COMPARISON OF THE STRENGTH AND RATE OF CONTRACTION AS CRITERIA OF MYOCARDIAL CONTRACTILITY

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KEY WORDS: isolated myocardium; contractility; temperature; stretching; frequency of contractions.

In the course of previous studies on the dog heart–lung preparation [4] and cat ventricle [6] it was postulated that rate of contraction has advantages over force when temperature effects on contractility of heart muscle are analyzed. The aim of the present investigation was to compare these parameters when estimating contractility of the isolated myocardium. The time course of the force and rate of contractions of the myocardium was studied both during a change of temperature and during a change in the length of the myocardium and frequency of its contractions.

EXPERIMENAL METHODS

Experiments were carried out on papillary muscles of the right ventricle of the cat heart. The size of the preparations did not exceed 8 mm in length and 1 mm in diameter. After excision the muscle was placed in a chamber containing a solution whose temperature could be controlled between 37 and 5°C with an accuracy of ±0.2°C. For stimulation, above-threshold square pulses 5-20 msec in duration (the duration was increased in the course of cooling) were applied from an ÉSU-1 electrostimulator. Measured changes in length of the myocardium were carried out by means of a special stretching device. In the course of the experiment the preparation was bathed with modified Krebs–Henseleit solution of the following composition (in mM): NaCl 118.0, KCl 2.7, $CaCl_2$ 2.5, KH_2PO_4 1.0, $MgSO_4$ 1.2, $NaHCO_3$ 12.0, glucose 5.55. The solution was saturated with a mixture of 95% O_2 and 5% CO_2 (pH 7.3-7.4). Mechanical activity of the muscle was recorded under isometric conditions by means of a 6MKhlS mechanotron on an N-338 automatic writer. All the experiments began after stimulation of the preparation for 30 min at 30°C with a frequency of 0.25 Hz and initial stretching by 10% relative to the initial length of the muscle. In all experiments the maximal force of isometric contraction, the time taken for the maximal force to develop, or the time of contraction and the mean rate of contraction which, under isometric conditions, is directly proportional to the maximal rate of contraction [10], were determined.

The investigation comprised three series of experiments. In series I, undertaken on 36 papillary muscles, the time course of the developed force, the duration of development of the force and rate of contraction were studied and the temperature was lowered from 37 to 5°C. The preparation was cooled at the rate of 0.2-0.5°C/min. Stimulation was carried out at the optimal frequency for the given temperature [5] and with constant stretching of the muscle by 40%.

In the experiments of series II, on 18 preparations, dependence of the force, time, and rate of contraction of the muscle on the degree of its stretching, expressed as a percentage of the initial length of the preparation, was studied at temperatures of 37, 30, and 20°C and at optimal frequencies of stimulation for these temperatures.

In series III, on 12 preparations, the effect of frequency of stimulation on the time course of the above-mentioned parameters was studied at the same temperatures as in series II and with constant stretching of the muscle by 40%. The frequency of stimulation at a given temperature was changed, starting from a value at which previous contractions did not affect the parameters of the following contractions.

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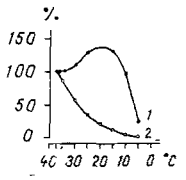

Fig. 1

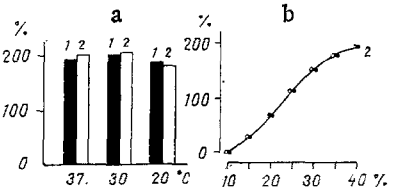

Fig. 2

Fig. 1. Time course of force (1) and rate (2) of contraction of isolated cat myocardium (in % of initial values) during a change of its temperature. Abscissa, temperature (in °C).

Fig. 2. Increase in force (1) and rate (2) of contraction of cat myocardium (in % of initial values) during an increase in its length from 10 to 40% at different temperatures (b) and dependence of increase of force and rate of its contraction on degree of stretching at temperatures between 37 and 20°C (a). Abscissa: a) temperature (in °C), b) degree of stretching (in % of initial length).

