# ROLE OF THE PAIN COMPONENT IN THE ORGANIZATION OF THE CHEMOSENSORY TASTE REACTION

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The food of animals and man may contain harmful components with nocigenic properties. The intake of food from the external environment is under the chemosensory control of the tongue. We have as yet no sufficiently complete idea of the peripheral mechanisms of protective reactions to pain, but there is indirect evidence of the existence of a structural and functional organization at the sensory periphery, which provides the pain component of taste sensitivity. First, several nocigenic additives (alkaloids of red and black pepper, mustard) evoke a nociceptive response and alter bitter and salt taste [5]. Second, the presence of a pain inducer such as histamine in the taste buds [2] and, third, the presence of fibers (pain afferents), reacting to substance P (SP), and penetrating to the site where histamine is found [4, 6-9].

The aim of this investigation was to study the structural and functional organization of the orosensory periphery, maintaining the nocigenic component of taste sensation.

## EXPERIMENTAL METHOD

Experiments were carried out on adult noninbred male rats weighing 250 g. Sources of histamine in the taste buds and the reaction of the mast cells to a chemical nocigenic taste stimulus [a solution of red pepper, the juice of the lily *Calla (Richardia, Zantedeschia)*, polymyxin, etc.] were detected by the method described previously [2]. On the same preparations, after fluorescence-histochemical staining of the sections with a 1% aqueous solution of toluidine blue, mast cells were identified There were two series of behavioral experiments. In series I the physiological role of histamine and SP-positive fibers in the transmission of nociceptive taste sensation and in the mechanism of licking movements was studied For this purpose, capsaicin (50 mg/kg) was injected in a volume of 0.2 ml 3 times subcutaneously into the experimental animals on the 2nd-4th days of postnatal development. After 2 months the animals were tested for consumption of pungent substances and water. In this series of experiments the number of licking movements was recorded during the first 20 min after water deprivation for 24 h. In series II the choice of substances was studied in the two-bottle test on SP-denervated animals (after treatment with capsaicin) and with their SP-ergic nerve fibers intact (control group). The following solutions were used as taste stimuli: quinine hydrochloride ($1 \cdot 10^{-4}$ M, $2 \cdot 10^{-4}$ M), sucrose (0.1 M), and common salt (1%). All solutions were at room temperature. Concentrations of sucrose and salt were close to the preferred values, while quinine solutions were close to the level of rejection.

*Deceased.

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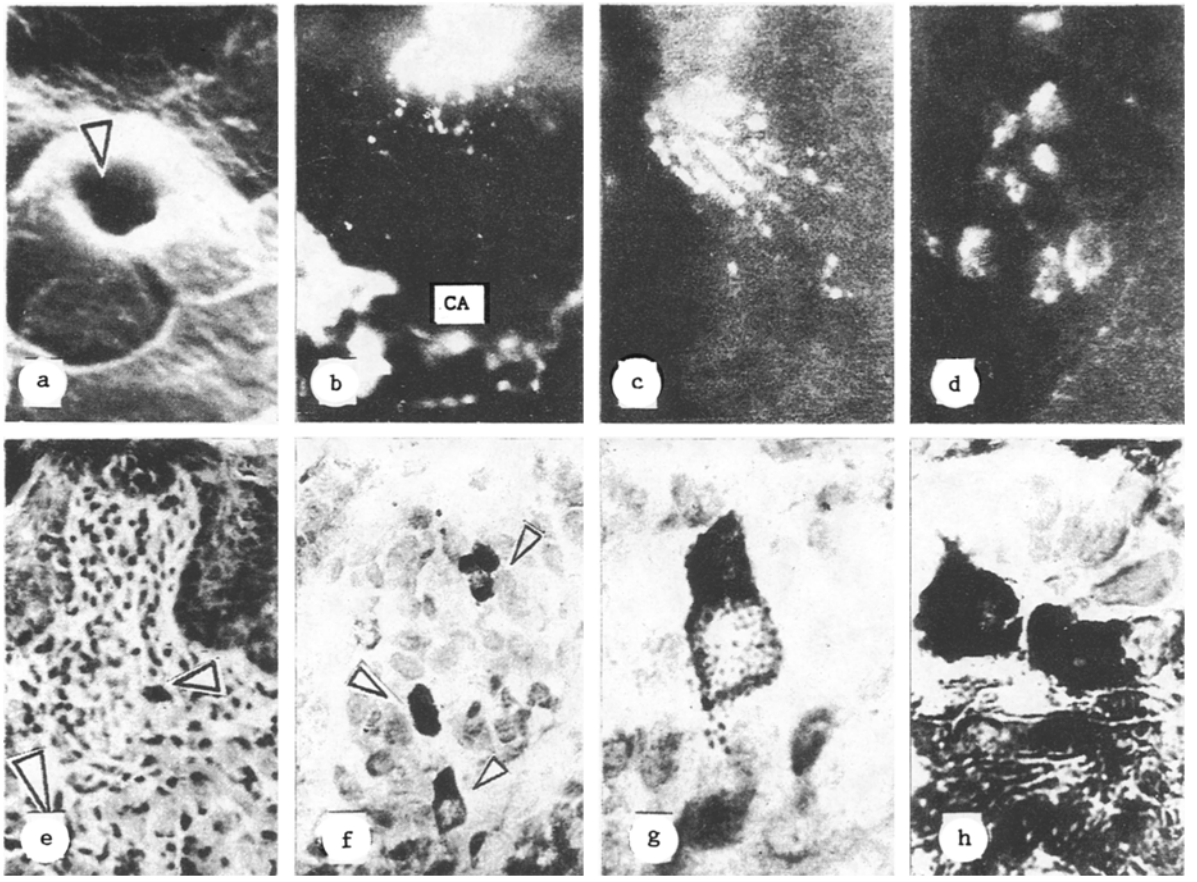


