AFFERENT CONNECTIONS OF THE PREFRONTAL CORTEX IN CATS

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The frontal cortex, which performs integrative functions, plays an important role in the mechanisms of pain perception and, in particular, in the formation of the emotional (affective) component of nociceptive sensation [2]. This view is supported by the results of research on primates, which demonstrated the presence of direct connections of the orbitofrontal cortex with thalamic structures involved in the conduction of nociceptive excitation [14]. From the morphological and functional points of view the orbitofrontal cortex of the cat is the precursor of the anterior zones of the frontal cortex in primates and man and consists of the gyrus proreus and the anterior part of the orbital gyrus, the first of which is classified as the prefrontal cortex [10]. Allowing for the presence of direct projections of the prefrontal cortexes to the antinociceptive structures of the midbrain [6], it is important to investigate efferent projections from cortical regions and deep brain formations to local areas of the prefrontal cortex, for research into this problem has been very limited [9, 11].

The aim of this investigation was to study both cortical and subcortical projections to local areas of the prefrontal cortex in cats.

EXPERIMENTAL METHOD

Experiments were carried out on eight adult cats weighing 3-3.5 kg. Under pentobarbital anesthesia (40 mg/kg) a unilateral microinjection of 0.18 μl of a 50% aqueous solution of horseradish peroxidase (Sigma, USA) was given by means of a microsyringe and micromanipulator in the course of 30 min at one or two points of the dorsal part of the lateral surface of the proreal gyrus (Fig. 1). After 48-72 h the brain of the anesthetized animal was perfused with a mixture of 0.4% paraformaldehyde and 1.25% glutaraldehyde, made up in 0.1M phosphate buffer (pH 7.4). Subsequent treatment of the brain was in accordance with Mesulam's retrograde axonal transport method.

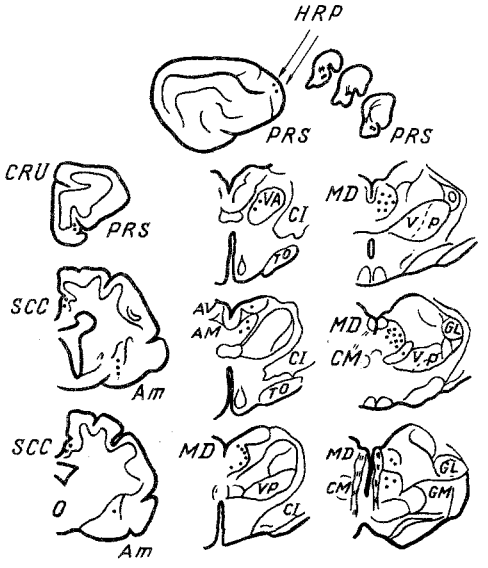

Fig. 1. Diagram of distribution of labeled neurons (dots) on frontal brain sections of cat after injection of microdoses of horseradish peroxidase into dorsal regions of prefrontal cortex (arrows). Am — n. amigdaloideus basilaris, AM — n. anterior medialis, AV — n. anterior ventralis, CI — capsula interna, CM — n. centrum medianum, CRU — s. cruciatus, GL — corpus geniculatum laterale, GM — corpus geniculatum mediate, HRP — horseradish peroxidase, MD — n. medialis dorsalis, PRS — s. presylvius, SCC — s. corporis callosi, TO — tractus opticus, VA — n. ventralis anterior, VP — n. posterior.

