Structural and Functional Organization of the Pain Sensitivity Component of Lingual Mechanoreceptor Structures

Z. V. Lyubimova, S. A. Subrakova, A. A. Nikitina, and O. P. Zelenkova

Translated from *Byulleten' Eksperimental'noi Biologii i Meditsiny*, Vol. 120, № 10, pp. 357-361, October, 1995
Original article submitted January 17, 1995

Examination of the structural and functional organization of tactile receptor structures in the rat tongue shows that the filiform mechanosensory papillae occupying the anterior free surface of the tongue are innervated by adrenergic, cholinergic, and peptidergic fibers. The location and sources of histamine are identified. All these components are thought to be involved in organizing the pain sensitivity of mechanosensory lingual formations.

Key Words: *tongue; histamine; innervation; mechanosensory papillae*

In the rat, the dorsal surface of the tongue contains several types of mechanoreceptor formations [1], the largest of which is represented by a population of filiform papillae on the anterior free surface of the tongue. These papillae share the same receptor-bearing surfaces with gustatory papillae (Fig. 1, *a*, *b*) and are primarily responsible for control over the nocigenic component of food entering from the external environment.

The sensory lingual structures exercising control over nocigenic stimuli have been studied inadequately. During the past decade, evidence has been gathered implicating such a pain inducer as histamine in the organization of pain sensitivity in taste perception [2,3].

Although tactile structures are located near chemosensory structures, they are supplied by different nerves and also have different receptor-related mechanisms, the tactile receptor structures being primarily sensitive to pain and the gustatory ones secondarily sensitive.

The organization of filiform papillae remains largely unexplored. Little is known about their innervation and nothing about the mechanisms of their pain sensitivity.

The purpose of the present study was to investigate the structural and functional organization of the tactile receptor structures responsible for pain sensitivity.

MATERIALS AND METHODS

The objects of the study were filiform papillae of the anterior free surface of the tongue in adult rats. Their nerve supply was examined using impregnation with silver salts (Campos and Bielschowsky-Gros methods), a fluorescent histochemical stain for biogenic amines (Falck's method [8]), and a histochemical stain for acetylcholinesterase (ACh) (Karnovsky's method [10]) with counterstaining by cresyl violet after Nissl.

The adrenergic and cholinergic components of innervation as well as histamine-containing structures of sensory lingual formations were examined both in intact rats and in rats in which the sympathetic nerve supply had been interrupted with guanidine sulfate [5] or to which capsaicin had been administered during the neonatal period [14].

Department of Human and Animal Anatomy and Physiology, Moscow State Pedagogical University (Presented by A. D. Ado, Member of the Russian Academy of Medical Sciences)

