10. Y. Tsukada, H. Watahe, et al., in: Alpha-Fetoprotein (Proceedings of an International Conference), R. Masseyeff, ed., Paris (1974), p. 521.
11. C. W. Young, G. Schochetman, and D. A. Karnofsky, Cancer Res., 27, 526 (1967).

HEMATOPOIESIS IN RATS AFTER DESTRUCTION OF THE POSTERIOR HYPOTHALAMIC NUCLEI ASSESSED BY BONE MARROW TOTAL CELL COUNT

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The effect of bilateral electrocoagulation of nuclei of the mammillary body and the posterior hypothalamic nucleus on the total cell count in the bone marrow was studied in rats. Destruction of the posterior hypothalamic nuclei led to inhibition of erythropoiesis. The number of mitoses and the total number of erythroid cells were reduced. Granulocytopoiesis, however, was stimulated. Proliferative activity and the total number of immature granulocytes in the bone marrow of the rats were increased.

KEY WORDS: hypothalamus; mammillary body; posterior hypothalamic nucleus; erythropoiesis; granulocytopoiesis.

According to data in the literature destruction of the hypothalamus (especially the nuclei of its posterior part) affects the composition of the blood erythrocytes [2, 5-7]. The present writers have shown in recent investigations [3, 4] that destruction of the posterior hypothalamic nuclei leads to inhibition of erythropoiesis and stimulation of granulocytopoiesis. A decrease in proliferative activity and in the relative percentage of erythroid cells together with an increase in the number of mitoses and in the relative percentage of cells of the granulocyte series were observed in the bone marrow of animals with injured posterior hypothalamic nuclei. Maximal changes were observed on the 3rd day after the operation. It was accordingly decided to study the absolute composition of bone marrow cells of animals at this period.

EXPERIMENTAL METHOD

Experiments were carried out on 78 male rats weighing 250-350 g (18 experimental, 17 control, and 43 intact animals). By means of a stereotaxic apparatus bilateral electrical coagulation of the nuclei of the mammillary body and of the posterior hypothalamic nucleus was carried out with a direct current of 2 mA for 5 sec. A platinum electrode 100 μ in diameter was used for this purpose.

On the 3rd day after the operation the blood vessels of the brain were perfused initially with physiological saline, later with a 10% solution of neutral formalin. The brain was fixed in a 10% solution of neutral formalin for 2-4 weeks, after which it was mounted in gelatin solutions of increasing concentration (from 12 to 24%). To determine the location and volume of the focus of destruction, serial sections through the brain were cut to a thickness of 25-30 μ in the frontal plane and stained by Nissl's method.

Bone marrow for counting the total number of myelokaryocytes and the myelograms was taken from the femur. The total number of myelokaryocytes was counted in 1 mm^3 bone marrow. The experimental results were compared with values for bone marrow taken from two or three intact rats.

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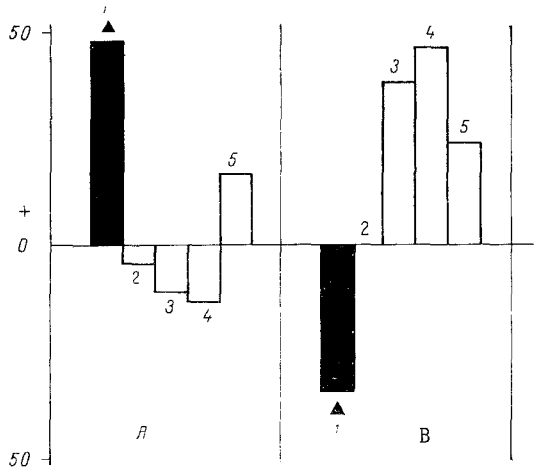

