EFFECT OF THICKNESS OF ISOLATED PAPILLARY MUSCLES ON STRENGTH OF CONTRACTION AT DIFFERENT FREQUENCIES

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The maximum strength of contraction developed by strips of papillary muscles of the left ventricle of rats varied inversely with the thickness of the strip. Strips of different thicknesses showed completely different relationships between concentration strength and frequency, if the increase in frequency was gradual. These differences disappeared if the change to a high frequency was sudden. The function of thick fibers was more considerably affected by blocking of glycolysis with monoiodoacetate. The results are in agreement with the view that an increase in thickness of muscles is accompanied by development of hypoxia in the central zones of the muscles through an increase in length of the oxygen diffusion pathway.

Isolated papillary muscles from the ventricles of mammals are widely used at the present time for physiological research. With a decrease in oxygenation of isolated muscles, the stability of their function is ensured by utilization of factors limiting the oxygen consumption of the muscles: hypothermia and a low frequency of stimulation. Although some workers [13] do not consider that the thickness of the papillary muscles is a factor determining their function, it is evident that with an increase in thickness, the length of the oxygen diffusion pathway from the solution to the central zones of the muscles must also increase.

The role of this factor was examined in the present investigation in which the function of strips of different thickness, taken from the papillary muscles, was compared.

EXPERIMENTAL METHOD

Strips of the papillary muscles of the left ventricle of male albino rats weighing 250-350 g were gripped by steel clips and placed in a glass chamber filled with Krebs's solution warmed to 30° and saturated with 5% CO_2 + 95% O_2, in a tube 150 cm long. The composition of the solution was as follows (in μmoles/liter): NaCl 120, KCl 4.8, $CaCl_2$ 2.5, KH_2PO_4 1.2, $MgSO_4$ 2.5, $NaHCO_3$ 25, glucose 5.56; pH 7.3-7.4.

The muscles were stimulated by means of electrodes placed in the solution on both sides of the muscle and parallel to it. The pulse duration was 5 msec, initial frequency 10/sec, and amplitude 10-20% above threshold for preventing excitation of sympathetic nerve endings [8].

Under isometric conditions, the maximum strength of contraction developed by each muscle strip during a gradual increase in its initial length was determined. The strength was measured by means of wire resistance transducers and a TU-4m tensometric amplifier and recorded on a Cardiovar VI instrument. To compare the strength of contraction of different muscles, the value of the maximum contraction developed was determined by dividing the force developed by the muscle by the area of cross section [13]. The latter was calculated from the weight and length of the strip, assuming that the muscle is a cylinder.

After measurement of the force, isotonic contraction conditions were created in which the muscle lifted a constant load, and the inotropic response was determined from the degree of shortening, as mea-

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TABLE 1. Functional Indices of Muscles of Different Thickness

	Muscles			Significance of difference
	thin 1	medium 2	thick 3	
Number	4	7	6	
Weight of muscles (in mg)	1.1±0,2	2,2±0,17	3,95±0,2	$P_{1-2}<0,01$ $P_{2-3}<0,01$
Area of cross section (in mm^2)	0,24±0,03	0,51±0,03	1,04±0,06	$P_{1-2}<0,01$ $P_{2-3}<0,01$
Maximum force developed (in g force)	0,76±0,11	0,83±0,08	0,92±0,22	$P_{1-2}>0,05$ $P_{2-3}>0,05$
Maximum tension developed (in g force/mm^2)	3,13±0,26	1,62±0,19	1,06±0,3	$P_{1-2}<0,01$ $P_{2-3}>0,05$
Maximum force developed by 1 mg myocardium (in g force)	0,7±0,05	0,38±0,02	0,22±0,07	$P_{1-2}<0,01$ $P_{2-3}<0,05$

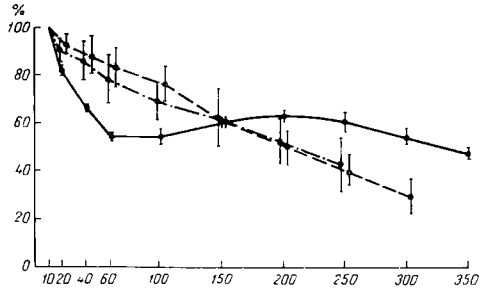

Fig. 1. Frequency of contractions as a function of degree of shortening, expressed in percentages of initial length (at frequency of 10/sec) for thin (continuous line), medium (broken line), and thick (line of dots and dashes) strips of papillary muscles of rats.

sured by a capacitance transducer and 51 BO2 amplifier (Disa Electronic). At this stage of the experiment, the response of the muscles to an increase in the frequency of stimulation and to blocking of blycolysis by monoiodoacetate (1 mmole/liter) was studied.

