A STUDY OF HIGHER NERVOUS ACTIVITY IN EXPERIMENTAL TUBERCULOSIS

COMMUNICATION II: A STUDY OF MOTOR-DEFENSE CONDITIONED REFLEXES IN DOGS

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The study of the central nervous system's role in different pathologic conditions has recently become of paramount importance.

Higher nervous activity in experimental tuberculosis has been studied almost exclusively by the method of salivary and motor-food conditioned reflexes [4-6, 10-13]. T. F. Ryumina [9,10] and others have shown, however, that the unconditioned reflexes of animals are depressed from the very first days following the infection, and this, of course, cannot but affect the character of conditioned reflex activity.

We used motor-defense conditioned reflexes electrocutaneously reinforced as an index of higher nervous activity with experimental tuberculosis in dogs.

Experimental Methods

A system of conditioned motor-defense reflexes was developed in dogs in a sound-proof chamber by V. P. Petropavlovskii's method [7], with certain modifications. The unconditioned stimulus was a supraliminal inducing current. The conditioned stimuli employed were a bell, a buzzer (differentiation), a touch, and a light. While the reflexes were being developed, the conditioned stimuli were each given alone for 5 seconds of their 20-second total action time. Later, each stimuli actually acted alone for 20 seconds because, when there was an expressed conditioned reflex, the dog, by lifting its paw, automatically cut off the current for the total action time of the conditioned stimulus. The autonomic component of the reflex was calculated according to the depth and rate of the respiratory movements of the chest. The experimental data were recorded on a kymograph tape, and entered in the official report. Higher nervous activity was evaluated according to a seven-point graded scale we worked out, taking into account the interrelation and gradation of the quantitative and qualitative indices of the motor conditioned reflex; the more adequate and absolute the reflex, the higher it was rated on the scale.

After the system of conditioned reflexes was developed, the dogs were intravenously infected on this "background" with a virulent culture of Mycobacterium tuberculosis (Walle strain) in a dose of 0.75 mg/kg of weight. We then observed the dynamics of higher nervous activity in the animals. At the same time, we systematically recorded the clinical indices, the general condition of the animals, and their behavior outside the chamber.

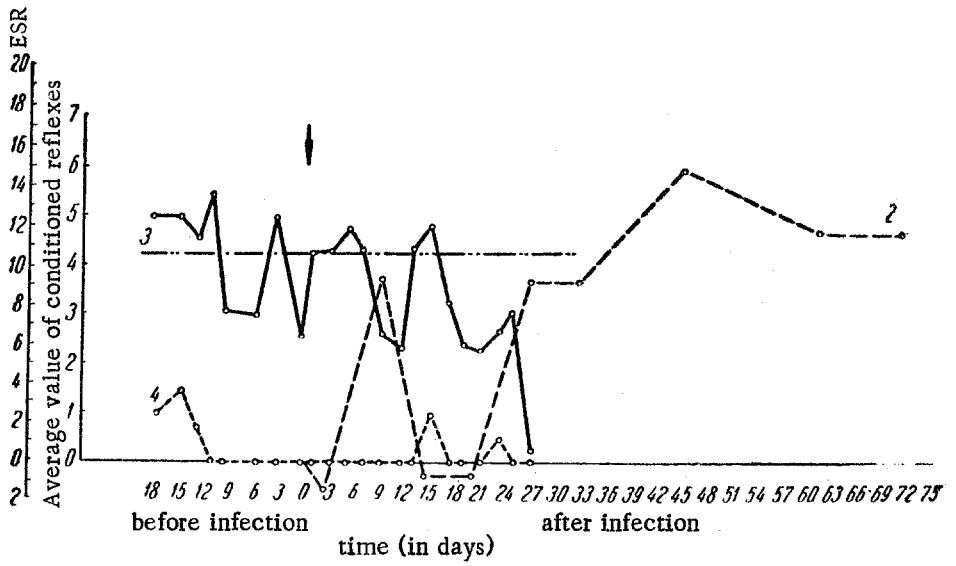

Fig. 1. The dynamics of the motor-defense conditioned reflexes in the dog Zhuchka compared with certain clinical indices after infection. Graded according to the conditional seven-point scale: 1) average value of positive conditioned reflexes; 2) average value of negative conditioned reflexes; 3) average preinfection level of positive conditioned reflexes; 4) E.S.R. (in millimeters per hour in relation to the original level).

