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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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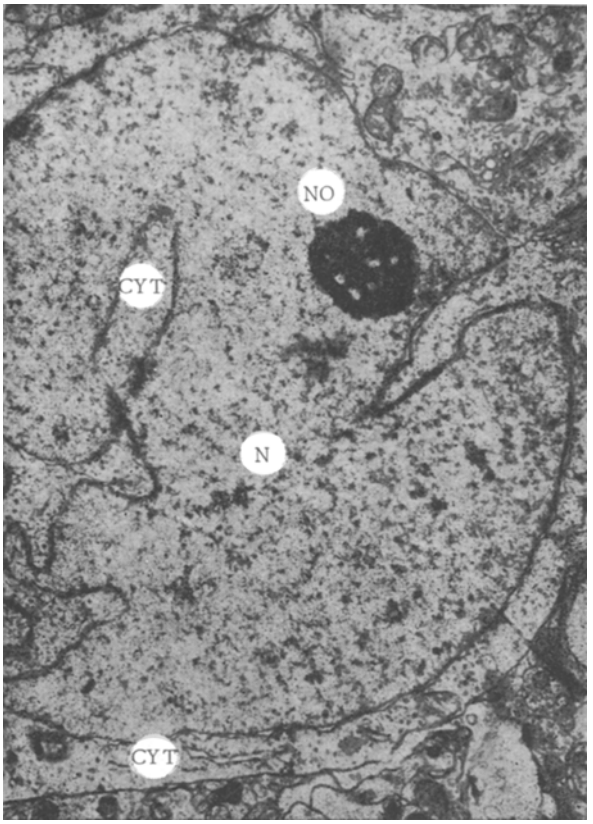


Fig. 1. Changes in configuration of nucleus in nerve cells from surface layers of sensomotor cortex in alcohol poisoning. Reduction in quantity of nuclear substance and in area of cytoplasm. N) Nucleus; NO) nucleolus; CYT) cytoplasm. 8000 ×.

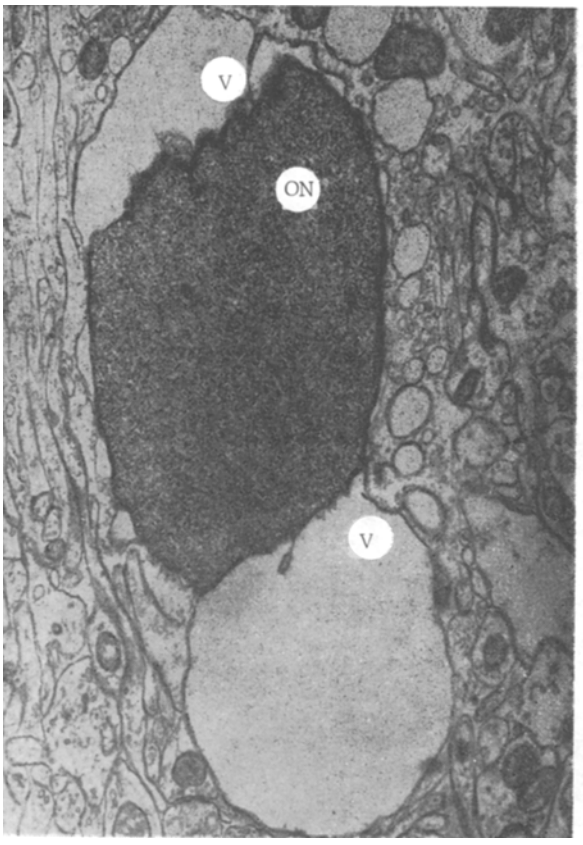
These changes in tissue and structural elements of the cortex during chronic alcohol poisoning were basically similar in character to changes described previously by one of us (N. I. A.) and also by other workers [1, 7, 8]. They consisted of perivascular edema of the astrocytic glia, slowing and vacuolation of the cytoplasm and its organoids, accumulation of lipofuscin granules in nerve and glial cells, etc.

As the present investigation showed, in chronic alcohol poisoning the nerve cell nuclei also changed. In the normal cerebral cortex nerve cell nuclei are round or oval in shape. Irregularly shaped nuclei, with projections into the cytoplasm or, conversely, with indentations filled with cytoplasm, were found much less frequently in the control animals.

In the experimental animals changes in configuration of the nuclei were found in many cortical neurons. The nuclei became multilobar, with uneven and curiously shaped outlines. In some cells the indentations into the nucleus reached almost to the opposite pole of the nuclear membrane, and in that case the separate parts of the nucleus were joined together only by a narrow isthmus of nuclear material (Fig. 1). The nucleoli in such nuclei were most frequently eccentrically placed, closer to the nuclear membrane. Against the background of the pale karyoplasm, the chromatin was uniformly scattered over the nucleus, without forming masses of any kind or forming only small aggregations. In some places dilatation of the perinuclear cistern was observed near such nuclei.

Usually in cells with a nucleus of altered shape the area occupied by the cytoplasm was considerably reduced. Separate parts of the nuclear membrane in cells of this kind touched the membrane surrounding the cell or were separated from it only by a narrow band of cytoplasm.

