EFFECT OF STRETCHING ON ELECTRICAL ACTIVITY OF HUMAN MYOCARDIAL CELLS

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Under pathological conditions the atria are often overloaded by pressure or volume and undergo appreciable overstretching. This is observed, for example, in patients with atrial septal defects or mitral stenosis. Consequently, overstretching may potentially be a pathogenetic factor. The character of electrical activity in the myocardial cells of such patients has been studied in fair detail [4, 1]. There is also information on the action of the principal cardiotropic drugs on electrogenesis of the myocardiocytes in congenital and acquired heart defects [2, 8]. However, the effects of stretching have not been studied.

The object of this investigation was to demonstrate how stretching affects electrical activity of the atrial myocardium of patients with cardiac septal defects (CSD) and mitral stenosis (MS).

EXPERIMENTAL METHOD

Experiments were carried out on thin strips of myocardium (length 7-10.0 mm, cross section 1.0 mm^2), excised from the trabeculae of the auricles of patients with MS and CSD. Removal of the auricles was an essential step in the operations. The strips were fixed in a transparent plastic bath with a capacity of 5 ml and perfused with Krebs' solution aerated with carbogen. The temperature of the solution was 32-33°C, its pH 7.3-7.4, and the rate of perfusion 7-10 ml/min. Above-threshold pulses 3-5 msec in duration were used for stimulation, through massive platinum electrodes (field stimulation). Pulses of stimulating current were applied through an isolating unit. Electrical activity was recorded by means of glass microelectrodes filled with 3 M KCl solution, under static and dynamic conditions of stretching. During static stretching the muscle was stretched from L_o to L_{max} and electrical activity was recorded by a stationary electrode, which was inserted into the preparation after each 10% of stretching. L_o is the length at which passively and actively developed tensions are close to zero, L_{max} the length at which the actively developed muscle tension is maximal. During dynamic stretching the muscle was stretched and then returned to L_o (cyclic deformation) at a constant velocity of between 0.03 and 0.3 mm/sec. In this case electrical activity was recorded by means of floating microelectrodes. The recording was considered to be successful if an action potential (AP) was recorded from one cell throughout cyclic deformation of the muscle. Altogether 20 preparations were studied.

EXPERIMENTAL RESULTS

During static stretching changes in AP occurred starting from stretching equal to 10% of L_o. Two-component APs, consisting of a prepotential (the first component) and a subsequent faster, high-voltage spike (second component; Fig. 1) were observed most frequently in the atrial myocardium of patients with congenitial and acquired cardiac defects (Fig. 1). During stretching, the origin of the second component began to be delayed: the greater the stretching, the greater the delay. For instance, when $L = L_o$ the delay was 130 msec, at $L = L_o +$ 15% L_o it was 460 msec, and $L = L_o +$ 20% L_o it was 660 msec. Lengthening of the delay of appearance of the second component corresponded to delay of the second contraction, which resembled an extrasystolic contraction (Fig. 1, II). Finally, starting from a certain moment (for example, 25% of L_o) the second component disappeared completely and the force of the contractions decreased appreciably (Fig. 1, II).

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0007-4888/82/9303-0249$07.50

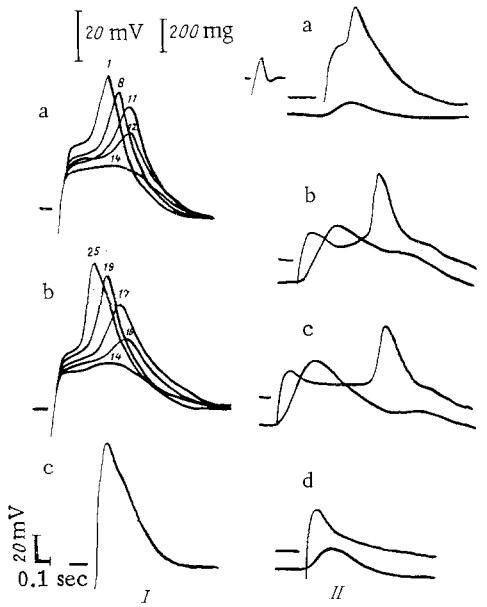

Fig. 1. Effect of stretching on electrical activity and contractility of human myocardium. I) Dynamic stretching: a) two-component AP (1-14) during continuous stretching of myocardium of patient with MS; 1) AP at length equal to L_o, 140 AP at length equal to L_o + 25% L_o; b) recovery of AP during continuous return of muscle length to L_o; c) typical AP for normal myocardium. II) Electrical and mechanical activity during static stretching: a) AP of preparation with length L_o (AP is preceded by artifact when microelectrode was located extracellularly); b) stretching by 10% of L_o; c) stretching by 20% of L_o; d) stretching by 25% of L_o.

During static stretching, after stretching eliminating the second component, this could reappear with time Moreover, the second component could gradually come closer to the first. This fact is evidence that the effects of stretching depend on time and, consequently, dynamic conditions are necessary in order to study the effect of stretching.

