THE EFFECT OF ADRENALIN ON THE CONTRACTURES OF A FROG'S RECTUS ABDOMINIS MUSCLE INDUCED BY POTASSIUM CHLORIDE AND PROPSERINE

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In this work, we studied the effect of adrenalin on acetylcholine, potassium and proserine contractures of a frog's rectus abdominis muscle.

EXPERIMENTAL METHODS

The experiments were performed on muscles obtained from Rana temporaria males during the fall-winter period. A preparation made from two unseparated rectus abdominis muscles was placed in a bath 15 ml in volume. For 1-1½ hrs before the experiment, the muscle was left at rest under an adequate load (a small rod weighing about 1.0-1.5 g) with intensive aeration and periodic exchange of the Ringer's solution. The Ringer's solution consisted of the following: 6.5 g NaCl, 0.14 g KCl, 0.12 g $CaCl_2$ and 0.2 g $NaHCO_3$ in 1 liter of water.

EXPERIMENTAL RESULTS

The first series of experiments confirmed Büch's data (1923) to the effect that adrenalin, regardless of its concentration, has no apparent effect on the development of acetylcholine contracture of a frog's rectus abdominis muscle (Fig. 1).

The next series of experiments examined the effect of adrenalin on the development of potassium contracture. We found the potassium contracture to be highly sensitive to adrenalin. Adrenalin, as Fig. 2 shows, definitely inhibits the development of potassium contracture of a frog's rectus abdominis muscle, even in a concentration of $1 \cdot 10^{-10}$, and almost completely inhibits it in concentrations of $1 \cdot 10^{-6}$. This inhibitory effect is rather durable. The muscle's reaction to potassium chloride was restored an average of 30-45 min after the adrenalin was washed out.

The extraordinary sensitivity of the potassium contracture to adrenalin and the failure of adrenalin to effect the acetylcholine contracture are strong arguments to the effect that the contracture effected by potassium chloride is due to the direct action of potassium ions on the contractile proteins of the muscle. If this is true, the difference in adrenalin's effects on acetylcholine and potassium contractures of a frog's rectus abdominis muscle can be utilized to analyze the action mechanism of other substances too.

We conducted experiments inducing muscle contracture by means of proserine. Used in a concentration of $2 \cdot 10^{-5}$ for 12 min, proserine induced a marked contracture. Adrenalin, used for 30 min in a concentration of $5 \cdot 10^{-7}$ inhibited the proserine contracture by more than 50% (Fig. 3).

Experiments with a leech's muscle were performed to determine whether the inhibitory effect of adrenalin on potassium contracture of a frog's rectus abdominis muscle were accidental or whether it could be demonstrated on other test objects.

In concentration of $1 \cdot 10^{-3}$, potassium chloride caused the leech's muscle to relax rather than contract. When the muscle was left in a proserine solution ($5 \cdot 10^{-7}$) for an hour, a $1 \cdot 10^{-3}$ concentration of potassium chloride caused a strong contracture. Under the influence of adrenalin in a concentration of $1 \cdot 10^{-6}$, the same concentration of potassium chloride induced no reaction in the proserinized muscle; the development of the contracture was totally inhibited. After the adrenalin had been washed out, potassium chloride again caused a marked contracture (Fig. 4).

There is a great deal of data available concerning the part played by potassium in muscle contraction. The formation of actomyosin is known to occur in the presence of potassium ions. After analyzing the literature data

and experimental material, D. N. Nasonov [4] demonstrated conclusively that "under conditions of injury or excitation, the non-ionized fraction of potassium and phosphates stably combined with the protoplasm is liberated and changes into

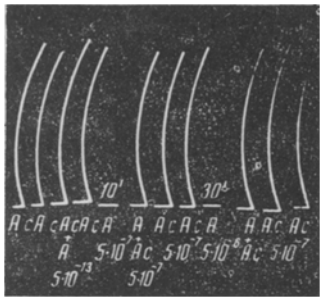


Fig. 1. Failure of adrenalin to affect development of acetylcholine contracture of frog's rectus abdominis muscle. Ac) Acetylcholine added to bath in final concentration of $5 \cdot 10^{-7}$, washed out after 3 min; A) adrenalin added to bath.

