CHANGES IN THE BLOOD CHOLESTEROL CONCENTRATION DURING ELECTRICAL STIMULATION OF THE HYPOTHALAMUS

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Various workers have shown [1, 2] that a disturbance of cholesterol metabolism leads to the development of atherosclerosis. Clinical observations [6, 7, 9] have demonstrated the important role of the nervous system in the etiology and pathogenesis of atherosclerosis. In this connection there is considerable interest in the problem of the regulation of cholesterol metabolism by the various divisions of the central nervous system and, in particular, by the hypothalamus. The hypothalamus is known to regulate the metabolism of water, carbohydrates, lipids, and proteins. So far as the cholesterol metabolism is concerned, only isolated investigations on this subject have so far been published.

Elevation of the blood cholesterol level in elderly persons is attributed to an increase in the activity of certain hypothalamic centers with age [5]. Destruction of the hypothalamic region with an electric current led within a day or two to an increase in the blood cholesterol concentration [8]. Puncture of the diencephalic region in rabbits with a needle led to a significant increase in the blood cholesterol concentration [10]. It will be clear from these facts that changes in the blood cholesterol concentration have been studied only after severe injury to the hypothalamus. The mechanism of the influence of the hypothalamus on the blood cholesterol level remains unexplained. In the investigations so far published no relationship has been established between the change in the blood cholesterol concentration and the localization of the injury in the hypothalamus.

Recognizing that the part played by the hypothalamus in cholesterol metabolism has received inadequate study, we have performed chronic experiments in which we studied the effect of electrical stimulation of the various parts of the hypothalamus on the blood cholesterol concentration.

EXPERIMENTAL METHOD

The investigations were carried out on 5 dogs 18-20 h after feeding. Blood was taken from a vein in the forelimb. The total blood cholesterol concentration was estimated by a modification of the method of Engel'gardt and Smirnova. Oxalated blood (0.1 ml) was hydrolyzed with 1 drop of 50% KOH for 25 min in a boiling water bath, and 1.5 g anhydrous sodium sulfate was added to the hydrolyzate. Cholesterol was extracted three times with chloroform. The Liebermann-Burchard test was performed on the total volume of chloroform and the intensity of the color determined with a type FEK-M photoelectric colorimeter.

After the blood cholesterol concentration had been determined in intact animals, the operation of implantation of multipolar electrodes into the hypothalamus was performed. The technique of implantation of electrodes into the hypothalamic region has been described previously [3, 4]. Essentially, it is as follows. Through a burr hole in the temporal bone multipolar electrodes, mounted in a thin horseshoe-shaped plate made of Plexiglas or motion picture film (after removing the emulsion), were applied to the hypothalamic region anteriorly and posteriorly to the stalk of the hypophysis. A Plexiglas shoe with pins for connecting the stimulating current was fixed to the temporal bone by means of a specially constructed device.

Changes in Blood Cholesterol Concentration during Stimulation of Various Parts of the Hypothalamus

Dog's name	Date of experiment (1962)	Before stimulation	During stimulation	After stimulation		Maximal variation (in mg%)
				15 min	30 min	
	Anterior part					
Kashtan	19/I	140	117	115	110	−30
	23/I	125	120	110	100	−25
	25/I	130	125	120	120	−10
	1/II	120	115	110	110	−10
	3/II	130	110	110	110	−20
Kazbek	27/I	120	110	112	100	−20
	29/I	120	112	108	113	−12
	30/I	135	125	120	115	−20
	31/I	110	98	100	95	−15
	Posterior part					
Kazbek	10/II	100	110	115	100	+15
	12/II	105	110	120	117	+15
Tobik	16/IV	120	138	138	125	+18
	28/IV	120	132	133	130	+18
	15/IV	110	122	120	120	+12
Enot	19/IV	122	133	132	130	+11
	18/IV	105	117	120	122	+17
	12/IV	120	125	130	135	+15
	Middle part					
Zbonok	22/I	115	138	140	120	+25
	24/I	110	125	135	115	+25
	26/I	125	105	110	115	−20
	31/I	140	138	128	120	−20
Enot	12/VI	110	120	130	115	+20
	14/VI	107	122	130	115	+23
	15/VI	123	115	95	107	−28
Tobik	24/II	112	130	132	110	+20
	27/II	110	120	130	112	+20
	29/II	150	145	138	130	−20

The investigations proper were carried out on dogs with 4-pole electrodes implanted into different areas of the hypothalamus. The position of the electrodes was verified after the operation roentgenographically, and then with the naked eye in sections of the hypothalamus. After the operation of implantation of the electrodes, for a period of 7-10 days the blood cholesterol concentration was investigated without application of stimulation. In each experiment the blood cholesterol concentration was first investigated before stimulation. Next, different parts of the hypothalamus were stimulated for 3 min with a sinusoidal current from a type ZG-10 audiofrequency generator (current 0.5 mA, voltage 5 V, frequency 60 cps). Blood for determination of the cholesterol concentration was taken during and 15 and 30 min after the end of stimulation.

