

contralateral kidney during splanchnic nerve stimulation without altering the value of the maximal glucose reabsorption in the two kidneys.

In the kidney on the side of splanchnic nerve stimulation maximal reabsorption of glucose was thus unchanged although the rate of the filtration process was reduced. After adrenal demedullation splanchnic nerve stimulation increased filtration in the contralateral kidney but had no effect on maximal glucose transport in the two kidneys. Consequently, maximal glucose reabsorption was unchanged during small fluctuations in glomerular filtration. The adrenergic fibers of the splanchnic nerve evidently have no direct influence on the velocity of maximal glucose transport in the proximal tubules of the kidneys.

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#### POTENTIATION AND RESTITUTION OF HEART MUSCLE CONTRACTION IN RATS ADAPTED TO EXERCISE

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UDC 612.176

The original amplitude of contraction of strips of myocardium determined the inotropic response to paired stimulation. The higher the initial amplitude, the lower the degree of potentiation and the higher the degree of restitution of contraction. For equal amplitude, the degree of potentiation of myocardial contraction of exercise-adapted rats was greater and the degree of restitution smaller than in the control. These changes probably reflect changes in the ion transport system of the myocardial cells.

**KEY WORDS:** isolated papillary muscles; paired stimulation; restitution and potentiation of contractions; adaptation to exercise.

The dynamics of the amplitude of premature and potentiated contractions of a muscle during paired stimulation with different intertrial intervals can be used to assess the rate of restitution and subsequent potentiation of contraction. The central role of  $\text{Ca}^{2+}$  as a regulator of the contraction process suggests that the rate of

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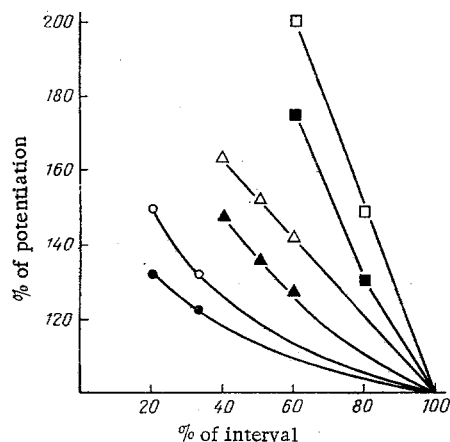


Fig. 1

Fig. 1. Degree of potentiation of amplitude of contractions of myocardial strips from control (shaded symbols) and adapted (unshaded symbols) rats as a function of interval between main and additional pulses, expressed as a percentage of initial value of interval for that particular frequency. Frequency of pulses per minute: 40 (circles), 120 (triangles), 240 (squares). Each point is mean of 8-11 experiments.

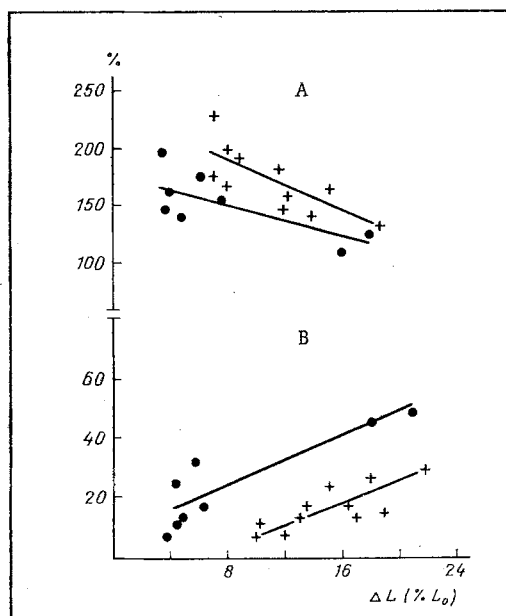


Fig. 2

Fig. 2. Degree of potentiation (A) and degree of restitution (B) as functions of initial amplitude of contraction at a frequency of 120/min for myocardium of control (dots) and adapted (crosses) rats. Amplitude of contraction in each experiment expressed as a percentage of initial length of muscle.

restitution of contraction reflects the rate of accumulation of  $\text{Ca}^{2+}$  in regions of the sarcoplasmic reticulum, and that the degree of potentiation reflects the magnitude of additional  $\text{Ca}^{2+}$  accumulation in these regions [12, 15].

During massive hypertrophy of the heart caused by an experimental defect the rate of uptake of  $\text{Ca}^{2+}$  by elements of the sarcoplasmic reticulum is reduced [9, 14]. This is combined with an increase in the rate of restitution [2] and a decrease in the degree of potentiation [3, 4]. In the case of moderate hypertrophy arising as a result of adaptation of animals to physical exertion, changes in the contractile function are largely opposite to those arising during massive hypertrophy of the heart [5].

In this investigation the rate of restitution and degree of potentiation of myocardial contraction were determined in rats adapted to exercise.

#### EXPERIMENTAL METHOD

Rats were adapted to exercise by making them swim in water at  $32^{\circ}\text{C}$  for 30-60 min daily for 7-11 weeks. The increase in relative weight of the left ventricle in the experimental animals compared with the controls was  $7 \pm 1.2\%$ . Strips of the papillary muscles of the left ventricle, with a calculated area of cross section of 0.5-1.0  $\text{mm}^2$ , were made to contract by electrical stimulation and to lift a small constant load in Krebs' solution with a  $\text{Ca}^{2+}$  concentration of 1.2 mM at  $30^{\circ}\text{C}$ . The use of isolated strips avoided possible differences in the thickness of the papillary muscles resulting from training and growth of the animals, which limits the contractile function, especially if the frequency of contractions is high [1, 11]. The design of the apparatus for recording isotonic contraction of the muscles was described previously [3, 4]. The mechanogram was recorded on a Disa Electronic oscilloscope, by means of a 51V21 capacitance transducer.

