Remarkable synchronization in fluctuations in NADH concentration in the glycolytic oscillator and spontaneous changes in tension of SM of the portal vein has recently [8] been demonstrated. When the membrane voltage of intestinal SM, generating slow waves, was clamped spontaneous inward currents were recorded [5]; in our opinion, these inward currents are connected with the activity of a cytoplasmic oscillator which was not identified by the authors cited.

The glycolytic oscillator in vascular smooth-muscle cells thus plays the role of trigger mechanism for the generation of rhythmic twitch contractions. It can be postulated that glycolysis supplies the mechanisms of Na^+-and K^+-transport and of pacemaker potential formation with energy, and energy formation in the Krebs' cycle is closely connected with processes determining the magnitude of the tension developed by SM.

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EFFECT OF DESTRUCTION OF THE PARAVENTRICULAR AND MEDIOBASAL HYPOTHALAMUS ON PAIN SHOCK IN RABBITS

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KEY WORDS: hypothalamus; shock; electrical stimulation

It was shown recently that injection of antagonists of opioid peptides improves the state of animals with endotoxic [7], hypovolemic [4], and electrically induced pain shock [2]. This suggests that opioid peptides participate in the pathogenesis of shock states. The paraventricular nuclei of the hypothalamus are known to contain relatively high concentrations of enkephalins [8] and this region is known to take part in the regulation of functions of the pituitary [1], which produces opioid peptides [8]. The only concentrations of β-endorphinergic cells in the brain have been identified in the mediobasal hypothalamus [3].

The object of the investigation described below was accordingly to study the effect of destruction of the paraventricular and mediobasal hypothalamus on the course of pain shock in rabbits.

EXPERIMENTAL METHOD

Experiments were carried out on 15 noninbred rabbits of both sexes weighing 2.2-2.8 kg. The arterial pressure (BP) of the animals (by a direct method), the heart rate (HR) and respiration rate (RR) were recorded. A state of shock was induced by electrical stimulation with a sinusoidal current through two electrodes, one located actually on the sciatic nerve, the

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TABLE 1. Changes in BP, HR, and RR of Rabbits after Induction of Shock and Disruption of Various Hypothalamic Zones

Experimental conditions	Animals undergoing mock operation			Animals with destruction of mediobasal hypothalamus			Animals with destruction of paraventricular hypothalamus		
	BP, mm Hg	HR, beats/min	RR, cycles/min	BP, mm Hg	HR, beats/min	RR, cycles/min	BP, mm Hg	HR, beats/min	RR, cycles/min
Background	81,4±8,9 / 71,0±11,5	264,6±23,7	80,8±36,1	83,8±10,8 / 69,5±7,7	276,8±25,5	66,5±18,5	80,7±15,6 / 67,8±12,6	257,7±33,2	87,0±34,4
After stimulation	48,2±10,2 / 43,6±9,9	286,4±28,4	99,0±11,7	42,5±11,4 / 35,5±12,1	255,3±41,1	86,0±14,9	51,8±13,7 / 44,7±11,1	319,0±28,4	107,3±19,2
Before destruction (65th minute)	38,6±10,2 / 33,4±9,2	270,0±41,2	82,6±9,1	38,5±6,8 / 30,8±4,0	258,0±29,7	80,3±18,9	50,2±13,9 / 43,3±13,5	311,7±16,1	102,7±29,0
Immediately after destruction	—	—	—	39,3±4,7 / 32,7±6,7	193,5±58,4	78,0±14,7	52,5±19,3 / 45,2±17,7	296,3±27,7*	104,7±12,3*
10 min after destruction	30,8±10,7 / 25,0±11,1	219,5±71,6	60,5±27,8	21,3±6,8 / 12,7±3,1	228,0±60,0	72,0±10,0	55,0±18,4 / 47,4±17,0	303,2±19,0	106,4±23,0
20 min after destruction	—	—	—	—	—	—	52,0±21,1 / 43,0±21,8	305,2±16,9	107,6±21,3

*P < 0.05 compared with animals undergoing mock operation and animals with destruction of mediobasal hypothalamus.

