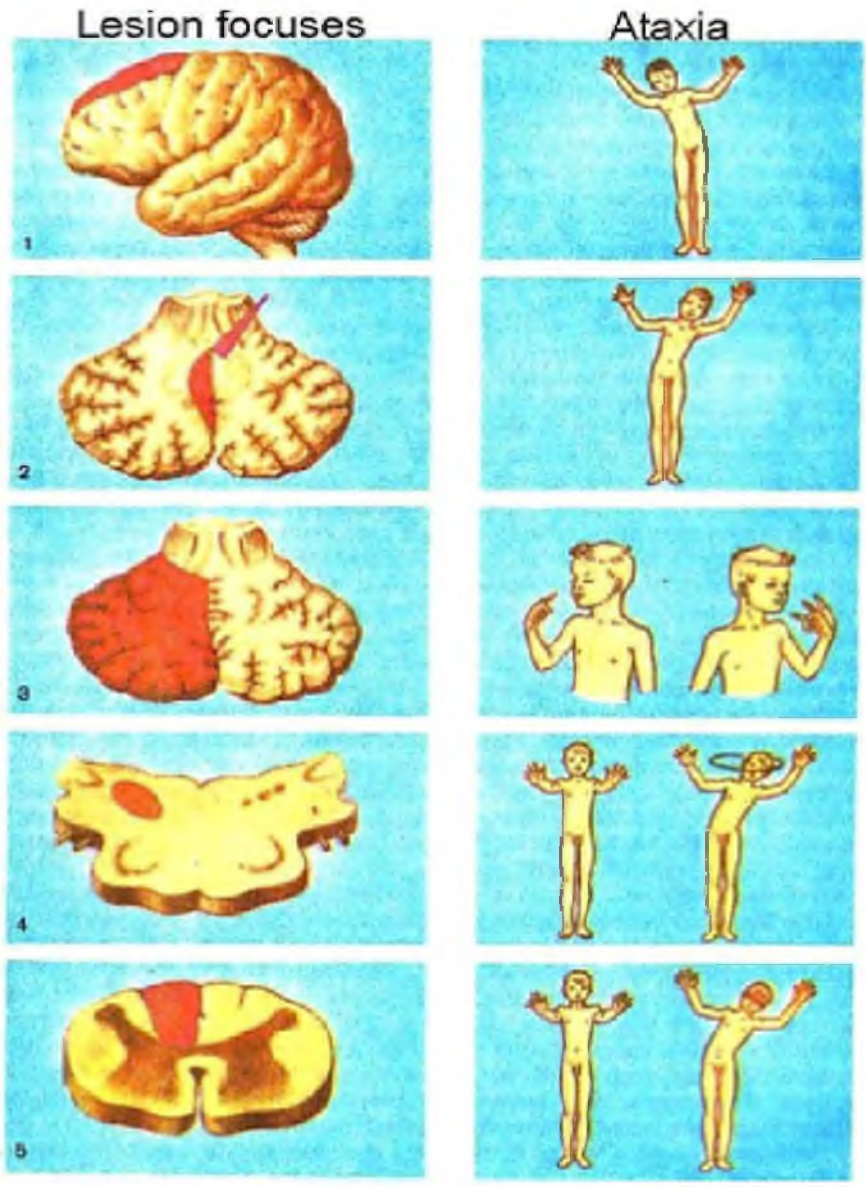


Fig.50. Symptoms of cerebellum lesion

Extrapyramidal part of nervous system

Extrapyramidal system includes structures of big hemispheres cortex, basal ganglia (Fig.51), cerebellum, reticular formation, descending and ascending tracts.

Functions: it provides involvement of all motor systems of brain, perfects movements making them economic and automatic.

Strio-pallidal system:

Striatum (more young formation) (Fig.52) includes caudate nucleus and putamen.

Pallidum includes globus pallidus, black matter, red nucleus, subthalamic nucleus.

Myelination of striatal tracts comes to end of 5-th month age. Newborns possess pallidal features.

Cortical center of extrapyramidal part includes premotor area (field 6), temporal and occipital areas.

Connections of strio-pallidal system.

1. Tract connecting to ending motor tract and muscle.
2. Mutual connections with various parts of extrapyramidal system and big hemispheres cortex
3. Afferent pathways (Fig.53):

- rubrospinal tract of Monakov
- reticulospinal tracts
- tegmental-spinal tract from corpora quadrigemina
- tracts to motor nuclei of cranial nerves.

Afferent signals from thalamus, cerebellum, reticular formation, great brain cortex create continuous corrective flow.

Signs of a pallidum lesion.

Lesion of pale globule and black matter causes parkinsonism – hypertonic-hypokinetic syndrome.

It occurs at a lesion of pale globule, black matter. Total restraint, hypoexpressions of movements (hypokinesia), muscle rigidity are characteristics. Static tremor is present. The person has face like mask. Beginning of arbitrary movements is difficult. Walking is with shallow steps. Voice is quiet, monotonic. Handwriting is small.

Signs of a striate body lesion. Striatic syndrome.

Hyperkinetic-hypotonic syndrome includes hypotonia or dystonia and different non-arbitrary violent excessive movements – hyperkinesias.

Chorea is lesion of midbrain tegmentum, lentiform and caudate nuclei. Unrhythmic fibrillations are typical.

Myoclonias are unrhythmic and unsynchronic contractions of various muscles of trunk, abdomen.

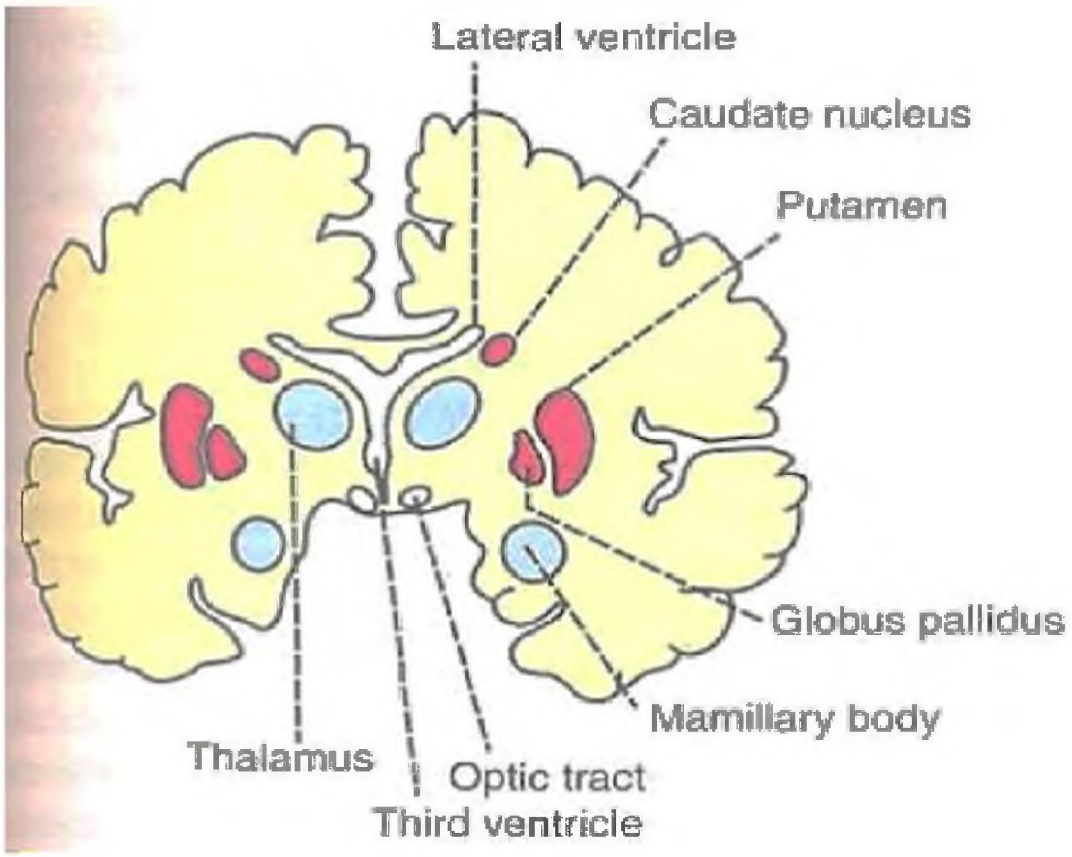


Fig.51. Basal ganglia.

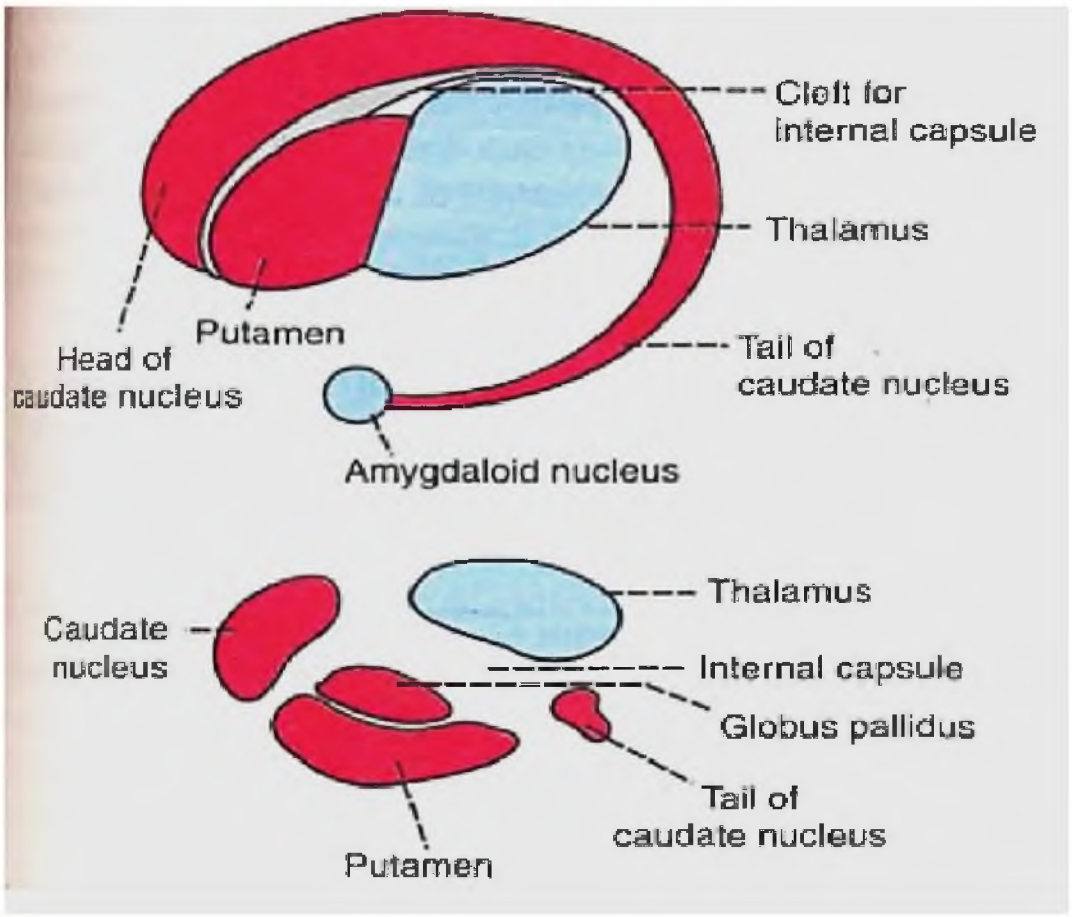


Fig.52. Corpus striatum.

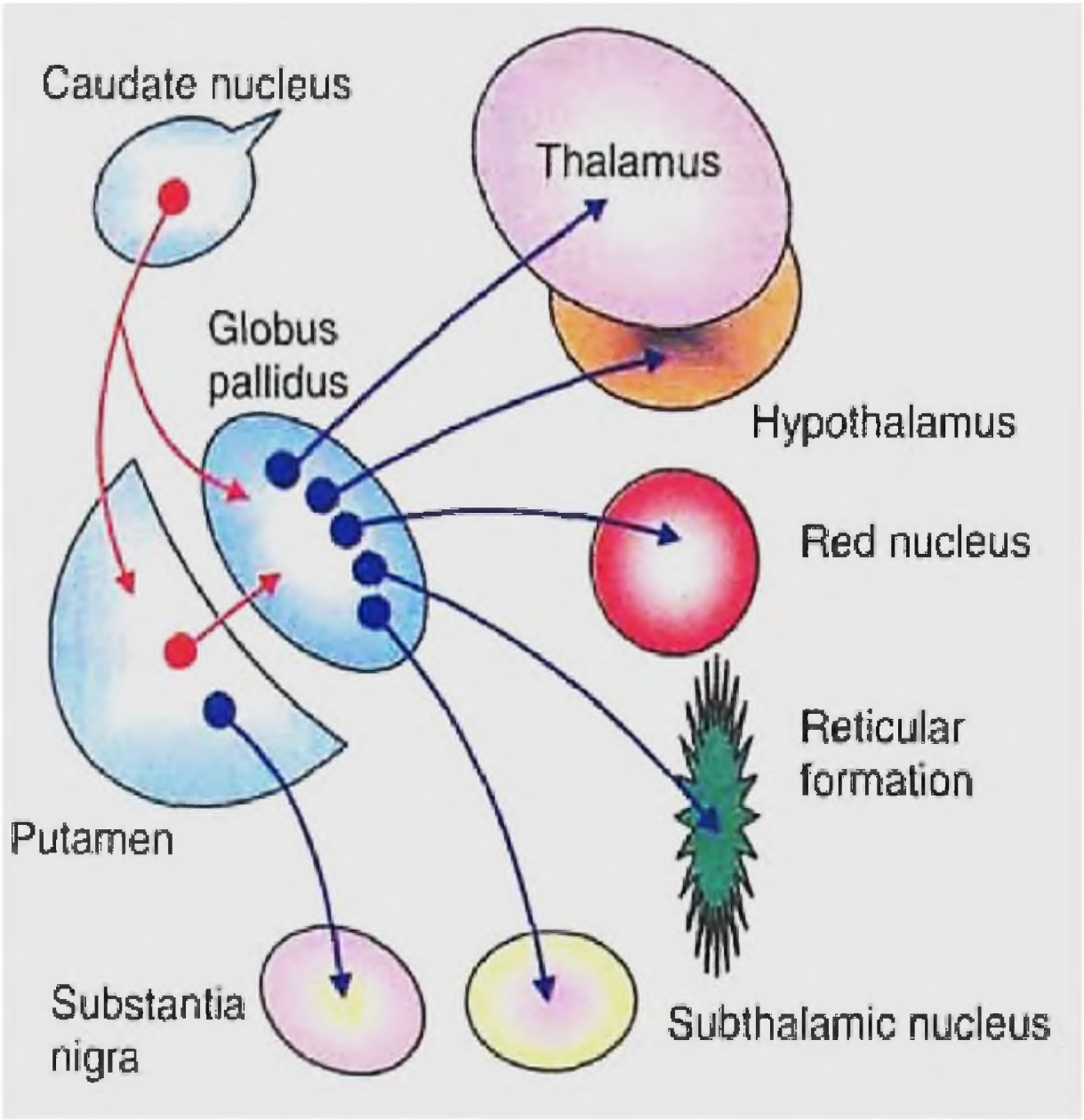


Fig.53. Efferent and intrinsic connections of corpus striatum.

Role of neurotransmitters in the functions of basal ganglia

The functions of basal ganglia on motor activities are executed by some neurotransmitters released by nerve endings within basal ganglia. Following neurotransmitters are released in basal ganglia.

Dopamine: It is released by dopaminergic fibers from substantia nigra to corpus striatum (putamen and caudate nucleus – nigra strial fibers). The deficiency of dopamine leads to Parkinsonism.

Gamma aminobutyric acid (GABA): It is secreted by intrinsic fibers of corpus striatum and substantia nigra.

Acetylcholine: It is released by fibers from cerebral cortex to caudate nucleus and putamen.

Substance P and enkephalins: These are released by fibers from globus pallidus reaching substantia nigra.

Noradrenaline: This is secreted by the fibers between basal ganglia and reticular formation.

Among all these neurotransmitters, dopamine and GABA are inhibitory neurotransmitters. So, the dopaminergic fibers and the fibers releasing GABA are inhibitory fibers. All other transmitters possess excitatory function.

4.Materials for auditory self-work.

Materials and methods: bed.

Investigation object: human being.

Task 1. To investigate movement coordination (Fig.54)

Romberg's pose - the investigated person is proposed to move his feet together, to rise his head, to put his hands alongside his trunk. To determine whether his pose is stable. Complicated Romberg's pose: the doctor proposes to the investigated person to stretch his hands forward horizontally. Initially his eyes must be opened, than closed. Cerebellum functions disorders are accompanied by unstable pose (falling forward is observed at vermis anterior parts injuries; ahead - at vermis caudal parts disorders).

Walking - the investigated person must go on right line with his opened eyes, then with closed ones. At good performing these tests the investigated person is proposed to go on right line such that sock of one foot was touched to the heel of the other one.

Phalanx walking - step movements towards; the investigator put his attention to the step clearance and to the possibility of fast stoppage at sudden order (at injury one can see ataxic walking: legs are significantly extended and putted forward).

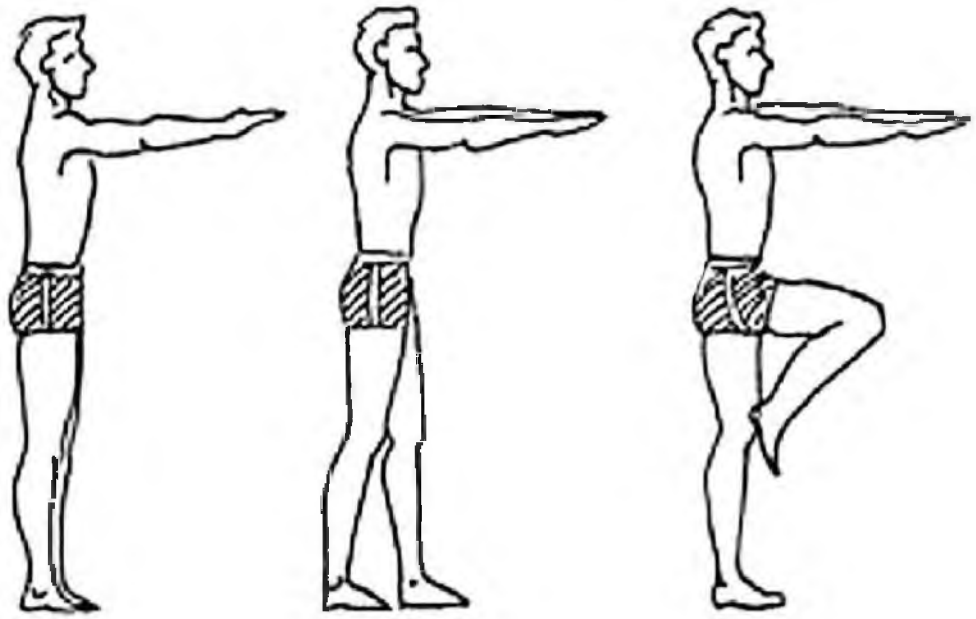


Fig.54. Investigation of movement coordination

Task 2. Asynergy investigation

Babynsky probe (Fig.55) - the investigated person lies on solid bed, he is asked to cross his hands on his thorax and to stand up (legs are raised without legs in people with cerebellum injury).

Ozhehovsky probe - the investigated person while his standing is strongly leant on doctor's palm. At sudden taking doctor's hands away the investigated person must be on his place, must be unmoved or turned ahead (in sick person this probe leads to the turning his trunk forward).

Stuart-Holms's probe - upper extremities proximal parts asynergy is checking. The hand putted till horizontal state investigated person must strongly bend in crural joint (antebrachium and hand in pronation state, hand is in fist). Doctor tries to straighten the investigated person antebrachium out and at sudden resistance stoppage the investigated person hand mustn't beat himself in his thorax. For the control the investigator's second hand must be putted to the place of allowed beat. In a healthy person muscles-antagonists are involved quickly and the beat is prevented.

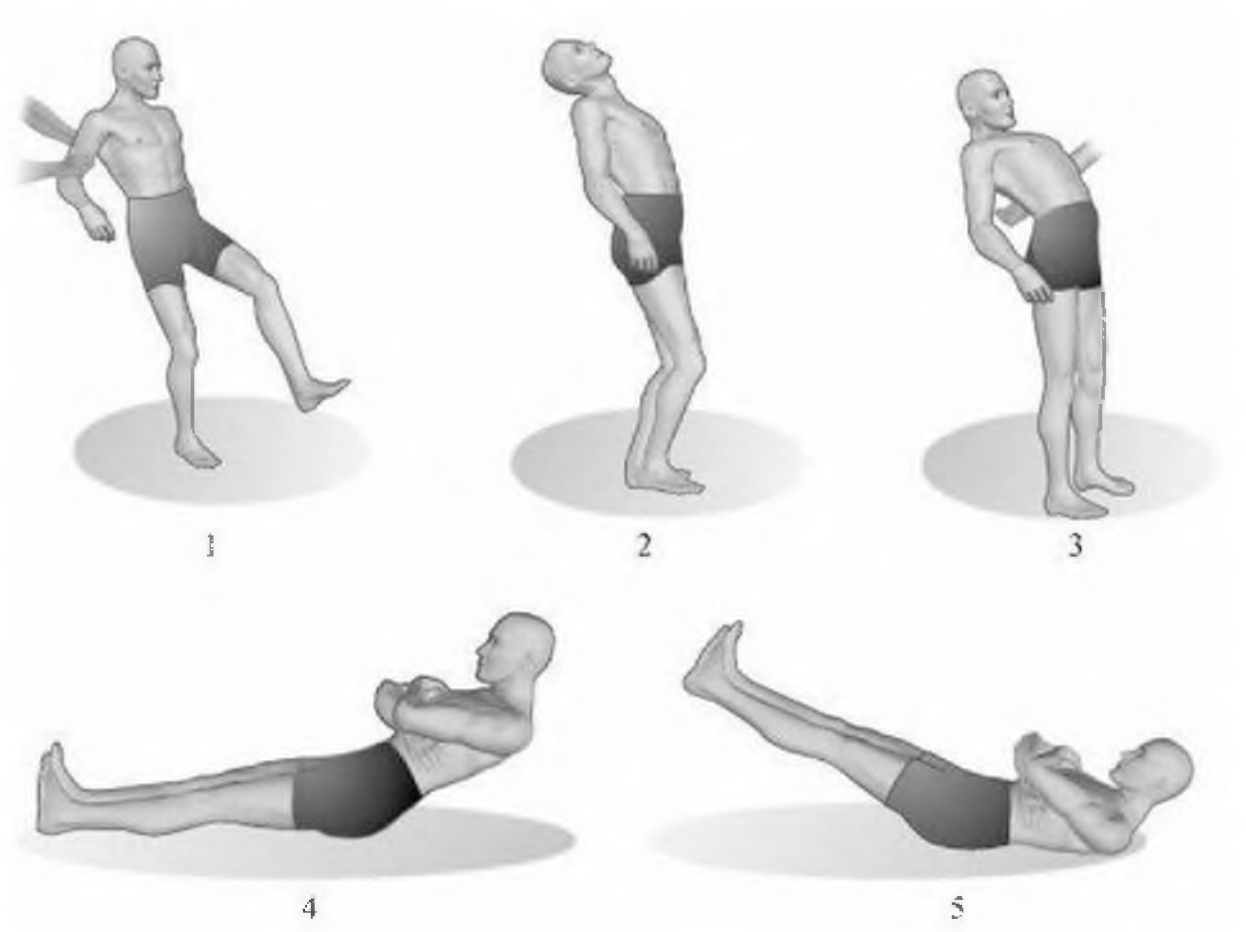


Fig.55. Asynergy investigation

1. Walking; 2. Normal body inclination; 3. Pathological body inclination;
4. Babynsky probe (normal condition); 5. Babynsky probe (pathology condition).

Task 3. Dynamic ataxy investigation

Finger-nose probe (Fig.56) - investigated person while his standing with closed eyes must touch nose ending by his index finger. To pay the attention to finger movement trajectory (locomotor ataxy existence) and putting to mentioned place (dysmetry existence), finger's tremor.

Fig.56. Finger-nose probe

Heel-knee probe (Fig.57) - the investigated person while sitting at the chair must touch by heel of one foot the knee of another one and to draw by it through tibia down. To mention locomotor ataxia absence or presence and dysmetry from lower extremities.

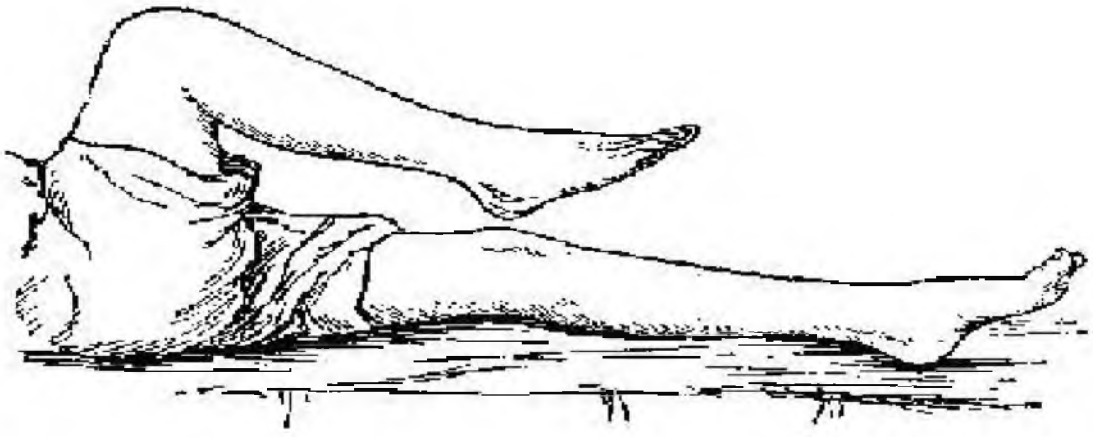


Fig.57. Heel-knee probe

Probe to adiadochokinesis- investigated person while his sitting must at the same time (simultaneously) by two hands stretched forward to perform pronation and supination. At disturbance of movement synchronism and equality one can determine adiadochokinesia on the side where the extremity is retarded.

Probe to the movement proportionality - the investigated person must stretch his hands forward by his palms up, the fingers are diverged. At order to turn hands by

their palms down. At cerebellum injury side one can determine excessive rotation - dysmetry.

Task 4. To put the attention to:

1. At cerebellum injury speech is slowed, speech fluency, explosed, scanding-accents are not on necessary syllable.
2. The writing in sick people is large, uneven; the person hasn't draw the circle.
3. There is rhythmic eyeballs fluctuation at sight towards and up - nistagm.

4. Materials for self-control:

1. Cerebellum connections with other CNS parts.
2. Cerebellum irritation and removal effects.
3. Cerebellum influence on organism vegetative functions.
4. Cerebellum influence on motor acts.
5. Clinical expressions occurring at cerebellum injury, their physiological mechanisms.
6. Intermediate brain physiology: thalamus, hypothalamus and epithalamus.
7. Basal ganglia physiology.

Lesson 16. Brain cortex function in motor activity regulation. Brain cortex activity investigation. Electroencephalography.

Before performing this lesson, you should study the introductory material presented here.

1. Lecture course.

2. Moroz V.M., Shandra O.A. Physiology. - 2011. Unit III. Chapter 7.

3. Guyton A.C., Hall J.E. Textbook of Medical Physiology. - 2011. Unit XI. Chapter 60.

Relevance of the topic.

Electroencephalography represents the functional state of the nervous system. This widespread method is useful for diagnostics. Because we spend about one-third of our lives sleeping, sleep disorders can have a significant impact on our quality of life.

1. Objectives:

To know: technique and mechanism of EEG, EEG rhythms, sleep stages, their relationship to the brain waves, the neural mechanisms of sleep, sleep disorders.

To be able to: evaluate of EEG, draw EEG.

2. Topic content.

The cerebral cortex is the site of the intellectual functions that make us human and that make each of us a unique individual. The cerebral cortex is generally arranged in six layers. It has been subdivided on the basis of cytoarchitectural differences by K. Brodmann (Fig.58.). He identified 47 distinct areas that have specific functional characteristics, and his numbering scheme is still in common use today in both research and clinical settings.

Neurons receive input from many subcortical structures by way of the thalamus and also from other regions of the cortex via association fibers. Cortical neurons, in turn, project to a wide range of neural structures, including other areas of the cerebral cortex, the thalamus, the basal nuclei, the cerebellum, the brainstem, and the spinal cord.

The cerebral cortex is divided into distinct functional areas, some of which are devoted to the processing of incoming sensory information, others to the organization of motor activity, and still others primarily to what are considered "higher intellectual functions" (Fig.59.).

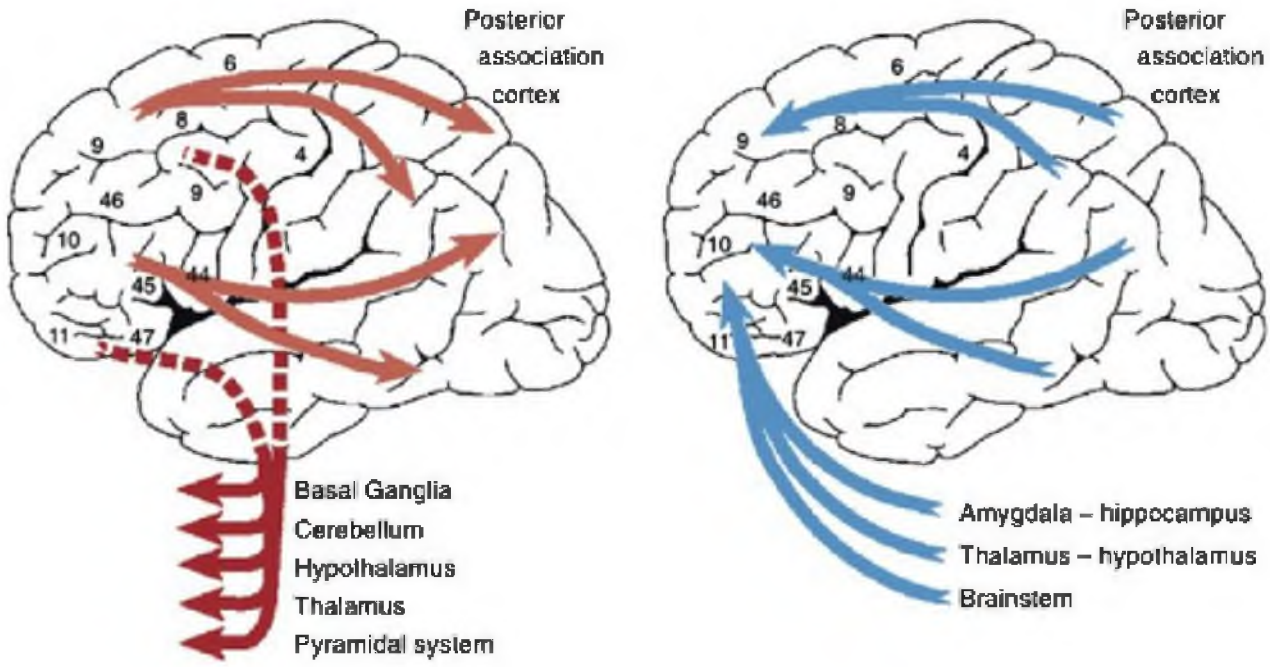


Fig.58. Interrelation between different brain areas. Cytoarchitecture areas of cerebral cortex by Brodmann.

Correlation of neocortical cytoarchitecture and function.

1. Frontal lobe (Brodmann areas 4, 6, 8-12, 32, and 44-47):

a. premotor cortex (area 6) is responsible for generating a plan for movement, which is transferred to the primary motor cortex for execution.

b. primary motor cortex (area 4) corresponds to the precentral gyrus. It is responsible for the execution of volitional movements. Origin of the corticospinal and corticonuclear pathways.

c. Broca's motor speech centre (areas 44 and 45) correspond to the inferior frontal gyrus.

d. prefrontal nonmotor areas (areas 9-12) are concerned with executive functions including emotional control and other aspects of cognitive function.

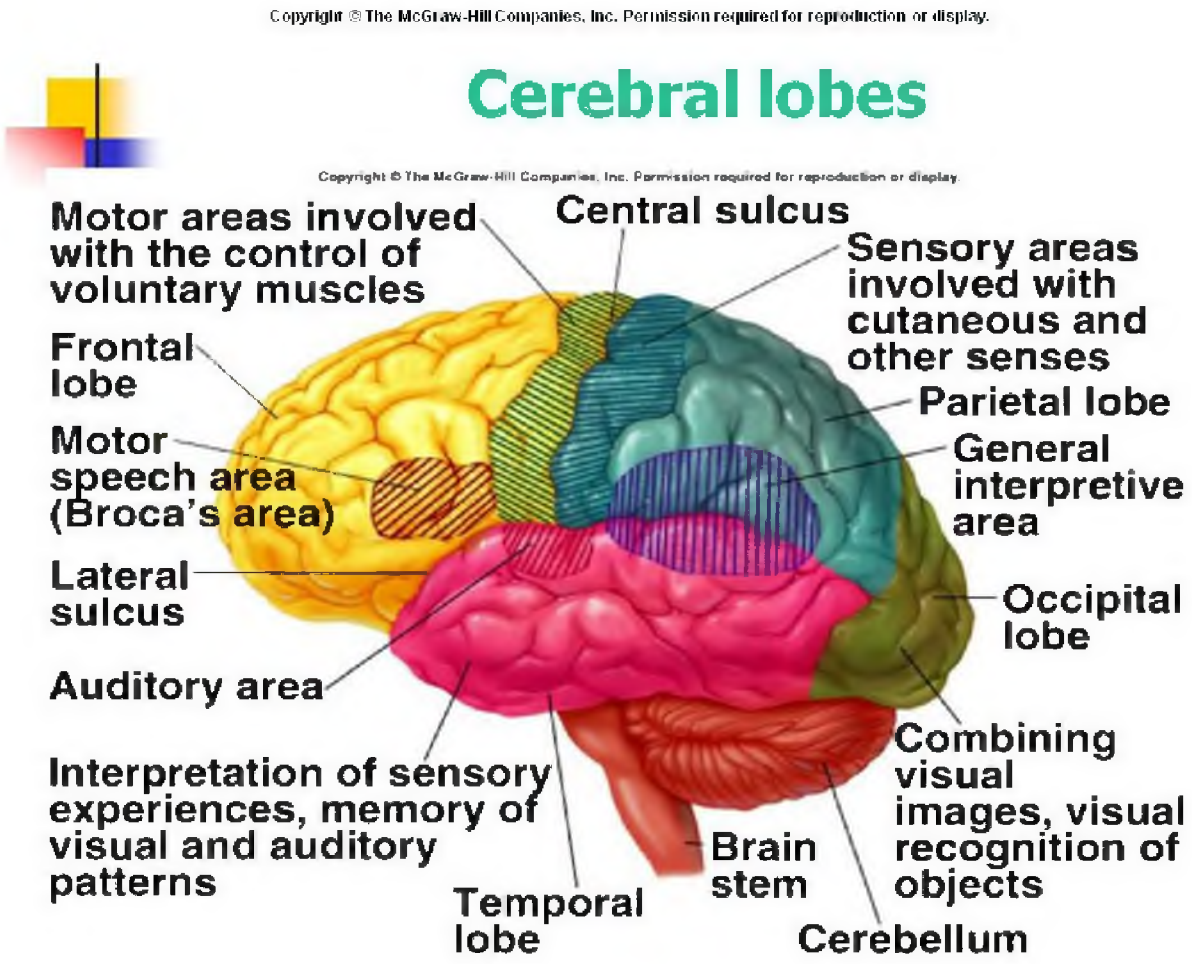


Fig.59. Functional areas of the human cerebral cortex.
(By The McGraw-Hill Companies. Inc.)

2. Parietal lobe (areas 3, 1, 2, 5, 7, 39, 40, and 43):

a. primary somatic sensory cortex (areas 3, 1 and 2) is located in postcentral gyrus; it is concerned with discriminative sensory, stereognosis, tactile localization.

b. inferior parietal lobule (areas 39, 40) consists of supramarginal and angular gyri, which in relation to reading and writing in the dominant hemisphere as higher integrative areas for language. It is part of the posterior speech area. In the nondominant hemisphere, these areas relate to our concepts of visual space.

c. superior parietal lobule (areas 5, 7) is sensory associational cortex.

3. Temporal lobe (areas 20-22, 27-28, 35-38, 41-42):

a. primary auditory cortex (areas 41, 42) is involved in the processing of auditory information.

b. Wernicke's receptive speech centre (area 22) corresponds to the superior temporal gyrus (for most people, this centre is in the left hemisphere). It is concerned with the reception and interpretation of spoken language.

4. Occipital lobe (areas 17-19):

a. V1 visual cortex (area 17) corresponds to the striate cortex and functions as the primary visual projection area.

b. V2-V5 visual areas (areas 18,19) function as visual association areas, also they are involved in the fixation and following of objects.

Language is the ability to communicate using symbols organized by a system of grammar to describe things and events and to express ideas. Several areas in the left hemisphere are involved in language.