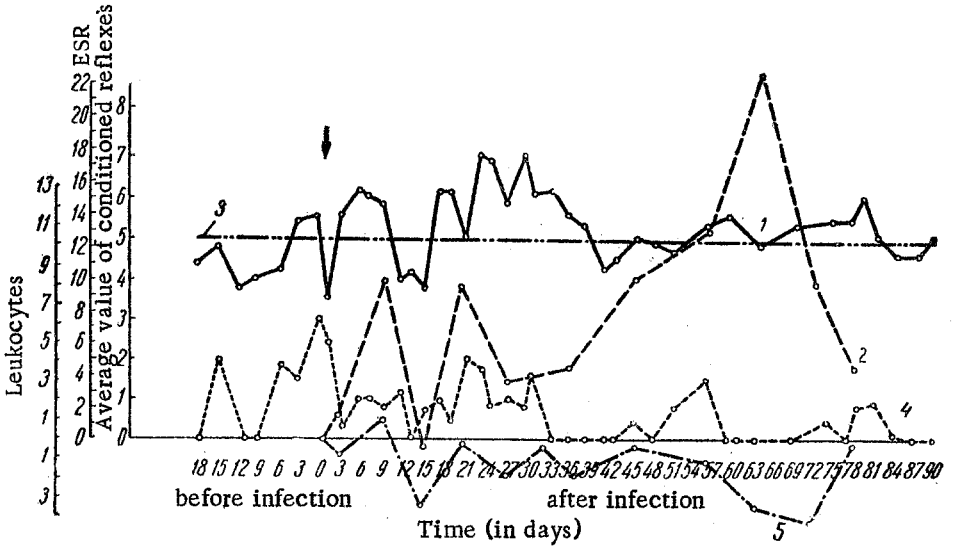

Fig. 2. The dynamics of the motor-defense conditioned reflexes in the dog Pal'ma compared with certain clinical indices: 1) average value of positive conditioned reflexes; 2) average value of negative conditioned reflexes; 3) average preinfection level of positive conditioned reflexes; 4) E.S.R. (in millimeters per hour in relation to the original level); 5) leukocytes (in thousands in relation to the original level).

The three dogs on which the observations were conducted can be described as follows:

1. A sheep dog named Zhuchka, 3-4 years old. Affectionate and timid with people, aggressive with other animals.

2. A mongrel named Pal'ma, 3-4 years old. Quiet and affectionate with people, indifferent to other dogs. Strongly expressed passive-defense reaction to new surroundings.

