Neurophysiological Changes in the Frog Taste Nerve Responses Induced by Chronic Ethanol Injection

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As has now been demonstrated, chronic ethanol injection induces various changes in the morphostructural organization of the taste receptor apparatus in animals. The dynamics of these changes is dependent on the duration of alcoholization. In the early period (7-30 days of ethanol injection) the predominant changes are function-related, with shifts of a compensatory character such as swelling, lightening, and contour erosion of receptor-carrying cells and their apical processes and sensory nerve endings [1]. Prolonged ethanol injection over 3-10 months results in the development of destructive processes and atrophy of the taste buds, as well as degeneration of the taste nerve fibers [1,2].

In addition, a significant reduction of acetylcholinesterase activity in structures of the taste organ and sensory fibers is recorded under chronic alcoholization [3].

These morphological and histochemical changes in the organization of the taste receptor apparatus are accompanied by impairment of its functional activity. The data on a decrease in impulse frequency in the taste receptors' response to stimulation of the tongue with test solutions speak in favor of this conclusion [1].

For further elucidation of the effect of ethanol on taste receptor apparatus functioning, we analyzed the impulse response latency (L) of the taste receptors to different taste stimuli and studied the frequency-temporal characteristics of these responses under chronic ethanol injection.

MATERIALS AND METHODS

The experiments were performed on 65 frogs kept under laboratory conditions at +10°C. Ethanol injections were carried out as described earlier [1]. Control animals received water. Electrophysiological experiments were performed on the frogs that had been immobilized by destruction of the brain and spinal cord 7 (group I), 14 (group II), 30 (group III), 60 (group IV), and 90 (group V) days after the first ethanol injection. Each group included 5 control and 8 experimental animals. To exclude the narcotic effect of ethanol, its administration to the experimental animals was stopped 1-1.5 days prior to the electrophysiological experiments. The impulse responses of the taste receptors to stimulation of the tongue with different taste stimuli (0.5 M NaCl, 0.5 M glucose, 0.25 M sucrose, 0.3 mM quinine chloride, 1.25 mM HCl, and tap water) were recorded with bipolar silver electrodes from the glossal branch of the glossopharyngeal (taste) nerve. The test solutions were applied in a volume of 5 ml to the dorsal surface of the tongue during 15 sec. Subsequently, the tongue was thoroughly washed with Ringer solution. The interval between stimulations constituted 2-3 min. The period between the appearance of the electrical artefact elicited by the contact of the taste stimulus with the tongue and the generation of the first nerve impulse was taken as the im-

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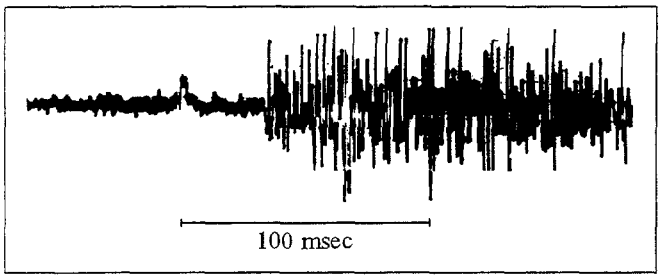

Fig. 1. Electrical artefact and impulse response of the frog taste nerve to stimulation of the taste receptors.

pulse response latency (L) (Fig.1). Average L values were compared using the Student *t* test.

RESULTS

The impulse response latency in the experimental animals proved to be dependent on the type of taste stimulus and inceased on average 3.5 and 4.5 times for sucrose and glucose, respectively, almost 2 times for salt, water and quinine, and 4 times for acid stimuli after 7-14 days of ethanol injection in comparison with the corresponding indexes in the control animals (Table 1).

After 30 days, although the ethanol injections were continued, the response latency tended to shorten. This is probably connected with the compensatory-adaptational mechanisms switched on to normalize the functional activity of the taste receptor apparatus. By this time the response latency of the chemoreceptors for sweet stimuli had decreased more than 2-fold in comparison with the previous period. However, the differences in L values in receptor responses to salt, water, quinine, and acid were insignificant; their average values decreased by 4-19 msec (Table 1).

The inhibitory effect of ethanol on the taste receptor apparatus under chronic alcoholization became more expressed after 2 months and led to a new rise in response latency. On average, the response latency of the taste receptors to stimulation with sucrose, glucose, salt, water, quinine, and acid exceeded the values in intact animals 4, 5, 2, 3, 2, and 4 times, respectively (Table 1). For further ethanol injections during 30 days the response latency remained at a constant level.

