RELATIONSHIP BETWEEN MECHANICAL NOISE AND CONTRACTURE LEVEL IN THE RAT PAPILLARY MUSCLE

S. I. Zakharov, K. Yu. Bogdanov, and L. V. Rozenshtraukh

UDC 612.172:612.731.8]-085.23

KEY WORDS: myocardium, contracture, mechanical noise.

Myocardial preparations at rest possess spontaneous mechanical activity. This activity is expressed as low-amplitude fluctuations of resting potential of the muscles with a frequency of 1 to 5 Hz (mechanical noise) [4, 7], or as fluctuations of optical density of the resting muscle [8]. Overloading myocardial preparations with Ca^{++} (low-sodium solution, cardiac glycosides) leads to the appearance of increased mechanical noise only [4, 7]. Similar factors acting on preparations of cardiomyocyte cultures induce asynchronous mechanical oscillations, even though electrical activity was completely suppressed [2, 5]. It can be postulated that the forms of mechanical activity of the myocardium described above are due to intensification of cyclic work of the sarcoplasmic reticulum in response to an increased intracellular Ca^{++} concentration in the same way as occurs in skinned fibers [3]. It has been stated that fluctuations of intracellular Ca^{++} may be the cause of extraexcitation in the myocardium [6], and this stimulates interest in the study of mechanical noise.

The main parameter indicating an increase in intracellular Ca^{++} is contracture of the preparation. In this investigation the relationship was studied between the magnitude of mechanical noise and the level of contracture of the rat papillary muscle during exposure of the myocardium to various factors. This problem has not previously been specially studied.

EXPERIMENTAL METHOD

The papillary muscle was isolated from the right ventricle of the rat heart. The mean length of the isolated muscle was 2.4 mm and their mean diameter 0.5 mm. The muscle was placed in a perfusion chamber (volume 7 ml) and connected by a Kapron thread to a highly sensitive (6 V/g) 6MKh1B mechanotron. The intrinsic noise of the mechanotron corresponded to a mechanical signal with amplitude of 10-15 μg. The preload on the muscle was 1 g/mm^2. Modified Tyrode solution (NaCl-150 mM, KCl-4mM, $MgCl_2$-0.5 mM, TRIS-HCl-25 mM, $CaCl_2$-5.4 mM, glucose 10 mM), pH 7.4, was oxygenated with 100% O_2 at 22 ± 1°C or 35°C. The rate of perfusion was 7 ml/min. Experiments were carried out both on freshly isolated muscles (unadapted preparation) and also on muscles after stimulation for 2 h (adapted preparation). Mechanical noise within the frequency range from 0.25 to 5 Hz and contracture of the preparation were recorded on a two-channel automatic writer (Gould-Brush 2400, USA). To produce hypoxia in the muscle, glucose was excluded from the perfusate and it was saturated with 100% N_2. In this case pO_2 in the perfusion chamber was reduced from 500 mm Hg in the control to 25 mm Hg during hypoxia. In some experiments 125 mM of Na^+ in the perfusate was replaced by Li^+. Noradrenalin was used in a concentration of 10^{-5} M and NaCN in a concentration of 3 mM, with removal of glucose from the solution.

EXPERIMENTAL RESULTS

The mean amplitude of mechanical noise of the freshly isolated muscle at 22°C was 0.45 ± 0.3 mg (n = 5) and its frequency was 1.48 ± 0.1 Hz. This noise consisted of a sequence of waves, symmetrical relative to the isoelectric line, uncorrelated with time. In the course of adaptation the muscle relaxed and the amplitude of mechanical noise diminished (Fig. 1). After 2 h of stimulation the resting voltage of the preparation became stable and the noise amounted to 0.1 ± 0.07 mg, whereas its frequency characteristics were virtually unchanged.

