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ULTRASTRUCTURAL CHARACTERISTICS OF CHANGES IN THE SENSOMOTOR CORTICAL NEUROPIL DURING LONG-TERM PROTEIN-CALORIC DEFICIENCY

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In the growing organism whose diet is deficient in protein, one of the most vulnerable organs is the brain [13, 14]. Numerous investigations on rodents (rats and mice) have been devoted mainly to the study of the effect of protein-caloric deficiency on the brain during late embryonic and early postnatal development. The reason is evidently that it is during this period that processes of neurogenesis take place actively in the brain of experimental animals. Yet from the clinical point of view it is more important to study the effect of protein-caloric deficiency on the infant at the time when he ceases to be fed on his mother's milk. It has been shown that infants between 6 months and 3 years of age most often suffer from diseases such as kwashiorkor and marasmus, which later often lead to low intelligence and mental backwardness [8]. It is at this time that processes of gliogenesis, myelinization, and growth of nerve cells and establishment of nervous connections take place in the child's brain. In the rodent brain the corresponding processes are most active during the first month of postnatal development [2, 7].

Considering the fact that most nerve cells in mice are formed during the period of embryonic development [15], i.e., significantly earlier than exposure to underfeeding began, the most significant changes might be expected in the structures of the neuropil. The study of the neuropil also seemed to be indicated in the investigation to be described below because it is in the neuropil that the main interneuronal interactions that lie at the basis of the mechanisms of integrative brain activity take place.

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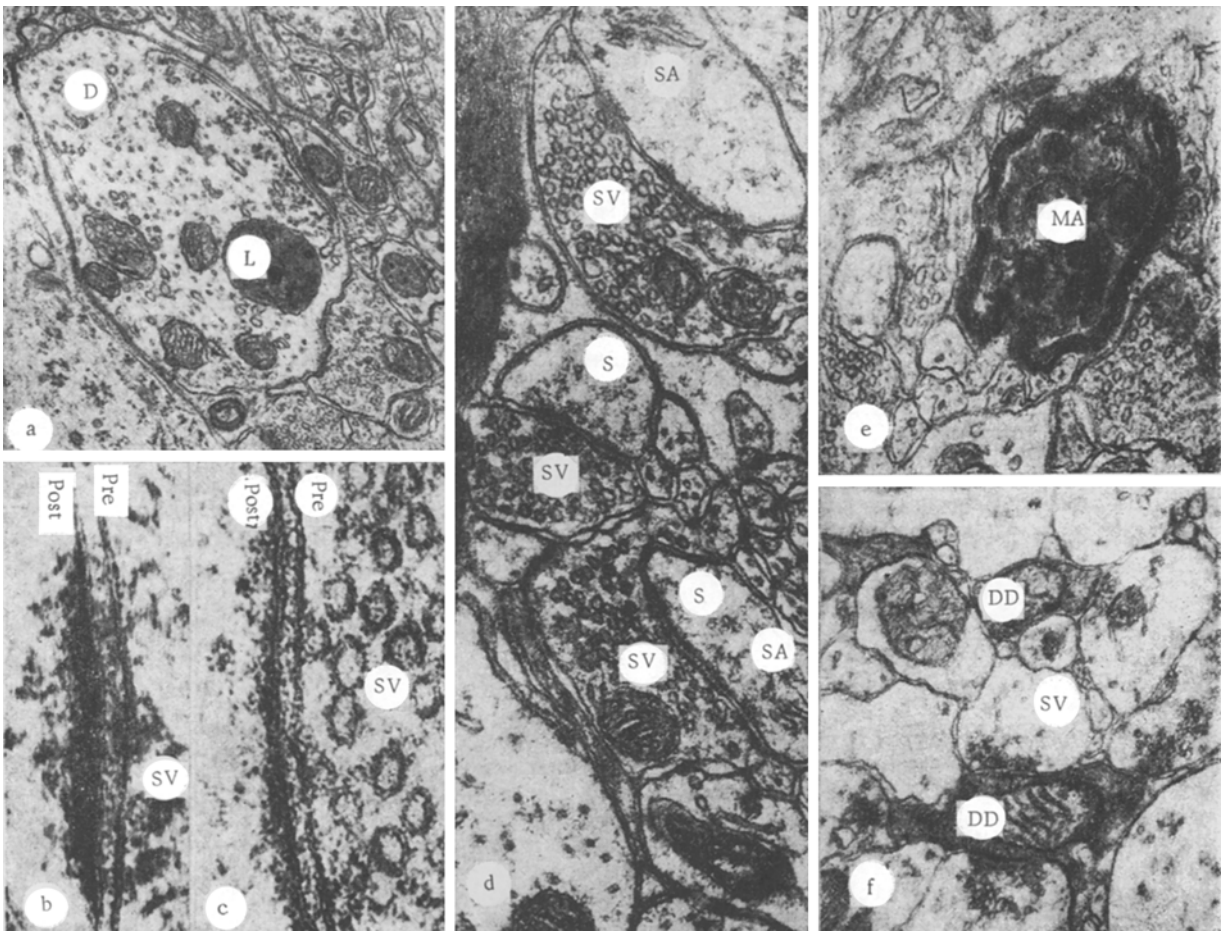

