REACTIVITY OF CHOLINOCEPTIVE CORTICAL NEURONS TO THE REPEATED ACTION OF ACETYLCHOLINE

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The participation and important role of the cholinergic system in the integrative activity of the brain have been demonstrated in many investigations [3]. The results of analysis of the reactive properties of cholinoceptive neurons in higher levels of the brain to acetylcholine (ACh) are accordingly of definite interest.

The action of ACh in the cerebral cortex has been studied by microiontophoresis in several investigations [7, 8, 11]. It has been shown that most neurons are sensitive to acetylcholine and give various excitatory and inhibitory responses to it [4, 6-10]. Meanwhile the plastic properties of cholinergic inputs of cortical neurons have not been adequately studied, and in this connection the mechanisms of participation of the brain cholinergic system in the organization of higher nervous functions remain unexplained.

An effective approach to the study of this problem is to determine the characteristics of the reactive properties of cholinoceptive neurons to repeated microiontophoresis of ACh [1, 2]. If ACh is applied in this way in physiologically adequate doses and conditions, it induces no pathological changes in the ultrastructure of the nerve cells or, evidently, in the balance between the ACh pools in nerve endings [5], but exerts its effect directly on the postsynaptic membrane of cholinoceptive neurons.

This communication gives the result of analysis of the plastic properties of cholinergic inputs of neurons in the rate sensomotor cortex during repeated application of ACh and their relationship with the character of the response to the mediator.

EXPERIMENTAL METHOD

Experiments were carried out on adult albino rats weighing 200 g, immobilized with D-tubocurarine, locally anesthetized with procaine during the operation, and artifically ventilated. The method of preparation of the electrodes and experimental objects was described fully by the writers previously [1]. ACh (0.5 M solution, pH 7.0) was applied microiontophoretically by currents of between 10 and 150 nA. ACh was applied 20 times (duration of iontophoresis 0.5 sec, interval between applications 30 to 120 sec).

The spike discharge of the neurons was led to the input of a microcomputer. The shape of the spike and the presence of a refractory period of over 1 msec on the interval histogram were monitored continuously. Peristimulus histograms, averaged for 20 presentations, with a bin of 200 msec and epoch of analysis of 14-30 sec were transformed into sequences of signs, the number of which was equal to the number of bins in the poststimulus part of the histograms. Under these circumstances a "plus" sign (+) indicated that the bin content did not exceed the value of $\bar{x} \pm \sigma$, and a "minus" sign (–) indicated that they did not exceed the value of $\bar{x} \pm \sigma$, where $\bar{x}$ and σ are the values of the mean and standard deviation for data in the prestimulus part of the histogram for a period of 4 sec. The remaining bins were replaced by "blank" signs. The times of the beginning and end of the excitatory components of the responses were fixed by these sign sequences, and values of the mean were calculated within their limit on the basis of averaged histograms, corresponding to 1-5, 6-10, 11-15, and 16-20 applications of ACh. Values of the mean for the background were calculated for the same histograms. The numbers obtained, made to correspond with the serial numbers of ACh ap-

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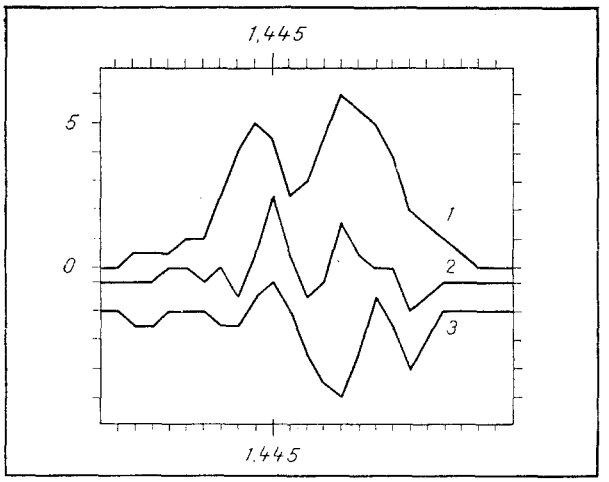