- **Wernicke's area** is located in the **posterior part of the superior temporal gyrus** behind the auditory cortex. It is concerned with comprehension of auditory and visual information. It projects via the **arcuate fasciculus** to **Broca's area.**

- **Broca's area,** is in the **posterior part of the inferior frontal gyrus** in front of the inferior end of the motor cortex. Broca's area processes the information received from Wernicke's area into a detailed and coordinated pattern for vocalization and then projects the pattern via a speech articulation area in the insula to the motor cortex, which initiates the appropriate movements of the lips, tongue, and larynx to produce speech.

The angular gyrus behind Wernicke's area appears to process information from words that are read in such a way that they can be converted into the auditory forms of the words in Wernicke's area.

Language Disorders.

Language ability can be impaired selectively, with little or no change in the senses of vision or hearing, by brain damage in either the parietal-temporal junction or the frontal lobe. This impairment, termed aphasia, is a disturbance of the comprehension and formulation of language.

1. Damage to **Wernicke's area** causes **sensory (receptive) aphasia**, in which there is difficulty understanding written or spoken language.

Usually, sensory aphasia is combined with **alexia** (the inability to read).

2. Damage to **Broca's area** causes **motor (expressive) aphasia**, in which speech and writing are affected, but understanding is intact (Tab.9.).

Often, motor aphasia is combined with **agraphia** (the inability to express language in writing). Damage to the angular and supramarginal gyri are associated with dysgraphia, dyscalculia (defect of calculations), left-right confusion and finger agnosia.

Table 8. Characteristics of Broca's and Wernicke's aphasias.

Motor (Broca's) aphasia	Sensory (Wernicke's) aphasia
Halting speech	Fluent speech
Tendency to repeat phrases or words (perseveration)	Little spontaneous repetition
Disordered syntax	Syntax adequate
Disordered grammar	Grammar adequate
Disordered structure of individual words	Contrived or inappropriate words
Comprehension intact	Comprehension not intact

Language is a highly lateralized function of the brain residing in the left hemisphere. The left hemisphere is usually dominant with respect to language, even in left-handed people. Lesions of the left hemisphere cause aphasia. The right hemisphere is dominant in facial expression, intonation, body language, and spatial tasks.

Electroencephalography (EEG) registers bioelectrical activities that are generated by the cerebral cortex. EEG represents the sum of the excitatory and inhibitory synaptic potentials. Differences in electrical potential and changes in these differences over time can be amplified, displayed on an oscilloscope, and recorded on paper or in digitized form.

The main indications for EEG:

- confirmation of the diagnosis of epilepsy and determination of the type of epilepsy;
- brief, episodic impairment of consciousness of unknown etiology;
- longer-lasting disturbances of consciousness;
- common and legal criterion of brain death;
- sleep studies.

Technique. Electrodes are placed on the scalp according to the internationally standardized 10-20 system. EEG records may be **bipolar** or **unipolar.** Bipolar records show fluctuations in potential between two cortical electrodes; unipolar records show potential differences between a cortical electrode and a theoretically indifferent electrode on some part of the body distant from the cortex. Magnitude of the potential fluctuations at the scalp is 10-100 μ the potential fluctuations V. They are amplified and recorded on paper in 12 parallel channels. Certain maneuvers (e.g. opening and closing the eyes, hyperventilation, and rhythmic photo stimulation) affect the EEG tracing in characteristic ways and may induce pathological waves in patients with epilepsy.

The potential fluctuations are called brain waves. There are 4 types of brain waves, distinguished by differences in amplitude (mV) and frequency (Hz) (Fig.60.):

1. **Alpha (α) rhythm** has a frequency of 8-13 Hz. It's recorded especially in the parieto-occipital area. It dominates the EEG when a person is awake and resting, with the eyes closed. It's suppressed when a person opens the eyes, receives sensory stimulation, or engages in a mental task.

2. **Beta (β) rhythm** has a frequency of 14-30 Hz. The EEG is said to be **desynchronized;** it displays low-voltage. It occurs in the frontal to parietal region. This rhythm is accentuated during mental activity and sensory stimulation.

3. **Theta (θ) – rhythm** has a frequency of 4-7 Hz. It is normal in children and in drowsy or sleeping adults, but a predominance of theta waves in awake adults suggests emotional stress or brain disorders.

4. **Delta (δ) rhythm** has a frequency of 1-3 Hz. Infants exhibit delta waves when awake, and adults exhibit them in deep sleep. A predominance of delta waves in awake adults indicates serious brain damage.

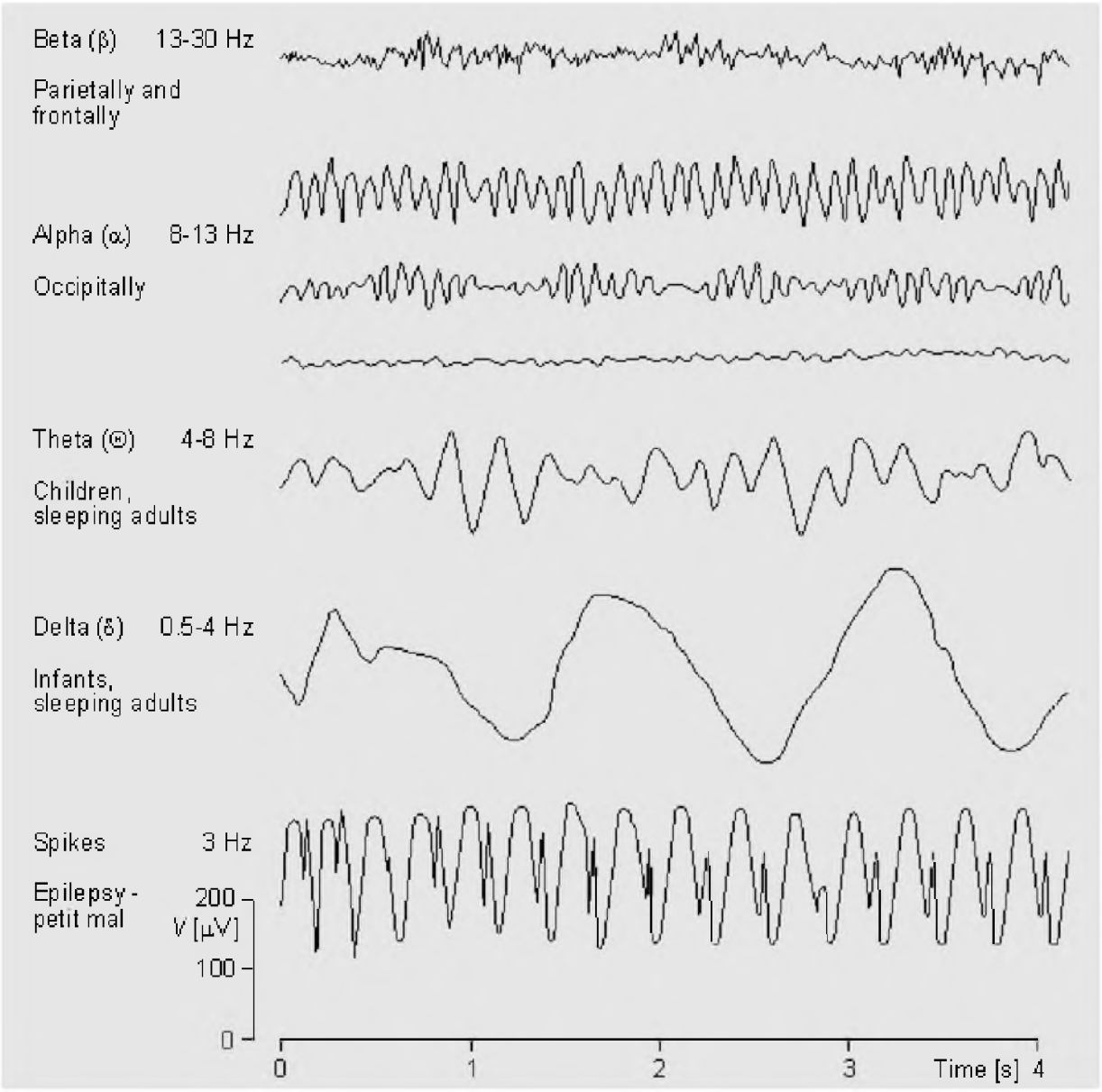


Fig.60. EEG rhythms.

A **CT scan**, also known as **computed tomography scan**, and formerly known as a **computerized axial tomography scan** or **CAT scan**, makes use of computer-processed combinations of many X-ray measurements taken from different angles to produce cross-sectional (tomographic) images (virtual "slices") of specific areas of a scanned object, allowing the user to see inside the object without cutting.

Digital geometry processing is used to further generate a three-dimensional volume of the inside of the object from a large series of two-dimensional radiographic images taken around a single axis of rotation. Medical imaging is the most common application of X-ray CT. Its cross-sectional images are used for diagnostic and therapeutic purposes in various medical disciplines. The term "computed tomography" (CT) is often used to refer to X-ray CT, because it is the most commonly known form. But, many other types of CT exist, such as positron emission tomography (PET) and single-photon emission computed tomography (SPECT).

CT produces data that can be manipulated in order to demonstrate various bodily structures based on their ability to absorb the X-ray beam. Although, historically, the images generated were in the axial or transverse plane, perpendicular to the long axis of the body, modern scanners allow this volume of data to be reformatted in various planes or even as volumetric (3D) representations of structures.

CT scanning of the head (Fig.61) is typically used to detect infarction, tumors, calcifications, haemorrhage and bone trauma. Of the above, hypodense (dark) structures can indicate edema and infarction, hyperdense (bright) structures indicate calcifications and haemorrhage and bone trauma can be seen as disjunction in bone windows. Tumors can be detected by the swelling and anatomical distortion they cause, or by surrounding edema. Ambulances equipped with small bore multi-sliced CT scanners respond to cases involving stroke or head trauma. CT scanning of the head is also used in CT-guidedstereotactic and radiosurgery for treatment.

Magnetic resonance imaging (MRI) of the head provides superior information as compared to CT scans when seeking information about headache to confirm a diagnosis of neoplasm, vascular disease, posterior cranial fossa lesions, cervicomedullary lesions, or intracranial pressure disorders. It also does not carry the risks of exposing the patient to ionizing radiation. CT scans may be used to diagnose headache when neuroimaging is indicated and MRI is not available, or in emergency settings when hemorrhage, stroke, or traumatic brain injury are suspected.

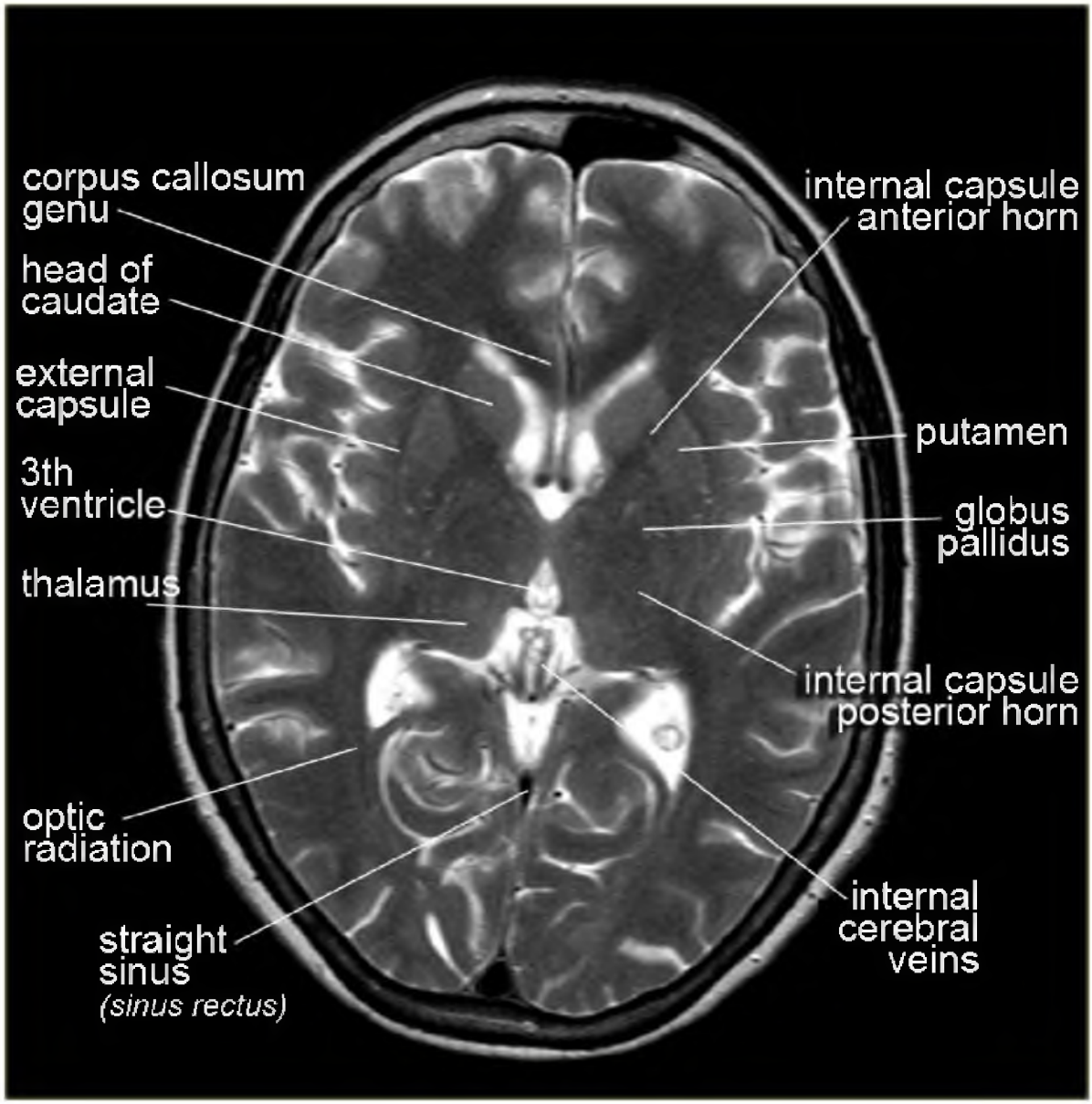


Fig.61. Computed tomography of human brain. By Robin Smithuis, Radiology department, Rijnland Hospital Leiderdorp, Netherlands (2008).

3. Materials for auditory self-work.

Task 1. Evaluation of EEG.

Choose EEG segment that equals 1,0 sec and count similar oscillations for 1 sec. Determine rhythm. For altitude determining (in mcv) compare oscillation height with calibrating graphic.

Draw EEG fragments in copy-book.

4. Materials for self-control:

Control questions:

1. Brain cortex structure by Brodmann.
2. Brain cortex areas involved in speech.
3. Some types of speech disorders.
4. EEG as a diagnostic method.
5. EEG rhythms classification.

Lesson 17
Practical skills on the content modules 4. Situational tasks solving on the content modules 4.

Questions for self-control:

1. Spine motor reflexes, their reflex arches, physiological importance.
2. Spine conductive function. Spine reflexes dependence on brain centers activity. Spinal shock.
3. Posterior brain motor reflexes, decerebrative rigidity.
4. Midbrain motor reflexes, their physiological importance.
5. Cerebellum, its functions, injury symptoms.
6. Thalamus, its functions.
7. Basal ganglia, their functions, injury symptoms.
8. Brain cortex structure by Brodmann. Types of aphasia.

By the link below you can find additional information (situational tasks) for preparing: **(Physiology Poltava)**

https://www.facebook.com/profile.php?id=100013316025779

Content module 5: Autonomic nervous system role in visceral functions regulation.

Lesson 18. Autonomic nervous system structural-functional organization, its role in visceral functions regulation.

Before performing this lesson, you should study the introductory material presented here.

1.Lecture course.
2.Moroz V.M., Shandra O.A. Physiology. - 2011. Unit IV, Chapter 8.
3.Guyton A.C., Hall J.E. Textbook of Medical Physiology. - 2011. Unit XI, Chapter 61.

Relevance of the topic.
Knowledge of the role of the autonomic nervous system is critical for understanding the function of any of the major organ systems. It is the primary mechanism for the involuntary control and coordinated activity of smooth muscle of visceral organs, cardiac muscle, glands and is essential for most homeostatic processes.

1. Objectives:

To know: the anatomical organization of the sympathetic and parasympathetic nervous systems; the major functions of the sympathetic and parasympathetic nervous systems; enteric nervous systems; the neurotransmitters and receptors employed at different synapses of the ANS.

To be able to: compare the somatic and autonomic nervous system, differentiate between the structures of the sympathetic and parasympathetic divisions.

2. Topic content.

The autonomic nervous system (ANS) is the part of the nervous system that controls most visceral functions of the body such as blood pressure, gastrointestinal secretion, sweating, body temperature, reproduction and other activities. The ANS innervates and regulates: smooth muscle, cardiac muscle, glands. The ANS (or visceral motor system) is distinct from the somatic nervous system (Fig.62.), which innervates skeletal muscle (Tab.9.).

Table 9. Comparison of somatic and autonomic nervous system.

Feature	Somatic	Autonomic
Effector	Skeletal muscle	Glands, smooth muscle, cardiac muscle
Control	Voluntary	Involuntary
Efferent pathway	One nerve fibre from CNS to effector; no ganglia	Two nerve fibres from CNS to effector; synapse at a ganglia
Effect on target cells	Excitatory	Excitatory or inhibitory
Effect of denervation	Flaccid paralysis	Denervation hypersensitivity
Neurotransmitters	Acetylcholine	Acetylcholine or norepinephrine

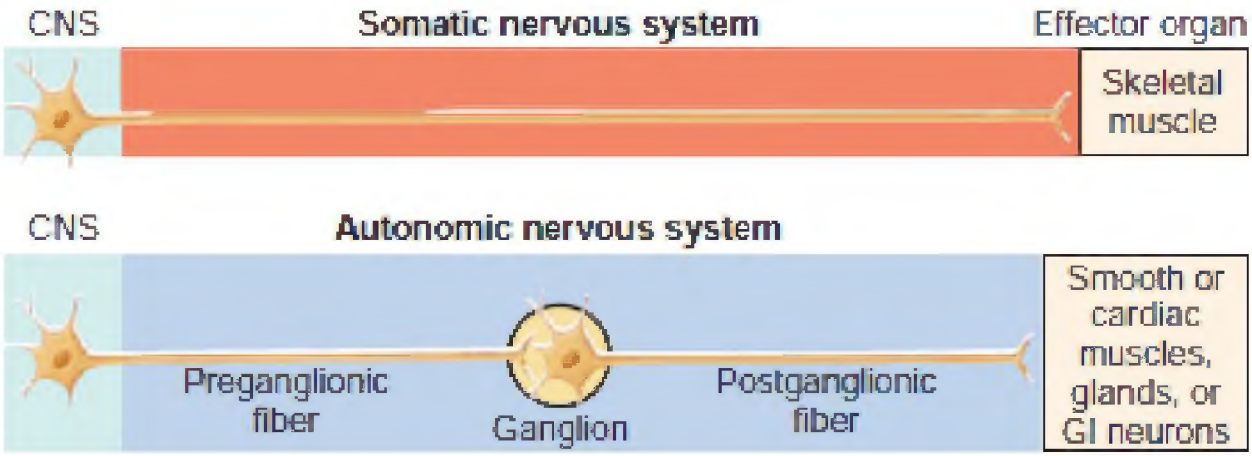


Fig.62. Efferent divisions of somatic and autonomic nervous system.

Organization of the ANS

The ANS has three divisions (Tab.11.):

- **sympathetic nervous system (SNS)** organizes involuntary responses that prepare the body for exertion (**fight-or-flight response**), activation occurs in response to stress;
- **parasympathetic nervous system (PNS)** organizes involuntary activities of the visceral organs in a state of relaxation (**rest-and-digest condition**);
- **metasympathetic (enteric) nervous system** is located in the walls of the visceral organs, e.g. the gastrointestinal tract that functions to regulate motility along the tract, secretion, and absorption across the gut epithelium.

Table 11. Comparison of sympathetic and parasympathetic divisions.

Feature	Sympathetic	Parasympathetic
Origin in CNS	Thoracolumbar	Craniosacral
Ganglia location	Paravertebral ganglia and prevertebral ganglia near spinal cord	Terminal ganglia near target organs
Fibre length	Short preganglionic Long postganglionic	Long preganglionic Short postganglionic
Preganglionic neurotransmitter	Acetylcholine	Acetylcholine
Postganglionic receptor	Nicotinic	Nicotinic
Postganglionic neurotransmitter	Norepinephrine	Acetylcholine
Effector organ receptor	$\alpha_1,\alpha_2,\beta_1,\beta_2$	Muscarinic
Effects of system	Often widespread and general	More specific and local

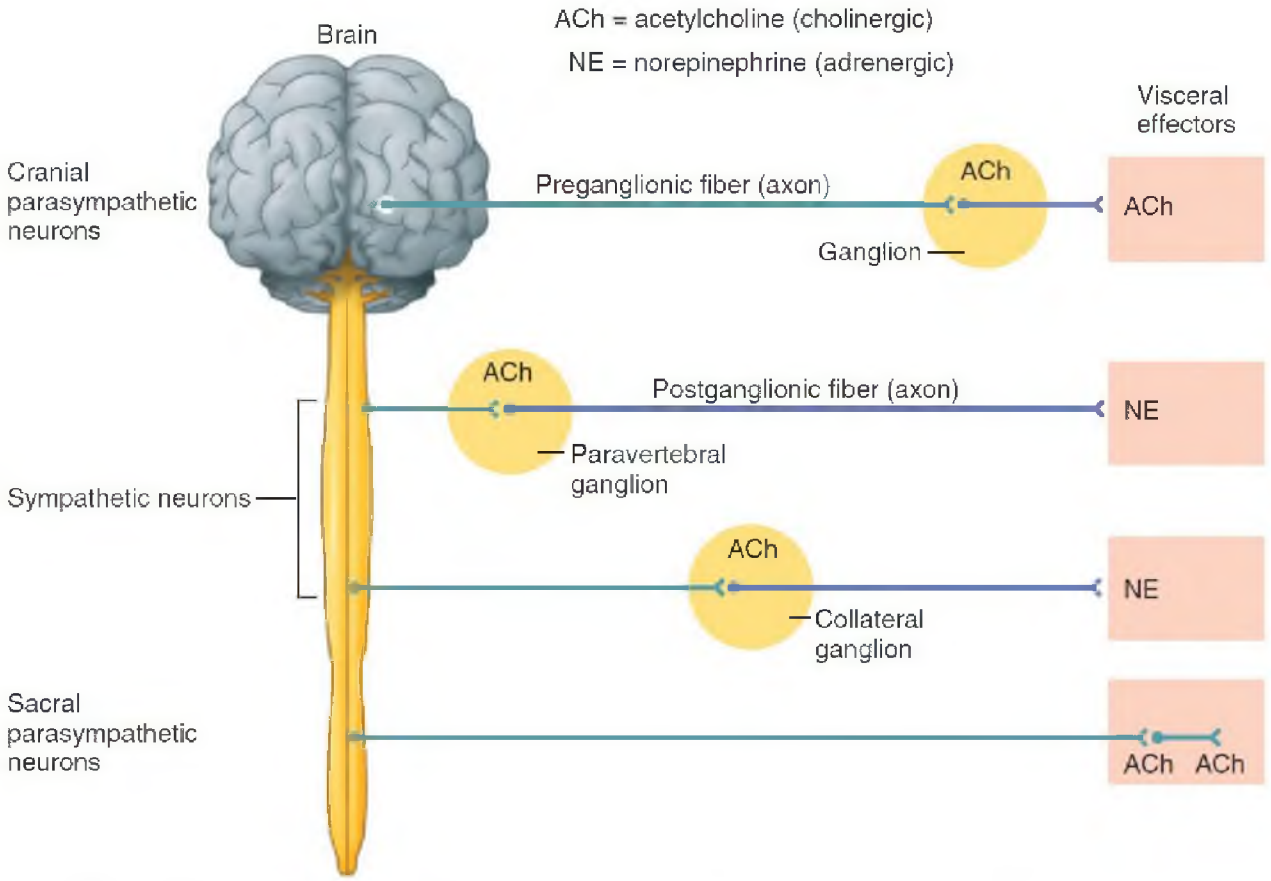


Fig.63. Organization of the sympathetic and parasympathetic divisions.

Sympathetic division:

1. **preganglionic neurons** are arranged in the intermediolateral nucleus of the **lateral horn** of the thoracic and upper lumbar spinal cord (T_1-T_{12}, L_1-L_2):

a. most preganglionic neurons are **short** and terminate in the **paravertebral ganglia** (sympathetic chain ganglia or **sympathetic trunks**). Generally, there are 3 cervical, 10-11 thoracic, 3-5 lumbar, and 3-5 sacral, and 1 coccygeal ganglion sympathetic ganglia on each side. The inferior cervical ganglion and the first thoracic ganglion fuse to form the *stellate ganglion*;

b. some preganglionic neurons lead to **prevertebral sympathetic ganglia** (e.g., celiac ganglia, superior and inferior mesenteric ganglia, pelvic plexus);

c. some preganglionic axons innervate the **adrenal medulla**, which is considered a special sympathetic ganglion modified for endocrine function (the chromaffin cells secrete catecholamines: epinephrine and norepinephrine);

d. use **acetylcholine (ACh)**, which binds to nicotinic (ionotropic) receptors on postganglionic neurons (Fig.63.);

2. **postganglionic neurons** directly innervate the smooth muscle of blood vessels and glands, reproductive organs, skin, cardiac muscle and pacemaker nodes of the heart:

a. unmyelinated postganglionic axons travel with peripheral nerves of the body to reach their widely distributed targets (Fig.64.);

b. most use **norepinephrine**, which binds to α and β adrenergic (metabotropic) receptors (except sweat glands, which use ACh).

Parasympathetic division:

1. preganglionic neurons are located in the nuclei of cranial nerves III, VII, IX, and X; sacral spinal cord segments (S_2-S_4):

a. preganglionic axons travel a long distance to innervate **parasympathetic ganglia** in or very close to end organs;

b. use **acetylcholine** (nicotinic receptors on postganglionic neurons);

c. the *sacral component* exits the spinal cord via ventral roots and form the *pelvic nerves (nervi erigentes).* These nerves mingle with sympathetic fibers of the inferior hypogastric plexuses to form the pelvic visceral plexus lateral to the rectum, bladder, and uterus (Fig.64.).

2. postganglionic neurons in the parasympathetic ganglia *(terminal* or *intramural ganglia)* directly innervate the smooth muscle of the eyes, viscera and reproductive organs, cardiac muscle and the glands of the head (Tab.12.):

a. since neurons are already in or near end targets, their unmyelinated axons travel a very short distance to innervate peripheral tissue;

b. use **acetylcholine** (muscarinic receptors).

c. both preganglionic and postganglionic parasympathetic neurons release molecules in addition to the principal transmitter at their terminals. These include neuropeptides, most prominently vasoactive intestinal peptides, which act as modulators of the postsynaptic response to the main transmitter.

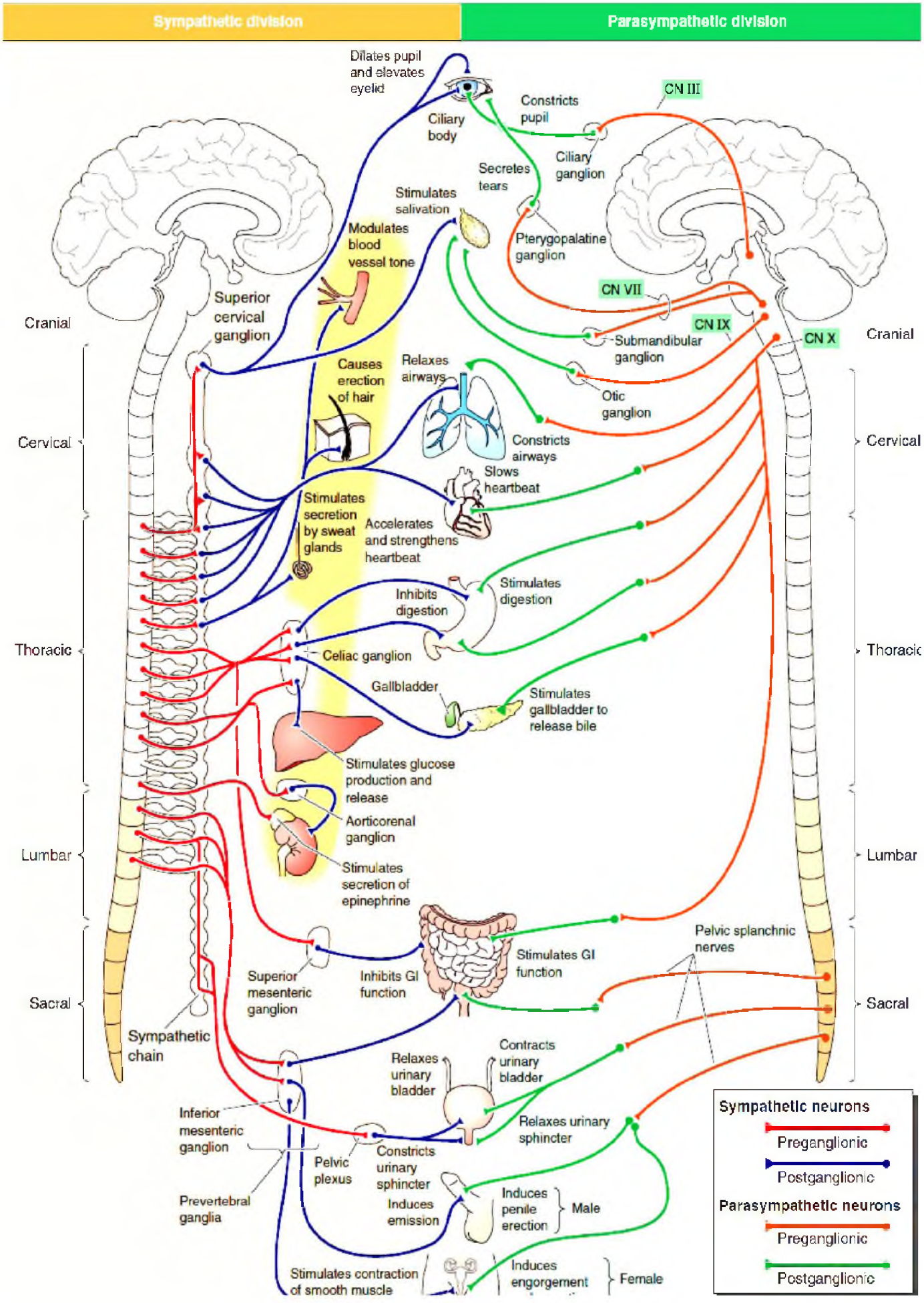

Sympathetic division
Parasympathetic division
Dilates pupil and elevates eyelid
Ciliary body
Constricts pupil
CN III
Ciliary ganglion
Secretes tears
Stimulates salivation
Modulates blood vessel tone
Pterygopalatine ganglion
CN VII
CN IX
CN X
Submandibular ganglion
Otic ganglion
Cranial
Superior cervical ganglion
Causes erection of hair
Relaxes airways
Constricts airways
Slows heartbeat
Cervical
Stimulates secretion by sweat glands
Accelerates and strengthens heartbeat
Inhibits digestion
Stimulates digestion
Thoracic
Celiac ganglion
Gallbladder
Stimulates gallbladder to release bile
Stimulates glucose production and release
Aorticorenal ganglion
Stimulates secretion of epinephrine
Lumbar
Pelvic splanchnic nerves
Stimulates GI function
Inhibits GI function
Superior mesenteric ganglion
Sacral
Sympathetic chain
Relaxes urinary bladder
Contracts urinary bladder
Relaxes urinary sphincter
Inferior mesenteric ganglion
Pelvic plexus
Constricts urinary sphincter
Induces emission
Induces penile erection
Male
Prevertebral ganglia
Stimulates contraction of smooth muscle
Induces engorgement
Female
Sympathetic neurons
Preganglionic
Postganglionic
Parasympathetic neurons
Preganglionic
Postganglionic

Fig.64. Autonomic nervous system effects.

Table 12. Some effects of autonomic nervous system

Effector organ	Receptor type	Sympathetic nervous system effect	Parasympathetic nervous system effect
Eye:			
iris muscles	α_1	pupil dilation (mydriasis)	pupil constriction (miosis)
ciliary muscle	β_2	relaxes (far vision)	contracts (near vision)
Heart:			
SA node	β_1	↑ heart rate	↓ heart rate
AV node	β_1, β_2	↑ conduction velocity	↓ conduction velocity
Atria and ventricles	β_1, β_2	↑ contractility	↓ contractility
Arterioles:			
coronary	α_1, α_2	constricts	–
	β_2	dilates	–
skin	α_1, α_2	constricts	–
skeletal muscle	α_1	constricts	–
	β_2	dilates	–
visceral	α_1	constricts	–
salivary glands	α_1, α_2	constricts	dilates
Veins	α_1, α_2	constricts	–
	β_2	dilates	–
Lungs (bronchiolar smooth muscle)	β_2	relaxes (bronchodilation)	contracts (bronchoconstriction)
Salivary glands	α_1	↓ secretion	↑ watery secretion
	β_2	↑ enzyme secretion	
Gastrointestinal tract:		inhibits digestion	promotes digestion
motility	α_2,β_2	decreases	increases
sphincters	α_1	contracts	relaxes
secretion	α_2	inhibits	stimulates
Liver	α_1,β_2	glycogenolysis, gluconeogenesis	–
Gallbladder	β_2	relaxes	contracts
Pancreas:			
exocrine part;	α_1	inhibits secretion	stimulates secretion
islets of	α_1	inhibits secretion	–
Langerhans	β_2	stimulates secretion	
Adipose tissue	α_2,β_3	lipolysis	–
Kidney	α_1	↓ renal perfusion	–
	β_1	↑ renin secretion	
Urinary bladder:		urinary retention	stimulates urination
detrusor muscle	β_2	relaxes	contracts

sphincter	α_1	contracts	relaxes
Uterus	α_1 β_2	contracts in pregnancy relaxes	variable
Genitalia	α_1	ejaculation	erection
Skin arrector pili muscle sweat glands	 α_1 α_1 AChR	 pilomotor contraction secretion from hands, feet generalized secretion	 – – –

Cranial nerves:

1. **Oculomotor nerve (CN III)** controls the lens and pupil of the eye. The preganglionic fibers from **Edinger-Westfall nucleus** (midbrain) enter the orbit and terminate in the ciliary ganglion behind the eyeball. Postganglionic fibers enter the eyeball and innervate the ciliary muscle, which thickens the lens, and the pupillary constrictor, which narrows the pupil.

2. **Facial nerve (VII)** regulates the tear glands, salivary glands, and nasal glands. The preganglionic fibers from the **superior salivatory nucleus** (pons) split away and form two smaller branches. The upper branch ends at the **pterygopalatine ganglion**. Postganglionic fibers then continue to the **lacrimal** and **nasal glands**. The lower branch ends at the **submandibular ganglion**. Postganglionic fibers from here supply **submandibular** and **subligual salivary glands**.

3. **Glossopharyngeal nerve (IX)** regulates salivation. The preganglionic fibers from the **inferior salivatory nucleus** (medulla) end in the **otic ganglion**. The postganglionic fibers innervate the **parotid salivary gland**. CN IX also carries afferent information about blood pressure and gas composition from carotid sinus and carotid body.

4. **Vagus nerve (X)** carries about 90% of all parasympathetic preganglionic fibers. The preganglionic fibers are from the **nucleus ambiguous** and **dorsal motor nucleus**. It forms three networks in the chest - the **cardiac plexus** (to the heart); the **pulmonary plexus** (to the bronchi and blood vessels into the lungs); and the **esophageal plexus** (regulates swallowing). These plexuses give off anterior and posterior **vagal trunks,** each of which contains fibers from both the right and left vagus nerves. These trunks innervate liver, pancreas, stomach, small intestine, kidney, ureter, and proximal half of the colon.

Neurotransmitters and receptors of the ANS

Preganglionic fibers of the sympathetic or parasympathetic nervous system and postglionic fibers of the parasympathetic nervous system release acetylcholine (ACh) as the neurotransmitter. They are cholinergic.

Cholinergic receptors (Tab.13.):

1. **Nicotinic receptors:**

- are located in the autonomic ganglia (N_N) of the sympathetic and parasympathetic nervous systems, and at the neuromuscular junction (N_M);
- excitatory, ionotropic receptors (increase influx of sodium);
- are activated by ACh or nicotine and blocked by ganglionic blockers (e.g., hexamethonium) in the autonomic ganglia, but not at the neuromuscular junction (they are blocked by curare).

2. **Muscarinic receptors:**

- are located in the gastrointestinal tract and CNS (M_1), heart (M_2), smooth muscle and glands (M_3), CNS (M_{4-5});
- inhibitory in the heart (e.g., decreased heart rate), G_i-protein coupled receptors (↓ cAMP);
- excitatory in smooth muscle and glands (e.g., increased GI motility and secretion) G_q-protein coupled receptors (IP_3/DAG/Ca^{2+});
- are activated by ACh and muscarine and blocked by atropine.

Atropine effects include pupillary dilation, relaxation of bronchiolar muscle, and reduction of peristalsis and secretion in the stomach.

