EFFECTS OF BRIEF AND PROLONGED STIMULATION OF THE HYPOTHALAMUS ON THE FREE AND COMBINED CHOLESTEROL CONTENTS OF BLOOD

Yu. N. Bordyushkov and L. Kh. Garkavi

Experimental Department (Director: Prof. M. A. Ukolova),
Rostov-on-Don Scientific-Research Institute of Roentgenology,
Radiology, and Oncology (Director: P. N. Snegirev),
Ministry of Health, RSFSR
(Presented by Member of the Academy of Medical Sciences A. V. Lebedinskii)
Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 55, No. 6,
pp. 61-64, June, 1963
Original article submitted August 10, 1961

The few papers which have been published on the central nervous regulation of cholesterol metabolism have dealt with changes in cholesterol content following disturbances of conditioned reflex activity [5], in inflammatory conditions of the brain [2, 3], and under conditions of generalized experimental stimulation of the brain [7, 8]. The role of glial elements of the brain in regulation of cholesterol metabolism has also been studied [2, 4]. However, the part played in cholesterol metabolism by the separate divisions of the brain has not until now been studied, and this applies in particular to the hypothalamus, whish is known to regulate the metabolism of a number of other steroids (sex hormones and corticoadrenal hormones) [10, 11].

We have shown [1] that the level of blood cholesterol rose sharply following brief stimulation of the hypothalamic region. Similar stimuli applied to the cerebral cortex and the cerebellum did not affect the level of blood cholesterol. Implantation of electrodes into the brain caused a transient raising of the blood cholesterol level, lasting for 5-7 days after the operation.

In the present research, we have made a further study of the effects of brief and prolonged stimulation of the hypothalamic region on the levels of free and combined cholesterol in blood.

EXPERIMENTAL METHOD

We used 53 male and female white rats for our experiments. Their diet was not varied over the period of the experiments. Implantation of the electrodes was effected according to Ukolova and Bordyushkov [9], and main current (alternating), stepped down through a transformer, was used for stimulation, measuring the potential with the aid

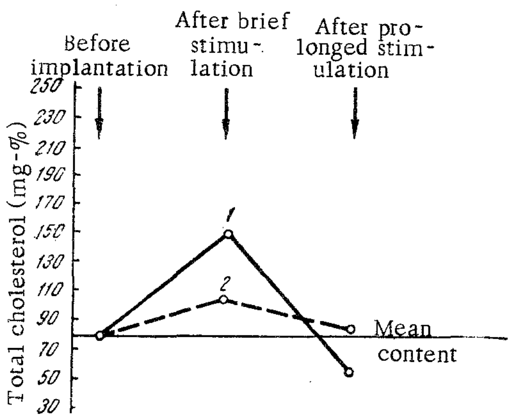

Fig. 1. Effect of brief and prolonged stimulation of the hypothalamus (1) and cortex (2) of rats on their blood cholesterol content.

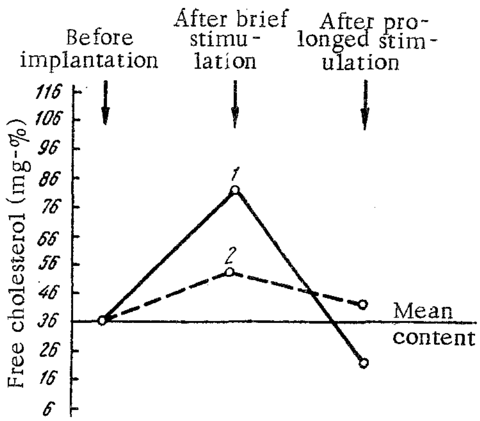

Fig. 2. Effect of brief and prolonged stimulation of the hypothalamus (1) and cortex (2) of rats on the free cholesterol content of their blood.