Fig. 1. Ultrastructural changes in neuropil of mouse sensomotor cortex during protein-caloric deficiency. a) Lysosome in cytoplasm of dendrite (38,000 ×); b, c) synaptic junctions with spines on dendrites of control and experimental animals, respectively (166,000 ×); d) destructive elements of the spinous apparatus (48,000 ×); e, f) increase in electron density of exoplasm and cytoplasm of myelinated axon (40,000 ×) and of small dendrites (26,000 ×). D) Dendrite, L) lysosome, S) spine, SA) spinous apparatus, SV) synaptic vesicles, DD) dark dendrite, MA) myelinated axon, Pre) presynaptic, and Post) postsynaptic membrane.

Accordingly, the aim of the investigation was to study electron-microscopic changes in the sensomotor cortex of mice exposed to protein-caloric deficiency from the 10th through the 40th day of life.

EXPERIMENTAL METHOD

Experiments were carried out on CBA mice. Lactating females were put on synthetic diets 10 days after giving birth to their offspring: a control diet and an experimental diet containing 50% of nutrient matter accountable for by cellulose, compared with the control [4]. At the age of 22 days the young mice were weaned on to synthetic diets. The experimental animals were very backward in development. By the 40th day their body weight averaged 57% of that of the control mice. The animals were killed 1 month after the beginning of the experiment. The brain of six control and six experimental animals (under pentobarbital anesthesia) was fixed by intravital perfusion with a mixture of 4% paraformaldehyde and 2.5% glutaraldehyde in phosphate buffer (pH 7.4, molarity 0.1M), and then postfixed in a solution of 2% OsO_4 in the same buffer, stained with uranyl acetate, and embedded in Araldite. In semithin sections 1 μ thick, stained with methylene blue, layer V of the cortex was identified and blocks trimmed so that the sections included this particular layer. Ultrathin sections were stained by Reynolds' method and examined in the Tesla BS 500 electron microscope.

EXPERIMENTAL RESULTS

Changes were found in the ultrastructure of the principal components of the neuropil; dendrites, axon terminals, myelinated axons, and synaptic junctions in animals kept under conditions of protein-caloric deficiency, compared with the same parameters in the control mice. For instance, single lysosomes 0.4-0.5 μ in diameter (Fig. 1a) were found in the cytoplasm of large and medium-sized dendrites in the experimental animals, but not in the control. The distribution of the microtubules, mitochondria, and bound and free ribosomes in these dendrites was indistinguishable from the control.

Destructive changes accompanied by a sharp increase in electron density of the cytoplasm and axoplasm, corresponding to the dark type of degeneration, were observed in individual dendrites and myelinated axons (Fig. 1e, f).

The ultrastructure of the axon terminals in layer V of the cortical area studied varied considerably. Some of them had a translucent matrix, containing a reduced number of synaptic vesicles, and with the appearance of large, irregularly shaped vesicles. The ultrastructure of terminals of this kind was similar to that observed in the pale type of degeneration of axon terminals.

