VISCERAL NOCICEPTIVE PATHWAYS

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Abstract. *Autonomic afferent neurons extending from visceral organs to the spinal cord and brain stem are visceral afferent components of spinal and cranial nerves. The bodies of these neurons, as well as the bodies of somatic afferent neurons, are located in the ganglia of the posterior roots. Visceral afferent nerves cross the autonomic ganglia, but do not form synapses with them and enter the spinal cord or the brainstem together with somatic afferent fibers of the same nerves. Both visceral and somatic afferents form reflex connections with the preganglionic autonomic neurons of the trunk and spinal cord. Thus, they are functionally related to them, but are not their anatomical component. Visceral afferents converge on the neurons of the optic nerve, as well as somatic nociceptive afferents.*
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Visceral pain occurs as a result of the phenomenon of multiple high-frequency discharges of visceral afferents, which normally perform homeostatic rather than nociceptive functions. In particular, visceral afferents may exhibit low-frequency activity in response to moderate dilation of hollow organs, but respond with a flash of high-frequency discharges to their sharp and excessive stretching. The resulting pain is felt in those dermatomes whose somatic neurons are projected in the same segments of the spinal cord. The peculiarities of visceral organ innervation should be taken into account when choosing the level of puncture and catheterization of the epidural space during interventions on certain visceral structures. For example, the skin of the scrotum is innervated from the sacral segments, at the same time, when operating on the testicles, the upper sensory level of the epidural block is not lower than T10. This is due to the fact that visceral afferents from the testicles, together with sympathetic lugs , enter the spinal cord at the Th10 level. During cesarean section, for adequate anesthesia, the upper level of the block should reach at least the mid-thoracic segments. This is due to the fact that the visceral and parietal peritoneum have a rather large severity. Uterine traction causes peritoneal distension and, as a consequence, pain in those cases when the upper level of the block is insufficient to block all nociceptive fibers coming from the peritoneum.

Transmission of nociceptive information within the spinal cord A number of neurotransmitters, neuromodulators and their characteristic receptors are involved in the transmission processes at the level of SMR.

They can be divided into two main groups:

1) excitatory transmitters secreted by primary nociceptive afferents or interneurons of the spinal cord;

2) inhibitory transmitters released by spinal cord interneurons or supraspinal structures.

The endings of primary afferent hairs contain excitatory amino acids (aspartate and glutamate), peptides (substance P, calcitonin-gene-linked peptide) and neurotrophic factor, which act as neurotransmitters and are released from terminals under the influence of stimuli of various intensities. Depolarization of the endings of primary enzyme fibers leads to the release of

glutamate, which activates postsynaptic ionotropic AMPA receptors. Aspartate and especially glutamate are the main excitatory transmitters. Glutamate causes rapid short-term depolarization of neurons of the second order. Substance P and neurokinin are responsible for delayed long-term depolarization. Excitatory amino acids act on various receptors, in particular AMPA and NMDA (metabotropic glutamate receptors). Activation of AMPA receptors causes the entry of Na+ ions into the cell, its depolarization and subsequent rapid activation NMDA receptors. At the same time, signaling information related to localization and intensity of nociceptive stimulation is rapidly transmitted. With this model of "physiological" pain, high-intensity stimulation produces short-term localized pain, the stimulus-response relationship between the afferent input from the injury zone and the reaction of the neurons of the posterior horns of the spinal cord is predictable and easily reproducible.

The summation of repeated stimuli from C fibers leads to a progressive increase in the depolarization of the postsynaptic membrane and the removal of the Mg2+ block from the ion channels of NMDA receptors. The mechanisms of this effect include the effect of glutamate on ionotropic NMDA receptors, metabotropic glutamate receptors (mGluR), as well as the effect of the P substation on neurokinin (NK1) receptors. At the same time, there is a rapid, progressive increase with each stimulus in the frequency of generation of action potentials by SPSM neurons, which has been called the phenomenon of "inflating" the activity of SPSM neurons (in English-language literature - "wind-up").