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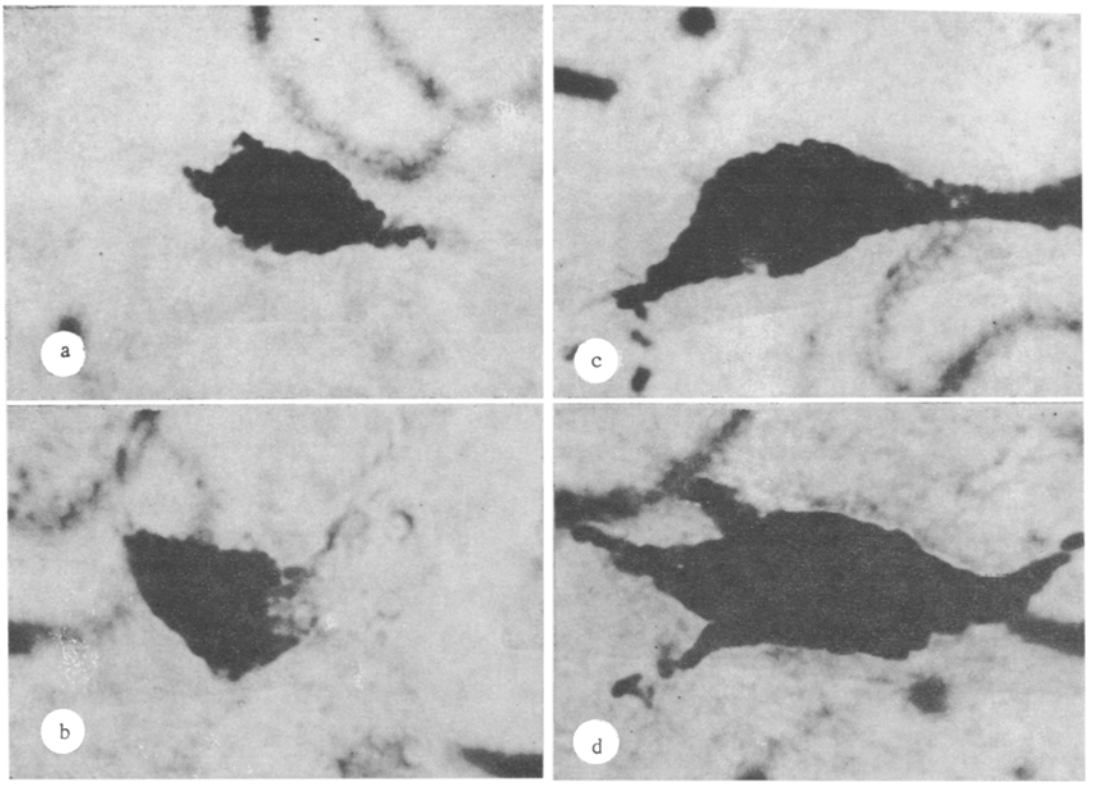

Fig. 2. Retrograde labeling of neurons in cingulate cortex (a), in amygdaloid nucleus (b), and in mediodorsal thalamic nucleus (c, d; MBI-15 microscope; magnification 40 × 7 × 1.6).

EXPERIMENTAL RESULTS

In experiments with unilateral injection of microdoses of horseradish peroxidase into the dorsal regions of the lateral proreal gyrus labeled neurons were discovered in the cingulate cortex and caudal part of the prefrontal cortex of the telencephalon, in the amygdaloid complex, and in thalamic structures of the brain (Fig. 1, Fig. 2).

The retrogradely labeled cells in the cingulate and caudal prefrontal cortex were pyramidal neurons. These neurons were distributed ipsilaterally relative to the side of injection and were located in layer III, the cells in which are the main source of association fibers.

Labeled cells in the cingulate cortex were found in the agranular area 24. According to data in the literature [15], this cortical formation is the anterior limbic region, which receives afferents from the anterior medial thalamic nucleus. Even though there were so few labeled neurons it can be concluded that direct projections of the cingulate cortex to the prefrontal cortex exist, especially in the dorsal part of the lateral surface of the proreal gyrus.

No labeled neurons were observed after these local injections in the somatosensory cortex. A very few labeled neurons were found in the aymgdaloid complex, in the anterior part of the basolateral nucleus. These labeled neurons were strained more palely than in the cingulate cortex. Many labeled neurons were found in the thalamus in the mediodorsal nucleus. Labeled neurons were arranged in groups in the middle and lateral parts of the nucleus, they sometimes outlined its lateral border, and they were fusiform or polygonal in shape. Labeled neurons were never found in the specific ventrobasal complex of the thalamus, but they were observed in the parafascicular complex. In addition, labeled neurons were found in the anterior thalamic nuclei, both ventral and medial, and also in the ventral anterior nucleus.

