EFFECT OF NORADRENALIN ON ELECTRICAL AND CONTRACTILE PROPERTIES OF SMOOTH-MUSCLE CELLS OF THE PULMONARY ARTERY

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Muscle cells of the pulmonary artery have no spontaneous activity. Electrical stimulation of these cells leads to the formation of electronic potentials unaccompanied by any change in isometric contraction of a strip of the artery. Noradrenalin, in a concentration of 10^{-8} g/ml, causes depolarization of the muscle cell membrane by 5-7 mV and a marked increase in contraction of the muscle strip. Under these conditions, catelectronotonic depolarization was accompanied by contraction of the strip, but anelectrotonic hyperpolarization by its relaxation. Phentolamine, an α-adrenoblocker, prevents the noradrenalin effect, indicating a role of α-adrenoblockers in the mechanism of the excitatory action of noradrenalin on the smooth-muscle cells of the pulmonary artery.

KEY WORDS: smooth muscle of pulmonary artery; volt–ampere characteristic curves; muscle contraction; noradrenalin; phentolamine.

Opinions differ on the mechanism of contractions evoked by noradrenalin (NA) in the smooth muscle cells of arteries. Some workers associate contraction of the muscle with the depolarizing action of NA on the membrane of these cells [3, 4]. However, depolarization does not always accompany NA-induced contraction [5, 8, 10-12], whereas contraction can be caused by potassium depolarization in the absence of NA [5, 6, 9]. On this basis it has been suggested that depolarization and NA can activate contraction of muscle cells independently [7]. However, experiments with potassium rule out membrane depolarization as the cause of muscular contraction, for under these conditions other properties of the membrane also change, notably its permeability to different ions [3, 4].

A method was used by means of which the membrane conductance of smooth-muscle cells during the action of NA could be monitored and the effect of the resting potential (RP) on their contractile activity could be investigated.

EXPERIMENTAL METHOD

Smooth-muscle cells of the rabbit pulmonary artery were chosen as the test object. The artery was cut into circular strips 1.5-mm wide and up to 8-mm long. Electrical potentials were recorded by intracellular glass electrodes with a resistance of not less than 30 mΩ. Meanwhile the contractile activity of the preparation was recorded [1]. To increase the effectiveness of the stimulating current, an isotonic solution of sucrose was passed between the stimulating electrodes. An area of muscle between the stimulating electrodes was isolated with rubber partitions [2]. One of the stimulating electrodes was immersed in isotonic KCl solution bathing the area of muscle to the left of the sucrose bridge. On the right side the muscle strip was bathed in Krebs' solution, warmed to 36°C. The microelectrode was inserted into this part of the muscle; a second stimulating electrode was placed in the same part of the chamber.

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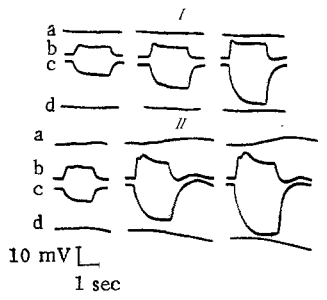

Fig. 1

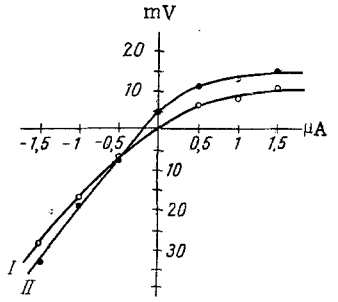

Fig. 2

Fig. 1. Simultaneous recording of electrotonic potentials and isometric contraction of smooth-muscle cells of pulmonary artery in Krebs' solution (I) and after addition of noradrenalin in a concentration of 10^{-8} g/ml (II). a, b) Isometric contraction of strip of pulmonary artery and catelectrotonic potentials evoked by depolarizing current of 0.5, 0.75, and 1 μA respectively; c, d) anelectrotonic potentials evoked by hyperpolarizing current of 0.5, 0.75, and 1 μA and isometric contraction of strip of pulmonary artery respectively.

Fig. 2. Volt–ampere characteristic curves of smooth-muscle cells of pulmonary artery in Krebs' solution (I) and after addition of noradrenalin in a concentration of 10^{-8} g/ml (II).

