3. I. P. Anokhina, V. Z. Gorkin, L. N. Ovchinnikova, *et al.*, *Alcohol Alcohol.*, **26**, No. 5-6, 559-565 (1991).
4. P. Chomchinsky and N. Sacchi, *Anal. Biochem.*, **162**, 156-159 (1987).
5. A. Z. Drozdov, B. M. Kogan, and I. P. Anokhina, *Alcohol Alcohol.*, **23**, No. 5, 343-350 (1988).
6. J. Engel and U. Rydberg, *Acta Pharm. Toxicol.*, **57**, 336-339 (1985).
7. J. M. Khanna, A. San-Marina, H. Kalant, and A. D. Le, *Genetic Aspects of Alcoholism*, K. Kiinmaa *et al.* (Eds.), Vol. 37, London (1989), pp. 207-217.
8. B. Tabakoff and P. Hoffman, *Ibid.*, pp. 127-146.

Changes in Neurons of the Caudate Nucleus in Experimental Alcoholism

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Reversible changes in caudate neurons and their dendrites in line with the components of compensatory reaction in oligodendrocytes are observed in rats during the first 3 weeks of a 12-month alcoholization period. After 2-4 months of alcoholization (the development of dependency), degenerative changes occur in caudate neurons and their dendrites system were evident. By the end of the 12-month period of alcohol intoxication, intensified deafferentation of the dendritic system was observed, suggesting functional insufficiency of the caudate nucleus.

Key Words: *alcohol; caudate nucleus; neurons; dendrites*

Morphofunctional organization of the caudate nucleus (CN) can be regarded as a subcortical association center involved in the regulation of brain integrative activity [6,10,11,13].

It was shown that CN is involved in neurophysiological mechanisms underlying the development of alcoholism and associated extrapyramidal disturbances [2]. However, structural organization of CN in chronic alcohol intoxication has been poorly investigated. In guinea pigs given small doses of alcohol over a short period, changes in neurons were detected not only in the neocortex but also in the CN [5]. Swollen and shrunken cells and occasional ghost cells were observed in CN of rats receiving alcohol for 1-3 months, while most CN neurons were swollen in rats after 6-12 months of alcohol consumption [3]. As we are aware, changes occurring in dendrites and dendritic spikes of experimentally alcoholized animals have not been studied, although these structures play an important role in primary processing of information received by the neuron and in the synaptic mechanisms of brain activity.

In the present study we examined changes in caudate neurons and in their dendrites with large numbers of spikes occurring in chronic alcohol intoxication (12 months).

MATERIALS AND METHODS

Rat model of chronic alcohol intoxication (alcoholization) was developed at the Department of Higher Nervous Activity, Moscow State University [7].

Rats were given a 30% alcohol solution instead of water from specially designed drinking bowls containing sucrose solution (150 g/liter) to increase alcohol consumption. The standard chow was supplemented with penicillin (daily dose 10,000 U) and polyvitamins (0.1-0.15 g). Control rats received an alcohol-free ration. Daily alcohol consumption was 2-3 ml per rat during the first 10-20 days, rose to 8-10 ml over the next 2-2.5 months and then to 14-17

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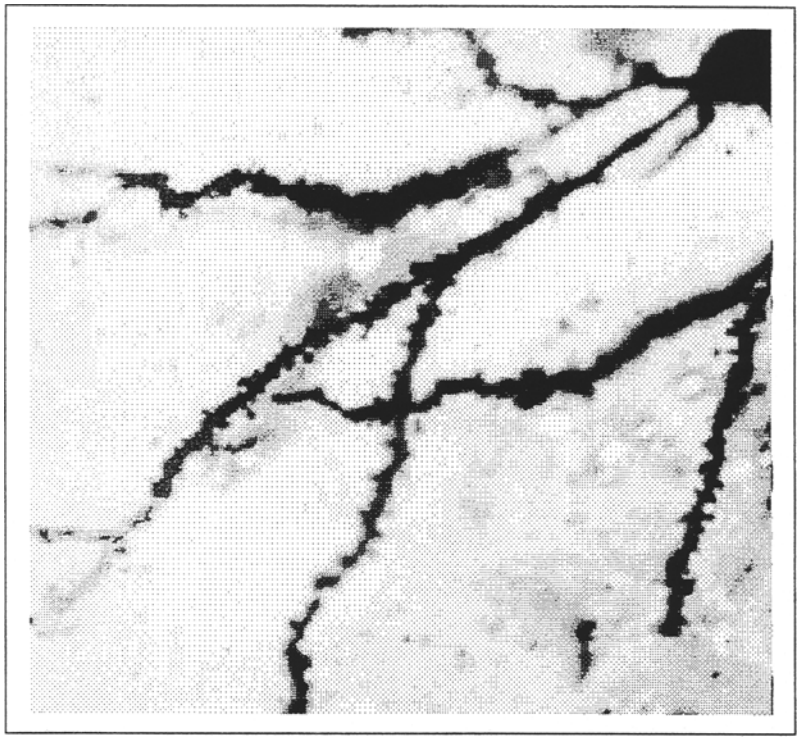

