ULTRASTRUCTURAL CHANGES IN THE NEUROHYPOPHYSIS DURING AUTOLYSIS

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Transplantation of organs and tissues, including of endocrine glands, has nowadays become a constant necessity, for existing hormonal treatment cannot completely replace the function of glands of internal secretion. A method of transplantation of the pituitary gland on its arteriovenous connections, together with nuclei of the anterior hypothalamus, in the form of a single hypothalamo-hypophyseal complex, has been developed and introduced into clinical practice [7], and has resulted in functioning not only of the anterior lobe of the pituitary gland (adenohypophysis), but also of its principal posterior lobe (the neurohypophysis). However, important criteria such as the permissible times of removal and preservation of viability of the hypothalamo-hypophyseal complex for transplantation have not yet been finally established and need morphological verification.

The aim of the present investigation was to determine the viability of the neurosecretory cells of the posterior lobe of the pituitary gland on the basis of criteria of preservation of their ultrastructure at different times after removal of the material.

EXPERIMENTAL METHOD

Light-optical and electron-microscopic investigations were carried out on 25 noninbred albino rats. The animal's brain was removed from the cranial cavity under ether anesthesia immediately after decapitation. This procedure lasted virtually not more than 5 min. The material taken at these times constituted the control group. In the other series of experiments material was taken 30 min and 1, 3, and 6 h after decapitation. Fixation of the tissue for light microscopy was carried out in 10% formalin solution by Lillie's method, and embedded in paraffin wax. Sections were stained with hematoxylin and eosin and by Nissl's method. Material for electron microscopy was treated by the traditional method. The preparations were studied in "Tesla BS-500" and "Philips-201-C" electron microscopes. The state of the cells of the neurohypophysis at different times after removal of the material was assessed by comparison with descriptions of its normal structure given in the literature [2, 6, 8].

EXPERIMENTAL RESULTS

The light-optical study of the neurohypophysis at all the above times of autolysis revealed no appreciable changes in its structural components compared with the control.

The results of electron microscopy are described for individual structures and times of taking of the material. The density of the chromatin was reduced in the nuclei of the pituicytes and of individual nerve cells of the neurohypophysis 30 min after decapitation, and was distributed uniformly with zones of slight condensation. The perinuclear space throughout the perimeter of the nuclei was uniform and consisted of a narrow slit. The cytoplasmic membranes were intact except those of the mitochondria, which in some cells had undergone focal swelling or appeared moderately swollen with intact cristae and with a matrix of low electron density. In other cells the mitochondria were represented by pale vacuoles, surrounded by a double membrane (Fig. 1a).

Herring's bodies were filled with elementary, disintegrating, and residual neurosecretory granules, with mitochondria with fragmented cristae, neurofibrils, and residual organelles in their center. The hyaloplasm had a matrix of average electron density with

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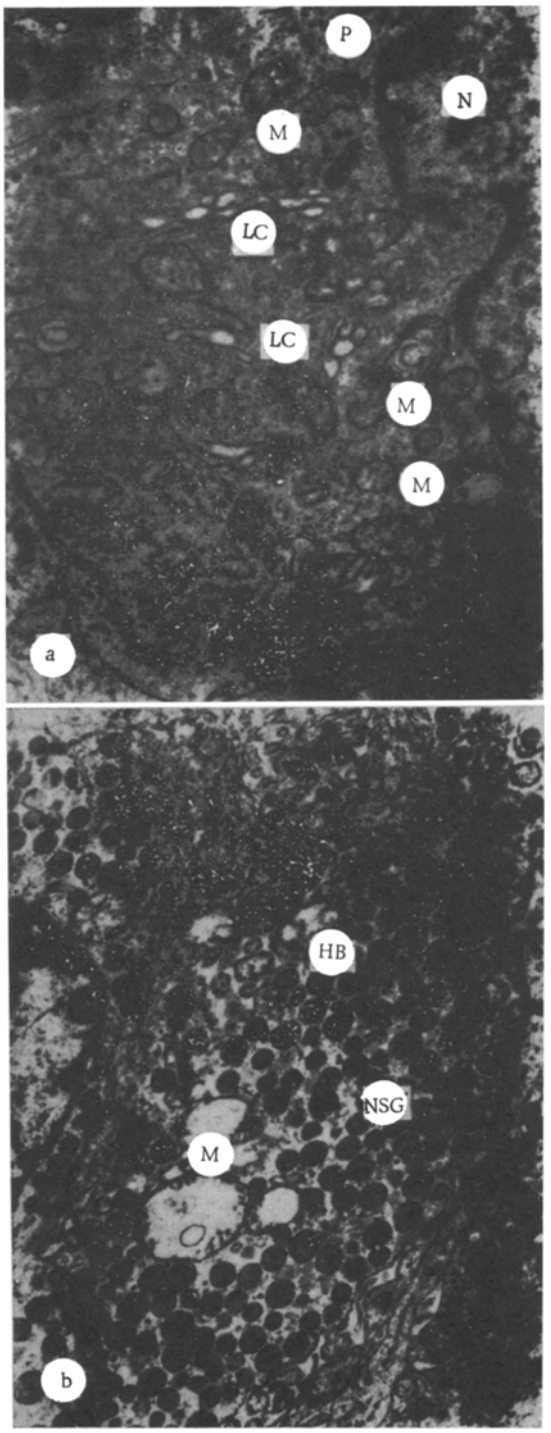