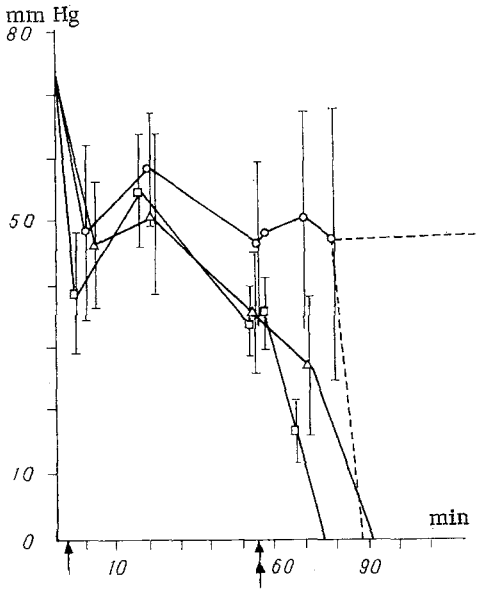

Fig. 1. Changes in blood pressure of rabbits after induction of shock (arrow) and after destruction (double arrow) of paraventricular (circles) and mediobasal (squares) hypothalamus, and in animals undergoing mock operation (triangles).

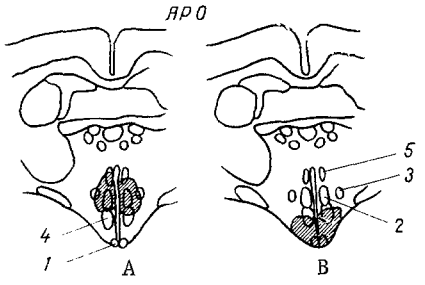

Fig. 2. Superposition of regions of hypothalamic destruction whose injury led to improvement of autonomic parameters (A) or did not affect them (B) in shock on corresponding plan of atlas [9]. 1) Arcuate nucleus, 2) dorsomedial nucleus, 3) fornix, 4) ventromedial nucleus, 5) paraventricular nucleus.

other in the region of the ipsilateral hip joint. Electrical stimulation with variable frequency and voltage (from 10 Hz to 10 kHz and from 1 to 120 V, respectively) was applied continuously until BP, after an initial rise, fell to its original values. The hypothalamic structures were identified from stereotaxic coordinates [9] and destroyed by an anodal current of 1.2-2.0 mA applied for 40 sec. After the end of the experiments, the brain was removed, fixed in formalin, and examined histologically to determine the location and volume of the lesion.

For statistical analysis of the data, Student's t test for independent samples and factor dispersion analysis were used.

EXPERIMENTAL RESULTS

Data on the time course of changes in the various parameters studied after application of the shock-inducing factors are given in Table 1 and Fig. 1. Table 1 shows that immediately

after the end of shock-inducing stimulation BP was reduced by 39.5%, and this was accompanied by a small increase in HR and RR. After a small transient rise of BP 20 min after the end of stimulation, a further decline of BP, HR, and RR was observed. By 50-55 min after induction of shock, the fall of BP amounted to 47.4%. HR and RR remained raised by 7.2 and 11.1%, respectively.

In five animals undergoing a mock operation (without destruction of the hypothalamus), BP 65 min after induction of shock was lowered by 63% (Fig. 1) and HR by 17% and RR by 24.7% (Table 1). All the animals of this group died on average 90.0 ± 52.4 min after induction of shock.

In 10 rabbits, when BP had fallen on average by 47.2%, which was 65 min after the induction of shock (9-165 min), the hypothalamic structures were destroyed.

The lesions in four rabbits, as the histological control showed, were located mainly in the mediobasal hypothalamus (Fig. 2). In these animals, after destruction, a further fall in BP compared with its previous level occurred, to 64.9% compared with the original value. HR and RR were virtually unchanged at this time. BP 10 min after destruction or 75 min after induction of shock had fallen by 81.8% (Table 1), which did not differ significantly from the values of BP in animals of the control group during this period of time after the induction of shock. The mortality in this group of animals was 100% on average 84.1 ± 52.4 min after induction of shock (31-136 min), which also did not differ significantly from the control.

In the remaining six animals, the lesions were located mainly in the paraventricular hypothalamus (Fig. 2). Immediately after destruction, the BP of these animals showed a further slight fall of 5.4% compared with its level before destruction (Table 1). HR fell by 5.4% but RR was virtually unchanged. BP 10 min after destruction was 10.1% higher than in the period immediately before destruction, so that it differed significantly ($P < 0.05$) from the values of BP in animals undergoing the mock operation and in animals with destruction of the mediobasal hypothalamus in this period after induction of shock (Table 1; Fig. 1).

