

Mediator systems of the CNS

Mediator systems are represented by neurotransmitters, specific nuclei in which these substances are synthesized primarily in the CNS, pathways through which these neurotransmitters are released and subsequently bound to receptors.

Through these pathways, ``chemical mediators *flow through the neurons, which aid and stimulate CNS functions. Mediators are highly specific substances and often affect specific areas of the brain.*

5 steps of neurotransmission:

1. **uptake/synthesis**
2. **storage**
3. **release**
4. **binding to receptors**
5. **inactivation**

Cholinergic System

It is formed by neurons synthesizing *acetylcholine*.

The nuclei are stored in the hemispheres and in the stem. The main core is **ncl. basalis Meynerti** (Ch4), Septum verum, ventral arm of Brock's bundle. It belongs to the basal ganglia and some of the nuclei of the reticular formation. Neurons of the septum verum project to the Hippocampal formation, nc. basalis projects throughout the neocortex, and the RF nuclei send axons to the thalamus.

The cholinergic system has an *excitatory effect* on neurons and is primarily released at the presynaptic terminals of the neocortex, where it facilitates transmission at excitatory cortical synapses.

Acetylcholine synthesized from choline and acetyl coenzyme A by **choline acetyltransferase** (ChAT). Subsequently, Ach is transported by a vesicular transporter to vesicles, where it is stored and released from there. The function consists in involvement in **processes of memory and learning, motor skills, regulation of wakefulness and sleep, as well as motivation and reward**.

'In the periphery, Ach plays a role in neuromuscular transmission, it is a neurotransmitter of both parasympathetic and preganglionic fibers, and also of parasympathetic postganglionic fibers, and it also plays an important role in pain modulation. It can also occur as non-neuronal, it is used in immunity, respiration and processes in the skin.

Monoaminergic system

It is formed by groups of neurons located mainly in the nuclei of the reticular formation in the brainstem. The axons of the neurons of this system are characterized by abundant collateralization and innervation of a large number of CNS structures.

Division of the monoaminergic system:

- **catecholaminergic:**
 1. *noradrenergic* – synthesizes noradrenaline
 2. *dopaminergic* – synthesizes dopamine
- **serotonergic** - synthesizes serotonin

Dopaminergic system

The dopaminergic nuclei are designated **A8-A10. The most important is the substantia nigra - pars compacta (A9) and medially from it the area tegmentalis ventralis (A10). Fibers from the substantia nigra project to the striata** and to a lesser extent to the **globus pallidus**. Fibers emerging from the area tegmentalis ventralis form the so-called *mesolimbic dopaminergic system* and terminate in the striatum ventrale, pallidum ventrale, in the septum verum, in the amygdala and in the cerebral cortex, mainly in the prefrontal and primarily motor area .

Function:

- effect on sympathetic ganglia;
- receptors D1 like family (**D1 and D5'**) – **increase the effect of adenylate cyclase**;
- receptors D2 like family (**D2, D3, D4**) – **reduce the effect of adenylate cyclase**;
- the key role of dopamine is **motivation**, then **addiction**, regulation of the hypothalamo-pituitary system and **motility**, nociception.
- *'reduced concentration of dopamine in the striatum' → Parkinson's syndrome* (hypokinesia, rigidity, shaking).
- **reduced concentration in the prefrontal cortex** → *disorders of memory, attention, motivation, schizophrenia, depression, substance addiction, eating disorders.*

Noradrenergic system

Its neurons are located in the **reticular formation** of the pontine and medulla oblongata and are referred to as **nuclei A1-A7**. The largest and most important noradrenergic nucleus is the locus coeruleus (A7), located under the base of IV. cerebral ventricles. Descending and ascending fibers emerge from it. Descending fibers go to the anterior and posterior horns of the spinal cord, to the sensitive nuclei of the cranial nerves, and to the cerebellum, where they terminate on the dendrites of the Purkinje cells. Ascending fibers end mainly in the hypothalamus and thalamus (in nc. VPL and nc. VPM). Strong projections also go to the neocortex and the hippocampal formation. Noradrenergic fibers do not enter the striatum and pallidum.

Function:

- *innervation of small vessels of the brain* and regulation of cerebral circulation
- noradrenergic fibers are part of the **activating ascending system reticular formation (ARAS)**

Serotonergic system

Most of the neurons of this system are stored in the '*rapheal nuclei of the reticular formation*'. Their axons enter ascending and descending bundles, directed to all "cortical areas" and to all structures of the "limbic system". Others end in the striatum, thalamus, hypothalamus, brainstem, cerebellum, and spinal cord.

Function:

- ascending component activity causes **mood swings** and *behavioural disturbances*
- fibers ending in the back corner of the spinal cord affect the "transmission of pain signals", their stimulation causes "analgesia"
- reduction of serotonin synthesis causes **depression, sleep disorders** to *insomnia*

Histaminergic system

Most of the neurons are located in the posterior thalamus and the histamine produced by them affects the transmission of **painful signals, motor activity and thermoregulation**.

Glutamate System

Glutamate is the main **excitatory mediator** in the CNS. It is produced by most neuronal mammalian systems. It is contained in most brain pathways. During a long excitatory action caused by the release of glutamate, the affected neurons are damaged and eventually destroyed.

In order for an excitatory AMPA to manifest, an inhibitory one must first be established.

GABAergic system

Gamma-aminobutyric acid (GABA)

Inhibitory Mediator

Ionotropic GABA A and metabotropic GABA B receptors

Important pathways to the cerebellum, causes chloride channel opening = hyperpolarization. Modulates monosynaptic and polysynaptic transmission of nociceptive information, presynaptically selects the afferent flow of information to the CNS.

Decreased amount of GABA: Huntington's chorea, epilepsy, anxiety.

Links

Reference list

- SECOND, Rastislav – GRIM, Miloš. *Anatomy of the Central Nervous System*. 1. edition. Prague : Galen; Carolinum, 2011. ISBN 978-80-246-1895-1.
- ŠIHÁK, Radomír. *Anatomy 3*. 2. edition. Grada Publishing, 2004. 692 pp. ISBN 978-80-247-1132-4.

Done by: Eisa Jbara