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INTERATRIAL DIFFERENCES IN MYOCARDIAL REACTIVITY AND ITS CHANGES FOLLOWING EXERCISE ADAPTATION

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Considerable atrioventricular differences in reactivity of the rat myocardium have been described [1, 6]. However, interatrial differences in myocardial reactivity have still received only little study. Interatrial differences in changes in myocardial reactivity during adaptation of animals to exercise likewise have not been studied. Exercise adaptation of rats is known to increase the inotropic effects of adrenomimetics [5] and the chronotropic action of acetylcholine [2], and also to modify the chronoinotropic reactions of the myocardium [3, 4].

The aim of the investigation described below was to study interatrial differences in inotropic effects of adrenomimetics and acetylcholine and changes in the frequency of contractions, and also differences in the changes in myocardial reactivity in the left and right atria during adaptation of rats to physical exercise.

EXPERIMENTAL METHOD

Wistar rats initially weighing 200-230 g were trained beforehand to run on a treadmill, and were adapted to exercise five times a week for 10-45 min each time, with a gradual increase in the speed of movement of the belt from 10 to 19 m/min in the course of 3 weeks [4]. Animals tolerating a complete training course (6 weeks) were used in the experiments. Animals of the same age served as the control. The heart was removed after intraperitoneal general anesthesia of the animals with urethane (140-160 mg/100 g). After rinsing of the heart (retrogradely through the aorta) with oxygenated Krebs–Henseleit solution both auricles were amputated and strips of their ventral regions were fixed with silk ligatures between microscrews and force transducers (the 6M × 1c mechanotron in series with a rigid spring) in a thermostatically controlled (25°C) continuous flow (20 ml/min) chamber. After preliminary stretching of the preparations and stimulation for 1.5-2 h with a frequency of 0.5 Hz and with a voltage on the platinum electrodes of 1.5 times the threshold level, they were additionally stretched up to the suboptimal length. The reactivity of the preparations was assessed from relative (% of the initial level) changes in the developed force F, and the maximal and

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TABLE 1. Changes (Δ, %, M ± m) in Parameters of Mechanical Activity of Myocardium from Right and Left Atria of Control (C) and Exercise-Adapted (A) Rats in Response to an Increase in Frequency of Stimulation (from 0.5 to 1.0 Hz), and Superfusion with Acetylcholine ($5.6 \cdot 10^{-7}$ M), Adrenalin (10^{-6} M), and Noradrenalin ($3 \cdot 10^{-6}$ M)

Atrium		Increase in frequency of stimulation			Acetylcholine			Adrenalin			Noradrenalin		
		F	dF/dt_+	dF/dt_-	F	dF/dt_+	dF/dt_-	F	dF/dt_+	dF/dt_-	F	dF/dt_+	dF/dt_-
Right	C	−28±2	−30±2	−23±2	−43±4	−41±4	−39±4	30±5	42±4	33±3	70±11	62±6	56±6
	A	−39±2[2]	−33±5	−30±6	−51±3	−42±3	−42±3	71±15[2]	49±5	42±5[2]	155±25[2]	96±15[2]	81±15[2]
Left	C	−23±1[1]	−18±2[1]	−16±2[1]	−34±4	−25±2[1]	−24±2[1]	17±3[1]	25±3[1]	26±3	40±5[1]	43±6[1]	40±6
	A	−28±3[1]	−28±2[2]	−25±4	−30±3[1]	−28±4[1]	−31±4	31±[1,2]	24±3[1]	20±3[1]	68±12[1,2]	86±16[2]	73±15

Legend. F, dF/dt_+, and dF/dt_-) force developed by myocardial preparations, and maximal and minimal values of its first derivative. [1] and [2]) Interatrial differences ([1]) and effect of training on myocardial response ([2]) are significant. Number of experiments in responses to NA was nine (right atrium, C), 11 (right atrium, A), and 10 (left atrium); in all other cases it was 14.

minimal values of its first derivative (dF/dt_+ and dF/dt_-) in response to an increase in the frequency of stimulation to 1 Hz, and superfusion with acetylcholine ($5.6 \cdot 10^{-7}$ M), adrenalin (10^{-6} M), or noradrenalin ($3 \cdot 10^{-6}$ M). The measurements were made when the reaction reached a steady level. The difference from the control values, determined by Student's t test had a level of significance of $p < 0.05$.

EXPERIMENTAL RESULTS

In the control experiments, in response to all test stimulations the preparations of the right atrium responded more strongly than preparations of the left atrium (Table 1). For instance, the response of dF/dt_+ of preparations of the right atrium on average exceeded that of the left atrium by 1.7 times in the test involving increasing the frequency of stimulation (FS), by 1.6 times in response to superfusion with acetylcholine (ACh), by 1.7 times in response to superfusion with adrenalin (A), and by 1.4 times in the test with noradrenalin (NA). Interatrial differences in responses of F to ACh and responses of dF/dt_- to adrenomimetics were not sufficiently significant, although they were in the same direction. On the whole, the greater reactivity of the right atrium than the left was more clearly evident in responses of velocity (or more precisely, temporal) parameters of myocardial mechanical activity than in changes in F.

Adaptation of the animals to exercise increased the reactivity of both atria to adrenomimetics, but the right more so than the left. For instance, responses of F of the right atrium to A and NA were increased by 2.4 and 2.2 times, but responses of F of the left atrium by 1.8 and 1.7 times. Only the right atrium reacted with a greater increase in dF/dt_- to NA and a greater decrease in F to an increase in FS. The absence of any increase in the response of the left atrium to an increase in FS and also the absence of any change in the responses of both atria to ACh may have an adaptive role in view of the negative sign of these reactions. As regards the effect of exercise adaptation of the rats on interatrial differences in myocardial reactivity as a whole, an increase in the differences in the responses of F can be detected. For instance, responses of F of the right atrium on average differed from those of the left atrium in the test involving a change in FS by 1.39 times, compared with a difference of 1.22 times in the control experiments. The corresponding values for responses to A and NA were 2.29 and 2.28 compared with 1.76 and 1.75 in the control. In the trained animals, the interatrial difference in responses to ACh became significant. Meanwhile, under the influence of training of the animals the interatrial differences in responses of dF/dt_+ disappeared in the tests with FS and NA, although differences in the responses to ACh and A remained sufficiently well marked, i.e., responses to procedures mainly linked with cAMP-dependent intracellular regulation (by contrast with effects of NA and a change in FS, which are realized largely through Ca^{2+}-dependent regulatory processes). Under the influence of training, interatrial differences in the response of dF/dt_- to ACh and to a change in FS also disappeared, but differences in the response of dF/dt_- to A appeared.

Interatrial differences are thus found both in responses of the rat myocardium to regulatory influences, and in the effect of training of the animals on reactivity of the heart muscle. Training animals intensifies interatrial differences in myocardial reactivity, assessed relative to changes in developed force, in tests with ACh, NA, and an increase in FS, and over the whole range of recordable parameters of mechanical activity of the heart muscle in the test with A, probable evidence of the substantial physiological importance of these differences.

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