EFFECT OF CHOLINERGIC DRUGS ON SINGLE MECHANORECEPTORS (PACINIAN CORPUSCLES)

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Application of acetylcholine and nicotine to the intact Pacinian corpuscle does not induce spike activity but affects its sensitivity to mechanical stimulation: low concentrations ($1 \cdot 10^{-6}$ g/ml) increase it, high concentrations ($1 \cdot 10^{-4}$ g/ml) reduce it. This effect can be explained by the action of these substances on structures generating action potentials. Application of acetylcholine to the decapsulated Pacinian corpuscle induces spike activity. This response may perhaps be due to the action of acetylcholine on the mechanoreceptive site itself. Application of tubocurarine or hexamethonium depresses the sensitivity of the receptor to mechanical stimulation, and this may also point to a role of acetylcholine in the process of adequate excitation of the receptor.

KEY WORDS: Pacinian corpuscles; spike activity; action potential; acetylcholine.

The effect of cholinergic drugs on mechanoreceptors and the possible role of a mediator mechanism in excitation of Pacinian corpuscles (PC) have frequently been discussed in the literature [1-4]. However, in only one investigation [5] was an attempt made to study the response of PC to acetylcholine (AC). These workers found no effect of AC on PC. Since PC did not respond to KCl either, it was concluded that the drugs tested did not reach the sensory nerve ending.

In the investigation described below, the effect of AC and other cholinergic substances was studied on activity of single intact and decapsulated Pacinian corpuscles.

EXPERIMENTAL METHOD

A single PC together with its nerve fiber was isolated from the mesentery of an anesthetized (35 mg/kg pentobarbital, intraperitoneally) cat. The receptor was placed on two electrodes in a special bath filled with Hanks's solution (37° C). The PC were stimulated by means of a generator of mechanical vibrations, rigidly fixed to the bath. Action potentials (APs) and the stimulus were recorded on a two-channel oscillograph. In some experiments, the receptor was partially decapsulated from the distal part before application of the test solutions. The Hanks's solution, AC ($1 \cdot 10^{-6}$ and $1 \cdot 10^{-4}$ g/ml), nicotine ($1 \cdot 10^{-6}$ and $1 \cdot 10^{-4}$ g/ml), tubocurarine ($1 \cdot 10^{-6}$ g/ml), and hexamethonium ($1 \cdot 10^{-6}$ g/ml) were applied through a glass micropipet (tip diameter 0.1 mm).

EXPERIMENTAL RESULTS

Application of solutions of AC or nicotine changed the threshold of mechanical stimulation of the intact PC. The direction of the changes was determined by concentration (Fig. 1). In a concentration of $1 \cdot 10^{-6}$ g/ml, AC considerably increased the sensitivity of the receptor to an adequate mechanical stimulus, but reduced it in a concentration of $1 \cdot 10^{-4}$ g/ml. The action of nicotine was similar.

Considering that the capsule of PC is a powerful barrier to diffusion [6], the next step was to determine whether AC acts on the receptor segment of the nerve ending or on structures generating AP [7]. For

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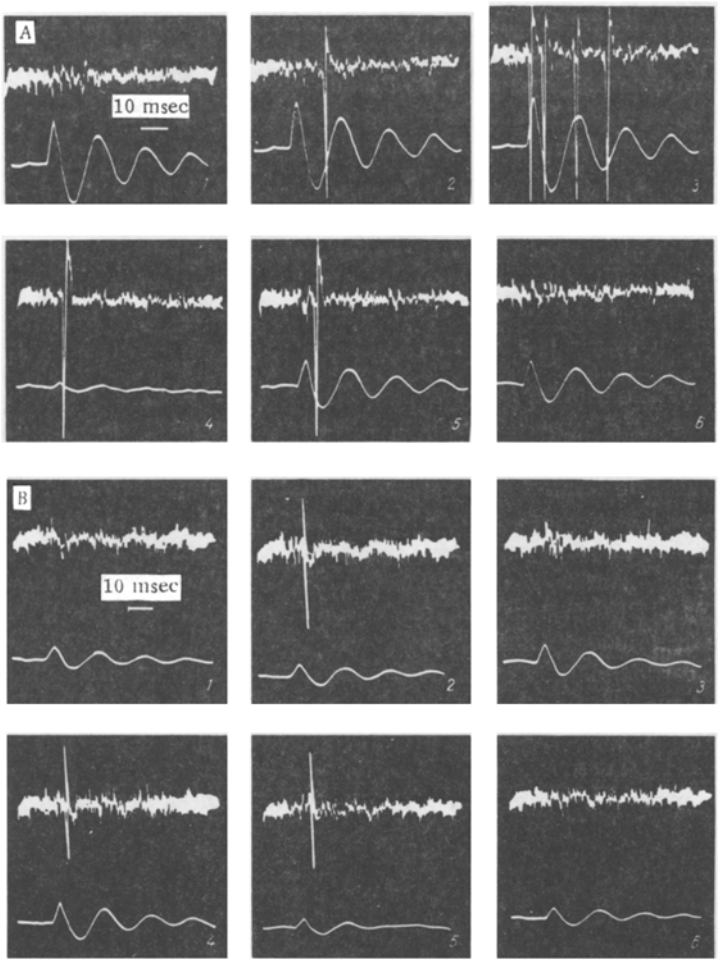