Subsequently, three animals of this group died on average after 80.2 ± 26.5 min (42-98 min). In two of these animals the dorsomedial hypothalamus was destroyed on one side only, but bilateral destruction of the medial zones of the lateral hypothalamic region and adjacent zones was present; in one animal, the lateral zones of the dorsomedial hypothalamus and adjacent structures were destroyed.

The remaining three animals of this group remained under observation for 3 h after destruction, and their BP before euthanasia was 68.7 ± 3.7/60.7 ± 3.7 mm Hg, HR was 272.3 ± 15.6 beats/min, and RR was 84.3 ± 36.7 cycles/min. In all these animals there was bilateral destruction of the paraventricular structures of the hypothalamus: the dorsomedial, paraventricular, and part of the ventromedial nuclei (Fig. 2).

Statistical analysis showed that values of BP, HR, and RR before induction of shock and before destruction of the hypothalamus, and also the duration of shock-inducing stimulation did not differ significantly in any of these animals, evidence of the homogeneity of the samples.

As the experiments showed, destruction of the mediobasal zones of the hypothalamus, containing β-endorphinergic cells, thus does not lead to any significant differences in the course of shock in the animals of this group or in animals undergoing a mock operation. Meanwhile, even partial destruction of the paraventricular zones of the hypothalamus, containing considerable concentrations of enkephalins [8], leads to improvement of the autonomic parameters of the animals, whereas after total destruction they are able to survive despite the development of pain-induced shock.

Since administration of naloxone improves the state of animals with shock [4, 6], it can be tentatively suggested that the improvement in the autonomic parameters observed in the above experiments in animals with shock after destruction of the paraventricular zones of the hypothalamus may be connected with a change in the activity of the endogenous opioid system.

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RELATIONSHIP BETWEEN ANAEROBIC ENERGY FORMATION AND MYOCARDIAL CONTRACTILITY DURING DISTURBANCE OF CORONARY PERFUSION

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Restriction of the blood and oxygen supply to the myocardium is accompanied by a switch from the aerobic to the anaerobic type of metabolism, which is regarded as an important compensatory mechanism maintaining the energy reserves of the myocardium under ischemic conditions. However, despite considerable activation of glycolysis and maintenance of a sufficiently high ATP level, myocardial contractility is reduced even in the earliest stages of ischemia. Many workers ascribe a decisive role in the change in myocardial contractility to a change in pH of the medium and, in particular, to lactate acidosis [14].

The object of this investigation was to study correlation between parameters of anaerobic metabolism in the heart tissues and the most informative parameters of myocardial contractility during a measured restriction of the coronary blood flow.

EXPERIMENTAL METHOD

Experiments were carried out on 50 dogs in which measured partial (by 70 and 90% for 30 min) restriction of the blood flow was carried out under conditions of closed-chest catheterization and autoperfusion of the circumflex branch of the left coronary artery [1]. The animals were anesthetized by intravenous injection of chloralose (80 mg/kg).

Myocardial contractility was studied by catheterization of the chambers of the heart and simultaneous recording of the intraventricular pressure and its rate of change (dp/dt), followed by calculation of various indices of contractility [9, 13]. After recording of the physiological parameters, part of the myocardium of the left ventricle was excised and placed in liquid nitrogen. The zone of ischemia and the myocardium at a distance from this zone were subjected to biochemical analysis, with quantitative determination of glycogen [10] and lactic acid [2], and of activity of glycolysis [8] and of phosphorylase [3]. Experiments with adequate perfusion (10 animals) served as the control. Multiple-factor correlation analysis was carried out with the Minsk-32 computer.

EXPERIMENTAL RESULTS

Reduction of the coronary blood flow by 70% was accompanied by a fall in the glycogen content in the zone of ischemia by one-third. An increase in the severity of the ischemia led to a more marked reduction in glycogen — to 54% of its initial level. Meanwhile, a considerable increase was found in glycolysis activity and in the lactic acid content — by 3-4 times compared with the control. Phosphorylase activity also increased in both groups of experiments,

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