BIOCHEMISTRY AND BIOPHYSICS

THE ROLE OF DYNAMIC CARDIAC NERVES IN THE REGULATION OF MYOCARDIAL TROPHICS

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I. P. Pavlov established the anatomic individuality of nerves which altered the strength of cardiac contractions, and devoted particular attention to the nature of these nerve fibers which he called "dynamic." Analysis of the action of these nerves on the heart led Pavlov to conclude that these were special nerves exerting a trophic effect on heart muscle. At the same time, Pavlov said, "this question may be raised and discussed, but not settled finally" [1].

It would appear that direct proof of trophic influences of dynamic nerves could be obtained only from biochemical examination of the myocardium. Of particular interest, therefore, is one of the recent communications of M. E. Raiskina [2] who showed that the "reinforcing" cardiac nerve increases the process of phosphorus fraction turnover in the myocardium (inorganic phosphorus, adenosinetriphosphoric and creatinephosphoric acids).

In the present work are presented results of investigations of the effect of dynamic cardiac nerves, parasympathetic and sympathetic, on the metabolic process of the myocardium. The following were taken as indices of myocardial metabolism: tissue respiration, content of phosphorus fractions (inorganic phosphorus, adenosinetriphosphate and phosphocreatine) and glycogen content.

METHODS

The experiments were performed on dogs of approximately the same age and weighing 8-13 kg. The dogs were kept under identical conditions and on identical diets; they were kept fasting for 24-30 hours prior to beginning the experiments.

Experiments were carried out at different times of the year. The thorax was opened under hexenal*-morphine anesthesia (artifical respiration), the vagus was followed along its course, and the cardiac branches leaving the inferior cervical sympathetic ganglion were dissected. The nerves were stimulated by induction current obtained from a Zimmerman apparatus with a 2 v accumulator. Stimulation of the nerves was from 1 to 4 minutes in duration. Cardiac activity was recorded on a smoked drum. Since interest centered on the influence of dynamic cardiac nerves on myocardial trophics only, the data of biochemical analysis reported in the present paper are concerned only with experiments in which stimulation of cardiac nerves led to changes in the strength of cardiac contractions (increase or decrease) without changes in cardiac rhythm. After a precisely determined period of time from the beginning of stimulation, a portion of the heart in the region of the left ventricle was removed; part of the tissue was frozen in liquid oxygen, while the remainder was used for determination of tissue respiration.

* Russian trade name.

Respiration was measured in a Warburg apparatus with alkali in the middle reservoir, using heart muscle macerated with phosphate buffer (pH 7.4) at 26°C.

Phosphorus fractions and glycogen were determined on heart muscle frozen in liquid oxygen. The frozen tissue was triturated. The proteins were precipitated with trichloracetic acid in the cold. Inorganic phosphorus was precipitated from protein-free filtrate, in the cold, by an equal volume of magnesial mixture, and estimated by the Fiske-Subbarow method. Phosphocreatine was determined in the filtrate after the precipitation of inorganic phosphorus: in the presence of molybdate in an acid medium, it broke down with the formation of inorganic phosphorus, which was estimated as described above. ATP (adenosinetriphosphate) was isolated as the barium salt from a separate portion of the trichloracetic filtrate, and determined by the amount of inorganic phosphate split off following 7-minute hydrolysis in 1N HCl on a boiling water bath. Inorganic phosphorus was determined simultaneously, but without preliminary hydrolysis in the other portion of the same solution.

Glycogen was isolated from the tissue, hydrolyzed and estimated as glucose by the iodometric method. In total, 50 experiments were performed: 27 with stimulation of the nerves, and 23 controls.

RESULTS

The whole dynamics of biochemical changes associated with a positive inotropic effect is represented graphically in Fig. 1. The diagram is based on the arithmetic mean of data expressed as percentage of control.

