EFFECT OF DIVISION OF THE VAGUS NERVES ON THE PROTEIN METABOLISM OF THE MYOCARDIUM IN DOGS

G. V. Chernysheva

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Severe degenerative changes in the heart are sometimes associated with disturbances of the activity of the nervous system, involving profound disturbances of the metabolic processes in the myocardium. These are intimately connected with morphological and functional changes in the myocardium and are regulated by complex neurohumoral mechanisms, in which a leading role is played by the parasympathetic and sympathetic divisions of the automatic nervous system.

One way of demonstrating the importance of these mechanisms is by excluding the parasympathetic innervation of the heart. Nevertheless, very few investigations have been made along these lines. After vagotomy, for instance, E. S. Troshanova [10] demonstrated a decrease in the glycogen content and in the succinate dehydrogenase activity in the heart muscle of rabbits. V. A. Govyrin confirmed these findings in experiments on cats and found that the ATPase activity of the heart tissue was lowered. In these circumstances there was no change in the content of adenosinepolyphosphate and creatinephosphate in the myocardium [2]. Histological investigations also revealed degenerative changes in the heart muscle after vagotomy [11]. However, no information could be found in the literature concerning the effect of vagotomy on the state of the contractile proteins of the myocardium responsible for performing its basic function.

In the present investigation the fractional composition of the myocardial proteins, the content of the principal contractile proteins, and their ATPase activity were studied after bilateral division of the vagus nerves, at the same time or successively.

Taking into consideration data in the literature concerning differences in the metabolic processes in the atria and ventricles [9], various parts of the myocardium were investigated.

EXPERIMENTAL METHOD

Experiments were conducted on dogs weighing 10-12 kg, including 18 control animals. In 12 dogs both vagus nerves were divided simultaneously in the neck. The animals were sacrificed on the 4th day. In 7 dogs vagotomy was performed in two stages: the left nerve was divided first, and the right vagus nerve 2 weeks later. One week after this the animals were sacrificed. In all the series of experiments the heart was extracted under ether anesthesia, with artificial respiration, washed with ice-cold physiological saline, and placed on ice. All subsequent procedures on the tissue were carried out in a cold room (±2°).

For fractionation of the myocardial proteins and isolation of myosin, I. I. Ivanov's method was used [4]. The ATPase activity of the actomyosin and myosin was determined by P. M. Zubenko's method [3], and the phosphorus was then determined by Lowry's method [16]. During investigation of the ATPase activity of the myosin no magnesium salts were added to the incubation mixture. The ATPase activity was calculated in terms of protein nitrogen.

To determine the state of the heart tissue after vagotomy, the cholinesterase activity was measured and the acetylcholine determined by Hestrin's method [14]. The cholinesterase activity of the tissue was expressed as the amount of acetylcholine broken down by 1 g tissue per hour of incubation. The experimental results were analyzed statistically by Student's method [8].

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Changes in Fractional Composition and Enzymic Activity of the Myocardium of Dogs after Division of the Vagus Nerves

