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# Trigeminal Sensor System of the Rat, Development and Morphofunctional Features

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**ABSTRACT**

In this article, was performed analysis and synthesis of literature data on the development and morphofunctional features of the trigeminal sensory system in rats. The sensory system of the trigeminal nerve or trigemenal sensory system plays an important role in the life of animals, as it is associated with vibrissae – sensitive hairs on the face and body, necessary for orientation in space and touch. Data on the development and morphofunctional features of the trigeminal sensory system of the rat will serve as the basis for the subsequent study of the nervous system of these animals, with the possible introduction of the results obtained into practical medicine.

**Keywords:** Rats; Neurons; Trigeminal Nerve

## Introduction

A frequent object of experimental biomedical research, including the study of the nervous system, is the rat. For an adequate interpretation of the obtained results and subsequent extrapolation to humans, it is important to have a clear understanding of the timing of the development and organization of the rat nervous system. The trigeminal sensory system or trigemenal sensory system plays an important role in the life of animals, as it is associated with vibrissae – sensitive hairs on the snout and body, necessary for orientation in space and touch. In humans, the trigeminal nerve is the main sensory nerve of the face and oral cavity and, in addition, carries efferents to the masticatory muscles, controlling their movements [1-4]. The purpose of the review is to analyze and systematize literature data on the development and morphofunctional features of the trigeminal sensory system in rat.

### Development of the Trigeminal Sensory System

The study of the distribution of zones of innervation of the trigeminal nerve in embryogenesis showed the important role of neurotrophic factors and their receptors in this process. Genetic studies have shown that peripheral target tissues of the trigeminal nerve secrete chemoattractants, promoting axon growth. Up to a certain stage, neurons do not depend on trophic factors, but from the moment the first branches of the neuropil reach the innervation zones, peripheral tissues begin the synthesis of attractants necessary for the further life of nerve cells [2,3]. Trigeminal nucleus neurons (ganglion neurons) form from ectodermal placodes and neural crest from days 9 to 14 of embryonic development. In the early stages of antenatal development (day 14), the nucleus of the trigeminal nerve adjoins the bend of the bridge, being in close proximity to the zone of innervation. Branching of the neuropil of neurons spread radially in the direction from the forebrain to the innervated organs. Over the next few days, the trigeminal ganglion rotates 90° so that the ventral mandibular neurons become lateral and the brainstem nuclei (also by 90º, so that the lateral neurons and the afferent pathways from the perikaryon to the mandible become dorsal) [2,3].

## Central Vibrissae Tract

Vibrissa follicles develop from the mesenchyme by the 14th day of embryogenesis, and by the 16th day the area of their afferent innervation is approximately the same size as in adult rats. The dendrites of the neurons of the trigeminal nucleus reach the brain stem on the 11-15$^{th}$ day of prenatal development, the thalamus – on the 14-15$^{th}$, the cerebral cortex (layer IV) – on the 16-21$^{st}$. The vibrissa tract itself, that is, the vibrissa communication system – the nucleus of the trigeminal nerve – the overlying parts of the brain develops mainly postnatally and is formed sequentially first in the brain stem (20 days of embryogenesis – 1 day after birth), thalamus (2-3 days of postnatal ontogenesis) and the cerebral cortex (3-5 days after birth). The development of afferent terminals is preceded by a period of asymmetric growth of dendrites and the migration associated with it, followed by accumulation of neuronal perikaryons in the area of the trigeminal nucleus facing towards the innervated organs.

The first signals received from vibrissae can be registered in the brainstem starting from the first day after birth, and in the cerebral cortex – from the 6th day of postnatal ontogenesis. The dimensions of the receptive fields approximately correspond to those in adult rats, however, newborn rat pups are characterized by a longer refractoriness period and impulse delay. By the 1st week of postnatal ontogenesis, peculiar barrel-shaped clusters of neurons surrounded by fibrous structures form in the IV layer of the neocortex. The diameter of these barrel columns is 100-400 μm. Each such structural unit is associated with certain large rat hairs – vibrissae [4]. GABAergic and serotonergic activity of neurons of the trigeminal nerve nucleus is detected from an early age, although it matures quite slowly, at least for 2 months. Moreover, in the early postnatal period, γ-aminobutyric acid causes excitation in the brain stem, and inhibition in the thalamus and cerebral cortex. In case of damage to the vibrissae before the formation of connections between the nucleus of the trigeminal nerve and the overlying parts of the brain, the formation of the vibrissae tract is disturbed. The critical period in this regard is: 1st day after birth for the brain stem, 2-3$^{rd}$ day for the thalamus and 3-4$^{th}$ day for the neocortex [2,3,5,6].

## Trigeminal Sensory System of Adult Rats

**Peripheral Nerves and Receptors**: The trigeminal nerve has three branches: ophthalmic, maxillary, and mandibular. In the rat, as in other mammals, the ophthalmic branch supplies the dorsum of the head, upper eyelid, supraorbital vibrissae, cornea, conjunctiva, nasal skin, and intranasal mucosa. The maxillary branch innervates the postorbital skin, upper lip, mystacial vibrissae, cheeks, palate, and upper teeth. The mandibular branch supplies the temporomandibular joint, the external auditory canal, the prioreceptors of the jaw muscles, the skin over the lower jaw, the lower lip, the mandibular mucosa, the teeth, and the anterior tongue. The dura mater and cranial blood vessels are innervated by afferents from all three branches. Sensory receptors are found in the skin and muscles of the rat's snout, oral and nasal mucosa, joints, and tendons [1-4]. The mediators in the afferent nerve endings are substance P and calcitonin, and in the cornea – galanin and the pituitary peptide that activates adenylate cyclase [6]. Irritation of nociceptors of the nasal mucosa is caused by both protective reflexes (sneezing) and neurogenic inflammation or disturbance of cardiorespiratory rhythms. Neurogenic inflammation is associated with vascular vasodilation, plasma extravasation, and mast cell degranulation. It often causes vascular headache [7].

