Chapter 6

Pathophysiology of the nervous system

6.1 The basic anatomical and physiological aspects

The nervous system forms a collection of specialized forms and specialized structures, the aim of which is to provide communication and feedback information of the organism with the outside world. The integration of all functions of the organism into a united reacting entirely called (the organic union) is equally important. The endocrine system has a role in the actualization of this duty. The dependence of the organism on the environment is given by its dependence on the outside energy sources, that change continuously. The organism has to be adapted to those changes all the time.

Any change in the environment can be considered as an action (stimulus) and the following change in the response of the organism is the reaction or answer. The quality and characteristics of the response are given by the characteristics of the organism (given genetically) and by the outside conditions (characteristics of the stimulus). Feed back relation will be formed between the stimulus and the response.

The stimulus is the specific change in the outside or inside environment, that affect the nervous system in a way that result in the generation of an impulse. Impulse is the change of the electrical processes that excite tissues, and that can spread via nerves or conductive membranes.

At a certain level of development there will be such a situation, where the response to a certain stimulus happens to be complicated variable and there will be selection of the specific answer. The organism reacts to the same stimulus variably depending on the variability of the situation.

There will be the formation of memory and this forms actualities. Further specialization of the system that has the ability to respond to outside stimuli by a specific reaction, learning depending on the fact that experience and memory leads into the formation of the nervous system.

The nervous system is composed by many types of cells:

- Cells specialized for the reception of stimuli from the outside or inside environments (receptors, sensors).
- Cells specialized for processing the received information, providing the contact and handling information in the network along with other parts of the nervous architecture (interneurons).
- Nerve cells – the neurons themselves, that gives the orders and reach the effect organ via their peripheral nerve endings (for example endocrine glands) or those reaching tissues (muscle) – effector neurons.
- Cells having only supporting or helping function in the nervous system (glial and satellite cells)

Upon the realization of the nervous function usually many nervous cells (the neurons) are interconnected in a form of a chain. The beginning of the
chain is usually formed by a sensor (a receptor) that is able to register a certain type of stimuli. The stimulus induces excitation on the membrane of the receptor cell, and this will spread in the network of neurons.

The nerve cells (the neurons) that are connected in this network will overtake the excitation in an unchanged form or modified form the will handle it to the other neurons till it reaches the effector. The excitation is represented by the change in the resting electrical potential of the neurons that spreads from the site of its generation to its vicinity or can be directed to a certain direction (for e.g. the site of contact with other neurons – synapses – are permeable only in one direction). The transmission of impulse to another neuron in the network takes place via synapses by the transmission of the potential excitation (the electrical transmission of excitation) or via some specific substance – neurotransmitter (humoral transmission).

The transmitter has a different chemical structure and is typical for certain part of the nervous architecture. The transmitter or its precursors are synthesized in the neuron body where they are passing to the peripheral branches of the cell, to the axon along to the synapses. The speed of transmission is 10–100 mm per 24 hours. The transmitter is usually stored in specific cell organelles (vesicles covered by membrane), by this way it is protected from the enzymes degradation. Contractile proteins such as stenin and neurin do present in the presynaptic part of the synapses. These might be stimulated by membrane stimulation and Ca\(^{2+}\) ions influx and by their contraction they bring the vesicle with the contained transmitter near the synapse. After the vesicle unites with the presynaptic membrane the transmitter is released to the synaptic cleft. The transmitter then reacts with the subsynaptic membrane receptor and activates them.

For e.g.: Ach. opens the Ca\(^{2+}\) channels directly, adrenaline on the other hand promotes its effect via the cAMP. As the result of the released mediator together with Ca\(^{2+}\) ions the subsynaptic membrane finally becomes highly permeable for the hydrated ions of Na\(^{+}\) (depolarization – excitation), or its permeability increases for even the less hydrated ions K\(^{+}\) and Cl\(^{-}\) (hyperpolarisation – inhibition). According to the characteristics of the change we may have an excitatory or inhibitory synapses. The exact morphological distinction of those two types of synapses can not be performed.

In some parts of the nervous system another way of transmission might take place. This transmission consist of some transmitters released from the neurons to the blood capillaries and those are transferred via blood stream to the place of their action. Due to the resemblance of these cells to the endocrine system they are hence called the neuroendocrine cells.

The transformation of the outside stimuli into a neuronal stimulation forms what is known as the code of the nervous system. The outside stimulus (mechanical, chemical, electromagnetic) is changed in the receptor to electrical activity, and a slow generator potential will be formed. If the generator potential reaches the threshold value it will evoke action potential in the nervous tissue. The size of the stimulus will be coded to frequent impulses. Such a coded information is during impulse conduction quite stable.

The level of organization of the nervous system in human is of variable degrees, that means that the nervous system forms a setting of relatively autonomic but on the other hand regulatory centers and functional and integration areas. We can differentiate 3 such levels:

- medulla oblongata,
- the subcortical area,
- the cortical area.

