phase of restoration of the background pH level (from the beginning of the pH shift toward the alkaline side until restoration of the pH to its basal or near-basal level).

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REGULATION OF THE CORONARY CIRCULATION DURING ACUTE EXPERIMENTAL STIMULATION OF HYPOTHALAMIC EMOTIOGENIC ZONES

V. L. Golubykh

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The predominant feature of responses associated with emotional stress, and to some extent in those simulated by stimulation of the hypothalamic emotiogenic zones, is elevation of the blood pressure (BP), which is due both to an increase in cardiac output and to systemic vasoconstriction [1-5]. How the coronary vessels react under these conditions is not quite clear. In experiments on anesthetized animals, a response of coronary vasoconstriction has been demonstrated during adrenergic β-receptor block [6, 8, 9] or in experiments under special conditions [7].

The reaction of the coronary vessels is largely dependent on the state of the organism as a whole and, in particular, it is determined by general anesthesia [10, 11, 14].

In experiments on unanesthetized cats, Nogina [3, 4] found an increased response of vasoconstriction accompanied by a rise of BP, depending on the severity of the emotional response to stimulation of the lateral hypothalamic nuclei. By contrast, vasodilatation was observed in dogs in the initial period of the response to excitation, evoked both by natural stimuli and by stimulation of the posterior hypothalamus [12, 13, 15].

Even a cursory glance at the data on centrogenic responses of the coronary vessels reveals their contradictoriness. Regulation of the coronary blood flow is known to be aimed mainly at satisfaction of the metabolic demands of the myocardium.

The object of this investigation was to study the neurogenic component of this response to stimulation of hypothalamic emotiogenic nuclei.

Laboratory of Regulation of the Heart and Coronary Circulation, All-Union Cardiologic Scientific Center, Academy of Medical Sciences of the USSR, Moscow.

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EXPERIMENTAL METHOD

Experiments were carried out on mongrel dogs with an average weight of 12 kg. Morphine was injected in a dose of 0.5 ml of a 2% solution/kg body weight. The animals were anesthetized with urethane and chloralose (300 and 45 mg/kg respectively). Bipolar electrodes, made of "Kavar" alloy (glazed), 150 μ in diameter with an interelectrode distance of 0.6-1 mm, were inserted into the lateral mammillary nucleus of the hypothalamus.

Thoracotomy was performed through an incision in the 5th intercostal space, the initial portion of the circumflex branch of the left coronary artery was mobilized and cannulated, and the blood flow was measured by an ultrasonic doppler flowmeter (designed by Voronezh Polytechnical Institute, Engineer Yu. N. Gusev). BP and the left ventricular pressure were recorded by a Statham electromanometer. The parameters were recorded on a Narco-Biosystem Inc. or Hewlett-Packard system 7758d recorder before stimulation, 5, 15, and 30 sec after the beginning of stimulation, and 5 and 30 sec after its end. The parameters of stimulation were: bipolar – 100 Hz, 2 msec, 1-4 V, duration 45 sec; monopolar – 5-10 V, remaining parameters the same.

Adrenergic β-receptors were blocked by Inderal, injected intravenously (10 mg/kg) and into the coronary circulation (1 mg).

The results of 12 experiments with a total number of 46 stimulations are described below. Some stimulations were carried out at constant pressure, during perfusion from a reservoir connected to the system perfusing the coronary artery. The resistance of the coronary vessels was calculated as the ratio between BP and the coronary blood flow at the end of diastole (in mm Hg/ml/min).

EXPERIMENTAL RESULTS

The initial BP during bipolar stimulation of the lateral mammillary nucleus of the hypothalamus averaged 97.1 ± 12.5 mm Hg, the coronary blood flow was 39.5 ± 14.6 ml/min, the left ventricular pressure was 106.9 ± 12.3 mm Hg, the pulse rate 127.5 ± 16.7 beats/min, and the calculated resistance of the coronary vessels 3.273 ± 0.763 mm Hg/ml/min (six experiments, 22 stimulations).

During bipolar stimulation of the lateral mammillary nucleus of the hypothalamus the resistance of the coronary vessels increased in 53.3% of cases in the first 5 sec of stimulation; the coronary blood flow showed a tendency to fall, and BP, the left ventricular pressure, and the pulse rate all increased (Table 1). In 46.7% of cases coronary dilatation was observed and was accompanied by an increase in the coronary blood flow, BP, and the other parameters. Meanwhile calculation showed a decrease in the resistance of the coronary vessels 15 sec after the beginning of stimulation. Vasodilatation was abolished by injection of Inderal (Table 2). Inderal also increased the rise in the coronary vascular resistance 5 sec after the beginning of stimulation.

Against the background of perfusion from a reservoir under constant pressure, 5 sec after the beginning of stimulation the coronary blood flow was reduced, so that the participation of Bayliss' myogenic mechanism in the response of elevation of the coronary resistance 5 sec after the beginning of stimulation could be ruled out.

The initial BP before monopolar stimulation of the lateral mammillary nucleus of the hypothalamus averaged 95.8 ± 6.9 mm Hg, the coronary blood flow was 49.9 ± 7.8 ml/min, the left ventricular pressure 114.1 ± 11.2 mm Hg, the pulse rate 144.6 ± 14.7 beats/min, and the calculated resistance of the coronary vessels 1.99 ± 0.09 mm Hg/ml/min (six experiments, 24 stimulations).

Monopolar stimulation of the lateral mammillary nucleus of the hypothalamus led to more marked vasoconstriction of the coronary vessels during the whole of the period of stimulation than bipolar stimulation of the same nucleus. In the first 5 sec from the beginning of stimulation coronary vasoconstriction was observed in 85.7% of cases, but it was most marked 30 sec after the beginning of stimulation (Table 1). In the cases of coronary vasodilatation that were observed the fall in their resistance was observed most commonly 15 sec after the beginning of stimulation (in 46.7% of cases).

