to this question may be of great practical importance, especially for groups of people whose skin is subjected to unfavorable external environmental factors during life and at work.

Thus as a result of the investigations a reversible increase in the force of adhesion was found between the keratinocytes both in the epidermis covering the scar formed at the site of a full-thickness wound and in the peripheral epidermis. This effect is of adaptive importance, for it can minimize cell losses and ensure rapid restoration of the epithelial cover and its barrier function.

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REPARATIVE CHANGES IN THE SENSOMOTOR CORTEX OF THE OFFSPRING AFTER MODERATE PRENATAL EXPOSURE TO ALCOHOL

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KEY WORDS: moderate prenatal exposure to alcohol; offspring; sensomotor cortex; reparative changes

Recently ever-increasing attention has been paid to the study of the effect of moderate prenatal exposure to alcohol on the development of the fetus and offspring. However, brain morphology has received little study in these cases. Leptomeningeal neuroglial heterotonia has been discovered in the frontal pole and the middle temporal gyrus, a decrease in density of the neurons and gliosis in the superficial layers of the frontal cortex, and reduction and dysplasia of the lateral geniculate body in the 6-month-old offspring of a monkey consuming 2.5 g/kg of alcohol once a week since the 40th day of pregnancy [9]. In the offspring of BALB/c mice with moderate prenatal exposure to alcohol the area of the corpus callosum and of the anterior commissure was reduced [10]. Delayed development and dystrophic changes of the cortical neurons were observed in the offspring of rats receiving alcohol in a dose of 2 g/kg body weight during pregnancy, at the light-optical level [8], together with changes in the ultrastructure of neurons [4], interneuronal connections [5], and capillaries [6] in the sensomotor cortex, lasting until the period of puberty.

In this publication attention is drawn to reparative changes in the sensomotor cortex of the offspring of rats with moderate prenatal exposure to alcohol.

EXPERIMENTAL METHOD

A model of alcoholic intoxication of pregnant females was developed at the Institute of Pharmacology, Academy of Medical Sciences of the USSR, where the experimental offspring were subjected to a preliminary physiological investigation. From the 1st to the 20th days of pregnancy, the mother rats received 20% alcohol

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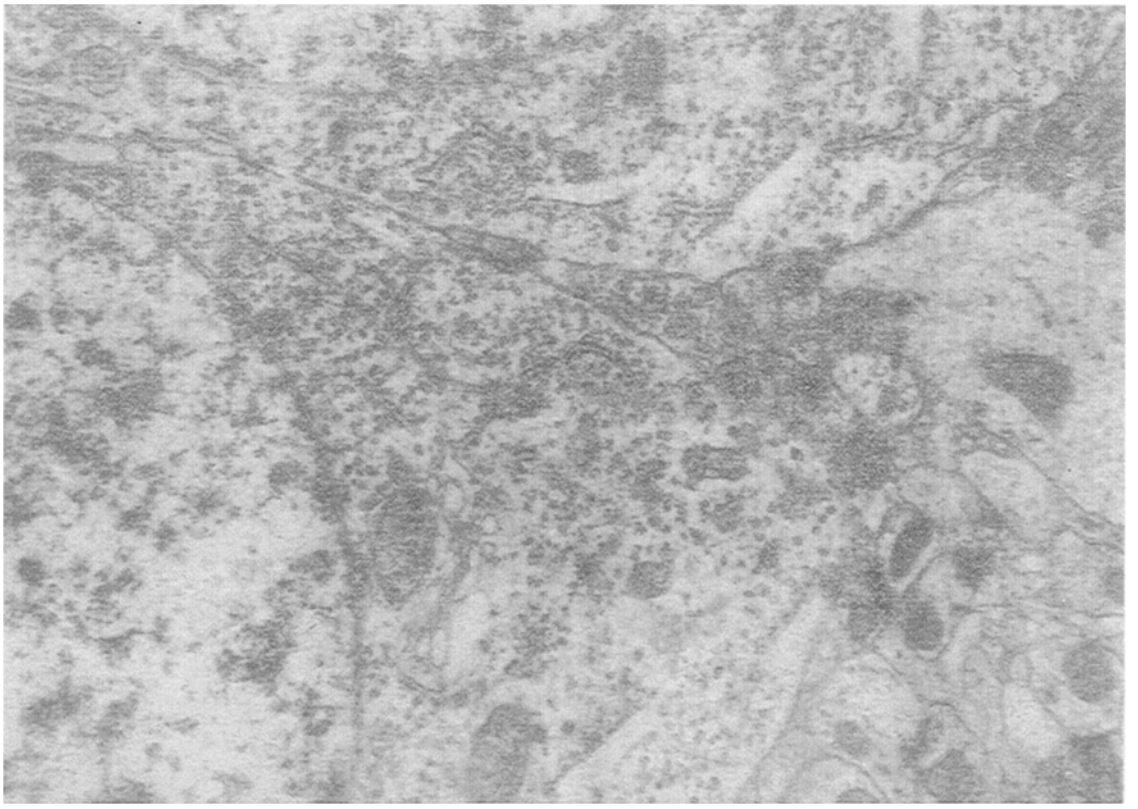

