EFFECT OF EXTRACARDIAC NERVES ON THE INTENSITY OF GLYCOGEN METABOLISM IN HEART MUSCLE

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After division of the left vagus nerve in the neck in rats the glycogen content in the heart muscle decreased and the intensity of its metabolism (based on incorporation of glucose-1-C^{14}) increased. Sympathetic denervation of the heart led to an increase in the glycogen content and a decrease in the intensity of its metabolism in the heart muscle.

KEY WORDS: rat heart; glycogen; sympathetic denervation.

The role of the extracardiac nerves in nutrition of the heart muscle is being increasingly widely studied at the present time [3-5]. The regulatory effect of the nervous system on the cell takes place through a system of intracellular regulation [2]. The question arises: Through which components of intracellular regulation does the trophic effect of the nervous system on the heart muscle manifest itself? Mediators and hormones exert their action primarily through the adenylate cyclase system [7, 9], with consequent changes in the intensity of glycogenolysis in the cell.

The object of the present investigation was to study the intensity of incorporation of glucose-1-C^{14} into the glycogen of the myocardium when extracardiac nervous influences on the heart are disturbed.

EXPERIMENTAL METHOD

Experiments were carried out on 85 rats. Sympathetic denervation of the heart was carried out in the animals by surgical removal of the cervical and upper thoracic sympathetic ganglia [1]. In the animals of another group the left vagus nerve was divided in the neck. The rats were used in the experiments 3 weeks after the operation. Glucose-1-C^{14} was injected intraperitoneally in a dose of 10 μCi/100 g body weight. The animals were decapitated 30, 60, and 120 min after injection of the label. The glycogen concentration in the myocardium of the left ventricle was determined with anthrone reagent by the method of Seifter et al. [11]. The radioactivity of glycogen was determined on the B-3 apparatus by means of an SBT-13 counter and expressed in counts/mg glycogen (specific activity). The radioactivity of glycogen also was calculated per gram of tissue.

TABLE 1. Changes in Glycogen Concentration in Heart Muscle during Disturbance of Nervous Regulation of the Heart (M ± m)

Conditions	Glycogen concentration (in mg %)
Control	415±11
Vagotomy	320±10 $P<0,001$
Desympathization	612±16 $P<0,001$

EXPERIMENTAL RESULTS AND DISCUSSION

The results of the investigation of glycogen in the heart muscle following disturbance of nervous influences on the heart are given in Table 1.

As Table 1 shows, after left-sided vagotomy the glycogen concentration in the heart muscle fell, but after partial sympathetic denervation of the heart it rose. These results, obtained in long-term experiments, indicate that disturbance of the relationship between the sympathetic and parasympathetic innervations of the heart leads to changes in glycogen metabolism in the heart muscle.

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TABLE 2. Intensity of Incorporation of Glucose-1-C^{14} into Glycogen of Heart Muscle during Disturbance of Extracardiac Nervous Influences on the Heart (M ± m)

Conditions	Radioactivity of glycogen at various times after injection of glucose-1-C^{14}					
	in counts/min/mg glycogen			in counts/min per glycogen in 1 g tissue		
	30 min	60 min	120 min	30 min	60 min	120 min
Control	220±16	370±11	172±23	892±31	1603±18	714±75
Vagotomy	442±48*	692±38*	192±21	1274±139*	2146±193*	567±52
Desympathization	105±13*	245±20*	97±9*	621±60*	1241±83*	570±13

* $P < 0.05$.

The results of investigation of the intensity of metabolism of the glycogen depots in the heart muscle during a disturbance of extracardiac nervous influences on the heart are given in Table 2.

As Table 2 shows, after left-sided vagotomy the incorporation of labeled glucose into the glycogen of the heart rose sharply. For instance, 30 and 60 min after injection of radioactive glucose the specific activity of glycogen in heart muscle rose strongly compared with the control, but by 2 h after injection it was falling. Consequently, in the vagotomized animals the incorporation of labeled glucose into cardiac glycogen was increased but its removal from the heart was accelerated considerably, i.e., renewal of the glycogen depots of the myocardium was intensified. After partial sympathetic denervation of the heart the specific activity of glycogen in the myocardium was lowered at all times after injection of labeled glucose.

The radioactivity of glycogen calculated per gram myocardial tissue after division of the left vagus nerve was increased 30 and 60 min after injection of the isotope, but reduced after sympathectomy. It can accordingly be concluded that the intensity of glycogenolysis in the heart muscle is changed when extracardiac nervous influences on the heart are disturbed.

The results thus show that in disturbances of the trophic influence of the extracardiac nerves on the heart the concentration of glycogen and the intensity of its metabolism in the heart muscle are altered. After left-sided vagotomy the rate of renewal of the myocardial glycogen depots is increased, but after sympathetic denervation, on the other hand, it is reduced.

In disturbances of the trophic influence of the vagus nerve on the heart the acetylcholine (AC) concentration in the myocardium is lowered [8, 15]. In the light of these facts, the increase in incorporation of glucose-1-C^{14} into myocardial glycogen after left-sided vagotomy found in the present experiments may be due to an increase in the predominance of tone of the sympathetic over the parasympathetic nervous system. Noradrenalin (NA) sharply increases adenylate cyclase activity and the formation of cyclic 3',5'-AMP in heart muscle [12, 13]. AC, on the other hand, inhibits adenylate cyclase and also increases the activity of cyclic 3',5'-phosphodiesterase, an enzyme hydrolyzing 3',5'-AMP to 5'-AMP [10, 14]. Consequently, after vagotomy increased formation of 3',5'-AMP in the heart muscle can take place not only through a change in the NA concentration, but also through a decrease in the AC concentration. An increase in the 3',5'-AMP activates the kinase of phosphorylase b. Activated kinase catalyzes the conversion of inactive phosphorylase b into its active form – phosphorylase *a*, which in turn catalyzes glycogen breakdown [6, 13].

After sympathetic denervation of the heart the NA content in heart muscle falls sharply [1]. An important role in the mechanism of the increased glycogen concentration and the decrease in the intensity of its metabolism in the heart muscle after desympathization may therefore be played by the decrease in adenylate cyclase activity and in the formation of 3',5'-AMP. There are thus grounds for considering that the change in intensity of glycogenolysis in the heart muscle following blocking of sympathetic or parasympathetic influences on the heart is connected with a decrease or increase in 3',5'-AMP formation as a result of a disturbance of the content of mediators and a change in the activity of enzymes of the adenylate cyclase system.

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