0007-4888/95/0010-0989$12.50

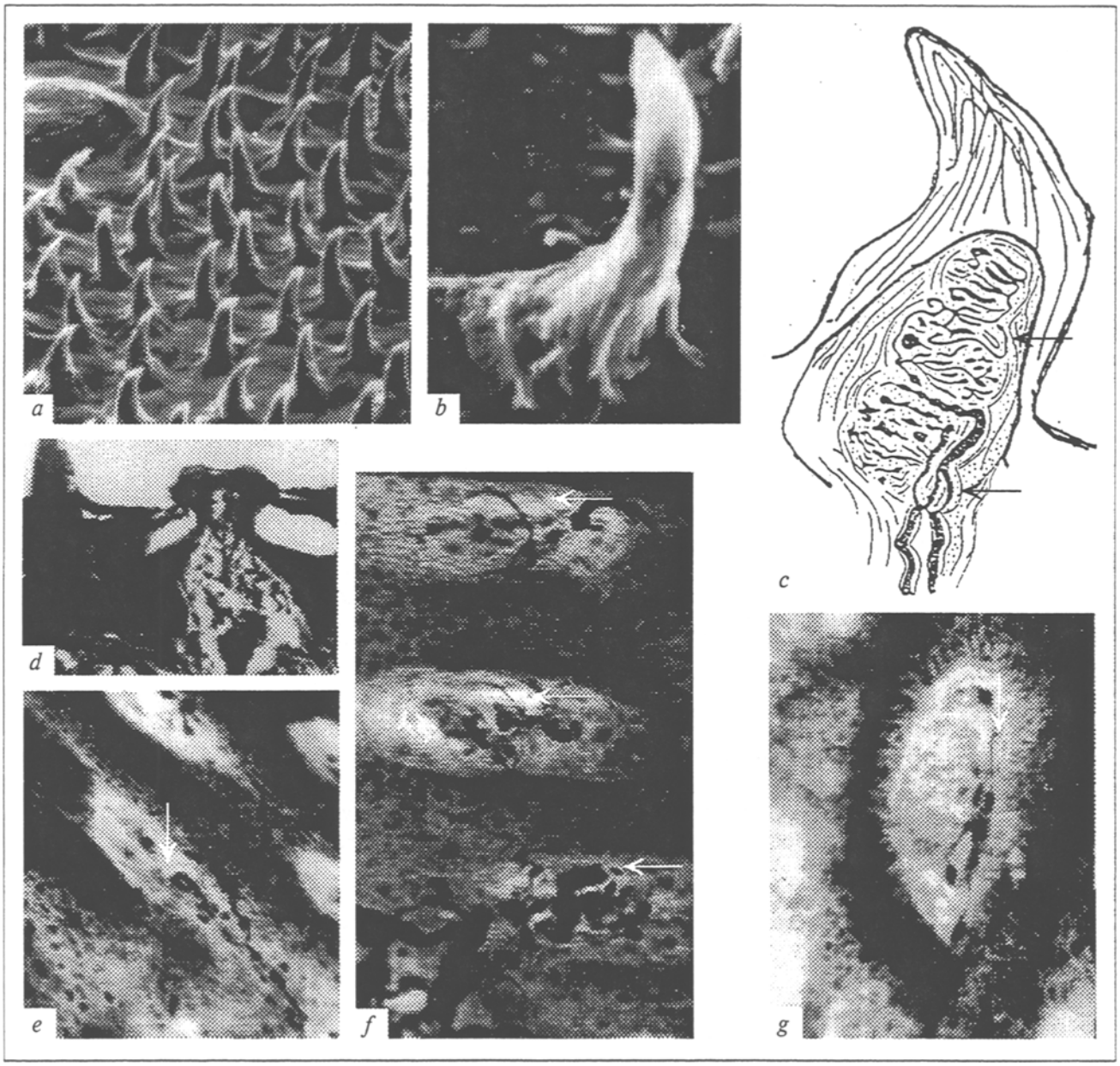

Fig. 1. Mechanosensory papillae in the rat tongue. *a* and *b*) filiform and fungiform papillae (scanning electron micrographs); ×200 in *a*, ×1100 in *b*. *c*) schematic structure of the tactile corpuscle in a filiform papilla; nerve fibers are indicated by arrows. *d*) fungiform and filiform papillae connected by structural proteins (impregnation after Bielschowsky–Gros); ×300. *e*, *f*, and *g*) innervation of filiform papillae (impregnation after Campos); tactile papillae are indicated by arrows; ×300 in *e*, ×560 in *f* and *g*.

RESULTS

Each filiform papilla has only one tactile corpuscle. Structural proteins of the papillary receptor-bearing surface (keratin) and connective tissue stroma (collagen and other proteins) form connections between the mechanosensory and chemosensory papillae (Fig. 1, *d*).

Each mechanosensory papilla is reached by a bundle of myelinated and unmyelinated nerve fibers (Fig. 1, *c*, *e*, and *f*). In the tactile papilla itself, however, fine fibers devoid of myelin were mainly detected (Fig. 1, *f* and *g* and Fig. 2, *a*).

Histochemical methods revealed fibers of cholinergic nature (Fig. 2, *b* and *c*). In rats administered capsaicin in the neonatal period, ACh-containing fibers of many chemo- and mechanosensory papillae had undergone considerable changes. Such fibers showed signs of degeneration such as increased varicosity, nonuniform swelling, and fragmentation (Fig. 2, *d*). It should be noted that fibers within the tactile corpuscle were affected more than the others. Such changes have been reported

