CHANGES IN CONTRACTILE ABILITY OF THE FROG'S MYOCARDIUM IN RELATION TO CONCENTRATION OF Na, K AND Ca IONS IN THE SURROUNDING MEDIUM

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The problem of the physiological action of different ions on excitable tissues has long been a subject of investigation. A major advance in this field was the discovery of the role of Na and K in generation of bioelectrical potentials. Extremely interesting data have been obtained on the role of Ca ions in the mechanism of contraction of heart muscle [2, 3, 7, 4, 17] and on the action of Na ions in inhibiting contractile activity [4, 10, 11]. The action of K ions on contraction of the myocardium has not been finally settled. Some investigators, for instance, have demonstrated the positive action of an excess of K ions on its contraction [6, 9] while others [5, 8] have reported the positive action of a deficiency of K ions in the medium in this respect. The possibility of a biphasic action of K ions on contractility has also been reported [1].

The object of the present investigation was to study the effect of Na, K, and Ca ions on the tone and contraction of heart muscle.

EXPERIMENTAL METHOD

For this purpose experiments were carried out in which a strip of myocardium from a frog's ventricle was placed in isotonic sucrose solution. It has been shown [12-16] that myocardium may contract for several hours in such a solution. To examine the action of individual ions, the chlorides of Na, K, or Ca were added to the sucrose solution. By recording changes in the tone or the amplitude of contractions of the strip of myocardium taking place after the addition of the various salts the effect of the individual ions on contractile function of the heart muscle could be determined.

In 78 experiments the tone of the strip of myocardium was recorded in conventional units by means of a long and almost balanced lever. In 17 experiments the amplitude of contractions of the myocardium in response to electrical stimulation of the muscle by over-threshold square pulses, 5 msec in duration and with a frequency of 0.15 Hz, were determined by means of a tensometric myograph and recorded on a loop oscillograph. As a first step in each experiment the heart muscle was kept for 1 h in Ringer's solution, and this was then replaced by one of the test solutions. After the muscle had been kept in the solution for 1.5 h, a weighed sample of myocardium was taken for estimation of the Na and K ion concentrations by flame photometry. Solutions of the following composition were used (concentrations of ions expressed in mmoles/liter). Ringer's solution: Na^+ (115), K^+ (2.5), Ca^{++} (1.2); isotonic sucrose solution; isotonic sucrose solution and K^+ (2.5); isotonic sucrose solution and Ca^{++} (1.2); isotonic sucrose solution, K^+ (2.5) and Ca^{++} (1.2); semiisotonic sucrose solution and Na^+ (57.5); semiisotonic sucrose solution, Na^+ (57.5), and K^+ (2.5); semiisotonic sucrose solution, Na^+ (57.5); and Ca^{++} (1.2). The solution bathing the muscle was changed every 15-20 min. The experiments were carried out at 18-22°.

EXPERIMENTAL RESULTS

Curves summarizing the changes in tone of strips of myocardium from the frog's ventricle in each of the 8 solutions listed above are given in Fig. 1. All the curves are plotted from the mean results of 8-12 experiments. The arrow indicates the time of changing the Ringer's solution, in which all the strips were kept for 1 h before the experiment, for one of the test solutions. It will be clear from Fig. 1 that the tone of the heart muscle fell in Ringer's solution (curve 1). If at the time indicated by the arrow this solution was replaced by isotonic sucrose solution, the tone of the strip of myocardium gradually increased (curve 2). If the Ringer's solution was exchanged for isotonic sucrose solution containing K ions the tone of the strip also increased, although not so much as in sucrose solution without K ions (curve 3). Addition

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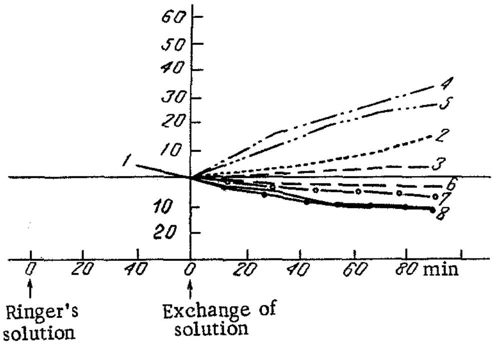

Fig. 1. Changes in tone of myocardium in solutions of different tonic composition. Abscissa) time after changing solution, in min; ordinate) conventional units. Explanation in text.