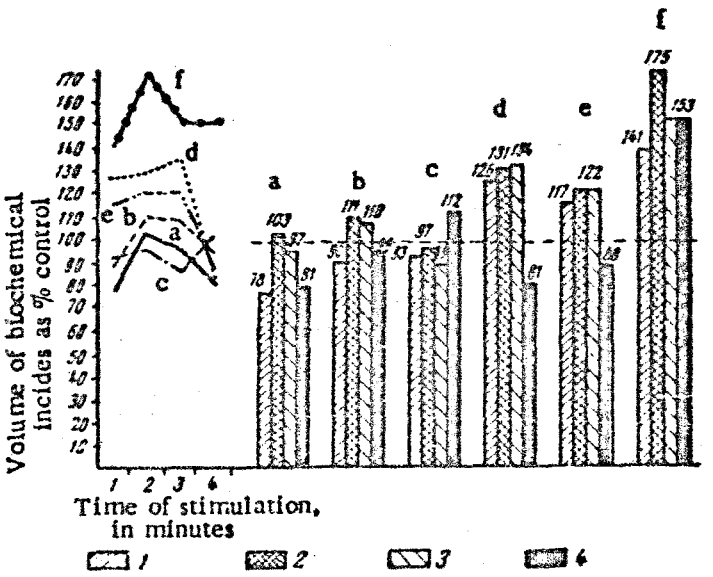

Fig. 1. Changes in biochemical indices of the myocardium with a positive inotropic effect. a) Tissue respiration; b) inorganic phosphorus content; c) phosphocreatine content; d) ATP content; e) phosphocreatine + ATP; f) glycogen content; 1) one-minute stimulation; 2) two-minute stimulation; 3) three-minute stimulation; 4) four-minute stimulation. Broken horizontal line – control (100%).

In the control experiments, biochemical analysis of the heart muscle was carried out without preliminary stimulation of the nerves. At first, an attempt was made to take the control sample and the sample following stimulation from the same heart. However, this had to be abandoned since trauma sustained by the heart in the process of obtaining the control sample resulted in severe changes in biochemical indices, and it was difficult to distinguish such changes from those occurring under the influence of dynamic nerves.

As can be seen from Fig. 1, stimulation of the reinforcing nerve led to changes in all the indices being considered, their nature depending on the duration of nerve stimulation. Thus, tissue respiration, depressed during the first minute of stimulation, reached and maintained the control level during the second and third minutes of stimulation, and again decreased during the fourth minute. Dynamics of the changes in inorganic phosphorus

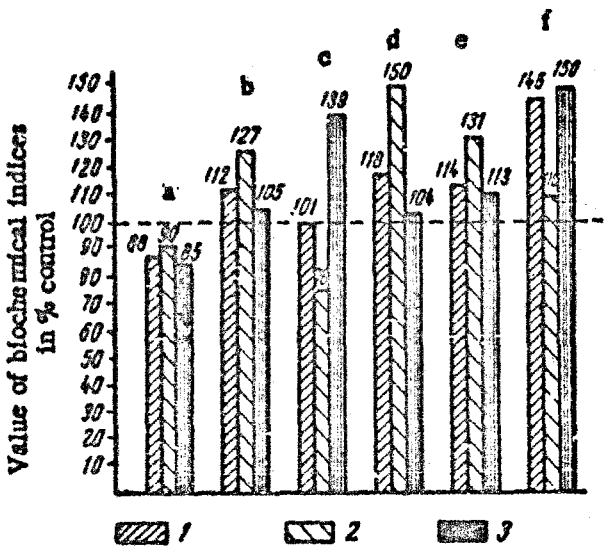

Fig. 2. Changes in biochemical indices of the myocardium with a negative inotropic effect. Legend as that in Fig. 1.

were analogous to those of respiration. Phosphocreatine content remained almost unchanged in the first 3 minutes, and only exceeded the control level to some extent during the fourth minute of stimulation of the reinforcing nerve.

