The amino acid taurine (like the dipeptide carnosine) has the property of neutralizing the toxic action of the hypochlorite anion and also of delaying the development of age-related opacities of the mammalian lens [10]. The identity of action of these two related compounds, which we have found, may perhaps lie at the basis of their anticataract effect.

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EFFECT OF MODERATE PRENATAL EXPOSURE TO ALCOHOL ON CORTICAL CAPILLARY ULTRASTRUCTURE IN THE OFFSPRING

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UDC 618.3-06:616.89-008.441.13]-092.9-07:616.831-053.31-076

KEY WORDS: capillaries; sensomotor cortex; offspring; moderate exposure to alcohol in pregnancy.

After exposure of the pregnant animal to alcohol, a wide spectrum of changes is observed in the offspring, ranging from the development of a full alcohol syndrome to its partial manifestations or finer disturbances of behavioral reactions [10]. In the offspring of animals exposed to prenatal intoxication with high doses of alcohol a decrease in size of the brain has been found, especially of the frontal region, together with polymicrogyria and thinning of the cortex [11], and a decrease in area of the corpus callosum and anterior commissure of the brain [13]. If there is moderate prenatal exposure to alcohol, leptomeningeal neuroglial heterotopia is found in the frontal pole, with a decrease in the density of the neurons and gliosis in the surface layers of the frontal cortex, and reduction and dysplasia of the lateral geniculate body [11]. Delay of development takes place, with changes in the neurons and interneuronal connections in the sensomotor cortex [4, 6, 8].

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(Presented by Academician of the Academy of Medical Sciences of the USSR O. S. Adrianov.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 113, No. 2, pp. 161-164, February, 1992. Original article submitted July 12, 1991.

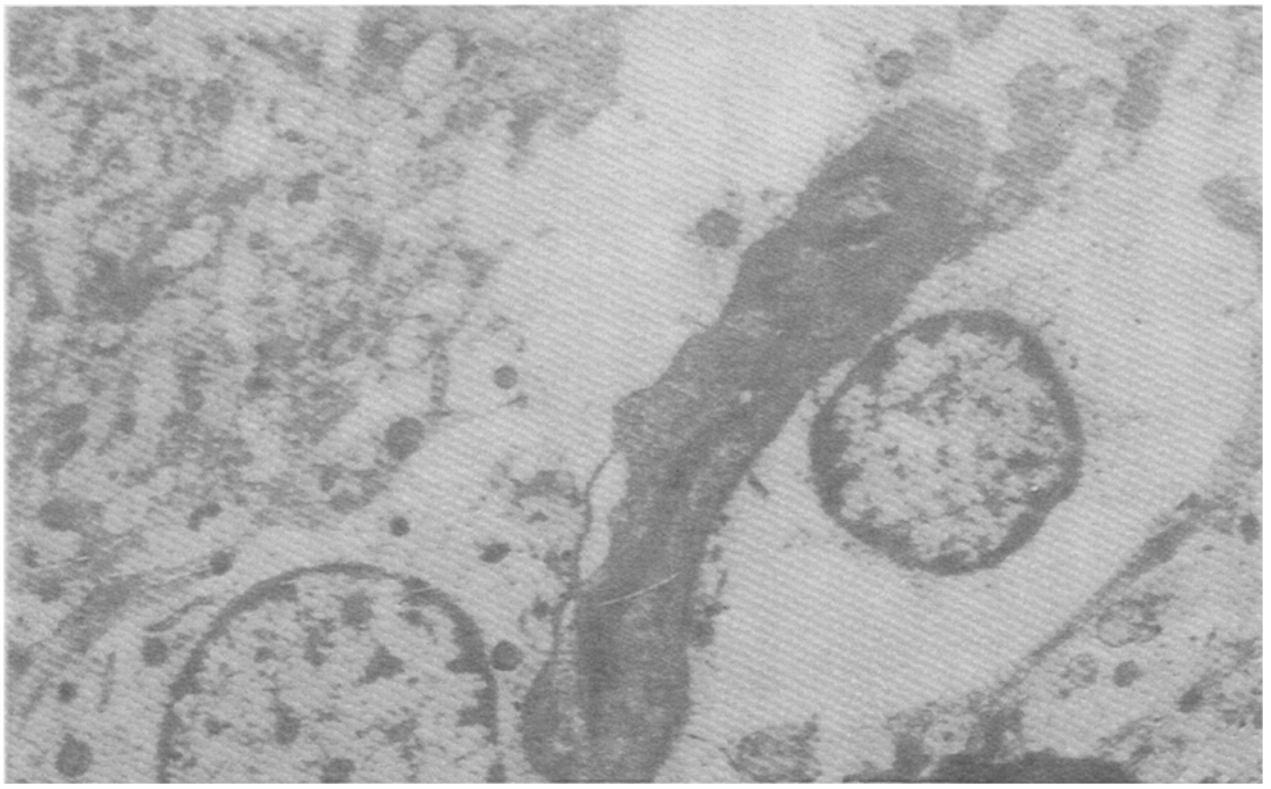

Fig. 1. Bodies of two astrocytes located near a modified capillary. Sensomotor cortex of 21-day-old rats exposed prenatally to alcohol. 3700×.