Dynamics of Change in Free and Combined Cholesterol Contents (mg-%) of Blood Following Stimulation of the Hypothalamus and Cerebral Cortex

Statistical indices	Before implantation of electrodes			After stimulation of the hypothalamus						Before implantation of electrodes			After stimulation of the cortex					
				brief			prolonged						brief			prolonged		
	Neishles's method	Lapin's method		Neishles's method	Lapin's method		Neishles's method	Lapin's method		Neishles's method	Lapin's method		Neishles's method	Lapin's method		Neishles's method	Lapin's method	
	total	total	free	total	total	free	total	total	free	total	total	free	total	total	free	total	total	free
M	81	80	37	151	148	81	58	56	23	90	80	36	106	104	54	86	85	42
σ	10	10	6	33	34	28	11	12	6	13	8	4	33	33	28	9	8	3
m	1,6	1,6	1,0	5,5	5,6	6,3	1,8	1,9	1,0	3,6	2,2	1,2	9	9	7,7	2,5	2,3	0,8
t				11	10	6,6	8,8	8,2	7,3	—	—	—	1,7	2,5	5	—	—	—
P				0,001	0,001	0,001	0,001	0,001	0,001	—	—	—	0,05	0,05	0,01	—	—	—

Note: Lapin's method was used in 13 of the analyses, and Neishles's method in 40 analyses.

of an avometer. Only threshold strengths of stimulus (causing somatic or vegetative reactions) were used. Stimuli of duration 40 sec were applied daily, being repeated 3 times at 3-5 min intervals. Blood samples were taken from the jugular vein. Blood cholesterol was determined in all samples by two different methods: Neishles's macromethod based on the color reaction with acetic anydride and sulfuric acid (total cholesterol), and Lapin's micromethod based on the color reaction with furfurol [6].

Electrodes were implanted into the hypothalamus of 40 animals, and into the cerebral cortex of 13 animals. The blood cholesterol was determined for each animal before implantation of the electrodes, and after brief (1-5 days) or prolonged (1-1½ months) daily stimulation. The location of the tips of the electrodes was established histologically, using Campo's silvering method. For the identification of the stimulated hypothalamic structures, we made use of Krieg's hypothalamic charts [13] and of Fifkova and Marsala's stereotactic atlas [12].

EXPERIMENTAL RESULTS

Our results showed that the changes in total and combined cholesterol contents of the blood varied according to the duration of stimulation. A short course (1-5 days) of electrical stimulation of the hypothalamus raised the blood cholesterol level, while prolonged further daily administration of threshold stimuli lowered the level (Fig. 1). The greatest changes were in the free cholesterol fraction (Fig. 2).

Similar brief stimulation of the cerebral cortex caused only a slight rise in blood cholesterol content (see the Table and Figs. 1 and 2).

The threshold for vegetative and somatic reactions changes considerably during the course of stimulation: the threshold potential was initially 0.15-0.2 V, while at the end of the course it had risen to 1-1.5 V.

Thus, over the whole course of stimulation of the hypothalamus, the blood cholesterol rises during its early atages, and then falls steeply to below the initial level at the end of the course. These effects might be explained on the assumption that when electrical impulses are applied to the nervous structures of the hypothalamus they initially cause stimulation, but that their effect changes to one of inhibition as the treatment is continued. This explanation is supported by the very great rise in the height of the threshold for somatic and vegetative reactions observed following prolonged stimulation.

A great variety of reactions was observed during stimulation of the hypothalamus. These included reactions of orientation, motor, feeding, sleep, yawning, washing, increased respiratory rate, narrowing of the palpebral fissure, and exophthalmic reactions. The most frequently observed reaction was that of orientation.

