Effects of stretch on mechanical and electrical properties of cardiac muscle

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Records were made of the effects of stretch on amplitude, velocity, and duration of contraction and on relaxation time, conduction velocity, transmembrane action potentials, and excitability. Similarities and differences between the hearts of homeotherms and poikilotherms are discussed.

METHOD

The muscle to be studied was held horizontally in a Lucite tissue bath of 30 ml volume. One end of the muscle was fixed by a clamp about 4 mm wide which held two platinum stimulating electrodes. The other end was tied with a silk thread to a vertical steel rod (R, Fig. 1) which was connected to a movable mount; by means of this mount the rod could be moved back and forth and the length of the muscle could be changed. A scale on the manipulator indicated changes in length in units of 0.1 mm. The rod, R, made contact with the pin of a mechanoelectric transducer tube (RCA 5734) which completed one arm of a bridge. Because the rod, R, was stiff, contractions of the muscle were, for practical purposes, isometric. The output of the bridge was connected to one channel of a dual-beam Dumont oscilloscope to record resting and contractile tension. The sensitivity of the transducer was determined before and after each experiment.

Transmembrane action potentials or surface electrograms were recorded simultaneously with tension. Transmembrane action potentials were recorded through glass microelectrodes filled by boiling in 3 M KCl. The average tip resistance was between 10 and 15 megohms. The microelectrode was connected through a chlorided silver wire to a cathode follower with input capacity neutralization (Bioelectric Instruments Co., Type D). The output of the cathode follower was connected to one of the beams of the oscilloscope.

Bipolar surface electrograms were recorded to measure conduction velocity. Surface electrodes were made of two parallel lengths of platinum wire imbedded in a short glass rod. The tip of the rod was ground down so that the wires, separated by 1 mm, were exposed only at their ends. The surface electrodes were connected to a
The composition of each is shown in Table I.

Three solutions were used as perfusion media in these experiments; the composition of each is shown in Table I. Mammals were anesthetized with Nembutal (30 mg/kg i.p.); fish and terrapins were pithed. The heart was removed and transferred to a container of the appropriate bathing medium under a continuous stream of oxygen-carbon dioxide. The desired tissue was removed from the heart and transferred to the tissue chamber where one end was attached to the vertical rod (R, Fig. 1) by a silk string and the other end was inserted into the jaws of the clamp containing the stimulating electrodes. The initial length of the preparation was determined by moving the rod to the position at which contractile tension just could be detected. Preparations were stimulated as soon as they were fixed in position. However, recordings were not made for at least 30 min to allow sufficient time for equilibration. Because few of the preparations exhibited spontaneous activity, they were stimulated unless otherwise noted. The stimulus intensity was three to five times threshold; and was constant throughout the experiment. At each length of the muscle, between 10 and 15 fibers were impaled at random, the resting potential was measured, and the amplitude and duration of the transmembrane action potential recorded. Conduction time was measured at each length of the muscle in two ways. In one, surface electrograms were recorded at two points separated by a constant distance. The time required for the electrical activity to travel between the stimulating electrode and each of the surface electrodes was measured and the conduction time over a fixed distance was calculated by difference. The distance between the two positions of the surface electrodes varied between 2-5 mm depending on the initial length of the muscle. Conduction time also was measured between two points on the surface of the muscles which had been marked with small bits of carbon.

Contractile tension was recorded simultaneously with either transmembrane action potentials or the surface electrograms. After recordings at one length had been completed, the muscle was stretched by a known increment and then it was allowed to equilibrate for 5-10 min so that the new steady resting tension was established. The end of relaxation time was considered the time when muscle tension had returned to the new base line at that length. The procedure was repeated at each length.

The errors of measurements did not exceed ±2 msec, which was about 5% of the shortest relaxation time. In this manner, the preparation was stretched until contractile tension passed through a maximum and then declined to a very low value or disappeared. The muscle then was released and the length at which contractile tension could just be detected was again recorded. By this criterion, all the muscles were slightly elongated after stretch. However, after 40-60 min these muscles returned to the same initial length as that measured before stretch.