EXPERIMENTAL RESULTS

The application of electrodes to the hypothalamus had no effect on the blood cholesterol concentration. Electrical stimulation of the hypothalamus caused changes in the blood cholesterol concentration, the character of which was dependent on the localization of the stimulation (see table).

Stimulation of the supraoptic nuclei (anterior part of the hypothalamus) caused a lowering of the blood cholesterol concentration by 10-30 mg%. In many of the experiments the maximal fall in cholesterol concentration was observed 30 min after stimulation of the hypothalamus. In some experiments the lowest level of the blood cholesterol was found 15 min after stimulation of the anterior part of the hypothalamus. The results of nine experiments on the dogs Kashtan and Kazbek are given in Fig. 1.

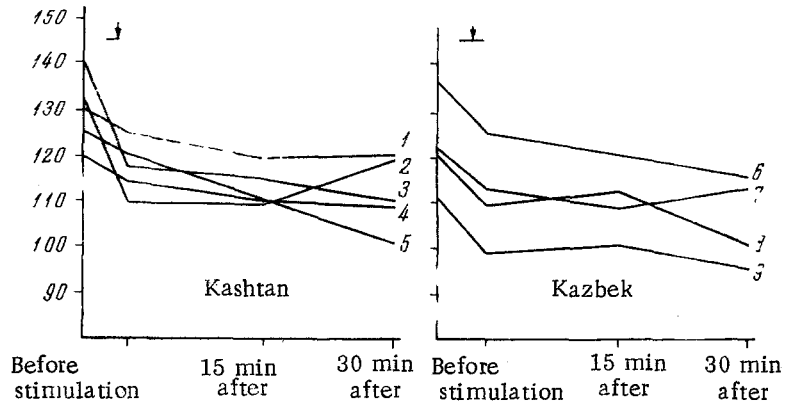

Fig. 1. Changes in blood cholesterol concentration during stimulation of the anterior part of the hypothalamus in the dogs Kashtan and Kazbek. Along the axis of ordinates – blood cholesterol concentration (in mg%); along the axis of abscissas – time of taking blood samples. The arrow denotes the moment of stimulation. Dates of experiments (1962): 1) 1/25; 2) 2/3; 3) 2/19; 4) 2/1; 5) 1/23; 6) 2/30; 7) 1/29; 8) 1/27; 9) 1/31.

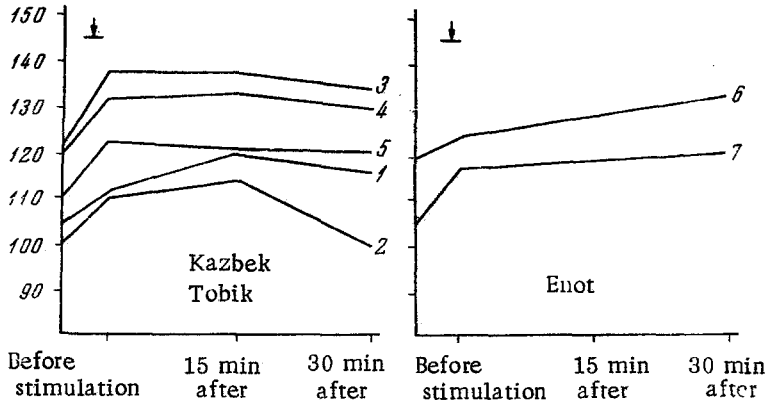

Fig. 2. Changes in the blood cholesterol concentration during stimulation of the posterior part of the hypothalamus in the dogs Kazbek, Tobik, and Enot. Legend as in Fig. 1. Dates of experiments (1962): 1) 2/12; 2) 2/10; 3) 2/28; 4) 2/16; 5) 3/15; 6) 4/12; 5) 4/18.

Stimulation of the mammillary bodies (posterior part of the hypothalamus) caused an increase of 11-18 mg% in the blood cholesterol concentration (see table). The maximal elevation of the blood cholesterol level was observed in most experiments 15 min after stimulation of the hypothalamus. The results of 8 experiments carried out on the dogs Kazbek, Tobik, and Enot are given in Fig. 2.