**Vibrissa:** Individual vibrissae are supplied by both deep and superficial nerves. In typical laboratory rats, each follicle receives approximately 250 nerve fibers. About one third of this sensory innervation consists of unmyelinated nerve fibers. In addition, the fur between the vibrissae is richly supplied with nerve endings [4]. The temporomandibular joint is innervated by afferents that form non-encapsulated receptors. Injections of irritants (eg, glutamate) into the joint cavity are used to simulate arthritis and deep craniofacial pain. Most often, female rats are used for this. In these animals, as in humans, there are gender differences in the sensitivity of the trigeminal nerve [8,9]. Teeth and periodontal ligaments receive innervation from myelinated and unmyelinated fibers. Nerve endings were found in the odontoblast layer, predentin, and pulp. The innervation of the incisors is the most complex due to the increased functional activity of these teeth in rats [10].

**Tongue:** Trigeminal afferents supply the surface epithelium, filiform and fungiform papillae of the anterior surface of the tongue, providing general somatic sensations. In addition, activation of the trigeminal nerve has been described in the perception of bitter taste (nicotine, caffeine).

## Neurochemistry of Afferent Synapses

Most peripheral nerve endings contain substance P or a peptide associated with the calcitonin gene ((Calcitonin gene-related peptide (CGRP)) [1,11,7].

**Trigeminal Ganglion:** The bodies of the neurons of most trigeminal afferents are located in the trigeminal ganglion, which lies in the middle cranial fossa of the base of the skull. The exception is neurons that receive part of the afferent fibers from the chewing muscles and the periodontium. Their pericarions are located in the mesencephalic nucleus of the trigeminal nerve of the brainstem. Ganglion neurons are pseudounipolar and surrounded by satellite cells. They are divided according to the size of the perikaryons into large (type A) and small (type B). There is some correlation between

cell type and their function. So, for example, large vibrissae afferents mainly go to type A neurons, while neurons innervating the cornea mainly belong to type B. Ganglion neurons are surrounded by a number of fibers including noradrenergic sympathetic axons, VIP-positive parasympathetic fibers, serotonergic fibers, and various peptidergic axons containing CGRP, substance P, cholecystokinin, galanin, and NO synthase [1,12].

**Cytoarchitectonics of the Trigeminal Ganglion:** The neurons that innervate the cornea lie in the anterior ganglion, and those that receive afferents from the lower jaw lie in the posterolateral. There is also a dorsoventral organization: in the dorsal region there are neurons supplying the cornea and supraorbital vibrissae, and in the ventral region - innervating the lower jaw [12].

**Neurochemistry of the Trigeminal Ganglion:** Large ganglion neurons (type A) are usually immunopositive for neuropeptide Y. Smaller and medium-sized neurons contain glutamate, substance P, CGRP, neurokinin A, somatostatin, VIP, GABA and galanin, chemokinin, melatonin, gastrin-releasing peptide. Substance P is usually localized in the cytoplasm of neurons with CGRP, in addition, a number of neurons simultaneously with CGRP can be immunopositive for both neuropeptide Y and enkephalins [12-16].

## Sensory Nuclei of the Trigeminal Nerve

The sensory nuclei of the trigeminal nerve include several clusters of neurons located in the cervical spinal cord, medulla oblongata and midbrain. The spinal cord contains: the spinal nucleus of the trigeminal nerve and the paratrigeminal nucleus. The spinal nuclei receive most of their afferent inputs from vibrissae. In the brainstem are located: the main sensory nucleus, the motor nucleus of the trigeminal nerve, the supramedial nucleus and the intertubular nucleus, which controls the movements of the jaws. In the midbrain - the mesencephalic nucleus, which sends afferents to the periodontal teeth of both the upper and lower jaws [1,11,2].

**Cytoarchitectonics:** Most sensory nucleus neurons are pseudounipolar, but small multipolar cells are also present.

**Neurochemistry of Sensory Nuclei:** The neuropil of the sensory nuclei contains: glutamate, CGRP and substance P. GABA is mainly present in the spinal nuclei. The mesencephalic nucleus contains GABAergic, glycinergic neurons, as well as cells immunopositive for aspartate and glutamate, gastrin-releasing peptide [13,17,15,16].

## Thalamic Switching Nuclei of the Trigeminal Nerve

The main tract passes through the medial part of the posterioventral and ventrobasal complex of somatosensory thalamic nuclei. Spinal sensory neurons also project to the intralaminar nuclei and the intermediate nuclei [1,11,18,19].

**Cytoarchitectonics and Neurochemistry:** The thalamic nuclei are composed of medium-sized multipolar GABAergic neurons [18].

**Somatosensory Areas of the Zone of Innervation of the Trigeminal Nerve in the Neocortex:** The vibrissa innervation zone has the most extensive representation in the neocortex. The fourth layer of the parietal cortex contains modules consisting of multipolar stellate GABAergic neurons and thalamic afferent fibers. Each module is associated with a specific vibrissa. Star-shaped neurons form synapses with cells of the 2nd, 3rd and 5th layers. Pyramidal neurons of the 5th layer of the neocortex, having received information from stellate cells, give efferents to the reticular thalamic nucleus, the superior striatum, the nuclei of the bridge and the sensory complex of the trigeminal nerve in the brain stem, providing the movement of vibrissae [18-22,1,5]. Thus, the data presented in this review on the development and morphofunctional features of the rat trigeminal sensory system will serve as the basis for further study of the nervous system of these animals with the possible implementation of the results obtained in practical medicine.

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