Fig. 1. Dendrites of a caudate neuron with dense spikes from a control rat. Golgi stain; magnification 400.

ml until the 6th month, and then dropped to 4-8 ml during the following 2 months before rising again. Rats were killed by decapitation after 10 and 20 days and 2, 4, and 12 months of alcoholization. The dorsolateral area of the CN receiving afferent inputs mainly from cortical regions responsible for the motor activity [12] was taken for investigation. The material was stained by the Nissl and Golgi methods.

Using an eyepiece micrometer (magnification 420), the spikes were counted per 10 μ of length in successive dendrite segments of neurons with closely spaced dendritic spikes. The results were analyzed using formulas for the evaluation of biological materials [4].

RESULTS

In the CN from control rats, the bulk of cells were medium-sized karyochrome cells with large nuclei and small cytoplasmic rim. They were characterized by the presence of 4-7 primary dendrites with few spikes and secondary and tertiary branches covered with numerous spikes (Fig. 1), 7.3±0.1 per micron of these branches.

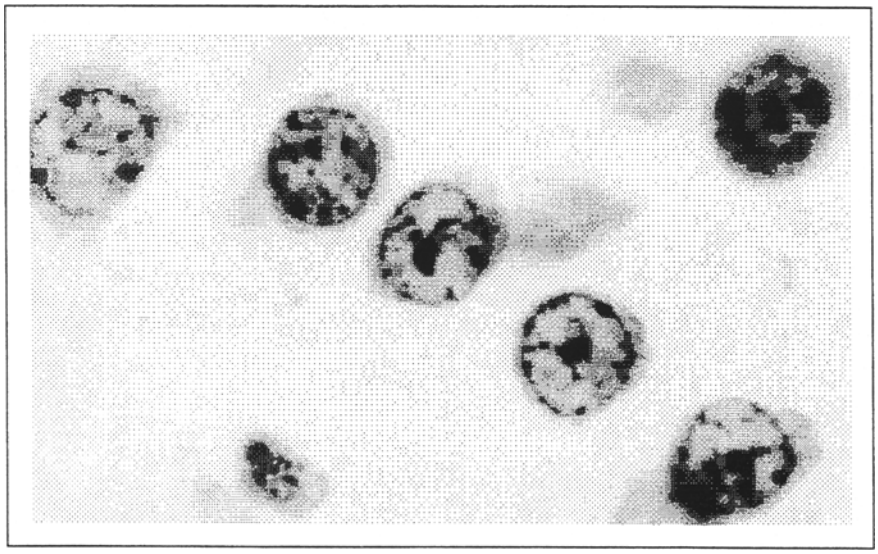

Fig. 2. Intracellular organization of caudate neurons from a rat alcoholized for 20 days. Nissl method, magnification 1000.

