# DESCENDING CONNECTIONS OF THE PARAFASCICULAR COMPLEX OF THE THALAMUS WITH THE PERIAQUEDUCTAL GRAY MATTER OF THE MIDBRAIN

G. F. Vasilenko and Z. V. Eliseeva

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KEY WORDS: periaqueductal gray matter; parafascicular complex; descending projections; degeneration; nociception.

To understand the mechanisms of formation of pain and of reflex anesthesia it is important to have a clear idea of the principles governing the organization and interrelations of both the mesencephalic and the thalamic nuclei, where pain signals are integrated and transmitted to the higher levels of the cerebral cortex.

According to the results of electrophysiological investigation, neurons of the parafascicular thalamic complex (CM-Pf)\* respond to nociceptive stimuli [4]. Unilateral destruction of the complex in animals weakens defensive reactions to nociceptive stimulation, whereas bilateral destruction completely abolishes them [15].

Injury to the CM-Pf complex in animals and also in man [5, 10,†11] induces analgesia, and for that reason Marburg regards CM as a modulator of nociceptive sensation.

Stimulation of the periaqueductal gray matter (PAG) also induces an analgesic effect, i.e., it leads to inhibition of discharges of posterior horn neurons evoked by nociceptive stimuli [12]. Analgesia also have been obtained during stimulation of this structure in man [3].

A large quantity of endogenous or natural opiates, simulating the effect of narcotics, but with much stronger action, has recently been found in PAG and also in the medial thalamic nuclei [14]. Ascending projections of PAG in the CM-Pf complex have been found in anatomical studies [8, 9]. However, the question of descending connections of the CM-Pf complex with PAG has not yet been adequately studied [2].

The object of this investigation was to study descending connections of the CM-Pf complex with PAG.

### EXPERIMENTAL METHOD

Stereotaxic operations with electrocoagulation of the CM-Pf complex were performed on adult cats anesthetized with pentobarbital. The animals were killed 3-5 days later by intravital perfusion of the brain with 10% neutral formalin. Frontal serial brain sections were treated by the Fink-Heimer method [6]. Parallel brain sections were stained by Nissl's method to determine the precise topography of the nuclei and to verify the site of coagulation.

#### EXPERIMENTAL RESULTS

Examination of serial sections through the brain stem revealed degenerated terminal fibers in the peri-aqueductal gray matter of the midbrain (PAG), surrounding the aqueduct of Sylvius.

According to Hamilton's classification [7], PAG can be divided both anatomically and functionally into three nuclei: medial, lateral, and dorsal. Each nucleus has its own definite type of cells and character of their distribution.

<sup>\*</sup>To describe the parafascicular and subparafascicular nuclei and the centrum medianum collectively the term "parafascicular complex of nuclei" [1] has been introduced, to correspond to the term centrum medianum—parafascicular complex used in the most recent publications by Western authors. †Refs. 8-13 are missing in the original Russian—Publisher.

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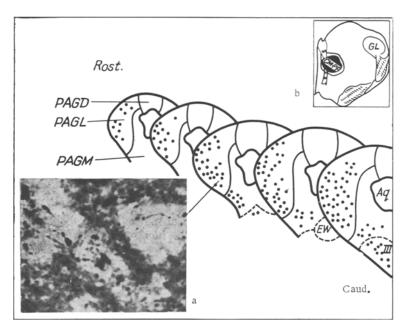


Fig. 1. Diagram of distribution of terminal degenerated fibers (dots) on frontal sections through PAG of midbrain after coagulation of CM-Pf complex. a) Terminal degeneration of fibers in PAG. Fink-Heimer method. Photomicrograph, MBI-15, magnification  $16 \times 40$ ; b) frontal section through brain indicating site of coagulation in parafascicular complex. Aq) Cerebral aqueduct, CM-Pf) centrum medianum-parafascicular complex, EW) Edinger-Westphal nucleus, GL) lateral geniculate body, PAG) periaqueductal gray matter, PAG D) dorsal PAG, PAGL) lateral PAG, PAGM) medial PAG, III) oculomotor complex. Direction rostro-caudal.