The number of organoids in the cytoplasm varied: in some cells the number of ribosomes, cisterns of the rough and smooth reticulum, mitochondria, and lysosomes was reduced. Those



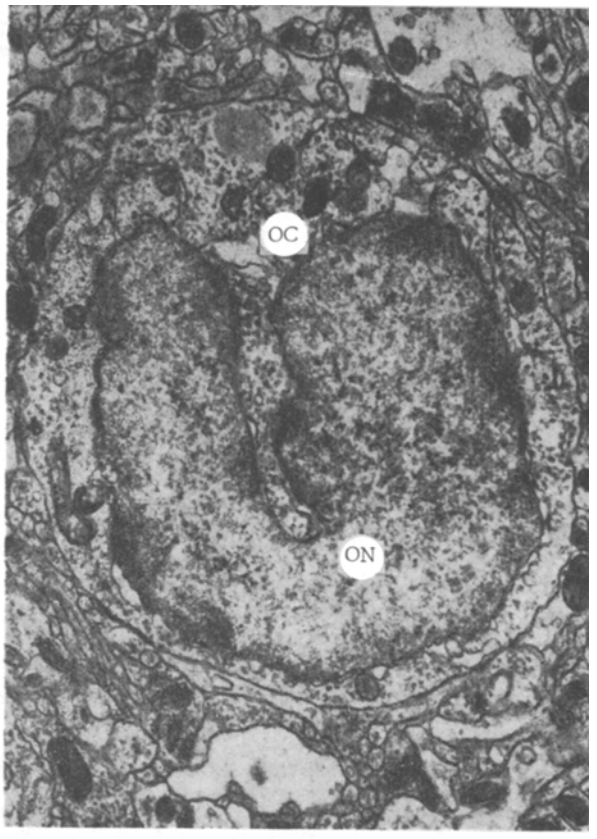


Fig. 2

Fig. 3

Fig. 2. Marked dilatation (vacuolation) of perinuclear cistern in an oligodendrogliocyte from the sensomotor cortex in alcohol poisoning. ON) Oligodendrogliocyte nucleus; V) vacuoles of perinuclear cistern. 12,000 ×.

Fig. 3. Folding of nucleus in oligodendrogliocyte from sensomotor cortex in alcohol poisoning. ON) Oligodendrogliocyte nucleus; OC) oligodendrogliocyte cytoplasm. 12,000 ×.

areas of cytoplasm which penetrated deep into the nucleus, in which there were only free ribosomes and polysomes, with occasional small mitochondria, were the least richly supplied with organoids.

In cells whose cytoplasm was vacuolated the nuclei remained round or oval in shape. The most characteristic and widespread change in the glial cells was vacuolation of the glioplasm and of the perinuclear cistern.

If microvacuolation predominated in the glioplasm, the perinuclear membrane in some cells formed multiple invaginations, almost equal in size, into the region of the glioplasm, and in other cells one or two vacuoles, much larger in size, projected near the nucleus (Fig. 2). Vacuolation of the perinuclear cistern was considerable in the oligodendrogliocytes. A more characteristic feature of astrocytes was microvacuolation and edema of the glioplasm. The nuclear structure of the glial cells showed no significant change. Changes in configuration and a greater degree of folding of the nucleus were observed in the oligodendrogliocytes, just as in nerve cells (Fig. 3). No changes in shape of the nuclei were found in the astrocytes.

Besides hydropic changes in chronic alcohol poisoning, processes leading to deformation and to changes in the ultrastructure of the nerve and glial cell nuclei thus also develop.

The functional role of folding of the nucleus has not yet been explained. Some workers consider that the increase in extent of the nuclear membrane as a result of folding of the nucleus in neurons is the result of reactive changes, associated with intensification of synthesis both in the nucleus and nucleolus, and also in the cytoplasm [2, 4].

In the present case, folding of the nuclei in chronic alcohol poisoning can hardly be regarded as a change in reactivity connected with intensification of synthetic processes, for in these cells there was a deficiency of nuclear material and cytoplasm, evidence rather of atrophy, leading to shrinking of the nucleus and to a decrease in size of the cells as a whole. This conclusion is confirmed by the results of physiological investigations which showed that the reactivity and lability of the brain structures are depressed in chronic alcoholism [3, 5].

In the case of those nuclei whose karyoplasm was rich in RNP granules and masses of chromatin were concentrated near the nuclear membrane, and the nucleolus also was close to the nuclear membrane, metabolic processes were evidently intensified.

However, in most cells with changes in the shape of the nucleus the karyoplasm did not have the characteristics described above and was poor in RNP granules and in masses of chromatin. The question arises whether changes in shape of the nucleus were the direct result of the action of alcohol or whether they developed secondarily on account of metabolic changes in the neurons and disturbance of nucleo-cytoplasmic relationships.

It can be tentatively suggested that both these factors may influence the development of changes in the nuclei of nerve and glial cells. The combination of a deficiency of nuclear material with a decrease in the area occupied by the cytoplasm, and also a decrease in the number and size of its organoids, indicated depression of metabolic activity and atrophy of these cells.

The increase in the number of cells of this kind, together with the hydropic and other changes in nerve and glial cells, must be responsible for the development of alcohol encephalopathy in the animals.

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