To determine the condition of the muscle after stretch, contractile tension as well as the various indices of electrical activity were measured at one or two lengths.

**DEFINITION OF TERMS**

**Initial length (L_i):** that length of the muscle at which contractile tension could just be detected. Optimal length (L_o): that length at which maximum contractile tension was recorded. Maximal length: that length at which contractile tension was reduced to a value of 0.2 g or less. Conduction time: the time, in milliseconds, required for the electrical activity to travel between two given points. Conduction velocity: conduction time per unit length (m/sec). Contraction time (time to peak tension, P): the time interval (after stimulation) required for the muscle to change from a fully relaxed state to a fully contracted state. Relaxation time (R): the time interval required for the muscle to change from a fully contracted state to a fully relaxed state.
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FIG. 2. Contractile tension, tension after release of muscle, T; initial length, L; optimal length, Lopt; maximal length, Lmax; contraction time after release of muscle, \( \Delta_t \); relaxation time, R; and the P/R ratio from a cat papillary muscle at various lengths. Immediately after releasing the muscle, contraction time as well as the relaxation time was changed (see text); P and R after release, \( \Delta_t \); P/R ratio after release, \( \delta \).

RESULTS

Cat papillary muscle. Papillary muscles from the right ventricle of the cat generally were chosen because of their almost cylindrical shape. All these muscles were less than 1 mm in diameter. Thinner muscles were thought more appropriate because of the possibility of more adequate diffusion of oxygen. The length of the muscle varied between 4 and 12 mm.

The effects of changes in length on isometric tension of cat papillary muscle are shown in Fig. 2, curve T. In the 18 muscles examined, it was found that as length increased, contractile tension increased, passed through a maximum, and then decreased to a minimal value. The effects of stretch on all the muscle parameters investigated were reversible even though the muscle had been stretched to a point where contractile tension was no longer recorded. If the muscle was checked immediately after release it was found that the initial length and the optimal length, as well as the contractile tension developed at the optimal length were greater than the initial values. Somewhat similar observations have been reported by Walker (8). However, if the muscles were allowed to rest for 1 hr before being tested again, the values of initial length, optimal length and maximum contractile tension were the same as those observed initially. The return of contractile tension after release suggested that, at least under the experimental conditions described, permanent fiber damage had not occurred.

The contraction time was constant between the initial length and the optimal length (Fig. 2, curve P). In the 18 cat papillary muscles examined, contraction time was \( 190 \pm 5 \) msec over this range of lengths. Beyond the optimal length, contraction time increased. Also, contraction time measured after release from excessive stretch was slightly increased although there was an increase in contractile tension as mentioned above.

If conduction time was measured between two points on the muscle 5 mm apart, conduction velocity apparently increased between the initial length and the optimal length (Fig. 2, curve VA, “apparent” conduction velocity). However, if the conduction time was measured between the ends of the muscle or between two carbon particles placed on the muscle before stretch was begun, then conduction velocity did not change between the initial length and the optimal length (Fig. 2, curve VT, true conduction velocity). At and above the optimal length, both values were the same and decreased with stretch (see Fig. 2). The average true conduction velocity, measured at the optimal length was 0.75 m/sec with a range of 0.5-1.2 m/sec. The surface electrograms recorded between the initial length and the optimal length were smooth in configuration, monophasic when recorded near the ends, and biphasic near the middle of the preparation. As the muscle was stretched beyond the optimal length, multiple deflections were observed, suggesting local asynchrony of activation in neighboring fibers.

At the initial length, relaxation time was almost the same as contraction time and averaged 140 msec. As shown in Fig. 3, the ratio of contraction time to relaxation time, the P/R ratio, was close to unity. As the muscle was stretched, relaxation time increased. Since contraction time was constant between the initial length and the optimal length, the P/R ratio between these lengths decreased. Beyond the optimal length relaxation time still was high, but since the contraction time also increased the P/R ratio increased slightly.

