EFFECT OF ADRENOCHROME ON ELECTRICAL CHARACTERISTICS OF *Helix pomatia* NEURONS

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UDC 616.895.8-092:616.831-008.94:577.175.522 + 612.822.3.014.46:577.175.522]-019:594

KEY WORDS: schizophrenia; neurons; mollusk.

According to one hypothesis the genesis of schizophrenia can be attributed to a disturbance of adrenalin metabolism and the appearance in the body of a toxic breakdown product of the mediator, adrenochrome. Adrenochrome has been shown to have a marked inhibitory action on dopamine monoamine oxidase in various structures of the rat brain, on tyramine and noradrenalin monoamine oxidase in the liver, kidneys, and in the brain [4], and to inhibit succinate dehydrogenase [2, 9], glyceraldehyde phosphate dehydrogenase, glucose-6-phosphate dehydrogenase, glutamate dehydrogenase, and cholinesterase activity in the blood serum and brain [8], and to reduce coenzyme A activity [10] and ATPase activity of rat erythrocytes and brain cells [8]. Since the inhibitory properties of adrenochrome for most enzymes may correlate with the weakening of enzyme-dependent processes in the brain in schizophrenia [1], it is natural to suggest that the effects of adrenochrome may be mediated through the cell surface and, in particular, the excitable membrane of the neuron. It was accordingly decided to study the effect of adrenochrome on electrical characteristics of the neuron membrane, and the results are described below.

EXPERIMENTAL METHODS

Experiments were carried out on neurons of the dorsal surface of the subesophageal ganglion complex of *Helix pomatia*, on the grounds that molluskan neurons have been used effectively in research to study the toxicity of the serum of schizophrenic patients [6]. The preparation was kept in a chamber with physiological saline as described by Sorokina [7]. Two microelectrodes, filled with 2.5 M KCl (resistance 5-10 mΩ) were inserted into a neuron. The ordinary technique of microelectrode recording and voltage clamping was used. The action of adrenochrome was tested 30 and 40 min after insertion of the electrodes. Adrenochrome was applied in concentrations of $5 \cdot 10^{-4}$ to $20 \cdot 10^{-4}$ M. In the course of the experiments the resting potential, action potential and, if the location of the electrodes in the cell permitted voltage clamping, the current-voltage characteristic curve were recorded.

EXPERIMENTAL RESULTS

In 38 experiments the effect of adrenochrome on neurons of *Helix pomatia* was studied for 60-80 min. The action of adrenochrome was expressed by depolarization and subsequent hyperpolarization of the membrane (Fig. 1, 1). Simultaneously with change in membrane potential, the frequency and amplitude of the spike discharge were reduced to 50-60% of their initial values. Changes in these parameters were periodic in character (Fig. 2, 1).

In 35% of cases against the background of solely alternating de- and hyperpolarization of the membrane, periodic transient shifts of membrane potential (PTSM) were observed (Fig. 1, 2-4). In different experiments the amplitude of the PTSM varied from 10 to 60 mV. This effect was observed on average 30 min after application of adrenochrome. The frequency and regularity of the PTSM varied: in 25% of cases they appeared with a period of 0.5 to 1 min (Fig. 1, 2), and in that case the regular cell discharge was transformed into bursting activity (Fig. 2, 2); in 10% of cases PTSM appeared only in the slow depolarization phase (Fig. 1, 3, 4).

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(Presented by Academician of the Academy of Medical Sciences of the USSR V. P. Kaznacheev.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 92, No. 9, pp. 312-313, September, 1981. Original article submitted February 4, 1981.

 0007-4888/81/9209-1208$07.50

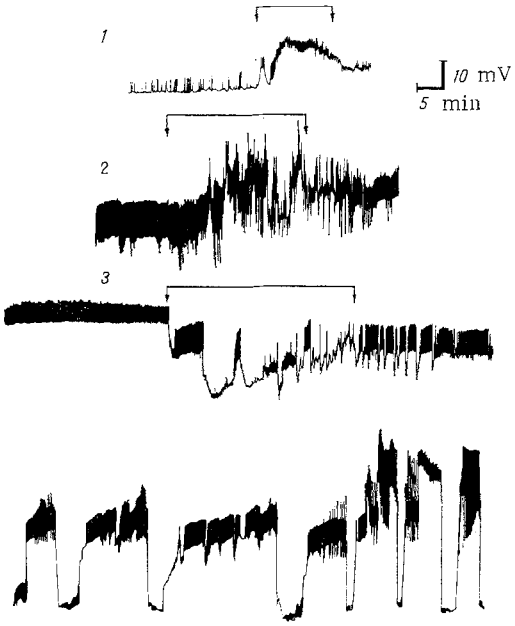

Fig. 1. Effect of adrenochrome on resting potential of neuron: 1) depolarization followed by hyperpolarization of membrane; 2-4) periodic shifts of membrane potential. Arrows indicate time of action of adrenochrome.