If we compare the development of the nervous system according to the development of that kind and species, then it is quite natural to notice the shift of the nervous system functions from the medulla oblongata to the brain in the human – we are talking about cranialization of the nervous functions. In the brain this shift is done from the lower subcortical areas to the cortex and hence the thalamocortical functioning complex – and this is known as the corticalization of functions. In man we may see the greatest centralization and integration of function and the relative autonomy of the lower areas is decreasing.

An important parameter, that can be consider as the functional principle of the nervous system organization is the combination of the stable (unchanged) reflex mechanisms with the great variability (plasticity). Plasticity is the landmark of the organic adaptation due to the effect of the external environment.
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It is basis is the ability to create temporary junctions, the process of learning and memory. Generally, the plasticity of the higher centers is higher than the plasticity of the lower centers.

The nervous system is morphologically divided into central nervous system (CNS), that constitutes of the brain, medulla oblongata and the peripheral nervous system, to which other parts of the nervous system belongs.

The autonomic nervous system is further more subdivided into sympathetic and parasympathetic, that regulates the vascular system, the glands and the smooth muscles.

The human brain is the most difficult and complicated organ in its intrinsic structure. It is situated in the cranial cavity and is divided into three major divisions:

- forebrain (prosencephalon).
- hindbrain (rhombencephalon)
- midbrain (mesencephalon).

The forebrain is divided into telencephalon and diencephalon. The forebrain is the conduction station of the tracts that joint the cerebral cortex to the lower compartments of the CNS and at the same time the center of the emotions. In this location there is also the center of the autonomic system regulation and the regulation center of the endocrine glands. The surface of the cerebrum is characterized by many convolutions (gyri and sulci) – the cerebral cortex, in which the neurons can lie and thereby maximizes their function, is the most developed part of the central nervous system. It consists of about 15 milliards neurons, that are interconnected with each other by means of their dendrites. Certain areas of the cerebral cortex have the character of so called projection centers, where some tracts end (from e.g. the sensory information from the peripheries). As the result of the analysis of the entering information there will be formation of orders for the lower parts of the central nervous system (for some effectors). The cerebral cortex performs even the higher integration and analytic activity, that is the basis of the higher nervous function (the second signal system).

The hindbrain is formed of the myelencephalon (medulla oblongata) and the metencephalon (pons and cerebellum). Life important (vital) centers for respiration, circulation, and cardiac and vascular activity are situated there. At the same time there is presence of the connecting fibers of many tracts that carry information from the peripheries to the higher centers. The cerebellum is the regulatory center of muscle tonus, muscular movement coordination and body balance.

The midbrain (mesencephalon) is the smallest, but functionally very complicated part of CNS. The subcortical optic, auditory, and motor centers as well as the center of body balance of others do present in the mid brain. Many tracts passes via the midbrain as well and these transfer information from the peripheries to the cerebral cortex and vice versa.

Medulla oblongata is the lowest part of the CNS. It forms the first center into which information are carried from the peripheries (cold, pain, heat, pressure and so on). These information are transferred from the medulla to higher centers or directly to the corresponding medullary motor centers that regulate the skeletal muscles and provide some involuntary reflexes (for e.g. the defense reflex). In the medulla there are also centers of the autonomic sympathetic and parasympathetic nervous system.

At this point we have to add that, the localization of functions (neuronal center for a specific function) has to be understood in relation with other parts of the nervous system. For example in the medulla oblongata the localization of functions is relatively constant and topographically exact. We might distinguish exactly the innervation of some muscle groups by one medullary segment. In the cerebral cortex although we might localize the entry of some sensory tracts (optic, hearing and so on) and the projection of, for example long direct motor tracts (pyramidal tracts), other functions and mainly those complex ones that require a wider sensory – motor interaction can be only vaguely localized. If for e.g. we are talking about the respiratory center specifically, it is not possible to be so specific in localizing some complex function such as consciousness, language, or sleep anatomically. This conclusion is important for the topical diagnosis during which we might suggest the localization of injury on the basis of functional disturbances.

The basic functional performance of the nervous centers are similarly as in the synaptic function the time and space summation and occlusion. The result of activation of a certain center can be larger in
The basic functional unit of the nervous system is reflex. Its structural basic unit is the reflex arc, that is formed of a receptor, an afferent sensitive pathway, the center (in the medulla or the brain), the efferent motor pathway, and the effector (muscle or gland). This structure enables the receive of information (receptor, free nerve terminal), the conduction of information to the center, the conduction of the efferent information to the effector (motor neuron) and the reaction of the effector. The simple reflexes are mediated via a direct reflex arc, i.e. The sensitive neuron is connected directly to the motor neuron – known also as the monosynaptic reflex (proprioceptive). If there is one or more neurons placed between the sensitive and the motor neuron, the reflex arc become indirect or multisynaptic. The direct reflex arc mediate reflexes, in which the receptor and the effector belong to one organ (e.g. contraction of muscle by hitting the corresponding muscle tendon). An indirect reflex arc mediates exteroceptive reflexes, where the receptor lies in a different organ than the effector organ (for the corneal reflex we need the connection between the sensitive nucleus of the trigeminal nerve (that inervates the cornea) with the motor nucleus of the facial nerve (that inervates the circular muscle of the eye). Even more complex reflex arcs are those known by the defense reflexes such as (cough, tear secretion, etc.) and others. Reflexes, that take place during normal conditions in the same way all the times are known as the unconditional reflexes (inborn). On those basic reflexes we may build the system of the conditional reflexes (acquired). A specific group is composed of instincts, that are considered as the most important unconditional reflexes.