Transmembrane action potentials recorded from cat papillary muscle at each length were examined for variations in shape, amplitude, and duration. Between initial length and optimal length, the amplitude of the resting potential, action potential, and overshoot did not change. The average resting potential was \( 90 \pm 5 \) mv and the transmembrane action potential was \( 105 \pm 5 \) mv. The rise time was about 1 msec. However, the shape and the duration of the transmembrane action potentials did not bear any apparent relationship to either the length of the muscle or its contractile tension. At the same length, various shapes of action potentials could be recorded from different areas. Since specialized conducting fibers have been shown to course along the...
length of the papillary muscle and merge with myocardial fibers at various points (g), the variety of shapes and durations observed was not considered significant.

As the muscle was stretched beyond the optimal length, the resting potential decreased and values as low as 50 mv were recorded at maximum length. The overshoot decreased in amplitude and eventually vanished when the resting potential reached 60 mv or less. In extreme stretch the rise time increased to 5-10 msec, suggesting an abnormal condition of the fibers. Electrical activity recorded at extreme lengths was more like local potential changes than propagated action potentials. The values of all the parameters described above returned to or approximated the initial values after the muscle had been released.

The ratio of the initial length of the muscle to the optimal length was calculated. Considering the small size of the muscles used and the somewhat arbitrary character of the definition of initial length used here, it was not surprising that the scatter in the values of this ratio was large. The average value in nine preparations was 1.46 with a range of 1.1-1.75. However, cat papillary preparation could not be stretched much beyond twice its initial length without a complete loss of contractile tension. This observation contrasts markedly with results obtained from the poikilothermic hearts, as shown below.

Comparison of cat papillary muscle with other preparations from homeothermic species. Preparations of cat auricular strips, hamster right ventricular wall, 13-lined ground squirrel right ventricular strip, and chicken auricular and ventricular strip were examined by the procedures described for the cat papillary muscle. Length-tension relationships observed in the other homeotherms were found to be similar to those shown for the cat papillary muscle. In all species examined, the auricular fibers exhibited a shorter contraction time and a higher velocity of conduction than the ventricular fibers of the same animal. Other responses of the fibers to stretch were similar to those described for the cat.

In all homeotherms maximal contractile tension decreased when the muscle was stretched beyond the optimal length. However, for a short range of lengths above the optimal length, contractile tension could be restored to the maximum values if the intensity of stimulation was increased. For example, in a preparation of hamster right ventricle, stimulated with 3 v, maximal contractile tension of 1.2 g was developed at the optimal length of 8 mm. When the muscle was stretched to 9 mm the contractile tension fell to 0.5 g but increased to 1.2 when the stimulus intensity was increased to 5 v. Similar observations were made with heart muscle fibers from all the different species examined in this survey. These results suggest that stretch causes a change in the excitability of the fibers. With excessive stretch, alternations in the magnitude of contractile tension suggested that not all fibers were contracting at the same time. Changes in the surface electrogram described above support this idea.

