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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TABLE 1. Changes in Parameters of Central Hemodynamics and Myocardial Contractility during Stimulation of Cardiac Augmentor Nerve (M ± m; P < 0.05).

Parameter tested	Before stimulation	During stimulation	Deviation from initial value, %
Systolic pressure in left ventricle, mm Hg	114,3±4,78	148,8±5,39	+30
End-diastolic pressure in left ventricle, mm Hg	7,2±0,52	5,5±0,38	—21
Pressure in aorta, mm Hg			
systolic	108±5,26	126±4,78	+16,6
diastolic	81,7±4,19	82,6±4,65*	+1
pulse	26,3±1,82	43,4±2,16	+65,2
CO, ml/min	1 730±133	2 440±160	+41
Stroke volume of heart, ml/min	16,7±0,93	23,01±1,33	+38,3
Rate of rise of pressure in left ventricle, mm Hg/sec	2597,2±155,4	5121,4±415,4	+97,2
Sonnenblick's index, sec^{-2}	3462,2±404,7	15 000±2 227	+333

*Not statistically significant.

TABLE 2. Concentrations of Catecholamines and DA in Myocardium during Stimulation of Augmentor Nerve (M ± m; P < 0.05)

Parameter studied, μg/g tissue	Right ventricle			Left ventricle		
	before stimulation	during stimulation	deviation from initial value, %	before stimulation	during stimulation	deviation from initial value, %
A	0,066±0,01	0,184±0,03	+178,8	0,061±0,01	0,2±0,05	+228
NA*	1,23±0,07	1,15±0,09*	—6,4	1,228±0,062	1,2±0,096*	—3,5
DA	0,74±0,008	1,4±0,027	+89,2	0,69±0,007	1,37±0,05	+98,5

*Not statistically significant.

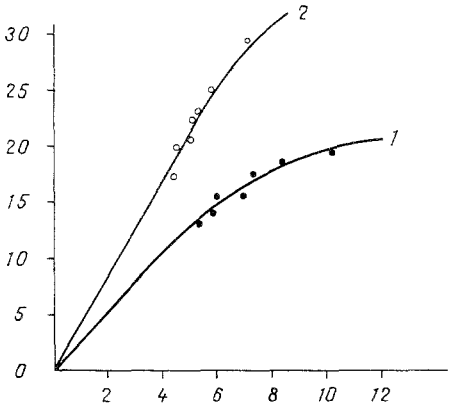

Fig. 1. Effect of stimulation of augmentor nerve on time course of contraction of left ventricle. 1) Control, 2) during stimulation. Abscissa, end-diastolic pressure (in mm Hg); ordinate, stroke volume (in ml/min).

EXPERIMENTAL METHODS

Experiments were carried out on 12 mongrel dogs. After induction of anesthesia with hexobarbital and intubation, sternotomy was performed. The aorta and left ventricle were catheterized through the carotid arteries and the coronary sinus through the right jugular vein. The right augmentor nerve was isolated by blunt dissection in the region of the inferior cervical sympathetic ganglion. The nerve was stimulated by means of the SUNS-01p stimulator, with voltage 6-8 V, frequency 80 Hz, and pulse duration 0.3 msec. Pressure and the ECG were recorded on a polygraph (Galileo, Italy). The cardiac output (CO) was determined by radiocardiography. The concentrations of adrenalin (A) and noradrenaline (NA) in

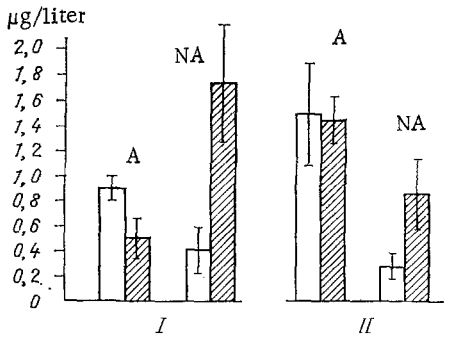

Fig. 2. Catecholamine concentration in blood from coronary sinus (I) and aorta (II) during stimulation of cardiac augmentor nerve. A) Adrenaline, NA) noradrenaline. Unshaded columns — before stimulation, shaded columns — during stimulation.

blood from the coronary sinus and aorta were determined by the trihydroxyindole fluorometric method. Concentratins of catecholamines and their precursors in the right ventricles were determined by liquid chromatography on the Hewlett—Packard multipurpose analyzer, using program 317. Experiments were carried out before and during interrupted stimulation of the nerve for 7 min [12].