Stimulation of the middle part of the hypothalamus did not have a constant effect on the blood cholesterol level. In most experiments its concentration increased and in roughly one-third of the experiments it fell. A relationship was observed between the initial cholesterol concentration in the blood and the character of its changes during stimulation of the hypothalamus. If the initial cholesterol concentration was 120 mg% or higher, stimulation of the middle part of the hypothalamus caused a decrease in the blood cholesterol. If the initial blood cholesterol concentration was below 120 mg%, stimulation of the middle part of the hypothalamus was accompanied by an increase in its level, most marked 30 min after stimulation. The results of 10 experiments involving stimulation of the middle part of the hypothalamus, carried out on the dogs Zvonok, Enot, and Tobik, are given in Fig. 3.

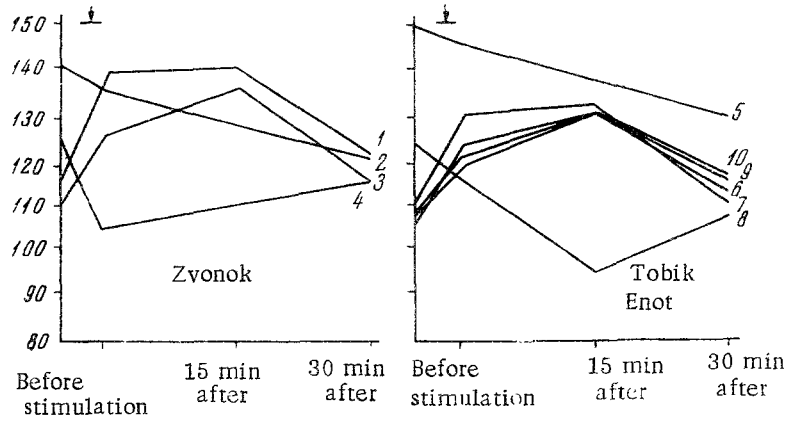

Fig. 3. Changes in the blood cholesterol concentration during stimulation of the middle part of the hypothalamus in the dogs Zvonok, Tobik, and Enot. Legend as in Fig. 1. Dates of experiments (1962): 1) 1/22; 2) 1/31; 3) 1/24; 4) 1/26; 5) 2/29; 6) 2/27; 7) 2/24; 8) 5/15; 9) 6/14; 10) 6/12.

It is an interesting fact that in all the experiments the change in the blood cholesterol concentration was clearly marked while the hypothalamus was actually being stimulated. This rapid reaction was probably attributable to the fact that the influences from the hypothalamus on the blood cholesterol concentration are transmitted by a nervous mechanism.

SUMMARY

Hypothalamus takes part in blood cholesterol control. Electrical stimulation of hypothalamus provokes changes in the blood cholesterol level. The character of these changes depends on localization of the stimulation. Electrical stimulation of the anterior part of the hypothalamus causes a fall, and of the posterior part – a rise in the blood cholesterol level. The change of blood cholesterol caused by electrical stimulation of the mid portion, of the hypothalamus depends on the initial blood cholesterol level. Stimulation of the mid portion of the hypothalamus raises an initially low, and lowers an initially high, cholesterol level.

LITERATURE CITED

1. N. N. Anichkov and V. D. Tsinzerling, In the book: Atherosclerosis [in Russian], Moscow (1953), p. 7.
2. N. N. Anichkov, In the book: Current Problems in Cardiology [in Russian], Moscow (1960), p. 7.
3. P. G. Bogach and A. F. Kosenko, Fiziol. zh. SSSR, 11, 989 (1956).
4. P. G. Bogach and A. F. Kosenko, In the book: Problems in Physiology [in Russian], No. 12, Kiev (1961), p. 3.
5. V. M. Dil'man, Ter. arkh., 2, 72 (1960).
6. A. L. Myasnikov, Vestn. Akad. Med. Nauk SSSR, 4, 15 (1950).
7. A. L. Myasnikov, Ter. arkh., 1, 32 (1954).
8. A. I. Seranova, In the book: Annual Report of the Institute of Experimental Medicine of the AMN SSSR for 1959 [in Russian], Leningrad (1960), p. 430.
9. E. M. Tareev, Ter. arkh., 5, 29 (1951).
10. F. K. Yarovoi, Transactions of the Crimean Medical Institute [in Russian], Vol. 17, Simferopol' (1957), p. 245.