Fig. 1. Ultrastructure of a pituicyte after 30 min. a) Swollen mitochondria (M), loosely arranged lamellar complex (LC), polysomes (P), in cytoplasm of a pituicyte. 14,000 ×; b) Herring's bodies (HB) — neurosecretory ending with neurosecretion granules (NSG): greatly swollen mitochondria (M) in center in the form of pale vacuoles surrounded by a membrane; (N) — nucleus 10,000 ×.

intact membranes (Fig. 1b). Numerous vessels of capillary type with a well-marked basement membrane and fenestrated endothelium were found among the pituicytes.

A similar picture of ultrastructural changes in the neurohypophysis also was observed 1 h after decapitation. A decrease in the quantity of chromatin in the central regions and its condensation along the nuclear membrane were observed in the pituicyte nuclei 3 h after

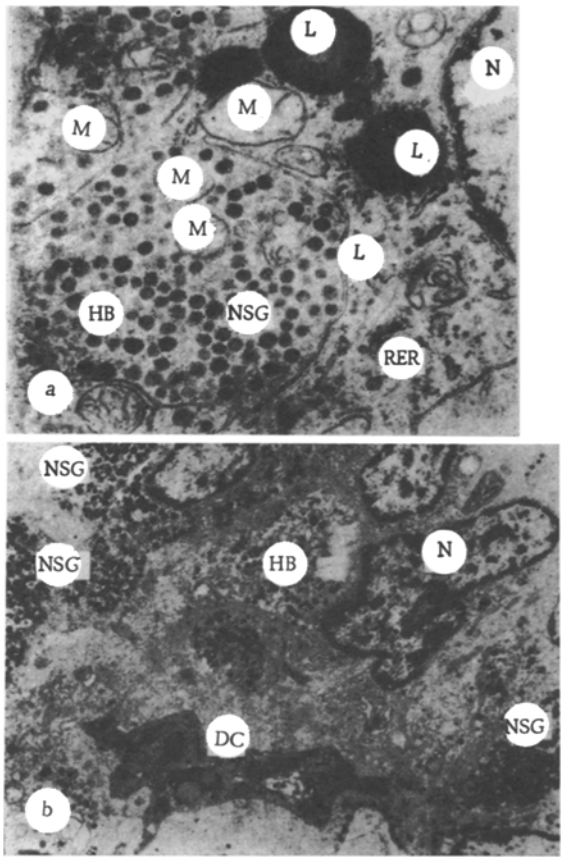

Fig. 2. Fragment of pituicyte: a) 3 h after decapitation lipid inclusions (LI), mitochondria with destroyed matrix and cristae in cytoplasm. In Herring's bodies (HB) granules of neurosecretion (NSG) and swelling mitochondria (M) are present. 14,000 ×. b) 6 h after decapitation. Destructively changed cells (DC) present among neurohypophyseal cells. Neurosecretion (NSG) is clearly defined in cytoplasm of cells in Herring's bodies (HB); (N) – nucleus 3400 ×.

decapitation. Considerable lipid accumulation, accompanied by swelling of the mitochondria, and also secondary lysosomes with membrane and granular cell components, forming large autophagic vacuoles, were found in the cytoplasm of individual cells. Elements of the lamellar complex were widened. Swollen mitochondria were found both in Herring's bodies and in the cytoplasm of the capillary endothelium. On the whole, however, most cells had a normal ultrastructure (Fig. 2a).

