CHANGES IN ACTIVITY OF THE TASTE RECEPTOR APPARATUS AND PREFERENCE FOR SODIUM CHLORIDE SOLUTION IN NEWBORN RATS TREATED WITH CAPSAICIN

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The discovery of substance P (SP) — immunoreactive nerve fibers in the taste buds of the rat and cat tongue [10, 12] — aroused great interest on the part of research workers in the role of this peptide in function of the taste receptor apparatus. Immunoelectron-microscopic studies of the structure and synaptic contacts in the taste buds of the vallate papillae of rats showed that these nerve fibers are probably not taste afferents. Meanwhile the use of fluorescence microscopy shows that after injection of SP the serotonin content in cells of the taste bud of the frog fungiform papillae is increased in the gustatory epithelium [7]. Electrophysiological experiments [2] have shown that injection of SP into the dorsal part of the rat tongue leads to potentiation of combined spike responses recorded from the nerve of taste — the chorda tympani — during stimulation of the receptor surface of the tongue by solutions of sodium chloride (NaCl) and citric acid; responses to sucrose and quinine under these circumstances were not significantly changed. Rats deprived of food and fluid, after subcutaneous injection, drank more NaCl solution than rats receiving injections of physiological saline or the fragment SP_{4-11} [2]. The mechanisms of the effect of SP on activity of the taste receptor apparatus in the course of NaCl consumption are thus not completely clear and require further study.

The aim of this investigation was to study function of the taste receptor apparatus under conditions of SP deficiency in the gustatory epithelium of adult animals. For this purpose the method of injection of capsaicin — a substance which destroys SP-ergic nerve fibers and neurons when used by this method, was adopted [11, 13, 14].

EXPERIMENTAL METHOD

Two liters of newborn laboratory rats were given subcutaneous injections, 24 h after birth, of 50 mg/kg of capsaicin ("Serva," West Germany), dissolved in the mixture of 10% ethanol with 10% Tween-80 in physiological saline [13, 14] (experimental group). Rats of the second litter received an injection of the solvent of the capsaicin alone (control group). After 4 weeks the rats were taken from their mothers, and after 5 weeks males and females were separated, after measurement of their rectal temperature, and they were kept in different cages. Throughout the investigation the young rats were weighed once a week; the development of their sense organs and growth of their hair were observed. Experiments were carried out on male and female rats. Twelve rats (six experimental and six control) were kept one to a cage, 7 weeks after birth, so that for a period of 5 days it could be ascertained what drink (0.1 M NaCl or water — W) the animals preferred, given unrestricted access (the two-bottle method). Preference was judged as the difference in the volumes of NaCl solution and W drunk and the following behavioral reactions were distinguished: consistent preference for W (the W reaction type) or NaCl (the NaCl reaction type), or a change of taste, i.e., an attraction for W instead of NaCl (NaCl → W), and to NaCl from W (W → NaCl). The NaCl and W → NaCl reaction types were interpreted as preference for NaCl, W and NaCl → W reactions were interpreted as preference for water [6].

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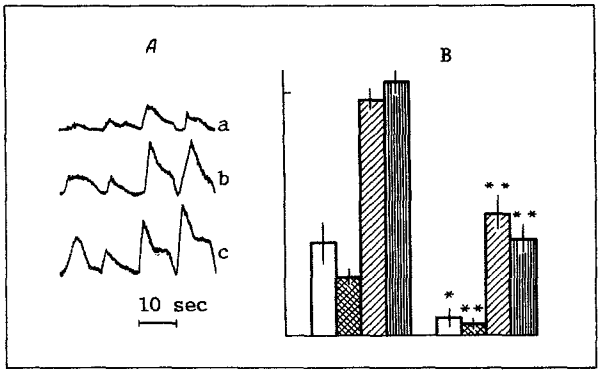

Fig. 1. Decrease in amplitude of taste responses in rats of experimental and control groups. A) Integral curves of taste responses (here and in Fig. 1B): a) left to right, sucrose, quinine, NaCl, and citric acid; b) taste responses in 8- and 16-week-old rats of experimental group; c) in 8-week-old rats of control group. Time marker 10 sec. B) Mean amplitudes of taste responses (standard error and $M \pm m$ shown) in 8-week-old rats of experimental (right) and control (left) groups. Abscissa, tasty substances; ordinate, amplitude of taste responses (in spikes/sec). $^*p < 0.05$, $^{**}p < 0.01$.

After the end of testing the animals were used in an electrophysiological experiment. Combined spike activity of the chorda tympani was recorded in rats anesthetized with pentobarbital (40 mg/kg) in response to stimulation of the receptor surface of the tongue with tasty solutions: 0.3 M sucrose, 0.01 M quinone sulfate, 0.1 M NaCl, and 0.1 M citric acid. Spike activity was recorded and converted into an integral curve by the method described previously [4]. The significance of differences was calculated by the Student—Fisher test.

