FUNCTIONAL STATE OF POSTERIOR HYPOTHALAMIC STRUCTURES OF RABBITS WITH EXPERIMENTAL TUBERCULOSIS

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An increase in the number of active neuron groups was found in the region of the posterior hypothalamic nucleus, most marked in the early periods after infection of rabbits with a virulent strain of Mycobacterium tuberculosis. In the basal portions of the posterior hypothalamus (supramamillary and mamillary region), the number of active neuron groups was reduced.

Investigations have shown [1,2,4-9,11,12,14,16] that the hypothalamus plays an important role in the development of protective reactions to infectious and antigenic stimuli. In particular, the work of Korneva and Khai [5-7,9] proved conclusively the important role of the posterior hypothalamic nucleus in antibody production. Pituitary ACTH, production of which is considered to be controlled by centers in the posterior hypothalamus [10,13,15,17], also undoubtedly participates in the processes of infection and immunity.

The present investigation was carried out to study functional properties of the posterior hypothalamus in experimental tuberculosis.

EXPERIMENTAL METHOD

Rabbits weighing 3-3.5 kg were used in the experiments. The animals were infected by intravenous injection of 0.15 mg of a culture of a virulent strain (No. 109) of Mycobacterium tuberculosis. The experiments were carried out on the 3rd-5th, 11th-16th, and 20th-25th days after infection. At each of these times four rabbits were used in the experiments. Control (healthy) rabbits (three groups, each with four animals) were investigated simultaneously.

Tracheotomy was performed under superficial hexobarbital anesthesia, Listhenon was injected intravenously, and the animals were maintained on controlled respiration (the DP-5 apparatus). The rabbit's skull was fixed in a stereotaxic apparatus, and the vault of the skull was exposed under local anesthesia (0.25% procaine). The experiment started 40-60 min after the operation, allowing the animal to awaken completely from the anesthetic.

Activity of groups of neurons was investigated by means of tungsten microelectrodes (tip 4-10 μ in diameter) using an extracellular recording technique. An electrophysiological apparatus (designed and built at the experimental workshops of the Institute of Experimental Medicine) incorporating a cathode follower was used. Recordings were made on film from the oscilloscope screen.

The microelectrode was introduced in accordance with stereotaxic coordinates into the posterior hypothalamic nucleus. Next, by means of a micromanipulator, it was advanced in steps of 60 μ for a distance of 3000 μ. The superior part of its track corresponded to the posterior hypothalamic nucleus, the inferior part to the mamillary region. The presence or absence of unit activity was observed at each 60-μ stage. Tracks of this type were investigated symmetrically on both sides of the 3rd ventricle.

After the end of the experiment, the electrode was fixed to the bones of the vault of the skull by means of acrylic glue, the bones of the vault were removed, and the brain widely exposed (only a narrow bridge of bone in which the electrode was fixed was left behind). Using a double-edged scalpel fixed in the holder of the stereotaxic apparatus, frontal sections of the brain tissue were cut anteriorly and posteriorly to the electrode and parallel to it, after which the animal's head was placed for 7-10 days in 10% neutral formalin solution. Frontal sections of the brain tissue were cut on a freezing microtome to determine the position

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TABLE 1. Functional State of Posterior Hypothalamic Structures (by 600-micron stages) in Rabbits with Tuberculosis

Time after infection	№	Zone	Number of 60-micron stages		m_p	Student's t criterion	P
			total	active			
3—5 days	1	1	88	66	4	1/6=8,7	<0,001
	2	2	80	30	5	2/7=0,65	>0,05
	3	3	80	36	5	3/8=1,66	>0,05
	4	4	80	12	4	4/9=9,7	<0,001
	5	5	80	12	4	5/10=14,0	<0,001
Control 1	6	1	88	18	4	—	—
	7	2	80	34	5	—	—
	8	3	80	47	5	—	—
	9	4	80	61	5	—	—
	10	5	74	63	4	—	—
11—16 days	11	1	88	51	5	11/16=5,3	<0,001
	12	2	80	25	5	12/17=1,06	>0,05
	13	3	80	27	5	13/18=0,8	>0,05
	14	4	80	10	4	14/19=6,5	<0,001
	15	5	80	9	3	15/20=12,5	<0,001
Control 2	16	1	88	19	4	—	—
	17	2	80	31	5	—	—
	18	3	80	31	5	—	—
	19	4	80	44	5	—	—
	20	5	80	64	4	—	—
20—25 days	21	1	88	32	5	21/26=3,1	<0,002
	22	2	80	13	4	22/27=1,5	>0,05
	23	3	80	3	0,5	23/28=6,2	<0,001
	24	4	80	3	0,5	24/29=6,2	<0,001
	25	5	80	0	0	25/30=10,9	<0,001
Control 3	26	1	88	14	4	—	—
	27	2	80	21	5	—	—
	28	3	80	32	5	—	—
	29	4	80	33	5	—	—
	30	5	80	48	5	—	—