Postganglionic fibres of the sympathetic nervous system release norepinephrine as the neurotransmitter. They are adrenergic.

Table 13. Agonists and antagonists of receptors

Receptor type	Location	Effects	Agonists	Antagonists
α_1-adrenergic	vascular smooth muscle	vasoconstriction	NE > Epi (phenylephrine)	Phentolamine Prazosin
α_2-adrenergic	presynaptic	regulate release of NE	NE > Epi (clonidine)	Yohimbine
β_1-adrenergic	heart	increasing heart rate and contractility	Epi > NE (dobutamine, isoproterenol)	Metoprolol
β_2-adrenergic	vascular and nonvascuiar smooth muscle	bronchodilation vasodilation	Epi > NE (terbutaline, isoproterenol)	Propranolol
β_3-adrenergic	adipose	lipolysis	Epi > NE (isoproterenol)	SR-59230A
N_M nicotinic	neuromuscular junction	skeletal muscle contraction	ACh (nicotine)	Tubucurarine
N_N nicotinic	ganglia of ANS	stimulation of SNS and PNS	ACh (nicotine)	Hexamethonium
M_1 muscarinic	stomach, CNS	activity of parietal cells; neuronal	ACh (muscarine)	Atropine Pirenzepine

		activity		
M_2 muscarinic	heart	decreasing of heart rate	ACh (muscarine)	Atropine
M_3 muscarinic	smooth muscle	contraction	ACh (muscarine, pilocarpine)	Atropine

Adrenergic receptors (adrenoreceptors) (Tab.13.):

1. **α_1-adrenergic receptors:**

- are located on vascular smooth muscle of the skin and splanchnic regions, the gastrointestinal and bladder sphincters, and the radial muscle of the iris;
- excitatory, G_q-protein coupled receptors (IP_3/DAG/Ca^{2+});

2. **α_2-adrenergic receptors:**

- are located on presynaptic membrane of adrenergic nerve terminals (autoreceptors), platelets, fat cells, and the walls of the GI tract (heteroreceptors);
- inhibitory, G_i-protein coupled receptors (↓ cAMP).

3. **β_1-adrenergic receptors:**

- are located in sino-atrial node, atrio-ventricular node, and cardiac muscle;
- excitatory (e.g., increased heart rate, conduction velocity, contractility), G_s-protein coupled receptors (↑ cAMP);

4. **β_2-adrenergic receptors:**

- are located on vascular smooth muscle of skeletal muscle, bronchial smooth muscle, and in the walls of the GI tract and bladder; produce relaxation;
- inhibitory, G_s-protein coupled receptors (↑ cAMP).

5. **β_3-adrenergic receptors:**

- are located in adipose tissue and GI tract;
- excitatory (stimulate lipolysis and GI motility), G_s-protein coupled receptors (↑ cAMP).

3. Materials for auditory self-work.

Task 1. Kerdoe's vegetative index (KVI)

The subject sits during 5-6 minutes. Determine heart rate (HR) of the subject and magnitude of arterial pressure (AP).

Calculate KVI by the formula: (1 – diastolic AP/HR)·100%

In healthy adults, KVI is from –10 to +10% (balance of ANS);

the predominance of SNS – KVI is more than +10%;

the predominance of PNS – KVI is less than –10%.

4. Materials for selfcontrol:

Control questions:

1. Comparison of the somatic and autonomic nervous system
2. Organization of the ANS
3. Metasympathetic nervous system
4. Comparison of sympathetic and parasympathetic divisions
5. Neurotransmitters and receptors of the ANS
6. Agonists and antagonists of the ANS

Lesson 19. Autonomic reflexes, their practical usage in clinics.

Before performing this lesson, you should study the introductory material presented here.

1.Lecture course.
2.Moroz V.M., Shandra O.A. Physiology. - 2011. Unit IV, Chapter 8.
3.Guyton A.C., Hall J.E. Textbook of Medical Physiology. - 2011. Unit XI, Chapter 61.

Relevance of the topic.
Autonomic (visceral) reflexes are very important for homeostasis and bodily functions (regulation of blood pressure, digestion, urination, etc). Autonomic reflexes are often tested in medicine.
1. Objectives:
To know: classification of the autonomic reflexes; compare the structure of somatic and autonomic reflex arc; the components of the autonomic reflexes.
To be able to: draw autonomic reflexes arcs; investigate autonomic reflexes; describe role of CNS in coordination of autonomic functions.

2. Topic content.

Autonomic reflexes are unconscious, automatic, stereotyped responses to stimulation, involving visceral receptors and effectors. They control many body functions such as blood pressure, respiration and digestion. The autonomic reflex arc contains the same components as the somatic reflex arc (Fig.65.):

- **receptor** (most autonomic sensory receptors are located in visceral organs, some – in skin);
- **sensory neuron** (most visceral afferent fibres are thin Aδ and C fibres;
- **integrating centre** (polysynaptic, most centres are located in the hypothalamus and brainstem, centres of urination and defecation – in the spinal cord);
- **motor neurons** (there are 2 motor neurones: preganglionic and postganglionic, with synapse in the autonomic ganglion);
- **effector** (cardiac muscle, smooth muscle or gland).

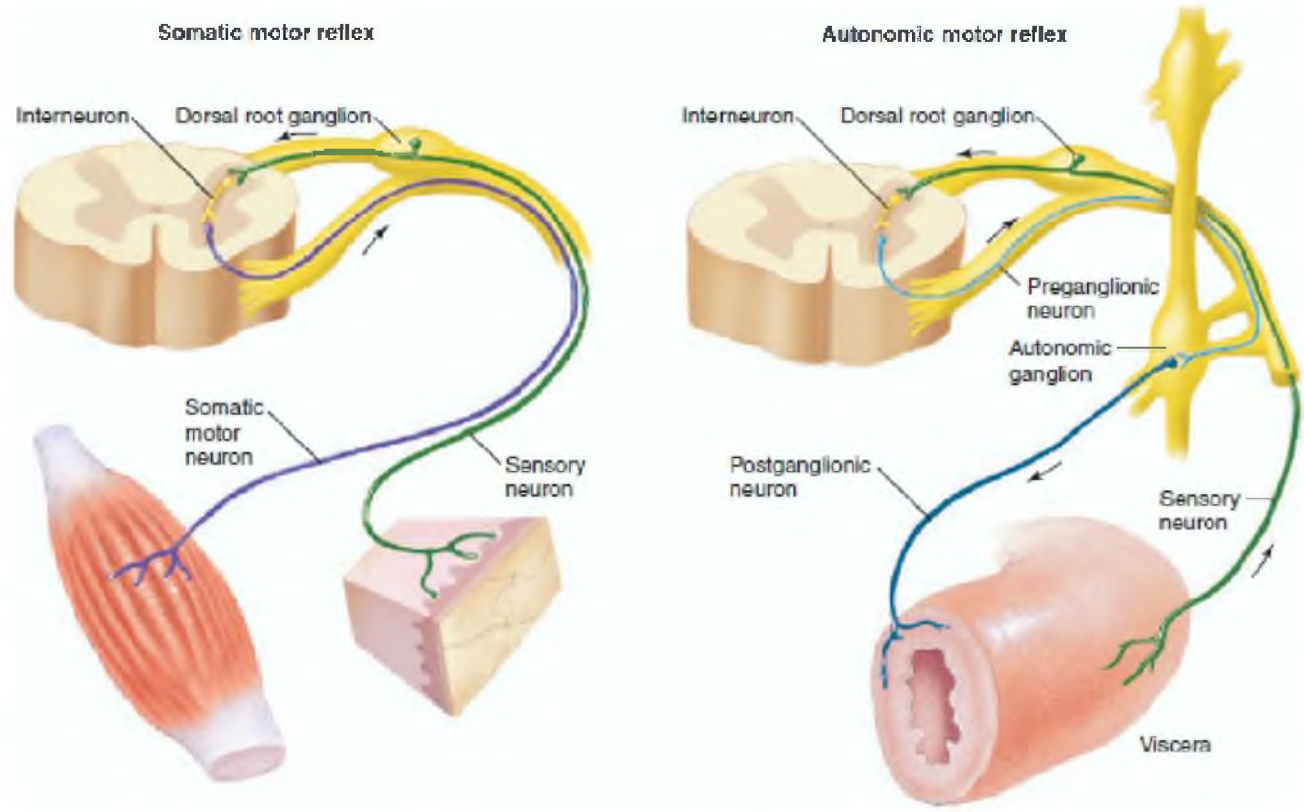


Fig.65. Comparison of a somatic and autonomic motor reflex.

Autonomic reflexes are also known as visceral reflexes because they involve the internal organs of the body.

Classification of autonomic reflexes:

1. ***Viscero-visceral reflexes***;
2. ***Viscero-somatic reflexes***;
3. ***Cutaneo-visceral reflexes***;
4. ***Viscero-cutaneous reflexes***;
5. ***Somato-visceral reflexes***.

Autonomic reflexes can divided according to organ systems (***cardiovascular, gastrointestinal, respiratory, sexual*** and others). Many of them have clinical significance (e.g. pupillary light reflex, sinocarotid reflex, oculocardiac reflex etc.).

Also, there are reflexes than do not have any CNS components:

1. ***Long reflexes*** have integrating centre;
2. ***Short reflexes*** are completely peripheral.

Autonomic reflexes are moderated and coordinated in a hierarchical, integrated fashion. They can engage simple responses at the local level (involving only part of one neuron), at the regional level (coordinated only by the autonomic ganglia), at the spinal cord level, brainstem level, and higher brain levels to coordinate more complex reflex responses. The higher level of complexity will require coordination of not only the sympathetic and parasympathetic responses as well.

Many autonomic reflexes are characterized by tonic activity. For each organ, there may be more of a parasympathetic or sympathetic tendency to the resting condition; it is the **autonomic tone** of the system.

Regulation of the ANS

Sensory information is integrated by different CNS structures collectively called the ***central autonomic network*** (CAN), which produces coordinated signals to the visceral motor, endocrine, and somatic motor outflow pathways. Although visceral motor activities are generally beyond conscious control, mental activity and emotional status clearly influence visceral structures. Thus, CAN integrates input from higher CNS centres involved in cognition and complex behavioural functions (Fig.66.).

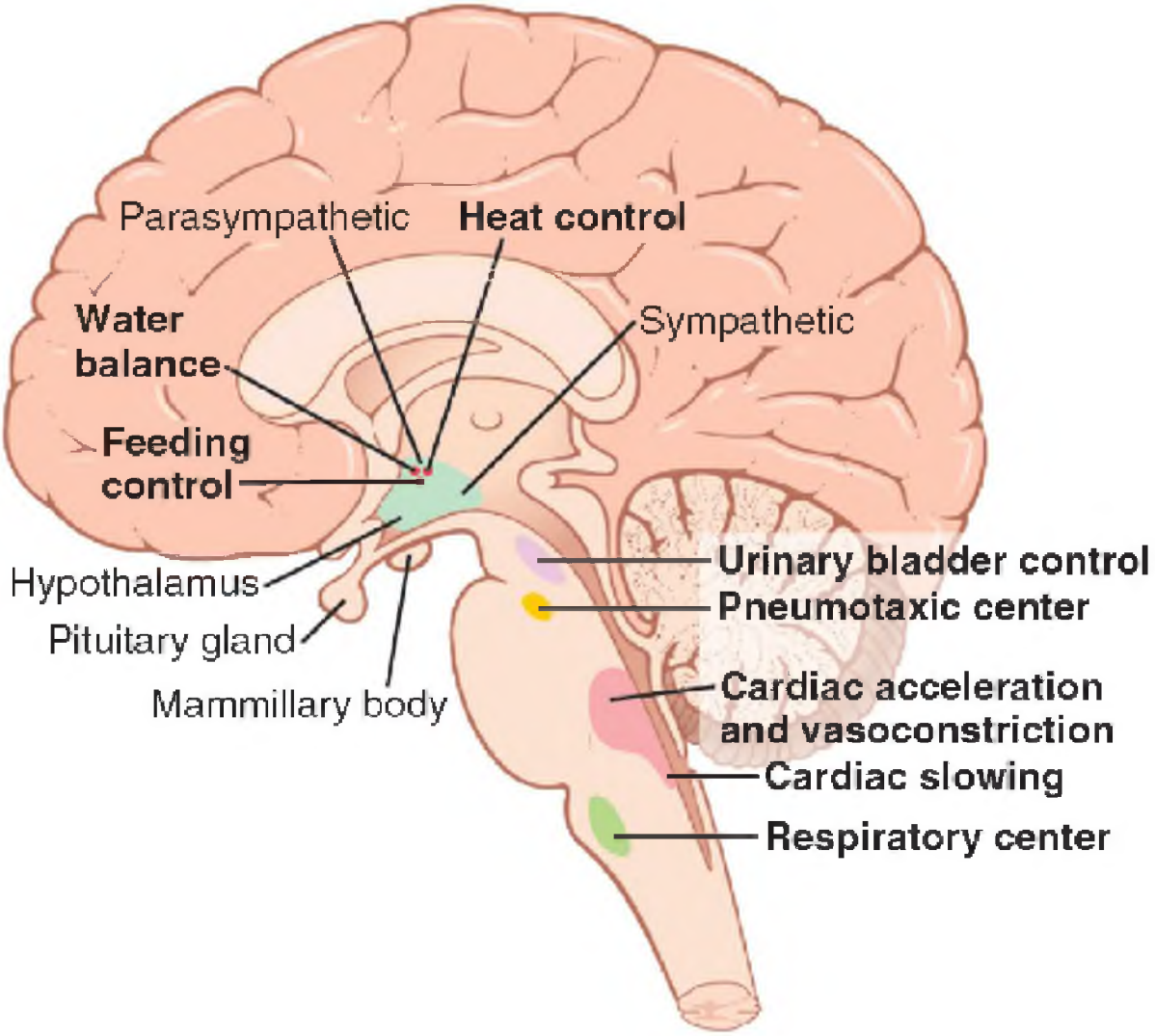


Fig. 66. Autonomic control areas in the brain.

The ***hypothalamus*** is the highest control centre of autonomic and endocrine functions. It directly regulates the activity of the anterior and posterior pituitary and has reciprocal connections with components of the CAN in the forebrain and brainstem. There are thirst, appetite-regulating, and temperature centres in the hypothalamus.

The ***amygdale*** is part of the limbic system involved in emotional responses. For example, when person is scared, the amygdale sends signals to the hypothalamus along the medial forebrain bundle and causes the fight-or-flight response of SNS.

Other cell groups that are important in autonomic regulation reside in the ***reticular formation of the brainstem***. For example, cells in the medulla are involved in cardiovascular regulation. This area is called the *vasopressor centre* because stimulation results in increased cardiac output and total peripheral vascular resistance. Areas such as this have been designated *centres* (e.g. the respiratory, vasomotor, pneumotaxic, swallowing, and vomiting centre).

3. Materials for auditory self-work.

Task 1. Dagnini-Ashner's reflex.

Determine the pulse frequency of the subject. Press on the eyeballs with increasing effort during 30 sec. Determine pulse rate again. Compare the received results. Slow down of heart rate (6-12 beats) shows normal autonomic reactivity (Fig.67.).

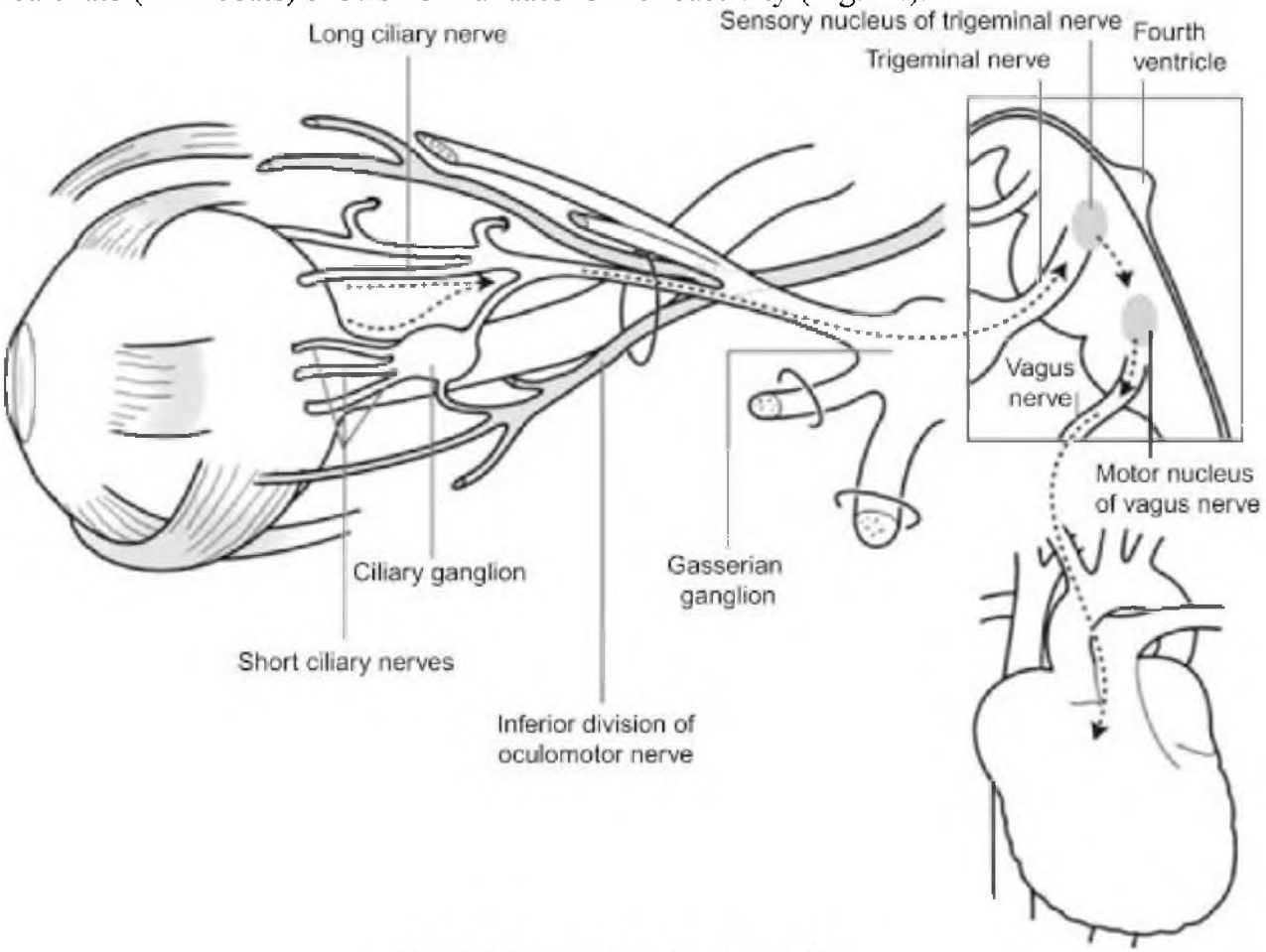


Fig.67. Dagnini-Ashner's reflex.

Task 2. Dermographism.

Dermographism – is reaction in response to stroking the skin. Blunt object (e.g. pen or spatula) is used to apply a light stroking pressure to the skin of forearm or chest. Examine

received stripes. Long white stripe shows the predominance of SNS tonus, red stripe – the PNS. White dermographism appears in 8-20 seconds and lasts 1-10 minutes. Red dermographism appears in 5-15 seconds and can last 1-2 hours.

Task 3. Orthostatic test.

The subject lies on his back during 5-6 minutes. Determine the pulse frequency of the subject. Then the subject stands up slowly. Take his pulse at once and after 1, 2, 5 and 10 minutes. Record all the measurements. The difference between pulse (when subject is lying and standing) is orthostatic heart rate (normally increase of 10-15 beats per minute).

Task 4. Pupillary light reflex

Stay with the subject in a darkened room for at least 1 minute, allowing his eyes to adjust to the dim light. The subject covers his right eye by holding a hand over the eye. Shine a narrow beam of light (from a pen flashlight) from the left side into the subject's left eye. Observe the pupil and describe what happens. Uncover the right eye and observe the size of the right pupil. The pupillary reflex in the other eye is called the consensual reaction (Fig.92.). Repeat this procedure from the right side.

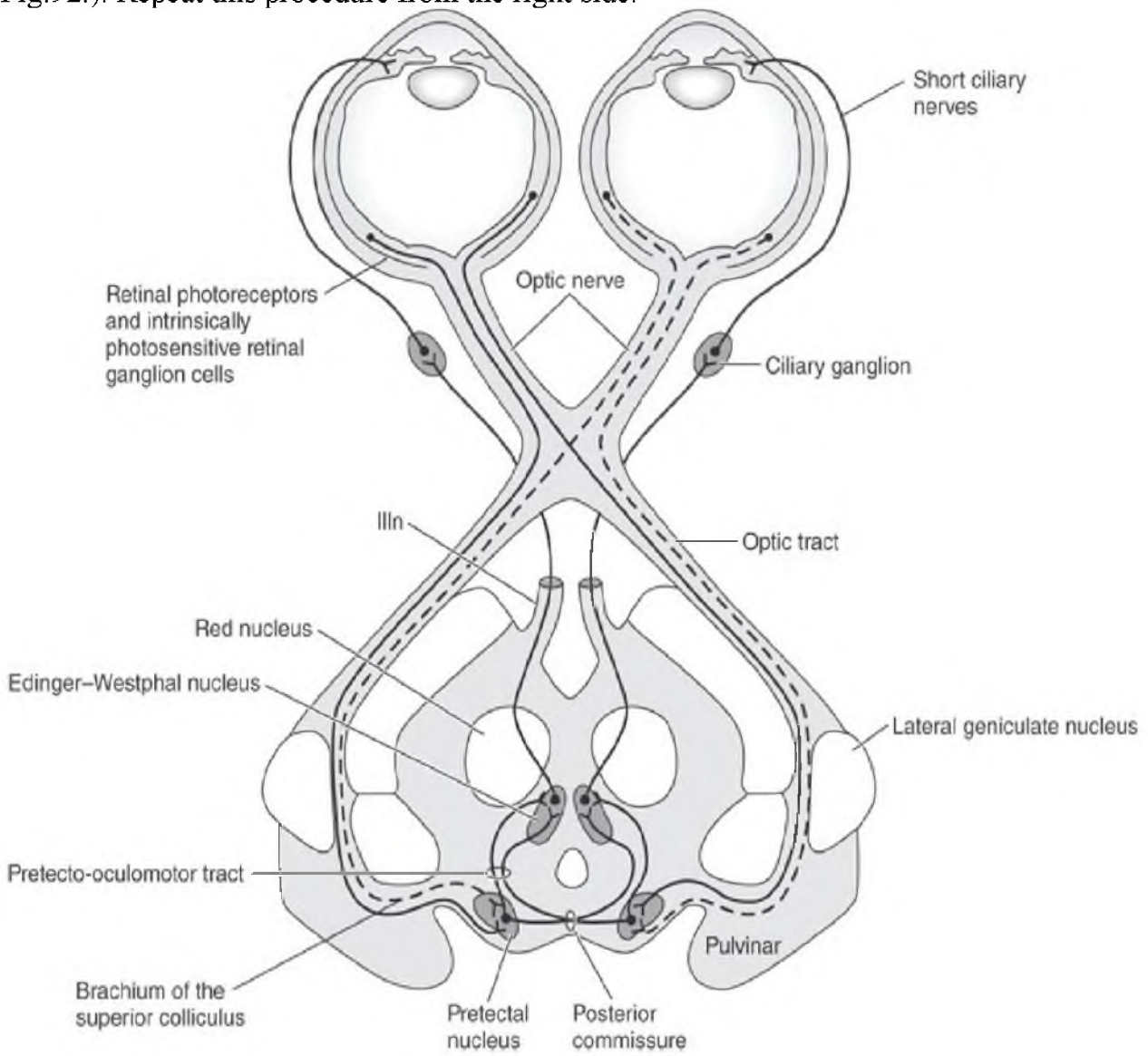


Fig.92. Reflex arc of pupillary light reflex.

4. Materials for self-control:
Control questions:
1. Autonomic reflexes, their classification.
2. Explain the difference in sympathetic and parasympathetic reflexes.
3. Examples of autonomic reflexes and their usage in clinics.
4. Role of higher centers of brain in autonomic regulation.

Content module 6: Endocrine glands role in visceral functions regulation.

Lesson 20. Humoral regulation, hormones action mechanisms to the target cells, hormones secretion regulation. Hypothalamic-hypophyseal system.

Before performing this lesson, you should study the introductory material presented here.

1.Lecture course.
2.Moroz V.M., Shandra O.A. Physiology. - 2011. Unit 5, Chapter 9.
3.Guyton A.C., Hall J.E. Textbook of Medical Physiology. - 2011. Unit 14.

Relevance of the topic.
Endocrine system play a key role in regulating almost all body functions, including metabolism, growth and development, reproduction and behaviour. Knowledge of endocrinology is necessary for early diagnosis and treatment of different disorders.
1. Objectives:
To know: hormone classes; main mechanisms of hormones action to organism cells; hypothalamic-hypophyseal system structure and functions.
To be able to: compare nervous and humoral regulation; analyze regulated parameters and make conclusions about endocrine glands functions.

2. Topic content.

Endocrine system consists of (Fig.69.):

- endocrine glands (ductless; secrete their products called hormones into the blood; e.g. thyroid gland);

- endocrine tissue (e.g. pancreatic islets of Langerhans);

- specialized cells in different organs (e.g. APUD system of gastrointestinal tract).

Hormones are substances that are produced and released by glands or specialized cells into the blood and influence the function or target cells. The target cells express hormone-specific receptors.

Types of hormone action (Fig.68.):

1. Autocrine (cells act on themselves);
2. Paracrine (target cells are located nearby);
3. Endocrine(distant action);
4. Neuroendocrine (hormones are released by neurons into the blood).

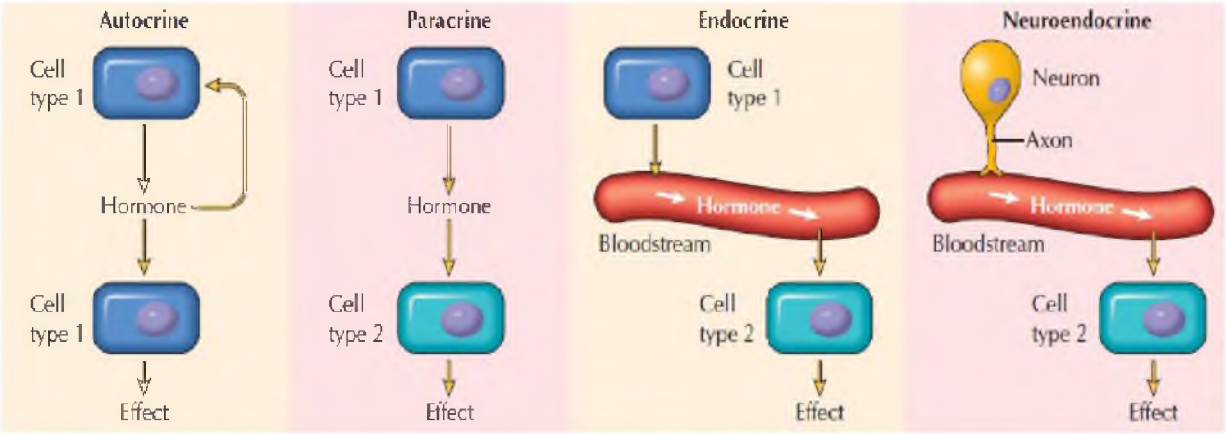


Fig.68. Types of hormone action.

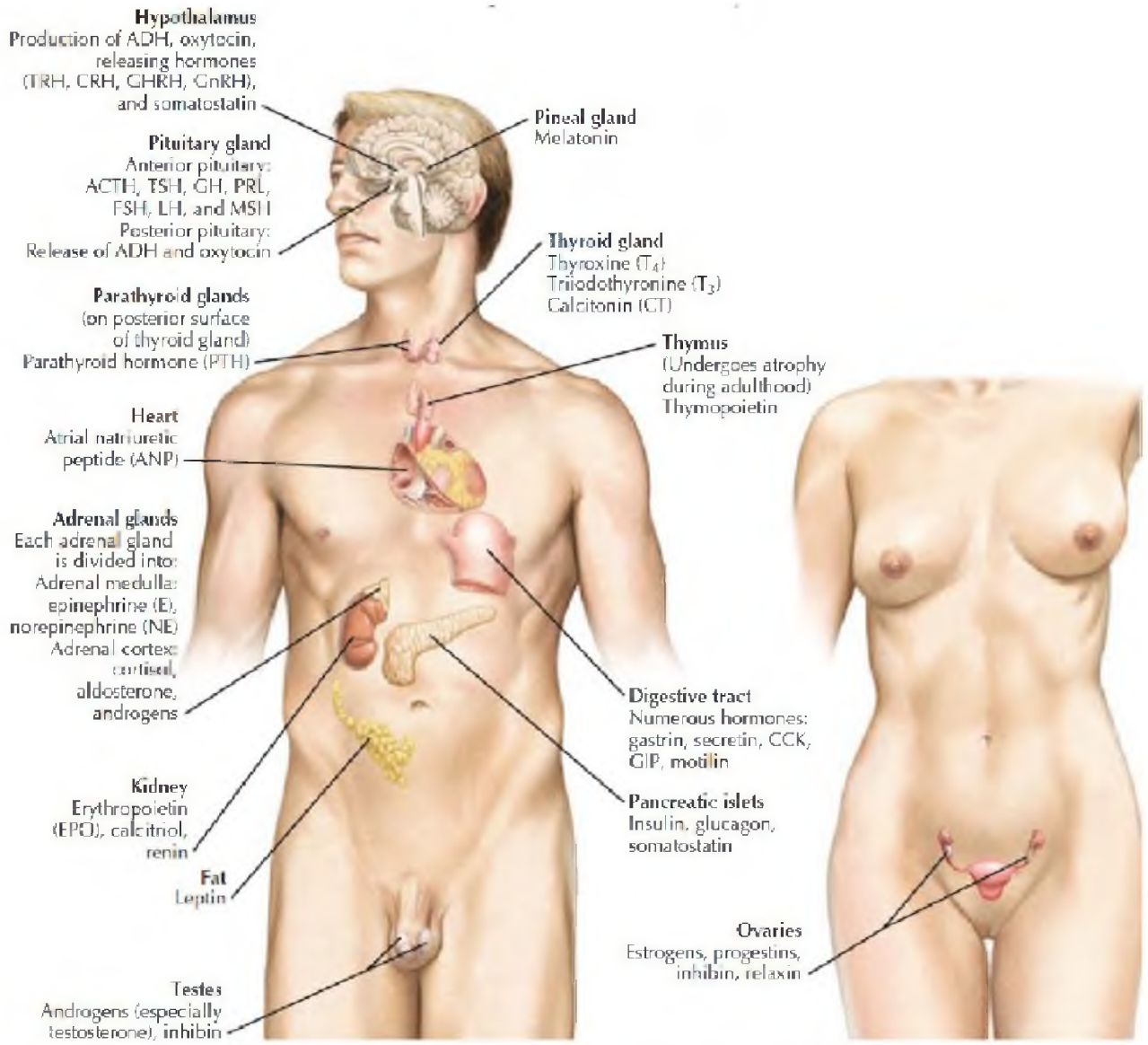


Fig.69. Organization of the endocrine system.

Chemical classification of hormones:

1. Derivates of amino acids:

a. tyrosine:

- thyroid gland (thyroxine and triiodothyronine);
- adrenal medulla (epinephrine and norepinephrine);

b. tryptophan:

- pineal gland (melatonin).

2. Proteins and polypeptides:

- hypothalamus (releasing hormones);
- anterior pituitary gland (thyroid-stimulating hormone, growth hormone, gonadotropins, prolactin, adrenocorticotropic hormone);
- posterior pituitary gland (antidiuretic hormone, oxytocin)
- pancreas (insulin and glucagon);
- parathyroid gland (parathyroid hormone);
- thyroid gland (calcitonin).

3. Steroid hormones (derived from cholesterol):
- adrenal cortex (cortisol, aldosterone);
- the ovaries and placenta (estrogen, progesterone);
- the testes (testosterone).

Mechanisms of hormone action

The location of a hormone's receptor proteins in its target cells depends on the chemical nature of the hormone.

1. Since the lipophilic hormones (steroids and thyroxine) can pass through the plasma membrane and enter their target cells, the receptor proteins for lipophilic hormones are located within the cytoplasm and nucleus. The activated hormone-receptor complex then binds with a specific regulatory (promoter) sequence of the DNA called the hormone response element, and in this manner either activates or repress transcription of specific genes (Fig.70.).

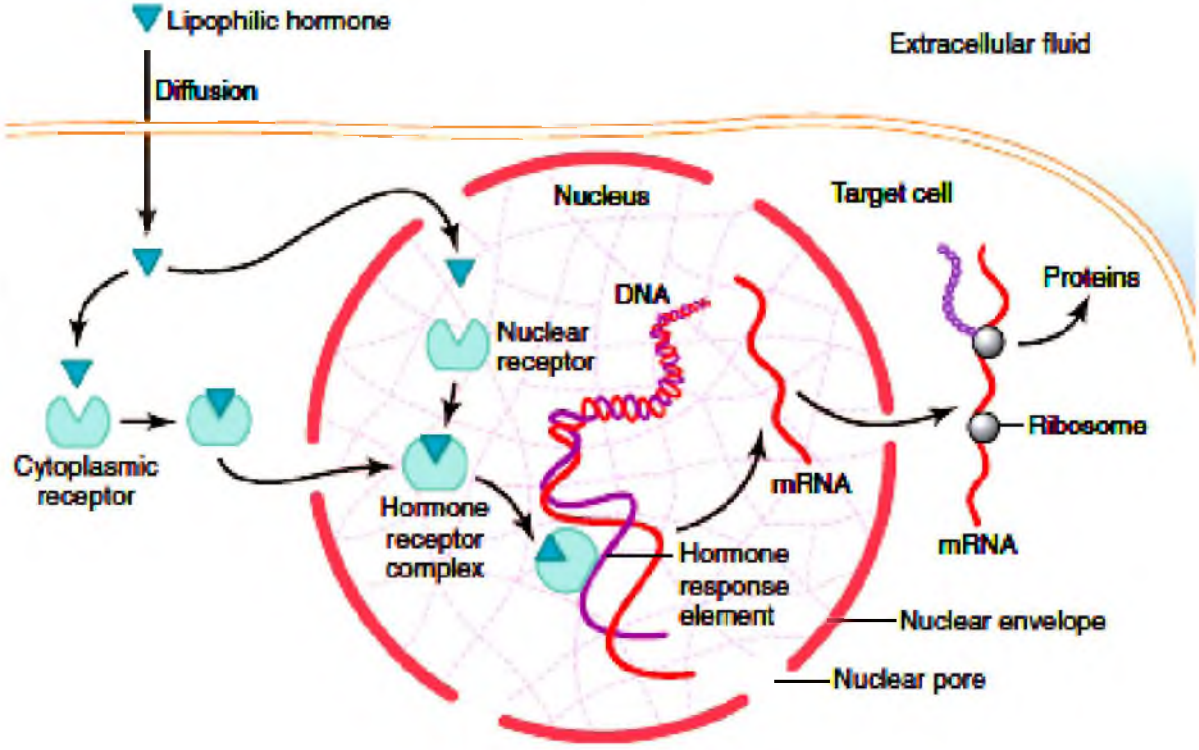


Fig.70. Mechanism of lipophilic hormone action.

2. Since the water-soluble hormones (catecholamines, glycoproteins and polypeptides) cannot pass through the plasma membrane, the receptor proteins are located on the outer surface of the membrane. In these cases, hormone action requires the activation of second messengers within the cell.

A. Adenylate cyclase – cyclic AMP second messenger system (Fig.71.).

Hormones that use the system: thyroid-stimulating hormone, growth hormone, gonadotropins, adrenocorticotropic hormone, angiotensin II (epithelial cells), catecholamines (β receptors), glucagon, calcitonin, somatostatin, secretin, vasopressin (V_2 receptors), parathyroid hormone, corticotropin-releasing hormone, human chorionic gonadotropin.

When one of these hormones binds to its receptor protein, it causes the dissociation of a subunit from the complex of **G_s-proteins**. This subunit moves

through the membrane until it reaches the enzyme **adenylate cyclase**, which converts ATP into **cyclic adenosine monophosphate (cAMP)**. Cyclic AMP activates **protein kinase**, which transfers phosphate groups to other enzymes in the cytoplasm. The activity of specific enzymes is either increased or inhibited by phosphorilation.