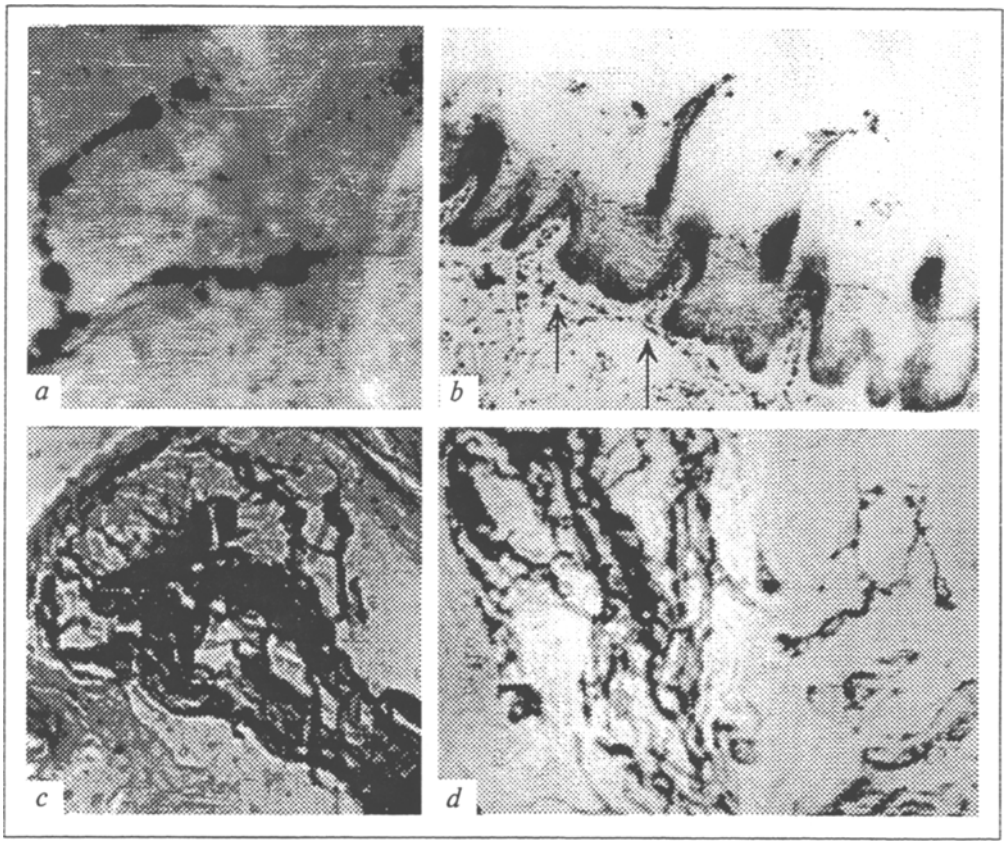

Fig. 2. Innervation of filiform and fungiform papillae in the rat tongue. *a*) nerve fibers accompanied by satellite cells in the tactile corpuscle of a filiform papilla. ×860. *b*) cholinergic innervation of filiform papillae (Karnovsky's method); nerve fibers are indicated by arrows; ×120. c) fungiform papilla, showing cholinergic nerve fibers supplying a taste bud. ×720. *d*) the same 1 month after neonatal administration of capsaicin. ×720.

as being characteristic of peptidergic fibers, in particular those containing substance P (SP) [13,14].

The fluorescent histochemical method demonstrated numerous adrenergic nerve fibers running to tactile papillae both together with blood vessels and separately. A sympathetic fiber frequently formed coils within the tactile papilla and, possibly, around other fibers as well (Fig. 3, *a* and *b*).

Tactile papillae were found to contain histamine, but, in contrast to the case in chemosensory papillae, its granules were arranged in a disordered manner. Histamine was most often detected in relation with collagen fibers that either formed the capsule of the tactile corpuscle or occurred in the connective tissue portion of the latter. Such histamine granules were clearly visible in both transverse and longitudinal sections of a tactile corpuscle (Fig. 3, *c*).

One source of histamine may be mast cells of the papillary stroma that actively respond by degeneration to stimulation of the dorsal surface of the tongue [3,9].

Chemical interruption of the sympathetic nerve supply did not alter the histamine level in the tactile papillae (Fig. 3, *d* and *e*), which suggests that biogenic amines accumulated in these papillae by independent mechanisms.

In rats administered capsaicin neonatally, adrenergic nerve fibers were preserved in both fungiform and tactile papillae (Fig. 3, *f*). This may be an indirect indication that capsaicin mainly destroys fibers containing active peptides rather than all fine fibers. Similar findings have been made for other central and peripheral structures [7,13, 14]. Histamine-containing granules were preserved in the capsaicin-treated rats.