Fig. 1. Localization of histamine-containing cells in sensory taste formations at the tip of the rat tongue: a) apical part of taste bud of fungiform papilla. Gustatory pore seen in center (arrow). Scanning microscopy. 6000×; b) Histamine in apical part of taste bud (arrow) and basal plexus of catecholaminergic fibers (CA). 720×; c) Histamine granules in apical part of taste bud. 720×; d) Histamine granules in basal cells of taste bud after application of pungent substance. 720×; e, f, h) Mast cells (arrow) in basal part of papilla. e) 100×; f) 400×; h) 900×. g) Degranulation of mast cell after stimulation by pungent substance. 720×; b, c, d) Fluorescence-histochemical method (Falck, Hillarp, et al., 1962). e-h) Stained with 1% aqueous solution of toluidine blue. h) With subsequent impregnation by Bielschowsky-Gros method.

## EXPERIMENTAL RESULTS

On the anterior free surface of the tongue, which is the first part to exercise chemosensory control over the food entering from the external environment, histamine is located in the region of the taste bud (Fig. 1a). Injection of activators of histamine synthesis, of its precursors, and of enzyme inhibitors revealed the distribution of histamine granules in the apical part of the taste bud of the fungiform papilla in the form of lobules (Fig. 1c). A network of adrenergic fibers, forming the perigemmal plexus in the basal part of the taste bud also was found in the papillae (Fig. 1b).

On application of pungent substances — histamine liberators — to the tongue histamine was released initially in the apical part of the papilla (Fig. 1b). In response to the chronic action of capsaicin a decrease was observed in the intensity of fluorescence of the cells, indicating a decrease in their histamine content (Fig. 1d). The source of histamine in the basal part of the bud could be mast cells, which are more often concentrated close to the small blood vessels of the connective and muscular layers, in the basal part of the taste papillae (Fig. 1e, f, h). During nociceptive stimulation (application of pungent substances) some degree of degranulation of the mast cells could be observed (Fig. 1f, g). This is in agreement with data in the literature indicating that exhaustion of histamine in the mast cells as a result of prolonged administration of substance 48/80, a histamine liberator, leads to weakening of perception of the pain stimulus [3]. The apical part of the cells of the taste buds of the foliate and vallate papillae of the rat tongue does not contain histamine (Fig. 2a, b). It was