The amount of ATP in the first 3 minutes was above the control level, and was significantly lowered only during the fourth minute. The myocardial glycogen content was increased during stimulation of the reinforcing nerve, reaching a maximum during the second minute.

Unlike the other indices, glycogen content did not drop below the control level throughout the period of stimulation (from 1 to 4 minutes).

The above-mentioned biochemical indices were also examined upon stimulation of the parasympathetic dynamic nerve, which produced weakening of cardiac contractions without slowing of the rhythm. Results of these experiments are presented in Fig. 2.

Figure 2 shows that tissue respiration was below the control level at all values of duration of stimulation. The amount of inorganic phosphorus exceeded the control level appreciably during the third minute. Phosphocreatine, unchanged during the first minute, was lowered during the third minute, and was considerably in excess of control upon four-minute stimulation. The amount of ATP, which increased upon 1-3 minute stimulation of the nerve, returned to control level during the fourth minute. Glycogen content remained above control level throughout.

All the indices studied were thus altered both in the presence of a positive and a negative cardiac inotropic effect.

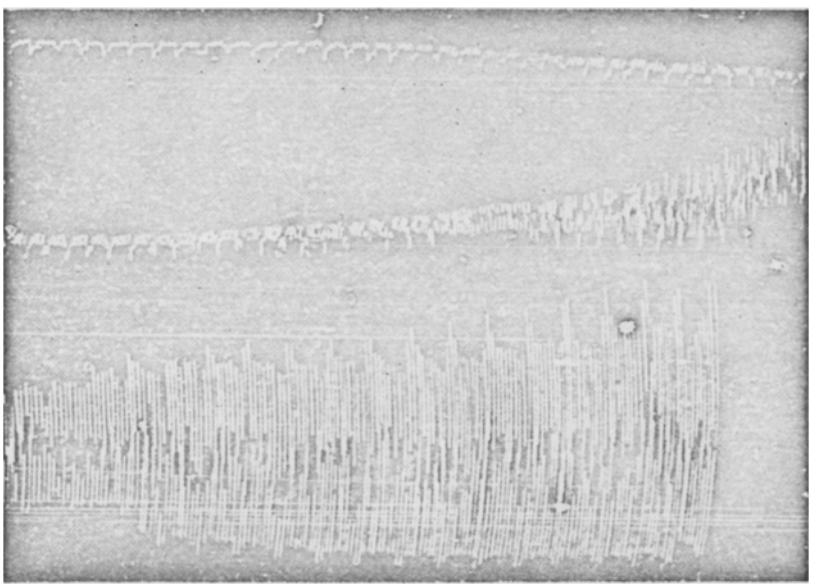

Fig. 3. The effect of reinforcing-nerve stimulation on cardiac activity. Records from above down: cardiac contractions – three tracings, time marker (1 sec); 2 lower tracings are continuation of the top trace.

When the reinforcing nerve is stimulated, the rearrangement of biochemical processes may be directed toward increasing the energy potential of the myocardium. The rapid transition of the heart muscle to increased work leads to respiratory depression, but the total content of ATP and phosphocreatine shows some increase rather than decrease. It may be assumed that more economic use of oxygen and enhancement of the anaerobic phase are involved. The amount of glycogen was altered in the process of stimulation, but remained above the control level without being affected by the duration of stimulation. Increased work following a positive inotropic effect on the heart and increased metabolism appear to result in more intensive breakdown and restoration of glycogen (V. A. Engelhardt's principle); such glycogen supercompensation has been observed in muscular work. All this suggests that the effect of the reinforcing nerve on myocardial metabolism is associated with considerable participation of glycogen. On stimulation lasting 2 and 3 minutes, respiration maintains the control level while the total high-energy bond (~ ph) values and glycogen remain above the control figure. Continuing increased cardiac work under the influence of the reinforcing nerve (on 4-minute stimulation), unaccompanied by increased partial pressure of oxygen, could conceivably lead to fatigue, since respiration decreased, as did the total ~ ph of the ATP.