In experiments on eight strips from the hearts of the control animals and 11 strips from the hearts of the adapted animals, after measurement of the basic indices of contraction and relaxation, the inotropic response was determined to paired stimulation at increasing frequency: 40, 120, and 240 pulses/min. The duration of the

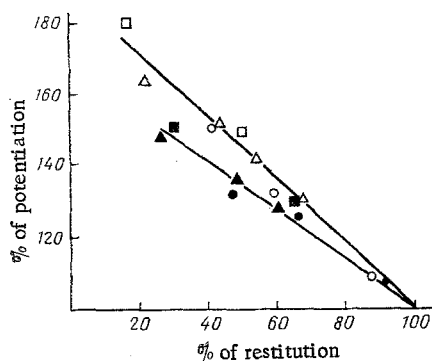


Fig. 3. Relationship between degree of restitution (abscissa) and degree of potentiation (ordinate) for myocardium of control (shaded symbols) and adapted (unshaded symbols) rats for a frequency of contractions of 40 (circles), 120 (triangles), and 240 (squares) per minute. Each point is mean of 8-11 experiments.

intertrial intervals varied under these circumstances from 150 to 1200 msec. The degree of potentiation was expressed as the ratio to the original amplitude of contraction at the given frequency, and the degree of restitution of amplitude in response to the second pulse of the pair was expressed relative to the amplitude of the preceding contraction. To compare the amplitude of contraction of strips with different lengths, the degree of real shortening was expressed as a percentage of the length of the strips.

#### EXPERIMENTAL RESULTS AND DISCUSSION

It will be clear from Fig. 1 that potentiation of the contractions increased as the intertrial interval was shortened and the frequency of contractions rose. At each frequency the degree of potentiation in experiments on the myocardium of the adapted animals was rather higher than in the control experiments, but the difference was not statistically significant.

The degree of potentiation in each group depended on the original amplitude of contraction. A high amplitude of contraction was combined with a low degree of potentiation (Fig. 2A). As Fig. 2A shows, the generally equal degree of potentiation in the experiments on the myocardium of the adapted animals was associated with a higher amplitude of contraction. For an equal amplitude the degree of potentiation was higher for the myocardium of the experimental animals than in the control. The amplitude of contraction also determined to some extent the degree of restitution for a given intertrial interval. A higher amplitudes was combined with a higher degree of restitution (Fig. 2B). According to the average data the difference between the control and experimental series was not significant, but for equal amplitudes the degree of restitution was lower for the myocardium of the experimental animals.

Other conditions being equal, the amplitude of contraction is determined by the degree of interaction between  $\text{Ca}^{2+}$  ions and contractile proteins. Contraction is absent if the  $\text{Ca}^{2+}$  concentration in the myoplasm is below  $10^{-7}$  M, but a concentration of  $5 \cdot 10^{-6}$  M is sufficient for maximal activation of the myofibrils [10]. It can be postulated that the increased amplitude of contraction in each group of experiments was due to the higher concentration of  $\text{Ca}^{2+}$  acting on the myofibrils. This hypothesis is supported by the decrease in the degree of potentiation and increase in the degree of restitution of the heart muscle found when the  $\text{Ca}^{2+}$  concentration in the solution is increased [7, 8, 13]. As Fig. 3 shows, at any of the frequencies tested, as the degree of restitution grew, the degree of potentiation in both groups fell. For the same degree of restitution, the myocardium of the adapted animals was characterized by an increased degree of potentiation.

The reciprocal relationship between the degree of restitution and the degree of potentiation is the essential rule of activity of heart muscle. It is observed under conditions when the initial strength or amplitude of contractions is varied within wide limits, for example, during an increase in the  $\text{Ca}^{2+}$  concentration [7, 13], the action of heavy water [6], or hypertrophy of the heart induced by an experimental defect [2, 3, 4]. This rule is perhaps determined by a redistribution of  $\text{Ca}^{2+}$  between the premature and potentiated contractions.

During adaptation to exercise changes in the degree of restitution and potentiation were opposite to the changes arising during compensatory hypertrophy of the heart [2, 3, 4]. Biochemical and physiological data

point to a decrease in the functional power of the mechanisms of ionic transport in the presence of massive hypertrophy of the heart [2, 3, 4, 9, 14]. This suggests that during adaptation to physical exercise, the power of the ionic transport system in heart muscle cells increases.

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#### EFFECT OF SALIVARY KALLIKREINS ON MICROVESSELS OF THE HAMSTER RETROBUCCAL POUCH AND RAT MESENTERY

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UDC 612.313.1/.8+577.156+612.335.5

The effect of purified human, rat, and hamster salivary kallikreins on microvessels of the rat mesentery and hamster retrobuccal pouch was studied by intravital microscopy. Dilatation of arterioles, a reduction in diameter of the venules, and an increase in the number of active capillaries were found. These effects differed depending on the species and organ concerned. Homogenates of the mesentery and retrobuccal pouch, proteins of the albumin type, histamine, and certain amino acids were found to activate the salivary kallikreins.

KEY WORDS: kallikrein; saliva; blood supply; digestive organs.

The physiological role of the salivary kallikreins in the digestive system has virtually not been studied except for their participation in the development of working hyperemia of the salivary glands [12].

The object of this investigation was to study the effect of purified salivary kallikreins on the microcirculation in the rat mesentery and hamster retrobuccal pouch.

#### EXPERIMENTAL METHOD

The effect of purified kallikreins isolated by the writers' own methods from rat, hamster, and human saliva [3, 5], on microvessels 10–75  $\mu$  in diameter in the mesentery and retrobuccal pouch was studied in ex-

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