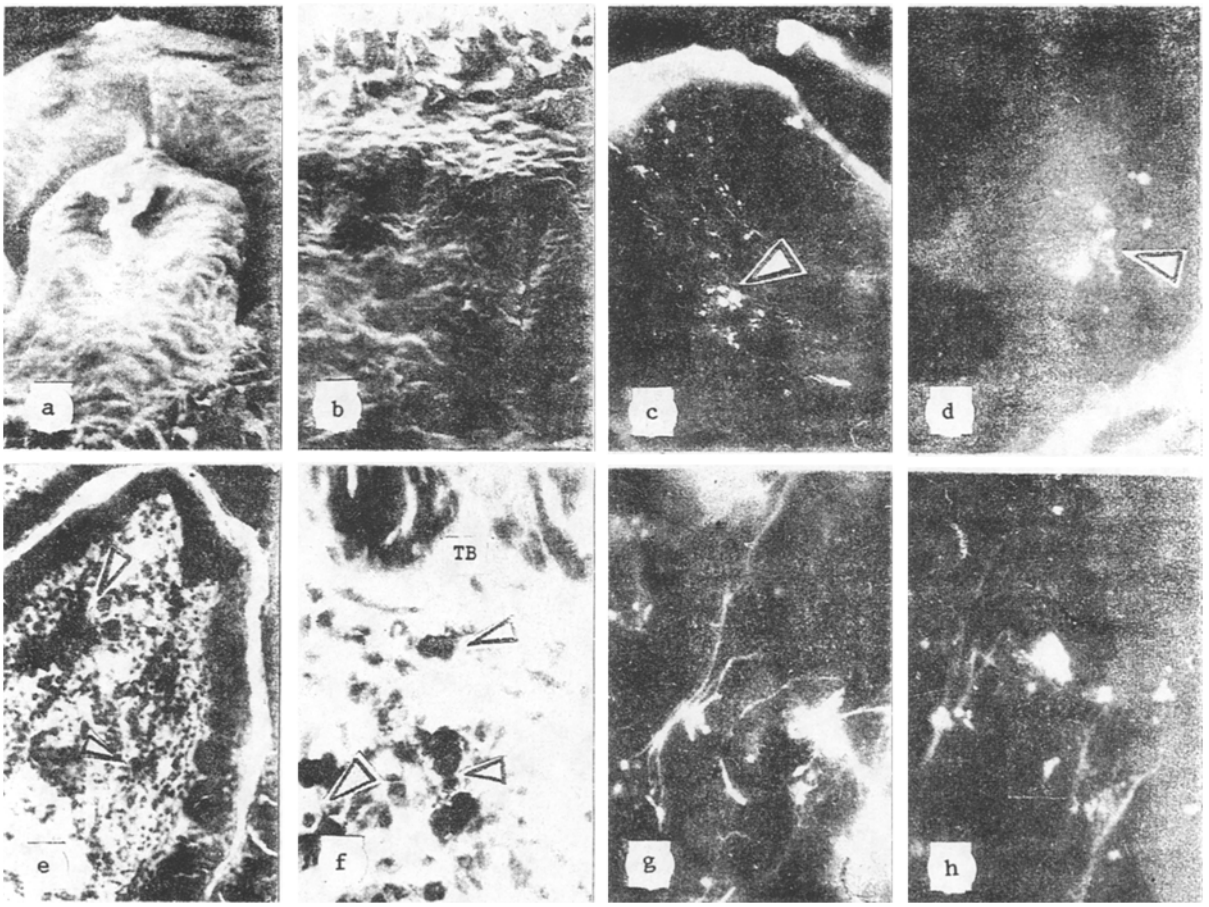


Fig. 2. Localization of histamine-containing cells in chemosensory formations of body and root of rat tongue: a) vallate papilla. 100×; b) Foliate papilla. 100×; c) Histamine-containing granules (arrow) in stroma of vallate papilla. 320×; d) Histamine granules (arrow) in basal part of taste bud of vallate papilla 720×; e, f) Mast cells (arrow) in stroma of vallate papilla. TB) Taste bud; e) 100×, f) 900×; g) collagen fibers and histamine granules. 720×; h) Collagen fibers and mast cells. 720×. a, b) Scanning microscopy; c-h) fluorescence-histochemical method (Falck, Hillarp, et al., 1962). e, f) Stained with 1% aqueous solution of toluidine blue.

shown by the fluorescence-histochemical method that histamine is located mainly in the stroma of the papilla (Fig. 2c) in the basal part of the taste bud (Fig. 2d). The main source of histamine, reacting to pungent substances in these papillae, is evidently the mast cells (Fig. 2h), the number and state of which vary depending on the duration of action of nocigenic chemical components of the food on the tongue. Histamine granules are often found close to the collagen fibers and are probably connected with them (Fig. 2c, g).

