THE ROLE OF THE CEREBRAL CORTEX AND SUBCORTICAL CENTERS IN THE REGULATION OF BLOOD CHOLESTEROL LEVELS

COMMUNICATION I: CHANGES IN BLOOD CHOLESTEROL LEVEL ON FORMATION OF A CONDITIONED REFLEX TO RESPIRATORY INHIBITION IN RABBITS

P. S. Khomulo

Chair of Pathologic Physiology (Chief – Professor N. T. Shutova), Pediatric Medical Institute, Leningrad

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Disorders of lipid metabolism and particularly that of cholesterol play an important role in a number of pathologic processes, such as atherosclerosis of blood vessels, lipid nephrosis, cutaneous xanthomatosis and others [1, 7, 8].

The work of S. S. Khalatov [7, 8], A. A. Znachkova [3], P. D. Gorizontov [2], N. T. Shutova [9] et al has shown that there is increased diminution of cerebral cholesterol and a rise in blood cholesterol level on emotional excitation, oxygen starvation, intoxication and destructive processes in the brain. On the basis of these facts S. S. Khalatov concluded that a number of hypercholesterinemic conditions were of cerebral etiology.

It was later shown that prolonged narcotic inhibition led to a decrease in blood serum cholesterol and its increase in the brain [4, 6].

Stimulation of the carotid sinus by bacterial filtrate of enteric bacillus [5] and electric stimulation of the brain [10, 11] led to a rise in blood cholesterol.

In the present work investigation of the blood cholesterol levels (using the Engelhardt-Smirnova micro-method) during changes in the functional state of the cerebral cortex and subcortical structures was undertaken.

EXPERIMENTAL

2 series of experiments were carried out on 10 rabbits. Following thrice-repeated estimation of blood serum cholesterol in 4 rabbits its level was determined on formation of a conditioned reflex to defensive reflex inhibition of respiration. The intervals between determinations in the course of the whole investigation did not exceed 5 days.

The sound of a metronome served as the conditioned stimulus. Unconditioned inhibition of respiration was produced by stimulation of the nasal mucosa by threshold doses of CO₂ admitted under a certain pressure onto a reflector held by means of a mask near the animal’s nose. The distance between the reflector and the nose was 5 mm. The mask and reflector did not cover the animal’s eyes, nose or ears and did not restrict its movements.

The sound of the metronome preceded the action of CO₂ by 3-4 seconds. 6 combinations of the stimuli with 5 minute intervals were used during the experiment; the pneumogram, the application of stimuli and the time were recorded on a kymograph (Fig. 1, C).

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Formation of the conditioned reflex passed through the stage of conditioned reflex increase in the rate of respiration and decrease in the amplitude of respiratory movements (Fig. 1, B). The typical form (cessation of respiration) of the conditioned reflex (Fig. 1, D) was established in rabbits (No. 2 and 4). In two other rabbits (No. 3 and 1) the reflex in most cases manifested itself by increased rate and decreased amplitude of respiration (Fig. 1, B) and only in 5-7% by cessation of respiration.

The first series included 217 experiments using a conditioned stimulus and 168 blood serum cholesterol estimations. The animals were kept under observation for 6 months.

RESULTS

During the formation of the conditioned reflex, as early as 10-15 days after the beginning of the experiments (60-80 combinations) all the rabbits showed a 25-30% decrease of blood serum cholesterol. On further prolonged work with the animals the average content of cholesterol decreased by 50% (Table 1) as compared with the average initial level. The maximal decrease noted towards the end of the procedure amounted to 80% in some cases.

A comparison of the number of positive responses to the conditioned stimulus (increase in respiratory rate with decrease in amplitude, cessation of respiration) and the degree of decrease of blood serum cholesterol shows that in the case of rabbit No. 3 the conditioned reaction appeared in a smaller percentage of cases than in other rabbits and the decrease in blood serum cholesterol in the same rabbit was insignificant (Table 2).

Therefore the decrease in cholesterol content is in direct ratio to the extent to which the conditioned reflex is pronounced.

On prolonged and continuous work with the animals disturbances of conditioned reflex activity were observed, which manifested themselves in a decrease of positive responses to the conditioned stimulus. These disturbances as a rule corresponded with minimal blood serum cholesterol levels. Towards the end of a two-months interval following termination of experiments using a conditioned stimulus the blood serum cholesterol remained decreased in 2 rabbits; in two others the cholesterol level exceeded the original value by 60-75%.

In the second series of experiments the blood serum cholesterol levels were studied in rabbits under conditions of dietary cholesterol "loading" against a background of conditioned reflex activity.

Observations were carried out successively on 3 groups of animals. In each group there were 2 experimental and 2 control rabbits which received cholesterol in equal amounts. In the first and second groups, experiments using a conditioned stimulus were begun on the experimental animals after 4-6 feeds of cholesterol when its level had risen 3-4-fold as compared with the initial content.

First group (Table 3). Experimental rabbits No. 1 and 4 and control rabbits No. 5 and 6 were given 0.5 g crystalline cholesterol in 40 ml milk. The increment of cholesterol in the blood serum towards the end of feeding found in the experimental rabbits was 5 and 8 mg % respectively. In the course of the same period of feeding the cholesterol increment in control rabbits was 164 and 166 mg %.

Figure 1. Respiration in rabbit during various periods of the formation of conditioned reflex. Records (from above down): respiration, beginning of stimulation, time marker in seconds; the figures refer to the serial number of combination of stimuli. M – metronome in A, B, C, D.