EXPERIMENTAL RESULTS

Electrical stimulation of the cardiac augmentor nerve was accompanied by a marked positive inotropic effect (Table 1). The systolic pressure in the left ventricle was increased by 30% (from 114.3 to 148.8 mm Hg). The end-diastolic pressure in it had a tendency to fall. A considerable rise of pulse pressure was noted in the aorta, indirect evidence of an increase in CO [2]. Direct determination of CO showed that it was increased by 41%. This marked degree of strengthening of cardiac activity took place virtually without any change in heart rate [1]. As a result, the stroke volume of the heart was increased. The time course of parameters of the contractile function of the myocardium indicated a considerable increase in myocardial contractility. The rate of rise of the pressure in the left ventricle during stimulation of the nerve was 5121 mm Hg/sec, for an initial value of 2597.2 mm Hg/sec. The index of myocardial contractility of the left ventricle increased to 15,000 sec^{-2} (3462 sec^{-2} in the control). Information on changes in the contractile function of the myocardium also was obtained by calculating the "left ventricular function curve," the ratio between the end-diastolic pressure in the left ventricle and its stroke volume [11]. As Fig. 1 shows, during stimulation of the augmentor nerve this curve was shifted upward and to the left, indicating an increase in contractility of the left ventricle.

This type of response of the heart to stimultion of the augmentor nerve was accompanied by release of NA into blood in the coronary sinus. As a result a sharp rise in the NA concentration was observed in blood from the sinus (from 0.4 to 1.72 μg/liter) and in the arterial blood, i.e., from 0.243 to 0.83 μg/liter (Fig. 2). The adrenaline concentration in blood from the coronary sinus fell under these circumstances from 0.91 to 0.5 μg/liter. The study of the concentrations of catecholamines and their precursor dopamine (DA) in the myocardium of both ventricles gave the following result (Table 2). The concentration of the sympathetic mediator in the myocardium of the left and right ventricles changed very little in response to stimulation of the nerve compared with the initial state (It fell by 3.5-6.4%). The DA level in the myocardium increased during stimulation of the nerve in tissues of both the left and the right ventricle, by 98.5 and 89.2% respectively. The practically unchanged NA level in the myocardium was accompanied by accumulation of A in it. The concentration of A in the heart muscle under these circumstances increased in the right ventricle from 0.066 to 0.184 μg/g and in the left from 0.061 to 0.2 μg/g.

The positive inotropic effect which appeared in response to stimulation of the cardiac augmentor nerve depends on liberation of the neuromediator NA into the synaptic space. Catecholamines, by increasing the cAMP concentration in the myocardium, increase the level of tension developed by the heart muscle and the rate of its rise [15]. In the present ex-

periments an increase in the force and rate of the cardiac contractions was observed during stimulation of the nerve. The raised blood NA concentration in the coronary sinus was found to be directly dependent on the increase in myocardial contractility. The NA concentration in heart muscle is known to be determined by relations between several factors: on the one hand, utilization of mediator in the course of cardiac activity, on the other hand, replenishment of its reserves through resynthesis of the mediator in the sympathetic neurons innervating the heart and, to a lesser degree, on account of its uptake from the blood [6]. In the present experiments, despite considerable entry of NA into the blood, its concentration in the myocardial tissue remained practically unchanged. This phenomenon can be explained by activation of mechanisms of synthesis of NA and its reassimilation by nerve endings (neuronal uptake). The rise in the DA level in the myocardium confirms the view that NA synthesis does not lag behind its consumption, and makes good the neuromediator used up during stimulation under these conditions. Another factor capable of maintaining the NA concentration at the necessary level is its binding and preservation in the tissue depot if adequate quantities of ATP are present [14]. Accumulation of ATP in the myocardium during stimulation of the augmentor nerve [3] is a favorable factor for preservation of adequate NA concentrations in the heart muscle. Meanwhile intensive uptake of A from the blood by the specific tissue of the myocardium may be assumed to take place. This is confirmed by the accumulation of this hormone in heart muscle during stimulation of the nerve. The increase in the A concentration in myocardial tissue is proof of activation of its extraneuronal uptake. Adrenaline is known to have a stronger effect on the adenylate cyclase system than NA [16]. Activation of metabolic pathways induced by A shifts them toward energetically less favorable conditions. Meanwhile data in the literature on an increase in the concentration of glycogen and high-energy phosphorus compounds in the myocardium during stimulation of the augmentor nerve [3, 4] suggest that the A which accumulates in the myocardium takes part in realization of the positive inotropic effect to a far lesser degree than NA, and that it does not have any unfavorable action on cardiac function. This is also demonstrated by our own observations, which indicate no increase in the A concentration in blood from the coronary sinus.

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