MORPHOLOGICAL ANALYSIS OF THE STATE OF THE HYPOTHALAMO-HYPOPHYSEAL NEUROSECRETORY SYSTEM AND THE THYROID GLAND OF ALBINO MICE SUBJECTED TO PROLONGED SALT LOADING

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During prolonged salt loading, the secretion of a neurosecretory substance into the blood stream is observed initially (first phase), and this is followed by restoration of its original concentration (the second phase) [11].

The object of the present investigation was to examine the possible functional relationship between the hypothalamo-hypophyseal neurosecretory system (HHNS) and the thyroid gland and also to determine the mechanism by which the neurosecretory influences are effected.

EXPERIMENTAL METHOD

Experiments were carried out on noninbred male albino mice initially weighing 14-23 g. The animals in the experimental group received their normal ration of dried oats and bread, with a 5% NaCl solution instead of drinking water. Material was taken from three animals at the same time of day on the 3rd, 6th, 9th, 11th, 14th, 21st, and 30th days. The animals in the experimental group at first grew emaciated and sometimes died, but toward the end of the experiment they were observed to gain in weight. The brain, fixed by Carnoy's method, and the pituitary and thyroid, fixed by Bouin's and Zenker's methods, were investigated. Paraffin sections of the brain were stained with gallocyanin by Einarson's method and by Feulgen's method, while similar sections of the pituitary and thyroid were stained with paraldehyde-fuchsin by the Gomori – Gabe method and with azan by Heidenhain's method. Karyometry of the nuclei of the neurosecretory cells was carried out on enlarged photomicrographs, and histophotometry of the neurosecretion in the principal posterior part of the neurohypophysis was carried out by means of the MF-4 microphotometer by an original method [13]. The results of measurement of the height of the cells forming the thyroid epithelium were analyzed by statistical methods: 4 cells in each follicle, making 240-270 cells in the whole gland, and the internal diameter of the follicle were measured.

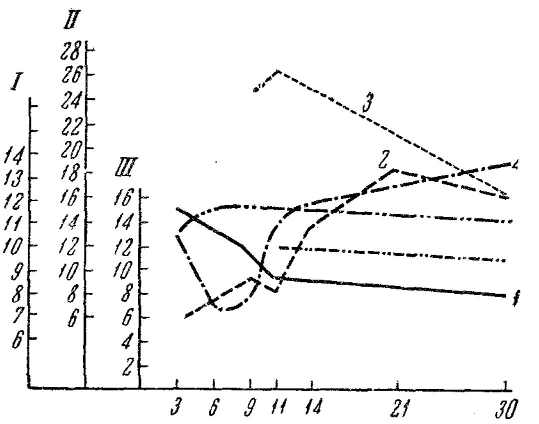

Fig. 1. Dynamics of changes in the indices of the state of the hypothalamo-hypophyseal neurosecretory system and thyroid gland. Along the axis of ordinates: I) height of thyroid epithelial cells (in μ; 1 – control, 2 – experiment); II) amount of neurosecretion in the posterior lobe of the pituitary (in conventional units; 3 – control, 4 – experiment); III) area of nuclei of cells of the supraoptic nucleus (in $cm^2 \cdot 10^{-6}$; 5 – control, 6 – experiment). Along the axis of abscissas – days of the experiment.