Note. Student's criterion of significance of the difference was determined for lines in the table corresponding to serial numbers of stages represented as fractions.

of the electrode track in the hypothalamus. * Only those experiments were analyzed in which the electrode track corresponded to that indicated in Fig. 1. After the experiment, the animal was autopsied to determine the stage and degree of development of tuberculosis.

To estimate the severity of the tuberculosis from the period of survival of the animals, groups of 5 rabbits were infected simultaneously with the experimental animals with the same dose of mycobacteria.

EXPERIMENTAL RESULTS AND DISCUSSION

The assumption was made that in the case of excitation of the investigated structures, the number of active 60-μ stages along the track of the microelectrode will be increased, and in the case of inhibition it will be decreased [3]. The electrode track (3000 μ) was divided into 5 zones, each of 600 μ, the superior zone corresponding to the posterior hypothalamic nucleus (zone 1), and the inferior (zone 5) to the mamillary region.

The total number of 60-μ stages investigated in each of the 600-μ zones and the number of active stages in each zone were counted. Both these indices were determined for the group of animals as a whole and they were compared with each other in accordance with statistical rules for a binomial distribution.

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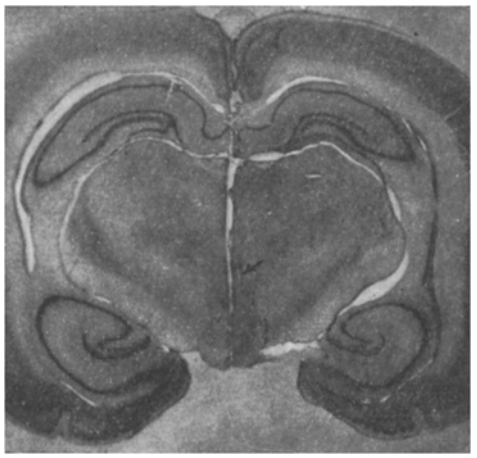

Fig. 1. Frontal section through rabbit's brain at the posterior hypothalamic level. Track of an electrode can be seen to the left of the 3rd ventricle (marked by arrow). Track passes through posterior hypothalamic nucleus and ends in region of mamillary bodies (5 ×).

The experimental results are given in Table 1. In zone 1, corresponding to the posterior hypothalamic nucleus, a considerable increase in the number of active neuron groups was observed at all periods after infection. The increase in activity was particularly marked at the beginning of the disease (3rd-5th day after infection).

At this period no pathomorphological changes visible to the naked eye were present. Activity was high also on the 11th-16th day after infection. At this period, specific pathological changes appeared in the lungs and other organs, and by the end of this period, the changes were of considerable severity.

In the terminal period of the disease (20th-25th day after infection), the activity of this zone was considerably reduced, although it remained higher than in the control animals.

In zones 2 and 3, no statistically significant difference in activity was found between the experiment and control, except in the last period when the decrease in activity in zone 3 was significant.

In zones 4 and 5, corresponding to the supramamillary and mamillary regions, a considerable decrease in activity was present at all periods after infection.

This decrease was all the more obvious because in the control animals these zones possessed the highest activity.

Rabbits infected with the same dose of mycobacteria and left to determine their period of survival died on the 24th-29th day after infection.

The results described indicate considerable changes in the function of the posterior hypothalamic structures in tuberculosis. These changes appear in the early stages of the disease, and they cannot therefore be attributed entirely to the harmful action of the infection. They probably reflect the manifestation of physiological measures against the disease.

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