Fig. 1

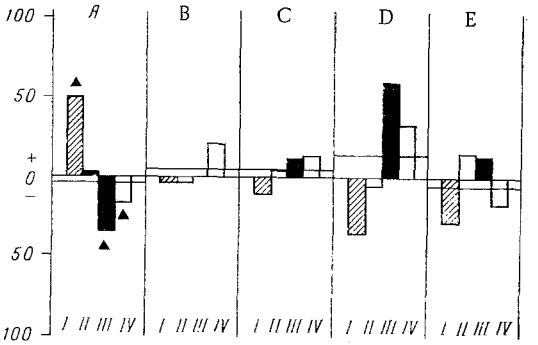

Fig. 2

Fig. 1. Changes in mitotic index of granulocytes (A) and erythroblasts (B) of bone marrow in rats on 3rd day after destruction of posterior hypothalamic nuclei. Abscissa: 1) posterior hypothalamus, 2) first control group, 3) second control group, 4) anterior hypothalamus, 5) middle hypothalamus; ordinate, mitotic index (in % of values for intact rats); ▲ — $P<0.05$.

Fig. 2. Changes in total number of bone marrow cells of rats on 3rd day after destruction of posterior hypothalamic nuclei. A) Posterior hypothalamus (experiment), B) first control group, C) second control group, D) anterior hypothalamus, E) middle hypothalamus. Abscissa: I) immature granulocytes, II) mature granulocytes, III) erythroid cells, IV) lymphocytes; ordinate, absolute number of bone marrow cells (in % of values for intact rats). Continuous line represents total number of myelokaryocytes. ▲ — $P<0.05$.

Control investigations were undertaken on the following groups of animals: on animals with insertion of electrodes into the nuclei of the posterior hypothalamus, without subsequent electrocoagulation (first control group), animals in which subcortical structures outside the hypothalamus (lateral geniculate body) were destroyed (second control group), animals in which nuclei in the anterior part of the hypothalamus (supraoptic and paraventricular nuclei) were destroyed; animals in which nuclei in the middle part of the hypothalamus (dorsomedial and ventromedial nuclei) were destroyed.

The numerical results were subjected to statistical analysis [1].

EXPERIMENTAL RESULTS

On the 3rd day after destruction of nuclei in the posterior hypothalamus the animals showed a tendency for the total number of myelokaryocytes, on average per 20,000 cells, to decrease. Significant differences in the number of myelokaryocytes, however, were not observed between the experimental and control animals.

After destruction of the posterior hypothalamic nuclei of the rats the number of mitoses in granulocytes was increased on average by almost 1.5 times ($P<0.001$; Fig. 1). Changes in proliferative activity of the granulocytes in the control animals were within limits of physiological variations. The proliferative activity of the erythroblasts of the experimental rats was reduced on average by 34% ($P<0.001$). In animals of the first control group the number of mitoses in erythroblasts was unchanged. In rats with destroyed nuclei of the anterior and middle parts of the hypothalamus and in the rats of the second control group, the increase observed in proliferative activity of the erythroblasts was not significant.

The total number of immature granulocytes in the bone marrow of animals with destroyed nuclei in the posterior part of the hypothalamus was significantly increased by 1.5 times (Fig. 2). After destruction of the nuclei of the posterior hypothalamus the total number of erythroid cells was reduced on average by 35% (P 0.001). The total number of lymphocytes