Analogically we might evaluate the function of the CNS as well. There are 3 main functions dominant, basic and complementary to each other:

1. The transfer of information from the peripheries.
2. The central processing of information.
3. The conduction of information from the center to the effector organs.

Information reaches the CNS via many channels – specific pathways conduct information from a certain sensory system to specific nuclei. Yet in the brain stem some collaterals emerge from the retic-
ular formation to the reticular (nonspecific) projection system of the thalamus. By this way information from multiple sensory systems are collected in the reticular formation and they form the nonspecific afferent pathway system. Its importance lies in the parallel transfer of information to the higher compartments of the CNS, by which it can promote adequate reactions to the information brought up by special pathways. The nonspecific systems have a higher number of synapses, a longer latency, but they effect the extend and the depth of the information. There are some places in the subcortical and cortical level where information are collected from different modalities and these are known as the association centers (nuclei). The information that reaches the CNS, is evaluated and it can serve for the regulation of some functions, to evoke others, or possibly to stop them, or to keep them active. Nervous centers are interconnected even on the same level – horizontal junction. These are:

1. Local junctions, that provide connection between the nuclear neurons. For e.g. between different layers of the cerebral cortex.
2. The homolateral associations, that promote the transfer of information among different nuclei at the same level of the CNS.
3. The collateral commisures, that mainly join the homolateral brain centers (but in the cerebral cortex it joins the heterolateral centers as well).

** Interruption of the commisures of the brain is known as split brain. ** There will be loss of coordination of functions of both hemispheres, and the result is a negative effect on intellect functions.

**The efferent systems** are adapted to transform the instructions (the descending efferent pathways):

- **Somatomotor efferent neurons** form two main systems:
  1. Pyramidal and extrapyramidal tracts where the extrapyramidal is more neuronal and it provides the coordination of multiple centers in different parts of the of the CNS.
  2. Peripheral motor neuron, that is common for both tracts and together with the muscle fibers it forms a motor unit.
- **The efferent vegetative tract** (glandular and visceromotor) forms bundles of tiny fibers, that joins the vegetative nuclei at different levels. Their topography is not exactly known.

The interconnection of the nerve centers forms circles of nerve tracts, that are the basis of the coordination of afferent and efferent systems at different levels of CNS. Some other parts also belongs here such as the reciprocal connections of the cerebral cortex and thalamus, the circles of the limbic system and the feedback fibers of the extrapyramidal tracts and others. The ascending and descending tracts are known as the vertical junctions (to be differentiated from horizontal junctions).

Anatomical and physiological notes about the structure and function of the nerve system is important from the pathophysiological point of view of the disease cases that may take place in the nervous system, and consequently can be of influence.

The basic protective system of the CNS constitutes of the cranium (skull) and the vertebral column, where we might find the central part of the brain and the spinal cord. The rigidity of the skeleton is yet a disadvantage during an increase in the intra cranial pressure because the cranium is composed of only a potential space to compensate the increasing pressure and hence there will be a gradual compression of the brain tissues with some serious regulatory disturbances. The brain lies in the cerebral cavity and it is covered by many covers (meninges) in a way that it actually swims in the cerebrospinal fluid. The cerebrospinal fluid circulates freely in the subarachnoid space covers the whole brain surface and its ventricles surface. And hence it is quite clear that this place forms a good culture media via which different – and mainly – infections diseases that might affect the whole surface of the brain and spinal cord (for e.g. meningitis) might find a way in. On the other hand errors and disturbances in the cerebrospinal fluid circulation causes an increase in the intracranial pressure and hydrocephalus.

The most important thing is an intact nondisturbed function and structure of the meninges. The course dura mater (meaning literally “hard mother”) is composed of two layers, which the venous sinuses formed between them. The outermost layer forms the periosteum tightly attached to the bone (endosteal layer, it actually serves as the peristoi). The inner dura (meningeal layer) is firm, and in some ar-
Neuronal injury

Neurons are very sensitive to many external and internal unfavorable effects. We are mainly talking about anoxia, hypoglycemia, viral infections, metabolic disorders, vitamin deficiency (for e.g. vitamin B) and so on. The resulting effects of these factors on the nervous system mainly depends on the degree of injury of the throphic function of the neuron and the maintenance of its integrity. The decisive factor is the site of injury, type of the nerve cell, but other factors also have a great value (for e.g. the degree of cellular differentiation, the relation to glial cells etc.). During some physical or chemical effects there might be either reversible short lasting injury or an irreversible neuronal injury. Neuronal injury might be of many degrees:

1. Functional injury caused for e.g. by pressure (hypoxia, that is reversible with the following normalization.
2. Death of an axon without interruption to the endoneural tubes.
3. Axonal death with interruption of the endoneural tubes.