Alterations of Cortical Neurons and Their Dendrites After Chronic Alcohol Intoxication

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Translated from *Byulleten' Eksperimental'noi Biologii i Meditsiny*, Vol. 122, No. 10, pp. 467-470, October, 1996
Original article submitted August 20, 1995

Alterations occurring in the neurons of rat sensorimotor cortex 1, 2, and 4 months after a 4-month alcohol intoxication and 1 and 4 months after a 1-year alcoholization are studied by the methods of Nissl and Golgi. Pronounced dystrophic changes in cortical neurons and dendrites as well as reparative processes in the cell body are revealed 1 month after a 4-month intoxication. The recovery period for the upper cortical layer neurons (phylogenetically younger) is faster than that of neurons from the lower layers (phylogenetically older), as well as that of hypochromatous *vs.* hyperchromatous cells. Normalization of dendrite structure is slower than that of the cell body. Four months after a 1-year alcohol intoxication the structure of cortical neurons and dendrites is not restored.

Key Words: *alcohol withdrawal; sensorimotor cortex; neurons; dendrites*

Morphological alterations of the brain after alcohol withdrawal are poorly investigated. It was demonstrated that changes in guinea pig brain neurons are preserved for 7-10 days after a 3 month alcohol intoxication [7]. In rats, acute changes in blood vessels, glial cells, and neuron caused by an 8-month discontinuous alcoholization disappear 2-7 days after alcohol withdrawal [2].

The nature of changes in rat brain vessels, neurons, and glial cells depends on the duration of chronic alcoholization. Withdrawal of alcohol for 1 month after a 3-6-month intoxication reduces morphological changes in brain structures; however, after 9-12 months of alcoholization pathological processes still occur [1]. Previously, we showed that the majority of brain neurons and dendrites in the upper layers of the cortex restore their structure within 2 months after a 2-month alcoholization [4], while structural alterations in the lower layer neurons are preserved within this time period.

Our goal was to characterized the alterations of brain neurons and dendrites after chronic alcohol intoxication.

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MATERIALS AND METHODS

The model of chronic intoxication developed at the Moscow State University [5] was employed. The structure of rat brain cortex (n=15) was studied 1, 2, and 4 month after a 4-month alcoholization and 1 and 4 months after a 1-year alcoholization.

The methods of Nissl and Golgi were used.

RESULTS

One month after withdrawal of alcohol, as well as during a 4-month alcoholization [5], dystrophic changes predominated in cortical neurons: swelling, chromatolysis, and karyocytolysis. They were accompanied by transformation of some neurons into ghost cells and replacement of dead cells by the glia. Highly hyperchromatous small neurons, sometimes clusterized, and occasional "shrunken" neurons were seen.

Hyperchromatous neurons have been associated with mental retardation [3], while the appearance of "shrunken" neurons has been regarded as an adaptive response (cellular mummification) [8].

Reparative processes were observed in some neurons: the nucleus was located near the nuclear membrane (this frequently occurred in the cytoplasm zone with reduced content of the basophilic substance),

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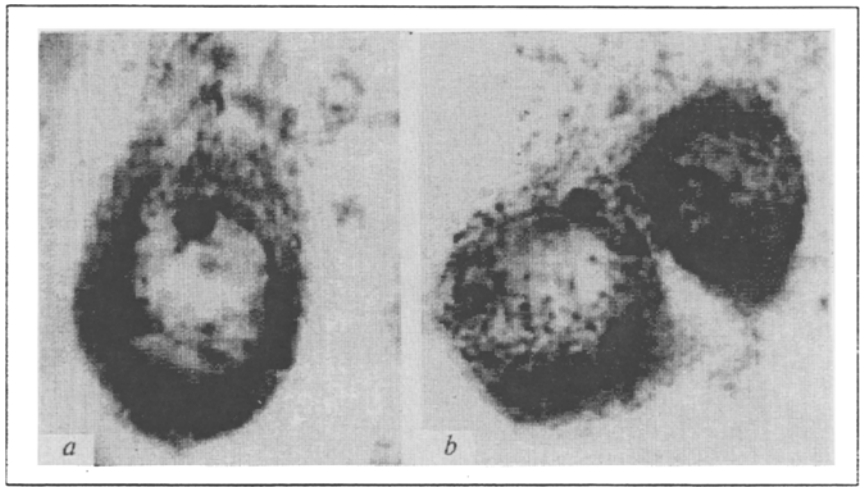

Fig. 1. Dislocation of the nucleolus to the nuclear membrane, polar thickening of the membrane, juxtanuclear hyperchromaticity of the cytoplasm (*a*), migration of the nucleolus into the cytoplasm (*b*). Neurons in layer V of the sensorimotor cortex 1 month after a 4-month alcohol intoxication. The Nissl method. ×750.

polar thickening of the karyolemma, juxtanuclear hyperchromaticity of the cytoplasm (Fig. 1, *a*). In some neurons, the nucleus was lying in the cytoplasm (Fig. 1, *b*). This may facilitate RNA transport into the cytoplasm in order to maintain the function of neurons, which are practically in the state of necrobiosis.