Thus, our study of the morphofunctional and histochemical characteristics of tactile papillae demonstrated a whole set of heterogeneous elements, each of which is capable, to a certain extent, of mediating peripheral pain sensitivity. These elements include the primary afferent SP-ergic fibers exhibiting cholinergic activity and also adrenergic fibers and the biogenic amine histamine associated with structural proteins of the capsular space.

Acetylcholine, catecholamines, serotonin, and histamine can elicit a sensation of pain in high concentrations. In low concentrations, these biologically active substances increase the excitability of afferent endings [6]. As our study showed, histamine granules in a tactile corpuscle occur in close association with structural proteins that make up the papillary stroma. This association of histamine-containing structures and collagen fibers may explain the mechanism by which this complex is involved in the organization of a peripheral pain response. From this standpoint, the question of pain sensitivity at

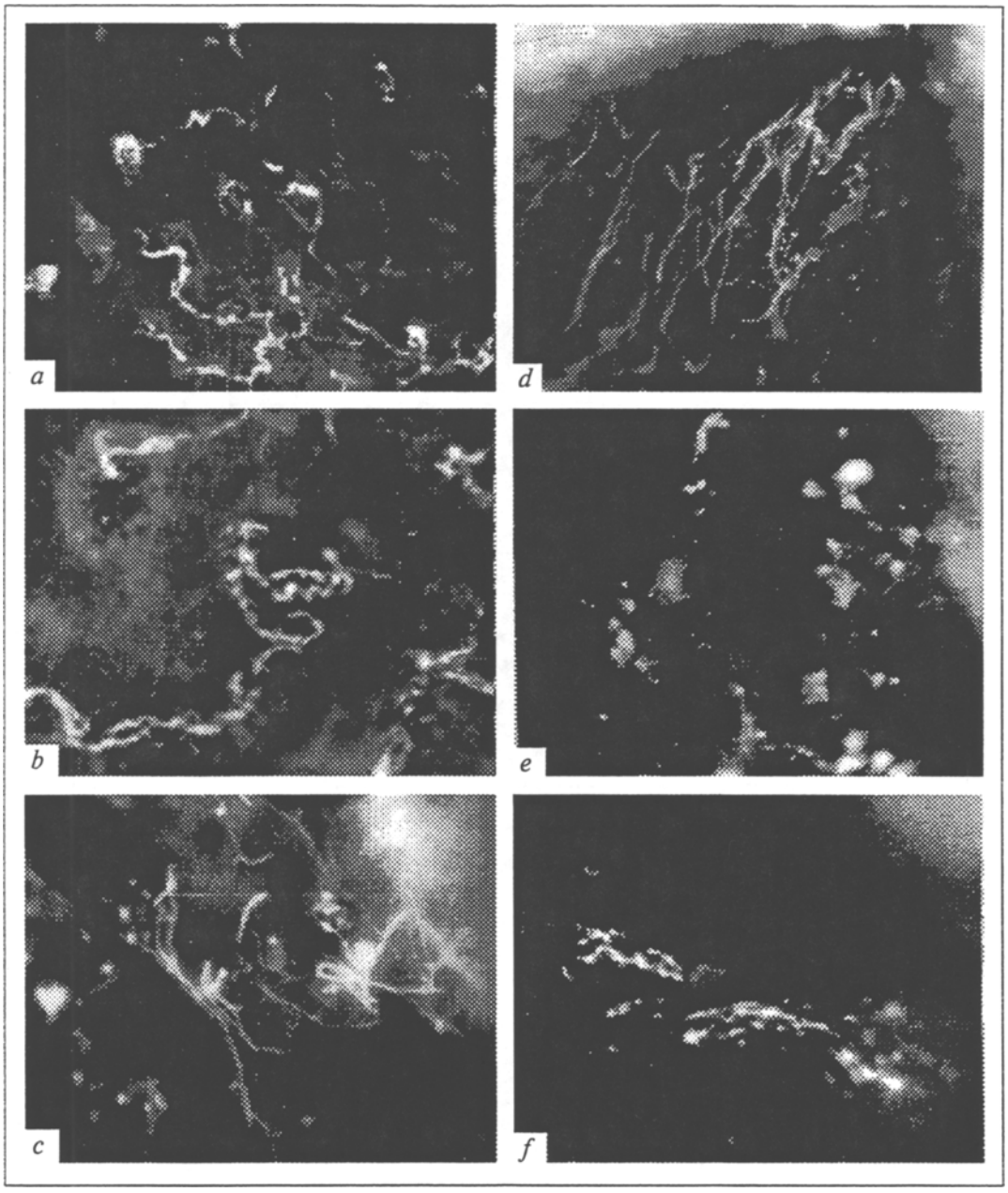

Fig. 3. Fluorescent histochemical demonstration of biogenic amines in tactile papillae of the rat tongue (Falck's method). *a* and *b*) adrenergic nerve fibers supplying lingual filiform papillae; ×180 in *a*, ×360 in *b*. *c*) histamine granules associated with collagen fibers in the connective tissue of a tactile papilla; ×540. *d* and *e*) filiform papilla from a rat with interrupted sympathetic nerve supply; ×360 in *d*, ×540 in *e*. *f*) adrenergic nerve fibers in lingual tactile papillae after neonatal administration of capsaicin. ×360.

the sensory periphery is first and foremost one of the excitation of primary sensory afferents by chemical means: the application of a mechanical nocigenic stimulus may result in degranulation of the mast cells in contact with collagen and other structural fibers and in histamine release. The release and accumulation of this pain inducer may affect the terminal portions of primary afferents. Endogenous histamine is known to be capable of raising the sensitivity of primary afferents from a subnocigenic to a nocigenic level, thereby enhancing their sensitivity to the mechanical stimulus [6]; moreover, impulses may be generated by the nerve fibers themselves.