Thus the chemosensory apparatus of the tongue includes structures responding by release of histamine to chemical substances contained in the food: these may be pungent and substances with a pungent and bitter (in the present experiments) taste [alkaloids of pepper, namely piperine and capsaicin, antibiotics — polymyxin, the juice of the lily *Calla* (*Richardia*, *Zantedeschia*), and so on], Incidentally, the anterior free surface of the tongue is the first to participate in the evaluation of the food stimulus and the histamine of its papillae is located near the surface of the tongue — in the apical part of the taste buds. This facilitates contact between the receptor surfaces of the cells and nocigenic chemical and physical stimuli. Apical histamine may play the role of local chemical mediator, rapidly triggering a whole series of nocigenic peripheral reactions, with which the taking or rejection of food is connected. In the foliate and vallate papillae, which monitor the composition of the food undergoing processing in the mouth, and located in the depth of the mouth, the nocigenic component of the taste reaction is connected with the histamine in the basal part of the taste buds.

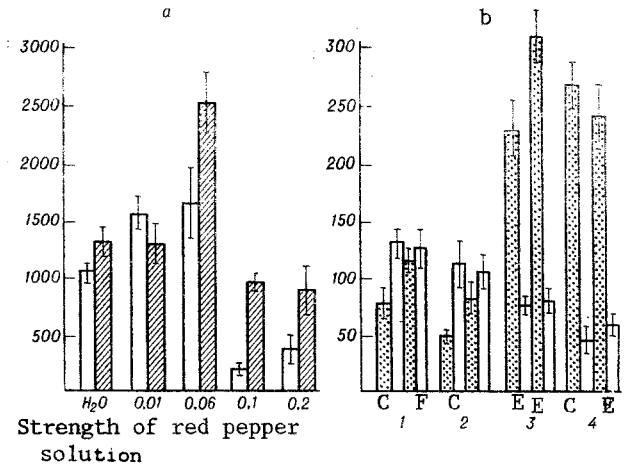


Fig. 3. Changes in taste sensation in rats: a) number of licking movements (ordinate) in animals consuming water and a red pepper solution of varied concentrations; unshaded columns — control, shaded — experiment; b) two-bottle test. Quantity of fluid drunk (ordinate, ml/kg); unshaded columns — $H_2O$, shaded — solution; 1) quinine hydrochloride $1 \cdot 10^{-4}$ M — $H_2O$; 2) quinine hydrochloride $2 \cdot 10^{-4}$ M — $H_2O$; 3) NaCl 1% — $H_2O$; 4) sucrose 0.1 M — $H_2O$; C) control, E) experiment.

Analysis of the character of the drinking behavior of the rats showed active consumption of pungent solutions in high concentration by animals under chronic treatment with capsaicin. Rats of the experimental group performed more licking movements pungent during consumption of solutions in high concentration compared with the controls (Fig. 3a). The results of experiments with choice of substances in the two-bottle test by experimental and control animals showed that animals of both group preferred both salt and sweet solutions, but rats of the experimental group drank less sweet solution than the controls (Fig. 3b). The percentage of preference of sucrose by animals of the experimental group was 75.7% and of the control group 82.5%. Meanwhile the experimental animals drank more salt solution than the controls, The percentage of preference was 73.7% and 66.4% respectively, The taste sensation was appreciably modified in relation to the bitter solution. Whereas the control animals rejected the $1 \cdot 10^{-4}$ solution of quinine hydrochloride by 41.5%, the experimental animals did so by only 3.68%, i.e., for denervated rats quinine in a concentration of $1 \cdot 10^{-4}$ M was close to the hedonic threshold. With an increase in the quinine concentration to $2 \cdot 10^{-4}$ M animals of both groups increased their rejection of quinine (by 58.3% in the control and 23.1% in the experiment). On the whole the quantity of fluid consumed in the combination (NaCl 1% — $H_2O$), (quinine hydrochloride [$1 \cdot 10^{-4}$ M and $2 \cdot 10^{-4}$ M] — $H_2O$) by animals of the experimental group was greater than that consumed by the controls; in the combination (sucrose 0.1 M — $H_2O$) animals of the experimental group drank much less liquid than the controls.

Subcutaneous postnatal injection of capsaicin, leading to destruction of SP-ergic nerve fibers, thus appreciably modifies taste sensation, more especially in relation to bitter substances.

Thus histamine-containing cells and SP-ergic fibers of the chemosensory formations of the tongue constitute the structural and functional organization maintaining the peripheral pain response in taste sensation as a means of monitoring the content of harmful chemicals entering the body with the food.

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