Long-term potentiation (DVP) is induced by high- frequency stimulation, while enhanced responses of neurons are recorded after the termination of the stimulus that caused them. This phenomenon is included in the mechanisms of "pain memory" at the level of the hippocampus, as well as the formation of sensitization of spinal cord neurons. Intensive and prolonged stimulation increases the excitability of the neurons of the eye. Electroneurophysiological studies have revealed two main mechanisms for enhancing postsynaptic responses. This is "inflation" caused by low-frequency stimulation of C-fibers (but not A-delta fibers), and DVP induced by high-frequency stimulation and exceeding in duration the effect of the stimulus that caused it. An increase in the intracellular concentration of Ca2+ ions, due to their enhanced entry through the ion channels of NMDA receptors, as well as release from intracellular depots, activates a number of intracellular kinase cascades. Subsequent changes in the kinetics of ion channels and/or the activity of receptors, the formation of additional receptors in membranes increase the efficiency of sympathetic transmission. Changes in the reactivity of the neurons of the optic nerve and the functional conductivity of A-beta mechanosensitive fibers, as well as the intensification of downward "facilitating" influences contribute to the development of secondary hyperalgesia (i.e., a decrease in pain thresholds beyond the directly injured tissues).

Descending modulating conducting paths Descending neuronal pathways suppress pain perception and efferent responses to pain. The cerebral cortex, hypothalamus, thalamus and the centers of the brain stem (near -conductive gray matter (OVSV), large suture nucleus, blue spot) send descending axons to the spinal cord, which allows modulating the transmission of nociceptive information at the level of visual perception. Terminals of descending axons inhibit the release of nociceptive neurotransmitters from primary afferents, and also weaken the response of second-order neurons to nociceptive stimulation.

Descending axons from the OVSV are projected into the reticular formation, and then descend into the spinal cord, where they form axons with inhibitory neurons of the SDD and other

neurons . Axonal terminals from the suture nucleus are projected into the SCM, where they release serotonin and norepinephrine. Axons descending from the blue spot modulate transmission at the level of SPSM due to the release of norepinephrine and activation of postsynaptic alpha-adrenergic receptors.

GABA and enkephlinergic interneurons in the VSM also provide local inhibition of nociception. The descending pathways are involved in the modulation of the transmission of nociceptive information at the spinal level, due to presynaptic action on primary afferent fibers, postsynaptic action on projection neurons or due to action on the insertion neurons of the posterior horns. These processes involve both direct corticofugal (efferent) and mediated (via modulating structures such as near-conducting gray matter) pathways from the cerebral cortex and hypothalamus.

The relative balance between inhibitory and facilitating influences varies depending on the type and intensity of the stimulus, as well as the time elapsed since the injury. Serotonergic and noradrenergic pathways in the posterior-lateral ropes are involved in the implementation of descending inhibitory effects, serotonergic pathways are also involved in facilitating effects. Thus, analgesia can be achieved by increased inhibition (opioids, anti- depressants) and/or restriction of activating stimulation (local anesthetics, ketamine). Conducting nociceptive stimuli from the spinal cord to supraspinal structures There are several ascending tracts involved in carrying nociceptive stimuli from the spinal cord to supraspinal structures , in particular spinothalamic, spinoretic, spinomesencephalic and spinolimbic. The main route of nociceptive information transmission is the spinothalamic tract (STT). CTT consists of two pathways: the lateral neospinothalamic (NSTT) and the medial palaeospinothalamic (PSTT).

NSTT is projected into the neotamus , whose cells transmit nociceptive impulses directly to the somatosensory zones of the cerebral cortex. In this case, there is a rapid perception (localization) of pain and avoidance reactions. The lateral tract also provides discrimination of pain, its sensory characteristics (pulsating, burning, etc.). PSTT is a slow lysynaptic tract that is projected into the reticular activating system, near- tap gray matter and medial thalamus. The cells of the medial thalamus project into the frontal and limbic zones of the cortex. PSTT is involved in the perception of prolonged acute pain, chronic pain. In addition, it provides the perception of poorly localized unpleasant sensations long after the initial injury.

Perception. The central link of the nociceptive system. The whole set of pain sensations, behavioral reactions and emotional coloring of pain is formed during the transmission of nociceptive information from the structures of the spinal cord to the medulla, forebrain and cerebral cortex along the pathways. The spinothalamic pathway originates from the primary afferent terminals of the I and II plates of the SPSM into the thalamus, from where nociceptive information on thalamocortical connections is transmitted to the somatosensory areas of the cortex. The spinothalamic pathway provides a discriminatory perception of pain sensations (determining the source of pain and the type of left stimulation).

The spinoreticular and spinomesencephalic tracts project into the medulla oblongata and the brainstem, thus participating in the formation of homeostatic__ and vegetative reactions in response to nociceptive stimulation. They also give projections into the cerebral cortex, taking part in the formation of the emotional-affective component of pain. The spinoparabrachial pathway is formed from the surface neurons of the I plate of the posterior horns of the spinal cord and is projected into the ventro- medial hypothalamus and the central nucleus of the amygdala.

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