

BIOCHEMISTRY AND BIOPHYSICS

INFLUENCE OF THE INTENSIFYING PAVLOV NERVE ON THE ALBUMIN OF THE CARDIAC MUSCLE

M. F. Bondarenko and M. E. Raiskina

From the Department of Pathophysiology (Chairman-Prof. P. D. Gorizontov) Central Institute for Training Physicians (Director V. P. Lebedeva), Moscow

(Received December 15, 1954. Presented by Acting Member of the Acad. Med. Sci. USSR S. E. Severin)

The capacity, discovered by L. P. Pavlov [5], of the cardiac nerve to exert a favorable influence on the strength of the cardiac contractions enabled him to present the hypothesis that this nerve produces its effect by interfering in the intimate trophic processes going on in the heart.

In the work of M. E. Raiskina [6], it was shown by means of radioactive phosphorus that stimulation of the intensifying nerve increases the speed of renewal of inorganic phosphorus, creatine phosphate and adenosinetriphosphate in the cardiac muscle.

In the light of the findings contained in the literature [4, 8] on the influence of adenosinetriphosphate on the structural properties of the contractile albumin of the muscle actomyosin, it appeared to us to be of interest to clarify whether the changes in the exchange of adenosinetriphosphate and creatine phosphate in the heart are coupled, upon stimulation of the intensifying nerve, with changes in the contractile albumins of the cardiac muscle.

In order to estimate the changes in the individual albumin components of the muscular fiber, the method of electrophoretic investigation is very convenient. This method, based on the different motilities of the albumin fractions in the electric field, makes it possible to identify the basic components in the albumin extract from the muscles.

In many investigations carried out with this method of the skeletal muscle [11, 13], the following basic albumin fractions were recognized in the albumin extract: actomyosin (α -myosin), β -myosin, myogen and myoalbumin.

Separate investigations of the albumins of the cardiac muscle [9, 10] showed that the basic albumin fractions of the heart were analogous to the fractions of the skeletal muscle, and only differ from them quantitatively.

We have not found in the literature data on the changes in albumins of the cardiac muscle under nervous influences. Information on the influence of direct electrical stimulation of the skeletal muscle on its albumin composition is therefore of interest.

Dubuisson [12] on an electrophoretic tracing of the muscle frozen in a state of maximum contraction, found an increase in the myogen with a simultaneous sharp drop in α -myosin and complete disappearance of β -myosin. The author also found in this case a manifestation of a new albumin fraction which he called contractin, which, as was later shown, had earlier been described as γ -myosin. These changes apparently reflect exhaustion of the muscle excited with direct electrical stimulation.

In the present work, we studied the state of the albumins of the cardiac muscle with an increase in the strength of its contractions under the influence of Pavlov's intensifying nerve.

EXPERIMENTAL METHODS

The experiments were conducted on dogs. The thorax of the animals under morphine-barbamyl narcosis was dissected and artificial respiration arranged.

In the chest cavity, according to the scheme proposed by I. P. Pavlov, the intensifying nerve of the heart was exposed. The effect of its stimulation was estimated by the changes in arterial pressure, the amplitude of the cardiac contractions, and by electrocardiograms. After tentative stimulation of the intensifying nerve with an induction current from the Duby-Reimon coils, the dog was given fifteen-minute periods of rest. Then on the basis of stimulation of the intensifying nerve, and in the control series of the basis of the normal activity, the apex of the heart was quickly cut away and frozen in liquid nitrogen.

The frozen cardiac muscle was ground into powder from which the albumins were extracted with 0.5 ml potassium iodide solution after one hour on ice. The total amount of albumin was determined refractometrically and according to Kjeldahl. Dialysis was carried out against a phosphate buffer pH 7.4 and with an ion strength of 0.35, for 10-16 hours in a refrigerator.

For the purpose of electrophoresis a 1937 model of the Tiselius-Svenson apparatus was used. The duration of electrophoresis was 10 hours with a voltage gradient 1.53 v/cm. The optically recognized albumin fractions were photographed. The relative content of the fractions was determined planimetrically on enlarged electrophorograms.

The method of electrophoretic investigation of the muscular fiber albumins has been described earlier in detail [1].

EXPERIMENTAL RESULTS

In 8 dogs, cardiac samples were taken during normal activity and in 8 others during stimulation of the intensifying nerve.