Laboratory of Electrophysiology of the Heart, Institute of Experimental Cardiology, All-Union Cardiologic Scientific Center, Academy of Medical Sciences of the USSR, Moscow. (Presented by Academician of the Academy of Medical Sciences of the USSR E. I. Chazov.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 97, No. 6, pp. 643-645, June, 1984. Original article submitted May 12, 1983.

0007-4888/84/9706-0701$08.50

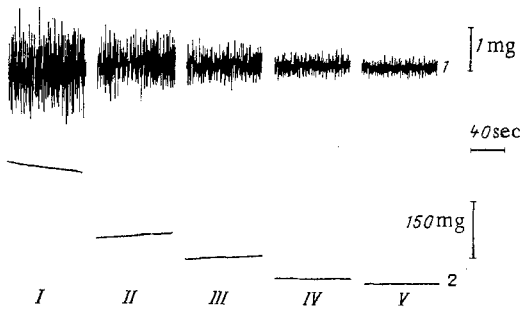

Fig. 1

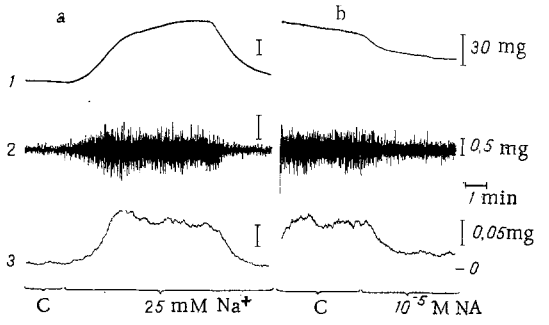

Fig. 2

Fig. 1. Changes in mechanical noise (1) and tone (2) of rat papillary muscle during adaptation. I) Noise and tone of preparation immediately after immersion in perfusion chamber; II) 5 min, III) 20 min, IV) 60 min, V) 100 min after stimulation of preparation at frequency of 0.7 Hz. Temperature 22°C.

Fig. 2. Correlation between contracture (1), mechanical noise (2), and its mean-square amplitude (3) on perfusion of muscle with solution with low sodium concentration (a) and under the influence of 10^{-5} noradrenalin (b). C) Control part of trace, NA) noradrenalin. Temperature 35°C.

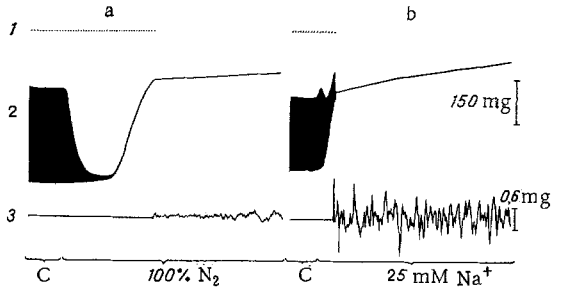

Fig. 3. Disappearance of mechanical noise against the background of hypoxic contracture (a) and its reappearance after reoxygenation during perfusion with low-sodium solution (b). Action of hypoxia and of low-sodium solution was studied against the background of continuous stimulation of the preparation. When contracture reached a magnitude equal to the initial source of contraction, stimulation was discontinued and noise was recorded at a faster tape winding speed. 1) Time marker (10 sec), 2) force of contraction, 3) mechanical noise. C) Control region of trace. Temperature 22°C.

On replacement of the control Tyrode solution by a solution with low sodium concentration and containing Li^+, contracture developed, the maximum of which could reach 300 mg; at the same time the amplitude of mechanical noise was increased (Fig. 2a). The mean frequency of mechanical noise and its amplitude in the low-sodium solution were closely similar to the noise characteristics of the unadapted preparation. During exposure to low-sodium solution for 2 min the amplitude of mechanical noise and of the developing contracture correlated closely ($r = \pm 0.96$). Later, however, correlation between these parameters weakened and could actually become negative (Fig. 2a).

Catecholamines have been shown to cause relaxation of the mammalian myocardium [9]. We studied the action of noradrenalin on the unadapted preparation and found that relaxation of the muscle under the influence of this agent was accompanied by a decrease in amplitude of mechanical noise with a high degree of correlation ($r = \pm 0.97$) (Fig. 2b).

