MORPHOLOGICAL AND FUNCTIONAL STATE OF THE HYPOTHALAMO-HYPOPHYSEAL NEUROSECRETORY SYSTEM IN EXPERIMENTAL FLUOROSIS

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Experimental fluorosis was induced in rats by daily subcutaneous injection of sodium fluoride in a dose of 12 mg/kg for 12 weeks. Similar and synchronous changes were found in the supraoptic and paraventricular nuclei of the hypothalamus in the periods of poisoning and recovery. Changes in the hypothalamo-hypophyseal neurosecretory system found in the latter period can be attributed to the cumulative properties of fluorine.

Chronic fluorine poisoning is a form of geographical and occupational pathology whose importance has increased sharply in recent years with the use of fluorine compounds in industry, agriculture, and medicine. This has led to justified interest in the study of the intimate mechanisms of fluorine poisoning. However, insufficient attention has been paid to the state of the hypothalamo-hypophyseal neurosecretory system (HHNS) in this condition. In particular, the only investigation published in this field is that of Mietkiewski et al. [16] who studied the state of this system in guinea pigs during poisoning with sodium fluoride for 5 weeks, but the investigation did not continue into the subsequent recovery period.

In the study of experimental fluorosis in rats the morphological and functional state of the HHNS was investigated in the periods of poisoning and recovery.

EXPERIMENTAL METHOD

Male albino rats (90) weighing initially 100 ± 20 g received daily subcutaneous injections of sodium fluoride in a dose of 12 mg/kg for 12 weeks and the changes in their HHNS were studied in 40 of these animals during 12 weeks of the recovery period. The control consisted of 40 rats of the same sex and weight not receiving fluorine. Tests were carried out 2 days and 1, 2, 4, and 12 weeks after the beginning of poisoning and also after 1, 4, 8, and 12 weeks of the recovery period. To preserve the anatomical integrity of the HHNS the hypothalamus was removed en bloc with the pituitary and fixed in Bouin's fluid. Serial paraffin frontal sections were stained with aldehyde-fuchsin by Gomori's method.

EXPERIMENTAL RESULTS

The neurosecretory nuclei of the anterior hypothalamus of the control animals were composed of large pear-shaped or irregularly triangular cells. The cell nuclei were large and spherical with well-defined nucleoli. The cytoplasm of the cells was filled with neurosecretory material (NSM) to an extremely variable degree (Fig. 1a). Most of the fibers of the hypothalamo-hypophyseal tract run in the middle zone of the median eminence where considerable deposits of neurosecretion were found. The outer zone of the median eminence was palely stained with aldehyde-fuchsin. The neurohypophysis (Fig. 1b) consisted of numerous

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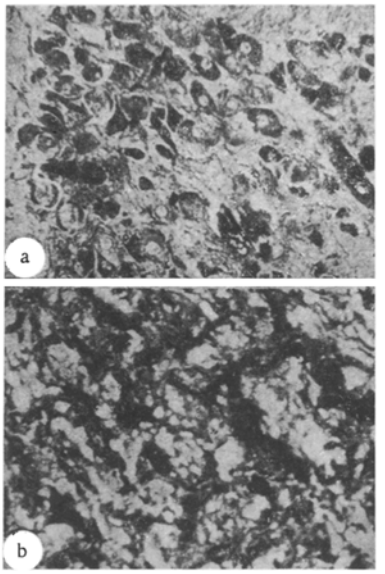

Fig. 1

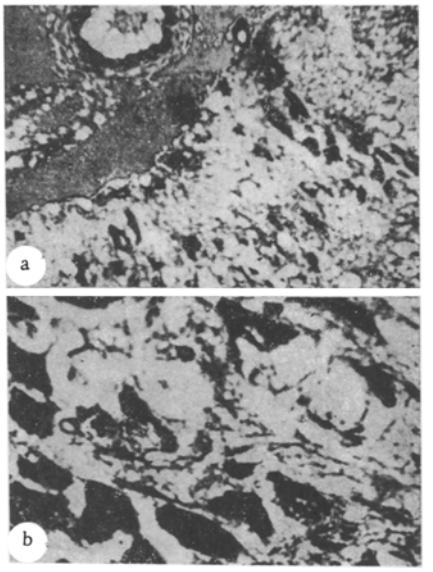

Fig. 2

Fig. 1. Content of NSM in cells of supraoptic nucleus (a) and neurohypophysis (b) of control rat. Gomori's aldehyde-fuchsin, magnification: a) 120 ×, b) 250 ×.