Protein fractions	Statistical criterion	Normal conditions			After division of vagus nerves					
					simultaneous division			successive division		
		left ventricle	right ventricle	atria	left ventricle	right ventricle	atria	left ventricle	right ventricle	atria
Sacroplasmic proteins (in mg nitrogen/g moist tissue)	$M \pm m$ P	8,7±0,35	8,5±0,4	7,7±0,37 <0,02	8,9±0,4	8,0±0,4 <0,01	6,5±0,3	8,4±0,5	8,2±0,32	5,9±0,4 0,001
Myofibrillary proteins (in mg nitrogen/g moist tissue)	$M \pm m$ P	9,0±0,55	8,8±0,42	6,5±0,3 0,01	9,3±0,6	9,1±0,4	6,8±0,4	9,1±0,5	8,3±0,38	6,9±0,29
Actomyosin (in mg nitrogen/g moist tissue)	$M \pm m$ P	6,6±0,22	6,5±0,3	4,21±0,31 <0,01	5,2±0,29 0,01	6,6±0,33	4,4±0,25	6,4±0,3	6,1±0,4	4,2±0,16
Myosin (in mg nitrogen/g moist tissue)	$M \pm m$ P	1,72±0,08	1,57±0,1 0,02	0,86±0,02 <0,001	1,38±0,5 0,01	1,61±0,07	0,97±0,031	1,57±0,04 0,02	1,67±0,06	1,0±0,02
Fraction "T" (in mg nitrogen/g moist tissue)	$M \pm m$ P	2,36±0,7	2,40±0,065	2,31±0,09	3,83±0,088 <0,01	2,3±0,1	2,2±0,13	2,31±0,15	2,0±0,18	2,4±0,06
Solid residue (in %)	$M \pm m$ P	22,0±0,8	22,8±0,5	21,2±0,5 <0,01	22,3±0,5	23,0±0,65	20,9±0,42 0,01	2,31±0,4	22,9±0,55	21,3±0,3
ATPase activity of phosphorus (in mg P/mg nitrogen): Actomyosin	$M \pm m$ P	0,44±0,01	0,37±0,035	1,0±0,04 <0,001	0,95±0,08 <0,001	0,68±0,065 0,001	1,44±0,07 <0,01	0,76±0,09 <0,001	0,70±0,1 0,01	1,0±0,02
Myosin	$M \pm m$ P	0,10±0,01	0,14±0,03	0,25±0,1 <0,001	0,15±0,025 0,01	0,12±0,04	0,29±0,06	0,12±0,02	0,12±0,02	0,28±0,05
Cholinesterase activity (in mg acetylcholine/g tissue/60 min)	$M \pm m$ P	11,1±1,35	14,08±0,57	28,97±1,2 0,001	5,66±0,23 <0,001	6,51±0,55 <0,001	15,66±0,7 <0,001	7,7±0,5 0,001	8,15±0,33 <0,01	14,8±0,91 0,001

EXPERIMENTAL RESULTS

Investigation of the tissue of different portions of the heart of the healthy dogs revealed no difference in the total content of sarcoplasmic and myofibrillary proteins in the tissues of the right and left ventricles (see table). Likewise there was no significant difference in the ATPase activity of the actomyosin of these portions of the heart. However, the myosin content in the left ventricle was higher than in the right. The atrial tissue differed considerably from the ventricular, for it contained less sacroplasmic and, in particular, less contractile proteins, constituting the main mass of the myofibrillary proteins. These results are in agreement with those reported by other investigators [13, 15, 17].

The ATPase activity of the actomyosin and the myosin isolated from the atrial tissue, calculated in relation to the nitrogen of these proteins, was higher than in the ventricular tissue (see table). A same pattern was observed by A. V. Palladin [6]. The cholinesterase activity also was higher in the atria, presumably because of the distinctive pattern of the innervation of the atria (see table). This suggestion is supported by the results of histochemical investigations conducted by E. M. Krokhina and E. K. Plechkova [5].

Hence the differences in the content of contractile proteins and in the enzymic activity between the ventricles and atria were evidently due to the different functions performed by these divisions of the heart.

Simultaneous and successive division of the two vagus nerves had no effect on the content of sarcoplasmic proteins in the right and left ventricles and slightly lowered their content in the atria.

After the simultaneous division of both vagus nerves the content of the principal contractile proteins – actomyosin and myosin – remained unchanged in the right ventricle and the atria, and fell by 21% below the normal level in the left ventricle. In these circumstances the total content of the myofibrillary proteins was unchanged as a result of an increase in the content of the fraction of the myofibrillary proteins soluble in media with low ionic strength, which I. I. Ivanov calls fraction "T" [4]. After the successive division of the vagus nerves these changes were not observed.

The ATPase activity of the actomyosin of all divisions of the heart increased after one-stage vagotomy. The ATPase activity of the myosin rose only in the left ventricle. After successive vagotomy the increase in the ATPase activity was less pronounced. The cholinesterase activity of the ventricular and atrial tissues fell by more than half after successive vagotomy.