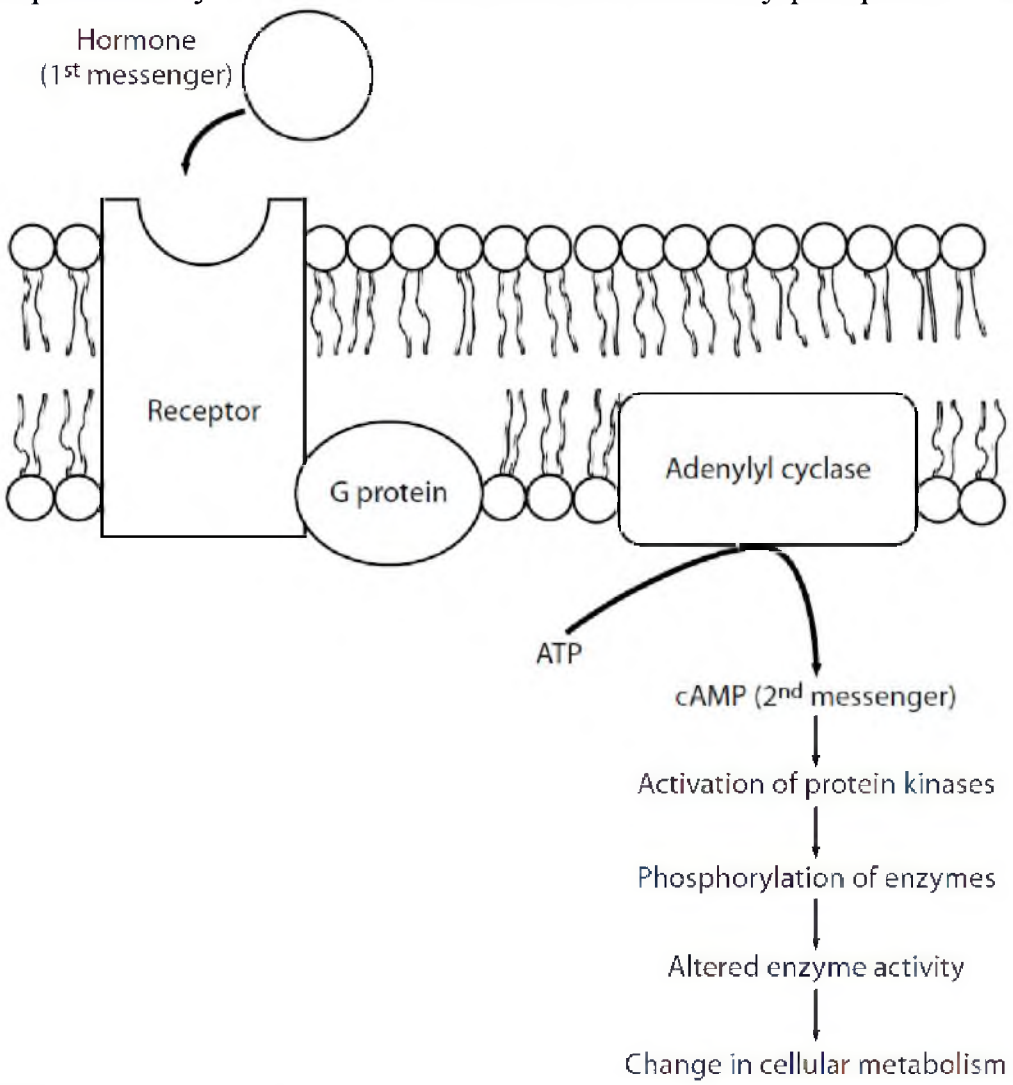


Fig.71. The cyclic adenosine monophosphate (cAMP) mechanism.

B. The phospholipase C – Ca^{2+} second messenger system (Fig.72).

Hormones that use the system: catecholamines (α receptors), vasopressin (V_1 receptors), oxytocin, gonadotropin-releasing hormone, growth hormone-releasing hormone, angiotensin II (vascular smooth muscle), thyrotropin-releasing hormone.

The hormone binds to its receptor on the outer surface of the membrane. Hormone-receptor interaction stimulates the activity of *G_q-protein* and then membrane enzyme, **phospholipase C**. It catalyzes the conversion of phospholipids in the membrane (especially phosphatidylinositol biphosphate) to **inositol triphosphate** (IP_3) and **diacylglycerol** (DAG). Diacylglycerol activates **protein kinase C**. IP_3 diffuses to the endoplasmic reticulum, where it binds to its receptor proteins and causes the opening of **Ca^{2+} channels**. Ca^{2+} that enters the cytoplasm, binds to and activates a protein called **calmodulin**. Calmodulin activates protein kinase, which phosphorylates other enzyme proteins.

In addition, the lipid portion of DAG is arachidonic acid, precursor for the prostaglandins and other local hormones.

C. Tyrosine kinase second messenger system.

Hormones that use the system: insulin, growth hormone, prolactin, leptin, insulin-like growth factor 1. The receptor is itself a kind of enzymes known as a tyrosine kinase. Tyrosine kinase adds phosphate groups to the amino acid tyrosine within the proteins.

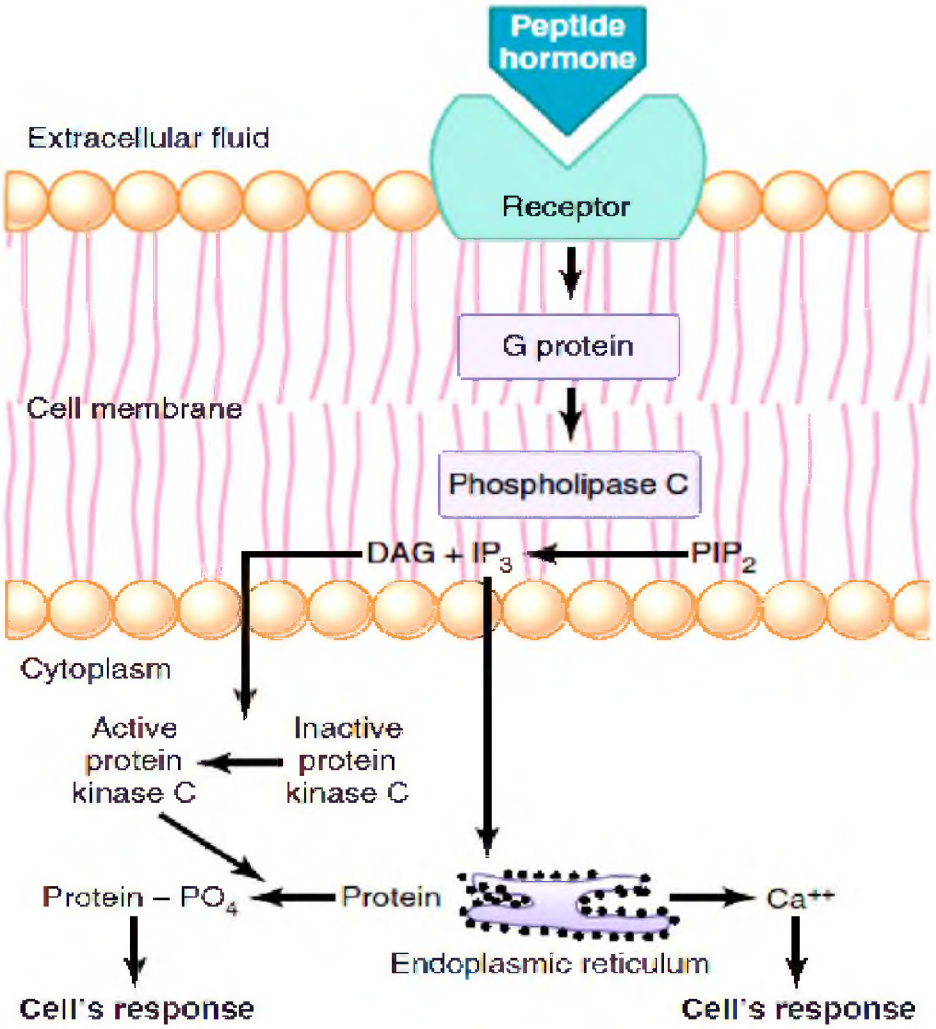


Fig.72. Mechanism of phospholipase C – Ca^{2+} second messenger system.

Hypothalamic-pituitary system

Hypothalamus controls anterior pituitary gland by secretion of the releasing and inhibitory hormones (factors).

Hormones from hypothalamus are transported directly to anterior pituitary gland through hypothalamic-hypophysial portal blood vessels (Fig.73.). Thus, only anterior pituitary receive high concentration of the hypothalamic hormones.

Hormones of hypothalamus:

1. ***growth hormone-releasing hormone (GHRH)*** stimulates growth hormone (GH) secretion by somatotrophs;

2. ***growth hormone-inhibitory hormone (GHIH)*** or **somatostatin** (SS, SRIF) inhibits growth hormone secretion by somatotrophs and ;

3. ***corticotropin-releasing hormone (CRH)*** stimulates adrenocorticotropic hormone (ACTH) secretion by corticotrophs;

4. ***thyrotropin-releasing hormone (TRH)*** stimulates thyroid-stimulating hormone (TSH) secretion by thyrotrophs;

5. ***gonadotropin-releasing hormone (GnRH)*** stimulates follicle-stimulating hormone (FSH) and luteinizing hormone (LH) secretion by gonadotrophs;

6. ***prolactin-inhibitory hormone (PIH)*** or **dopamine** inhibits PRL secretion by lactotrophs.

Hormones of anterior pituitary gland (adenohypophysis)

The anterior pituitary gland produces 6 hormones (Table 14.) which enter the systemic circulation and have effects on other endocrine glands. They are called tropic or trophic hormones.

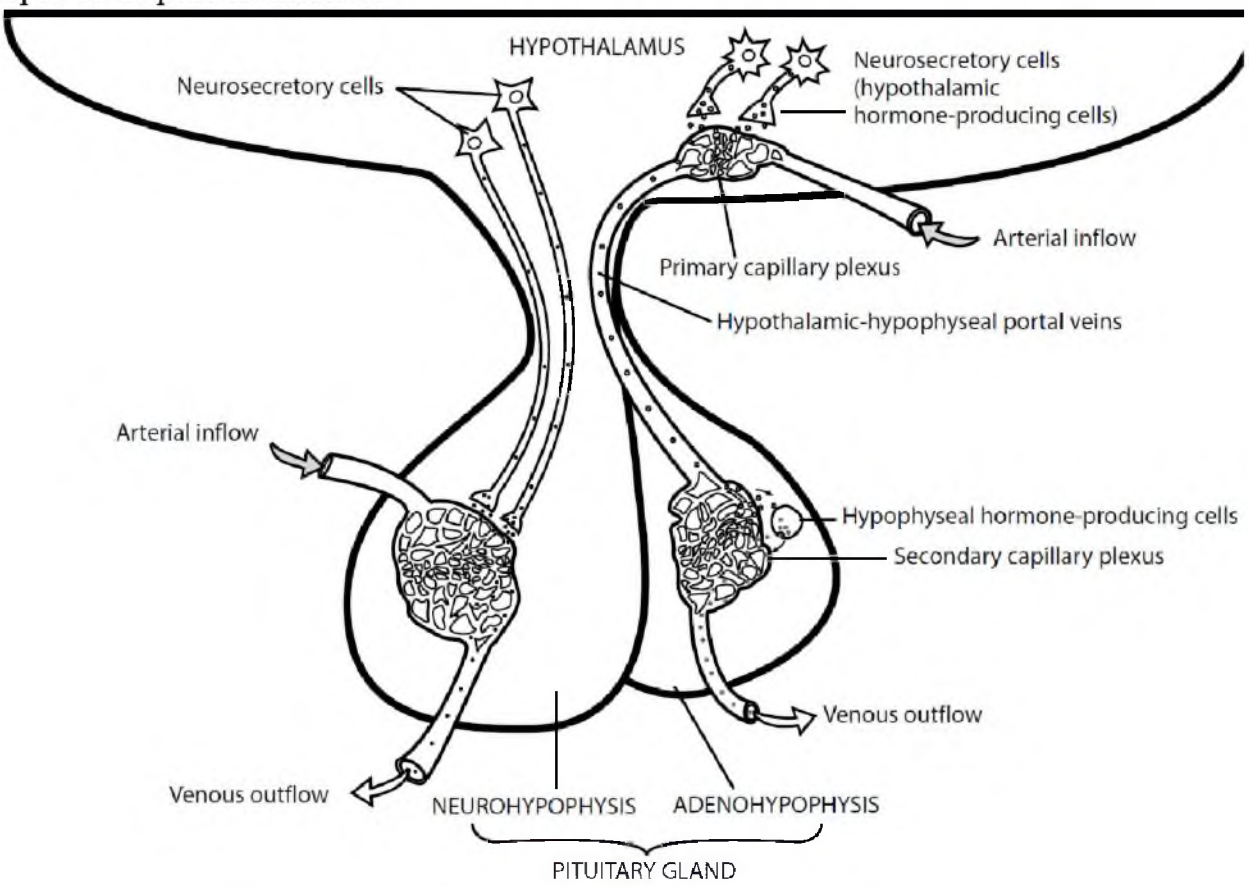


Fig.73. Hypothalamic-pituitary system function.

Table 14. Hormones of anterior pituitary gland.

Hormone	Target	Physiologic actions	Regulation of secretion
Adreno-corticotropic hormone (ACTH)	Adrenal cortex	↑ secretion of glucocorticoids and androgens; maintain size of adrenal cortex	+ CRH; - glucocorticoids
Thyroid-	Thyroid	↑ secretion of thyroid hormones;	+ TRH;

stimulating hormone (TSH)	gland	maintain size of follicular cells	- thyroid hormones
Growth hormone (GH)	Most tissue	↑protein synthesis and body growth; lipolysis; ↑ blood glucose	+ GHRH; - somatostatin
Follicle-stimulating hormone (FSH)	Gonads	gamete production; estrogen production in females	+ GnRH; - sex steroids, inhibin
Luteinizing hormone (LH)	Gonads	ovulation and formation of corpus luteum; ↑ estrogen and progesterone secretion by ovaries; ↑ testosterone secretion by testes	+ GnRH; - sex steroids
Prolactin (PRL)	Mammary glands	milk production in lactating females	+ TRH; - PIH

1. ***Adrenocorticotropic hormone (ACTH)*** regulates function of adrenal cortex. It stimulates the synthesis of glucocorticoids (cortisol and corticosteron) and androgens (dehydroepiandrosterone). ACTH also maintains size of the zona fasciculate and the zona reticularis of adrenal cortex, elevated ACTH level leads to hypertrophy and hyperplasia of adrenal cortex. Its secretion has pulsatile and diurnal pattern (the highest levels occurring in the morning). Corticotrophs synthesize ACTH as part prohormone ***proopiomelanocortin (POMC)***. POMC can be cleaved into **ACTH**, **β-lipotropin**, **β-endorphin** and **α-melanocyte-stimulating hormone** (MSH). Synthesis of ACTH is regulated by the hypothalamic-pituitary-adrenal axis. ACTH secretion is stimulated by low cortisol levels, sleep-wake transition, stress, ADH, hypoglycaemia and it is inhibited by somatostatin and high cortisol levels (negative feedback).

Clinical correlation

Excessive ACTH secretion causes **Cushing disease**. Deficiency of ACTH causes **secondary adrenocortical insufficiency**.

2. ***Thyroid-stimulating hormone (TSH)*** regulates function of thyroid gland. It stimulates secretion of thyroid hormones and maintains size of thyroid follicles. Synthesis of TSH by thyrotrophs is regulated by the hypothalamic-pituitary-thyroid axis (Fig. 74.).

Clinical correlation

Excessive levels of TSH causes an enlargement of thyroid gland called **goiter**. Deficiency of TSH causes **hypothyreoidism**.

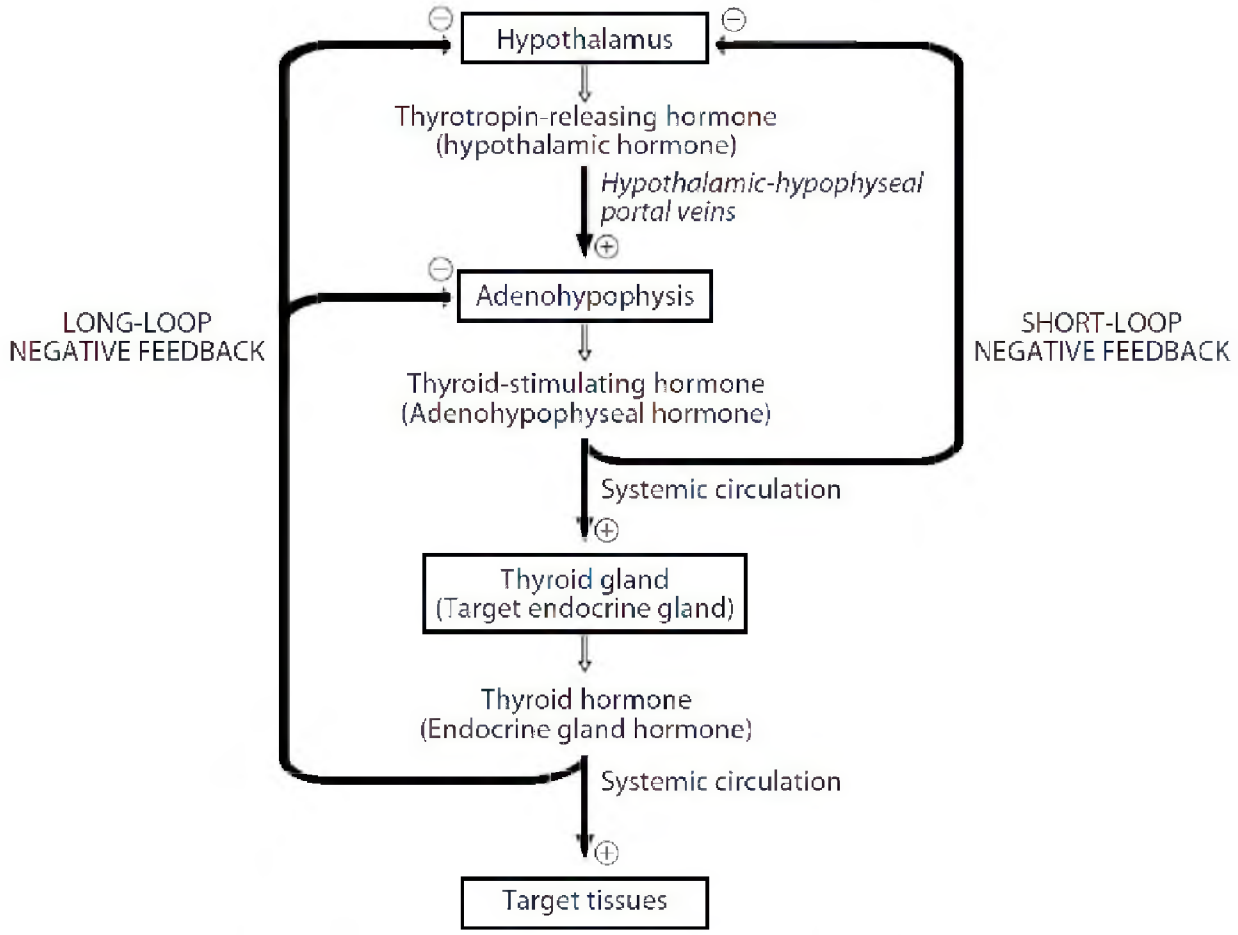


Fig.74. The hypothalamic-pituitary-thyroid axis.

3-4. ***Gonadotropins: follicle-stimulating hormone (FSH) and luteinizing hormone (LH)*** regulate reproductive function and sexual development.

Synthesis of FSH and LH by gonadotrophs is regulated by the hypothalamic-pituitary-gonad axis.

Actions of FSH:

a. the development of follicles in the ovaries;

b. spermatogenesis in the testes;

c. secretion of estrogens by the ovary;

Actions of LH:

a. ovulation and luteinization of the ovulated follicle;

b. secretion of estrogens and progesterone by the ovary;

c. secretion of testosterone by the Leydig cells of the testes.

5. ***Growth Hormone (GH)*** or ***somatotropin*** promotes growth of the body and has effects on metabolism. Synthesis of GH in somatotrophs is regulated by GHRH and somatostatin of hypothalamus. GH is secreted in a pulsatile pattern.

Stimulatory factors of GH secretion: hypoglycaemia, ↓free fatty acids, starvation, arginine, hormones of puberty, stress, exercise, slow wave sleep, α-adrenergic agonists.

Inhibitory factors of GH secretion: hyperglycaemia, obesity, pregnancy, senescence, somatostatin, somatomedins, GH, β-adrenergic agonists.

Most of the effects of GH are not direct but are mediated by the syntheses and release of somatomedins (insulin-like growth factors) by the liver and other tissues.

There are two types of somatomedins:

- **somatomedin B** (insulin-like growth factor 2) plays an important role in the growth of fetus.
- **somatomedin C** (insulin-like growth factor 1) occurs growth-promoting effects.

Actions of GH:

a. stimulation of linear growth;

b. stimulation of protein synthesis and organ growth, increase in muscle mass (anabolic effect);

c. stimulation of lipolysis, ketogenic effect;

d. increased amino acids uptake and protein synthesis;

e. decreased glucose uptake and increased glucose production by the liver;

f. increased insulin secretion and causes insulin resistance (diabetogenic effect).

Clinical correlation

Hyposecretion of GH during childhood causes **pituitary dwarfism**. It is associated with short stature, delayed puberty, and mild obesity. GH deficiency is treated with human growth hormone replacement. Treatment is ineffective in case of **Laron dwarfism** (defective GH receptors).

Oversecretion of GH during childhood causes **gigantism** (result of growth hormone-secreting adenoma).

Hypersecretion of GH in an adult causes **acromegaly**. It is associated with increased hands, foot, and organ size, change of facial features and insulin resistance. It is treated with somatostatin analogues (octreotide).

6. ***Prolactin (PRL)*** regulates milk production (galactopoiesis or lactogenesis) in the mammary glands and breast development.

Synthesis of PRL in lactotrophs is stimulated by estrogens and prolactin-releasing factor (TRH). Blood prolactin level is increased in postpartum period with further decreasing by 6 months. Breast-feeding (suckling) stimulates PRL secretion and decrease dopamine release. Dopamine inhibits PRL production.

Actions of PRL:

a. stimulates development of the breast (with estrogens and progesterone) at puberty and during pregnancy;

b. stimulates milk production (induces synthesis lactose, lactalbumin, casein, and milk fats);

c. suppresses ovulation. Suckling and prolactin inhibit GnRH release and cause lactational amenorrhea.

Clinical correlation

Prolactin deficiency leads to failure to lactate.

Hypersecretion of PRL causes **galactorrhea**, **amenorrhea** (in females) and **infertility** (inhibition of GnRH secretion). It is treated with dopamine agonists (e.g. bromocriptine).

Hypopituitarism (deficiency of all anterior pituitary hormones) can result from trauma, shock, blood loss and ischemia (e.g. during peripartum period, Sheehan syndrome). It leads to hypothyroidism, retarded growth, hypogonadism, and adrenocortical insufficiency.

Hormones of posterior pituitary gland (neurohypophysis)

The hormones from **hypothalamus** (supraoptic and paraventricular nuclei) to posterior pituitary gland are transported by nerve fibers of hypothalamo-hypophysial tract. The posterior pituitary gland stores in bulbous nerve terminals and releases two hormones:

1. ***Antidiuretic hormone (ADH)***, also known as ***vasopressin***, regulates body fluid osmolarity. ADH is nonapeptide that is synthesized primarily in the supraoptic nuclei of hypothalamus and released from the posterior pituitary. ADH secretion is stimulated by a high osmolarity of the blood (detected by osmoreceptors of hypothalamus), hypovolemia and a decrease in blood pressure. Also, pain, hypoglycaemia, nausea, drugs (nicotine, opiates) can activate ADH secretion. Atrial natriuretic peptide (ANP), ethanol, α-adrenergic agonists, and cold inhibit ADH secretion.

Actions of ADH:

a. causes vasoconstriction through V_1 receptors and increases peripheral vascular resistance and blood pressure;

b. increases of water reabsorption in the kidneys (distal tubules and collecting ducts) by regulating the water channel proteins called aquaporins through binding toV_2 receptors and production of cAMP.

Clinical correlation

Hyposecretion of ADH causes **neurogenic (central) diabetes insipidus** It is associated with polyuria, polydipsia and hypernatraemia. It is treated with ADH analogue. Defect in V_2 receptors causes **nephrogenic diabetes insipidus**.

Hypersecretion of vasopressin causes **SIADH** (syndrome of inappropriate antidiuretic hormone secretion) which is associated with hypervolemia, hyponatraemia, and high blood pressure.

2. ***Oxytocin*** is nonapeptide that is synthesized primarily in the paraventricular nuclei of hypothalamus and released from the posterior pituitary. Oxytocin secretion is stimulated by afferent nerve impulses from nipple during breast-feeding and from the female reproductive tract during childbirth.

Actions of oxytocin:

a. contractions of myoepithelial cells in the mammary gland, which result in the milk-ejection reflex and milk letdown in a lactating woman;

b. contractions of uterus during labour.

Clinical correlation

Injections of oxytocin may be given to a induce labour. Oxytocin administration during postpartum period decreases the danger of bleeding and promotes uterine involution.

4. Materials for self-control:

Control questions:

1. Humoral regulation factors, their characteristics and classification.
2. Nervous and humoral regulation connection.
3. Endocrine system's structural-functional organization.
4. Hormones action mechanism.
5. Hormone receptors, G-proteins, secondary messengers, their role.
6. Hormonal secretion regulation.
7. Hypothalamic-hypophyseal system.
8. Hypothalamus hormones.
9. Hormones of anterior pituitary gland.
10. Hormones of posterior pituitary gland.

Lesson 21. Hormones role in regulating the psychic, physical development, body linear growth and homeostasis (hormones of thyroid gland, parathyroid glands, pancreas).

Before performing this lesson, you should study the introductory material presented here.

1.Lecture course.
2.Moroz V.M., Shandra O.A. Physiology. - 2011. Unit 5, Chapter 10, 11, 12.
3.Guyton A.C., Hall J.E. Textbook of Medical Physiology. - 2011. Unit IX. Chapter 77-81.

Relevance of the topic.

Endocrine system play a key role in regulating almost all body functions, including metabolism, growth and development, reproduction and behaviour. Knowledge of endocrinology is necessary for early diagnosis and treatment of different disorders.

1. Objectives:

To know: physiological functions hormonal regulation characteristics, mechanisms of hormones action on organism.
To be able to: analyze regulated parameters and make conclusions about endocrine glands functions.

2. Topic content.

Thyroid gland

Thyroid gland secretes thyroid hormones (thyroxine (T_4), triiodothyronine (T_3)) in follicular cells and calcitonin in parafollicular or C cells.

Thyroid hormones regulates body development and rate of metabolism. TSH regulates thyroid hormones production and thyroid gland growth. TSH secretion, in turn, is regulated by TRH and negative feedback by thyroid hormones.

Production of thyroid hormones (Fig.75.):

a. synthesis of thyroglobulin and exocytosis into the lumen of the follicle;

b. iodide trapping (iodide enters the follicle cell via Na^+/I^- cotransporter (the I-trap) and exins into the lumen via I^-/Cl^- antiporter);

c. oxidation of iodide by thyroid peroxidase;

d. iodination of tyrosine residues of thyroglobulin (formation of monoiod tyrosine (MIT) and diiodtyrosine (DIT);

e. coupling reactions (thyroid peroxidase binds two DIT, forming T_4);

f. endocytosis of the mature thyroglobulin, proteolysis and releasing of thyroid hormones into the blood.

The thyroid gland produce mostly T_4. It is then converted to T_3, which is about four times more active. In the blood, the most of thyroid hormones are bound to albumin, transthyretin, and thyroxine-binding globulin (TBG).

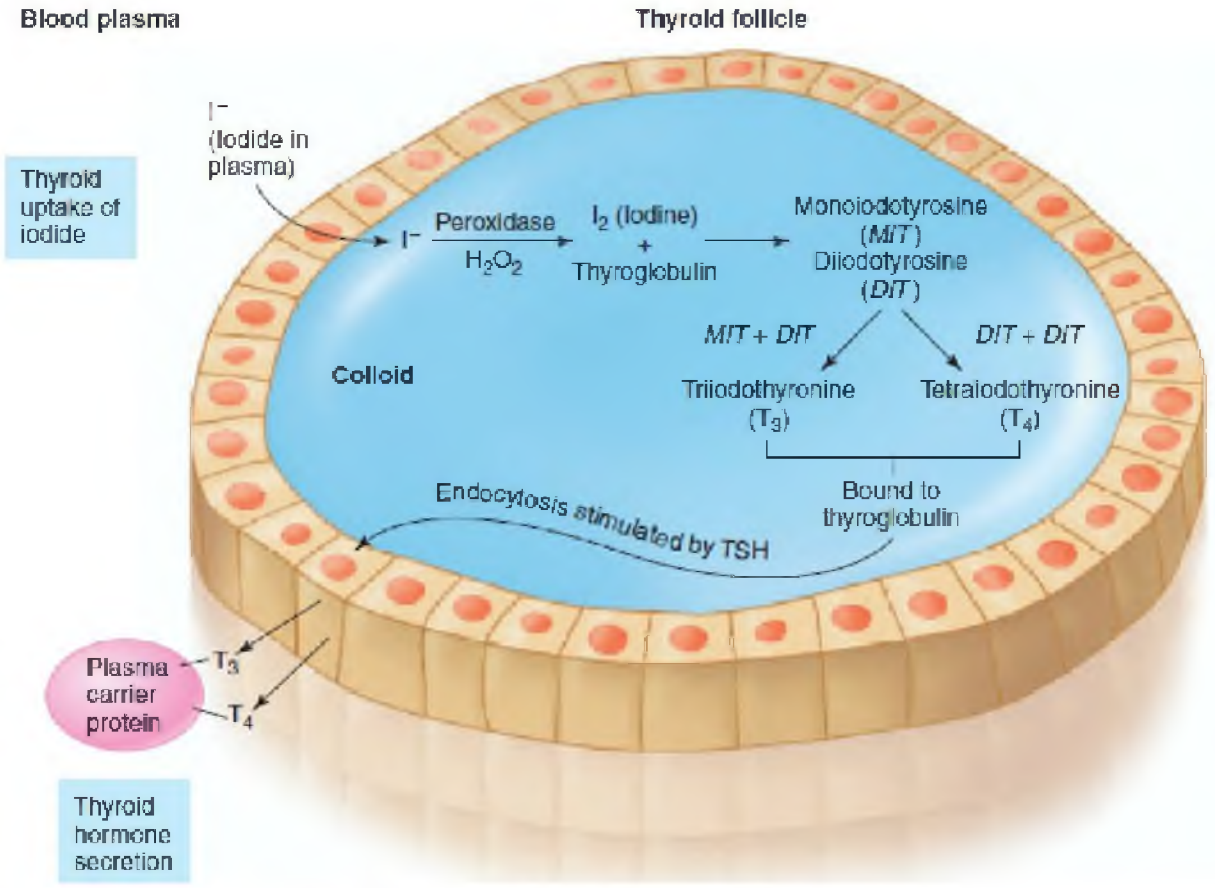


Fig.75. Production of thyroid hormones.

Actions of thyroid hormones:

a. stimulate synthesis of many enzymatic and structural protein, but also activate proteolysis, net effect is catabolic;

b. stimulate lipolysis, glycogenolysis, gluconeogenesis;

c. contribute to normal CNS development in the perinatal period;

d. stimulate growth processes (promote bone formation);

e. regulate energy metabolism, increase basal metabolic rate (BMR) and oxygen consumption by increasing the activity of the Na^+-K^+ ATPase;

f. increase body heat production (thermogenic action) by synthesis of uncoupling proteins;

g. increase cardiac output and respiration due to *permissive effect* for catecholamines (induce β-adrenergic receptors).

Clinical *correlation*

Hypersecretion of thyroid hormones (**hyperthyroidism** or **thyrotoxicosis**) is caused by thyroid-stimulating immunoglobulins (TSI), which activate TSH receptors (**diffuse toxic goiter** or **Graves' disease**) or excessive TSH secretion. Hyperthyroidism has antianabolic effects (loss of weight and muscle weakness), stimulates energy metabolism (↑ BMR, body temperature), increases excitability, causes exophthalmos, sweating, tremor, dyspnea, excessive sweating, and tachycardia. It is treated with drugs, which inhibit synthesis of thyroid hormones or surgical removal of gland.

Hyposecretion of thyroid hormones (**hypothyreoidism**) leads to **myxedema** in adults (associated with edema, decreased appetite, fatigue, hypotension, hypothermia,

slowing of mental function, somnolence, constipation, etc.) and **cretinism** in children (associated with mental and growth retardation). Hypothyreoidism can result from lack of iodine (endemic goiter) as well as autoimmune Hashimoto's disease. It is treated with thyroid hormone replacement therapy.

Pancreas

The pancreas contains about 1 million endocrine clusters of cells, known as islets of Langerhans, which compose 1-2% of the pancreatic mass. **Islets of Langerhans** consist of about 2500 cells:

1. A cells (α-cells) secrete glucagon (20%);
2. B cells (β-cells) secrete insulin (65%);
3. D cells (δ-cells) secrete somatostatin (10%);
4. F cells or PP cells secrete pancreatic polypeptide (5%).

Insulin is a peptide consisting of A chain and B chain. The β-cells firstly produce preproinsulin, after removal of signal peptide it converts to proinsulin and then proteases cleave the connecting peptide (C peptide), yielding insulin. Determination of C peptide is an important diagnostic test for insulin secretion level.

Insulin secretion is regulated by different factors:

1. Stimuli of insulin secretion: hyperglycaemia, increased blood free fatty acids and amino acids; gastrointestinal hormones (gastrin, secretin, cholecystokinin, gastric inhibitory peptide); glucagon, growth hormone, cortisol; potassium; β-adrenergic stimulation; parasympathetic stimulation, acetylcholine; insulin resistance; obesity (Fig.76.).

2. Inhibitors of insulin secretion: hypoglycaemia; fasting; exercise; somatostatin; α-adrenergic activity; leptin.

Actions of insulin:

1. On carbohydrate metabolism (decrease blood glucose):

a. increases glucose uptake into cells by increasing of permeability of cell membrane and number of glucose transporters (GLUT 4) into target cells such as muscle and adipose;

b. promotes peripheral utilization of glucose and inhibits gluconeogenesis;

c. stimulates glycogenesis and inhibits glycogenolysis.

2. On protein metabolism (anabolic effect):

a. increases amino acids uptake into the cell;

b. increases protein synthesis.

3. On fat metabolism:

a. promotes synthesis of fatty acids and triglycerides;

b. inhibits lipolysis and oxidation of fatty acids.

c. stimulates cholesterol synthesis in the liver.

Glucagon is peptide of α cells, which stimulates mobilization and utilization of stored nutrients in the fasting state.

Glucagon secretion is stimulated by hypoglycaemia, fasting, increased blood amino acids, and cholecystokinin. Insulin; increased blood fatty acids, somatostatin inhibit glucagon secretion.

Action of glucagon:

a. stimulates glycogenolysis;
b. stimulates gluconeogenesis (increases blood glucose);
c. inhibits glycogenesis and glycolysis;
d. stimulates lipolysis and ketoacid formation.

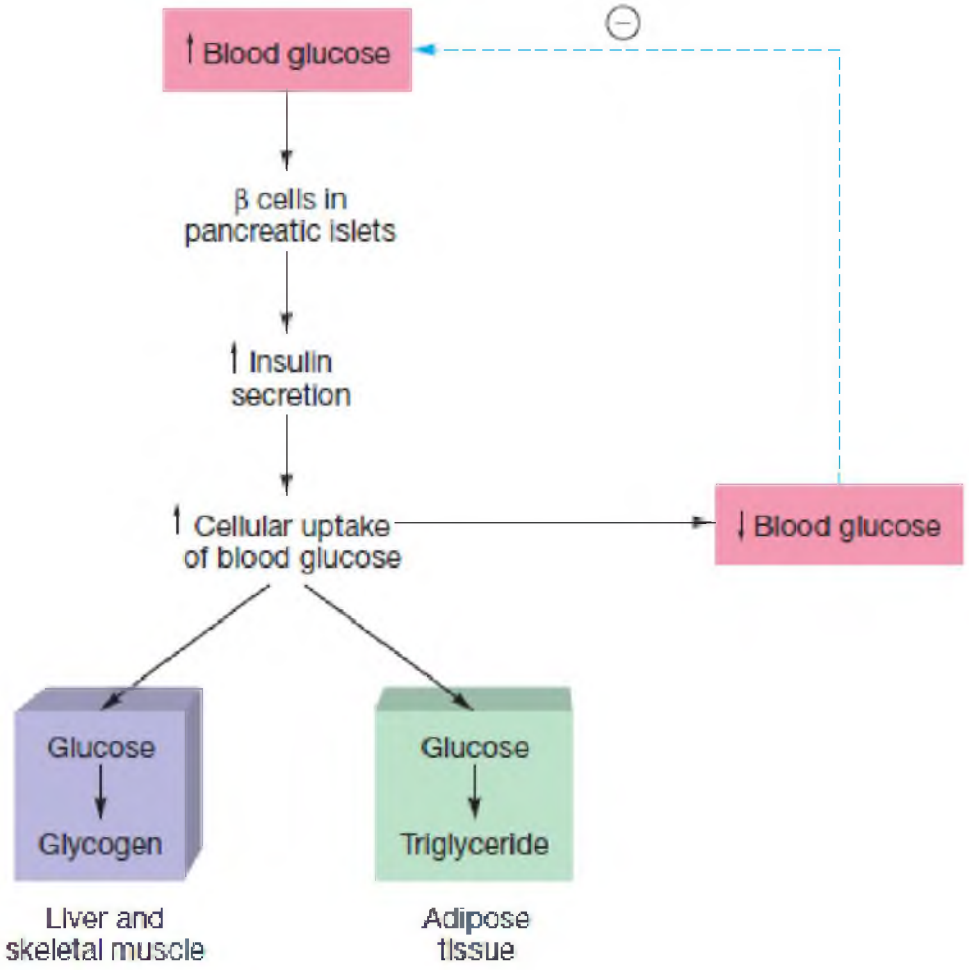


Fig.76. Regulation of blood glucose.

