its normal inhibitory effect on the respiratory center. That is why, despite the normal composition of the blood gases, the patient needs additional stretching of the muscles and additional artificial ventilation of the muscles, which causes hypocapnia. The latter, in turn, makes it necessary to increase the hyperventilation still more. However, the primary reason why hyperventilation is necessary in patients with paralysis of the respiratory muscles is insufficiency of the inhibitory Hering–Breuer reflex.

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# CHANGES IN BLOOD CHOLESTEROL AND TRIGLYCERIDE LEVELS DURING SELF-STIMULATION AND AVOIDANCE REACTIONS


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Change in the blood cholesterol and triglyceride levels during self-stimulation and avoidance reactions were studied in rabbits of both sexes. Self-stimulation was accompanied by a significant fall in the blood cholesterol and triglyceride levels. During the avoidance reaction the character of changes in the cholesterol level varied. In avoidance reactions of the "aggression" type the blood cholesterol was raised, whereas in reactions of the "fear" type it was lowered. The maximal deviation of the blood cholesterol from its initial level in all types of reactions was observed 15-30 min after stimulation.



KEY WORDS: electrical stimulation of the hypothalamus; self-stimulation and avoidance reactions; lipids.


In an earlier chronic experimental investigation [8] it was shown that compulsive stimulation of the emotiogenic zones of the hypothalamus through implanted electrodes, giving rise to qualitatively different emotional behavioral responses, both negative and positive, is accompanied by opposite changes in the blood cholesterol level.

In the investigation described below, in order to obtain more objective conclusions regarding the appearance of a positive emotional state in the animal, the self-stimulation method was used; according to most investigators, this method is associated either with the appearance of an emotional state of positive sign only, or with predominance of positive components in the emotional state [2-5, 15]. The avoidance reaction was used as the criterion of a negative emotional state. The character of changes in the blood cholesterol and, in some cases, the triglyceride levels were investigated in these states.

## EXPERIMENTAL METHOD

Experiments were carried out on 20 adult rabbits of both sexes weighing 3-3.5 kg. Bipolar nichrome electrodes 0.1 mm in diameter were implanted into the brain structures by a random method [14] in accordance with coordinates of a stereotaxic atlas [16]. To obtain a self-stimulation reaction the electrodes were inserted into the region of the lateral hypothalamus and medial forebrain bundle, and to obtain negative emotional and

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TABLE 1. Effect of Self-Stimulation Reaction on Changes in Blood Cholesterol and Triglyceride Levels in Rabbits (M ± m)

| Indices of lipid metabolism | Initial level | Time of taking blood after end of self-stimulation, min | | | |
|---|---|---|---|---|---|
| | | 3 | 15 | 30 | 60 |
| Cholesterol, mg% | 45,4±3,1 (30—60) | 33,9±3,04 (20—50) | 30,8±3,01 (20—50,5) | 31,8±2,4 (24—50) | 38,2±1,95 (30—51) |
| *n* | 11 | 11 | 10 | 10 | 10 |
| *P* | | <0,01 | <0,01 | <0,01 | <0,01 |
| Triglycerides, mg% | 46,36±2,3 (37—53) | 29,3±2,5 (23—40) | 27,7±3,2 (22—42) | 24,2±1,0 (21—28) | 30,9±2,8 (21—36) |
| *n* | 6 | 6 | 6 | 6 | 6 |
| *P* | | <0,01 | <0,01 | <0,01 | <0,01 |

Legend. Here and in Table 2, limits of variations shown in parentheses.

behavioral avoidance reactions they were inserted into the ventro- and dorsomedial nuclei of the hypothalamus. A sinusoidal current with a strength of between 10 and 100 $\mu$A and a frequency of between 20 and 60 Hz was applied to the electrodes.

To teach self-stimulation skills a stimulator with time relay [1], giving constant duration of stimulation (1 sec), was used. To press the lever the rabbit used its teeth or mouth.