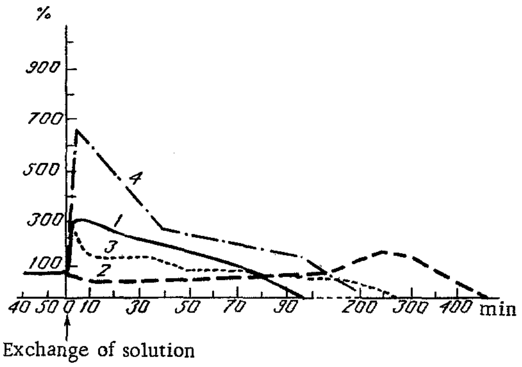

Fig. 2. Dynamics of changes in amplitude of contractions of a strip of myocardium in solutions of different ionic composition. Abscissa) time after exchanging solution; ordinate) amplitude of contractions (in percent). Explanation in text.

of Ca ions to the sucrose solution greatly increased the tone of the heart muscle (curve 4). If the solution bathing the muscle contained both K and Ca ions together, the effect of Ca ions in increasing the muscle tone was less pronounced (curve 5).

In every case when an increase of myocardial tone was observed, no Na ions were present in the solutions bathing the muscle. It is clear from Fig. 1 that if Na ions were added to the test solutions, the tone of the myocardium was reduced. This difference was seen particularly clearly when the effects of solutions differing in the presence or absence of Na ions are compared (curves 2 and 6, curves 3 and 7, curves 4 and 8, curves 5 and 1).

The results of determination of the concentration of K and Na ions in the samples of myocardium confirmed the important role of Na ions in the maintenance of muscle tone. It was found that in every case when the tone of the myocardial strip was increased, the concentration of Na ions in the myocardium was always below 30% of the initial value after 1.5 h. Roughly identical concentrations of K in the myocardium were found when the muscle tone was increased and decreased. The results obtained thus showed that Ca ions increase myocardial tone while Na^+ ions have the opposite effect. To maintain constant tone, a definite ratio between the concentrations of Ca^{++} and Na^+ ions is evidently necessary, as was pointed out by Niedergerke and Lüttgau, [10, 11], who considered that this ratio corresponds to $\frac{Ca^{++}}{[Na^+]^2}$. K ions have no appreciable action on myocardial tone, or they may diminish it very slightly.

The amplitude of the contractions in response to electrical stimulation in solutions of varied ionic composition shows more complex changes. It will be seen from Fig. 2 that when the Ringer's solution was exchanged for isotonic sucrose solution without the addition of any ions, the amplitude of the contractions was increased three times in the first 2-5 min and remained high for 1 h, falling only gradually (curve 1). When the Ringer's solution was replaced by isotonic sucrose solution with the addition of Ca ions the amplitude of the contractions increased about six times in the first few minutes, and then fell gradually for 1.5 h, although at the end of this time it was still twice the initial amplitude (curve 4). A much smaller increase in amplitude of the contractions was observed when the Ringer's solution was replaced by sucrose solution containing K ions. In the first few minutes the amplitude of the contractions was doubled, after which it fell rapidly, although it still remained above the initial level (curve 3). If, however, the Ringer's solution was replaced by sucrose solution containing Na ions, the amplitude of the contractions diminished by 20% and remained so for 1 h, after which the amplitude of its contractions gradually increased by 2-2.5 times for a period of 5-6 h, followed by a second decrease in amplitude of the contractions (curve 2).

In attempting to explain the results obtained, it must be assumed that the contractions produced by electrical stimulation depend not only on the contractile ability of the myocardium, but also on the excitability of the muscle. The authors consider that in the period soon after the muscle is placed in sucrose solution, when a slight loss of Na takes place, the excitability of the muscle changes slightly and its contractile ability is clearly increased. In the subsequent period, with a marked decrease in the Na content in the myocardium, the excitability falls sharply, so that the contractions of the muscle in response to electrical stimulation diminish considerably or may even cease altogether. This is the situation when the muscle is kept in isotonic sucrose solutions with the addition of K and Ca ions. If, however, the strip of myocardium is kept in a solution whose isotonicity is due half to sodium chloride and half to sucrose, the loss of Na by the muscle is small, so that the muscle contractions not only are not increased, but may even be decreased by comparison with those in Ringer's solution, because of the absence of Ca ions in the solution. The decrease in Na concentration in the myocardium takes place only after a few hours, as a result of which the amplitude of the contractions is increased. However, since the excitability is also diminished in these circumstances, after a short time the muscle contractions in response to electrical stimulation cease altogether.

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