Fig. 1. Fragments of dystrophically changed double neurons with local ruptures of cytolemmas and signs of repair in sensomotor cortex of 30-day-old experimental rat. 5800×.

solution by gastric tube in a dose of 2 g/kg body weight. An electron-microscopic investigation was made of the sensomotor cortex of 15 experimental and 15 intact rats, aged 21, 30, and 60 days (5 rats each from different litters in each age group). The material was processed by the standard formula. Ultrathin sections were stained with uranyl acetate and lead citrate, and examined and photographed in a "Hitachi HV-11E" electron microscope (Japan).

EXPERIMENTAL RESULTS

Besides signs of delayed development of the sensomotor cortex and of dystrophic changes in the neurons, interneuronal connections, and capillaries, the repair processes also developed in the experimental offspring, and they were particularly marked at the age of 1 month. A characteristic feature of compensatory and adaptive character was the presence of duplicated nerve and glial cells, open capillaries, and approximation of the bodies of neurons or astrocytes to a capillary. The ultrastructure of the double neurons was one of polymorphism. In one type the cytolemmas were in contact only for a small distance, and mainly they did not touch each other; reparative changes were clearly seen: hyperplasia of the lamella component of the Golgi apparatus, which could become curved in shape, concentration of rough vesicles and mitochondria in the zone of the Golgi apparatus, and hypertrophy of some of the vesicles. The nucleus of one cell could be located in the center and could have deep invaginations. Many double neurons showed signs of dystrophic and reparative changes. In some cells the contacting membranes were thickened at discrete points, and their osmiophilia was greatly enhanced. Besides foci of translucency in the cytoplasm and destruction of elements of the Golgi apparatus close to the thickened regions of the cytolemma, cisterns of the rough endoplasmic reticulum were localized, together with groups of mitochondria and separate lysosomes, evidence of more intensive metabolism in these zones. The nuclei were displaced toward the zone of contact of the cytolemmas, and their activation took the form of enlargement of the nucleolus, an increase in the number of nuclear pores, and displacement of the paranucleolar bodies toward the nuclear membrane. Other neurons showed local rupture of the contacting cytolemmas. Slit-like translucencies, edema, and blurred outlines of individual cisterns of the Golgi

