ULTRASTRUCTURAL CHARACTERISTICS OF BRAIN CAPILLARIES IN OLD ANIMALS DURING HYPOXIC HYPOXIA

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The ultrastructure of the brain capillaries during hypoxia has been well studied both experimentally and in autopsy material [1]. The age differences in the pathomorphology of the brain and functional changes in different parts of the CNS in hypoxic states in clinical geriatrics and in old animals under experimental conditions also are known [2, 5]. Much attention has been paid to the study of the effect of hypoxia on ultrastructure of the brain capillaries during aging. At the same time, age changes in the fine structure of the capillaries affect their reactivity and determine the character of responses of the microvessels in old animals and people to experimental procedures and to harmful factors [4].

The object of this investigation was to study ultrastructural differences in the response of the brain capillary walls in old animals to hypoxic hypoxia.

EXPERIMENTAL METHOD

The brains of 30 male albino rats of two age groups — adult (6-8 months) and old (28-30 months) — were the test objects. Hypoxic hypoxia was induced by inhalation of gas mixtures with a reduced oxygen concentration in a pressure chamber. The experiments were carried out in the Department of Hypoxic States (Head, Dr. Med. Sci. A. S. Kolchinskaya), A. A. Bogomolets' Institute of Physiology, Academy of Sciences of the Ukrainian SSR. Details of the experimental conditions are given in Table 1.

The walls of capillaries in the mammillary bodies were studied. Interest in this region was due not only to the particular features of its blood supply (1004 ± 156 capillaries/mm^3) and its functional role as an important component in neurohumoral regulation, but also to the fact that, of all the nonsecretory nuclei of the hypothalamus, it is the one that is most subject to the influence of age [3].

The mammillary bodies were fixed in 3% glutaraldehyde solution in phosphate buffer, pH 7.4, postfixed in 1% osmium tetroxide solution, and embedded in Epon-812. Sections were

TABLE 1. Experimental Conditions and Distribution of Animals among Series

Experimental conditions	Series of experiments	Age of animals	Oxygen concn. in gas mix., %	Duration of experiment	Number of animals
Control (intact rats)	I	Adult	—	—	5
	II	Old	—	—	6
Exposure in pressure chamber	III	Adult	14,2	1 h	3
	IV	Old	14,2	1 h	4
	V	Adult	11,85	1 h	2
	VI	Old	11,85	1 h	2
	VII	Adult	7	1 h	2
	VIII	Old	7	1 h	2
	IX	Adult	5,3	20 min	2
	X	Old	5,3	20 min	2

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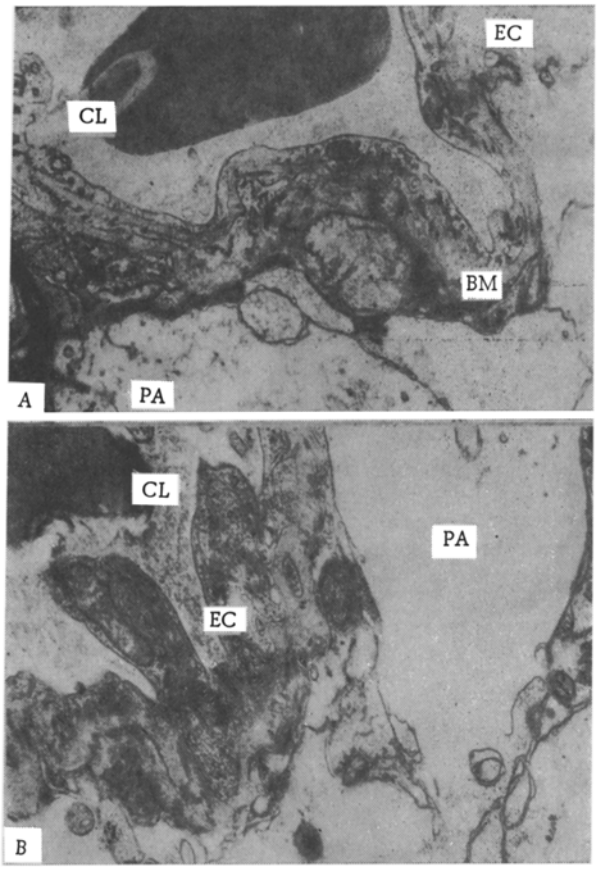