The influence of the intensifying nerve on the functional state of the heart has earlier been described in detail [7]. In the majority of experiments, alongside an increase in arterial pressure an increase in the amplitude of cardiac contractions was observed. The typical changes in blood pressure upon stimulation of the intensifying nerve, on the basis of which the cardiac samples were taken, are depicted in Fig. 1.

Figure 2 presents the electrophoregram of the albumins of the cardiac muscle in normal conditions and Fig. 3 with stimulation of the intensifying nerve. Both electrophoregrams include the following albumin fractions: myoalbumin, S-P interval, actomyosin (α -myosin), β -myosin and myogen. However, it is difficult to judge by the appearance of the tracing the quantitative content of the albumin fractions. The results of planimetric determination of the albumin fractions in the cardiac muscle in normal conditions and upon stimulation of the intensifying nerve are presented in Tables 1 and 2.

In the cardiac muscle of the dogs, in exactly the same manner as had been noted in rabbits, the bulk of the albumins is formed of the myosin complex, which in the majority of cases can be broken down into actomyosin (α -myosin, and β -myosin). Its content in the cardiac muscle was on average, 58.3%.

On the electrophoregram of the albumins of the cardiac muscle taken upon stimulation of the intensifying nerve, no new fractions, as compared with the fractions detected in normal conditions, were identified. Nor did the electrophoretic motility of the fractions change.

The basic change in the albumin fractions of the cardiac muscle with stimulation of the intensifying nerve consisted, as is clear from the tables, in an increase of the content of albumin of the basic contractile complex, including actomyosin and α -myosin. The relative content of the myogen decreased. In view of the fact, that the total content of the albumin in normal conditions and with stimulation was uniform, the decrease in amount of myogen with stimulation of the intensifying nerve may be considered as absolute.

The increase discovered by us in the amount of the contractile albumins in the heart with stimulation of the intensifying nerve may take place through transformation of some albumins into others — of the albumins of the muscular plasma into contractile albumin of the myofibril. This point of view is in line with the conception of G. E. Vladimirov [3], who postulated that the amount of myosin in the muscles according to the degree of development of the organism may grow both through its re-formation and through formation of myogen and myoalbumin from easily soluble albumins.



Fig. 1. Change in arterial pressure upon stimulation of the intensifying nerve. Significance of tracings (from top to bottom): arterial pressure (torsion manometer), arterial pressure (mercury manometer), zero line, indication of stimulation, indication of time. Arrow indicates moment of "taking" of the heart.



Fig. 2. Electrophoregram of the ascending boundary of the albumin fractions of the cardiac muscle in normal conditions (see Table 1, Experiment of March 24, 1953). 1) Myoalbumin; 2) S-P interval; 3) Myosin; 4) Myogen.

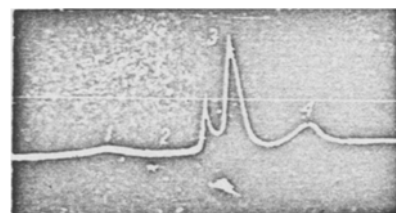


Fig. 3. Electrophoregram of the ascending boundary of the albumin fractions of the cardiac muscle upon stimulation of the intensifying nerve (see Table 2, Experiment of April 2, 1953). Significance of tracings as in Fig. 2.

TABLE 1

Albumin Fraction Content in Cardiac Muscle of Normal Dogs (in %)

Date of Experiment	Sex of dog	Weight of dog (in kg)	Albumin fractions					Myogen
			Myoalbumin	S-P interval	Myosin			
					α	β	Total	
31/V 1952 r.	Female	12.0	11.0	3.2	—	—	50.2	35.6
20/III 1953	„	11.0	9.1	3.3	13.2	51.8	65.0	22.6
24/III 1953	Male	12.0	9.2	5.7	10.7	48.4	59.1	26.0
10/IV 1953	Female	12.0	9.3	3.1	12.7	47.3	60.0	27.6
14/VI 1953	„	12.2	11.1	—	—	—	63.5	25.4
8/VII 1953	„	9.5	5.1	6.2	—	—	62.0	26.7
13/VII 1953	Male	13.5	8.2	1.4	39.2	16.8	56.0	34.4
15/VII 1953	„	13.5	7.5	4.3	—	—	50.8	37.4
Average			8.8	3.8			58.3	29.5

TABLE 2

Albumin Fraction Content in Cardiac Muscles of Dogs upon Stimulation of the Intensifying Nerve (in %)