Together with a rise in the latency values in these periods, we observed changes in the nature of the responses to salty and acid irritants. Figure 2 demonstrates the frequency-temporal characteristics of the taste reaction to irritation of the tongue with 0.5 % sodium chloride in the control and experimental (after 3 months of ethanol injection) animals. As follows from Fig. 2, *a*, the summed impulse reaction of the taste receptors to salt stimulus of a certain concentration is represented by an initial phasic and a subsequent tonic response. The impulse frequency of the phasic response (that lasted 9 sec) reached its maximum (665 imp/sec) 1 sec after stimulation was begun, decreased gradually to 209 imp/sec later on, and remained at that level until the end of stimulation. In other words, the phasic response gave way to a tonic response. In this experimental animal the afferent impulsation frequency decreased, the peak of the phasic response was also observed 1 sec after the beginning of stimulus application, but the response duration dropped to 4 sec. During this period the impulse frequency fell from 224 imp/sec to 64 imp/sec.

The initial phasic response was followed by a second wave of excitation and the impulse frequency increased to 144 imp/sec The second peak of impulse activity was observed 7 sec after stimulation was started and lasted only 1 sec. The impulse frequency then gradually decreased (Fig. 1, *b*).

According to current views, the latency of impulse responses of the taste receptors to taste stimuli recorded from sensory nerve fibers is defined as the sum of the time spent on adsorption of irritants on the cell membrane and interaction

TABLE 1. Impulse Response Latency (msec) of Taste Receptors to Taste Stimuli as a Function of Alcoholization Period ($M \pm m$)

Duration of ethanol injections (days)	Sucrose	Glucose	Taste stimuli			
			Salt	Quinine chloride	Acid	Water
7–14	133.29±8.11 (14)	134.71±12.48 (14)	31.5±1.73* (16)	181.37±11.08* (13)	120.0±11.8* (12)	68.69±7.32* (13)
30	61.38±4.1* (8)	60.89±3.07* (9)	27.38±0.92* (8)	170.91±8.7* (11)	101.6±11.54* (10)	55.5±4.13* (11)
60–90	164.36±9.41* (11)	157.0±7.2* (9)	32.22±2.34* (9)	194.22±8.32* (9)	188.89±11.72* (9)	111.63±12.52* (8)
Control	38.93±10.05 (15)	30.54±2.59 (13)	16.71±0.79 (14)	87.92±7.12 (12)	28.31±2.07 (13)	34.77±1.82 (13)

Note. Asterisk denotes of differences in comparison with the control $p<0.05$. Number of animals shown in parentheses.

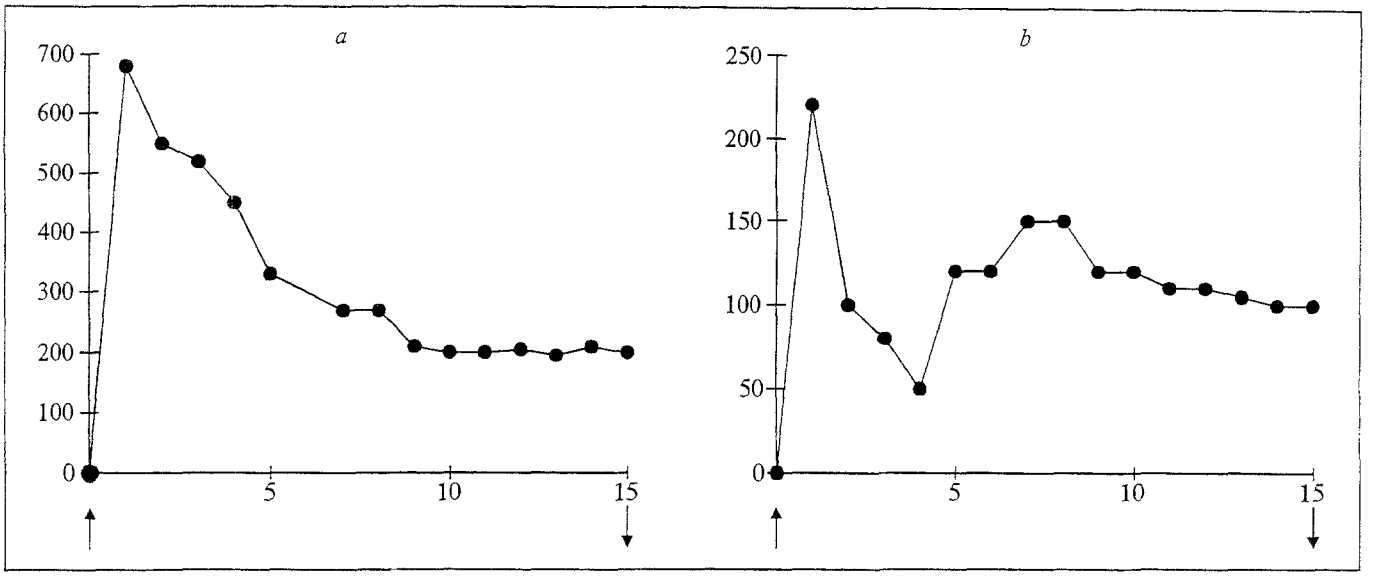

Fig.2. Dynamics of impulse response of taste receptors to stimulation with 0.5 M sodium chloride, recorded from the glossopharyngeal nerve of the control (*a*) and experimental (*b*) animals after 3 months of ethanol injections (a separate example). Abscissa: course of reaction (sec); ordinate: number of impulses/sec. Arrows point to the beginning and end of stimulation.