The most marked degeneration of nerve fibers after coagulation of the CM-Pf complex was found in the lateral nucleus of PAG (Fig. 1). These were very fine, fragmented, disintegrating fibers (Fig. 1a). Tracing the degeneration in frontal serial sections through PAG in the rostro-caudal direction revealed some tendency for the number of degenerated fibers to increase in the part of the nucleus where it attained its largest size, and also in the region bordering on the tegmentum. The lateral nucleus of PAG contained the largest neurons of all PAG nuclei, with many adjacent glial cells. As Hamilton [8] points out, the lateral nucleus of PAG has the most extensive connections with other brain structures compared with the medial and dorsal nuclei.

This can perhaps be explained by the position of this nucleus, which forms the outer circle of this formation. The paleo-spino-thalamic bundle, which passes through the nucleus laterally, conducting nociceptive sensation, gives off collaterals in PAG which, if they do not end on neurons of the lateral nucleus, pass through it. It is the neurons of the lateral nucleus of PAG which send their axons to cells of the parafascicular nucleus of the thalamus [8].

Considerable degeneration of terminals of nerve fibers also was observed in the ventral part of the medial nucleus, and only single altered fibers were impregnated in the dorsal nucleus of PAG.

Some selectivity of projection of fibers of the CM-Pf complex to the lateral nucleus and, to some extent, to the ventral part of the medial nucleus of PAG may be evidence that it is these parts of the central gray matter of the midbrain that are concerned with nociception. We know that PAG not only participates in the formation of pain and emotions, but also is concerned in regulation of the autonomic function of the body. It can be tentatively suggested that the dorsal nucleus and the ventral part of the medial nucleus are more closely related to these functions. However, to solve this problem special investigations will be necessary. All that is clear is that the contradictory nature of the numerous data connected with functional activity of PAG has arisen because of the view that this formation is structurally homogeneous.

It should be pointed out that the type of PAG neurons as defined by Ramon-Moliner [13] corresponds to the isodendritic type of neurons forming the "brain core." This is the simplest type of neurons in the CNS and it is characterized by straight, long dendrites with few branches, which gave rise to nerve cells with a complex dendritic pattern. Our preliminary electron-microscopic studies have shown that PAG contains pectiniform synapses such as are described for phylogenetically old brain formations.

It can thus be concluded from these results that there are direct descending connections between the CM-Pf complex and the lateral nucleus of PAG, and data in the literature indicate the presence of ascending projections of PAG to that thalamic structure, thus confirming the general principle of two-way connections for brain structures.

Considering data in the literature showing that neurons of CM-Pf and PAG respond to nociceptive stimuli and that these formations received projections or collaterals from the paleo-spino-thalamic bundle, it can be suggested that the brain structures which we have investigated, located in the "brain core," are directly concerned with the transmission and reception of slow, diffuse pain, on account of which the patient most frequently seeks medical advice.

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## ULTRASTRUCTURAL STEREOLOGIC STUDY OF CARDIAC MYOCYTES IN MYOCARDIAL ATROPHY

L. M. Nepomnyashchikh and L. V. Kolesnikova

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To stimulate general pathological processes or the action of extremal factors, starvation is frequently used [4-6, 8]. In the investigation described below a quantitative morphological study was made of the principal ultrastructures of the cardiomyocytes of the left ventricular myocardium of rats in the course of total starvation.

#### EXPERIMENTAL METHOD

Experiments were carried out on 19 sexually mature Wistar rats (females) weighing initially  $237.1 \pm 3.3$  g. The experimental rats were divided into three groups and totally deprived of food (but allowed water ad libitum): the animals of group 1 were starved for 2 days, those of group 2 for 5 days, those of group 3 for 10 days. Control animals were given a balanced diet of adequate amount. The experimental and control animals were weighed and decapitated at the end of the experiment. After rapid removal of the heart from the chest and determination of the absolute weight of the heart, the relative weight of the organ was calculated.

Laboratory of Pathological Anatomy and Histocytometry, Department of General and Clinical Pathology, Institute of Clinical and Experimental Medicine, Siberian Branch, Academy of Medical Sciences of the USSR, Novosibirsk. (Presented by Academician of the Academy of Medical Sciences of the USSR V. P. Kaznacheev.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 89, No. 7, pp. 107-111, July, 1980. Original article submitted November 28, 1979.