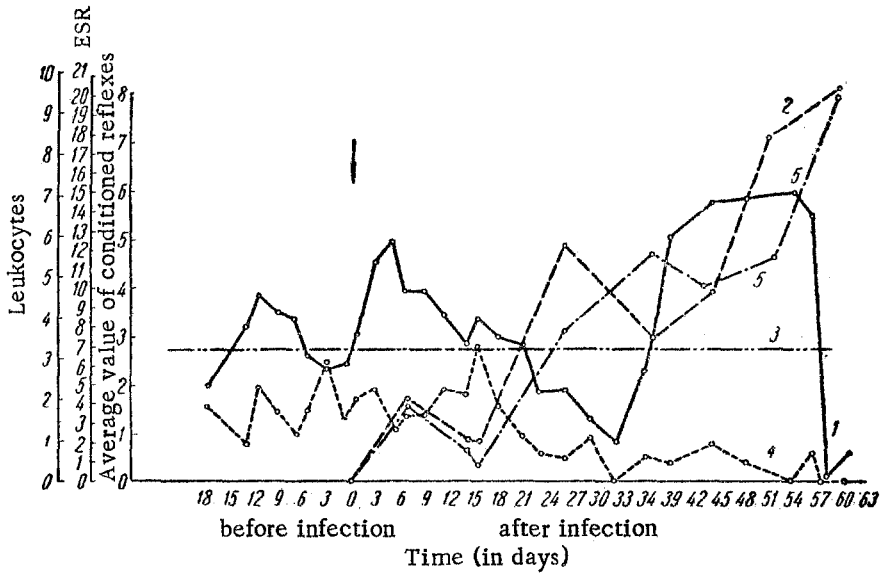

Fig. 3. The dynamics of the motor-defense conditioned reflexes in the dog Ryzhii compared with certain clinical indices. Symbols the same as in Fig. 2.

3. Ryzhii, a cross between a female sheep dog and a male mongreal, 2-3 years old. Strongly developed orientation and playful reflexes. Very active, movements impulsive and impetuous, respiration uneven.

Experimental Results

On the thirteenth day after infection, the dog Zhuchka began to appear weak and to be slightly unsteady in her gait. This weakness increased sharply on the 29th day; the dog sagged against the straps on the bench, and dyspnea and sharply expressed movements of exhaustion were observed. The dog died 85 days after infection. An autopsy was performed,* which demonstrated more than four liters of serous exudate in the abdominal and pleural cavities. The lungs, liver, and kidneys were studded with miliary tubercles.

During the first 26 days of observations after the infection, the motor-defense reflexes in this dog, graphically expressed, formed two waves; the first peak was observed on the 5th-7th day after infection; the second, on the 15th day (Fig. 1). After the infection, conditioned reflex activity retained the circular character observed before it, and the average value of the positive conditioned reflexes almost matched the preinfection level. The differentiation was absolute at the time of the first peak, but became slightly disinhibited to the first buzzer, although still absolute to the second, during the time of the second peak. There was a considerable increase in the inertia of the accelerated respiration constituting the aftereffect, and this, together with the intensification of the intersignal reactions (general unrest and frequent shifting of the paws during the five-minute interval) should evidently be regarded as an indication of increased defense center excitability.

Starting the 31st day after infection, we observed in the dog Pal'ma sluggishness, "drunken" gait, and some sagging in the straps; at the same time, the passive-defense reaction became stronger, and a sharply expressed depth phobia developed. The dog was sacrificed on the 180th day after infection in a condition of extreme cachexia. The autopsy disclosed a few submiliary and miliary tubercles in the lungs and kidneys.

As compared with the preinfection period, motor-defense conditioned reflexes of Pal'ma improved considerably on the 3rd-9th and 16th-39th days after infection: they became strictly adequate, the differentiation became stronger, and the dog's paws shifted more frequently during the intersignal interval (Fig. 2). The aftereffect, especially to the light, became sharply prolonged: the dog did not drop its paw for 25-28 sec after the stimuli were cut off. The aftereffect expressed in frequency of respiratory movements also increased to five times the original level (before infection). A new positive conditioned reflex was rapidly developed (to a tone 1 per second in frequency), becoming apparent in clear and adequate form at the third combination; the differentiation to this (tone 1 per 5 seconds in frequency) became total at the fifth use of the differentiation stimulus.

* The autopsies on the dogs were performed by M. A. Simanovskii.

