INTRACELLULAR REGENERATION OF LATERAL HYPOTHALAMIC NEURONS IN RATS AFTER RESUMPTION OF FEEDING

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KEY WORDS: intracellular regeneration, ultrastructure of neuron, resumption of feeding.

Previous investigations [2, 3] yielded evidence of substantial injuries to the ultrastructure of neurons in the lateral hypothalamic region (LHR) of the rat brain after starvation for 7 days. The possibility that the submicroscopic changes arising in cells of the CNS during prolonged starvation may be reversible is of tremendous scientific interest from both the theoretical and the practical point of view.

The time course of intracellular regenerative processes in neurons of the anterior, middle, and posterior parts of LHR of the rat brain at different times after the discontinuation of food deprivation was studied in the investigation described below.

EXPERIMENTAL METHODS

Experiments were carried out on 25 male Wistar albino rats weighing initially 190-220 g. After food deprivation for 7 days the animals were allowed free access to food and drink. The animals were anesthetized with ether 10, 20, 30, 50, and 70 days after the beginning of resumption of feeding, and the animals' brain was fixed by perfusion. Brain fragments, after dehydration, were embedded in a mixture of Araldite and Epon-812. Ultrathin sections were cut on an LKB Ultratome (Sweden) and examined in the HU-600 electron microscope (Hitachi, Japan).

EXPERIMENTAL RESULTS

Ten days after resumption of feeding, cisterns of the rough endoplasmic reticulum (RER) in most neurons of LHR of the rat brain were lengthened and their number was increased. In some neurons a connection could be observed between single cisterns of RER and the perinuclear membrane (Fig. 1), evidence of regeneration and the formation of new cisterns. The number of ribosomes and polysomes, most of which were located on membranes of the cisterns of RER, was increased. There was a marked increase in the number of mitochondria in the cytoplasm of the neurons and many tiny mitochondria appeared, evidence of their formation de novo. Elements of the lamellar apparatus were hypertrophied, and marked proliferation of its cisterns was observed in some neurons, possibly in connection with activation of the transport of materials in these cells in the recovery period. The number of lysosomes of different sizes in the cytoplasm of individual neurons was increased. In addition, the nucleus of the neurons was rich in chromatin granules, adjacent to the inner side of the karyolemma, which accordingly appeared to be greatly thickened. Pores were clearly visible in the karyolemma, with many chromatin granules in them, as a result of which the pores looked like dark bridges connecting the karyoplasm and cytoplasm. Near the outer nuclear membrane, in the perikaryon, groups of chromatin granules were found. All these findings are evidence of the active role of the nuclear apparatus in the restoration of the structures of the neurons after resumption of feeding.

It will be noted that 10 days after the begining of resumption of feeding, besides restoration of the ultrastructure of the majority of neurons in LHR of the brain, individual

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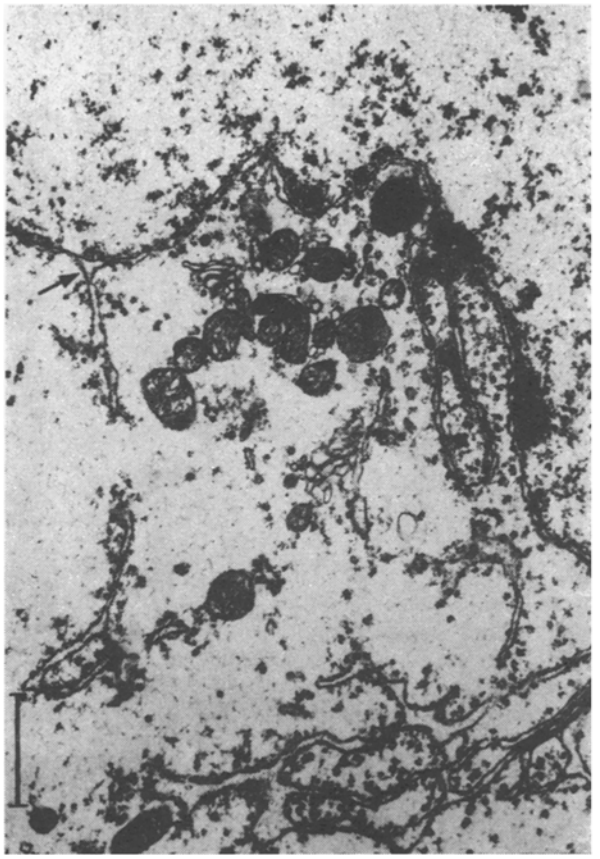