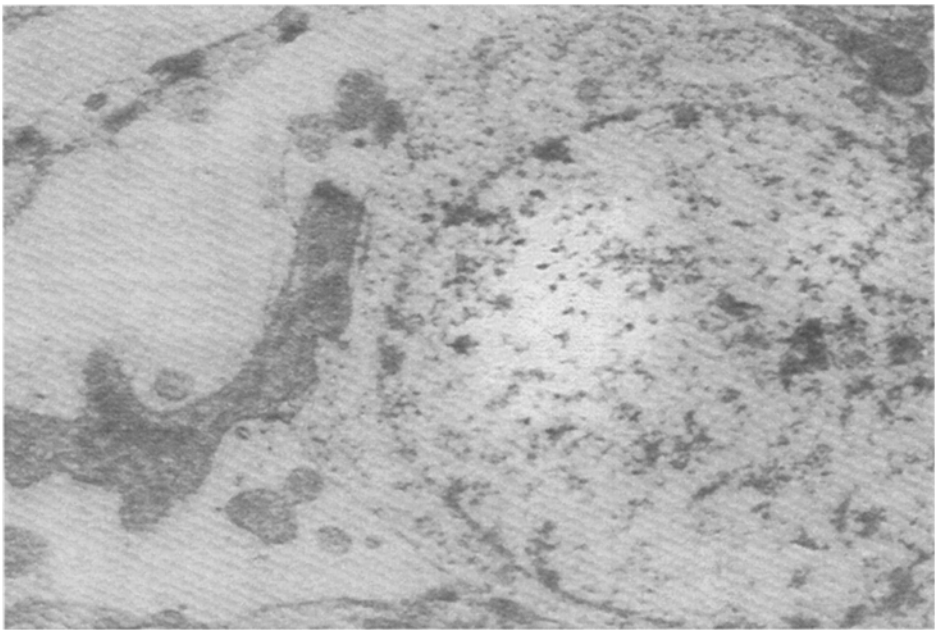

Fig. 2. Body of a neuron in sensomotor cortex of 30-day-old rat exposed prenatally to alcohol lies close to a modified capillary. 4800×.

Changes in brain structure and function in the offspring after prenatal alcohol intoxication of the mother have received little study. It has been shown experimentally that long-term consumption of alcohol before pregnancy leads to a tendency toward increased excitability of the CNS at the age of one month and inhibition of motor activity, with some increase in the response at the age of two months [9]. In the month-old offspring the aggressive reaction, and the rate of formation and consolidation of the conditioned defensive reflex are considerably reduced, although microscopic changes of the brain structures are absent [3]. In the early stages of postnatal ontogeny disturbances of the ultrastructure of the protein-synthesizing and energy-providing systems of cortical neurons have been discovered [5], with disturbances of the organization of interneuronal connections [6], indicating a possible role of oxygen insufficiency in the pathogenesis of these lesions.

The aim of this investigation was to study the ultrastructure of cortical capillaries in the offspring following exposure of the mother to a moderate dose of alcohol during and before the onset of pregnancy.

EXPERIMENTAL METHOD

Models of alcohol intoxication of pregnant rats and female rats before pregnancy were developed at the Institute of Pharmacology, Academy of Medical Sciences of the USSR, where the experimental offspring underwent a preliminary physiological investigation. In the first series of experiments, female rats weighing 200-220 g were given 20% alcohol solution by gastric tube in a dose of 2 g/kg from the first through the twentieth days of pregnancy. The sensomotor cortex of 15 experimental and 15 intact rats aged 21, 30, and 60 days (5 rats from different litters in each age group) was studied. In the second series, female rats weighing initially 180-200 g received 5% alcohol solution instead of water for 1 month before mating, followed by 10% alcohol solution for 2 months. The sensomotor cortex of the offspring at the age of 14 and 21 days was removed for investigation. The material was processed by the standard formula and ultrathin sections were stained with uranyl acetate and lead citrate and examined in the Hitachi HV 11E electron microscope (Japan).

EXPERIMENTAL RESULTS

The experiments showed that the ultrastructure of the cortical capillaries of intact 21-day-old rats was similar to that of the mature animals. In the third week of life, mainly capillaries with a round or oval lumen (on cross section) or a cylindrical lumen (on longitudinal section) were present in the cortex. Occasionally capillaries were seen with an irregular slitlike lumen, and these were considered to be nonfunctioning [7]. Some capillaries contained blood cells, others did not. The thickness of the capillary endothelium was quite uniform although greater in the zone of the nucleus. The nuclei, which were most frequently spindle- and sickle-shaped, contained finely granular material and marginal concentrations of chromatin. The cytoplasm contained an endoplasmic reticulum, a Golgi apparatus, mitochondria of variable number, size, and electron density, and pinocytotic vesicles. The basement membrane was quite uniform in thickness and was composed of thin fibers. Bodies of pericytes were distributed in its ramifications, but processes were more numerous. The ultrastructure of the nucleus and cytoplasm of the pericytes was similar to that of the endotheliocytes. The capillaries were surrounded by outgrowths of nerve and glial cells. The latter covered a large part of the surface of the vessel and their cytoplasm was almost free from organelles.