Compensatory migration of the nucleolus into the cytoplasm was observed in newborn monkeys fed a protein-deficient diet [10] and in hypothalamic neurons of aged and old people [9].

The dendrites, particularly their terminal segments, were convoluted, which indicates the loss of tonicity. Their basal branches were thin and hypochromatous, implying disorders of the information processing and synaptic transmission in the brain.

Two months after a 4-month alcohol intoxication, the structure of the upper layer neurons was restored. The structure of the lower layer neurons remained practically unchanged (Fig. 2).

Four months after a 4-month intoxication, the majority of hypochromatous neurons restored their structure, the intensity of the cytoplasm staining in hyperchromatous cells decreased, and the nucleus and nucleolus become discernible. Although deafferentation of dendrites slightly decreased (occasional spikes were seen on altered dendrites), their structure was not restored.

One month after a 1-year alcoholization, there were no noticeable structural changes in cortical neurons and their dendrites. The number of neurons in the cortex decreased, accumulations of glial cells, chromatolytic changes, karyocytolysis, ghost cells, and clusters of highly hyperchromatous and shrunken cells with the nucleolus in the cytoplasm and disrupted plasma membrane were seen. Disruption of the plasma membrane and migration of the nucleolus are typical of necrobiotic cells [6]. The dendrites were convoluted, thinned, and "fenestrated"; occasional spikes appeared on their secondary branches (Fig. 3).

There were no considerable differences between neuronal alterations 1 and 4 months after a 1-year alcoholization. Necrobiotically altered neurons with the nucleolus located in the cytoplasm (Fig. 4, *a*), hypochromatous cells with compensatory changes in the cytoplasm, and hyperchromatous neurons with swollen apical dendrites containing large nucleolus (Fig. 4, *b*) were seen.

Thus, our findings show that the recovery of neurons and dendrites after 4 months of alcohol intoxication is faster in the upper (phylogenetically younger) than in the lower (phylogenetically older) layers of the brain cortex. Compensatory processes are more intense in hypochromatous than in hyperchromatous neurons, while normalization of the den-

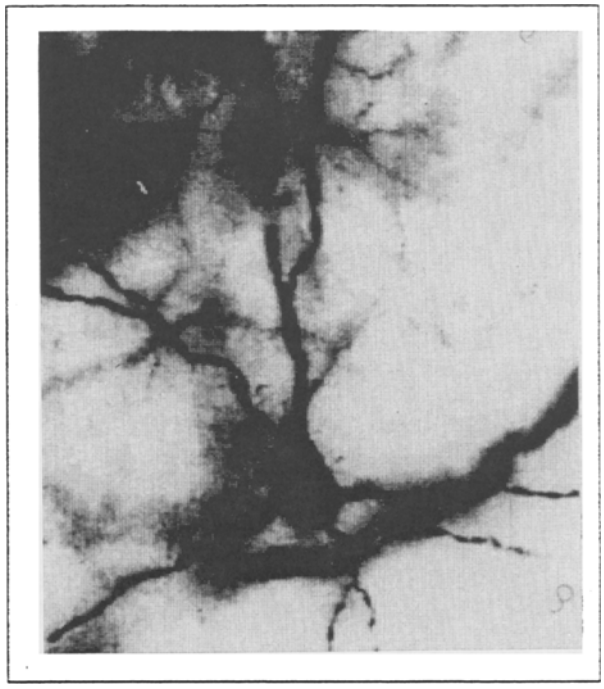

Fig. 2. Dendrites in layer V of the sensorimotor cortex 2 months after a 4-month alcohol intoxication. The Golgi method, ×200.