**Table 1. Composition of modified Tyrode's solution used for various species**

<table>
<thead>
<tr>
<th>Constituent</th>
<th>Mammalian Tyrode's</th>
<th>Avian Tyrode's</th>
<th>Turtle Tyrode's*</th>
</tr>
</thead>
<tbody>
<tr>
<td>NaCl</td>
<td>137</td>
<td>137</td>
<td>130</td>
</tr>
<tr>
<td>NaHCO₃</td>
<td>12</td>
<td>12</td>
<td>11.9</td>
</tr>
<tr>
<td>Dextrose</td>
<td>5.1</td>
<td>5.1</td>
<td>5.6</td>
</tr>
<tr>
<td>KCl</td>
<td>2.7</td>
<td>2.7</td>
<td>2.7</td>
</tr>
<tr>
<td>MgCl₂</td>
<td>0.5</td>
<td>0.5</td>
<td>0.5</td>
</tr>
<tr>
<td>Na₂HPO₄</td>
<td>1.8</td>
<td>1.8</td>
<td>0.34</td>
</tr>
<tr>
<td>CaCl₂·H₂O</td>
<td>2.7</td>
<td>2.7</td>
<td>1.4</td>
</tr>
<tr>
<td>O₂</td>
<td>95%</td>
<td>95%</td>
<td>98%</td>
</tr>
<tr>
<td>CO₂</td>
<td>5%</td>
<td>5%</td>
<td>4%</td>
</tr>
</tbody>
</table>

Values indicate concentration, in mmoles/liter. * Turtle Tyrode's solution also was used for the fish.

Comparison of cat papillary muscle with preparations from poikilotherms. Auricular and ventricular strips from terrapin heart and ventricular strips from the heart of the carp were examined as described in METHODS. The composition of the bathing media used for these tissues is shown in Table 1. The temperature in these experiments was 30 C for the terrapin heart and 20 C for the carp. Higher experimental temperatures could not be used because of deleterious effects on the tissues.

One of the striking differences between the preparations from poikilotherms and the homeotherms was the effect of stretch on the development of contractile tension. Whereas stretching a homeothermic heart muscle 50-100% beyond its initial length considerably diminished or abolished entirely the development of contractile tension, poikilothermic hearts were capable of developing half the maximal contractile tension at three to five times the initial length. The effect of stretch on the poikilothermic heart differed in other ways from that described for cat papillary muscle. As shown in Fig. 4, curve T, contractile tension of terrapin ventricle increased with mild stretch and decreased with excessive stretch. As in the homeotherms, true conduction velocity was constant between the initial length and the optimal length but the apparent conduction velocity increased. True and apparent conduction velocity coincided near the optimal length and declined beyond the optimal length. The velocity of conduction in the poikilothermic hearts was much lower than in the cat papillary muscle (0.2-0.5 m/sec). As in other species examined, velocity of conduction in terrapin auricular strips was higher than in ventricular strips.

The effect of stretch on contraction time in the poikilothermic hearts was unlike that in cat papillary muscle. Contraction time increased between the initial length and the optimal length and decreased beyond the optimal length (Fig. 4, curve P). Although stretch increased relaxation time, this effect was greater in the poikilotherms than in cat papillary muscle. A comparison of the effects of stretch on the ratio of contraction time to relaxation time in the terrapin ventricular strip (Fig. 5) with cat papillary muscle (Fig. 3) shows that, in the former experiments, between the initial length and the optimal length the ratio declined sharply at
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Fig. 4. Contractile tension, velocity of conduction, and contraction time recorded at various lengths from a terrapin ventricular strip. Contractile tension, T; conduction velocity, V; contraction time, P; initial length, L₀; optimal length, Lₒ; maximal length, L_max. Experimental temperature, 30 C.

Fig. 5. Contraction time, P; relaxation time, R; and P/R ratio recorded at various lengths from a ventricular strip of terrapin heart. Experimental temperature, 30 C.

first and then remained constant. In the cat, on the other hand, the P/R ratio declined gradually with stretch. Beyond the optimal length the ratio increased slightly in cat papillary muscle as well as in the terrapin heart.

The transmembrane resting potentials recorded from terrapin heart ranged between 70 and 80 mv. Stretch beyond the optimal length caused the amplitude of the resting potential as well as the action potential and the overshoot to decrease. The overshoot never exceeded 5-10 mv. Ventricular strips from the carp exhibited resting potentials in the range from 60 to 65 mv and an overshoot of 5 mv. Both decreased in amplitude when the muscle was stretched excessively.