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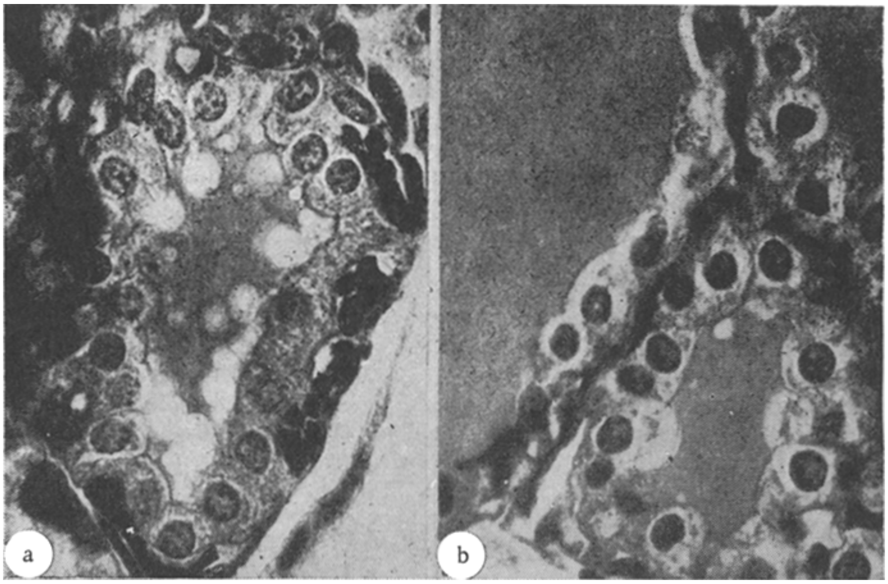
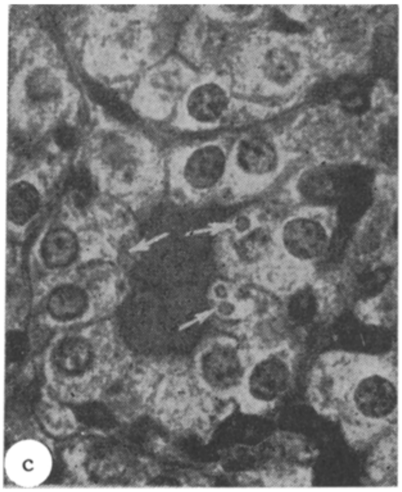

Fig. 2. Principal types of follicles in the thyroid gland. a) Control, zone I, 3rd day after the beginning of the experiment; b) experiment, zones I-III, 3rd day; c) experiment, zone III, 6th day. The arrows indicate droplets of intracellular colloid. Azan. Objective 30×, ocular 10×.

EXPERIMENTAL RESULTS

The results are given in Fig. 1.

Three days after the beginning of the experiment the thyroid of the control animals contained follicles in three states: zone I (including the upper and lower parts of the gland and the part next to the trachea) contained follicles measuring about 20 × 25 μ, of various shapes, with numerous resorption vacuoles (Fig. 2a) with cells 6-18 μ in height. In the apical parts of the cells vacuoles were often seen, and occasionally droplets of intracellular colloid were present; zone II – the outer zone of the macrofollicles, up to 90 μ in size, with homogeneous colloid and containing no resorption vacuoles. The height of the cells was 4-16 μ; the inner zone of the microfollicles, up to 10 × 20 μ, in the central part of the gland. The follicles were oval in shape and contained homogeneous colloid and cells 4.8-13.2 μ in height with basal nuclei, and hardly any vacuoles in the cytoplasm. The mean height of the cells of the thyroid epithelium for the gland as a whole was 12.20 ±0.2 μ. On the 9th day after the beginning of the experiment the follicles in zones I and II in the control animals measured up to 60×90 μ and contained a moderate quantity of slightly vacuolated colloid and cells 8.4-12 μ in height, sometimes with a few apical or basal vacuoles and centrally situated nuclei. In zone III, the follicles measured up to 12×18 μ and the height of the cells was 6.0-8.4 μ. The mean height of the cells in the gland was 10.45±0.17 μ. On the 11th-30th day of the experiment in the thyroid of the control animals there was a well-defined tendency for depression of the functional activity [1-6, 10]. For instance, the mean height of the cells in the gland on the 11th day was 9.12±0.12 μ, and on the 30th day it was 8.47±0.24 μ.

Hence, in the control animals at different periods of the experiment the thyroid was in a moderately active functional state with a tendency for its activity to diminish towards the end of the experiment. In the neurohypophysis a decrease in the content of neurosecretory substance was observed toward the end of the experiment. These changes in the thyroid and neurohypophysis were evidently related to age.

In the experimental animals, 3 days after the salt loading began, the follicles in zone I of the thyroid were large, measuring up to 30 × 90 μ, and they contained a few resorption vacuoles and cells measuring 9.6 × 14.4 μ. The nuclei of these cells lay in the apical or central part of the cytoplasm, and the latter also contained apical (few) and basal (many) vacuoles. In addition, intracellular colloid was often seen. Zone II contained macrofollicles, measuring up to 100 μ, with dense colloid, not containing resorption vacuoles, and with low cells 3.6-7.2 μ in height. In zone III, the follicles measured up to 15 × 30 μ and contained homogeneous colloid with rare single resorption vacuoles (Fig. 2b). The height of the cells was 4.8-8.4 μ and they contained intracellular colloid. The mean height of the cells was 7.68 ± 0.12 and 7.33 ± 0.11 μ.