Fig. 1

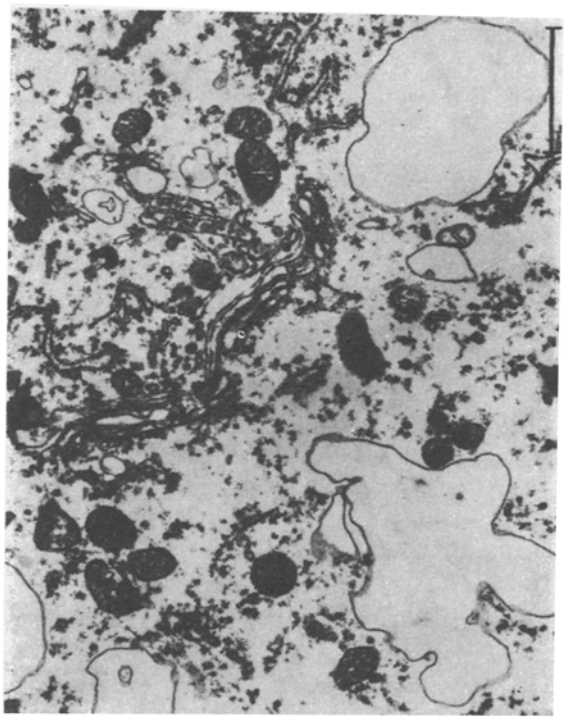

Fig. 2

Fig. 1. Intracellular regeneration in neuron in posterior part of LHR of rat brain 10 days after termination of food deprivation. Arrow indicates formation of cisterns of rough endoplasmic reticulum from perinuclear cistern. Scale: 1 μ.

Fig. 2. Increase in number of mitochondria and components of Golgi complex in large neuron in posterior part of rat LHR during persistence of marked ultrastructural changes (vacuolation of cytoplasm) 20 days after resumption of feeding. Scale: 1 μ.

large nerve cells with marked changes in the form of chromatolysis and vacuolation of the cytoplasm, which we observed during starvation, especially on the 7th day [3], still remained. The number of these changed neurons and the degree of their ultrastructural disturbances were higher in the posterior part than in the anterior part of LHR. In the middle part of LHR very slight morphological changes persisted only in single neurons, in the form of moderate peripheral chromatolysis and some degree of vacuolation of the cytoplasm. At this stage of the experiment the number of "paired" neurons was reduced, but neurons with marked folding of the nuclear membrane, and with an eccentric arrangement of their nucleus and nucleolus, still remained, characteristic morphological features of compensatory processes, observed during food deprivation [3].

After 20 days of feeding of the animals the ultrastructure of most nerve cells in the middle part of LHR was almost indistinguishable from that of intact rats, the only difference being that in single cells small vacuoles were still observed in the cytoplasm with focal peripheral chromatolysis. In the anterior and, in particular, in the posterior part of LHR, against the background of numerous normal cells there were also single neurons with marked dystrophic changes, in the form of total chromatolysis and the presence of large vacuoles (Fig. 2). However, even in these altered neurons there were ultrastructural features of intracellular regeneration: many small mitochondria appeared, accompanied by proliferation of components of the endoplasmic reticulum. "Paired" cells still remained in the posterior part of LHR, accompanied by neurons with deep investigations of the karyolemma.

The structure of the neurons in the middle part of LHR 30 days after resumption of feeding was back to normal, but in the anterior and, in particular, in the posterior part of LHR

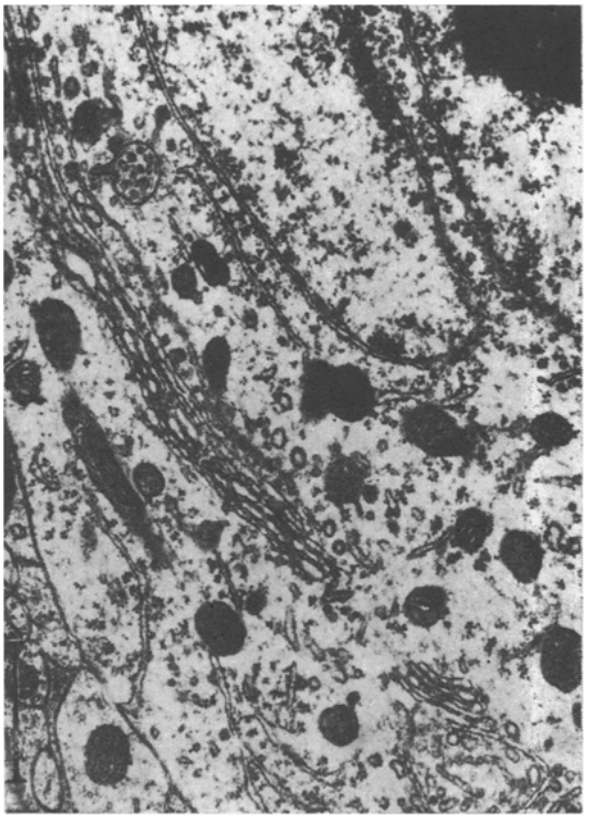

Fig. 3. Hyperplasia of cytoplasmic mitochondria-organelles, and of vesicular and cisternal components of Golgi complex in large neuron of posterior part of LHR of rat brain 30 days after resumption of feeding. Scale: 1 μ.