Clinical Indices in Experimental Dogs Before and After Infection

Clinical indices	Dog's name	Index*	Day after infection															
			2nd	7th	9th	11th	14th	16th	20th	26th	29th	32nd	36th	44th	46th	51st	59th	64th	71st
Weight (kg)	Zhuchka	22,0	—	—	—	20,5	—	—	18,4	—	—	—	12,6	—	—	—	—	—	—
	Pal'ma	26,0	—	—	—	24,6	—	—	22,3	—	—	—	20,5	—	—	—	—	19,2	—
	Ryzhii	29,0	—	—	—	26,4	—	24,6	24,2	—	23,2	—	21,7	20,8	—	—	18,3	—	—
Temperature	Zhuchka	39,0	38,7	39,5	40,1	40,8	40,3	—	40,0	—	—	—	—	—	—	—	—	—	—
	Pal'ma	39,0	38,3	39,2	39,4	39,8	40,0	—	39,3	—	38,7	—	38,8	—	38,8	—	38,7	39,0	—
	Ryzhii	38,4	—	39,9	40,0	40,5	40,0	39,6	—	—	39,6	—	39,5	—	—	—	39,1	—	—
ESR (mm/hr)	Zhuchka	5	3	—	15	—	4	—	4	—	—	15	—	—	21	—	—	18	18
	Pal'ma	2,5	4	—	12	—	2	—	12	—	—	—	7	—	12	—	—	25	12
	Ryzhii	2,5	—	7	—	—	5	5	—	15	—	—	10	12	—	20	23	—	—
Number of erythrocytes (in millions)	Zhuchka	5,0	4,78	—	4,46	—	4,29	—	4,22	—	—	3,41	—	—	3,4	—	—	3,15	2,4
	Pal'ma	5,0	4,79	—	4,03	—	4,04	—	4,21	—	—	3,94	3,27	—	3,82	—	—	4,37	3,8
	Ryzhii	4,5	—	4,03	—	—	4,34	4,05	—	3,84	—	—	3,44	3,14	—	3,43	4,09	—	—
Hemoglobin (in % according to Sahli)	Zhuchka	95	90	—	94	—	87	—	75	—	—	74	—	—	70	—	—	65	—
	Pal'ma	108	—	—	75	—	82	—	82	—	—	70	65	—	75	—	—	82	72
	Ryzhii	102	—	85	—	—	92	84	—	78	—	—	70	68	—	68	78	—	—
Number of leukocytes (in thousands)	Zhuchka	8,4	7,5	—	6,45	—	6,4	—	6,8	—	—	17,85	—	—	8,35	—	—	16,8	11,8
	Pal'ma	7,3	6,8	—	8,1	—	3,9	—	7,15	—	—	7,0	5,46	—	7,0	—	—	3,7	3,0
	Ryzhii	6,0	—	7,8	—	—	6,6	6,45	—	9,2	—	—	11,3	10,6	—	11,4	15,25	—	—

*Average indices before infection.

Sluggishness was observed in the dog Ryzhii starting the 7th-8th day after infection, and the playful reflex disappeared. Acute deterioration of condition (weakness, unsteady gait) was observed starting the 54th day. The dog died 63 days after infection. The autopsy disclosed 1.5 liters of serohemorrhagic exudate in the abdominal cavity, while the liver, lung, and kidneys were found to be completely overrun with miliary tubercles.

Before the infection, Ryzhii's motor-defense conditioned reflexes were marked by extreme instability, and their indices were usually low. The differentiation was incomplete. During the period comprised of the first to the ninth day after infection, the differentiation became somewhat reinforced, intersignal excitation increased, and the motor-defense positive conditioned reflexes improved, becoming clearer and more tonic. Then, after a nine-day slump, there was an abrupt and extraordinary improvement in conditioned reflex activity for 21 days. The reflexes to all the positive conditioned stimuli became sharper and more adequate than ever before, and the differentiation became stronger. Respiration became much slower. The aftereffect to the weak stimulus (the light) was enhanced (especially from the 34th to the 56th days): the delay in dropping the paw reached 12 sec.