EXPERIMENTAL RESULTS

Analysis of the postnatal development of the young rats showed that the increase in body weight over a period of 6 weeks was identical in the experimental and control groups, but by the 7th week the body weight of rats of the experimental group exceeded that of the control (171.8 ± 7.9 and 131 ± 5.6 respectively, $p < 0.01$). No significant differences were observed between the groups as regards the times of maturity in the young rats of the visual (opening of the eyes) and auditory (response to sound) systems, or of the switch to independent feeding. Meanwhile the appearance of hair on the body was observed 8 days earlier in rats of the experimental group than in the control (the 6th and 14th days respectively). This delay can be explained by deficiency of neurotrophic influences of the nervous structures of the skin, containing SP, whose normal development was disturbed as a result of the injection of capsaicin. The rectal temperature of rats of the experimental group, measured 5 days after birth, was higher (37.4 ± 0.2°C) than in young rats of the control group (36.8 ± 0.1°C, $p < 0.02$). Since we known [1, 3, 11] that exogenous administration of SP leads to lowering of the body temperature in rats, the hyperthermia in animals of the experimental group also indicates a deficiency of SP-ergic nervous structures regulating temperature homeostasis.

Analysis of bioelectrical activity of the taste receptor apparatus in 8-week-old rats showed that the amplitudes of the integral responses to stimulation of the tongue by sucrose, quinine, NaCl, and citric acid were less in rats of the experimental group than in the control (Fig. 1A). However, 16 weeks after birth the taste responses regained the control level (Fig. 1). Neuroanatomical studies have shown [11] that after neonatal injection of capsaicin into rats degeneration of unmyelinated primary afferent SP-ergic nerve fibers is observed in rats. Neonatal injection of capsaicin probably induces degeneration or underdevelopment of SP-ergic nerve fibers, found in taste buds [10, 12]. Since in response to exogenous administration of SP taste responses to NaCl and acid in the gustatory epithelium increased [2], reduction of the responses in rats of the experimental group can perhaps be explained by the absence of the excitatory effect of SP-ergic structures on the taste receptor apparatus. As experiments showed, 16 weeks after birth responses were restored, and this may have been connected with gradual regeneration of nerve fibers containing SP and incorporation of the peptide into the process of regulation of bioelectrical activity of the taste apparatus (Fig. 1).

It was shown previously that the reflex facilitatory influence of intraperitoneal injection of the peptide cholecystokinin on activity of the taste receptor apparatus of the rat is mediated by efferent fibers in the composition of the chords tympani and by cholinergic neurotransmitter mechanisms [5, 9]. The problem of the possible identity of cholinergic and SP-ergic nervous structures, with an excitatory action on activity of the taste apparatus, thus arises but requires further proof obtained by the aid of neurohistochemical methods.

Reduction of activity of the taste receptor apparatus in animals of the experimental group led to a decrease in the intensity of taste sensations and to a change of taste, i.e., to preference for W or NaCl. Keeping animals given the choice between NaCl and W under observation for 5 days showed that five of six rats of the experimental group preferred NaCl and one preferred NaCl and one preferred W, whereas all six rats of the control group chose W. The persistent preference for W rather than NaCl solution (the W reaction type), observed in the control rats, can be explained by the inhibitory effect of capsaicin solution on formation of the motivational system for NaCl consumption in rats, for normal intact rats are known to drink NaCl solutions with average concentrations willingly, whereas the sensitivity of the taste receptor apparatus to NaCl in rats of the control group remained at the normal level (Fig. 1). Increased attraction for NaCl solution in rats of the experimental group was accompanied by weakening of activity of the taste receptor apparatus, possibly due to a deficiency of taste sensations, but the effect of capsaicin on brain structures (hypothalamus, amygdala) responsible for motivation of salt consumption cannot however be ruled out.

Thus SP-ergic nerve fibers of taste buds probably play the role of a factor maintaining the optimal level of activity of the taste receptor apparatus, which is essential for the normal consumption of salt by the animals.

LITERATURE CITED

1. I. P. Ashmarin and M. F. Obukhova, Biokhimiya, **51**, 531 (1986).
2. A. I. Esakov, O. N. Serova, and N. A. Solov'eva, Abstracts of Proceedings of the 15th Congress of the I. P. Pavlov All-American Physiological Society [in Russian], Vol. 2, Leningrad (1987), p. 299.
3. V. E. Kluša, Peptides — Regulators of Brain Function [in Russian], Riga (1984).
4. O. N. Serova and K. V. Golubtsov, Byull. Éksp. Biol. Med., **85**, 631 (1978).
5. O. N. Serova and A. I. Esakov, Fiziol. Zh. SSSR, **71**, 1271 (1985).
6. O. N. Serova and A. I. Esakov, Zh. Vyssh. Nerv. Deyat., **36**, 150 (1986).
7. N. A. Solov'eva and A. I. Esakov, Byull. Éksp. Biol. Med., **98**, 389 (1984).
8. P. Oehme, M. Wienert, K. Hecht, and J. Bergman, Substance P: Some Problems in Chemistry, Biochemistry, Pharmacology, Physiology, and Pathophysiology [in Russian], Riga (1984).
9. A. I. Esakov and O. N. Serova, Motivation in Functional Systems, K. V. Sudakov (ed.), New York (1987), pp. 301-313.
10. J. M. Lundberg, T. Hokfelt, A. Anggard, et al., Acta Physiol. Scand., **107**, 389 (1979).
11. J. I. Nagy, Trends Neurosci., **5**, 362 (1982).
12. T. Nishimoto, M. Akai, S. Inagaki, S. Shiosaka, et al., J. Comp. Neurol., **207**, 85 (1982).
13. M. Schultzberg, G. J. Dockray, and A. G. Williams, Brain Res., **235**, 198 (1982).
14. H. Traurig, A. Saria, and F. Lembeck, Arch. Pharmacol., **327**, 254 (1984).
15. H. Yamasaki, Y. Kubota, H. Takagi, and M. Tokyama, J. Comp. Neurol., **227**, 380 (1984).