ADRENOSENSITIVE NEURONS OF THE MYENTERIC (AUERBACH'S) PLEXUS

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Experiments on the myenteric plexus of isolated strips of the small and large intestines showed the presence of adrenosensitive cells capable of responding to application of different concentrations of adrenalin (A) and noradrenalin (NA) by a distinct increase in firing rate. The greatest effect was obtained with NA; the range of action of which was wider (from 10^{-9} to 10^{-5} g/ml) than that of A. Addition of phentolamine to the surrounding solution in most cases prevented the appearance of these effects. Besides spontaneously discharging cells, "silent" neurons with no spontaneous activity also responded to the addition of A and NA. It is suggested that catecholamines may play a direct part in the modulation of processes carried out by neurons in the ganglia of the myenteric plexus.

KEY WORDS: *myenteric plexus; adrenalin; noradrenalin; adrenosensitive neurons.*

Among mechanisms controlling the activity of the muscular layers of the digestive tract an important role is played by adrenergic inhibitory systems of the intramural ganglia [9]. This conclusion is based, in particular, on the observed presence of catecholamines in the pre- and postsynaptic elements of the myenteric plexus [3, 4]. Attempts have accordingly been made [2, 7, 8, 10] to explain the effect of biologically active substances on the character of the electrical processes in the ganglia of the myenteric plexus. However, because of the fragmentary and contradictory nature of the results, no definite conclusion could be reached. Meanwhile, because of the exceptional role of the myenteric plexus in the organization of intestinal movements, the solution of this problem is of the utmost importance.

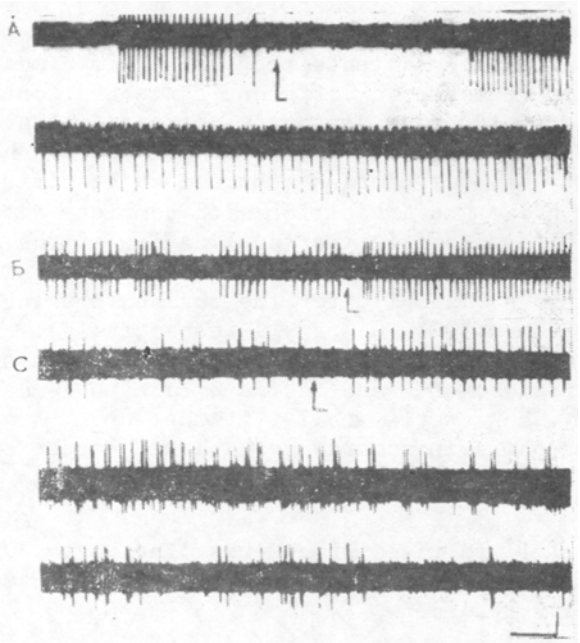

Fig. 1. Changes in character of spontaneous unit activity in myenteric plexus of cat small intestine in response to application of noradrenalin (10^{-9} g/ml). A and B) Response of neurons with "burst" type; C) with single type of activity. Here and in Fig. 2, arrows indicate times of application of drug. Calibration: 0.5 sec, 20 μV.

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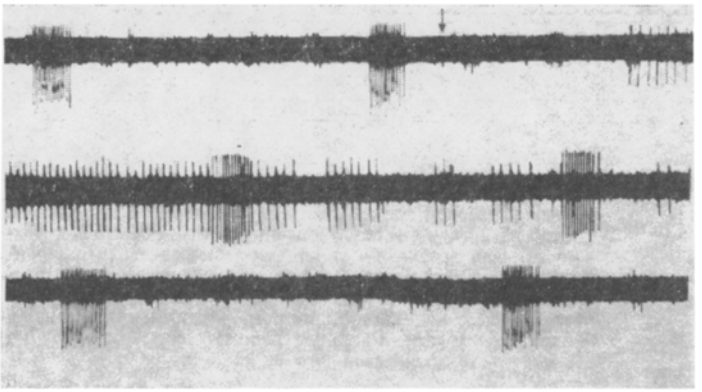

Fig. 2. Activation of "silent" neuron of myenteric plexus of cat large intestine during application of noradrenalin (10^{-9} g/ml).

The object of this investigation was to study neuronal activity in the myenteric plexus of the large and small intestines in response to the action of different concentrations of adrenalin (A) and noradrenalin (NA).