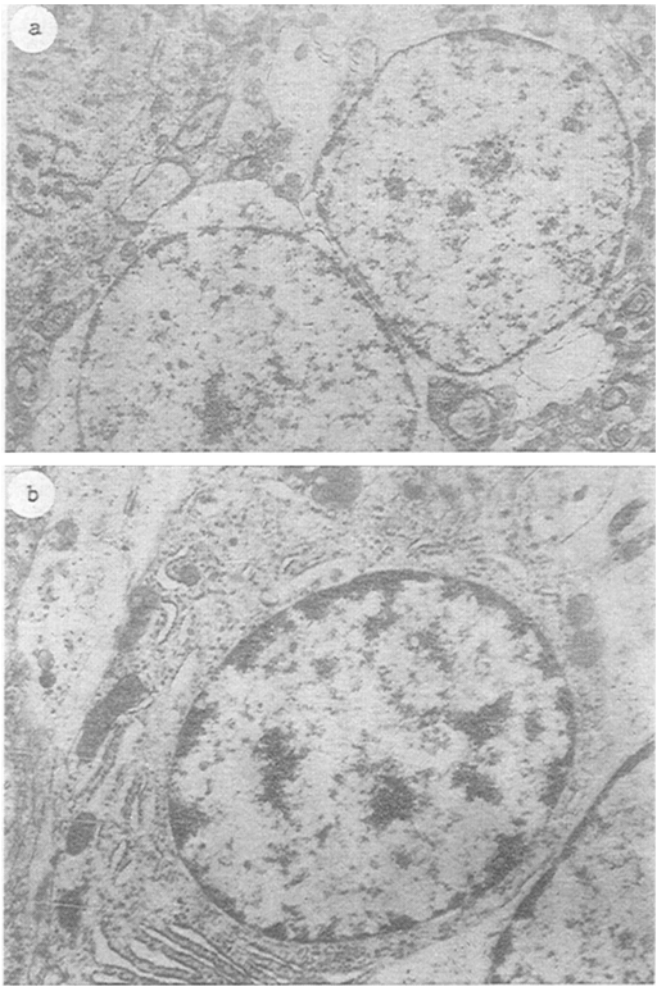

Fig. 2. Double pale astrocytes (a), pale astrocyte and oligodendrocyte (b) in sensomotor cortex of 30-day-old experimental rat. 3700×.

apparatus were detected in the cytoplasm, but in the immediate vicinity of the sites of rupture of the cytolemmas and of fusion of the cytoplasm the number of free polysomes and the area of the rough endoplasmic reticulum were increased, and multivesicular bodies appeared, i.e., synthetic processes were intensified. The nuclei in these double neurons were shifted more strongly toward the contacting cytolemmas and separated from them by a narrow layer of cytoplasm (Fig. 1).

Junctions between two neurons under pathological conditions have been observed by other workers also. The ultrastructure of paired neurons has been described in the cerebral cortex of rats with oxygen deficiency [2], of double neurons in the postischemic period [3], and of "paired" neurons in the lateral hypothalamic region after food deprivation [1]. These workers regard junctions between neurons as a compensatory reaction under particular pathological conditions.

Double glial cells of different types and ultrastructure also were found in our material. In most cases two astrocytes were in contact. They included cells with similar ultrastructure, possessing nucleus and cytoplasm of the typical structure, but the nuclei displaced toward the zone of contact contained larger marginal collections of chromatin. The cytoplasm of the other double astrocytes was deprived of organelles to a varied degree. An astrocyte with relatively few organelles at the periphery of the cytoplasm could be present in a pair with an astrocyte of irregular outline, containing vacuolelike cavities. The cell nuclei were strongly displaced toward the contacting cytolemmas and separated from them by a very narrow border of cytoplasm (Fig. 2a). Sometimes after destruction of the cytolemmas, the cytoplasm of the double astrocytes could be seen to be fused.