Fig. 1

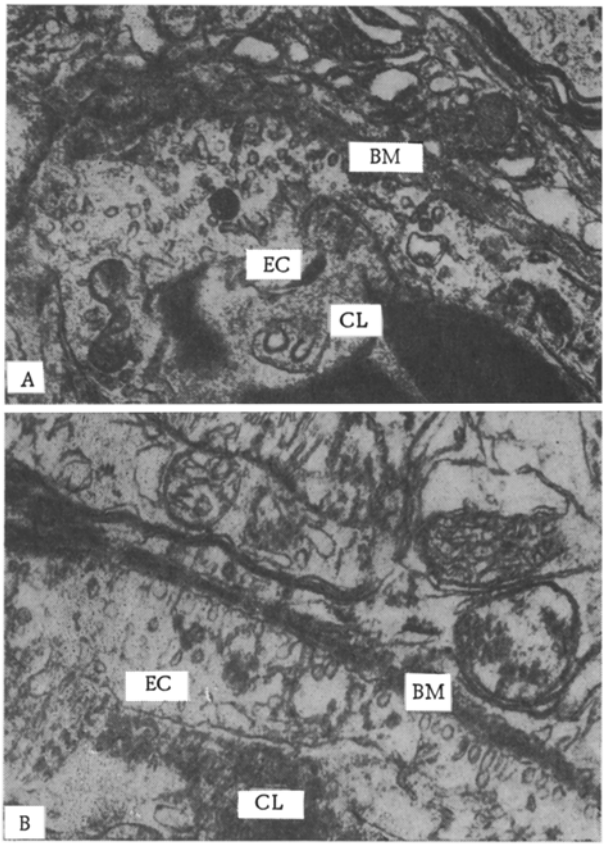

Fig. 2

Fig. 1. Moderate hydration of pericapillary processes of astrocytes in brain of adult rat in experiments of series III (A) and severe hydration of processes of astrocytes in brain of old rat in series IV (B). BM) Basement membrane; PA) processes of astrocytes; CL) capillary lumen; EC) endothelial cell. 30,000 ×.

Fig. 2. Marked micropinocytosis (arrow) in endothelial cell of brain capillaries of two adult rats. A) Series VII; B) series IX. 40,000 ×.