EXPERIMENTAL RESULTS

The RP of the smooth-muscle cells of the rabbit pulmonary artery, measured intracellularly, averaged 52±3 mV. In Krebs' solution these cells did not generate spontaneous action potentials (APs). Spontaneous contractions of the pulmonary artery also were absent.

Electronic potentials arose in response to electrical stimulation of the smooth-muscle cells. With weak currents (Fig. 1, I) the an- and catelectrotonic potentials were about equal in value. However, as the strength of stimulation increased, the amplitude of the anelectrotonic potentials rose proportionally to current strength, whereas the catelectrotonic potentials changed less substantially. At a certain level of current strength, a potential resembling a local potential appeared on the catelectrotonic potential. With an increase in the strength of the depolarizing current it increased slightly but did not change into an AP.

The volt–ampere characteristic curve (Fig. 2, I) shows that the smooth-muscle cell membrane behaves with respect to hyperpolarizing and weak depolarizing currents as a purely passive resistor. With an increase in strength of the depolarizing current the slope of the characteristic curve was sharply reduced and it became almost parallel to the current axis.

In Krebs' solution the electrotonic potentials were never accompanied by changes in isometric contraction of the segment of pulmonary artery. Consequently, depolarization of their membrane alone is insufficient to cause activation of the contractile mechanism of the muscle cells.

The addition of NA to the Krebs' solution in a concentration of 10^{-8}–10^{-7} g/ml led to depolarization of the smooth-muscle cell membrane by 5–7 mV. Electrotonic potentials were considerably increased during the action of NA (Fig. 1, II). Local potentials arising on the catelectrotonic potential during the action of NA changed their shape (an accessory slow wave appeared), but in that case also no AP developed. Stopping the depolarizing and hyperpolarizing currents was followed by the appearance of after-potentials, which were never observed in normal Krebs' solution.

Depolarization of smooth-muscle cells induced by NA was accompanied in all experiments by a marked increase in contraction of the strip of artery. Under these conditions contraction of the muscle became sensitive to a change in the RP level. The increase in muscle contraction produced by NA is shown in Fig. 3. After about 3 min, when the contraction was stabilized, a hyperpolarizing current caused relaxation and a depolarizing current caused contraction of the strip of artery. However, restoration of RP by the hyperpolarizing current to its initial value led to only slight relaxation of the strip.

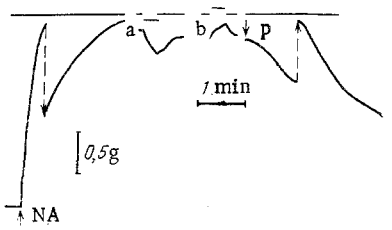

Fig. 3. Increase in isometric contraction of strip of pulmonary artery under the influence of noradrenalin (10^{-8} g/ml) and inhibition of noradrenalin effect by phentolamine ($5 \cdot 10^{-6}$ g/ml). Beginning of action of noradrenalin (NA) and phentolamine (P) indicated by arrows: a) relaxation of strip of artery under the influence of hyperpolarizing current; b) contraction of strip of artery under the influence of depolarizing current. Strength of current 1.25 μA. Top line records stimulating current. Broken line indicates displacement of record in direction of arrow.

Judging from measurement of the slope of the volt–ampere characteristic curve in Fig. 2, the resistance of the smooth-muscle cell membrane is increased by NA. Depolarization of the membrane was expressed as a shift of the volt–ampere characteristic curve along the voltage axis by an amount of depolarization equal to 5 mV.

The effect of NA was completely blocked by the α-adrenoblocker phentolamine in a concentration of $5 \cdot 10^{-6}$ g/ml (Fig. 3); the initial voltage and the values of RP and the electrotonic potentials were restored. This effect was not accompanied by a change in the contraction of the strip of artery.

The results indicate that NA stimulates the smooth-muscle cells of the pulmonary artery through α-adrenoblockers. The increase in resistance of the cell membrane produced by the action of NA indicates that the cause of depolarization was evidently a decrease in the permeability of the muscle cell membrane to potassium ions. Although contraction of the strip of pulmonary artery in the presence of NA became sensitive to a change in the RP level, the contribution of noradrenalin depolarization to the ensuing contraction of the strip of artery was negligible, for restoration of the initial RP of the cell by a hyperpolarizing current simply led to slight relaxation of the strip.

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