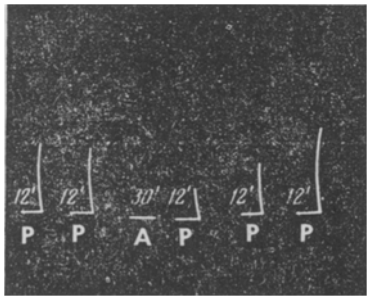
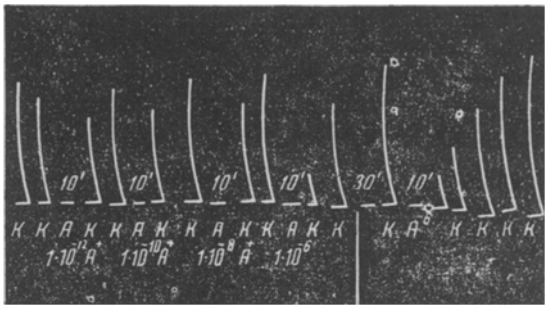


Fig. 3. Effect of adrenalin on development of proserine contracture of frog's rectus abdominis muscle. P) Proserine in a concentration of $2 \cdot 10^{-5}$, washed out after 12 min; A) muscle treated with adrenalin in a concentration of $5 \cdot 10^{-7}$ for 30 min; P) proserine in a concentration of $2 \cdot 10^{-5}$ after adrenalin was washed out.



pause

Fig. 2. Development of potassium contracture of frog's rectus abdominis muscle inhibited by adrenalin. P) Potassium chloride solution added to bath in a concentration of $1 \cdot 10^{-3}$, washed out after 3 min; A) adrenalin in order of tests: $1 \cdot 10^{-12}$, $1 \cdot 10^{-10}$, $1 \cdot 10^{-8}$, $1 \cdot 10^{-6}$.

a dissolved, ionized state. . . When the excitation ceases, the liberated potassium and phosphates are once more combined with the protoplasm."

V. A. Engel'gard and M. N. Lyubimova [3] established in 1959 that myosin possesses ATP activity, and Sent-Dzhiord'i [12] demonstrated in the laboratory that the ATP activity of potassium on a tonic muscle could be due the direct action of potassium ions on the colloid properties of the muscle proteins and on the phosphatase activity of myosin.

However, there are indications in the literature that the development of potassium contracture is connected to some extent with potassium's ability to liberate acetylcholine from the muscle tissue [2]. This is supported by the data of my work carried out in 1944-1946 [5], which show that a frog's rectus abdominis muscle subjected to the influence of proserine (a substance with an anticholinesterase effect) reacts to potassium ions by a stronger contraction. In 1946, however, Miquel [11] discovered that the rectus abdominis muscle contraction effected by neostigmine (proserine) and the potentializing effect of the latter on acetylcholine are maintained after total cholinesterase inhibition by diisopropyl fluorophosphate. This allowed the author to conclude that, apart from its anticholinesterase activity, proserine acts directly on the muscle.

Since adrenalin inhibits potassium and proserine contractures but does not affect the development of acetylcholine contracture, one can propose that proserine's effect on muscles is largely due to its ability to expel potassium ions from the muscle proteins. One can also assume that the muscle acetylcholine plays no part in the development of potassium contracture.

The known ability of adrenalin to inhibit the contractile reactions of mammals' denervated muscles [8] is probably based on the same mechanism as its inhibition of the potassium contracture of a frog's rectus abdominis muscle. The fact is that the potassium concentration in the blood increases sharply when the organism is under the influence of agents depolarizing the end-plates (succinylcholine, for example) [6]. The potassium ions liberated

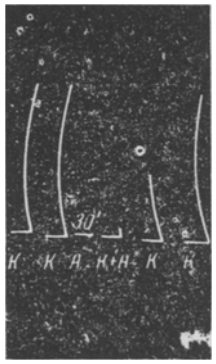


Fig. 4. Contracture of leech's proserinized dorsal muscle induced by potassium chloride. Adrenalin inhibition of contracture. KCl) Potassium chloride added to bath in a concentration of $1 \cdot 10^{-3}$; A) muscle in $1 \cdot 10^{-6}$ adrenalin solution. In the presence of adrenalin, the muscle did not react to potassium chloride. After the adrenalin was washed out, the reaction of the muscle to potassium chloride was gradually restored. The entire experiment was conducted in the presence of proserine in a concentration of $5 \cdot 10^{-7}$.

can cause a contractile reaction in a muscle denervated to exclude the influence of the sympathetic nerve. The preliminary administration of adrenalin prevents this reaction of the denervated muscle [1].

It is known fact that adrenalin tends to enhance the normal asymmetrical nature of potassium distribution between the cell and the environment and to restore any loss of this asymmetry [7, 10]. The fact that the ability of the muscle proteins to bind potassium ions increases under the influence of adrenalin probably sums up the mechanism of the latter's effect on contractures.

SUMMARY

Experiments were performed on rectus abdominis muscles in frogs. A study was made of the effect produced by adrenaline on the development of contracture during the action of acetylcholine, potassium chloride and proserine. As established, adrenaline depresses the development of potassium and proserine contractures of the frog's rectus abdominis. The known data are confirmed by the fact that adrenaline produces no effect on the development of acetylcholine contracture of the rectus abdominis in a frog. The mechanism of adrenaline action of the contractures, evidently, brings to muscle proteins increased ability to bind potassium ions.

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