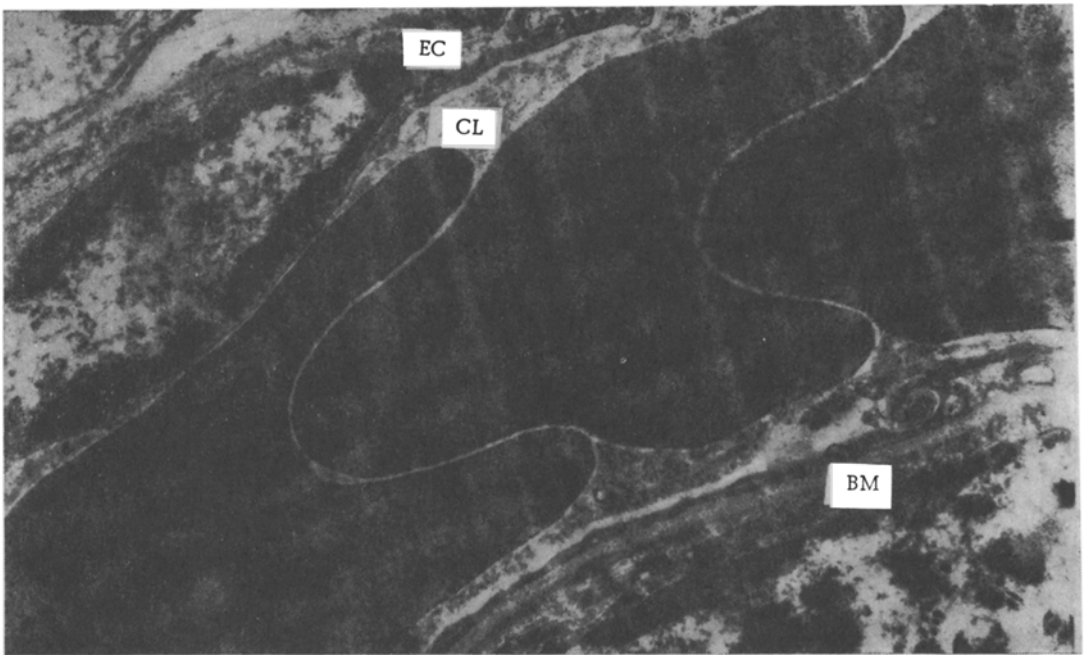

Fig. 3. Stasis of erythrocytes in brain capillary of old rat (series X). Focal translucencies of basement membrane [1]. 20,000 ×.