Clinical correlation

Diabetes mellitus is a disease of impaired insulin function, resulting in chronic hyperglycaemia (Tab.15.).

Table 15. Differences between type I and type II diabetus mellitus.

Characteristic	Type I (IDDM)	Type II (NIDDM)
Age of onset	Before 40 year (juvenile-onset diabetes)	After 40 year (adult-onset diabetes)
Mode of onset	Rapid	Gradual
Main cause	Absolute insulin deficiency	Insulin resistance or relative

		insulin deficiency
B cells of pancreas	Destroyed	Normal
Insulin level	Low to absent	Normal or elevated
Body weight	Not obese	Obese
Incidence of ketoacidosis	High	Low
Genetic predisposition	Moderate: concordance rate is < 50%	Strong: concordance rate is > 50%
Usual complication	Ketoacidotic coma	Hyperosmolar coma
Treatment with insulin	Essential	Usually not required
Treatment with oral hypoglycaemic drugs	Unresponsive	Responsive

Type 1 diabetes (**insulin-dependent diabetes mellitus**) is caused by destruction of β-cells by autoimmune attack. It is characterized by hyperglycaemia, loss of weight, metabolic acidosis (diabetic ketoacidosis), hyperkalemia, polyuria (osmotic diuresis), polydipsia (thirst), and polyphagia. It is treated with insulin replacement therapy.

Type 2 diabetes (**non-insulin-dependent diabetes mellitus**) is caused by insulin resistance, resulting from reduction in the insulin receptors. It is characterized by hyperglycaemia, obesity, hyperosmolarity, polyuria, and polydipsia. It is treated with weight reduction, sulfonylurea drugs (glyburide), which stimulate insulin secretion, and biguanide drugs (metformin), which activate insulin receptors.

Excessive production of insulin is usually due to tumour, **insulinoma**. It is associated with episodes of hypoglycaemia, headache, confusion, unconsciousness, palpitations, sweating, and convulsions.

Endocrine regulation of calcium homeostasis

Calcium plays an important role in many physiological processes (nerve excitability, neurotransmitter release, excitation-contraction coupling in muscles, blood clotting, etc.). Also, calcium is the most abundant mineral in the body (1-2 kg): 99% of calcium is in bones in the form of hydroxyapatite (Fig.77.).

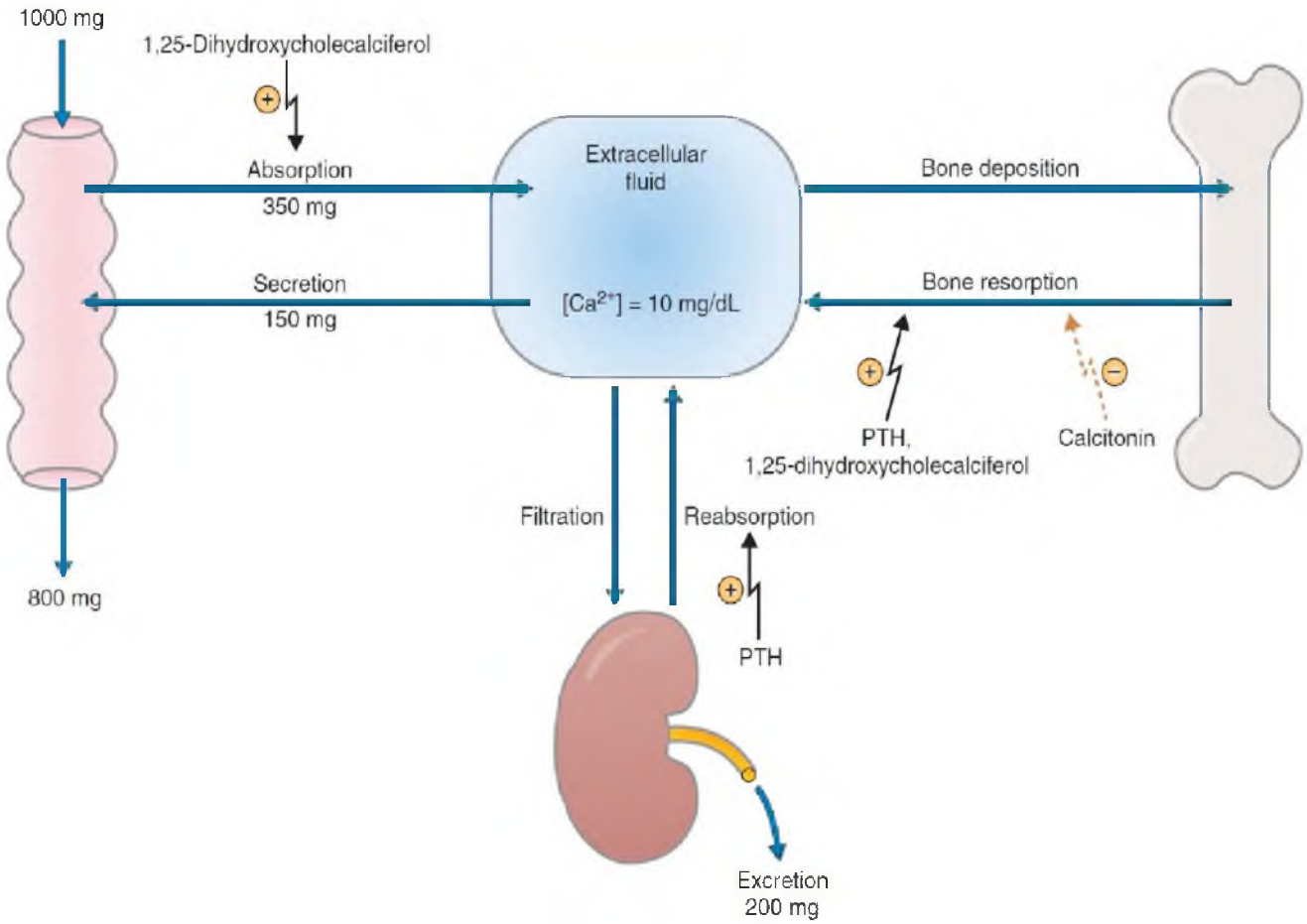


Fig.77. Calcium exchange.

Plasma calcium is regulated by parathyroid hormone, 1,25-dihydroxycholecalciferol and calcitonin. The same mechanisms are involved in regulation of phosphate concentrations.

Parathyroid glands

There are two pairs of parathyroid glands on the dorsal surface of the thyroid gland; the chief cells produce parathyroid hormone.

Parathyroid hormone (PTH) regulates plasma calcium concentration. The normal stimulus for secretion of PTH is a decrease in ionized calcium concentration. Low magnesium concentration also stimulates PTH secretion and 1,25-dihydroxycholecalciferol inhibits it. PTH increases calcium concentrations and decreases phosphates in blood.

Actions of PTH:

1. <u>At the bones</u>:

a. activates bone resorption and calcium and phosphate mobilization from bones;

b. simulates maturation of osteoclasts;

c. inhibits collagen synthesis by osteoblasts.

2. <u>At the kidneys</u>:

a. increases renal tubular reabsorption of calcium;

b. decreases renal tubular reabsorption of phosphate;

c. increases the formation of 1,25-dihydroxycholecalciferol.

Clinical correlation

Hyperparathyroidism leads to hypercalcaemia and hypophosphatemia. It is associated with extensive decalcification and multiple fractures (osteitis fibrosa cystica), kidney stone formation (urolithiasis), depression of CNS, muscle weakness, constipation, abdominal pain. It is treated with surgical removal of glands.

Hypoparathyroidism results in hypocalcemia and hyperphosphatemia. Hypocalcaemia increases the excitability of sensory and motor neurons and muscle cells (tingling or numbness, cramping, seizures, tetanic muscle spasms). It is treated with oral calcium supplement and active form of vitamin D. The complete absence of PTH (e.g. after removing of parathyroid glands) leads to death from hypocalcemic tetany.

Vitamin D_3 (cholecalciferol), its active form, ***1,25-dihydroxycholecalciferol (1,25-OH D_3)*** or ***calcitriol***, serves as a hormone in calcium regulation. Cholecalciferol can be provided by dietary sources or the action of ultraviolet light on 7-dehydroxycholesterol in skin. Vitamin D is converted to 25-OH D_3 in liver and then undergoes the second hydroxylation to 1,25-dihydroxycholecalciferol in the kidneys. Calcitriol increases both calcium and phosphate concentration in blood.

Actions of vitamin D:

1. <u>At the small intestine</u>:

a. increases calcium absorption (stimulates production of calcium binding proteins);

b. increases phosphate absorption.

2. <u>At the bones</u>:

a. increases bone remodelling and mineralization;

b. promotes actions of PTH on osteoclasts, increasing bone resorption.

3. <u>At the kidneys</u>:

a. increases renal tubular reabsorption of calcium;

b. increases renal tubular reabsorption of phosphate.

Clinical correlation

Vitamin D deficiency during childhood causes **rickets** (skeletal deformities and growth failure). It is treated with vitamin D supplement.

Vitamin D deficiency in an adult causes **osteomalacia** (impairment of bone mineralization leads to the softening of bones).

Excess of vitamin D (**vitamin D toxicity**) leads to calcinosis (calcification of soft tissues), kidney stone formation, hypercalcaemia, and cardiac arrhythmia.

Parafollicular cells of **thyroid gland** produce ***calcitonin (CT)***. Calcitonin secretion is stimulated by an increase in calcium concentrations and hormones of the gastrointestinal tract. CT decreases calcium and phosphate levels in blood.

Action of CT:

1. <u>At the kidneys</u>:

a. decreases renal tubular reabsorption of calcium;
b. decreases renal tubular reabsorption of phosphate.
2. At the bones:
a. decreases bone resorption;
b. inhibits osteoclasts.

CT deficiency or CT hypersecretion does not lead to clinical abnormalities of calcium concentrations. However, calcitonin is used for treatment of malignancy-related hypercalcaemia and osteoporosis.

4. Materials for self-control:
Control questions:
1. Hormones of thyroid gland.
2. Hormones of pancreas.
3. Hormones of parathyroid glands.
4. Role of vitamin D, calcitonin and parathyroid hormone in calcium homeostasis/

Lesson 22. Hormones role in regulating organism adaptation. Adrenal glands hormones. Hormones role in sexual functions regulation.

Before performing this lesson, you should study the introductory material presented here.

1.Lecture course.
2.Moroz V.M., Shandra O.A. Physiology. - 2011. Unit 5, Chapter 10, 11, 12.
3.Guyton A.C., Hall J.E. Textbook of Medical Physiology. - 2011. Unit IX. Chapter 77-81.

Relevance of the topic.
Endocrine system play a key role in regulating almost all body functions, including metabolism, growth and development, reproduction and behaviour. Knowledge of endocrinology is necessary for early diagnosis and treatment of different disorders.
1. Objectives:
To know: physiological functions hormonal regulation characteristics, mechanisms of hormones action on organism.
To be able to: analyze regulated parameters and make conclusions about endocrine glands functions.

2. Topic content.

Adrenal glands (suprarenal glands)

Adrenal glands consist of two distinct parts: adrenal cortex and adrenal medulla.

Hormones of adrenal cortex (Fig.78.):
Zona glomerulosa produces mineralcorticoids (aldosterone);
Zona fasciculate produces glucocorticoids (cortisol and corticosterone);
Zona reticularis produces androgens (dehydroepiandrosterone and androstenedione).

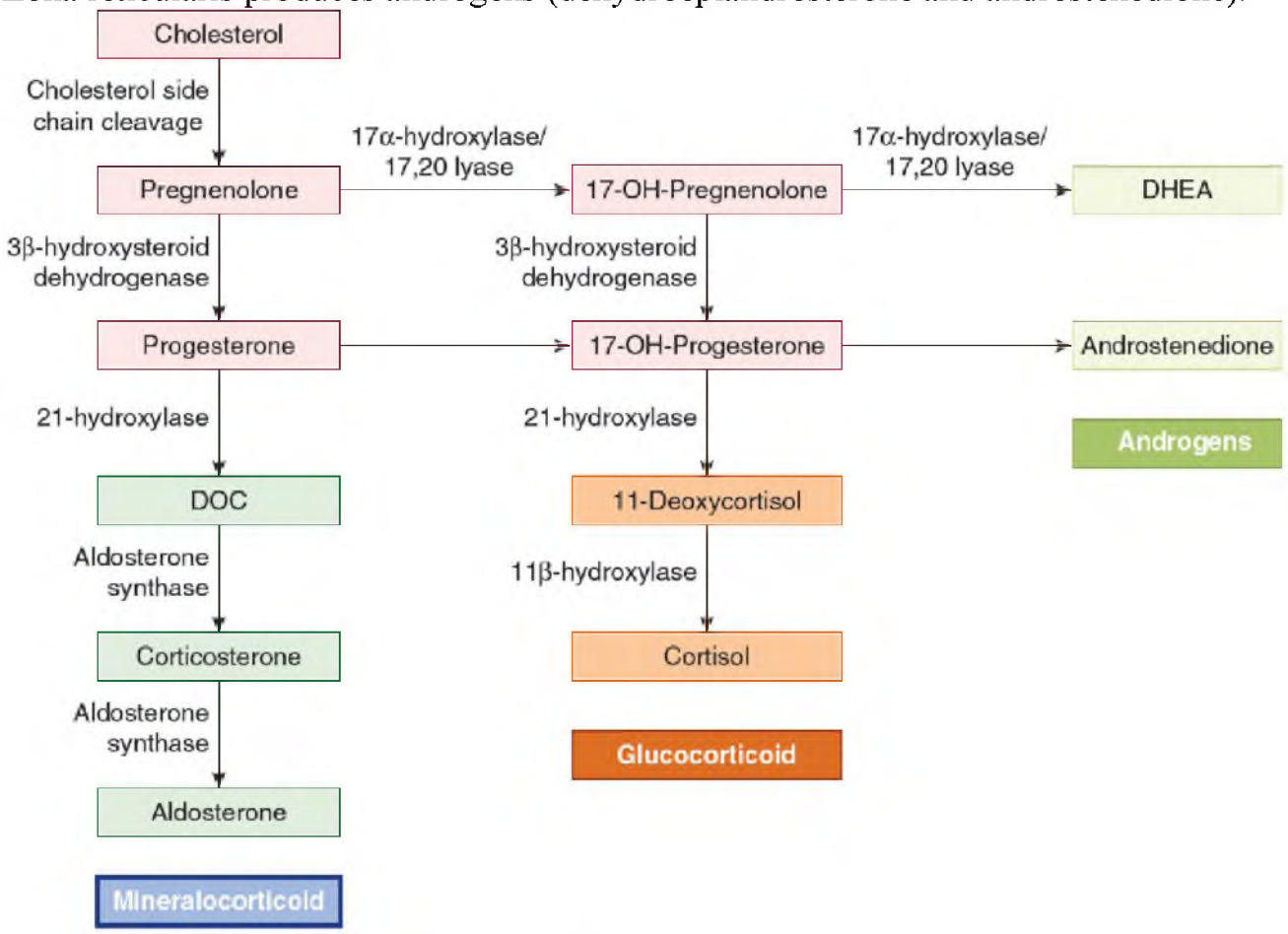


Fig.78. Synthesis of steroid hormones in the adrenal cortex.

1. ***Mineralcorticoids*** (***Aldosterone***) regulate sodium and potassium concentrations in plasma. Aldosterone secretion is stimulated by angiotensin II (renin-angiotensin-aldosterone system) and an increase in potassium in plasma. ACTH does not regulate aldosterone secretion but it has a tonic effect on aldosterone synthesis.

Actions of aldosterone:

a. increase **reabsorption of sodium** in renal tubules, and as a result, water retention and increasing of extracellular fluid volume, in excess, hypertension results;

b. increase **excretion of potassium** in renal tubules;

c. increase **excretion of hydrogen** in renal tubules.

Clinical correlation

Primary aldosteronism or **Conn's syndrome** (caused by aldosterone-secreting tumour) leads to hypernatraemia, hypokalemia, metabolic alkalosis, and hypertension. It is treated with surgery and aldosterone antagonist (spironolactone).

2. ***Glucocorticoids*** (***Cortisol***) regulates metabolic processes, suppresses of inflammatory responses, and modulate CNS function. Secretion of glucocorticoids is regulated by hypothalamic-pituitary-adrenal axis. The regulation of cortisol secretion has pulsatile and diurnal pattern (the highest rates occur in the morning).

Actions of glucocorticoids:

1. On carbohydrate metabolism (increase blood glucose):

a. stimulate of gluconeogenesis (activate synthesis key gluconeogenic enzymes and mobilize amino acids and glycerol for gluconeogenesis);

b. decrease uptake and utilization of glucose (anti-insulin effect);

c. increase secretion of glucagon and epinephrine that cause glycogenolysis, but also cortisol promotes hepatic glycogenesis.

2. On protein metabolism:

a. facilitate proteolysis, especially in skeletal muscle, skin, bone, and connective tissue and enhance release of amino acids;

b. inhibits synthesis of proteins (antianabolic effect),

c. increase synthesis of many plasma and liver proteins.

3. On fat metabolism:

a. promote lipolysis, ketogenesis and mobilization of fatty acids;

b. have lipogenic effect (due to compensatory hyperinsulinemia) and cause centripetal redistribution of fat;

c. stimulate leptin synthesis in adipose tissue.

4. Anti-inflammatory effects:

a. induce synthesis of ***lipocortins*** (inhibitors of phospholipase A_2), decreasing amount of arachidonic acid available for conversion to prostaglandins and leukotrienes that mediate inflammatory response;

b. decrease capillary permeability and reduce inflammatory exudations;

c. stabilize lysosomal membrane and inhibit release of proteolytic enzymes;

d. inhibit the release of histamine and serotonin from mast cells.

5. Immunosuppressive effects:

a. involution of the lymph nodes, thymus and spleen;

b. inhibit T-cells proliferation and release of interleukins;

c. reduce B-cells and decrease antibody production.

6. Permissive effects:

a. increase catecholamine synthesis and vascular responsiveness to them;

b. increase metabolic effects of glucagon and catecholamines.

7. Psychoneural effects:

a. decrease REM sleep and increase slow-wave sleep, high levels can cause insomnia;

b. influence the mood and behaviour, high levels can cause depression and irritability.

8. Other effects:

a. stimulate surfactant synthesis in the fetal lungs;

b. increase glomerular filtration rate, causing vasodilation of afferent arterioles;

c. increase red blood cell, platelet, and neutrophil counts and decrease eosinophil, basophil, and lymphocyte counts.

Clinical correlation

Hypersecretion of cortisol causes **Cushing's syndrome** (primary hyperplasia of adrenal cortex) or **Cushing's disease** (excess of ACTH). It is associated with centripetal obesity (moon face, buffalo hump), hypertension, hyperglycaemia and insulin resistance (steroid diabetes), osteoporosis, muscle wasting, striae, poor wound healing, immunosuppression, virilisation and menstrual disorders in females. It is treated with drugs which block steroid hormone synthesis or surgery.

Injury of the adrenal cortex causes **Addison's disease** (primary adrenocortical insufficiency). There is decreased synthesis of all adrenocortical hormones. It is associated with hypoglycaemia, rapid weight loss, weakness, dehydration, hypotension, hyperkalemia, and hyperpigmentation (increased ACTH and MSH level). It is treated with replacement of glucocorticoids and mineralcorticoids.

Also, exogenous glucocorticoids are administered to suppress immune response and prevent the rejection of transplanted organs. But synthetic glucocorticoids inhibit ACTH secretion and decrease production of natural glucocorticoids. The sudden discontinuation of treatment causes acute adrenal insufficiency.

3. ***Androgens*** (***dehydroepiandrosterone*** (***DHEA***) and ***androstenedione***) are male sex hormones.

Actions of androgens:

a. in males: similar to testosterone;

b. in females: stimulate growth of axillary and pubic hair and libido.

Clinical correlation

Hypersecretion of androgens causes **adrenogenital syndrome**. It is associated with suppression of gonadal function, masculinisation in females.

Hormones of adrenal medulla

The adrenal medulla is innervated by sympathetic nervous system, and secretion of its hormones is activated during "fight or flight" reaction (injury, pain, hypoglycaemia, anxiety, anger, cold). The chromaffin cells of adrenal medulla produce about 80% of ***epinephrine*** (***adrenaline***) and 20% of ***norepinephrine*** (***noradrenaline***). Biological effects of catecholamines are mediated through α_1-, α_2-, β_1-, β_2-, β_3- adrenergic receptors (see lesson 18).

Actions of epinephrine:

a. stimulation of glycogenolysis and lipolysis;

b. inhibition of insulin secretion and stimulation of glucagon secretion;

c. increases heart rate (tachycardia) and vascular resistance (peripheral vasoconstriction);

d. causes bronchial dilation;

e. inhibits peristalsis and constricts sphincters.

Clinical correlation

Hypersecretion of epinephrine (e.g. tumour of the adrenal medulla) is **pheohromocytoma** (associated with hypertension, tachycardia, palpitations, hyperglycaemia, headache, nervousness, profuse sweating).

Hyposecretion causes no clinical symptoms.

Endocrine regulation of reproductive function

Endocrine function of testes

The major hormone of testes is ***testosterone***. It is produced by Leydig cells. Testosterone in the blood is bound to sex hormone binding globulin (SHBG) or albumin. Testosterone is able to convert to dihydrotestosterone (DHT) and estrogens in tissues. DHT is the most active androgen (2-3 times more potent than testosterone). Secretion of testosterone is regulated by hypothalamic-pituitary-gonad axis. LH stimulates testosterone production. FSH stimulates spermatogenesis and function of Sertoli cells in testes. Sertoli cells produce ***inhibin***, inhibitor of FSH secretion.

Actions of testosterone:

a. differentiation and growth of the male genitalia during fetal life;

b. development of the secondary sex characteristics (hair distribution, bone growth, deepening of voice) at puberty;

c. stimulate spermatogenesis; libido;

c. anabolic effect (increase in muscle size);

e. stimulate erythropoiesis in the bone marrow.

Actions of DHT:

a. embryonic development of prostate;

b. descent of testes and phallic growth;

c. growth of axillary and pubic hair; male pattern balding;

d. activity of sebaceous glands.

Clinical correlation

Exogenous testosterone cannot achieve the local high concentration in the testis. It inhibits LH release and lead to suppression of endogenous testosterone production. Testosterone has an anabolic effect and causes an increase in muscle mass and strength (bodybuilders and athletes). Also androgen abuse is associated with aggressive behaviour and increased risk of liver tumours.

Endocrine function of ovaries and placenta

Ovarian hormones (estrogens and progesterone) are synthesized in the granulosa and theca cells of follicles: the theca cells produce androgens from cholesterol (mainly androstenedione), which diffuse into the granulosa cells. The granulosa cells convert androgens to estradiol and produce progesterone. Ovarian steroidogenesis is regulated by hypothalamic-pituitary-gonad axis. Secretion of female sex hormone has pulsatile pattern and follows a 28-day cycle. The menstrual cycle include follicular phase, ovulation, and luteal phase (Fig.79.).

In the follicular phase: FSH and LH stimulate estrogen secretion and follicular development. Estradiol has negative feedback on secretion of GnRH, FSH, and LH.

At midcycle: elevated estradiol levels has positive feedback on secretion of GnRH, FSH, and LH. The LH level rises sharply and induces ovulation of the mature oocyte.

In the luteal phase: corpus luteum produces progesterone, which has negative feedback on secretion of GnRH, FSH, and LH.

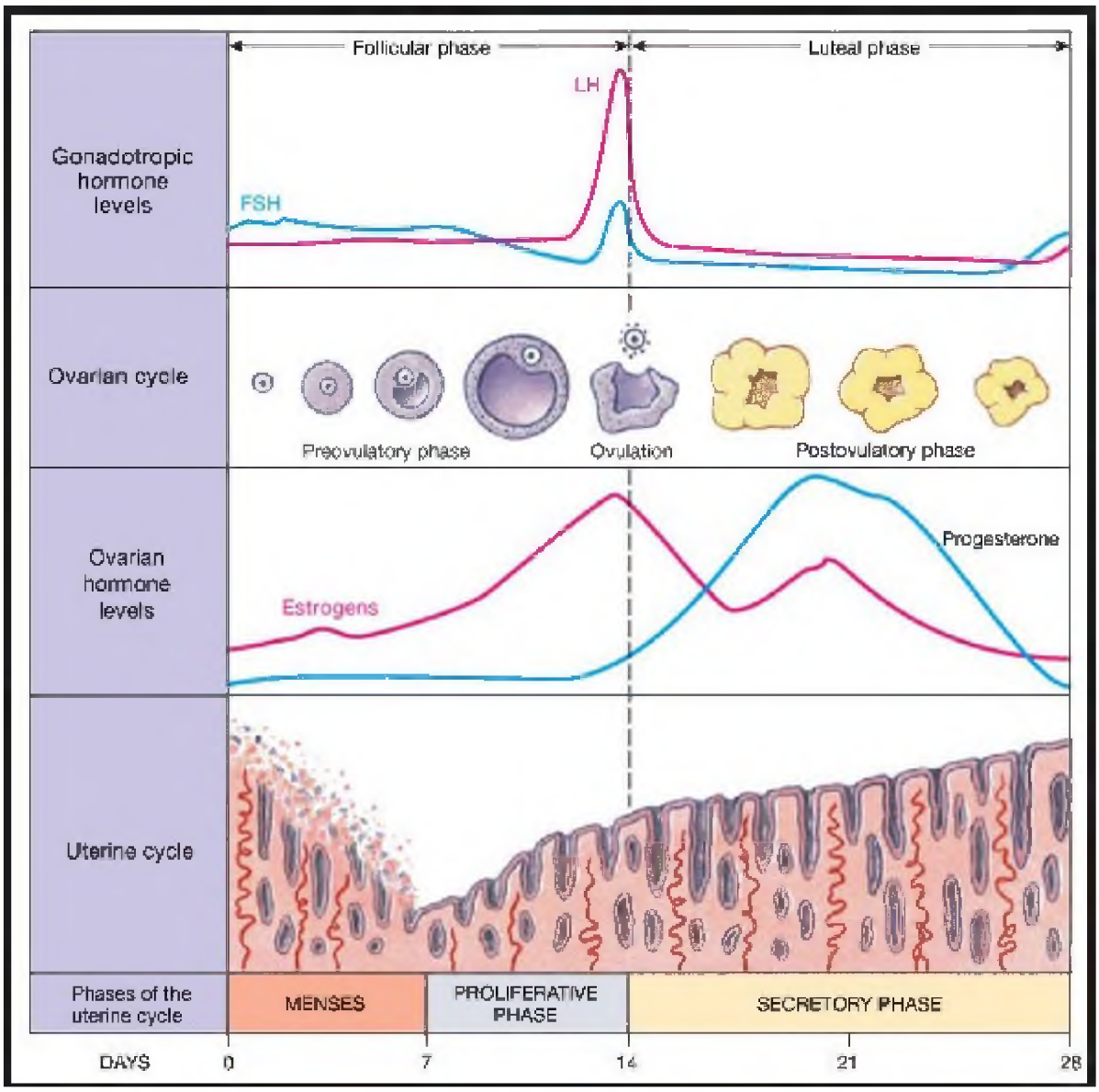


Fig.79. Hormonal production during the menstrual cycle.

There are 3 estrogens:

- ***estradiol*** (the most abundant and biologically active)'
- ***estrone*** (weak ovarian estrogen, in postmenopausal woman it is produced in liver and adipose tissue from androstenedione of adrenal cortex);
- ***estriol*** (it is secreted by placenta or liver from estradiol and estrone).

Progestagens (***progesterone*** and ***17α-hydroxyprogesterone***) are produced by theca luteal cells.

Estrogens in the blood are bound to SHBG or albumin. Progesterone is bound to transcortin or albumin.

Ovaries also produce 3 polypeptide hormones: ***inhibin*** and ***follistatin*** suppress the secretion of FSH, ***activin*** increases the secretion of FSH.

Actions of estrogens:

a. development and maintenance of female reproductive organs:

- in the ovaries cause proliferation of granulosa cells and enhance action of FSH; responsible for follicular development;

- *in the uterus* cause proliferation of endometrium and myometrium, increase uterine contractility;

- *in the fallopian tubes* stimulate ciliary activity and contractility;

- in the cervix make cervical mucus watery and elastic;

- *in the vagina* stimulate proliferation of epithelium;

b. development of the female secondary sexual characteristics at puberty;

c. promotes growth of mammary glands;

d. maintenance of pregnancy;

e. other effects:

- increase osteoblastic activity and promote deposition of bone matrix (anti-osteoporosis effect), stimulate bone maturation and epiphyseal closure;

- protein anabolic effect;

- neuroprotective and cardioprotective effects;

- increase synthesis coagulation factors, angiotensinogen, and transport globulin in the liver;

- decrease LDL (low-density lipoprotein) cholesterol.

Actions of progesterone:

a. arrests endometrial proliferation and induces secretory activity of uterus;

b. inhibits uterine motility;

c. promotes growth of mammary glands but suppresses milk production before parturition;

d. promotes implantation and maintains pregnancy;

e. other effects:

- modulates sexual behaviour;

- antagonizes the action of aldosterone;

- increase basal body temperature;

- stimulates of the respiratory centre.

Clinical correlation

Oral contraceptives contain combination of estrogen and progesterone or progesterone alone.

Antiprogesterone agents (mifepristone) are used for medical termination of pregnancy.

Placenta as endocrine organ produces:

- ***human chorionic gonadotropin*** (maintains the corpus luteum, stimulates the corpus luteum to produce progesterone, stimulates secretion of testosterone in the male fetus. It is produced by the trophoblast. HCG is detectable in urine in 14 days after fertilization and it is used for pregnancy diagnostic tests);

- ***human chorionic somatomammotropin*** (stimulates breast development and activates lipolysis and increases maternal blood glucose levels);

- ***relaxin*** (inhibits uterine motility);

- ***estrogens*** (maintain pregnancy);

- ***progesterone*** (maintains pregnancy).

3. Materials for auditory self-work.

Task 1. Pregnancy test

It is based on determination of human chorionic gonadotropin in the urine. The liquid front moves further and reaches a region where another immobile antibody is bound: Ab3 recognizing Ab1. When binding occurs here, this also triggers an enzymatic reaction leading to the appearance of a coloured line. The presence of this line proves that the urine sample moved all the way along the assay strip (Fig.80.).

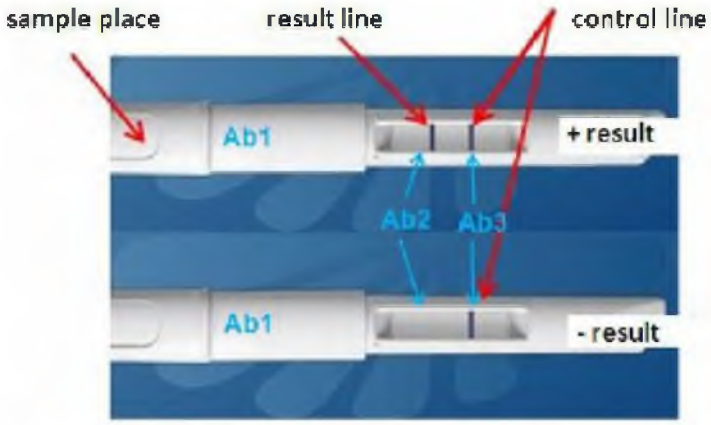


Fig.80. Pregnancy test.

4. Materials for self-control:

Control questions:

1. Hormones of adrenal cortex.
2. Hormones of adrenal medulla.
3. Hormones of testes, ovaries and placenta.

Content module 8: Sensory systems physiology. Special senses.

Lesson 23. Visual sensory system investigation.

Before performing this lesson, you should study the introductory material presented here.

1.Lecture course.

2.Moroz V.M., Shandra O.A. Physiology. - 2011. Unit XII, Chapters 35, 36.

3.Guyton A.C., Hall J.E. Textbook of Medical Physiology. - 2011. Unit IX, Chapters 50-53.

Relevance of the topic.
The visual system is sensory system that gives more information than others. The eyes gather information about the environment and brain form an image. Loss vision may represent a significant disability.

1. Objectives:

To know: the optical system of the eye and mechanisms of the focusing of an image on the retina; the molecular processes of photosensory transduction; modern theory of colour vision.

To be able to: draw the visual neuronal pathways; identify the layers of the retina; determine distance visual acuity, near point of vision.

2. Topic content.

Visual system

Anatomy of the eye:

Three coats of the eye (Fig.81.):

a. Outer fibrous layer (cornea and sclera);

b. Middle vascular layer or uvea (choroid, iris, and ciliary body);

c. Inner nervous layer (retina).

The eye consists of anterior, posterior, and vitreous chambers. The anterior and posterior chambers of eye are filled with aqueous humour. It is produced by the ciliary body and enters the posterior chamber and then anterior chamber through pupil. It is reabsorbed to canal of Schlemm and venous plexus. Aqueous humour supplies nutrition to cornea and lens and maintains intraocular pressure.

Clinical correlation

The normal intraocular pressure is 10-18 mm Hg. An increase in intraocular pressure due to obstruction of the outflow of aqueous humour is **glaucoma** (the peripheral vision is affected first).

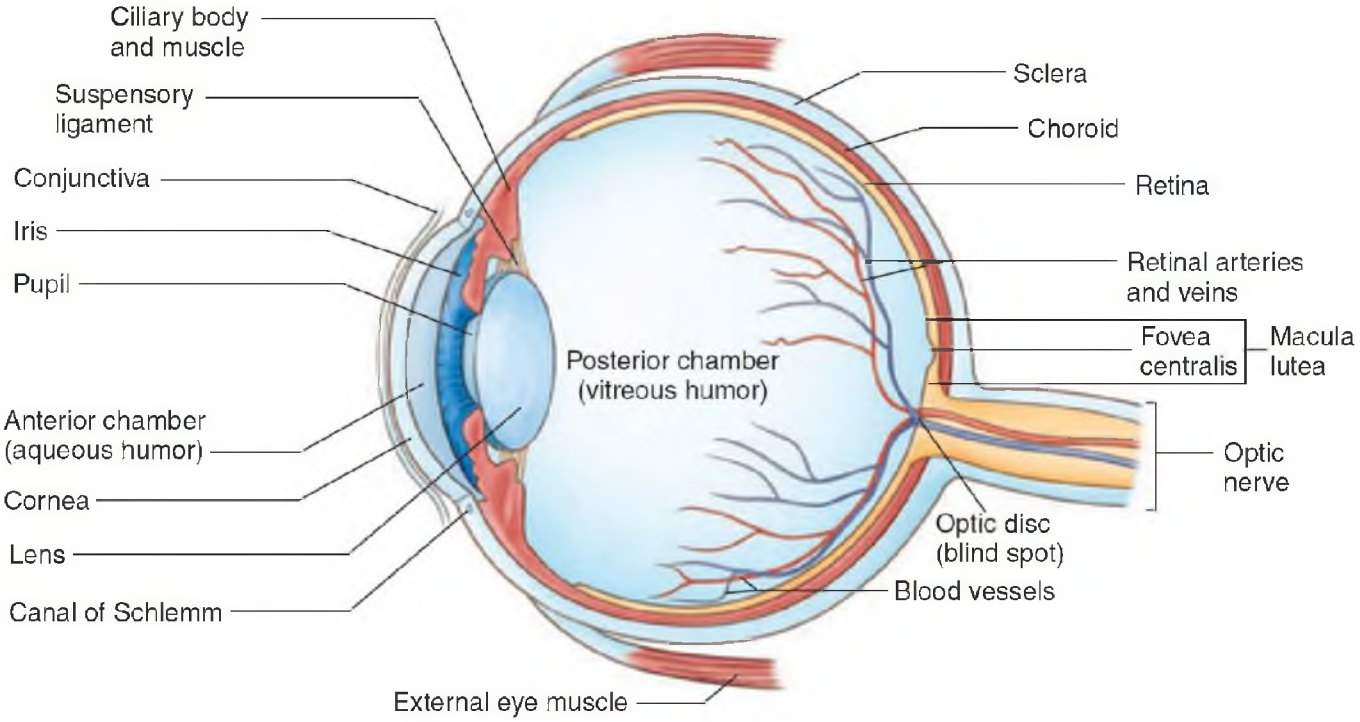


Fig.81. Anatomy of the eye.

Eye Optics:

The optical apparatus includes the cornea, the aqueous humour, the lens and the vitreous humour (Fig.82.). The light rays are bent and refracted to a point behind lens (**principal focus**). The distance between the principal focus and lens is the **principal focus distance**.