Fig. 1. Correlation between duration of excitatory component of response of neurons of ACh and time course of tonic and evoked activity during repeated action of mediator. Abscissa, logarithm of duration of excitatory component of response measured in second; ordinate, number of neurons exhibiting time course of activity, averaged for 2 neighboring points. 1) Distribution of neurons according to duration of excitatory component of response; 2, 3) distribution of neurons exhibiting time course of spontaneous and evoked activity respectively, according to duration of excitatory component of response. Zeros for curves 2 and 3 shifted relative to zero for curve 1 downward by 0.5 and 1.5 divisions, respectively.

plication, characterize the time course of evoked and spontaneous activity of the neurons investigated. On the basis of these data coefficients of linear correlation were calculated. Their values, if higher than +0.441 ($P < 0.05$), were considered as indicating significant growth, whereas values below −0.441 were taken as indicating a significant reduction in the corresponding type of unit activity.

EXPERIMENTAL RESULTS

A considerable part of the bulk of the responses of all 50 neurons tested to ACh was accounted for by the excitatory phase. Accordingly, reactivity to ACh was evaluated on the basis of the abundance of this component. The character of the time course of the response and tonic activity (TA) of the neurons was as follows. Stability of response and stability of TA were observed in 3 neurons, growth of the response and stability of TA in 4, reduction of the response and stability of TA in 7, stability of response and growth of TA in 6, growth of response and growth of TA in 9, reduction of response and growth of TA in 8, stability of response and reduction of TA in 3, and reduction of response and reduction of TA in 10 neurons. Growth of the response accompanied by reduction of TA was not observed in any of the neurons studied. Thus cholinoceptive neurons of the sensomotor cortex may be divided into three groups on the basis of the time course of their reactivity to ACh during its repeated application: those reducing (50% of cells), those increasing (26% of cells), and those not changing (24% of cells) their response. Of 38 neurons changing their reactivity to ACh, a change in the spontaneous firing rate was observed simultaneously with the change in reactivity in 27 (71% of cells) in the course of successive presentations of ACh. Incidentally, in 9 neurons which did not change the abundance of their responses a significant change in the spontaneous discharge frequency was observed.

The character of the time course of activity of cortical cholinoceptive neurons was found to depend on the duration of the excitatory component of their response to ACh. Incidentally, the duration of the excitatory component of the response was virtually independent of the quantity of ACh applied. The relationship between the character of the time course of activ-

ity of the neuron and the duration of the excitatory component of their response to the mediator is shown in Fig. 1, in which curve 1 shows the distribution of the test neurons by the durations of these components, whereas curves 2 and 3 show the type and abundance of the time course of spontaneous and evoked activity respectively. Values of the ordinate at each point on curves 2 and 3 are the algebraic sum of the number of neurons exhibiting an increase (above the zero for each graph) or a decrease (below the zero) of activity of a particular type. It will be clear from Fig. 1 that the probability that a neuron exhibits a time course of spontaneous or evoked activity during the repeated action of ACh is greatest when the duration (which is strictly specific for each nerve cell) of the excitatory component of their response is 3.2, 8.1, and 13.5 sec, and that the duration of excitation has a different relationshp to the direction of the time course of spontaneous and evoked activity.

The results of investigation of cholinoceptive neurons thus demonstrate differences in plasticity of inputs of the same chemical nature. Analysis of the plasticity of inputs of different chemical nature will provide a deeper insight into the mechanisms lying at the basis of learning and memory.

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EFFECT OF CALCIUM ON FORCE-FREQUENCY RELATIONSHIP AND RESTING POTENTIATION IN THE MYOCARDIUM OF ADULT AND OLD RATS

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The adaptive powers of the cardiovascular system are considerably reduced during aging [3, 7, 8]. Elucidation of the primary mechanisms lying at the basis of these changes is essential for the development of effective ways of increasing the adaptive capacity of the aging organism. Dependence of the developed tension, and the rate of contraction and relaxation on frequency enables the heart muscle to maintain optimal contractile activity during changes of rhythm. The rat myocardium is characterized by a negative chronoionotropic relationship [4, 13, 15]. The study of age changes in this relationship has shown that the velocity-force parameters of heart muscle during an increase in the frequency of stimulation to 5.0 Hz change less in old rats than in adult rats, and that the potentiation of contractions by an interval of rest also is depressed in the old myocardium [4]. The important role of Ca^{++} ions in the realization of chronoinotropic relations is well known [1, 2, 6], and changes in

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