The sensory formations of the tongue have a well-developed peptidergic nerve supply [11,12,15]. SP cannot be classed among the algogens but, as has been shown for chemosensory lingual structures [3,6], it may have a part to play in the organization of pain sensitivity.

This work received financial support from the Russian Foundation for Basic Research (Project No. 93-04-7301).

REFERENCES

1. Z. V. Lyubimova and A. I. Esakov, *Byull. Eksp. Biol. Med.*, **86**, № 12, 641-644 (1978).
2. Z. V. Lyubimova, A. A. Kurnosova, and A. I. Esakov, *Byull. Eksp. Biol. Med.*, **95**, № 6, 116-119 (1983).
3. Z. V. Lyubimova, S. A. Subrakova, and A. A. Nikitina, *Byull. Eksp. Biol. Med.*, **114**, № 12, 563-565 (1992).
4. V. M. Khayutin, in: *Interoceptors, Regulation of Physiological Functions, and Behavior* [in Russian], Leningrad (1976), pp. 230-247.
5. P. U. Angeletty, R. Levi-Montalcini, and F. Caramia, *Brain Res.*, **43**, № 2, 515-525 (1972).
6. S. M. Bond, F. Cervero, and D. S. McQueen, *J. Physiol. (London)*, **315**, 15 (1982).
7. S. H. Buck and T. F. Burcs, *Pharmacol. Rev.*, **38**, 179-226 (1986).
8. B. Falck and Ch. Owman, *Acta Univ. Lundensis*, **2**, № 7, 1-23 (1965).
9. S. Giuffrida, G. Parenti, T. Catti, *et al.*, *Pharmacol. Res. Commun.*, **20**, № 3, 243-244 (1988).
10. M. J. Karnovsky and L. Roots, *J. Histochem. Cytochem.*, **12**, 219-221 (1964).
11. L. Landblad, J. M. Lundberg, E. Brodin, *et al.*, *Acta Otolaryngol. (Stockholm)*, **96**, 485-493 (1983).
12. P. Montavon, K. Lindstrand, A. Luts, *et al.*, *Regul. Pept.*, **32**, 141-150 (1991).
13. J. I. Nagy, *Trends Neurosci.*, **5**, № 10, 362-365 (1982).
14. J. I. Nagy, M. Goedert, S. P. Hunt, *et al.*, *Neuroscience*, **7**, № 12, 3137-3151 (1982).
15. T. Nishimoto, H. Ishikawa, S. Wakisaka, *et al.*, *Anat. Rec.*, **212**, № 4, 430-436 (1985).