Date of Experiment	Sex of Dog	Weight of dog (in kg)	Albumin fractions					Myosin
			Myoalbumin	S-P interval				
					α	β	Total	
28/III 1953 r.	Female	11.3	6.6	3.7	33.0	41.5	74.5	15.2
1/IV 1953 ,	"	14.6	9.5	2.4	41.3	23.8	65.1	23.0
2/IV 1953 ,	"	9.0	7.5	1.8	15.2	56.6	71.8	18.9
27/IV 1953 ,	Male	6.1	8.9	3.5	34.9	27.6	62.5	25.1
15/VI 1953 ,	"	13.0	10.1	—	—	—	68.3	21.6
19/VI 1953 ,	"	12.6	9.4	5.8	—	—	62.7	22.1
6/VII 1953 ,	"	11.3	10.3	—	—	—	68.5	21.2
10/VII 1953 ,	"	10.2	9.1	—	—	—	70.6	20.3
Average			8.9	3.4	—	—	68.0	20.9

Our findings, however, may be interpreted differently. It was shown that in different stages of the contractile act, the strength of the link between the muscular fibers and the structural elements of the muscular fiber changed [12]. It may be assumed that stimulation of the intensifying nerve produces a fall in the firmness of the links of the contractile albumins and increase in firmness of the links of the easily soluble albumins. Thanks to this, during extraction in these conditions there is an increase in the output of the albumins of the myosin complex and a decrease in the output of the myogen fraction.

Consequently, the increase we found in the content of myosin may be a reflection of increased lability of its links with the structural elements of the muscular fiber.

There are grounds for believing that in the change of the firmness of the links indicated, an active role is played by adenosinetriphosphate, and that with stimulation of the intensifying nerve, together with an increase in the content of myosin, the metabolism of adenosinetriphosphate is speeded up and probably not accidentally.

Of interest is the quest as to what the increase in myosin content is associated with in the heart — with exhaustion of the cardiac muscle or, on the contrary, with improvement of its functional state.

On comparing the functional effect noted upon stimulation of the intensifying nerve with the corresponding electrophoregram (see Figures 1 and 3), we recognized that the increase in the myosin complex content in the cardiac muscle was combined with a very favorable functional effect (increase in arterial pressure, increased amplitude of cardiac contractions). A reverse manifestation — decrease in the myosin fraction — was found with acute anoxia of the cardiac muscle [2], i. e., with deterioration of the functional state of the heart.

Thus, the changes occurring under the influence of the intensifying nerve in the albumin structure of the cardiac muscle are further proof of the capacity of this nerve to influence favorably the trophic processes in the heart.

LITERATURE CITED

- [1] Bondarenko, M. F., Byull. Eksptl. Biol. i Med. Vol. 38, No. 10, pp. 70-73 (1954).
- [2] Bondarenko, M. F., Byull. Eksptl. Biol. i Med. Vol. 38, No. 11, pp. 43-46 (1954).
- [3] Vladimirov, G. E., Chemistry of Muscular Albumins* (Leningrad, 1940), pp. 49-61.
- [4] Ivanov, I. I., and Ivanova, T. I., Doklady Akad. Nauk. SSSR. Vol. 66, No. 5, pp. 895-898. (1949).
- [5] Pavlov, I. P., Complete Collected Works* (Moscow, 1951), Vol. 1, pp. 577-582.
- [6] Raikina, M. E., Byull. Eksptl. Biol. i Med. Vol. 41, No. 5, pp. 44-47 (1956). **

* In Russian

** See C. B. Translation.

- [7] Raiskina, M. E., Byull. Eksptl. Biol. i Med. Vol. 37, No. 6, pp. 16-24 (1954).
- [8] Engelgardt, V. A., and Lyubimova, M. N., Biokhimiya Vol. 7, No. 5-6, pp. 205-231(1942).
- [9] Blasius, R., Nowy, H., and Seitz, W., Klin. Wochschr. 31., No. 19-20, p. 478 (1953).
- [10] Cruck, S., Biochim. et Biophys. Acta. Vol. 10, No. 4, pp. 630-631 (1953).
- [11] Dubuisson, M., Biol. Revs. Vol. 25, No. 1, pp. 46-71 (1950).
- [12] Dubuisson, M., Experimentia, Vol 4, p 437(1948).
- [13] Jacob, J., Biochem. J. Vol. 141, p. 808 (1946).