IMPORTANCE OF CATECHOLAMINES IN DEVELOPMENT OF REFLEX DEGENERATION OF THE STOMACH WALL

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During the last decade neurogenic forms of degeneration and the influence of neurotropic substances on them have been studied in the Department of Pharmacology [3].

Physiological and pharmacological analysis of the degenerations caused by application of excessively strong stimulation to animals [8, 9] has demonstrated their reflex character, and on this basis the pathways of the reflexes disturbing tissue nutrition have been postulated. According to these views, afferent impulses arising from reflexogenic zones to which the stimulation is applied are transmitted to nonspecific pathways in the reticular formation of the brain, thereby evoking excitation of sympathetic centers situated in the hypothalamus.

Observations made by one of the authors (E. V. Moreva) have shown that electrical stimulation of the posterior hypothalamus leads to the appearance of degenerative changes in the gastric mucous membrane similar to those produced by reflex methods. The efferent part of the reflex arc is evidently formed by sypathetic nerves along which a flow of impulses disturbing trophic processes in the stomach tissue is transmitted. This is confirmed by data showing the protective action of sympatholytic drugs—dibenamine and octadin, and also of ganglion-blocking drugs—hexamethonium, tetraethylammonium, and so on [2].

Because of the undoubted participation of the sympathetic nervous system in the mechanism of development of reflex degeneration of the gastric mucous membrane, it was decided to investigate the catecholamine content in the tissue of the stomach wall after application of extremely strong stimulation to animals.

EXPERIMENTAL METHOD

Experiments were carried out on male albino rats weighing 200-250 g. The method developed by O. N. Zabrodin [7] was used to reproduce degenerative changes: fasting rats were immobilized and subjected to electrical stimulation for 3 h. Stimulation was carried out with rectangular pulses of alternating current generated by an electronic stimulator (frequency 50 Hz , voltage 6-7 V). Intact fasting rats were used as controls. All the animals were decapitated after 3 h.

The stomach tissue was immersed in liquid oxygen and ground to a powder. A weighed sample (200 mg) was transferred into 5% trichloroacetic acid solution and homogenized. The content of catecholamines was determined fluorometrically by Euler's method [11], modified by V. A. Govyrin [5].

Control determinations of catecholamines were carried out in each experiment for the noradrenalin; in particular, the adrenalin level varied somewhat in animals of the different groups.

EXPERIMENTAL RESULTS

The investigations showed that after electrical stimulation of immobilized rats for 3 h the catecholamine content was reduced in the tissues of the stomach wall. These changes were seen particularly clearly in relation to noradrenalin. In intact animals (11 experiments) the mean noradrenalin concentration was 0.64-0.24 μg/g weight of moist tissue, while after excessive stimulation the noradrenalin concentration fell in 5 experiments to 0 and in 5 cases to 0.21-0.16 μg/g. The changes in the adrenalin concentration in the stomach tissue were not so clearly defined. A decrease in the adrenalin concentration compared with the control was observed in 10 of 11 experiments, but because of the considerable scatter of the control and experimental data, no statistically significant decrease in this index could be established.

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Hence, application of excessively strong stimulation, causing degenerative changes to develop in the stomach wall, is accompanied by a decrease in the noradrenalin concentration in the stomach tissue, evidently as a result of exhaustion of catecholamine reserves following their more intensive liberation from the tissue depot under the influence of sympathetic impulses during prolonged, excessive stimulation. The fall in the noradrenalin level in the injured stomach tissue may be probably be regarded as a sign of the onset of degenerative processes, and may be a possible cause of these changes. However, it is difficult at present to judge what is responsible for the disturbance of nutrition of the stomach tissue—the injurious action of an excess of liberated catecholamines in the initial period of stimulation or the catecholamine deficiency developing later, in connection with which the normal level of tissue metabolic processes cannot be maintained. The first hypothesis is supported by data obtained in the authors' laboratory, according to which the early signs of impending degeneration in the stomach wall appear extremely rapidly. The results of electron-microscopic investigations carried out by I. S. Zavodskaya and A. A. Manina showed that excessive stimulation for 15 min leads to changes in the mitochondria of both the chief and the oxyntic cells. According to the observations of I. S. Zavodskaya and N. I. Zaskal'ko, stimulation for 15 min is also sufficient to cause depression of mitotic activity in the epithelium of the gastric mucous membrane, a phenomenon known to be one of the signs of neurogenic degeneration [6]. Adrenalin also possesses the same property of depressing mitotic activity of cells [1].

Hence, the results obtained in this investigation show that if changes take place in the catecholamine level in the tissues or, in other words, if their balance is disturbed, the course of trophic processes is also disturbed.

It is interesting to compare these results with others recently obtained according to which intravenous injection of low concentrations of noradrenalin restores the secretion of the gastric glands when these are exhausted by prolonged exposure to histamine and acetylcholine [4].

The results of these investigations afford further confirmation that the sympathetic nervous system, which in normal conditions maintains the level of tissue nutrition [10], may also disturb this level, giving rise to degenerative changes, during the transmission of excessively intensive impulses.

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