large neurons with chromatolytic changes and with vacuoles of different shapes in their cytoplasm still remained. In the posterior part of LHR sometimes "paired" cells were observed. In some large cells in the posterior part of LHR hyperplasia of the cytoplasmic organelles was observed, especially of the mitochondria, but also of the vesicular and cisternal components of the Golgi lamellar apparatus and of RER (Fig. 3). The ultrastructure of neurons in the anterior part of LHR was restored 50 days after the resumption of feeding, but in its posterior part, despite a considerable decrease in the number of altered cells compared with 30 days after resumption of feeding, individual large neurons still preserved their ultrastructural changes, in the form of peripheral chromatolysis and tiny vacuoles in various parts of their cytoplasm. At this time no "paired" cells remained in LHR. Restoration of the ultrastructure of neurons of the posterior part of LHR was not complete until the 70th day of resumption of feeding.

Ultrastructural changes observed during food deprivation for 7 days in the residual neurons of LHR in rats are thus reversible in character. After long-term food deprivation (for 7 days) the structure of neurons is restored through normalization of the ultrastructure of the cytoplasmic organelles and the formation of new ones, in accordance with Sarkisov's concept [4] of intracellular regeneration. An increase in the number of cytoplasmic organelles leads to intensification of synthetic processes, as a result of which neurons are supplied with building material and their structure gradually returns to normal.

After resumption of feeding the regenerative reaction of the neurons is aimed at eliminating the consequences of long-term starvation. In addition, gradual disappearance of those changes ("paired" cells, folding of the karyolemma, ectopia of the nucleus and nucleolus) which, during food deprivation developed as reparative adaptations in the neurons [1], is observed in the recovery period.

The intracellular regenerative processes in neurons in different parts of LHR differ in intensity. Repair processes begin initially and end sooner in neurons in the middle part (30th day), followed by in the anterior (50th day) part of LHR; normalization of neuronal structure in the posterior part proceeds more slowly and is not complete until the 70th day after resumption of feeding.

The results are thus not only of theoretical, but also of practical scientific importance, for they provide a basis for the development of methods of pathogenetic treatment of the diseases of starvation.

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QUANTITATIVE ANALYSIS OF DENDRITIC SPINES OF PYRAMIDAL NEURONS IN LAYER V OF THE SENSOMOTOR CORTEX OF RATS EXPOSED ON THE "KOSMOS-1667" BIOSATELLITE

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KEY WORDS: sensomotor cortex, factors of space flight, spines.

The study of the variability of the number of dendritic spines (DS) during exposure to various physiological or chemical factors [1, 3, 6-11] has shown that this parameter is sufficiently labile and reflects a functional principle expressed as unique adaptation of the neuron to changing environmental conditions, involving restoration or loss of synaptic connections. The rodent sensomotor cortex accounts for almost one-third of the neocortex and is the dominant factor in the formation of adaptive responses of rats, by comparison with the visual and auditory cortex [4].

The aim of this investigation was to study the number of DS on pyramidal neurons in layer V of the sensomotor cortex, which are densely covered with spines, in rats exposed for 7 days to space-flight conditions on the "Kosmos-1667" biosatellite and in control experiments.

EXPERIMENTAL METHODS

Four groups of male Wistar-SPF rats (three animals in each group) were used: the flight group (F), the animal house control for the flight group (AHC-1); the ground control experiment group (GCE), i.e., the animals of this group remained on the ground and were exposed to the action of spaceflight factors, excluding weightlessness; and the animal house control for this group (AHC-2). The animals were decapitated and during the next 3 min the frontal block of the sensomotor cortex (PA^s and PA^m, FPP according to [4]) was excised and impregnated by Golgi's method. Spines were counted under the "Ortholux" microscope (Leitz, West Germany) under a magnification of 312, along a 100-μ long segment of dendrites, densely covered with spines, of pyramidal neurons in layer V of the sensomotor cortex. The number of DS was counted separately in the right and left cerebral hemispheres on apical and oblique dendrites, passing through layer III-IV, on apical dendrites passing through layer I-II, and on basal dendrites. The absence of data for layer I-II in the left cerebral hemisphere is explained by the use of this part of the brain for other purposes. In each animal DS were

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