The character of biochemical changes in the myocardium described was observed in all the experiments involving the reinforcing nerve.

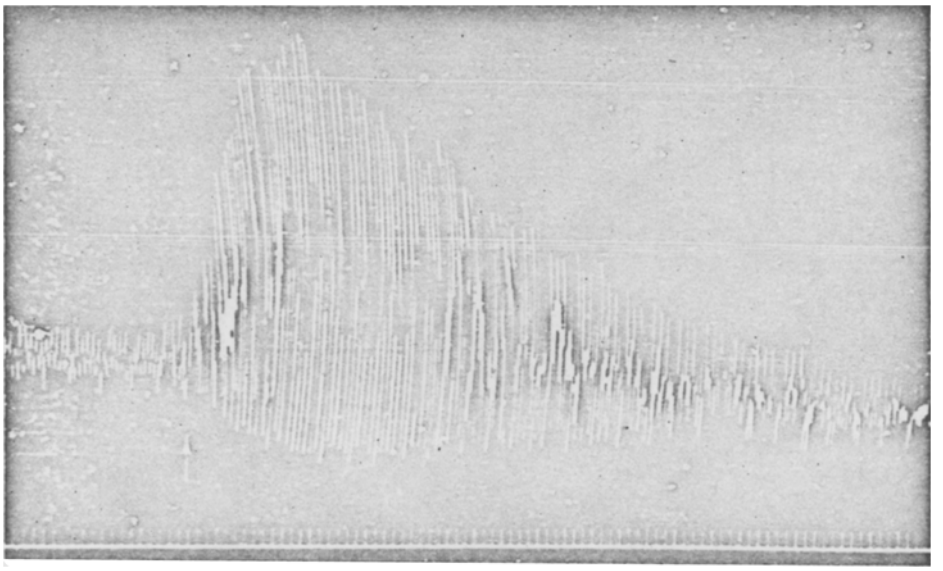

Fig. 4. The effect of reinforcing-nerve stimulation on cardiac activity. Records from above down: cardiac contractions; time marker (1 second).

The degree of changes in individual indices, however, fluctuated in different experiments with a correspondence, in some cases, between the extent to which physiologic effects were pronounced and the intensity of changes in the biochemical indices. In support of this, cardiograms of 2 experiments (Fig. 3 and 4) and corresponding biochemical data are presented.

Figure 3 shows that stimulation of the nerve led to fairly considerable increase in cardiac activity, which was associated with an adequate ~ ph content (117.7%) and glycogen content (296%).

In another experiment, the reinforcing nerve caused transient increase in the amplitude of cardiac contractions, with gradual return to the initial level on continuing stimulation (Fig. 4). Exceedingly low ~ ph (38%) and glycogen (88%) content was found to be associated with this.

The negative inotropic effect of dynamic parasympathetic cardiac nerves is, evidently, accompanied by changes in myocardial trophics in the direction of weakening breakdown processes and enhancing the synthesizing processes. Thus, despite depressed tissue respiration, the total content of ~ ph and glycogen remains above the control level. Thus both sympathetic and parasympathetic cardiac nerves lead to appreciable qualitative rearrangement of myocardial biochemical processes.

It was demonstrated in experiments on dogs, that the stimulation of dynamic heart nerves of sympathetic and parasympathetic origin (which evoke positive and negative inotropic effects) was associated with the change of contents of phosphorus fractions (inorganic phosphorus, adenosinetriphosphate and phosphocreatine) and, likewise, in the change of intensity of tissue respiration. These changes depended on the duration of the stimulation. The content of glycogen in all cases never went below the control level. The mechanism of these phenomena are discussed in their connection with the physiological effects.

LITERATURE CITED

[1] I. P. Pavlov, Collected Works,* vol. 1, p. 451.

[2] M. E. Raiskina, Byull. Eksptl. Biol. i Med. 41, No. 5, 44-47 (1956).

* In Russian.

** Original Russian pagination. See C. B. translation.