EXPERIMENTAL METHOD

Segments (4-6 cm long) of the large and small intestines of a cat were investigated and were placed in a bath containing continuously flowing oxygenated (95% O_2 + 5% CO_2) Tyrode solution, pH 7.1. The temperature of the solution in all the experiments was 37°C. By means of stainless steel needles the strip was fixed (from the side of the mucous membrane) to a Plexiglas plate on which a layer of 3-4 mm of wax was applied. The longitudinal muscular layer was removed. To reveal the plexus it was stained with $2 \cdot 10^{-5}$ M Methylene Blue solution for 4-5 min. Metal microelectrodes with a tip 2-5 μ in diameter and a resistance of 0.5-1 MΩ were used. The solutions of A and NA were applied to the surface of the myenteric plexus.

EXPERIMENTAL RESULTS

Spontaneous unit activity of the myenteric plexus consisted either of single discharges of varied pattern or bursts of 4 to 15 spikes. In response to different concentrations of solutions of A and NA, the discharge frequency increased. The responses differed in their latent periods (from 3 to 5 sec) and duration (from 10 to 15 sec). After the preparation had been been rinsed with Tyrode solution, the activity of most neurons returned to its initial level and only in a few cases was it replaced by prolonged inhibition with complete disappearance of activity. The ability of the cells to respond to a further application of the drug was usually restored after 10-30 min. Characteristically, neurons with "bursts" and single types of activity were more sensitive to NA than to A (Fig. 1), for the threshold value for NA was 2 or 3 orders of magnitude lower (10^{-9}-10^{-8} and 10^{-6}-10^{-5} g/ml, respectively). "Silent" cells, the character of whose activation was indistinguishable from that of the spontaneously active neurons, also responded to application of A and NA. As a rule these cells again became "silent" after excitation (Fig. 2). Characteristically, neither A nor NA affected the discharges of oscillator cells discharging in pairs in accordance with the master and slave principle [7, 10], but acted only on the slave neurons irrespective of the group to which it belonged.

Preliminary addition of phentolamine (10^{-5} g/ml) to the surrounding solution in 80% of cases prevented the appearance of effects of A and NA; propranolol (10^{-5} g/ml) caused no significant change in the structure of the activity recorded.

These effects of the catecholamines can evidently be explained primarily by simple interaction of A and NA molecules with the postsynaptic membrane, leading eventually to depolarization. In that case A and NA behave as ordinary chemical mediators. This hypothesis is confirmed by the results of histochemical investigations [3, 4] according to which presynaptic terminals of the myenteric plexus contained many adrenalin as well as acetylcholine vesicles. Exogenous radioactive NA is also concentrated in these structures. Finally, this hypothesis is also supported by the results of experiments with phentolamine, which indicates the presence of α-adrenergic receptors on the neuron [6, 7]. Another acceptable explanation is that catecholamines in this particular case facilitate the transmission of

excitation into the ganglia, by playing the role of modulators [5]. Which explanation is more in accordance with reality only closer investigations carried out for this purpose will show.

Neurons of the myenteric plexus in segments of the large intestine lying in the zone of innervation of the caudal mesenteric sympathetic ganglion, the cells of which have a regulatory effect on contractions of its distal part [1], were found to be most sensitive to A and NA. In this connection, neurons of the intramural ganglia in this region, it can be suggested, are more vulnerable to the influence of sympathetic postganglionic fibers than cells of the plexuses of the small intestine.

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CHANGES IN THE SYSTEMIC HEMODYNAMICS PRODUCED BY VASOPRESSIN IN DOGS DURING INDIVIDUAL DEVELOPMENT

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Indices of the central hemodynamics were studied in puppies aged 18-22 days and 2-3 months and in dogs aged 3-5 years after intravenous injection of synthetic vasopressin (0.8 unit/kg body weight). The pressor effect was strongest in the adult dogs and bradycardia in the puppies aged 18-22 days. The cardiac output was reduced in all animals and the peripheral resistance considerably increased. In adult dogs the external work of the left ventricle and the energy consumption of the heart were increased. In puppies a reduction in the volume velocity of ejection of blood and in the external work of the heart was combined with a smaller increase in energy consumption.

KEY WORDS: *systemic hemodynamics; vasopressin; individual development.*

Activation of hypothalamic neurosecretion and mobilization of neurohormones into the bloodstream are observed in response to the action of various stressors. Oxytocin and vasopressin, on entering the circulation, bring about various adaptive responses of the body. Meanwhile, many investigations [2, 5, 6, 8, 11-13, 20, 22] have shown that a similar response of the neurosecretory system is observed during the development of experimental hypertension and of essential hypertension in man. It is generally accepted that the neurohormones mobilized into the blood stream in these cases are implicated in the genesis of the pathological process and that they can cause the specific changes of hypertension. One method of studying the possible role of these hormones in the circulatory changes of hypertension is by the analysis of their intrinsic hemodynamic effects. The effect of vasopressin on indices of

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