There are known to be two types of contracture of myocardial preparations; in the first type contracture is caused by an increase in the Ca^{++} concentration in the myoplasm, whereas in the second, contracture is meta-

bolic and connected with the formation of rigor complexes when the concentration of high-energy compounds in the cell is deficient [10]. Prolonged contractures of the first type may change into the second type, and the higher the temperature of the perfusion solution the more rapidly does this change take place [10]. Contractures of the first type include those due to low sodium concentration, whereas metabolic contracture can be induced by the action of NaCN or hypoxia. It is evident that in metabolic contracture mechanical noise should disappear. We postulated that the weakening of correlation between the amplitude of noise and contracture in our experiments during the prolonged action of low-sodium solution is connected with the appearance of a metabolic component in the contracture. The appearance of mechanical noise in contracture induced by the action of sodium-free solution has been observed previously in atrial trabeculae of guinea pigs [4]. However, no correlation could be found between the magnitude of contracture and the parameters of mechanical noise in that study. The absence of correlation between noise and contracture during prolonged exposure (for tens of minutes) to low-sodium solution is probably connected with the appearance of a metabolic component in contracture.

Two types of contractures were compared in the present experiments: low-sodium and metabolic. The action of hypoxia on tone and mechanical noise of the papillary muscle is shown in Fig. 3a. It will be clear from the bottom part of the figure that mechanical noise was virtually absent during hypoxia despite considerable contracture. Continuous noise recording during hypoxia in the absence of stimulation shows that in the first minutes of hypoxic contracture mechanical noise could increase in amplitude very slightly, but it became lower in frequency. During the development of contracture the amplitude of noise decreased, and after 8-10 min of hypoxia the noise flattened out and disappeared (at 22°C), which was never observed in the low sodium solution. After reoxygenation of the papillary muscle, low-sodium solution induced equally strong contracture as hypoxia, but high-amplitude mechanical noise still remained (Fig. 3b).

High correlation was thus found between the level of contracture and the amplitude of mechanical noise during the first 1-2 min of action of the low-sodium solution at 35°C or in the course of 5-7 min at 22°C. Meanwhile no correlation whatever was found between these parameters in hypoxia. Similar results were obtained on metabolic contractures induced by NaCN.

Correlation also is absent between the amplitude of noise and contracture during the action of caffeine, which blocks the cumulative function of the sarcoplasmic reticulum [1]. As our experiments and data in the literature [4] showed, disappearance of mechanical noise during the action of caffeine is accompanied by transient contracture. It can be tentatively suggested that the amplitude of mechanical noise is directly connected with the concentration of myoplasmic Ca^{++} provided that the sarcoplasmic reticulum is intact and the contractile apparatus of the mammalian myocardium is functioning normally.

LITERATURE CITED

1. L. Blayney, H. Thomas, J. Muir, et al., Circ. Res., 43, 520 (1978).
2. J. M. Burt, J. Molec. Cell. Cardiol., 14, 99 (1982).
3. A. Fabiato, Fed. Proc., 41, 2238 (1982).
4. H. G. Glitsch and L. Pott, Pflüg. Arch. Ges. Physiol., 358, 11 (1975).
5. K. Goshima and S. Wakabayashi, J. Mol. Cell. Cardiol., 13, 489 (1981).
6. R. S. Kass, W. J. Lederer, B. W. Tsien, et al., J. Physiol. (London), 281, 187 (1978).
7. R. S. Kass and B. W. Tsien, Biophys. J., 38, 259 (1982).
8. E. G. Lakatta and D. L. Lappé, J. Physiol. (London), 315, 369 (1981).
9. M. Morad and E. L. Rolett, J. Physiol. (London), 224, 537 (1972).
10. R. Ventura-Clapier and G. Vassort, J. Mol. Cell. Cardiol., 13, 551 (1981).