Fig. 2. Changes in HHNS after poisoning for 12 weeks: a) hemorrhage near supraoptic nucleus, reduced content of NSM in its cells; b) two types of changes in neurons of supraoptic nucleus. Gomori's aldehyde-fuchsin, magnification: a) 80 ×, b) 320 ×.

interweaving neurosecretory fibers (axons), a network of capillaries, and glial cells. Many expansions of the axons, filled with deeply stained neurosecretory material (Herring's bodies) were found in this region.

The different periods of poisoning were characterized by differences in functional state of the HHNS, but the changes in the supraoptic and paraventricular nuclei were synchronous. For instance, 2 days after poisoning most neurons in these nuclei of the hypothalamus were large and palely stained, and almost free from neurosecretion. Granules of NSM were usually arranged at the periphery of the cytoplasm or around the border of the optically empty vacuoles. The nuclei of the neurons were large and pale, with clearly outlined nucleoli. In the region of the median eminence along the course of the fibers of the hypothalamo-hypophyseal tract the pools of NSM were appreciably enlarged. In the neurohypophysis the quantity of secretion was reduced. Individual concentrations of NSM granules were found immediately under the ependyma of the infundibulum. By the 4th week of poisoning the decrease in content of NSM in all parts of the HHNS was more marked. After poisoning for 12 weeks severe disturbances of the circulation were observed: dilatation of the pial vessels, which were congested with blood, and diapedetic hemorrhages. These hemorrhages, which varied in severity, were found in the region of the supraoptic nucleus in all cases (Fig. 2a). The nuclei of the anterior hypothalamus contained neurons with changes of two types: 1) palely stained cells in which neurosecretory granules resembling dust particles were diffusely distributed; 2) deeply stained cells whose cytoplasm was filled with a homogeneous mass of confluent granules. The nuclei of these cells were shrunken, obscured by NSM, and their nucleoli were indistinctly outlined (Fig. 2b). When extensive hemorrhages were found close to the supraoptic nucleus, the changes in the neurosecretory cells in that nucleus were mainly of the second type.

The content of NSM was sharply reduced in the region of the median eminence along the course of the fibers of the hypothalamo-hypophyseal tract and in the neurohypophysis. In addition, dilatation of the capillaries was observed in the neurohypophysis.

In tests carried out in the early stages of the recovery period a low content of NSM was observed in the neurons, together with an increase in the volume of the nuclei and hypertrophy of their nucleoli, evidence of hyperactivity of the hypothalamic nuclei. Cells with vacuolated cytoplasm were moderately numerous in them. At the later stages of the recovery period there was a sharp decrease in the number of these

neurons and also of neurons with homogenized cytoplasm. Even after 4 weeks of the recovery period granules of NSM were still not condensed into large masses. After 8 weeks of this period the changes taking place in the HHNS can be regarded as regenerative. This is shown by the increase in the NSM content in neurons of the anterior hypothalamic nuclei and also along the course of fibers of the hypothalamo-hypophyseal tract, both in the region of the median eminence and in the neurohypophysis. The distribution of NSM in the different parts of the HHNS 12 weeks after cessation of administration of sodium fluoride was indistinguishable visually from the control.

The first days of fluorine poisoning are thus associated with features reflecting increased activity of the HHNS. In chronic fluoride poisoning a disturbance of the function of the HHNS was observed, giving rise to severe pathological states of the secretory neurons of the anterior hypothalamic nuclei, manifested as pycnosis and homogenization of the cells or as a sharp decrease in their content of NSM. Similar changes in the nuclei of the anterior hypothalamus have been observed [13] under various experimental conditions. The predominance of severely damaged neurons at the height of poisoning may be connected with the circulatory disturbances in this region [7].

Many investigations have shown that the morphological and functional response of the supraoptic and paraventricular nuclei to various experimental procedures may differ in character [1, 3, 5, 6, 11, 15, 17]. On the other hand, synchronous and similar changes in these hypothalamic nuclei have been observed after burns [10], exposure to gravitational overloads [12] and hypokinesia [4], and also in fluorine poisoning [16].

A close connection has been established between the hypothalamus, adenohypophysis, and other glands of internal secretion, notably the thyroid. In particular, Voitkevich [8] considers that the state of thyroid function is reflected directly in the formation of neurosecretion. From this point of view the statement of Aleshin [2] that a synchronous and similar response is observed in the supraoptic and paraventricular nuclei during blocking of hormone formation in the thyroid gland by thyrostatic agents, is of definite interest. The thyrostatic effect of sodium fluoride observed by the writers in rats [9] is in agreement with the fact established previously that fluorine has a direct inhibitory effect on the adsorption of inorganic iodine [14]. In this connection the similar and synchronous changes in the supraoptic and paraventricular nuclei of the hypothalamus in experimental fluorosis are evidently due to the general toxic and thyrostatic action of fluorine. In the recovery period the HHNS remains for a long time in a state of functional stress, evidently due to the cumulative properties of fluorine.

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