Comparing the results of the observations on each of the three experimental dogs, one can distinguish certain common features of both the clinical picture of tuberculosis and the functional condition of the cerebral cortex. The common clinical symptoms comprised the following (see table): 1) increase in body temperature on the 9th-14th day, followed by a decrease; 2) progressive weight loss beginning the 5th-10th day after infection; 3) erythropenia throughout the postinfection period; 4) reduced hemoglobin content of the peripheral blood; 5) E.S.R. considerably accelerated, with maximal acceleration observed on the 46th-64th day; 6) positive Mantoux test on the 13th-15th day; 7) loss of appetite and change in general condition (sluggishness, ataxia) observed in all the dogs, but at different intervals after infection; 8) sectional demonstration of tuberculous tubercles, primarily in the lungs and kidneys. All these features leave no doubt as to the severity of the course of the tuberculous process.

As to conditioned reflex activity, graphically expressed, it formed two waves, or four phases, in all of the dogs: 1) on the 3rd-7th day after infection, an increase in the sum of the positive conditioned reflexes and reinforcement of the differentiations; 2) beginning the 9th day, some decrease in the sum of the positive conditioned reflexes; 3) then, at different times after the infection, a considerable increase in the sum of the positive conditioned reflexes: in Zhuchka, the 13th-15th days; in Pal'ma, the 16th-36th days; and in Ryzhii, the 39th-56th days after infection; 4) acute premortal decrease of all conditioned reflexes.

The most general features of the higher brain sections' reaction to tuberculous infection, therefore, occur during the first few days when the intervals and character of change in the motor-defense conditioned reflexes almost exactly coincided in the different dogs. The more individual features of the reaction appear later.

During the first phase, moreover, the increase and qualitative improvement in the defense conditioned reflexes, attended by increased general excitability (intersignal reactions, etc.), coincide with deterioration of the clinical indices of the tuberculous process (accelerated E.S.R., leukocytosis), while the opposite is true during the second phase, which is clearly evident upon comparison of Figs. 1, 2, and 3.

Before the last days of life, while the experimental dogs could still stand and move about, the motor-defense conditioned reflexes were clear and adequately expressed (the dog Zhuchka was, to some extent, the exception, as she developed symptoms of general intoxication very rapidly).

The authors of the works cited at the beginning of this article indicated a considerable decrease in the food conditioned reflex. They drew the general conclusion that the efficiency of the cerebral cortex as a whole regularly diminished under the influence of the infection.

In our experiments with motor-defense conditioned reflexes, however, we observed conditioned reflex activity to be extraordinarily stable; this seems to be due to the tonicizing effect of infection upon the defense center.

The data we obtained, therefore, casts doubt on the existing opinion concerning the disturbance of higher nervous activity which is alleged to occur under any circumstances in dogs with experimental tuberculosis. The change which takes place in food conditioned reflexes does not seem to be the general rule in the pathology of higher nervous activity. On the other hand, all these data can serve to point up the fact that, in research in higher nervous activity, it is not enough to ascertain only the physiological mechanism of a reaction; the biological significance of each of the animal's reactions must also be taken into account, as has been demonstrated particularly clearly in the works of G. A. Obraztsova [6], É. Sh. Airapet'yants [1], P. K. Anokhin [2], et al.

SUMMARY

After the elaboration and consolidation of a system of motor-defense reflexes in 3 dogs, the animals were infected intravenously with Mycobacterium tuberculosis (Walle strain) in the dose of 0.75 mg per kg of body weight. Four phases in the change of conditioned reflex activity were noted against the background of progressing disease: 1) improvement during the first days after the infection; 2) some reduction; 3) considerable and prolonged improvement; 4) preterminal reduction of the reflexes. The first phase coincided with the exacerbation of tuberculosis (increased erythrocyte sedimentation rate, leukocytosis), the second – with its temporary abatement (some normalization of the clinical indices). Later, such coincidence was not constantly observed. A suggestion was made as to the regular sequence characterizing the reaction of the higher portions of the brain to tuberculosis, i.e., the general features are manifested first, the individual, later. Our data on the absence of stable disturbance of defense reflexes during tuberculosis were compared with contrary results, obtained by the food reflex method (literature data). It is suggested that the defense center excitability is increased by the development of infection. A conclusion was drawn that the data obtained with the food conditioned reflexes are not applicable to the higher nervous activity as a whole.

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