The results of these experiments thus showed that simultaneous division of the vagus nerves had a more marked effect on the metabolic processes than the successive operation. Evidently in the case of successive division of the vagus nerves, compensatory and adaptive mechanisms are brought into play.

The one-stage exclusion of the parasympathetic innervation of the heart was reflected mainly in the contractile proteins of the left ventricle, and in these circumstances the increase in the ATPase activity of the actomyosin and myosin likewise were more marked in the left ventricle. In the normally working heart, the work performed by the left ventricle is 2.5-3 times greater than that performed by the right ventricle [1].

Considering that the cessation of vagus influences intensifies the sympathetic effects on the myocardium, the secreted catecholamines give rise to a change in the calcium concentration [12] and accelerate the ATP metabolism [7]. These findings are in agreement with the observed increase in the ATPase activity of the actomyosin and myosin and they are evidence of an increase in the utilization of energy necessary for the contractile activity of the heart. The decrease in the content of actomyosin and myosin in the left ventricle after vagotomy may probably be regarded as the result of intensified work of the heart, during which the synthesis of contractile proteins lags behind their breakdown. The results obtained thus demonstrate the participation of central parasympathetic influences in the regulation of the metabolic processes of the myocardium.

SUMMARY

The object of investigation was the influence of bilateral division of the vagus nerves in the neck on the fractional composition of the myocardial proteins, the content of the basal contractile proteins and the enzymatic activity. The cardiac ventricles and auricles were analyzed. The experiments were carried out on 37 adult dogs. The investigations showed that simultaneous division of the left and right vagus nerves was followed by a decrease in the content of actomyosin and myosin in the left cardiac ventricle.

In successive division of the vagus nerve no such changes were noted. Vagotomy caused an increase in the ATPase activity of actomyosin and myosin in all parts of the heart.

The activity of cholinesterase was markedly reduced. Changes in the enzymatic activity were more pronounced after a simultaneous division of both vagus nerves.

The decrease in the content of contractile proteins and the increase in their ATP-ase activity in the left ventricle were apparently due to an increased functional load on the left ventricle caused by vagotomy.

LITERATURE CITED

1. K. M. Bykov, G. E. Vladimirov, V. E. Delov et al., Textbook of Physiology [in Russian], Moscow (1954), p. 142.
2. V. A. Govyrin, In: The Evolution of Function [in Russian], Moscow–Leningrad (1964), p. 241.
3. P. M. Zubenko, A. D. Reva, and E. G. Plakhotishina, Biokhimiya, No. 1 (1950), p. 79.
4. I. I. Ivanov and V. A. Yur'ev, The Biochemistry and Pathobiochemistry of the Muscles [in Russian], Leningrad (1961).
5. E. M. Krokhina and E. K. Plechkova, In: The Physiology and Pathology of the Heart [in Russian], Moscow (1963), p. 263.
6. A. V. Palladin, É. B. Skvirskaya et al., Ukr. Biokhim. Zh., No. 1 (1947), p. 86.
7. M. E. Raiskina, Biochemistry of the Nervous Regulation of the Heart [in Russian], Moscow (1962), p. 241.
8. P. F. Rokitskii, Fundamentals of Variance Statistics [in Russian], Minsk (1961).
9. V. M. Rubel', Vopr. Med. Khimii, No. 3 (1964), p. 238.
10. E. S. Troshanova, Ukr. Biokhim. Zh., No. 3 (1952), p. 312.
11. I. A. Chernova, Arkh. Anat., Gistol. Émbriol., No. 7 (1960), p. 13.
12. V. A. Shidlovskii and I. A. Keder-Stepanova, Byull. Éksp. Biol., Vol. 30 (1950), p. 54.
13. E. Helander, Cardiologia, Vol. 41, Basel (1962), p. 94.
14. S. Hestrin, J. Biol. Chem., Vol. 180 (1949), p. 249.
15. J. Kovats, Nature, Vol. 163 (1949), p. 606.
16. O. H. Lowry et al., J. Biol. Chem., Vol. 162 (1946), p. 421.
17. H. Nowy, Z. Ges. Exp. Med., Vol. 131 (1959), p. 478.

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