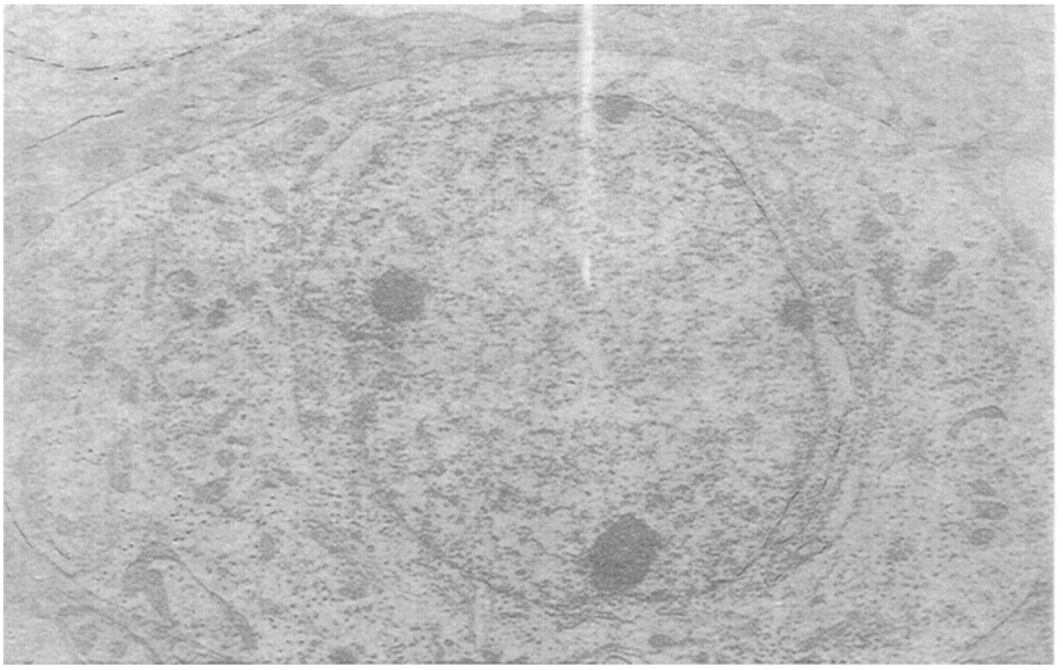

Fig. 3. Activation of nuclear and cytoplasmic structures in a dystrophically changed neuron in sensomotor cortex of 30-day-old experimental rat. 4800×.

A double astrocyte and oligodendrocyte was seen less frequently. The former had uneven outlines and contained translucent foci and membranous bodies in their cytoplasm; the displaced nucleus was separated from the cytolemma by a hardly visible border of cytoplasm. The cytoplasm of the oligodendrocyte was moderately osmiophilic and the cisterns of the rough endoplasmic reticulum were dilated; the mitochondria were distributed mainly around the periphery and the nucleus was less strongly displaced toward the region of the contacting membranes (Fig. 2b).

We previously [6] noted the compensatory character of this approximation of the bodies of neurons and astrocytes toward the basement membrane of the cortical capillaries in the offspring in this same model of exposure of the mothers to alcohol. Under these circumstances the capillaries were unevenly compressed and surrounded by a muff of edematous processes of perivascular astrocytes, in which the mitochondria were located close to the junction with the basement membrane.

Intracellular reparative regeneration constitutes the structural basis of reversibility of the dystrophic changes in nerve cells [7]. Repair processes in the dystrophically changed cortical neurons of the offspring, in the case of moderate prenatal exposure of the mothers to alcohol, are expressed as activation of the nucleus and cytoplasm. The characteristic features include a varied depth of invagination of the nuclear membrane, the presence of two nucleoli in the paranucleolar bodies, their displacement toward the nuclear membrane, grouping of the mitochondria, in which were patterns of their division (Fig. 3). Hyperplasia of the Golgi apparatus or of its lamellar component, an increase in the number of rough vesicles and lysosomes, and hypertrophy of individual mitochondria also were observed. In the 60-day-old experimental rats, proliferation of pale astrocytic processes was clearly defined in the neuropil of the sensomotor cortex, including near to synapses, indicating the possibility of "blocking" of some synaptic junctions by a type of feedback, in order to maintain processes of restoration in the neuron. Meanwhile in many synapses the synaptic vesicles were concentrated near the presynaptic membrane, and the contacting membranes were indistinct and considerably thickened, indicators of increased function of the synapses. In addition, multiple contacts between axon terminals were present on certain dendrites with the typical ultrastructure, possibly indicating intensification of the presynaptic afferentation. The smoothing out of differences in motor activity and learning in the experimental and control rats toward the age of two months can be explained by the presence of reparative changes and increased efficiency of synaptic transmission [8]. However, dystrophic changes in the neurons lasted until puberty and even in the adult experimental offspring, thus raising the question of a search for ways of eradicating brain damage at the earliest times of life.

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