The avoidance reaction was elicited by the use of the same apparatus. Self-stimulation and avoidance sessions lasted 30 min. All the animals took part in the experiments for 1 to 2 months.

Blood from the marginal vein of the ear was taken in some cases before and 3 min after the end of stimulation, and in other cases 3, 15, 30, and 60 min after stimulation. The blood cholesterol concentration was determined by the method in [11] and the triglycerides as in [12, 13].

To verify the location of the electrode tips morphologically the brain was fixed in 10% formalin solution. Sections were stained by Nissl's method.

## EXPERIMENTAL RESULTS AND DISCUSSION

Three types of reactions were observed during self-stimulation in the rabbits. In some cases there was only a self-stimulation reaction, in others a self-stimulation reaction accompanied by a food response and, finally, relatively weak self-stimulation with a predominant food response.

The avoidance reaction appearing in the rabbits after compulsory contact with the lever as a rule was mixed in character, as other workers also have found [4]. Nevertheless, two types of negative emotional and behavioral reactions could be distinguished: "fear" and "aggression." Whereas during a "fear" reaction the rabbits usually tried to hide in the corner or to squeeze against the floor, in the "agression" reaction the animals behaved actively: They stamped on the floor with their hind limbs, uttered threatening sounds and, when the provoking object was shown to them they pounced on it, and even after the end of electrical stimulation, for a long time they remained in a state of excitation – they stamped with their paws and continued to make threatening noises. In most cases, however, the predominant reaction of the animals was one of "fear."

The morphological control showed that the electrode tips were located in the lateral hypothalamic region (at the level of the tuber cinereum) in its dorsal, ventral, or lateral parts, and also in the lateral preoptic region (dorsal part). An avoidance reaction of "agression" type was observed when the electrode tips were located in the ventromedial nucleus of the hypothalamus and on the boundary between the ventro- and dorsomedial nuclei of the hypothalamus. An avoidance reaction of "fear" type was observed in some rabbits in which the electrode tips were located in the same structures, but also in the posterior hypothalamic nucleus, on the boundary between the ventro- and dorsomedial nuclei and the posterior hypothalamic nucleus, on the boundary between the dorsomedial and perifornical hypothalamic nuclei, and also in the dorsal part of the medial preoptic region between the paraventricular nucleus and the fornix.

Investigation of the blood-lipid levels showed that during self-stimulation there was a tendency in most rabbits for the cholesterol level to fall regardless of the type of responses which predominated. In some cases deviations of the cholesterol concentration from its initial level were not observed. On average, in 33 experiments on five rabbits the cholesterol level before stimulation was 38.6 ± 2.1 mg%, compared with 29.7 ± 2.18 mg% 3 min after the end of self-stimulation ($P < 0.01$).

TABLE 2. Changes in Blood Cholesterol Level during Avoidance Reactions in Rabbits (M ± m)

| | Indices of lipid metabolism | Initial level | Time of taking blood after end of stimulation, min | | | |
|---|---|---|---|---|---|---|
| | | | 3 | 15 | 30 | 60 |
| A | Cholesterol, mg% | 41,4±2,2 (35—45) | 48,3±3,6 (41—58) | 55,2±1,7 (48—60) | 52±3,0 (47—62) | 44±1,0 (41—50) |
| | *n* | 5 | 5 | 5 | 5 | 5 |
| | *P* | | <0,02 | <0,01 | <0,01 | <0,05 |
| B | Cholesterol, mg% | 50,3±2,5 (38—60), | 39,6±1,6 (29—50) | 36,4±1,6 (28—52) | 41,4±2,6 (34—55) | 47,8±2,8 (36—57) |
| | *n* | 10 | 10 | 10 | 10 | 10 |
| | *P* | | <0,01 | <0,01 | <0,02 | <0,05 |

Legend. A) Response of "aggression" type. B) response of "fear" type. P calculated by comparison with initial data.