The investigations thus show that the cingulate cortex sends direct projections into the prefrontal cortex of the cat brain, in agreement with data in the literature [11, 13]. It must be emphasized that projections from the cingulate cortex, according to data in the literature also [11], were purely ispilateral. In this context there is interesting information

to show that projections from the lateral prefrontal cortex of rats are unilateral, whereas those from the medial prefrontal cortex are bilateral [8].

Cingulo-frontal connections are evidently reciprocal in character, for local projections of the prefrontal cortex to the cingulate cortex have been demonstrated by methods of detection of degenerate fibers, but unlike afferent connections, they are bilateral [4].

The present investigation failed to disclose any direct projections from the insular cortex to the prefrontal region, although there is some evidence of their existence [11]. However, the authors cited emphasize that not all points of the proreal gyrus receive such projections. Moreover, data showing that neighboring points of the proreal gyrus can receive nonidentical afferent projections from the brain stem may serve as an indirect explanation [12].

The present investigation showed that the amygdaloid complex sends direct projections into the dorsal part of the prefrontal cortex, in agreement with the results of experiments using autoradiographic methods [9].

Since the cingulate cortex and the amygdaloid nucleus are components of the limbic system and are involved with integration of nociceptive stimulation [5, 7], it can be concluded from these results that cingulo-frontal and amygdaloid-frontal connections can be regarded as the afferent pathway for nociceptive impulses to the frontal cortex, participating in the formation of emotional responses. This conclusion is in good agreement with clinical observations showing that lobotomy depresses the emotional-affective component of nociceptive sensation in patients without changing the perceptual-discriminative response [3]. Moreover, direct projections of the mediodorsal thalamic nucleus and also of the anterior thalamic nuclei to the prefrontal cortex which, as Adrianov [1] has shown, are responsible for integration of vegetoemotional responses with complex forms of "frontal" activity, also have a significant influence on the mechanisms of formation of the emotional-affective component of pain perception.

LITERATURE CITED

1. O. S. Adrianov, Principles of Organization of Integrative Activity of the Brain [in Russian], Moscow (1976).
2. A. V. Val'dman and Yu. D. Ignatov, The Central Mechanisms of Pain [in Russian], Leningrad (1976).
3. L. V. Kalyuzhnyi, Physiological Mechanisms of Regulation of Nociceptive Sensitivity [in Russian], Moscow (1984).
4. O. E. Malakhova, O. S. Adrianov, and E. M. Popovkin, Byull. Éksp. Biol. Med., No. 4, 475 (1984).
5. M. N. Bagshaw and J. D. Pribram, Exp. Neurol., 20, 197 (1968).
6. E. O. Bragin, Z. V. Yeliseeva, G. F. Vasilenko, et al., Neurosci. Lett., 51, 271 (1984).
7. G. V. Goddard, Psychol. Bull., 62, 89 (1964).
8. W. O. Guldin and H. J. Markowitsch, J. Comp. Neurol., 215, 135 (1983).
9. J. E. Krettec and J. L. Price, J. Comp. Neurol., 172, 723 (1977).
10. H. J. Markowitsch and M. Pritzel, Acta Neurobiol. Exp., 37, 63 (1977).
11. H. J. Markowitsch, M. Pritzel, and I. Divac, Neurosci. Lett., 11, 115 (1979).
12. H. J. Markowitsch and E. Irle, Exp. Brain Res., 41, 233 (1981).
13. W. J. H. Nauta, in: Surgical Approaches in Psychiatry, ed. by L. Laitinen and K. Livingston, Baltimore (1973), pp. 303-314.
14. H. J. Ralston, Advances in Pain Research and Therapy, ed. by L. Kruger and J. C. Liebeskind, Vol. 6, New York (1984), pp. 183-195.
15. J. E. Rose and C. N. Woolsey, J. Comp. Neurol., 89, 279 (1948).