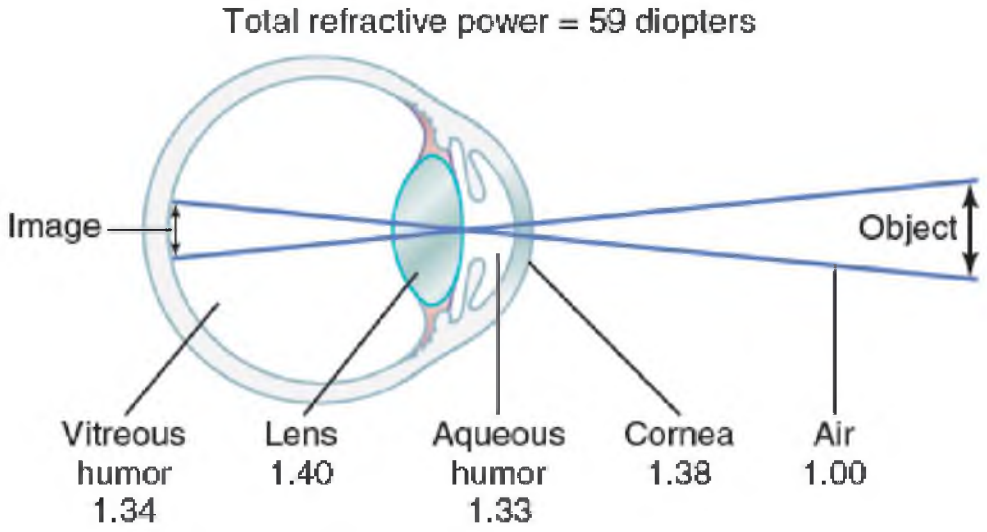


Fig.82. Optical components of the eye.

The total refractive power of the eye is 60 dioptres (D) at rest; most of refraction occurs as light passes through the cornea. Dioptre is equal to the reciprocal of the focal distance in metres.

The total refractive power of the lens can be changed from 13 D to 26 D.

Accommodation involves lens accommodation, pupil accommodation and convergence.

1. Lens accommodation is the process by which the curvature of the lens is increased**:**

a. when the lens is flat – far vision;

b. when lens is rounded – near vision.

The lens is held by circular lens suspensory ligament (zonular fibres) which is attached to ciliary body. Ciliary muscle contracts when the gaze is directed at near object. It relaxes zonular fibres and lens becomes more convex. The increasing of the lens curvature leads to the greater refractive power.

2. Pupil accommodation. The iris contains muscles that constrict or dilate the pupil. The pupil constricts (**miosis**) in the light to prevent the excessive entry of light. The pupil dilates (**mydriasis**) in the dark to allow more light to enter the eye.

The image is inverted and reversed with respect to the object. However, the mind perceives objects in the upright position despite the upside-down orientation on the retina because the brain is trained to consider an inverted image as the normal.

Clinical correlation

Common refractive defects (Fig.83.)

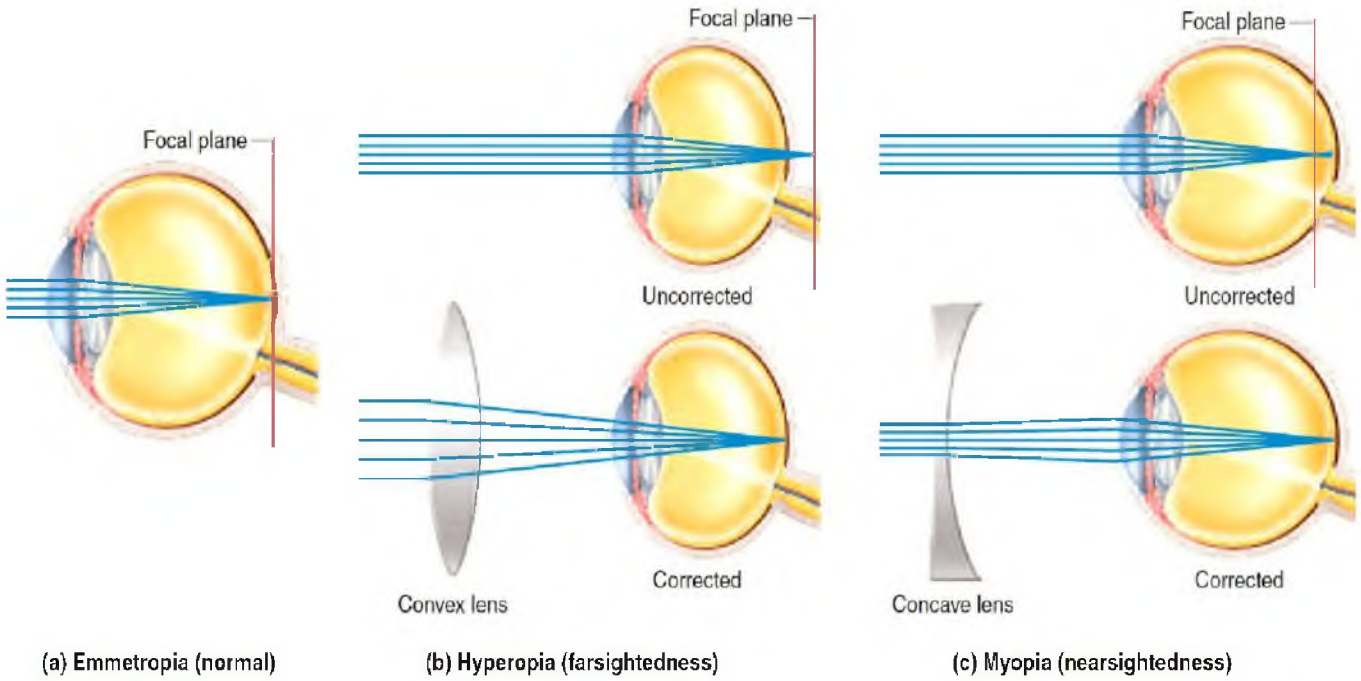


Fig.83. Defects of refractions and their correction.

1. **Presbyopia** – is reduced ability to accommodate for near vision with age; it is caused by declining flexibility of the lens.

2. **Astigmatism** – is inability to focus light rays that enter the eye on different planes due to uneven curvature of the cornea; corrected with cylindrical lenses;

3. **Hyperopia** or farsightedness – is inability to see the near objects clearly, the retina lies in front of the focal point of the lens due to shortening of axis of the eye; corrected with convex lenses, which cause light rays to converge.

4. **Myopia** or nearsightedness – is inability to see the distant objects clearly, the light rays are focused in front of the retina due to lengthening of axis of the eye; corrected with concave lenses, which cause light rays to diverge.

Retina – is the light-sensitive portion of the eye, containing the cones, which are responsible for colour vision, and the rods, which are mainly responsible for vision in the dark. Human eye can detect light rays of 370-740 nm.

Cells of retina (Fig.84.):

1. a three-neuron chain provides direct flow of visual information:

a. **photoreceptors**: sensory transducers; two main types - **rods** and **cones**;

b. **bipolar cells**: interneurons between photoreceptor and ganglion cells;

c. **ganglion cells**: their axons form the optic nerve (generate action potentials): on-centre/off-surround cells and off-centre/on-surround cells.

2. lateral interactions (e.g. lateral inhibition) are mediated by:

a. **horizontal cells**: between photoreceptors and bipolar cells;

b. **amacrine cells**: between bipolar cells and ganglion cells.

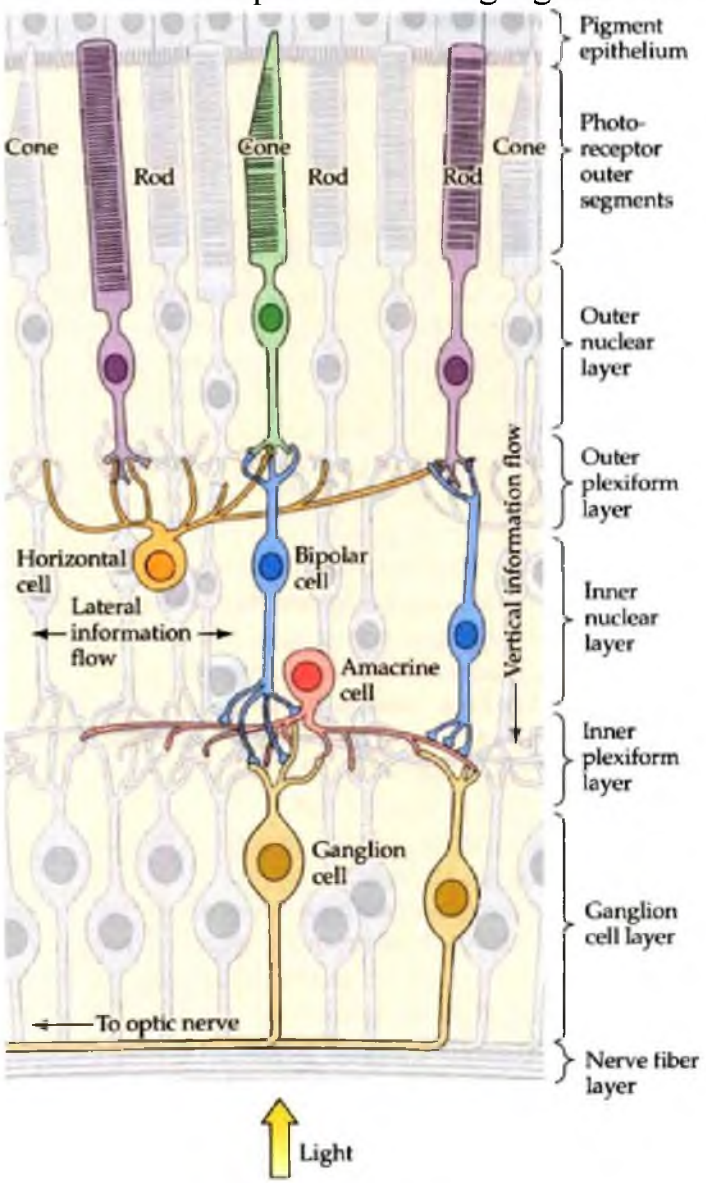


Fig.84. Retina.

Each eye contains about 120 million rods and 6 million cones. **Macula lutea** is small area in the retina which contains only cones. It is responsible for acute and detailed vision. Centre of macula is **fovea centralis**, region of the greatest visual acuity. There are no cones or rods in the **optic disc** (blind spot).

Visual pigments – these are light-sensitive chemicals that decompose on exposure to light and excite nerve fibres leading from eye. Rods contain rhodopsin (consists of opsin and 11-cis-retinal).

Phototransduction (Fig.85.):

1. **In the dark**: the photoreceptors are **depolarized** (approximately -40 mV).

a. high cGMP level leads to opening of cation (Na^+/Ca^{2+}) channels;

b. cations influx (dark current) keeps the rod in a depolarized state.

2. **In the light**: the photoreceptors are **hyperpolarized** (about -65 mV).

a. absorption of a photon of light by rhodopsin causes change in configuration from 11-cis-retinal to 11-trans isomer and generates metarhodopsin II;

b. ↓cGMP level and closure of the cation-selective channels lead to hyperpolarization.

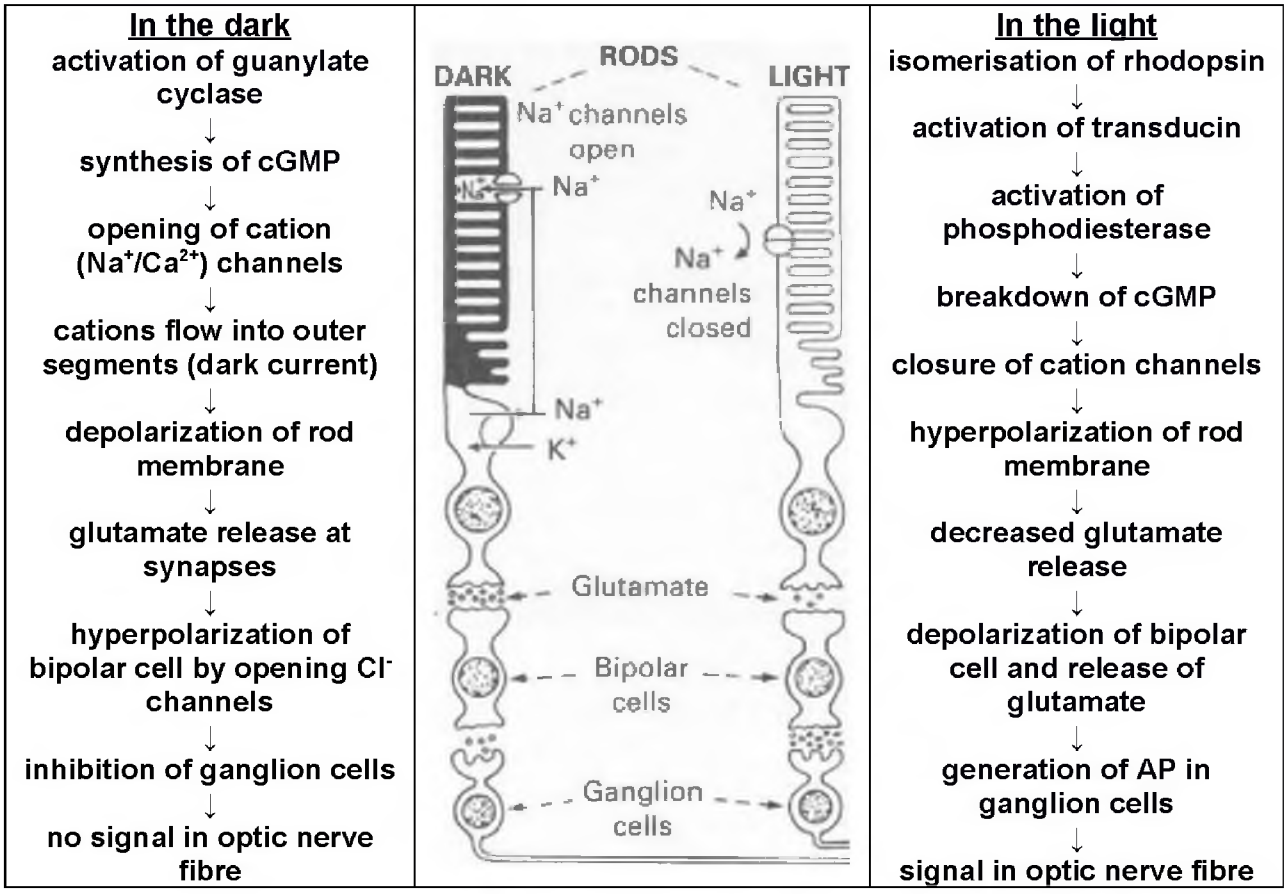


Fig.85. Phototransduction.

Rods and cones make different contributions to visual activity:

1. **scotopic vision**: very low level of illumination (only rods are activated);
2. **mesopic vision**: low level of illumination (both rods and cones are activated);
3. **photopic vision**: moderate and high levels of illumination (only cones are activated).

Interpretation of colour in the nervous system

Colour vision is based on three types of cones (Fig.86.):

1. short-wavelength (S) or **blue cones** (peak sensitivity at 420-440 nm);
2. medium-wavelength (M) or **green cones** (peak sensitivity at 531-555 nm);
3. long-wavelength (L) or **red cones** (peak sensitivity at 558-580 nm).

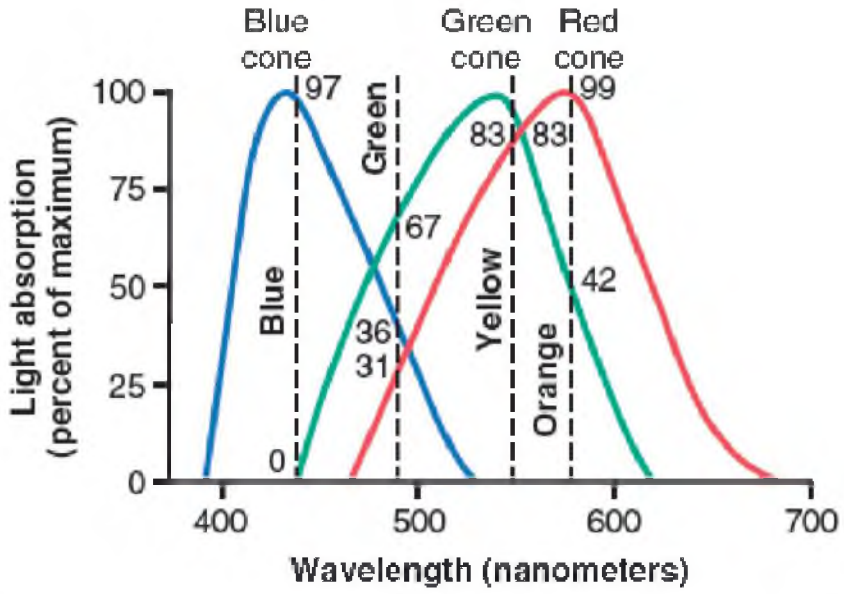


Fig.86. Stimulation colour-sensitive cones by monochromatic lights.

Clinical correlation

Night blindness (nyctalopia) is caused by significant deficiency of dietary vitamin A (also leads to xerophthalmia).

Colour blindness is genetic disorder and more common in males. Individuals with normal colour vision are called trichromats. Dichromats are individuals with only two cone systems; they may have protanopia, deuteranopia, or tritanopia.

Protanopia – loss of red cones.

Deuteranopia – loss of green cones.

Tritanopia – loss of blue cones.

The visual pathways

After nerve impulses leave the retina they pass backward through the optic nerves (Fig.87.):

1. Ganglion cell axons leave the retina at the optic disk and form the optic nerve.
2. About half of the optic nerve fibres cross the midline in the **optic chiasm** and project to the contralateral hemisphere; the other half stay ipsilateral;
3. Ganglion cell axons from the ipsilateral temporal hemiretina and contralateral nasal hemiretina form the **optic tract**.
4. axons exit the optic tract and terminate in the diencephalon and midbrain:

a. diencephalon:

- **lateral geniculate nucleus** (LGN) in the thalamus, relays visual signals through **optic radiation** to the **primary visual cortex;**
- **suprachiasmatic nucleus** of the hypothalamus, responsible for endogenous circadian rhythms;

b. midbrain:

- **superior colliculus,** involved in coordinating orientating responses to a visual stimulus;

- pretectum, involved in pupillary light reflex.

5. the principle projection to the visual parts of the cerebral cortex originates in the LGN and terminates in **primary visual cortex V1**, **Brodmann's Area 17** (also called the "striate cortex"), which is located in the banks of the **calcarine fissure** of the occipital lobe.

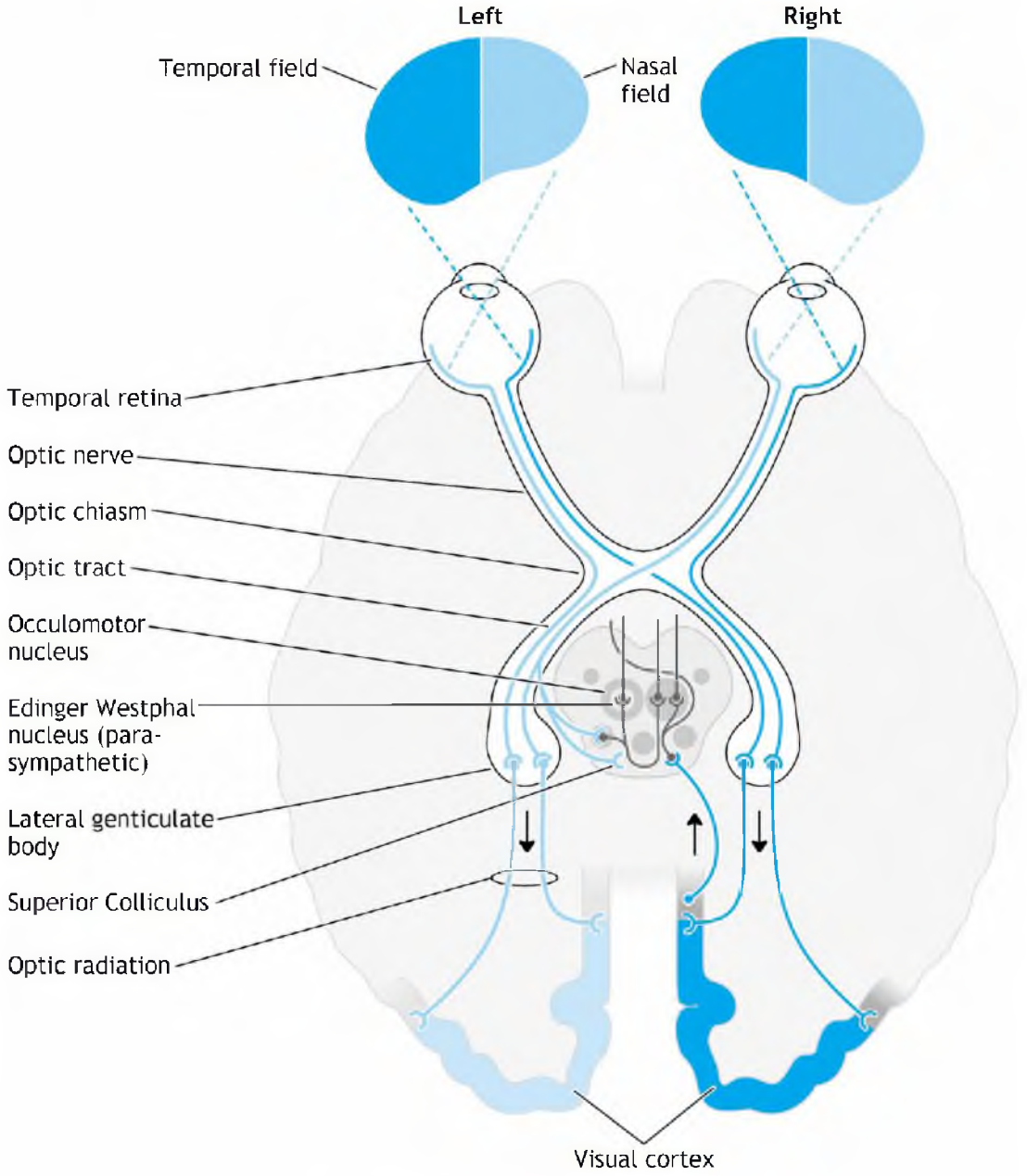


Fig.87. The visual pathways.

The **visual field** (Fig.88.) is the part of the surroundings from which the eyes can perceive light. It is what each eye sees. We divide the retina and the visual field in two halves: the temporal and the nasal parts.

Clinical correlation

Lesions of the optic pathways:

a. lesion of the optic nerve results in blindness in the ipsilateral eye;

b. lesion of the optic chiasm results in loss of vision in temporal fields (**bitemporal heteronymous hemianopsia**);
c. lesion of the optic tract results in loss of vision in the contralateral visual field (**homonymous hemianopsia**);
d. lesion of the primary visual cortex results in contralateral homonymous hemianopsia with **macular sparing** (loss of peripheral vision with intact macular vision).

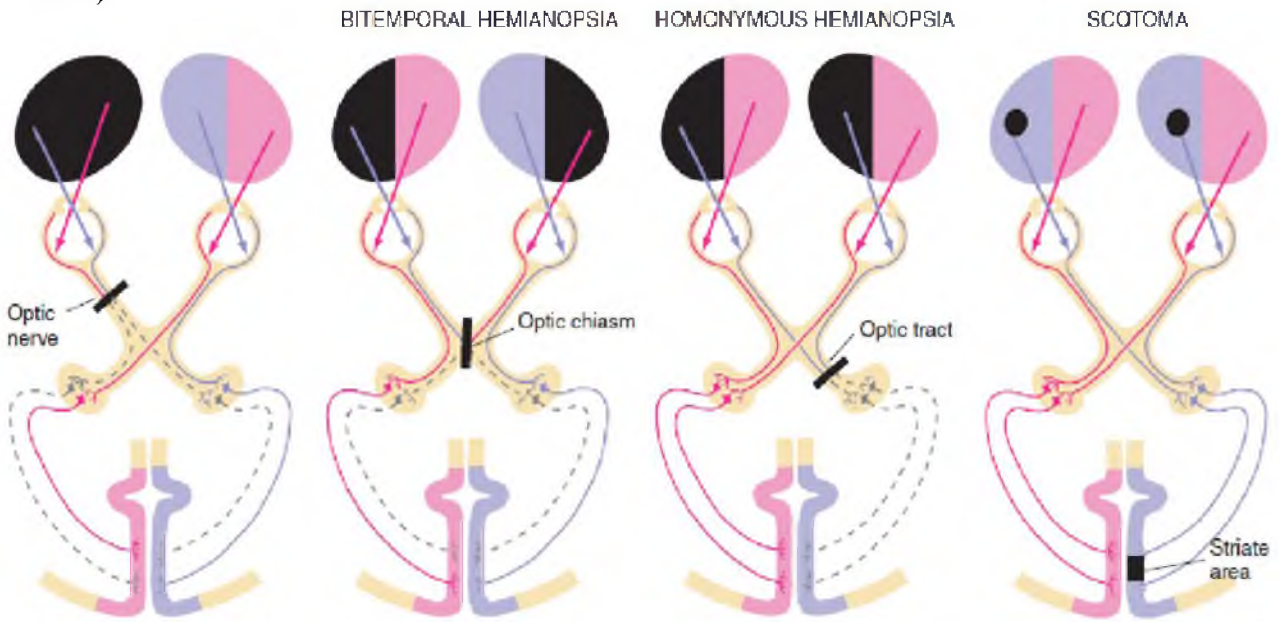


Fig.88. Optic lesions.

The central parts of the visual fields of the eyes coincide (**binocular vision**). Coordination of eye movements is very important for binocular vision. Eye movements is mediated by six muscles which are innervated by CN III (oculomotor), IV (trochlear), and VI (abducens): medial, lateral, superior, inferior, rectus musles, superior and inferior oblique muscles.

Types of eye movements:

1. Saccades (rapid movements when gaze fixes on object for a long time).
2. Smooth pursuit movements (when eyes follow moving objects).
3. Convergence movements (help to focus on near objects).
4. Vestibular movements (maintain visual fixation).

3.Materials for auditory self-work.

Task 1. Blind spot test.

Looking at Fig.89., hold the manual in both hands and extend both arms in front of you. Close your left eye. Keep your right eye open and focus on the dot. Slowly move the figure toward you. The X will disappear when it crosses your blind spot, but if you move the figure too fast, you will miss it.

Measure the distance the book is from your face when this happens. Then move the figure closer to your face, and the dot will reappear.

Blind spot distance for right eye: _____

Close your right eye. Keep your left eye open and focus on the X. Slowly move the figure toward you until the dot disappears. Measure the distance.
Blind spot distance for left eye: _____
Explain why the dot disappears and reappears.

Fig.89. Blind spot test.

Task 2. Test for visual acuity.

Stand 20 feet (6m) from the Snellen eye card (Fig. 90). Covering one eye, attempt to read the line with the smallest letters you can see. Walk up to the chart and determine the visual acuity (ability to distinguish between two-point light sources) of that eye. Repeat this procedure using the other eye.
An individual with normal visual acuity can read the line marked 20/20 from a distance of 20 feet.

Fig.90. Snellen acuity card.

Task 3. Test for astigmatism.

Stand about 20 feet away from an astigmatism chart (Fig.91.) and cover one eye. This chart consists of a number of dark lines radiating from a central point, like spokes on a wheel. If astigmatism present, some of the spokes will appear sharp and dark, whereas others will appear blurred and lighter because they are coming to a focus either in front of or behind the retina. Repeat this procedure using the other eye.

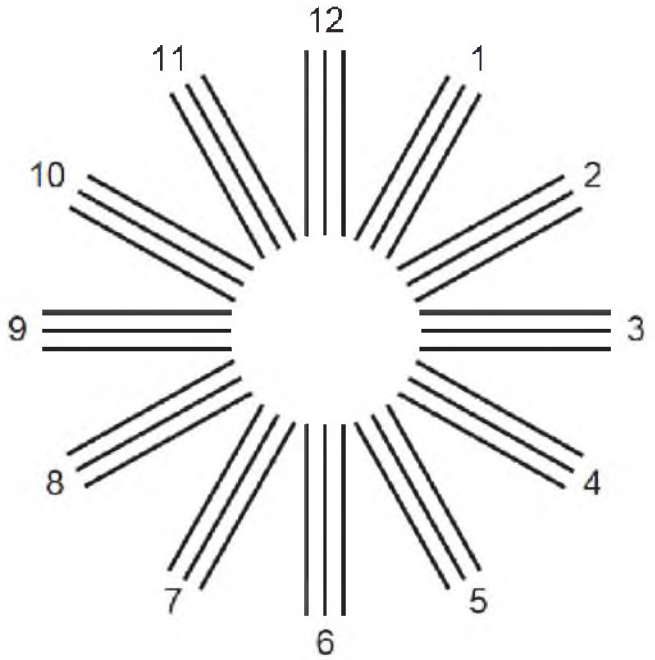


Fig.91. Astigmatism chart.

4.Materials for self- control:
Control questions:
1. Eye optic system characteristics.
2. Eye refraction and accommodation mechanism.
3. Pupil retraction, its mechanism and role.
4. Retina structure and its separate layers function.
5. Eye light sensitivity and adaptation.
6. Coloured vision.
7. Binocular vision.

Lesson 24. Auditory and vestibular sensory systems investigation.

Before performing this lesson, you should study the introductory material presented here.

1.Lecture course.

2.Moroz V.M., Shandra O.A. Physiology. - 2011. Unit XII, Chapters 35, 36.
3.Guyton A.C., Hall J.E. Textbook of Medical Physiology. - 2011. Unit IX, Chapters 50-53.

Relevance of the topic.
The outer, middle ear, and cochlea of the inner ear detect sounds. The utricle, saccule, and semicircular canals maintain balance and equilibrium. Both sensory systems contain specialized receptors called hair cells which convert mechanical energy into neural impulses. They provide the important information about environment.

1. Objectives:
To know: the structure and function of the external, middle, and inner ear; the anatomy of the vestibular labyrinth; explain the sensory transduction in auditory hair cells and in the vestibular labyrinth; the vestibular and auditory pathways; the organization of the vestibular and auditory cortex.
To be able to: Draw the vestibular and auditory neuronal pathways; identify the major structures of the cochlea; perform main tests that are used to determine the cause of hearing loss.

Vestibular sensory system

The vestibular system maintains balance and equilibrium by detecting movement (linear and angular acceleration) or change position of the head in space. Also, the vestibular system promotes stable visual fixation during head or whole body movement. Moreover, it contributes in sense of orientation in space (with visual information and somatic sensory proprioception).

Vestibular apparatus

Vestibular apparatus, also called the **membranous labyrinth**, is located in the bony labyrinth of the temporal bones. It is filled with endolymph (high K^+ / low Na^+) and surrounded by perilymph (low K^+ / high Na^+).

The membranous labyrinth consists of:

A. Two **otolith organs** (the **saccule** and the **utricle**) which detect linear acceleration and head position relative to the gravity;

B. Three perpendicular **semicircular canals**: horizontal (lateral), superior (anterior), and inferior (posterior) which detect angular (rotational) acceleration.

Sensory transduction

There are **hair cells** in otolith organs and semicircular canals that transduce mechanical signal (motion or change position of the head) into neural impulses.

A. The **utricle and saccule** contain sensory area called a **macula** which consists of hair cells and overlying gelatinous mass (**otolith membrane**) in which **otoliths** (crystals of calcium carbonate) are embedded.

Change of head position causes the otoliths and otolith membrane to slide relative to the epithelium. It displaces of the hair cells stereocilia and leads to *tonic* depolarization.

Linear acceleration causes shift and leads to *phasic* depolarization.

Utricle is orientated horizontally and detects acceleration forward and backward.

Saccule is orientated vertically and detects acceleration up or down.

B. The hair cells of **semicircular canals** are located in the **ampulla** which contains **cristae** (sensory epithelium) and overlaying gelatinous mass (called **cupula**). Hair processes (one **kinocilium** and many **stereocilia**) protrude into cupula. They are stimulated mechanically by the starting or stopping of rotatory head movements. The inertia of endolymph causes shift of the cupula in the opposite direction to the direction of rotation. The rotation in one direction leads to depolarization (if the stereocilia bend toward the kinocilium) or hyperpolarization (if the stereocilia bend away from the kinocilium).

The horizontal canal detects turning (e.g. shake head for "no").

The superior canal detects forward and back rotation (e.g. shake head for "yes").

The posterior canal detects left-to-right rotation (e.g. head tilt, a cartwheel).

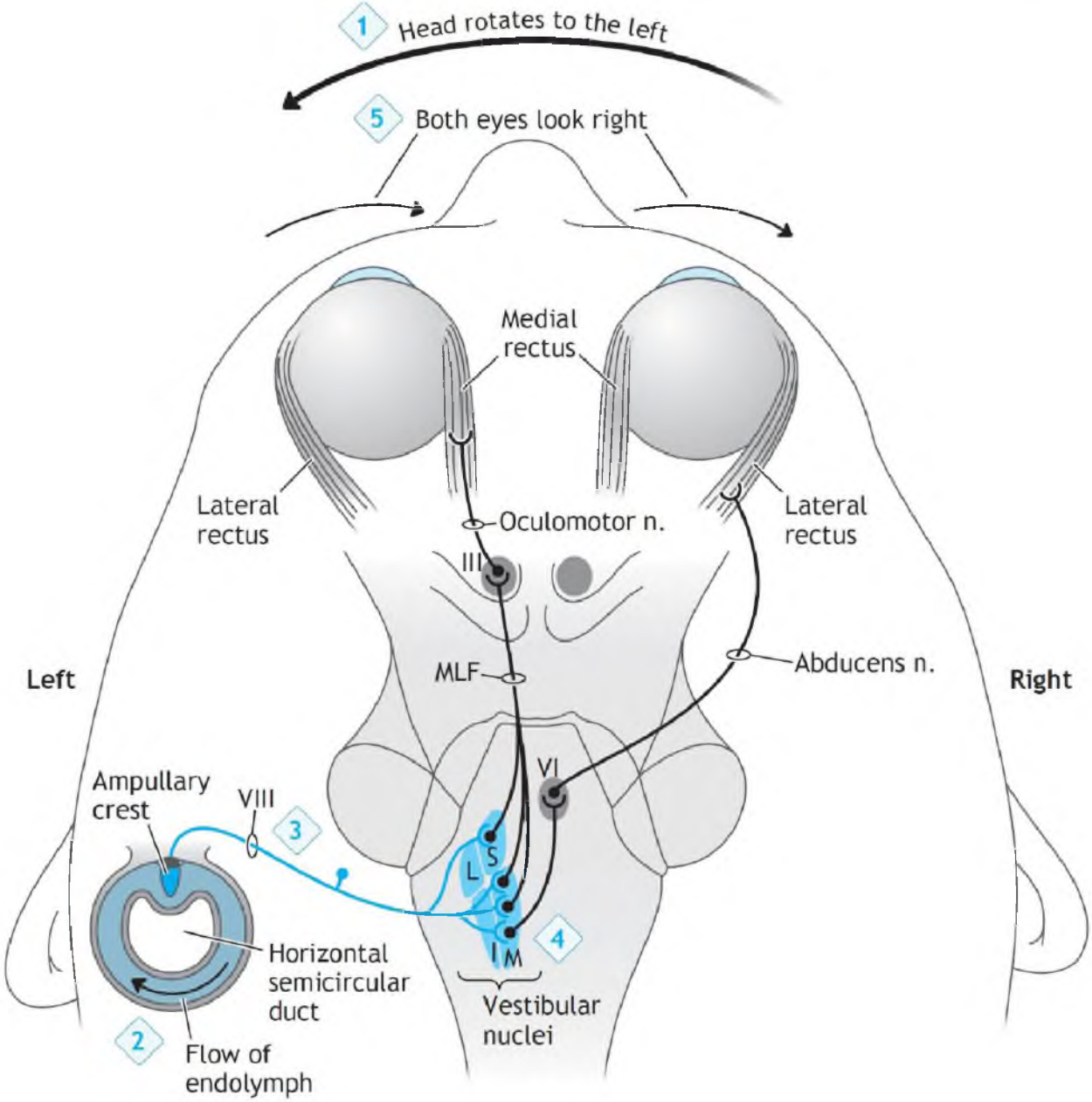


Fig.93. Vestibulo-ocular reflex.

The vestibular pathways (Fig.94.):

1. The first order neurons: **Scarpa's** or **vestibular ganglia** (vestibular portion of VIII cranial nerve which project to vestibular nuclei and cerebellum).

2. The second order neurons: **vestibular nuclei** in the medulla and pons (lateral (Deiters), medial, superior and inferior).

3. The third order neurons: the ventral posterior nuclei of the thalamus.

4. The neurons of the thalamus project to somatic sensory cortex (Brodmann's area 3a and 2) and parietal cortex (Brodmann's area 5).