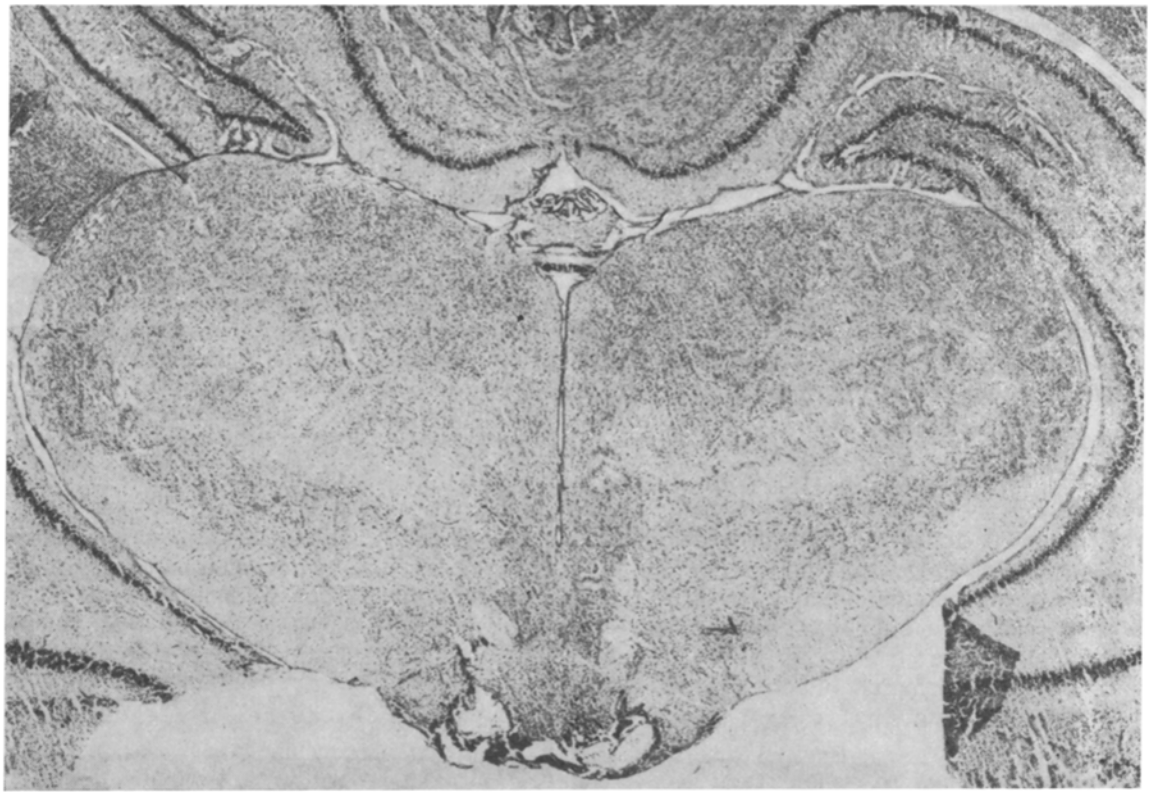

Fig. 3. Frontal section through brain of rat No. 54-2 with focus of bilateral electrolytic destruction of ventral and part of medial portions of medial nucleus of mammillary body.

also was reduced significantly in the experimental animals, on average by 18%. No such changes were found in the bone marrow of the control animals. Changes in the absolute number of bone marrow cells in the control animals of the first and second groups were within the limits of physiological variations. In the animals with destroyed nuclei of the anterior and middle parts of the hypothalamus the absolute number of erythroid cells was increased and the absolute number of immature granulocytes was reduced. These changes were not significant.

After destruction of nuclei in the posterior hypothalamus of the animals marked inhibition of erythropoiesis thus took place: The number of mitoses and the absolute number of erythroid cells were reduced. Stimulation of granulocytopoiesis, however, was observed: an increase in proliferative activity and in the absolute number of immature granulocytes.

The most marked changes in the bone marrow were observed after destruction in the region of the mammillary body. In rat No. 54-2 with bilateral injury to the medial nucleus of the mammillary body (Fig. 3), for instance, proliferative activity was sharply reduced by 60% and the total number of erythroid cells was reduced by more than 33%. The number of mitoses was more than doubled, and the total number of immature granulocytes was increased by 50%. Comparison of these results with those obtained previously [3, 4] and with data in the literature [2, 5-7] confirms the hypothesis that structures in the posterior part of the hypothalamus participate in the regulation of hematopoiesis.

LITERATURE CITED

1. L. S. Kaminskii, Analysis of Clinical and Laboratory Data [in Russian], Leningrad (1959).
2. E. L. Kan, in: Problems of Interoception, Regulation of Physiological Functions, and Behavior [in Russian], Leningrad (1976), p. 71.
3. Z. M. Likhovetskaya, in: Mechanisms of Regulation in the Blood System [in Russian], Part 1, Krasnoyarsk (1978), p. 134.
4. Z. M. Likhovetskaya and A. I. L'vovich, Byull. Éksp. Biol. Med., No. 8, 154 (1979).
5. S. Feldman, E. A. Rochmiewitz, and G. Izak, J. Lab. Clin. Med., 67, 713 (1966).
6. S. Halvorsen, Scand. J. Clin. Lab. Invest., 13, 564 (1961).
7. E. Mirand, J. Grace, G. Johnston, et al., Nature, 204, 1163 (1964).