The surrounding of up to 85% of the perimeter of the capillaries by pale astrocytic pedicles in an albino rat on the 21st day of postnatal life is an expression of the morphological and functional maturity of the blood—brain barrier [2]. In the 21-day-old experimental rats the predominant type of change in the cortical capillaries was spasm, sometimes irregular. The lumen of the capillary in some places was narrowed or almost completely closed, obstructing the blood flow and leading to cortical ischemia, and consequently, adversely affecting metabolism, structure, and function of the brain. Besides disturbance of the blood flow the ultrastructure of all components of the vascular wall of the capillaries showed changes: large vesicles and vacuoles could appear in the cytoplasm of the endotheliocytes, with considerable concentrations of chromatin in the nucleus, around the periphery; the basement membrane was thickened in places. The surface of the contracted capillaries as a rule was covered by a muff of greatly swollen astrocytic processes, creating a picture of marked perivascular edema. Characteristically the mitochondria in the edematous processes of the pericapillary astrocytes were located close or immediately next to the basement membrane of the capillary, another possible sign of compensatory-adaptive nature.

Fig. 3. Ultrastructure of capillary in sensomotor cortex of 21-day-old rat whose mother was exposed to alcohol before pregnancy. 3700×.

The proximity of bodies of astrocytes to modified capillaries, which is observed under pathological conditions and, in particular, in the brain of patients dying from stroke [1], is a noteworthy feature. In Fig. 1 the bodies of two astrocytes lie close to a capillary; the cytoplasm of one of them and the process of the other are free from organelles but contain vacuolar cavities.

It is also possible to see a neuron in close proximity to a capillary which is surrounded by a muff of edematous processes of astrocytes, sometimes with local lysis of the plasmalemma of the nerve cell and of an astrocytic pedicle.

Dystonia of cortical capillaries, swelling of pericapillary astrocytic processes, and proximity of a nerve cell to a capillary also were found in one of the experimental offspring aged 1 month. In this last case (Fig. 2) the cytoplasm of the neuron contained slitlike translucencies, observed in hippocampal neurons in the postischemic period [12]. Approximation of a nerve cell to a capillary evidently facilitates the direct transmission of nutrients from blood into neuron when the blood supply of the cerebral cortex is disturbed. In the sensomotor cortex of 2-month-old experimental rats the capillaries had a sufficiently wide lumen of irregular outline and the typical normal ultrastructure. However, severe swelling of the pericapillary processes of the astrocytes and a picture of perivascular edema still remained.

It can be concluded from these observations that an important pathogenetic factor in the disturbance of brain structure and function in postnatal ontogeny in offspring exposed prenatally to alcohol is a deficiency of the cerebral circulation, as a late manifestation of fetal hypoxia. In fact, compression of the isolated human umbilical arteries in vitro, with consequent impairment of umbilico-placental transport can be caused even by low doses of alcohol [14].

When the rats were exposed to alcohol before pregnancy, changes in the cortical capillaries of the offspring were less marked. Edema of the pericapillary astrocytes was not observed. At the age of 14 days significant changes were found in mitochondria of the endotheliocytes. Swollen organelles with residues of cristae on the inner membrane and mitochondria resembling vacuoles predominated. In the immediate vicinity of the nucleus there were solitary slitlike translucencies in the cytoplasm, which can be regarded as a manifestation of prenatal cerebral ischemia.

Polymorphism of the ultrastructure of the cortical capillaries was found in an experimental young rat aged 21 days. Capillaries with an almost typical ultrastructure but with accumulation of lipofuscin in the processes of the pericytes were present. Capillaries could be seen with a narrow slitlike lumen. The cytoplasm of their endotheliocytes and pericytes contained translucencies of different shapes, and the nuclei of some pericytes contained a dilated perinuclear cistern. Sometimes blood cells could be seen around one such capillary (Fig. 3), indicating increased permeability of the vessel wall.

Open capillaries with swellings of cytoplasm of the endotheliocytes into the lumen of the vessel were seen. There were also capillaries with a thick vessel wall, with swellings of cytoplasm of the endotheliocytes into the lumen of the vessel and with discrete long, thin outgrowths. The cytoplasm of these endotheliocytes was electron-dense and contained a well developed granular component of the endoplasmic reticulum, with round and oval mitochondria and pinocytotic vesicles. The basement membrane was quite wide with a distinct three-layered structure. Much of the capillary surface is covered with pale astrocytic processes. These are evidently immature capillaries, and may indicate slowing of development of the blood-brain barrier in the offspring of females taking alcohol before pregnancy.

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