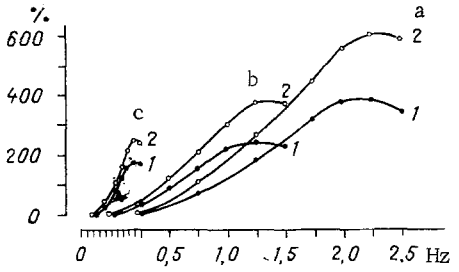

Fig. 3. Dependence of force (1) and rate (2) of contraction of cat myocardium (in % of initial values) on frequency of its stimulation. Abscissa, frequency of stimulation (in Hz): a) 37°C, b) 30°C, c) 20°C.

EXPERIMENTAL RESULTS

The experiments showed that the source of established contractions of the isolated cat myocardium increases as the temperature falls from 37 to 20°C, and then falls on further cooling to 5°C (Fig. 1). The increase in the force of contraction was 9 ± 1% at 30°C, 29 ± 1% at 25°C, and 39.2% of its initial value (31.9 ± 4.4 mN/mm^2 at 37°C; $P < 0.05$ in all cases) at 20°C. Cooling the heart muscle to 15°C caused a reduction in the increase of force to 33 ± 2% ($P < 0.05$;, but at 10°C the force no longer differed in magnitude from its initial value ($P = 0.1$). At 5°C the force of contraction fell sharply, to 22 ± 1% of its initial value ($P < 0.01$).

Unlike the force of its contraction, the rate of contraction of the myocardium decreased with a fall in temperature, starting from 37°C (Fig. 1). At temperatures of 35, 30, 25, 20, 15, 10, and 5°C the rate fell to 86 ± 7, 57 ± 4, 34 ± 3, 21 ± 2, 12 ± 1, 4.2 ± 0.3, and 0.7 ± 0.1%, respectively, relative to the initial value (319 ± 54 mN/sec/mm^2 at 37°C; $P < 0.01$ in all cases). The contraction time, in turn, increased successively during cooling of the myocardium: from 0.10 ± 0.01 sec at 37°C it lengthened by 20 ± 2, 90 ± 3, 280 ± 8, 560 ± 13, 1040 ± 23, 1990 ± 36, and 3140 ± 45% (relative to the initial value; $P < 0.01$ in all cases) at 35, 30, 25, 20, 15, 10, and 5°C, respectively.

In the experiments of series II the following results were obtained. Stretching the papillary muscle led to an increase in the force and rate of its contraction at all temperatures studied. The increase in the force and rate of contraction (in percentages of the initial value) caused by stretching the muscle by the same amount, was found to be the same regardless of temperature (in all cases $P < 0.5$). For example, during stretching by between

10 and 40% the force of contraction was increased at 37, 30, and 20°C by 190 ± 12, 202 ± 10, and 182 ± 9%, and the rate of contraction increased by 199 ± 14, 205 ± 14, and 176 ± 8%, respectively (Fig. 2a). The time course of the increase in force and rate of contraction on average for temperatures of between 37 and 20°C is shown in Fig. 2b. Unlike the force and rate of contraction, the duration of development of force was unchanged during stretching of the myocardium (in all cases $P > 0.5$).

In the experiments of series III an increase in the frequency of stimulation to its optimal value always increased both the force and the rate of myocardial contraction (Fig. 3). In particular, at 37°C the force and rate were increased by 383 ± 78 and 598 ± 120%, at 30°C by 251 ± 52 and 377 ± 78%, and at 20°C by 179 ± 39 and 250 ± 51%, respectively (in all cases $P < 0.01$). Meanwhile the contraction time was shortened with an increase in frequency by 30.8 ± 5.8% at 37°C, by 26.4 ± 3.5% at 30°C, and by 20.2 ± 4.6% at 20°C (in all cases $P < 0.05$).