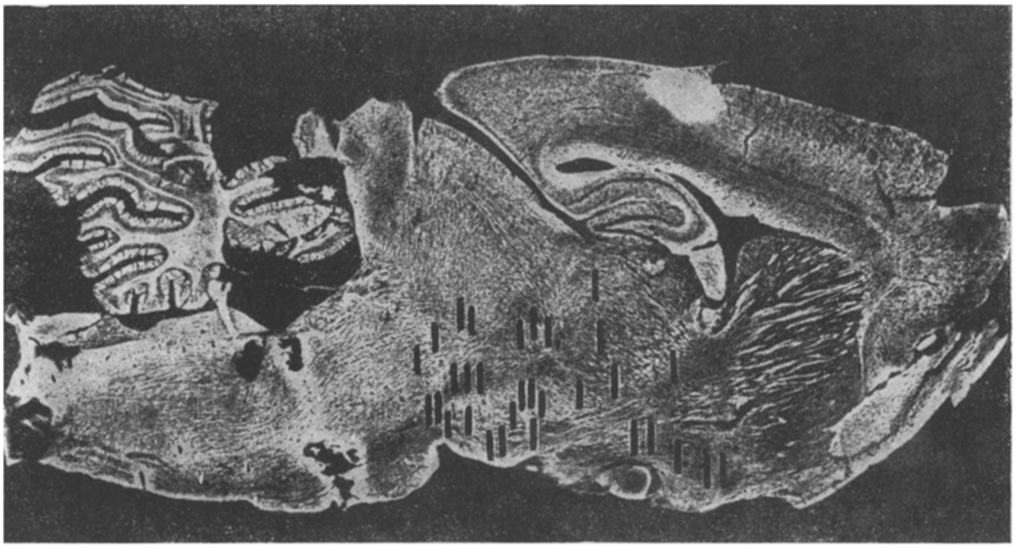

Fig. 3. Representation of the locations of the tips of stimulating electrodes, seen on a sagittal section of rat brain. Electrode tips are represented by dashes.

The tips of the stimulating electrodes were found in various nervous structures of the anterior, middle, and posterior hypothalamus (Fig. 3). In a few cases they were located in parts of the thalamus adjacent to the hypothalamus. The cerebral cortex was stimulated in 6 animals, the electrodes being implanted into various parts of the parietal lobe.

We would add that the same type of effect was given by stimulation of different hypothalamic nuclei, and that stimulation of a particular nucleus gave different effects, according to the duration of the course of stimulations. It is conceivable that our findings are due to some unspecific effect of hypothalamic nervous structures on cholesterol metabolism, which may be compared, on the one hand, with the unspecific activity of reticular formations, and on the other with the presence of adaptive response of the organism to the action of different stimuli.

Our findings permit the conclusion that hypothalamic region participates in regulation of cholesterol metabolism.

SUMMARY

Threshold-strength stimulation of the hypothalamus of white rats, under conditions of chronic experimentation, affected the blood cholesterol level differently, depending on the duration of the course of stimulations. The initial effect was to raise blood cholesterol, but after prolonged stimulation (1-1.5 months), the cholesterol content fell, following application of the stimulus, to below the initial level; the greatest changes were in the free cholesterol content. The same type of response was given by different hypothalamic structures. The part played by the hypothalamus in regulation of cholesterol metabolism is discussed.

LITERATURE CITED

1. Yu. N. Bordyushkov and L. Kh. Garkavi, Abstracts of Papers read at the XIII Congress of Physiologists of the Southern RSFSR, Rostov-on-Don (1960).
2. P. D. Gorizontov, Byulleten' Éksperimental'noi Biologii, No. 4, 6, p. 55.
3. P. D. Gorizontov, Arkh. pat., 4, No. 1 (1938), p. 82.
4. P. D. Gorizontov, Significance of the Brain in Cholesterol Metabolism [in Russian], Moscow (1940).
5. T. D. Dzidziguri, Byulleten' Éksperimental'noi Biologii, No. 2 (1959), p. 32.
6. L. N. Lapin, Trudy Samarkandskogo meditsinskogo Institute, 11 (1956), p. 103.
7. N. V. Okunev, Cholesterol-Protein Complexes. Proceedings, VIII All-Union Congress of Physiologists, Biochemists, and Pharmacologists [in Russian] (1955), p. 455.
8. A. I. Seranova. Proceedings, Symposium on Problems of Arteriosclerosis [in Russian], Leningrad (1959), p. 18.
9. M. A. Ukolova and Yu. N. Bordyushkov, Byulleten' Éksperimental'noi Biologii, No. 8 (1958), p. 126.
10. E. Endröczi, E. Kovacs, and K. Lissak. Kiserl. orvostud., 8, No. 5 (1956), p. 504.
11. B. Elerko, Arch. anat. micro., Bd. 46, No. 2, S. 159 (1957).
12. E. Fifkova and J. Marsala, Stereotaxis of Subcortical Structures of the Brain of Rats, Rabbits, and Cats [in Czech], Prague (1956).
13. W. J. Krieg, Quart. Bull. Northwestern University Med. School, 20, No. 2 (1946).

All abbreviations of periodicals in the above bibliography are letter-by-letter transliterations of the abbreviations as given in the original Russian journal. *Some or all of this periodical literature may well be available in English translation.* A complete list of the cover-to-cover English translations appears at the back of this issue.