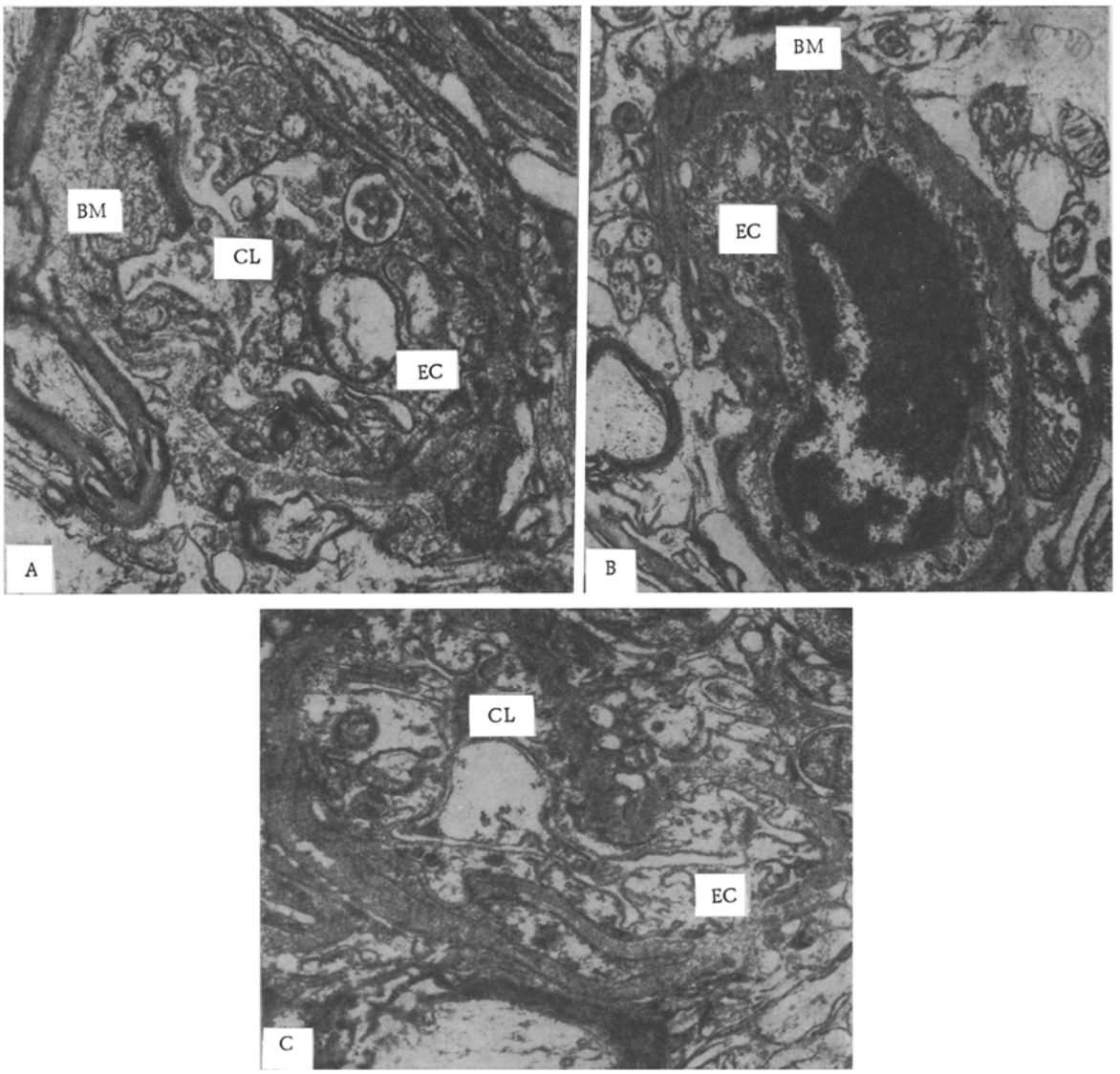

Fig. 4. Constriction and closing of lumen of brain capillaries of adult (A) and old (B and C) rats under conditions of hypoxic hypoxia. A) Series VII; B and C) series X. Abundance of dense chromatin in nucleus [1]. Endothelial cell in capillary wall of old rat, 20,000 ×.

cut on the LKB-III Ultrotome, stained with lead citrate [6], and studied in the JEM-100B electron microscope with an accelerating voltage of 60 kV.

EXPERIMENTAL RESULTS

Unequal changes were observed in the capillaries of the mammillary bodies of adult animals of series III and V. Besides vessels which preserved their ordinary structure, there were capillaries in whose walls reactive changes aimed at increasing their premeability were clearly visible: increased micropinocytosis, the appearance of large vacuoles in the cytoplasm of the endotheliocytes on account of meeting of the processes of their luminal membrane. Edema of the cytoplasm of the endothelial cells and foci of translucency of the noncellular component of the basal layer developed in the walls of some capillaries, evidence of a disturbance of transcapillary metabolism. Diapedesis of erythrocytes was observed. Moderate hydration of processes of astrocytes was present in the pericapillary glia (Fig. 1A), in which large mitochondria with distinct cristae and a juicy matrix, were distributed close to the capillary walls.

Exposure of the old animals in the pressure chamber (series IV and VI) led to further progression of edema of the cytoplasm of the endotheliocytes, destruction of the mitochondria, and accumulation of lipofuscin in the endothelial cells and pericytes. The fraction

of dense (inactive) chromatin in the nuclei was sharply increased. The lumen of many capillaries was closed because of swelling of the endotheliocytes. Stasis and diapedesis of erythrocytes were frequently seen. Total destruction of the basal layer was observed. Processes of pericapillary astrocytes were highly edematous (Fig. 1B). By contrast with adult animals, in the capillary walls of the old rats intensification of compensatory processes was observed in response to the experimental conditions (increased pinocytosis, the formation of large vacuoles in the cytoplasm) was less marked than in the original state.

With a decrease in the oxygen concentration in the inspired mixture (series VII-X) these age differences tended to disappear, for considerable degenerative changes developed in the capillary walls in this region in the adult animals also. Under these circumstances the intensive pinocytosis in the adult animals points to a compensatory increase in the intensity of transendothelial transport of materials (Fig. 2A, B). Marked edema of processes of pericapillary astrocytes was also the result of a disturbance of permeability of the vessel wall, which in turn led to interference with transcapillary metabolism. Changes in the pericapillary structures of nerve tissue in old animals were more distinct than in adult animals. The lumen of the vessels in the adult and, in particular, the old rats either was closed as a result of swelling of the edematous endotheliocytes, or was dilated because of stasis (Figs. 3 and 4). Erythrocytes were found outside the vessel also. However, it must be pointed out that in both adult and old animals there was no disturbance of the junctions between the endothelial cells or in the integrity of the vessel wall, evidence of the high stability of the structures of the blood–brain barrier (by contrast with capillaries elsewhere) [7]. Age differences in the response of the brain capillary walls to a harmful agent (in this case to hypoxia) can thus be reduced to the more rapid increase in the intensity of degenerative changes and the lower intensity of the compensatory processes in old animals. The more severe disturbances of other brain tissue elements surrounding the vessel are further evidence that their adaptive reactions are less effective.

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