Analysis of results reflecting the time course of the force of contraction during a fall of temperature shows that estimation of myocardial contracility on the basis of the parameter of force confirms the widely held view that its contracility is best at temperatures of about 20°C [1, 2, 7, 8, 11]. In that case, however, an evident contradiction arises between this conclusion and data on the pumping capacity of the heart, which is virtually absent at 20°C [4]. Meanwhile, the force of contraction of the cat papillary muscle at 37 and 10°C was found to be the same, although it is known that the pumping function of the heart of homoiothermic animals is completely suppressed at 10°C, indicating profound depression of myocardial contractility [4]. Meanwhile the rate of contraction of the isolated cat heart muscle is reduced by almost 80% during cooling from 37 to 20°C, and a fall of temperature to 10°C reduces the rate by 22 times.

Comparison of the time course of the force and rate of contraction thus shows that the rate of contraction is a more adequate and more sensitive criterion of the influence of cold on myocardial contracility than the force of contraction. It follows from this conclusion that cooling the myocardium depresses its contractility, as is confirmed by a decrease in the rate of contraction.

Comparative analysis of changes in the force and rate of contraction obtained during stretching the muscle or by increasing the frequency of its contractions under different temperature conditions suggests that the principal regulated parameter of contractility during exposure to these factors is the rate of contraction.

For instance, with an increase in length of the myocardium the time of its contraction is unchanged, i.e., an increase in the force of contraction under the influence of stretching is due entirely to an increase in the rate of contraction. Hence it follows that the principal controlled parameter of contractility in the Starling mechanism is not the force, but the rate of contraction. In turn, it will be clear from the account given above that the Starling mechanism is based on a relationship between the length of the heart muscle and the rate of its contraction.

When the effect of frequency of contractions on contractility of the myocardium is examined, it will become clear that an increase in the force of contraction, even if associated with a decrease in its time, during an increase in frequency is produced purely by an increase in the rate of contraction. The chrono-inotropic mechanism of self-regulation of mycardial contractility, just as in the Starling mechanism, thus controls contractility through a change in the rate of contraction, and changes in force are purely secondary. Consequently, chrono-ionotropic relations in the myocardium are in fact based on the relationship between the interval between contractions and the rate of contraction of the heart muscle.

Analysis of data in the literature [3, 9, 12] shows that changes in myocardial contractility obtained in other experimental situations can also be explained primarily by changes in the rate of contraction. However, usually this fact does not receive the attention it deserves, for most factors have little effect on contraction time at a constant temperature, and as a result the change in force is in the same direction as the change in the rate of contraction, so that the primary character of the rate criterion is masked.

It can be concluded from the facts described above that assessment of myocardial contractility by the use of contraction rate as the criterion is more justifiable than the use

of the force of contraction, not only during a fall in temperature of the myocardium but also during exposure to other physiological factors.

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ENDOGENOUS CATECHOLAMINES AND CARDIAC FUNCTION DURING STIMULATION OF THE AUGMENTOR NERVE

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The effect of the augmentor nerve on the force of cardiac contraction is well known [5, 10, 13], but the mechanism of this effect has been insufficiently studied. There have been one or two investigations of metabolic changes in the myocardium arising as a result of stimulation of the augmentor nerve. It has been shown, in particular, that the effect observed during stimulation of the nerve is due to the more rapid turnover of high-energy phosphorus compounds, namely ATP and acid phosphatase (AP), in the heart muscle [7]; a high concentration of glycogen and potassium ions has been found in the myocardium during this procedure [4]. The concentrations of catecholamines in the blood and myocardium have been studied [3, 9] during adaptation of the heart to prolonged sympathetic stimulation in dogs. In these experiments, sympathetic postganglionic mixed nerves were stimulated.

Meanwhile the question of the effect of stimulation of the augmentor nerve on myocardial catecholamine metabolism and the role of catecholamines in the realization of effects of the augmentor nerve have not yet been studied, and the investigation described below as carried out for this purpose.

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