On the 6th day after the beginning of the experiment, vacuoles were almost absent from the cells in all the zones but numerous droplets of intracellular colloid were present. These droplets were surrounded by a distinct and optically empty sphere (the pericolloid membrane [5]; Fig. 2c). The mean height of the cells of the thyroid epithelium was 7.94 ± 0.11 and 8.46 ± 0.15 μ.

On the 9th day of the experiment the follicles in zones I and II contained a small amount of badly stained colloid, numerous resorption vacuoles, and cylindrical cells from 8.4 to 14 μ in height. The cytoplasm of the cells contained many basal vacuoles, and the nuclei were situated usually in the apical part. In zone III the follicles measured up to 12 × 18 μ, the colloid was highly vacuolated, and the cells were of moderate height, 9.6-12 μ. The cytoplasm contained a few apical or basal vacuoles but no intracellular colloid. Often hardly any colloid was present in the follicles and their lumen became slit-like. The mean height of the cells was 10.1 ± 0.19 and 11.3 ± 0.14 μ.

On the 11th day of the experiment zones I and II contained distended, but not large follicles, filled with finely granular colloid, resorbed at the periphery, very similar to those in the experiment on the 9th day. In zone III, however, there were no completely empty follicles. The mean height of the cells was 8.25 ± 0.14 and 9.08 ± 0.12 μ.

On the 14th, 21st, and 30th days of the experiment the thyroids showed a tendency toward increased activity compared with the control. On the 21st day, for instance, the follicles of the gland contained little colloid, and in its central part they were almost empty. The height of the cells increased from 11.59 ± 0.18 μ on the 14th day to 13.88 ± 0.17 μ on the 21st day and 12.61 ± 0.16 μ on the 30th day.

The changes in the thyroid of the experimental mice compared with the control demonstrate a fall in the functional activity on the 3rd-6th day and an appreciable rise on the following days. Since on the 3rd-6th day numerous droplets of intracellular colloid were found in the cells of most follicles (of zones I and III), it may be concluded that the processes of colloid secretion were disturbed. It has been reported [1-6] that during inhibition of the thyrotropic reaction the sudden cessation of secretion of colloid from the cells into the blood stream is characterized by the presence of droplets of intracellular colloid.

The results of the study of the content of neurosecretion in the neurohypophysis showed that on the 3rd day of the experiment it was reduced by almost 50% (control 25.4 units, experiment 13.2 units), and on the 6th day it reached a minimum (6.6 units) or the neurosecretion had almost completely disappeared. Later, on the 9th day of the experiment, the quantity of neurosecretion gradually increased and reached the control level, which in some cases it exceeded on the 30th day. The nuclei of the neurosecretory cells of the supraoptic nucleus increased considerably (almost by 1.4 times) on the 6th day of the experiment, and then gradually diminished, although by the 30th day they were still larger in the experimental animals than in the controls.

Analysis of the results described above revealed reciprocal relationships between the functional activity of the thyroid and the HHNS. For instance, in the first phase of the experiment with salt loading (3rd-8th days), when the secretion of a very large quantity of hormones contained in the neurosecretory substance was observed from the neurohypophysis, inhibition of the functional activity of the thyroid took place; in the second phase, starting on the 9th-11th days, when the accumulation of neurosecretory material was observed in the neurohypophysis, an increase in the thyroid activity was observed. Next followed a period (from the 21st day of the experiment) when the quantity of neurosecretion in the neurohypophysis reached or even exceeded the control level, while high activity was observed in the thyroid. Similar results in relation to the state of the HHNS have been obtained in albino rats subjected to chronic salt loading, in which condition a decrease in the functional activity of the thyroid was also observed in the period of diminution of the quantity of neurosecretory substance in the neurohypophysis, [12]. A sharp decrease in the percentage uptake of I^{131} by the thyroid has also been described following administration of a single dose of highly concentrated sodium chloride solution [18].

The results obtained in the control animals also showed that an increase in the quantity of neurosecretion in the neurohypophysis is accompanied by an increase in thyroid activity.

It follows from all these results that the biologically active substances of the neurosecretion – the neurohormones – enter the general circulation in large amounts and for a long period (about 5 days), and inhibit the functional activity of the thyroid in the phase of secretion. It is postulated that during salt loading the neurohormones have a direct effect on the thyroid function by a para-adenohypophyseal mechanism [15]. These views have been confirmed by physiological investigations [7-9, 14, 16, 17, 19] showing that injection of large doses of neurohypophyseal hormones causes depression of the functional activity of the thyroid.

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