**DISCUSSION**

This study of the mechanical and electrical responses of heart muscle fibers from several species of animals has revealed a number of similarities in the properties of the various hearts, and several differences. In agreement with the findings of other workers, the effect of mild stretch (between the initial length and the optimal length) on the heart muscle fibers of all animals was to increase the contractile tension developed. Excessive stretch (beyond the optimal length) decreased contractile tension considerably or abolished it entirely. Stretch also increased the relaxation time in all preparations. At extreme lengths, alternation in the amplitude of contractile tension was observed in all preparations, suggesting that not all the fibers contributed to the development of contractile tension in any given twitch. Extreme stretch caused a decrease in resting potential, rate of rise, and overshoot of the transmembrane action potential. Surface electrograms were unaffected by mild stretch but extreme stretch decreased the amplitude of deflection and increased propagation time. Multiple deflections observed during extreme stretch suggested asynchronous activity in adjacent fibers.

The greatest differences in the response of heart muscle fibers observed in this survey were those between homeotherms and poikilotherms. Thus, whereas mild stretch increased contractile tension in all species, contraction time was unaffected in the homeotherms and velocity of contraction increased. In the poikilotherms, on the other hand, contraction time increased and velocity of contraction increased only slightly, if at all. Similarly, whereas extreme stretch brought about a decrease in contractile tension in all species, contraction time increased in the homeotherms but decreased in the poikilotherms. As a class, hearts of homeotherms failed to develop contractile tension when stretched beyond 50-100% of initial length. This behavior contrasted markedly with poikilothermic hearts which could be stretched two to three times the initial length before a marked reduction in the development of contractile tension was observed.

As pointed out above, it is possible to distinguish between an apparent and a true conduction velocity in these heart muscle preparations. When conduction time was measured between two marked points on the surface of the muscle, there was no change in conduction velocity as the muscle was stretched from the initial length to optimal length. Thus the true conduction time was not affected by this degree of stretch. However, if the conduction time was measured by moving the surface recording electrodes a known distance along the muscle, then the conduction velocity was observed to increase with stretch between the initial and the optimal length. This apparent change in conduction velocity was thought to result largely from changes in fiber orientation.

It would seem that the effect of stretch in decreasing the magnitude of contractile tension in these fibers in part could be explained in terms of a change in excitability. As the muscle was stretched beyond the optimal length, the threshold of some of the fibers was increased and these fibers failed to respond to the stimulus intensity usually employed. As a result contractile tension decreased but could be restored if the stimulus intensity raised so as to exceed the new threshold. Further stretch would again bring about a decrease in contractile tension which once more could be raised in the initial value by raising the stimulus intensity. This process could be repeated until the muscle was stretched so much that contractile tension decreased to a minimal value in spite of the application of maximal stimulus intensity. The effect of changes in stimulus strength is not thought to be due to catecholamine release since it was not apparent prior to overstretched (10, 11).

It is well known that the tension developed by skeletal
muscle also decreases when the fibers are stretched beyond the rest length. According to Huxley (12) the decline in tension occurs because the interdigitating filaments are pulled away from each other, leaving fewer points for contact during contraction. Although this mechanism may explain the decline in contractile tension of heart muscle fibers at extreme stretch and maximal stimulus intensity, it would seem that, before this stage is reached, stretch also brings about a decrease in excitability. When the stimulus intensity is only raised three to five times above threshold, as in the experiments described above, then the decreased excitability will cause contractile tension to decline. It may be that the effect of stretch on excitability is characteristic of heart muscle fibers, although such an effect on skeletal muscle may have been masked by the routine use of maximal stimulus intensity.

Another factor which may contribute to the decline in contractile tension when the muscle is stretched beyond the optimal length is the decrease in the velocity of conduction. In the homeotherms, increase in contraction time associated with the decline in contractile tension could be due to asynchrony of contraction in various fibers; however, the same reasoning would not apply to poikilothermic hearts in which contraction time decreases with stretch beyond the optimal length.

REFERENCES