The cytoplasm of the pituicytes and secretory neurons 6 h after decapitation was swollen, its outlines became less distinct and more diffuse, and they had the appearance of ameboid processes. Due to edema the cells were arranged a long distance apart. As a result of considerable swelling, destructive changes increased sharply in the organelles. The cytoplasmic membrane in some cells was torn and organelles and neurosecretory granules were dissipated into the intervellular space. Elements of the lamellar complex and cisterns of the rough endoplasmic reticulum were greatly dilated and vacuolated. Chromatin in nuclei of individual cells was distributed in dense, compact masses, and its clumps were enlarged (Fig. 2b). On the whole, after 6 h some clearing of the nucleus and cytoplasm of the neurohypophyseal cells was noted.

The same picture also was characteristic of Herring's bodies, where a decrease in the electron density of the hyaloplasm, rupture of its membrane in some areas, and gross swelling of the mitochondria could be clearly seen. However, despite the marked destructive changes in individual organelles, the neurosecretory granules underwent no changes of any kind, nor did the quantity of neurosecretion in them. Among cells of the neurohypophysis some were destroyed or showed evidence of lysis. As regards the microcirculatory bed, the blood vessels examined showed no destructive changes. Sinusoidal capillaries were tightly packed

with deformed erythrocytes. Incidentally, besides cells with destructive changes, perfectly normal cells with their structure preserved also were found even at this time.

The results agree with data in the literature on the general principles of autolysis of brain nerve cells. For instance, the time course of autolytic changes in intracellular organelles of the human and rat brain, described in [1, 9], could be traced in detail over a long period of time — from 1 to 24 h. The most general change in autolysis was shown to be swelling of all organelles of the nerve cells starting with the 1st hour after death. Anders [3] observed a satisfactory degree of preservation of the cerebral cortical ultrastructure in man during the first 3 h after death. Swelling of intracellular organelles has been described by many investigators who have studied postmortem changes in neurons and glial cells of the brain in both the early and late stages [4, 5, 10, 11].

No information could be found in the literature on postmortem changes in the neurohypophysis at the ultrastructural level.

As was pointed out above, mild autolytic changes in ultrastructures of the rat neurohypophysis were found in these experiments during the first 3 h, and this can be explained by the faster cooling of the rat neurohypophysis, with its exceptionally small volume. However, their swelling, especially of the mitochondria, which was noted in the early stages after death (during the first 30 min), when mitochondria with lysis of their cristae were found in some cells in the form of optically empty vacuoles, surrounded by a double membrane, also was a stable feature for all neurosecretory cells.

The "mosaic" pattern of the autolytic changes in the ultrastructural components of the rat neurohypophysis, manifested clearly at all times, must be particularly emphasized: besides well preserved cells (in the early stages), cells with definite signs of destruction also were present.

A no less important problem is the possible reversibility of the ultrastructural changes discovered. This applies in particular to mitochondria, for we know that a change in these organelles assumes their regeneration. Destruction of the outer membrane is evidently the main sign of death of these organelles. However, this phenomenon is observed quite rarely. It is therefore very difficult to assess the extremely widespread changes in the mitochondria as being exclusively autolytic.

Ultrastructural analysis of the secretory cells of the neurohypophysis (neurosecretory cells, pituicytes, Herring's bodies) of rats thus showed that at all times of autolysis the mitochondria underwent the greatest changes. Signs of destruction in these organelles were not found during the first 3 h. Nevertheless, with an increase in the duration of autolysis, a tendency was observed for destructive changes to increase in structures of the neurohypophysis. This was manifested particularly clearly after 6 h, when the cytoplasmic membrane of some cells ruptured, and their contents escaped into the intercellular space, whereas elements of the lamellar complex and rough endoplasmic reticulum showed vacuolation.

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