EXPERIMENTAL RESULTS AND DISCUSSION

The total number of muscle strips was subdivided into three groups on the basis of their weight (Table 1), and these were conventionally described as thin (weight 0.8-1.5 mg), medium (weight 1.6-2.8 mg), and thick (weight 3.1-4.8 mg). Comparison of the medium and thick fibers with the thin shows that an increase in weight and area of cross section by 2 and 4 times, respectively, was associated with a decrease in the contraction and force generated by 1 mg myocardium by about 2 and 3 times. This dependence of the strength of contraction of the strips on their thickness was not observed in the experiments of Spann et al. [13], using papillary muscles of cats. The reason for this difference may be, first, the fact that observations by the workers cited were restricted to six muscles, four of which had an area of cross section exceeding 1.2 mm^2, and second, the fact that the myocardial oxygen consumption of rats is several times higher than that of cats [5, 6, 10, 11, 15].

The fact that the strength of contraction was reduced in the thicker strips can be regarded as experimental confirmation of the hypothesis put forward previously by morphologists [1, 4, 12, 14], to the effect that an increase in the length of the oxygen diffusion path and the development of hypoxia in the center of fatigued muscle fibers may be among the probable causes of disturbance of the contractile function of the hypertrophied heart.

The dynamics of the degree of shortening during a gradual increase in the frequency of stimulation, when the muscle completed from 60 to 80 contractions at each frequency, is illustrated in Fig. 1. This relationship was the same for thick and medium muscles: any increase in frequency led to a decrease in amplitude, while for thin muscles there was a certain range of frequencies (from 100 to 200) within which the amplitude of shortening increased as in the staircase phenomenon. In addition, the thin muscles reproduced a higher frequency of contraction than the thick.

In other investigations conducted on the papillary muscles and strips of the ventricles of rats [2, 3, 7] at 37°, the relationship between the strength of the contractions and their frequency was identical to that observed by the writer for thick and medium strips (Fig. 1). Hoffman and Kelly [5] attempted to explain the absence of a positive inotropic effect of an increase in frequency, which is usual for mammalian ventricles [9], but the addition of rat plasma, pyruvate, or lactate to the perfusion fluid, or a change in the concentrations of potassium, sodium, and magnesium, proved ineffective. The sharp change in the ordinary

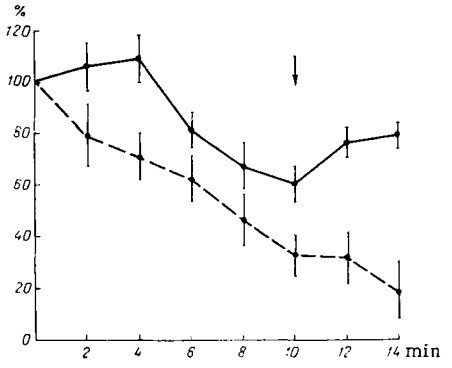

Fig. 2. Effect of monoiodoacetate on degree of shortening, expressed in percentages of initial length (before treatment with monoiodoacetate), of thin (continous line) and medium (broken line) strips of papillary muscles of rats. Arrow marks beginning of rinsing out of iodoacetate.

relationship between force of contraction and frequency in the thin strips (Fig. 1) suggested that the absence of a phase of increase in strength in the thick fibers was due to hypoxia and to an energy deficiency.

The following results are in agreement with this hypothesis. After a sudden change of frequency from 10 to 270/min, the amplitude of shortening of the thin and medium strips showed changes of an absolutely identical pattern: at first it fell to 30% of the initial value, then gradually rose to reach 75% of the initial value after 15 sec. Evidently the work of the muscle at a high frequency for 15 sec required much less expenditure of energy than during a gradual increase in frequency lasting for more than 5 min. This expenditure of energy could be fully compensated by the reserves of high-energy phosphates accumulating during work at low frequency.

During hypoxia of muscle tissue, the role of anaerobic glycolysis in the supply of energy for muscle function is known to increase. Blocking of glycolysis by treatment with monoiodoacetate for 10 min had an irreversible inhibitory action on the degree of shortening of the medium strips, whereas the thin strips recovered their amplitude of shortening almost to its initial level after rinsing out of the monoiodoacetate.

The progressive decrease in strength of contractions of thick strips during a gradual increase in frequency was thus evidently due to the development of hypoxia and a deficiency of energy for contraction in the muscles. This hypthesis suggests that the sharp difference between the inotropic response of the ventricle in rats from that of the ventricles of other mammals may not be so considerable if oxygenation of the myocardium is adequate.

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