Many axon terminals were characterized by numerous synaptic vesicles, which packed the axon endings tightly. As a rule the synaptic vesicles in these terminals lay at a distance of up to 30 nm from the presynaptic membrane. In synaptic junctions formed by these terminals the width of the synaptic space and of the postsynaptic thickening in the experimental material was on average 12% less than in the control (Fig. 1b, c). Comparative study of the ultrastructure of the synaptic junctions showed that the sharpest changes were found in synapses located on spines, with a significantly altered spinous apparatus. In the control it was a complex consisting of flat cisterns, alternating with electron-dense disks between them. In animals on a protein-deficient diet the regularity of alternation and the mutual arrangement of the components of the spinous apparatus was disturbed. Its cisterns were dilated, often irregular in shape, and the disks of electron-dense material were poorly defined (Fig. 1d).

The changes described above were not observed in all components of the neuropil. Some axon endings, synapses, and dendritic spines preserved their normal structure. However, the decrease in the number of actively functioning axon terminals and synaptic junctions can evidently be regarded as evidence of a significant reduction in the compensatory powers of the CNS.

It can be concluded from these observations that the highly specialized synaptic junction apparatuses, located on dendritic spines, i.e., those ultrastructural components of the neuropil which attain their highest development in the mammalian cerebral cortex and which are connected with the highest functions of the CNS [9, 10], are the structures that are most sensitive to malnutrition. In evolution and ontogeny of the nervous system these components of the neuropil are formed later than the others [3] and they are most sensitive to various influences [1, 6]. Dendrites of large and average diameter exhibit greater resistance to protein-caloric deficiency. However, the appearance of lysosomes in them is evidence of the existence of dystrophic processes, together with those of a compensatory and adaptive character. Some of the changes in axon terminals and myelinated fibers described by ourselves and by other workers (in earlier stages of starvation) are evidence of a number of destructive and, possibly, irreversible processes taking place in the structure of the neuropil in this type of situation [12]. Meanwhile, the arrangement of the synaptic vesicles at a considerable distance from the presynaptic membrane of the synaptic junctions is evidently the morphological expression of a disturbance of the mechanisms of synaptic transmission [5].

Finally, changes observed in this investigation in the structure of interneuronal junctions and, in particular, narrowing of the synaptic space of the postsynaptic thickening of the membranes, may be evidence of a disturbance of the ultrastructural bases of the mechanisms of long-term change of conductivity in synapses [6, 11].

The most sensitive structures of the CNS to the action of protein-caloric deficiency are thus the highly organized structures of the neuropil, recent in terms of evolution, which are probably the morphological basis for integrative brain activity.

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NUCLEAR ULTRASTRUCTURE OF CEREBRAL CORTICAL NERVE AND GLIAL CELLS IN EXPERIMENTAL ALCOHOL POISONING

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A combination of morphological changes in nerve and glial cells, nerve fibers, synapses, and blood vessels has been described [1, 7-10] in the literature on the action of alcohol on brain structure. However, the effect of alcohol poisoning on nuclear ultrastructure of the various brain cells has not been adequately treated [6, 7].

The object of this investigation was to study the action of alcohol on the morphology of nerve and glial cell nuclei under chronic experimental conditions.

EXPERIMENTAL METHOD

Experiments were carried out on 12 male rats (six experimental and six control) weighing 200 g. The experimental rats were kept on a water-free diet: instead of water they were given ethyl alcohol in 20° concentration to drink for 6 months. In the course of 1 day each rat drank about 10 ml alcohol. The structure of the sensomotor cortex was studied. Pieces of brain for electron-microscopic investigation were fixed in 5% glutaraldehyde solution, post-fixed in 1% OsO_4, and embedded in Araldite. Sections were cut on the LKB-III Ultrotome, stained by Reynolds' method [11], and examined in the JEM-100B electron microscope.

EXPERIMENTAL RESULTS

The morphological changes were similar in all the animals studied. Differences were expressed only in the degree of severity of these changes, which probably depended on various factors.

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