The APs in the myocardium of patients with MS and with CSD vary considerably, even in the same preparation [4, 2]. During static stretching, when the electrode had to be introduced into a new cell each time, it was impossible to be certain that only effects of stretching were being recorded. During dynamic stretching, when all recordings were made from one cell, these difficulties are abolished. Moreover, during dynamic stretching the evolution of the shape of the AP as a function of the velocity of cyclic deformation of the muscle can be observed continuously.

During dynamic stretching it was found that the second component was gradually delayed during stretching from 130 msec at $L = L_o$ to 220 msec at $L = L_o$ + 20% L_o; the rate of its rise and its amplitude fell (rate of rise 0.17 V/sec at $L = L_o$ and 0.06 V/sec at $L = L_o$ + 20% L_o), or even disappeared completely (Fig. 1, I). The amplitude of the first component also fell from 26 mV at $L = L_o$ to 14 mV at $L = L_o$ + 25% L_o. On the return of the length of the muscle to L_o, the original shape was restored, but the restoration was marked by some degree of hysteresis. For instance, at $L = L_o$ the amplitude of the first component before stretching was 26 mV, compared with 22 mV after the return to L_o. Conversely, the second component increased after cyclic deformation from 26 to 34 mV. This last phenomenon can easily be observed if the duration of delay or the amplitude of the second component is plotted as a function of muscle deformation during stretching and return of the length of the muscle to L_o.

APs could be recorded continuously from the same cell in the same preparation at three different velocities of cyclic deformation. The complete deformation cycle consisted of

stretching by 55% of L_o and the return to L_o. In this preparation a change in the shape of the AP occurred only starting from stretching amounting to 35% of L_o; at a velocity of 0.33 mm/sec (or 0.043 muscle length per second), moreover, the two components came closer together, after which the amplitude of both components fell, and finally a marked shortening of the repolarization phase of the AP occurred. On the return of the muscle length to L_o marked hysteresis was observed, and complete recovery of AP did not take place even when the muscle length was L_o. With an increase in the velocity of stretching to 0.06 mm/sec (or 0.09 muscle length per second) the change in the shape of AP was biphasic. Initially the two components moved apart, their amplitudes fell (the first component by 25%, the second by 75%), after which they again began to close up and the repolarization phase was greatly shortened. At a velocity of 0.3 mm/sec (or 0.43 muscle length per second) significant inhibition of the components was observed (the first was reduced from 55 mV at $L = L_o + 55\% L_o$, and the second from 30 mV to zero at $L = L_o + 55\% L_o$), together with marked hysteresis in recovery of the shape of AP.

During both static and dynamic stretching, when APs typical of the normal atrial myocardium were recorded (Fig. 1, I, c), no changes at all were observed during stretching up to 40%.

The effect of stretching on the normal myocardium has been described by several workers. It has been shown [3] that stretching by up to 30% of L_o did not change APs in Purkinje fibers. However, with a greater degree of stretching, a marked decrease in the steepness of AP was observed in the zero phase. Furthermore, in the reports of several studies of AP [5, 7] the stretched muscle was loosened in quick release experiments. Under these circumstances the principal changes took place in the repolarization phase. Data showing a significant change in AP during a sudden increase in volume of the frog ventricle also have been reported, and after stretching of the ventricle the configuration of AP was gradually restored [6]. The nature of the changes described is not known. It has been suggested that two-component APs are the result of a disturbance of conduction in the pathologically changed myocardium [4]. The prepotential in this case is regarded as electrotonic, the second component as the result of the calcium current induced by the prepotential. The results of the present experiments can easily be explained from this point of view: Stretching worsens conduction and, as a result, the prepotential, the rate of rise, and the amplitude of the second component are reduced.

The facts described above, in the writers' opinion, are of great practical importance. They show that stretching, even within physiological limits, may be an important pathogenetic factor causing extrasystolic contractions and affecting the tension developed by the muscle. It must be emphasized that a close connection exists in the pathologically changed human myocardium between electrogenesis and the Frank–Starling phenomenon.

LITERATURE CITED

1. P. B. Tsyv'yan and V. S. Markhasin, Fiziol. Zh. SSSR, No. 2, 271 (1981).
2. P. B. Tsyv'yan, "Electrical and mechanical activity of the myocardial cells of patients with congenital and acquired heart defects," Author's Abstract of Candidate's Dissertation, Kiev (1981).
3. J. Dubel and W. Trautwein, Cardiologia, 25, 344 (1954).
4. A. Fabiato and F. Fabiato, Circ. Res., 24, 296 (1971).
5. R. Kaufmann, M. J. Lab, R. Hennekes, et al., Pfluegers Arch. Gesamte Physiol., 324, 100 (1971).
6. M. J. Lab, Circ. Res., 42, 519 (1978).
7. M. J. Lab, Cardiovasc. Res., 12, 624 (1980).
8. E. R. Ten Eick and D. H. Singer, Circ. Res., 44, 534 (1979).