with receptor molecules; on the generation of the receptor potential; on the synaptic transmission of excitation from the receptor cell to the sensory nerve fibers; on the generation of the first impulse and its further conduction to the electrodes. The response latency is dependent on a number of factors, in particular, on the modality of the taste stimulus [5], which may be explained by the variability of the primary mechanisms of chemoreception. The results obtained confirm this supposition. In our experiments the responses of the taste receptors to sodium chloride were characterized by the shortest latency (16.7 msec on average), while the responses to quinine had the longest latency (87.92 msec). The latency of the responses to other stimuli (sucrose, glucose, acid, and water) had intermediate values and constituted 38.93, 30.54, 28.3, and 34.7 msec, respectively. Chronic ethanol injections led to an increase in the response latency, the process showing different dynamics for different stimuli. The latency prolongation was more pronounced for glucose, sucrose, and acid and less so for the other stimuli. The reason for such a different behavior should probably be sought in pecularities of the effect of ethanol on the primary mechanisms of chemoreception.

The ethanol-induced prolongation of the impulse response latency may be a result of disturbances in the transmission of taste stimuli to sensory nerve fibers and transformation of excitation into nerve impulses, as well as of a delayed course of all the steps starting with the adsorption of a taste stimulus on the cell membrane to the generation of the first impulse. Besides, it seems likely that impulse conduction along the nerve fibers to the recording electrodes is also slowed down. The morphofunctional changes recorded in receptory cells, synaptic formations, Ranvier's nodes, and other structures of the sensory nerve fibers under the action of ethanol support this conclusion [1,3].

Chronic ethanol administration was shown to induce changes in the dynamics of impulse responses of the taste receptors to salt and acid that were reflected in the appearance of a second peak of impulse frequency. It is probable that under these conditions, as additional chemosensory structures, the sensory nerve fibers located within the taste organ or outside of it, in the mucosal epithelium, become involved in chemoreception of these stimuli. In our opinion, as a result of destructive changes in the taste organ and impairment of the cell-cell contacts, taste irritants such as salt or acid excite not only receptor cells. Freely penetrating into the taste buds, they directly activate the nerve endings, leading to a momentary increase in impulse response frequency. In the normal situation chemoreception proceeds via a similar mechanism under the influence of strong salt irritants [4]. The appearance of a second peak of impulsation in the response of the taste receptors to 0.5 M sodium chloride 7 sec after the beginning of ethanol stimulation is reminiscent of the reaction of the taste receptors to stimulation with 1 M NaCl [4]. As a consequence, the precision of sensory analysis may be reduced and differentiation between stimuli of similar intensity may be impeded.

Thus, the results obtained, together with earlier data demonstrating a decrease in the frequency of afferent impulses in taste reactions, indicate that under chronic alcogolization the neurophysiological mechanisms involved in the functioning of the taste receptor organ become impaired, ultimately leading to distortion, or errors, in the coding of primary sensory information.

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PATHOLOGICAL PHYSIOLOGY AND GENERAL PATHOLOGY

Relationship between Inflammation and the Stress Reaction

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It is well known that the inflammatory process is accompanied by a change of the level of glucocorticoids and catecholamines in the blood [1,10]. But there is no consensus as to whether these changes are typical for the stress reaction. If there is an interrelation between these processes, then some aspects of inflammation pathogenesis appear in a different light. Considering the tissue damage inducing an inflammatory process to be a stress factor, it is also necessary to take into account such well-known consequences of the stress reaction as secondary alteration of cells [5,13], the development of which can exacerbate an inflammatory process, prolong its course, and even result in chronic inflammation.

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The aim of the present investigation was to establish whether an inflammation is accompanied by a stress reaction and how these processes interconnect dynamically.

MATERIALS AND METHODS

Ninety male albino rats were used in the experiments. An inflammation was induced by placing a celloidin plate 5×1 mm in size in the subcutaneous connective tissue of the shank of ether-narcotized animals. To assess the dynamics of the cell reaction in the inflammatory focus, the thickness of the cellular swelling, the density of neutrophils, macrophages, and fibroblasts in it, and the number of layers of fibroblasts in the capsule were measured on the histological preparations [3]. The duration of the inflammation stages was determined

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