Fig. 1. Application of AC in concentrations of $1 \cdot 10^{-6}$ (A) and $1 \cdot 10^{-4}$ (B) g/ml on intact PC: 1, 2) determination of threshold of excitation in Hanks's solution; 3, 4) after application of AC; 5, 6) after rinsing in Hanks's solution.

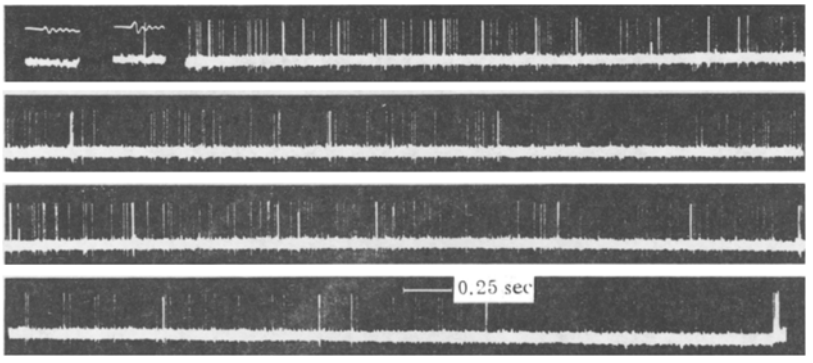

Fig. 2. Application of AC in concentration of $1 \cdot 10^{-6}$ g/ml on decapsulated PC. Record not continuous. First two frames represent determination of threshold of mechanical stimulus.

this purpose, the maximal possible decapsulation of the distal part of the receptor was carried out before AC application. Under these conditions, AC ($1 \cdot 10^{-6}$ g/ml) without any mechanical stimulus evoked a rhythmic train of APs lasting up to 5 min (Fig. 2). Since the distal part of the receptor was decapsulated, it can logically be supposed that under these circumstances the access of AC was facilitated to the mechanoreceptive part of PC but not to the segments generating APs.

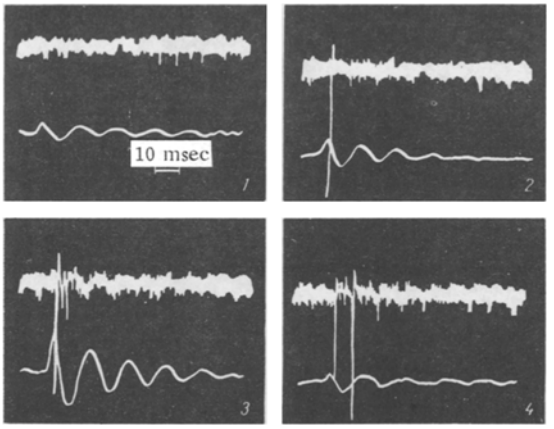

Fig. 3. Application of tubocurarine to decapsulated PC: 1, 2) in Hanks's solution; 3) application of tubocurarine; 4) after rinsing with Hanks's solution.

These results suggest that the substrate with which AC interacts differs whether it is applied to the intact or the decapsulated PC. In the first case, AC in a concentration of $1 \cdot 10^{-6}$ g/ml lowered the threshold of adequate stimulation but did not induce spike activity. Its absence might be explained by an inadequate AC concentration. However, spike activity did not appear after application of AC in a concentration of $1 \cdot 10^{-4}$ g/ml which, on the contrary, led to an increase in the threshold of excitation of PC to mechanical stimulation. Consequently, if applied to the intact receptor, AC did not reach the cholinergic receptor structures by interaction with which it could induce APs. The effect of AC on the intact PC is probably determined by its action directly on structures generating APs.

The appearance of spike activity after application of AC suggests that activation of the receptor by mechanical stimulation takes place with its participation. To verify this hypothesis (Fig. 3), PC decapsulated from the distal part were treated with tubocurarine ($1 \cdot 10^{-6}$ g/ml) and hexamethonium ($1 \cdot 10^{-6}$ g/ml). In both cases an increase in the threshold of excitation to mechanical stimulation was observed. Admittedly in no case was the receptor completely blocked.

These results suggest that AC participates in the reception of an adequate mechanical stimulus by PC, i.e., that synaptic transmission exists.

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