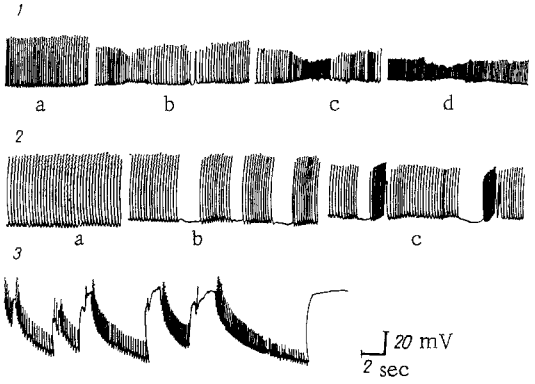

Fig. 2

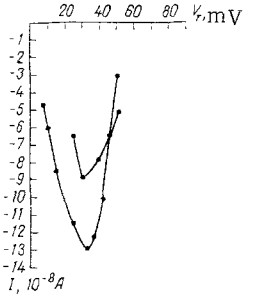

Fig. 3

Fig. 2. Effect of adrenochrome on action potential of nerve cell: 1) change in frequency and amplitude of spikes; 2) appearance of bursting activity; 3) spike activity of neuron during transient shift of membrane potential; a) control; b-d) 20, 30, and 40 min respectively after application of adrenochrome.

Fig. 3. Current—voltage characteristic curves before (1) and after (2) action of adrenochrome. Abscissa, voltage of testing pulse (in mV); ordinate, peak value of inward current (in A).

The difference in responses to adrenochrome application was evidently connected with the type of cell. A weak reaction (de- and hyperpolarization of the membrane by 3 mV throughout the period of observation and absence of PTSM) was characteristic of cells of the LPaZ type according to [5]. Well-marked PTSM were observed in cells of LP1-1, V, F, and RPa2 type (Fig. 2, 3).

Voltage clamp experiments (recording of the current—voltage characteristic curve) revealed a decrease in the inward current after application of adrenochrome (Fig. 3). The po-

tassium holding current recorded at the end of the testing pulse, 60 msec in duration, remained unchanged.

The results of the voltage clamping experiments show that the decrease in amplitude of the action potential under the influence of adrenochrome is connected not only with membrane depolarization, but also with a change in the characteristics of the ionic channels of the electrically excitable membrane and, in particular, with a decrease in maximal conductance of the inward current system.

It can be stated on the basis of the Goldman—Hodgkin—Katz equation for a steady field [11, 12] that since the resting potential reached its initial values or was below them during the periodic transient shift of membrane potential, its dynamics under the influence of adrenochrome was not due to changes in ionic composition but to changes in membrane structures responsible for permeability to sodium and potassium ions. Changes in these structures may be connected with the direct action of adrenochrome on the neuron membrane or may take place through the intervention of cell metabolism.

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SYNTHESIS OF THE SPECIFIC LENS ANTIGEN (δ-CRYSTALLIN) IN THE ADENOHYPOPHYSEAL ANLAGE OF CHICK EMBRYOS

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UDC 612.844.1.015.36:547.96]:612.433:612.646

KEY WORDS: adenohypophysis; chick embryos; crystallins.

The synthesis of crystallins is a specific biochemical sign of differentiation of the vertebrate lens. In their immunologic and physicochemical properties crystallins can be divided into several classes. For birds and, in particular, for hens there are three main classes of crystallins: α-, β-, and δ-crystallins. The first to appear during development of the lens in chick embryos are the δ-crystallins [10, 12], which account for most of the total quantity of lens proteins synthesized during embryonic development.

Recently δ-crystallins have been found immunochemically in cells of the adenohypophyseal anlage of chick embryos [2]. This a most interesting observation, for it may be evidence

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(Presented by Academician of the Academy of Medical Sciences of the USSR A. P. Avtsyn.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 92, No. 9, pp. 314-316, September, 1981. Original article submitted December 15, 1980.

0007-4888/81/9209-1210$07.50