Injection of Inderal against the background of monopolar stimulation of the lateral mammillary nucleus of the hypothalamus also led to an increase in the coronary vascular resistance, especially 15 and 30 sec after the beginning of stimulation, accompanied by a decrease in the coronary blood flow, a more marked rise in BP, and slowing of the pulse rate. Under these circumstances only vasoconstrictor responses of the coronary vessels were found.

TABLE 1. Effect of Stimulation of Lateral Mammillary Hypothalamic Nucleus on Principal Parameters of Cardio- and Hemodynamics (difference compared with initial values, given in text, in %)

Parameter	Stimulation						After end of stimulation			
	5 sec		15 sec		30 sec		5 sec		30 sec	
	B	M	B	M	B	M	B	M	B	M
Coronary blood flow	—3,4* 30,2±25,5	—1,9* 13,0*	—0,7* 55,9±30,4	1,4* 16,6*	8,2* 47,0±30,1	7,6* 44,3±35,9	—3,7* 36,1±22,7	—11,4±16,8 36,1±22,7	—3,2* 27,1±16,8	7,8* 23,6±9,8
Arterial blood pressure	8,0±4,6 8,6±4,0	11,4±5,3 —5,0*	18,3±13,3 27,0±8,1	19,4±9,4 5,2*	20,9±14,5 24,1±11,7	18,6±8,1 35,0±26,2	7,7* 18,9±12,4	5,5±4,8 21,7±20,8	0,2* 8,1±6,4	12,7±8,2 7,4±4,5
Coronary vascular resistance	21,1±18,9 —19,9±16,3	17,2±8,6 —11,0±4,9	17,2* —29,2±11,5	22,5±21,9 —8,4±7,9	19,4* —24,9±20,8	27,1±23,5 —5,6±3,7	1,9* —23,9±9,6	19,1±10,5 —6,7±4,4	15,0±14,8 —17,6±11,0	8,1±4,8 —12,1±5,8
Left ventricular pressure	4,1* 14,0±10,1	7,7±3,7 —8,8*	11,7±1,5 28,8±16,5	12,3±9,4 4,5*	14,2±11,7 28,0±8,8	23,5±23,0 28,9*	2,4* 24,3±13,6	5,7±3,6 23,0±23,0	5,6* 10,8±8,3	8,7* 7,3±6,6
Pulse rate	46,5±43,7 21,6±10,8	5,7* 0*	6,5* 57,8±39,6	3,2* 8,4±8,0	5,4±5,2 15,4±15,4	—2,3* 4,6*	3,0* 20,7±9,7	9,4±8,7 0,9*	6,6* 5,6±5,6	6,9* 1,4*

Legend. 1) Numerator — change in parameters during rise of coronary vascular resistance, denominator — during fall of coronary vascular resistance. 2) Asterisk indicates that changes are not statistically significant ($P > 0.05$). 3) Here and in Table 2: B — bipolar, M — monopolar stimulation.

TABLE 2. Effect of Stimulation of Lateral Mammillary Hypothalamic Nucleus on Principal Parameters of Cardio- and Hemodynamics after Intracoronary Injection of 1 mg Inderal (difference compared with original data, in %)

Parameter	Stimulation						After end of stimulation			
	5 sec		15 sec		30 sec		5 sec		30 sec	
	B	M	B	M	B	M	B	M	B	M
Coronary blood flow	—10,11±5,6	—9,5±9,0	19,2*	—18,2*	33,8±15,5	—3,6*	39,2±23,3	14,6*	9,2*	14,4*
Arterial blood pressure	47,5±10,2	38,3±26,4	80,0±16,8	81,8±16,4	85,4±16,4	77,9±55,3	57,0±19,0	48,7±38,8	47,1±28,2	14,8±6,5
Coronary vascular resistance	65,0±22,7	53,0±37,2	44,2±30,2	130,4±68,6	43,7±24,1	120,0±43,2	16,0±13,7	29,0*	36,2±4,9	7,5*
Left ventricular pressure	33,4±10,1	39,2±15,6	53,7±5,1	69,1±16,3	72,3±29,5	56,6±36,3	44,0±24,9	33,5*	60,4±46,0	21,0±2,1
Pulse rate	27,1*	—48,8±4,3	4,4*	—69,5±7,2	—3,9*	—23,4*	—21,2±1,7	14,8±13,7	—25,5±4,7	27,3*

*Changes not statistically significant.

The investigation thus showed that the high percentage of coronary vasoconstriction observed in the first 5 sec after the beginning of stimulation, whether bipolar or monopolar, points to the presence of direct vasoconstrictor influences arising during stimulation of hypothalamic pressor points, and spreading both to peripheral and coronary vessels. However, this constriction was of short duration and 15 sec after the beginning of stimulation it was replaced by a fall in the coronary vascular resistance. The reason for this is evidently the phenomenon known as functional sympatholysis: an increase in the work of the heart (elevation of BP, an increase in the pulse rate) and, consequently, marked activation of myocardial metabolism, make the coronary vessels "invulnerable" to constrictor influences. However, the action of Inderal, which blocks adrenergic β-receptors, discloses this masked vasoconstrictor effect of hypothalamic stimulation on the coronary vessels.

The disparity between coronary vascular reactions in the initial period of stimulation and during repeated stimulation in the course of the same experiment is evidence of the lability of the functional state of the hypothalamus. This conclusion is supported by the scatter of the data on the coronary blood flow obtained by Nogina [3, 4] in unanesthetized cats during stimulation of hypothalamic nuclei.

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