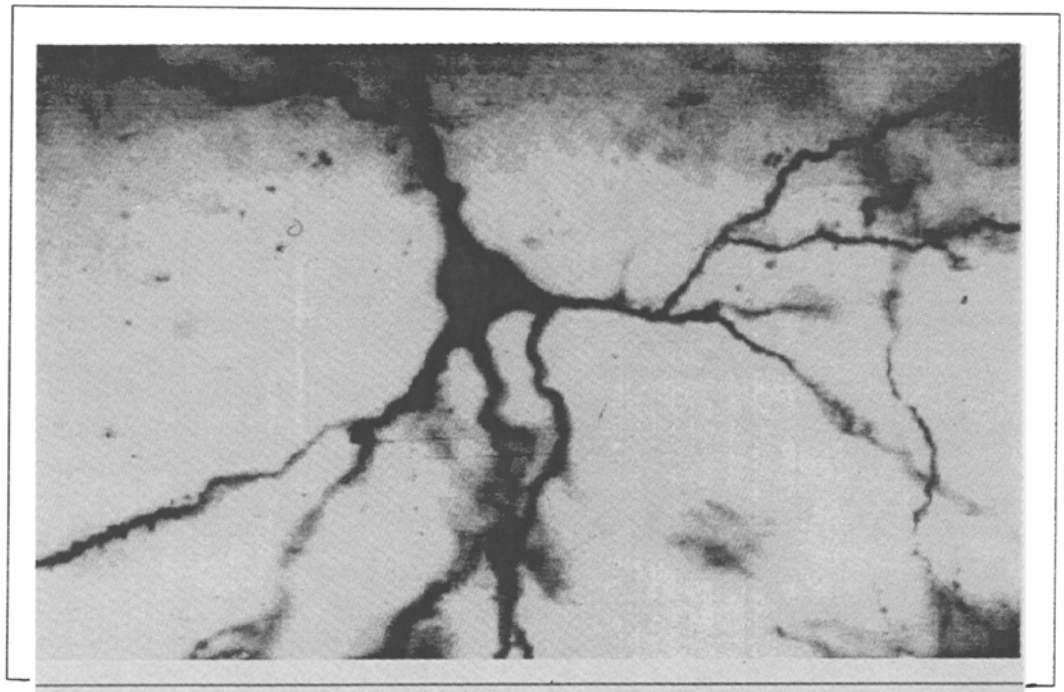

Fig. 3. Structure of dendrites of a layer V neuron 1 month after a 1-year alcohol intoxication. The Golgi method. ×300.

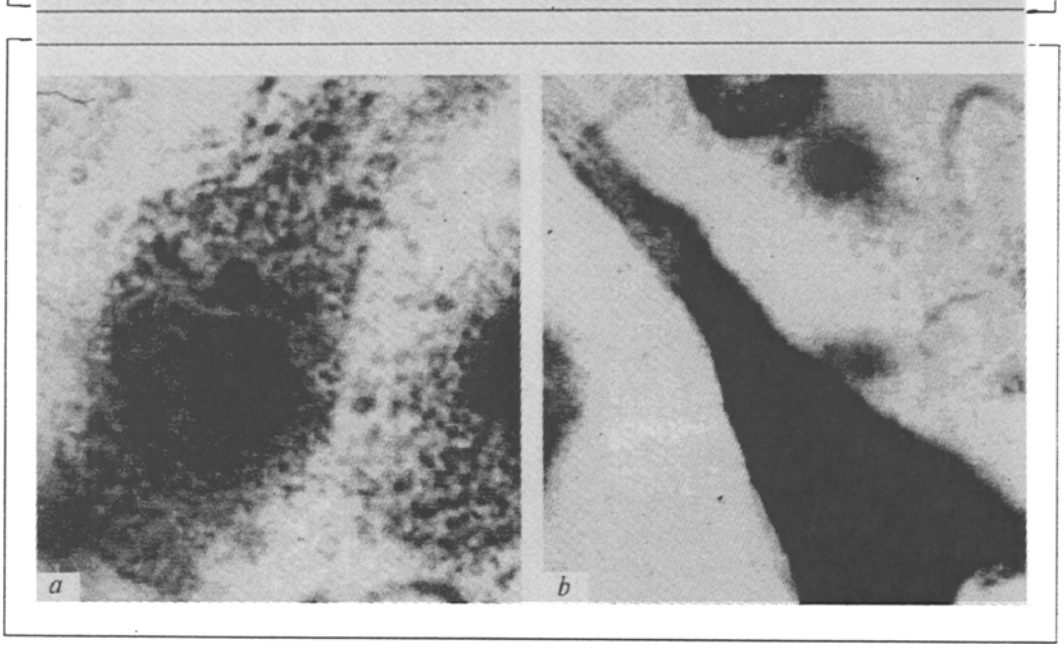

Fig. 4. Necrobiotic changes in neuron (*a*), decreased hyperchromaticity (*b*) in a large neuron of layer V 4 months after a 1-year alcohol intoxication. The Nissl method. ×750.

drite structure lags behind, particularly in the lower layer of the cortex. The structure of cortical neurons and dendrites is not restored within 4 months after a 1-year alcoholization.

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