In the series of experiments on male rabbits with a well-marked self-stimulation reaction, the dynamics of the blood levels of both cholesterol and triglycerides was studied for 1 h after the end of stimulation. Altogether 11 experiments were carried out on five rabbits. The decrease in the blood cholesterol concentration noted above 3 min after self-stimulation became more marked with time and the minimal level was reached on average 15-30 min after its end; after 60 min the mean cholesterol level was still lower than initially (Table 1).

The dynamics of changes in the blood triglyceride level also was similar after self-stimulation (Table 1).

During periodic sessions of self-stimulation considerable fluctuations in the blood triglyceride level and, to a lesser degree, of the cholesterol level were observed in some rabbits. In rabbit No. 56, for example, the triglyceride concentration rose from 32 to 244 mg% and the cholesterol level from 30 to 62 mg%. Additionally, investigation of the blood triglyceride level revealed a so-called rebound effect [4], i.e., after self-stimulation leading to a marked decrease in the blood triglyceride level, on the following days their level increased considerably, probably on account of a rise in the blood sugar concentration during self-stimulation [6]. No clear relationship was found between the frequency of self-stimulation and the degree of deviation of the blood lipid levels. No difference likewise was found between changes in the blood lipid levels during self-stimulation reactions obtained from different structures of the hypothalamus, nor was any definite correlation observed between changes in the blood lipid level and the food response accompanying self-stimulation.

Analysis of the dynamics of changes in the blood cholesterol concentration during avoidance reactions was carried out only in animals with well-marked emotional and behavioral reactions of the "aggression" or " fear" types.

Altogether five experiments were carried out on male rabbits with "aggression" reactions, in which the blood cholesterol was significantly increased as early as 3 min after stimulation (Table 2), and reached a maximum after 15 min. In some of these rabbits the blood cholesterol level had fallen to normal after 60 min.

In avoidance reactions of the "fear" type observed in 10 experiments on male rabbits, on the other hand, a significant fall in the blood cholesterol level was found 3 min after the end of stimulation (Table 2), the lowest level being reached after 15 min. In some rabbits the blood cholesterol returned to its original level 60 min after stimulation.

Changes in the blood cholesterol level in the two types of negative emotional and behavioral avoidance reactions of the "aggression" and "fear" types were thus opposite in character. The dynamics of the changes in the blood triglyceride level was not so clearly defined.

In control experiments on five rabbits with implanted electrodes, when blood was taken at the same time intervals but hypothalamic stimulation was not applied, the blood cholesterol level remained virtually unchanged – deviations did not exceed 3%.

Changes observed in the blood cholesterol level of rabbits by the use of the more objective method of reproducing different emotional states in animals confirmed results obtained by the writers in experiments on dogs [8, 9]. Because of the changes in the blood cholesterol concentration in the two types of negative emotional and behavioral reactions of "aggression" and "fear" it is possible to use rabbits, which are herbivorous animals not consuming exogenous cholesterol, as experimental objects with which to study changes in lipid metabolism in various emotional states.

The mechanism of the parallel changes in the blood lipid levels during self-stimulation and avoidance reactions of the "fear" type calls for special study. As the present writers [10] and others [7] showed previously, chronic (for 4 months) stimulation of negative emotiogenic zones of the hypothalamus in unrestrained animals with an autonomous microstimulator, causing the appearance not only of reactions of "aggression" but also of "fear" (accompanied by transient hypolipidemia in the case of short-term stimulation), leads to the development of a lasting endogenous rise in the blood cholesterol and triglyceride concentration. Meanwhile, chronic stimulation of the positive emotiogenic zones of the hypothalamus in rabbits under the same experimental conditions [9] is not accompanied by any significant changes in the blood cholesterol or triglyceride levels. These differences are not only of theoretical interest, but also of practical importance for they are vital to the understanding of the pathogenetic mechanisms of the onset and development of atherosclerosis, since elevation of the blood cholesterol and triglyceride levels is one of the "risk factors" for the development of this form of cardiovascular pathology.

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