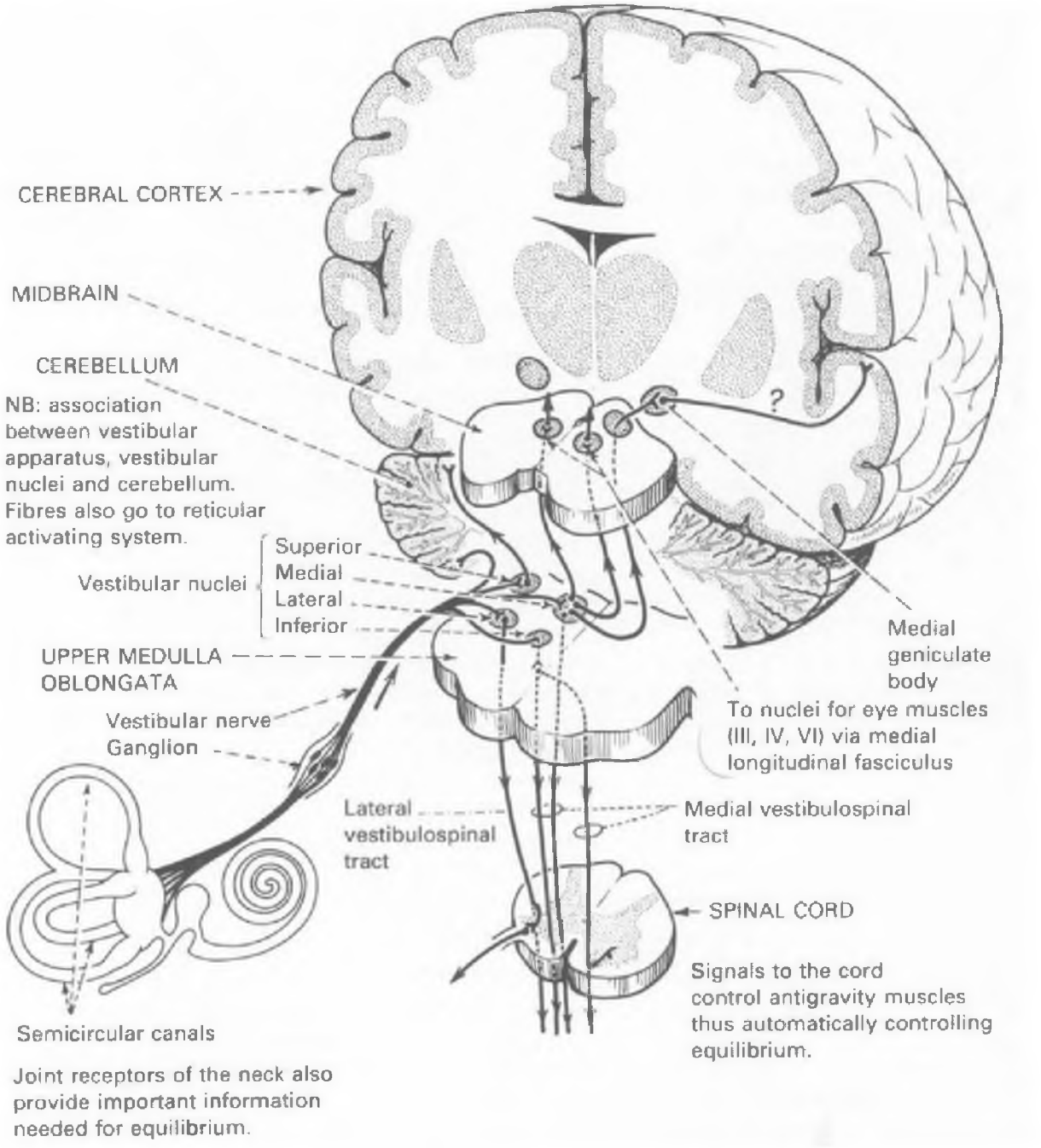


Fig.94. Vestibular pathways.

5. Other vestibular projections:

a. descending **medial and lateral vestibulospinal pathways** to spinal cord occur **postural reflexes** controlling equilibrium (medial pathway regulates head and neck position, lateral – excites extensor muscles);

b. excitatory projections to the contralateral abducens nucleus and inhibitory projections to the ipsilateral abducens nucleus through medial longitudinalis fasciculus (**vestibulo-ocular reflex**) (Fig.93.);

c. **vestibulocerebellar tract** or directly to flocculonodular lobe of cerebellum (regulates balance and eye movements);

d. output to autonomic centers in the reticular formation (mediates nausea).

Clinical correlation

Motion sickness can be explained by sensory conflict during adaptation to linear and rotational acceleration. It leads to dizziness, nausea, vomiting, and **vertigo** (false sensation of rotation in the absence of actual rotation).

Meniere's disease is an inner ear disorder caused by irritation of the vestibular labyrinth (endolymphatic hydrops). It is associated with attacks of dizziness, nausea, vomiting, vertigo, vestibular **nystagmus** (slow rhythmic oscillation of the eyes to one side followed by fast reflex movement of the eyes in the opposite direction), hearing impairment, and **tinnitus** (ringing in the ears).

Auditory sensory system

Hearing – is the sense by which sounds are perceived.

Sound: Vibrating air molecules generate spherical pressure waves that are characterized by their amplitude (loudness), frequency (pitch) and phase (temporal displacement). Humans can detect sound in the frequency range from 20 Hz to 20000 Hz. Intensity of sound is measured in **decibels** (dB). $dB = 20 \log P/P_0$, where P - sound pressure, P_0 - reference pressure measured at the threshold frequency. Speech has an intensity of about 60 dB and frequency from 300 to 3500 Hz. Sounds more than 100 dB can damage the peripheral auditory apparatus.

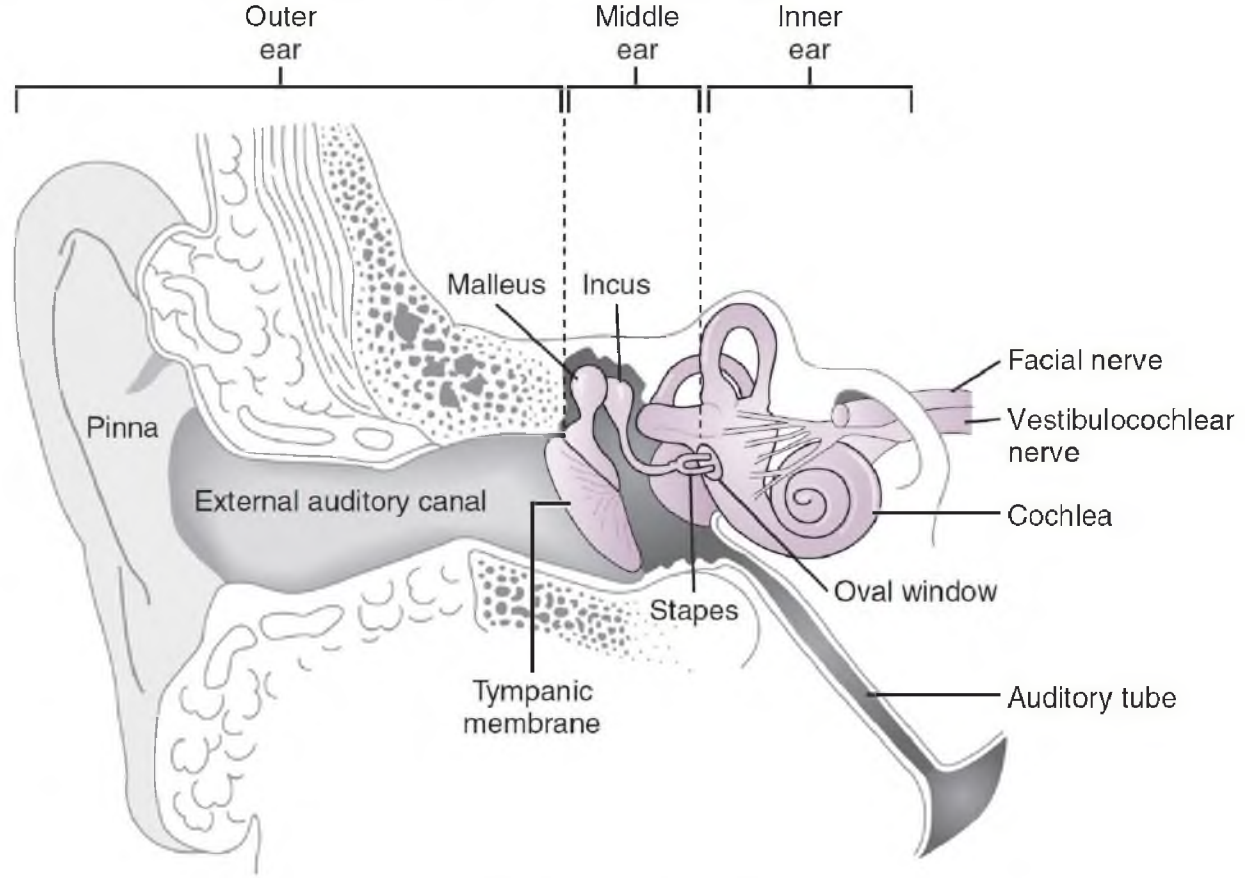


Fig.95. Anatomy of the ear.

Ear can be divided on 3 parts (Fig.95.):

1. **Outer ear** (pinna, the external auditory canal) gathers sound waves and directs them to the **tympanic membrane** (eardrum). It also plays a role in sound localization.

2. **Middle ear** (tympanic membrane, three **ear ossicles** (**malleus**, **incus**, and **stapes**)) transmits sound from air to the inner ear: sound waves cause the tympanic membrane to vibrate. In turn, the ossicles vibrate, pushing the stapes into the oval window and displacing fluid in the inner ear. The middle ear amplifies the pressure of acoustic energy by the lever action of the ossicles and the concentration of sound waves from the large tympanic membrane onto the smaller **oval window**.

There are two muscles in the middle ear: tensor tympani muscle pulls the malleus and decreases vibrations of the tympanic membrane; stapedius muscle pulls the stapes out of the oval window. Their action (**attenuation reflex**) protects the acoustic apparatus against damaging sounds, decreases sensitivity to own speech, and masks low-frequency sounds.

The middle ear opens via the **auditory (Eustachian) tube** into the nasopharynx. The tube opens during chewing, swallowing, and yawning, keeping the air pressure on the two sides of the tympanic membrane equalized.

3. **Inner ear** (bony labyrinth (semicircular canals, cochlea, and vestibule) and ducts called the membranous labyrinth, auditory nerve) transduces mechanical energy into neural signals to the brain.

Cochlea is small, coiled (2¾ turns) structure surrounded by bone, divided by **Reissner's membrane** and the **basilar membrane** into 3 fluid-filled channels (**scala vestibuli, scala tympani** and **scala media**). The cochlear partition terminates before the apical end of the cochlea, allowing for continuity between the scala vestibuli and scala tympani (at the **helicotrema**).

The cochlear partition contains the **organ of Corti**, which consists of the **basilar** and **tectorial membranes** (Fig.96.)**.** The basilar membrane supports inner and outer hair cells; the **inner hair cells** are the sensory receptor cells of the cochlea. The cochlear partition contains a smaller channel (scala media), which contains **endolymph** (with high levels of K^+).

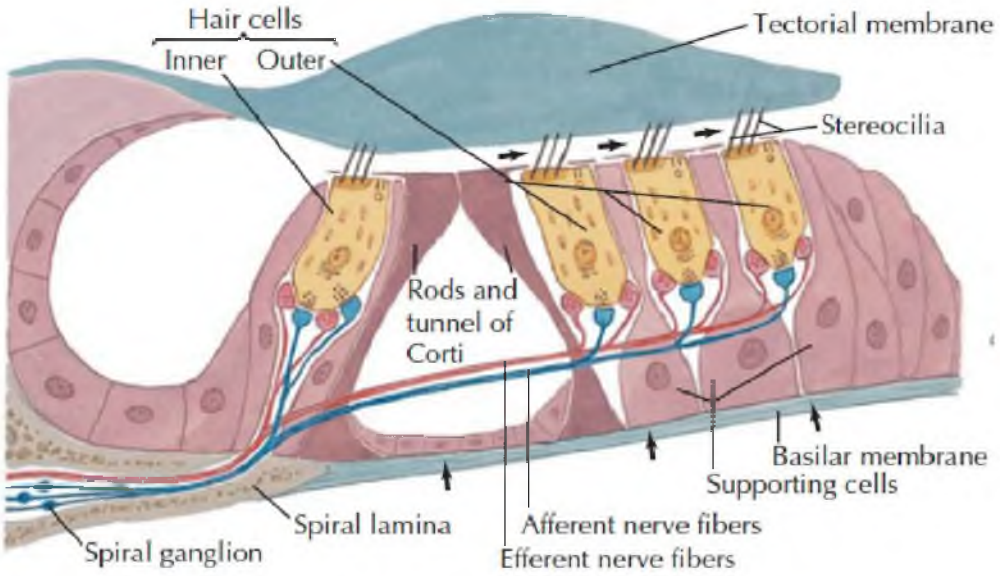


Fig.96. Spiral organ of Corti.

Sensory transduction:

a. vibration of the basilar membrane leads to shearing motion between basilar and tectorial membranes in which the stereocilia of hair cells are embedded;

b. motion bends the stereocilia, their deformation toward the longest stereocilia leads to inward flow of K^+ and depolarization;

c. depolarized hair cells release neurotransmitters and cause action potential in the auditory nerve;

d. deformation of the stereocilia away from the longest stereocilia leads to closure of K^+ channels and hyperpolarization.

Different sound frequencies stimulate hair cells in different parts of basilar membrane:

- high-frequency sound causes vibration at the base of the basilar membrane;
- low-frequency sound causes vibration at the apex of the basilar membrane.

The auditory pathways (Fig.97):

1. The first order neurons: in the **spiral ganglion** of the cochlear nerve (CN VIII).

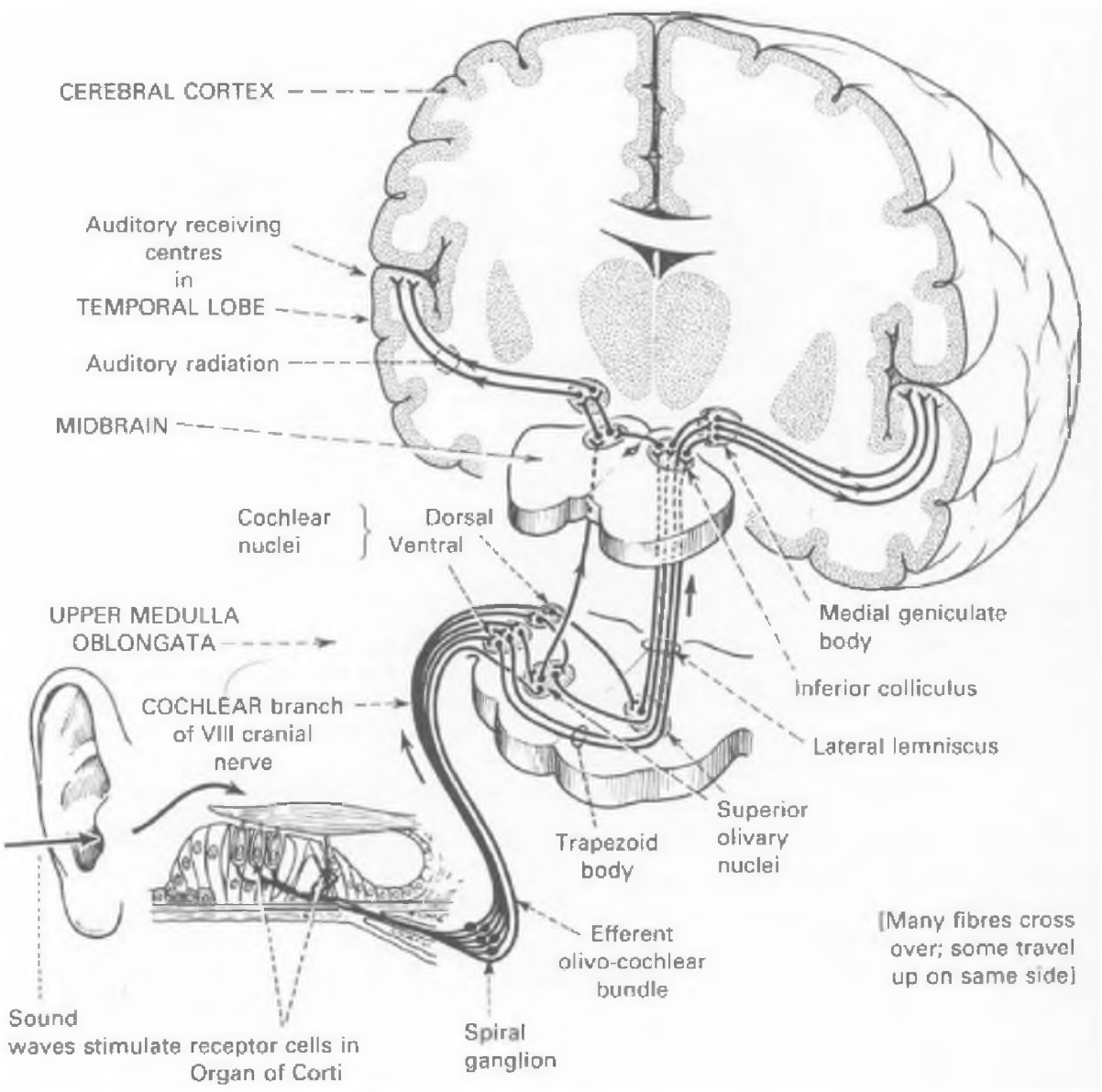


Fig.97. Auditory pathways.

2. The second order neurons: in the **cochlear nuclei** which project to targets on both sides of the brainstem:

- **medial superior olive** (sound localization is based on interaural timing differences);

- **lateral superior olive** (sound localization is based on interaural intensity differences);

- **inferior colliculus** (projection from lateral lemniscus is involved in coordinating orientating responses to an auditory stimulus).

4. The third order neurons: **medial geniculate body** project through internal capsule (**auditory radiation**) to the primary auditory cortex.

5. **Auditory temporal lobe cortex**:

- **primary auditory cortex** that receives highly tonotopic input from the medial geniculate body; also maps binaural interactions;

- additional, higher-order auditory areas (**Wernicke's area**, a division of the auditory cortex that is specialized for comprehending speech).

Clinical correlation

Conduction deafness is caused by impairment of external or middle ear (e.g. cerumen impaction, otitis media, and otosclerosis).

Sensorineural deafness results from damage to the inner ear, auditory nerve or auditory pathway.

Presbycusis is reduced ability to hear high-frequency sounds with age; it is caused by loss of hair cells in the organ of Corti.

3.Materials for auditory self-work.

Task 1. Weber test

Choose a subject from your group. Have the subject sit with the head erect and facing forward. Strike a tuning fork and place it medially on the subject's head (bone conduction). Ask the subject if the sound is equally loud in both ears or louder in one ear.

If the sound is equally loud in both ears, the subject either has normal hearing or bilateral deafness (equal hearing loss in both ears). If the subject has unilateral deafness, conduct the Rinne test to determine if hearing loss is conduction deafness.

Task 2. Rinne test

Strike a tuning fork and place it on the subject's mastoid process to test hearing by conduction. Ask the subject to tell you when the sound can no longer be heard. Immediately place the still-vibrating tuning fork close to the subject's ear to test hearing by air conduction. If the subject can hear the tuning fork again when it is placed next to his or her ear, the subject does not have conduction deafness in that ear (Tab.16.).

Table 16. Interpretation of auditory tests.

Test	Normal	Conduction deafness	Partial sensorineural deafness
Weber test: sound is heard better	equally loud in both ears	in the affected ear	in the unaffected ear
Rinne test: better conduction (air or bone)	air > bone, both ears	bone > air in the affected ear; air > bone in the unaffected ear	air>bone, both ears

4.Materials for self-control:

Control questions:

1. Structure of vestibular apparatus.
2. Sensory transduction in semicircular canals and otolith organs.
3. Vestibular pathways.
4. Anatomy and function of the inner, middle, and inner ear.
5. Excitation process formation in auditory analyzer.
6. Auditory pathways.
9. Binaural hearing, its physiological importance.
10. Types of deafness.

Content module 8: Behaviour physiological bases. Higher nervous activity.

Lesson 25. Conditioned reflexes formation and inhibition investigation. Behaviour congenital and innate forms investigation: attention, learning and memory, motivations and emotions, thinking, and consciousness.

Before performing this lesson, you should study the introductory material presented here.

1.Lecture course.
2.Moroz V.M., Shandra O.A. Physiology. - 2011. Unit XIII, Chapter 38.
3.Guyton A.C., Hall J.E. Textbook of Medical Physiology. - 2011.

Relevance of the topic.
Conditioned reflexes form the basis of learning and give better adaptation. Conditioned reflexes prepares person for future activities (e.g. eating, avoidance of danger). They mat be applied in clinical and psychological practice. Higher nervous functions are very essential to make up the human mind.

1. Objectives:
To know: differences of conditioned reflexes and unconditioned reflexes, classification of conditioned reflexes, conditioned reflexes formation and inhibition mechanisms, higher brain functions physiological mechanisms,.
To be able to: perform conditioned reflex in human being, to draw schematically reflectory arc of conditioned reflex, to assess higher brain functions in a person.

2. Topic content.

Unconditioned reflexes are individual and specific stereotype reactions of organism on the outside and inside irritants, which are fastened genetically and realized with the help of CNS. Complicated unconditioned reflexes are instincts.

Conditioned reflex is a systemic adaptive reaction, individually acquired during life or special study and based on the temporary connection between conditioned irritant and unconditioned action. This is individual experience acquirement due to environment variation. Associative or conditioned experience acquirement takes special place among these behavioural forms. Conditioned reflexes are formed at definite conditions of organism ontogenesis and are disappeared at their absence comparatively to unconditioned reflexes (Tab.17.). Complicated conditioned reflexes are dynamic stereotype.

Table 17. Difference between the conditioned and unconditioned reflexes

Unconditioned reflex	Conditioned reflexes
Inborn reflexes	Acquired after birth
Have species specificity	Have individual specificity
Constant	Temporary
Elicited by adequate stimuli	Elicited by varied stimuli
Receptive field is determined	There is not a certain receptive field
Involve brain stem and spinal cord	Involve brain cortex
Form on the basis of genetic program	Form on the basis of unconditioned reflexes
Provide survival of species	Provide behaviour and higher nervous activity

Classification of conditioned reflexes

I. <u>According to biological importance</u>:

1 nutritional;

2. defensive;

3. homeostatic.

II. <u>According to reflex reaction</u>:

1. somatic (motor);

2. visceral.

III. <u>According to receptors</u>:

1. exteroceptive;

2. interoceptive;

3. proprioceptive.

IV. <u>According to a way of formation</u>:

A. **Classical conditioned reflexes** (they are established by a conditioned stimulus (CS), followed by an unconditioned stimulus (UCS)) (Fig.98.):

1. ***Primary*** (1 unconditioned stimulus + 1 conditioned stimulus);

2. ***Secondary*** (1 unconditioned stimulus + 2 conditioned stimuli);

3. ***Tertiary*** (1 unconditioned stimulus + 3 conditioned stimuli).

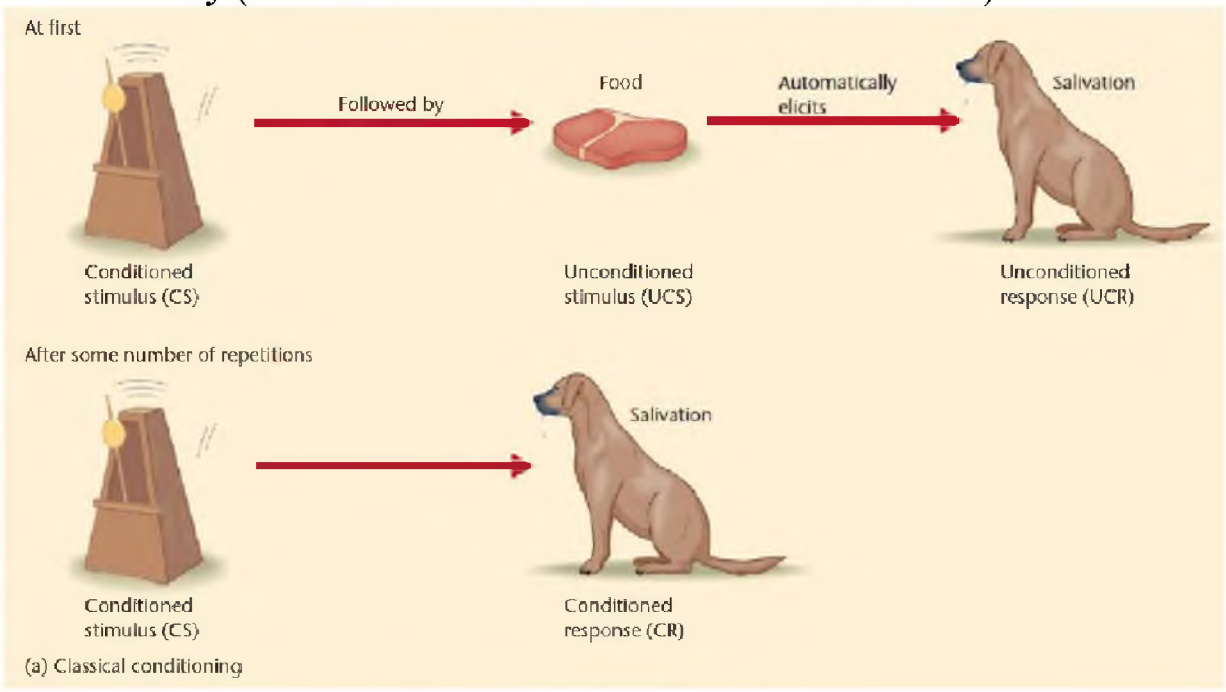


Fig.98. Classical conditioning.

B. **Instrumental or operant conditioned reflexes** (they are established by a conditioned stimulus, followed by a reward or a punishment).

Operant conditioning can be broken down into four types:

1. ***Positive reinforcement*** (when a behaviour is strengthened and the probability of it recurring increases because a positive was the result).

2. ***Negative reinforcement*** (when a behaviour is strengthened as a result of avoiding or stopping a negative condition).

3. ***Punishment*** (when a behaviour is weakened and the probability of the behaviour recurring decrease due to a negative condition).

4. ***Extinction*** (when a behaviour is weakened because the result did not lead to a positive condition or a negative condition).

V. <u>According to relation of conditioned and unconditioned stimulus</u>:

1. Natural (conditioned and unconditioned stimuli are connected, e.g. smell and taste of food);

2. Artificial (conditioned and unconditioned stimuli aren't connected, e.g. light or sound and food).

VI. <u>According to timing between CS and UCS</u> (Fig.99):

1. simultaneous,
2. forward;
3. traced;
4. delayed;
5. backward.

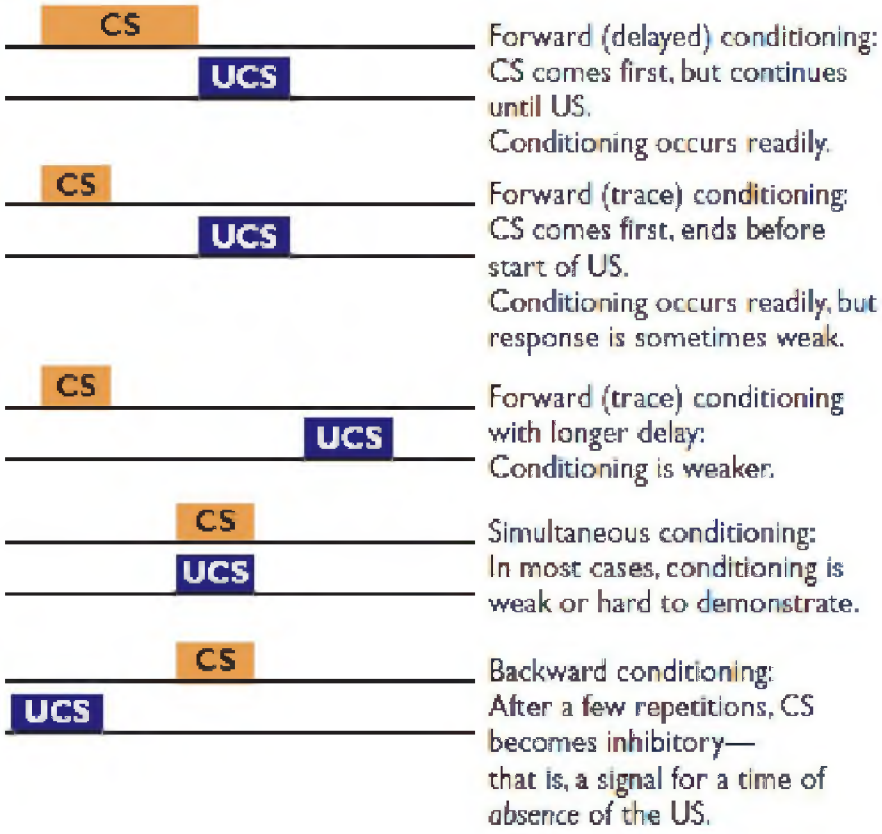


Fig.99. Types of conditioning.

Rules for formation of the conditioned reflexes

1. Coexistence in time, several times repeated, of the indifferent agent and the unconditioned stimulus;

2. The indifferent agent should somewhat precede (1-5 sec) the unconditioned stimulus;

3. Unconditioned stimulus should be stronger by its biological importance;
4. Conditioned stimulus should be indifferent;
5. Absence of other stimulus that could induce externally caused inhibition;
6. The animal should be healthy and active.
7. Stimuli from the visceral organs should be excluded;
8. The experiments should take place at the same time every day.

Stages of formation of the conditioned reflexes:

1. Stage of generalization;
2. Stage of specialization.

Acquired reactions constant change occurs in course of life. One conditioned reflexes are fixated, others disappear quickly and then after several time are restored. It is connected with conditioned reflexes inhibition appearance or working out.

Inhibition of conditioned reflexes

1. **Unconditioned (external)** (conditioned reflex is inhibited by simultaneous excitatory process):

a. **external** (result of action of new unconditioned stimulus that distracts attention and causes orienting reflex);

b. **transmarginal** (appears if the conditioned stimulus is too strong; it has protective function.).

2. **Conditioned (internal)** (inhibitory effects in the cortical centre of conditioned reflex):

a. **extinction** (if conditioned stimulus isn't reinforced by unconditioned stimulus for many times);

b. **differentiation** (if there are two similar stimuli and one of them isn't reinforced);

c. **delayed** (result of delay of the unconditioned stimulus);

d. **conditioned inhibitor** (combination of two conditioned stimuli isn't reinforced).

Phases of inhibition:

1. **paradoxal** (weaker stimulus causes stronger reaction);
2. **ultraparadoxal** (negative reflexes will perform the response, positive will be inhibited);
3. **equalizing** (stimuli with different strength cause equal response);
4. **inhibitory** (response will be less for all the stimuli).

Higher nervous activity

Gnosis is an ability to recognize and correctly interpret incoming stimuli in a particular sensory modality. Lesions of the association cortex can result in difficulty recognizing, identifying, and naming different categories of objects. These disorders are called agnosias.

Agnosia is an inability to recognize sensory stimuli even though sensation as such is intact.

1. visual agnosia is concerned is associated with damage to the occipital lobe (areas 18, 19). The patient without visual impairment cannot recognize objects on sight, but can name the object after feeling or hearing it.

2. tactile agnosia is an inability to recognize objects by touch (astereognosis if both hands are affected). It is associated with lesions of the parietal lobe (area 40).

3. auditory agnosia is an inability to recognize objects by sound and distinguish speech from non-speech sounds. It is associated with lesions of the temporal lobe.

4. prosopagnosia is the inability to recognize and identify faces (damage to the inferior temporal cortex).

5. autotopagnosia is difficulty recognizing parts of one's body.

Praxis is an ability to perform sequences of actions and goal-directed execution of complex actions.

Apraxia is disturbance in the goal-directed execution of complex actions or sequences of actions. Cortical lesions causing apraxia are usually on the left side.

1. ideomotor apraxia: the individual components of a single action cannot be put together correctly.

2. ideational apraxia: the individual actions can be performed, but cannot be combined into more complex sequences.

Cerebral asymmetry

Laterality is the idea that the two cerebral hemispheres have separate functions (Fig. 100, Tab.18.). One hemisphere is specialized in sequential-analytic processes (the **categorical** or **dominant** hemisphere), the other one – in visuospatial relations (the **representational** or **nondominant hemisphere**).

Hemispheric specialization is related to handedness. Damage of dominant hemisphere leads to aphasia, and dyscalculia; damage of nondominant hemisphere results in agnosia, astereognosis, and anosognosia.

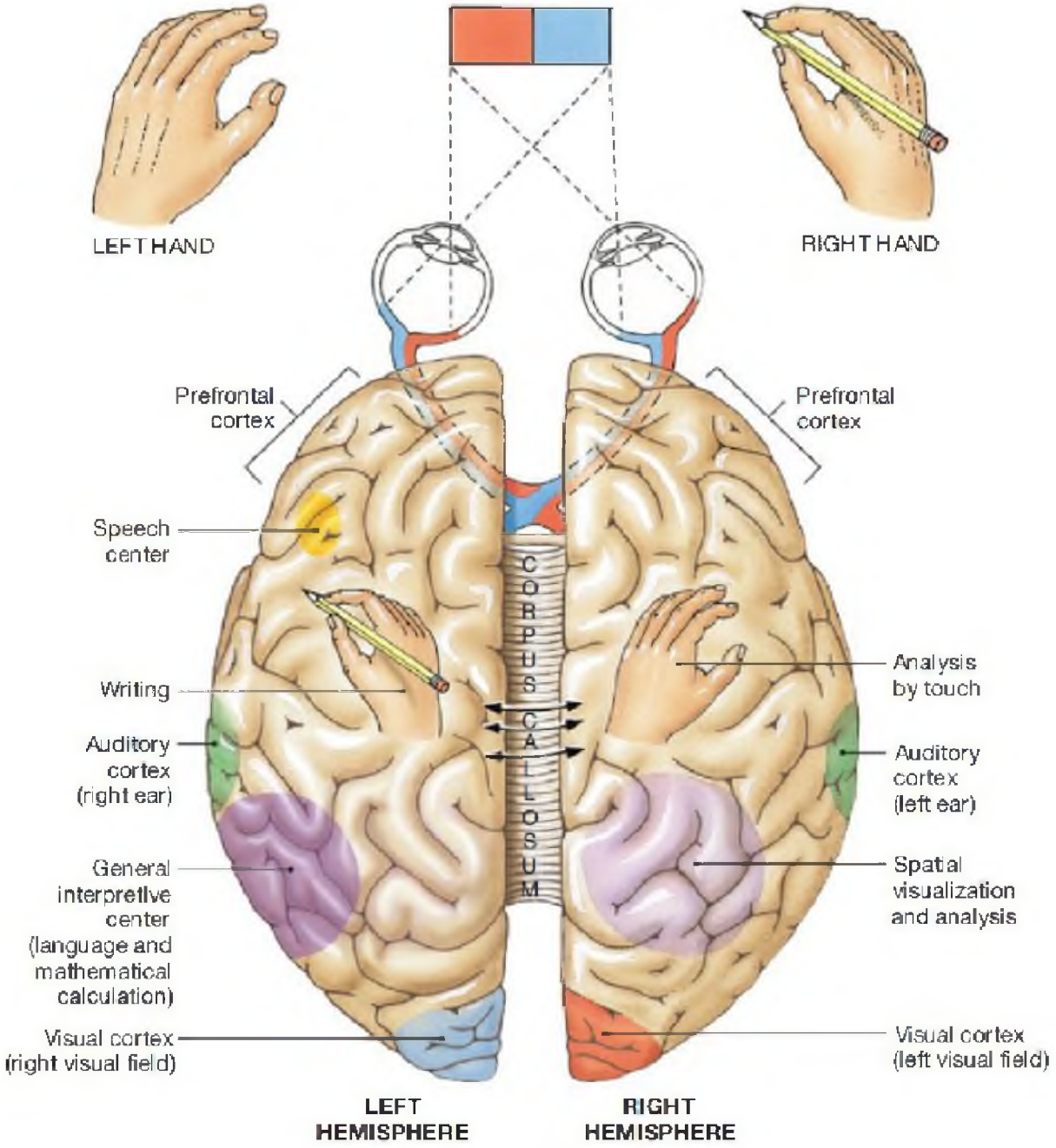


Fig.100. Cerebral laterization.

Table 18. Cerebral asymmetry.

Left hemisphere functions	Right hemisphere functions
Control movement on the right side	Control movement on the left side of the body
Analysis of right visual field	

Stereognosis (right hand)	Analysis of left visual field
Lexical and syntactic language	Stereognosis (left hand)
Producing and understanding language	Emotional colouring of language
Writing	Producing and perceiving nonverbal information
Speech	
Mathematical skill	Visuospatial orientation
Analytical ability	Rudimentary speech
	Imagination, insight
	Recognition of face, image

Learning is acquisition of the information and change in behaviour as a result of experience. According to social learning theory, there are four processes which influence learning: attention, motivation, behaviour, and memory.

Memory is the ability to retain and recall the information.

Classification of memory (Fig.101.):

I. **Sensory memory** (holds information <1sec).

II. **Short-term memory** (lasts seconds to hours).

III. **Long-term memory** (stores memories for years and sometimes for life):

1. **Explicit (Declarative)**:

a. ***Episodic*** (memory for events);

b. ***Semantic*** (memory for facts: words, language, rules).

2. Implicit (Nondeclarative):

a. ***Associative learning*** (classic and operant conditioning);

b. ***Non-associative learning*** (habituation and sensitization);

c. ***Priming*** (facilitation of recognition of words or objects by prior exposure to them);

d. ***Procedural memory*** (skills and habits).

The processing of information that converts short-term memory into long-term memory is known as **consolidation** and occurred in **hippocampus**.

Short-term memory is based on temporary memory trace in neural circuit (**reverberation**). **Working memory** keeps information available, usually for very short periods (18-20 sec), while the individual plans action based on it.

Long-term memory is a storage area capable of holding vast amounts of information. Basis mechanism of long-term memory is structural synaptic changes (development of new neuronal circuits by the formation of new synapses) and facilitation of synaptic transmission. It includes:

- post-tetanic potentiation;
- sensitization;
- habituation;

- long-term potentiation (LTP);
- long-term depression (LTD).

Long-term memory has been divided into two types that are consolidated and stored using different neuronal pathways.

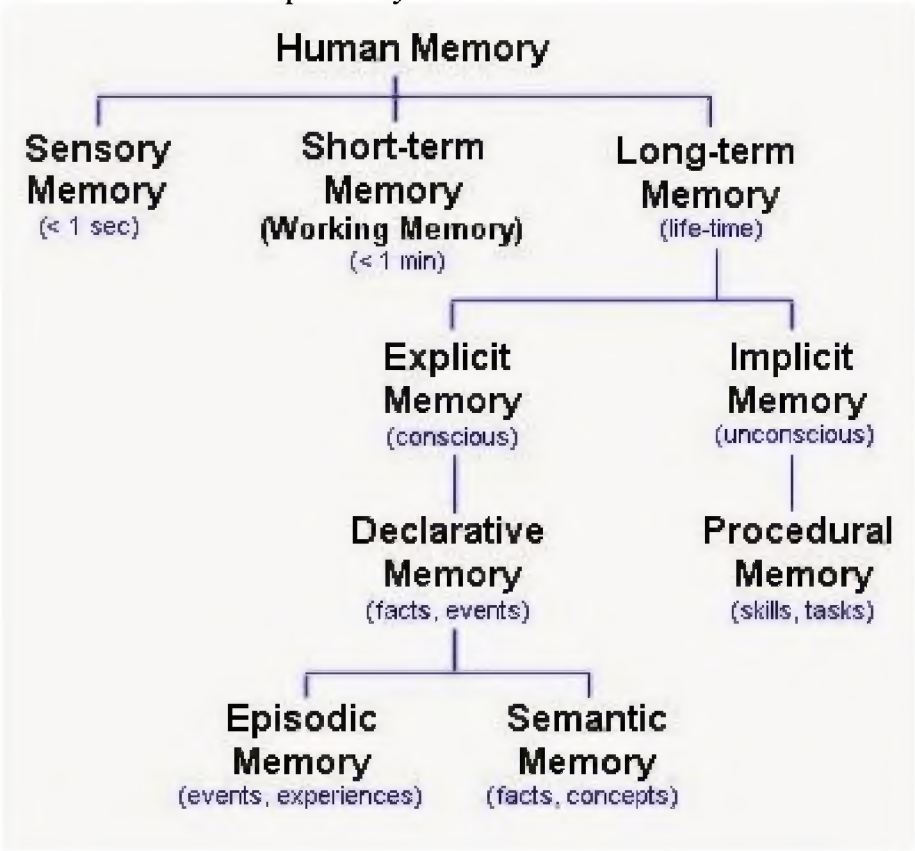


Fig.101. Types of memory.

Implicit memory, which is automated and does not require conscious processes for either creation or recall, involves the amygdale, striatum, cerebellum, motor cortex, and reflex pathways. Information stored in implicit memory is acquired slowly through repetition.

Explicit memory can be verbally expressed. It requires conscious attention for its recall. The neuronal pathways involved in this type of memory are in the temporal lobes of neocortex.

Clinical correlation

Amnesia– is the loss of memory.

Anterograde amnesia is inability to remember newly acquired information; amnesia for events that occur after some disturbance to the brain.

Retrograde amnesia is inability to remember events that happened before the brain damage occurred.

H.M.'s history. H.M. received the surgery (bilateral medial temporal lobectomy) in an attempt to treat his severe epilepsy and that caused anterograde amnesia. H.M. was extensively studied; his doctors discovered many mechanisms of formation of long-term memories (e.g. the hippocampus is involved in consolidation of memory and recalling of episodic memory).

Motivation is defined as internal signals (need or desire) to act a certain way to achieve a goal. They shape voluntary behaviour.

Properties: they create an increased state of CNS arousal or alertness, create goal-oriented behaviour, and they are capable of coordinating disparate behaviour to achieve that goal.

Maslow's hierarchy of motivations:

a. physiological;

b. safety needs;

c. love and belongingness;

d. esteem needs;

e. self-actualization needs.

Many motivated behaviours stop when the person has reached a certain level of satisfaction, or satiety, but they may also continue despite feeling satiated.

An emotional response consists of 3 components:

1. behavioural (muscular movements that are appropriate to the situation);

2. autonomic (facilitates the behaviours and provide quick mobilization of energy);

3. hormonal (reinforces the autonomic responses).

Emotions can be considered in terms of a relation between an individual and the environment based on the individual's evaluation of the environment, disposition toward the environment, and the actual physical response to it.

Brain structures for emotional processing

Two main structures in the ventral and medial forebrain—the so-called "limbic" forebrain (Fig.94.) - are critically involved in emotional processing: the **amygdala** and the **orbital-medial prefrontal cortex.**

Output to "downstream" effector systems involves both classical motor pathways (pyramidal system) and less-well defined (extrapyramidal) pathways that mediate emotional expression (recall the parallel pathways that govern emotional and volitional facial expressions).

Amygdala:

1. associates sensory stimuli with rewards and punishers;

2. especially important in threat/fear processing and fear-based social assessments;

3. deficits produced by amygdala lesions can be understood in terms of a failure of emotional associative learning and an absence of threat/fear signalling.

Orbital-medial prefrontal cortex:

1. involved in emotional processing, interpretation of social cues, planning appropriate social behaviour, and formation of advantageous decisions in real-life circumstances (≈ reason);

2. emotional learning, especially when primary reinforcers are scents and food;

3. involved in ongoing analysis and modification of behaviour when reinforcement contingencies are rapidly changing (emotional re-learning);

4. necessary for the assessment of future consequences and the implementation of advantageous decisions;

5. damage causes impaired emotional experience and expression, impaired rational decision making, especially in personal and social affairs, pathological inability to make advantageous decisions in real life situations.

Cognition means thinking, gaining knowledge, and using knowledge. Human cognition cannot deal with all the information that the world provides.

Thinking uses concepts (mental grouping of a set of objects or events on the basis of important common features) and applies past experiences to present thoughts. Thinking aids in problem solving by using algorithms and heuristics.

Intelligence is ability to acquire and use knowledge. IQ test is used for measuring of intelligence. IQ = (mental age/chronological age)×100.

Attention is cognitive process enabling person to respond to some stimuli more than others at any given time or to remember some more than others.

Classification of attention:

1. **Non-volitional** (without making any conscious effort):

a. **enforced** attention (is aroused by the instincts);

b. **spontaneous** attention (produced by the sentiments).

2. **Volitional** (demands the conscious efforts):

a. **implicit** attention (a single act of volition is sufficient);

b. **explicit** attention (needs repeated acts of will to sustain it).

There are four different types of attention:

1. **Selective** attention (a focus to only one thing at once);
2. **Sustained** attention (a focus for a long period of time);
3. **Divided** attention (a focus on two events at once);
4. **Executive** attention (a focus on completing steps to achieve a goal).

Attention depends on different factors: external (nature, intensity, variety, repetition of stimulus) and internal (interest, motives, mood and attitude).

Attention-deficit disorder is characterized by easy distinction, impulsiveness, moodiness, and failure to follow through ton plans.

3. Materials for auditory self-work.

Task 1. Classical conditioning of the eyeblink reflex.

Unconditioned stimulus – an air puff directed to eye (Fig. 102.). Conditioned stimulus – is an auditory tone.

The subject has to put on special glasses with fixed tube for air. A puff of air blows to the cornea of the eye and causes blink (unconditioned response). An auditory tone doesn't cause blink. Sound the tone and then blow a puff of air into subject's eye. Repeat this combination (in which the tone is followed by air puff) 5-10 times. After a few repetitions, subject will start to close his eyes as soon as he hears the tone.

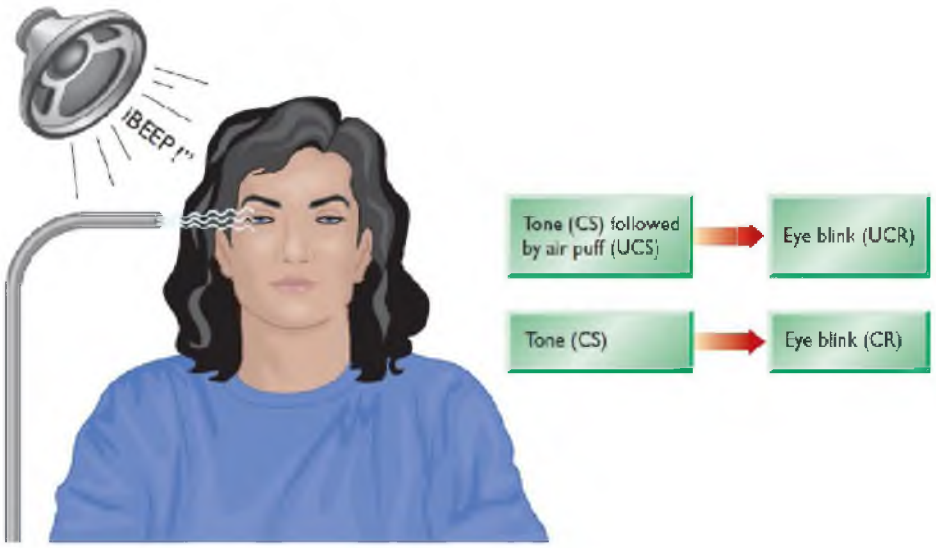


Fig.102. The eyeblink reflex.

Task 2. Inhibition of the eyeblink reflex.

Perform 2 experiments for inhibition of the eyeblink reflex:
- external inhibition (add any new stimulus during action of conditioned stimulus, e.g. light);
- extinction (repeatedly present 5-10 conditioned stimulus (the tone) without unconditioned stimulus (no air puff). After a few trials, you will see extinction of the eyeblink reflex.

Task 3. Short-term memory

Prepare a list of 20 unrelated words by writing these down in advance. Read this list slowly two times to the group of participants and ask to repeat. Then write down a list of 20 related words organized into 4-5 related categories (e.g. furniture: chair, table, sofa, bookcase; animals: dog, cat, lion, tiger; weather: rain, snow, cloud, sunshine etc.). Read slowly and ask to repeat. Determine whether the number of words recalled for the disorganized list on average is less than the number of words recalled for the organized list.

Task 4. Hand preference questionnaire

1. Imagine the centre of your back is itching. Which hand do you scratch it with?
2. Interlock your fingers. Which thumb is uppermost?
3. Imagine you are applauding. Start clapping your hands. Which hand is uppermost?
4. Wink at and imaginary friend straight in front of you. Which eye does the winking?
5. Put your hands behind your back, one holding the other. Which hand is doing the holding?
6. Someone in front of you is shouting but you cannot hear the words. Cup your ear to hear better. Which ear do you cup?

7. Count to three on your fingers, using the forefinger of the other hand. Which forefinger do you use?
8. Tilt your head to one shoulder. Which shoulder does it touch?
9. Fixate a small distant object with your eyes and point directly at it with your forefinger. Now close one eye. Now change eyes. Which eye was open when the fingertip remained in line with the small object? (when the other eye, the non-dominant one, is open and the dominant eye is closed, the finger will appear to move to one side of the object.)
10. Fold your arms. Which forearm is uppermost?

4. Materials for self-control:
Control questions:
1. Compare conditioned reflexes and unconditioned reflexes.
2. Classification of conditioned reflexes.
3. Mechanism of development of conditioned reflexes.
4. Inhibition of conditioned reflexes.
5. Learning: definition, classification, role.
6. Classification of memory.
7. Memory mechanisms.
8. Biological significance of emotions.
9. Emotions types and main theories.
10. Attention: types, mechanism.
11. Brain asymmetry.

Lesson 26. Sleeping, its types, phases, physiological role. HNA (higher nervous activity) types investigation.

Before performing this lesson, you should study the introductory material presented here.

1.Lecture course.
2.Moroz V.M., Shandra O.A. Physiology. - 2011. Unit XIII. Chapter 39, 40.
3.Guyton A.C., Hall J.E. Textbook of Medical Physiology. - 2011. Unit XI. Chapter 58, 59.

Relevance of the topic.
Because we spend about one-third of our lives sleeping, sleep disorders can have a significant impact on our quality of life.The higher nervous activity type (temperament) is acquired nervous system features which determine organism interconnection with environment and find their reflection in all organism functions.

1. Objectives:

To know: sleep stages, their relationship to the brain waves, the neural mechanisms of sleep, sleep disorders, temperament types, character.

To be able to: draw EEG of different sleep stages, investigate individual-typological peculiarities.

2. Topic content.

Sleep and Wakefulness

Sleep is an active, reversible behavioral state, which is characterized by decrease of brain activity and response to stimuli of the environment.

Two separate types of sleep have been defined on the basis of physiologic parameters (Fig.103.):

1. NREM (non-REM) sleep is subdivided into 4 **stages of sleep:**

- **stage 1**: the state of transition between wakefulness and sleep (drowsiness), characterized by low-voltage and relatively frequent brain waves.

- **stage 2**: deeper sleep, characterized by slower brain waves and increasing in amplitude. EEG during this stage is generally irregular, contains periods of theta activity, **sleep spindles** (short clusters of wave of 12-14 Hz) and **K-complexes** (sharp high-amplitude waves).

- **stage 3**: moderate to deep levels of sleep, characterize by further decreases in EEG frequency (contains 20-50% delta activity) and further increase in amplitude.

- **stage 4**: the deepest level sleep, also called "slow-wave sleep" (SWS), it is characterized by high amplitude delta waves (more than 50%). SWS indicates that neuronal activity is highly synchronized. During this stage a person is least responsive to outside stimulation.

2. **REM** (rapid eye movement) **sleep** ("paradoxical sleep"): EEG activity in REM sleep resembles the waking state. Most (but not all) dreaming occurs in REM sleep. During REM sleep, most large skeletal muscles (except for respiration musculature) are actively hypotonic; certain visceral motor activities (cardiac output, respiration, blood pressure) are increased; thermoregulation ceases.

During the night sleep alternates between periods of REM and non-REM sleep. Each cycle is approximately 90 minutes long, containing 20-30 minutes of REM sleep with progressive increases in the duration of REM sleep through the night.

Neural mechanisms of sleep

1. awake state is promoted by the activation of serotonergic (raphe nuclei), cholinergic, histaminergic (tuberomammillary nucleus), orexinergic, and noradrenergic (locus ceruleus) neurotransmitter systems which activate widespread regions of the CNS.

2. non-REM sleep is induced by the **suppression** of these activating systems by inhibitory neurons in the ventrolateral preoptic nucleus (VLPO) of the hypothalamus, which is activated by the basal forebrain. The accumulation of **adenosine** in basal forebrain leads to sleep, therefore, caffeine (adenosine receptor antagonist) is stimulant.

3. REM sleep is promoted by cholinergic input from the brainstem to visual cortex: **PGO** (ponto-geniculo-occipital) **waves**.

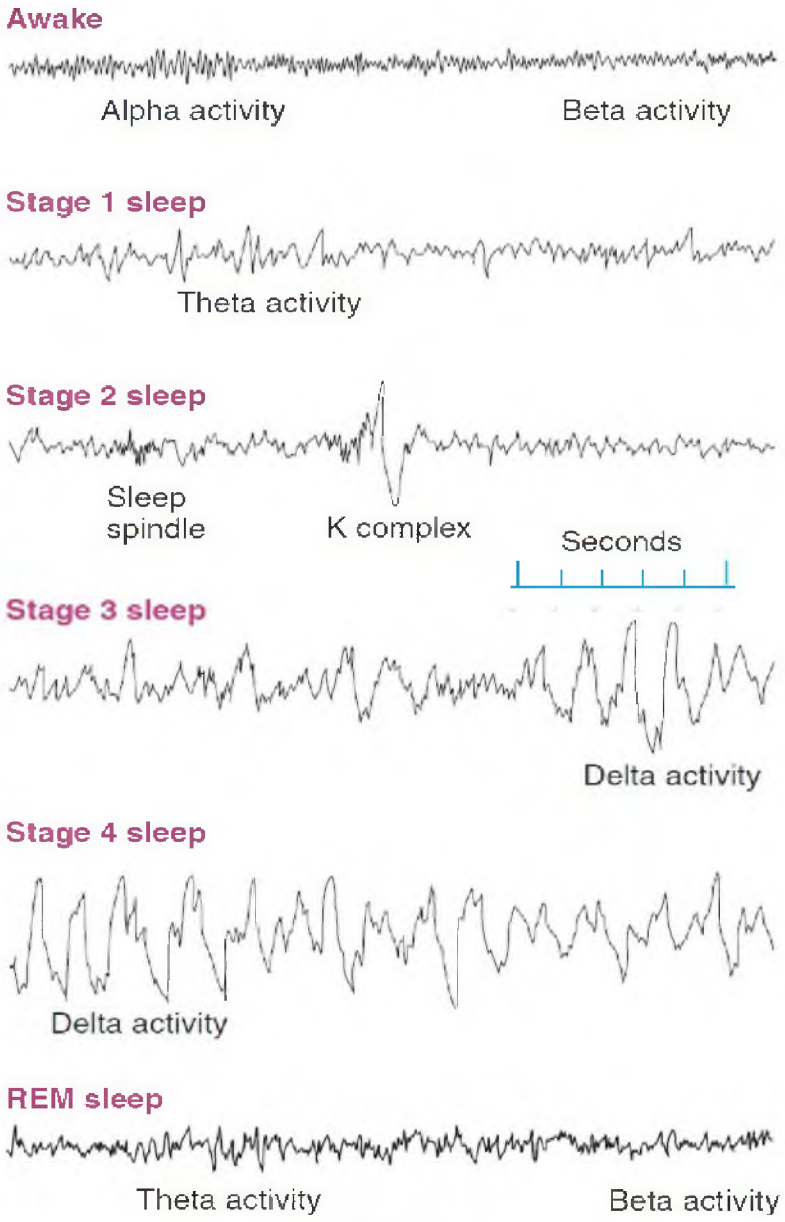


Fig.103. EEG sleep stages.

Clinical correlation

Sleep disorders

1. **Insomnia** is the most prevalent sleep disorder (affects about 15% of the population), characterized by an inability to fall asleep or often waking up during the night.

2. **Sleep apnoea** refers to a pattern of interrupted breathing during sleep that affects many people. Stimulation of the respiratory muscles temporarily ceases many times during a night. Decreasing in oxygen level repeatedly awakens the patient, who is deprived of SWS and REM sleep. It leads to sleepiness during a day.

3. **Narcolepsy** ("sleep attacks"): a patient becomes drowsy or falls asleep (fragments of REM sleep) at inappropriate times and places. The narcolepsy symptoms consist of excessive daytime sleepiness, sleep paralysis, cataplexy (sudden

muscle weakness caused by strong emotions), and hypnagogic hallucinations. This condition is associated with a defect in hypocretin/orexin activity.

4. **Restless leg syndrome (RLS):** the patient feels discomfort inside the legs that cause an irresistible urge to move the legs.

5. **Parasomnias** are characterized by undesirable behaviours during sleep. They include **sleepwalking** (somnambulism), **sleep talking** (sominloquy), **bruxism**, **sleep terrors**, and **nocturnal enuresis**, which are NREM disorders.

HNA types

Temperament is the combination of mental, physical and emotional traits of a person; natural predisposition.

There are a lot of theories how temperament traits can be classified and organized.

According to ancient Greek medicine temperament is the mixture of the four main humors (sanguis, chole, melan chole, phlegma), the relative proportions of which were supposed to determine physical and mental constitution (Fig.95.).

Hippocrates-Galen temperaments:

1. **sanguine** – predominance of *sanguis* (blood);
2. **choleric** – predominance of *chole* (bile);
3. **melancholic** – predominance of *melan chole* (black bile);
4. **phlegmatic** – predominance of *phlegma* (mucus).

I. Pavlov demonstrated the connection between features of nervous system and behavioral responses.

Pavlov used such categories as:

- **strength of excitation** – is the ability of nerve cells to withstand a powerful stimulus without going into a state of defensive inhibition (strong or weak);
- **equilibrium of nervous processes** – is the ratio of excitation and inhibition by magnitude (balanced or imbalanced);
- **mobility of excitation and inhibition** – is the rate of disappearance of one process and its replacement by another (mobile or inert).

Pavlov's temperament types:

1. **strong**, **balanced**, **mobile** – lively type (sanguine);
2. **strong**, **balanced**, **inert** – calm type (phlegmatic);
3. **strong**, **imbalanced** – strong excitatory type (choleric);
4. **weak** type (melancholic).

Also, Pavlov distinguished ***human types of HNA***, according to concept of the first and second signal system:

1. **Artistic** type (predominance of the first signal system);
2. **Intellectual** type (predominance of the second signal system);
3. **Mixed** type.

Eysenck's typology:

1. **Stable extraverts** (sanguine)
2. **Unstable extraverts** (choleric)
3. **Stable introverts** (phlegmatic)
4. **Unstable introverts** (melancholic)

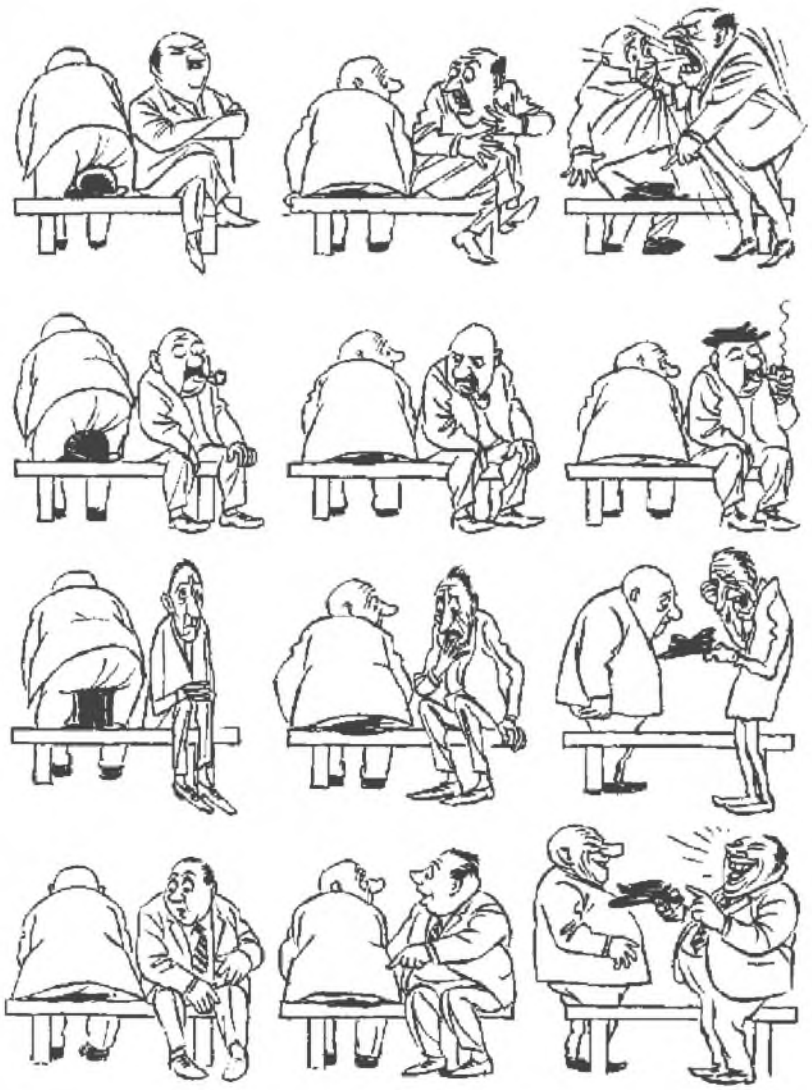


Fig.104. Different types of behaviour depending on temperament.

3. Materials for auditory self-work.

Task 1. Eysenck's Personality Questionnaire

Try to decide whether YES or NO represents your usual way of acting or feeling.

1. Do you often long for excitation?
2. Do you often need understanding friends to cheer you up?
3. Are you usually carefree?
4. Do you find it very hard to take no for an answer?
5. Do you stop and think things over before doing anything?
6. If you say you will do something do you always keep your promise, no matter how inconvenient it might be to do so?
7. Do your moods go up and down?
8. Do you generally do and say things quickly without stopping to think?
9. Do you ever feel 'just miserable' for no good reason?
10. Would you do almost anything for a dare?
11. Do you suddenly feel shy when you want to talk to an attractive stranger?
12. Once in a while do you lose your temper and get angry?
13. Do you often do things on the spur of the moment?
14. Do you often worry about things you should have done or said?
15. Generally do you prefer reading to meeting people?

16. Are your feelings rather easily hurt?
17. Do you like going out a lot?
18. Do you occasionally have thoughts and ideas that you would not like other people to know about?
19. Are you sometimes bubbling over with energy and sometimes very sluggish?
20. Do you prefer to have few but special friends?
21. Do you daydream a lot?
22. When people shout at you do you shout back?
23. Are you often troubled about feelings of guilt?
24. Are all your habits good and desirable ones?
25. Can you usually let yourself go and enjoy yourself a lot at a lively party?
26. Would you call yourself tense or 'highly strung'?
27. Do other people think of you as being very lively?
28. After you have done something important, do you come away feeling you could have done better?
29. Are you mostly quiet when you are with other people?
30. Do you sometimes gossip?
31. Do ideas run through your head so that you cannot sleep?
32. If there is something you want to know about, would you rather look it up in a book than talk to someone about it?
33. Do you get palpitations or thumping in your hear?
34. Do you like the kind of work that you need to pay close attention to?
35. Do you get attacks of shaking or trembling?
36. Would you always declare everything at customs, even if you knew you could never be found out?
37. Do you hate being with a crowd who play jokes on one another?
38. Are you an irritable person?
39. Do you like doing things in which you have to act quickly?
40. Do you worry about awful things that might happen?
42. Have you ever been late for an appointment or work?
43. Do you have many nightmares?
44. Do you like talking to people so much that you never miss a chance of talking to stranger?
45. Are you troubled by aches and pains?
46. Would you be very unhappy if you could not see lots of people most of the time?
47. Would you call yourself a nervous person?
48. Of all the people you know, are there some whom you definitely do not like?
49. Would you say that you were fairly self-confident?
50. Are you easily hurt when people find fault with you or your work?
51. Do you find it hard to really enjoy yourself at a lively party?
52. Are you troubled by feelings of inferiority?
53. Can you easily get some life into a dull party?
54. Do you sometimes talk about things you know nothing about?
55. Do you worry about your health?
56. Do you like playing pranks on others?
57. Do you suffer from sleeplessness?

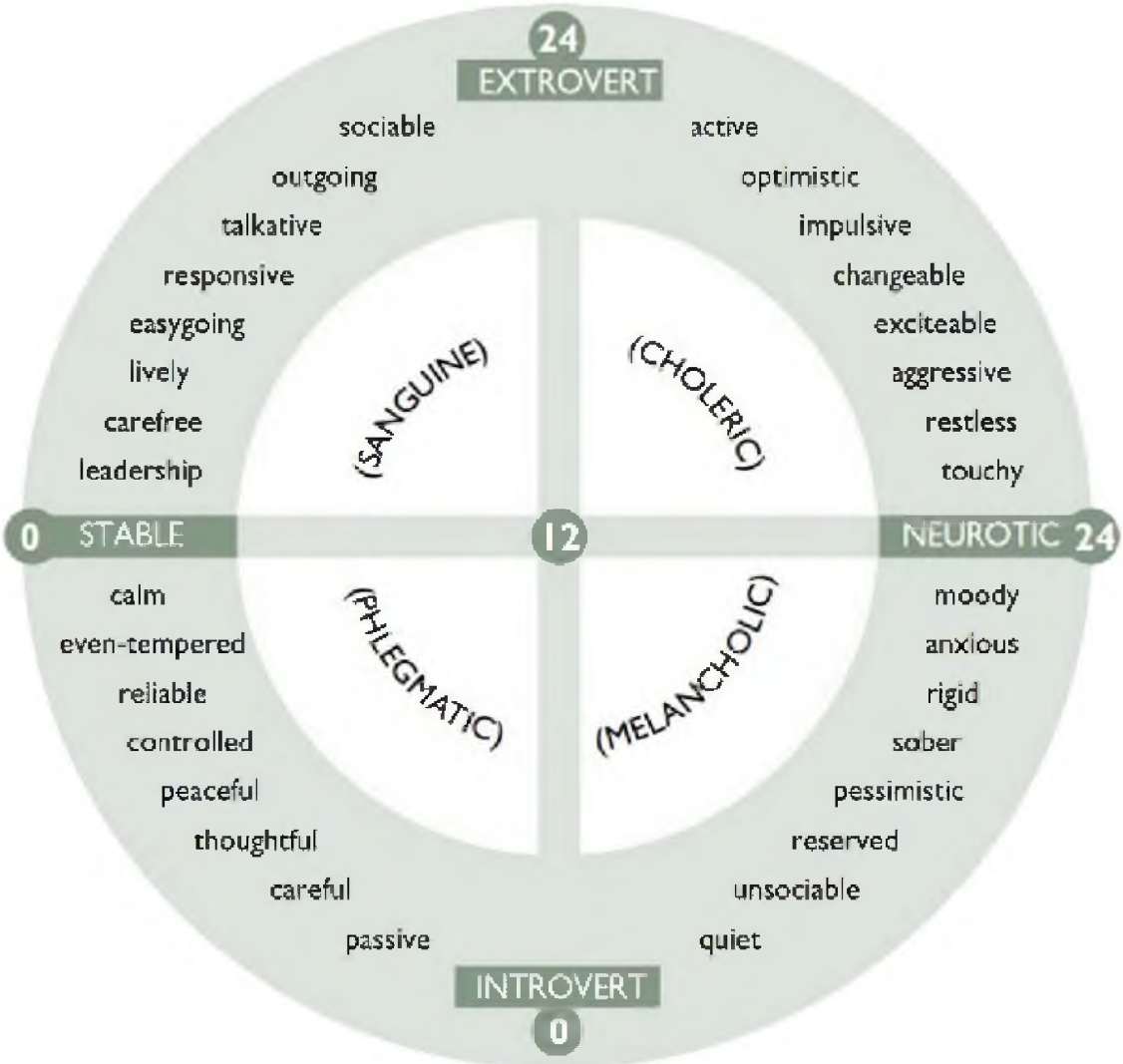


Fig.105. Eysenck chart.

SCORING (Fig.97.)

Extroversion/Introversion

If you answered Yes then add *one point*:

1; 3; 8; 10; 13; 17; 22; 25; 27; 39; 44; 46; 49; 53; 56

If you answered No then add *one point*:

5; 15; 20; 29; 32; 34; 37; 41; 51

Neuroticism/Stability

If you answered Yes then add *one point*:

2; 4; 7; 9; 11; 14; 16; 19; 21; 23; 26; 28; 31; 33; 35; 38; 40; 43; 45; 47; 50; 52; 55; 57

Lie Scale

If you answered Yes then add *one point*:

6; 24; 36

If you answered No then add *one point*:

12; 18; 30; 42; 48; 54

0-3 (sincere); 4-6 (situational); 7-9 (lying)

4. Materials for self-control:

Control questions:

1. Sleep stages.
2. Sleep mechanisms.
3. Sleep disorders.
4. The higher nervous activity types classifications before and after I.P. Pavlov.

Lesson 27-28

Credit module controlling the managing module 1: General physiology, CNS physiology, higher integrative functions

Questions for self-control

1. Resting potential, origin mechanisms, its parameters, physiological role.
2. Action potential, origin mechanisms, its parameters, physiological role.
3. Excitability. Depolarization critical level, cellular membrane depolarization threshold.
4. Cell excitability changings during single action potential development.
5. Excitation conduction mechanisms through nervous fibers.
6. Excitation conduction regularities in nervous fibers.
7. Excitation conduction mechanisms through nervous-muscular synapse.
8. Excitation t and contraction conjugation. Skeletal muscles contraction and relaxation mechanisms.
9. Muscular contractions types: single and tetanic; isotonic and isometric.
10. Representation about reflex. Reflectory arc structure and its links functions.
11. Receptors, their classification, excitation mechanisms.
12. Proprioreceptors, their types, functions. Muscular spindles structure and functions.
13. Excitation conductive mechanisms and regularities in central synapses.
14. Central inhibition types. Pre- and post-synaptic inhibition developmental mechanisms.
15. Excitation and inhibition summation with CNS neurons.
16. Spine motor reflexes, their reflectory arcs, physiological importance.
17. Spine conductive function. Spine reflexes dependence on brain centers activity. Spinal shock.
18. Posterior brain motor reflexes, decerebration rigidity.
19. Midbrain motor reflexes, their physiological importance.
20. Cerebellum, its functions, injury symptoms.
21. Thalamus, its functions.
22. Limbic system, hypothalamus, their functions.
23. Basal ganglia, their functions, injury symptoms.
24. Sensory systems, their structure and functions.
25. Gustatory (taste) sensory system, its structure, functions, investigative methods.
26. Olfactory sensory system, its structure and functions.
27. Somato-sensory system, its structure and functions.
28. Pain physiological mechanisms.
29. Opiate and non-opiate antinociceptive organism systems, their importance.
30. Anesthesia physiological mechanisms.

31. Auditory system, its structure and functions.
32. External and middle ear functions. Internal ear, sound signals frequented analysis.
33. Visual system, its structure and functions.
34. Major visual functions and their investigative methods.
35. Behavior biological forms. Innate behavioral forms. Instincts, their physiological role.
36. Acquired behavioral forms. Conditioned reflexes formation conditions, their differencies from non-conditioned ones.
37. Memory, kinds and formation mechanisms.
38. Needs and motivations, their role in behavior formation.
39. Emotions, formation mechanisms and biological role.
40. Neocortex functions and human being higher nervous activity.
41. Emotions biological and informational theory, their role in behavior formation.
42. Brain big hemispheres cortex functional asymmetry, its integrative function.
43. Speech, its functions, formation physiological bases.
44. Thinking. Abstract thinking development in a human being. Cerebral structures role in thinking process.
45. Human being higher nervous activity types. Temperament and character.
46. The higher nervous activity age aspects in a human being.
47. Human being working activity physiological bases.
48. Physical and mental activity peculiarities. Optimal working regimens.
49. Fatigue physiological bases. Active rest and its mechanisms.
50. Human being working activity age changings.
51. Sport physiological bases. Trainings optimal regimens compiling principles.
52. Sleep, its kinds, phases, cortex electrical activity, physiological mechanisms.
53. Autonomic nervous system structure general plan. Autonomic reflexes, their reflectory arcs.
54. Autonomic nervous system synapses, their neurotransmitters, receptors and blockers of conduction in synapses.
55. Sympathetic nervous system effects on visceral functions.
56. Parasympathetic nervous system effects on visceral functions.
57. Metasympathetic system role in visceral functions regulation.
58. Humoral regulation, its differences from nervous one. Humoral regulation factors characteristics.
59. Hormones features, their main effects. Hormones actions mechanism to the target cells.
60. Humoral regulation contour. Hormonal secretion regulation by endocrine glands.
61. Hypothalamic-hypophyseal system role in endocrine glands functions regulation.
62. Somatothropic or growth hormone, thyroxin and triiodthyronine, insulin role in body linear development, as well as organism physical and psychical development regulation.
63. Calcitonin, parathormone, calcitriole role in calcium and phosphates ions constancy in blood regulation.

64. Pancreas hormones role in organism functions regulation.
65. Thyroid gland (T_3, T_4) hormones role in organism functions regulation.
66. Female sexual system physiology, its functions, sexual hormones role.
67. Male sexual system physiology, sexual hormones role.
68. General representations about non-specific organism adaptation to the stress situation. Hormones role in non-specific adaptation.
69. Sympathetic-adrenal system role in the regulation of non-specific organism adaptation to the stress situation.
70. Hypophyseal-suprarenal system role in the regulation of organism non-specific adaptation to the stress situation. Glucocorticoids and mineralocorticoids main influencings on the organism.

By this link you can find additional information (situational tasks) for the Module 1 preparing: **(Physiology Poltava)**
https://www.facebook.com/profile.php?id=100013316025779

For improving your skills please use this link for Krok-1 tests training https://www.testcentr.org.ua/uk/krok-1

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Навчальний посібник англійською мовою

Тетяна Запорожець
Марія Рудь
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Фізіологія

МОДУЛЬ 1: "ЗАГАЛЬНА ФІЗІОЛОГІЯ ТА ВИЩІ ІНТЕГРАТИВНІ ФУНКЦІЇ"

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