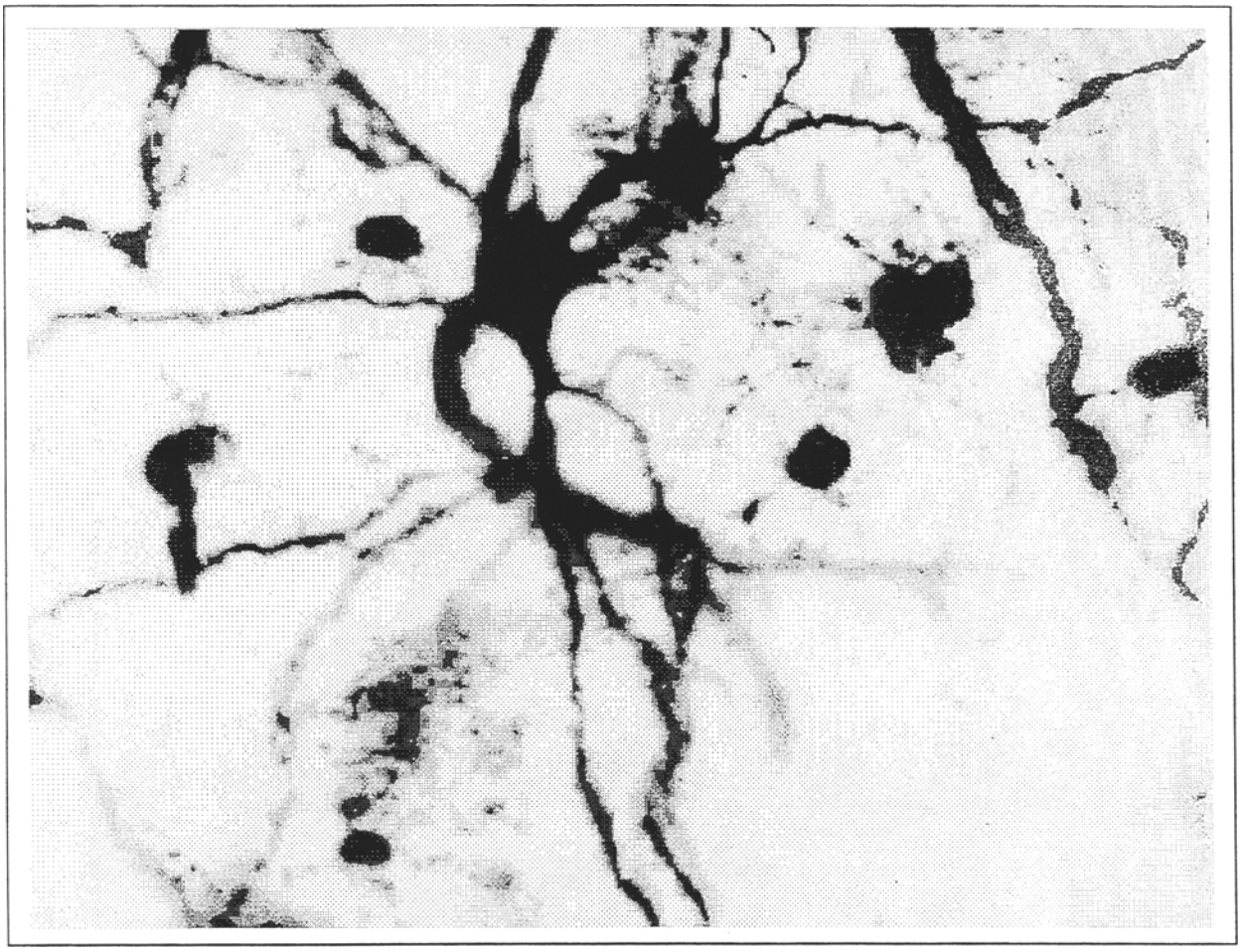

Fig. 3. Dendrites of a caudate neuron from a rat alcoholized for 20 days; oligodendrocytes appear swollen and gliodendritic "junctions" can be seen. Golgi method, magnification 300.

After 20 days of alcohol intoxication, no substantial changes in the intracellular organization of medium-sized caudate neurons were apparent (Fig. 2), but the number of impregnated dendritic spikes decreased considerably (to 2.3±0.07), and thin weakly stained areas appeared on some branches, presumably indicating impaired conductivity of these dendrites. On the other hand, oligodendrocytes undetectable by the Golgi method in intact animals were impregnated. Most of them had a round or oval body and short processes, which is a characteristic feature of swollen (so-called "drainage") oligodendrocytes (Fig. 3). The emergence of such oligodendrocytes, some processes of which may form gliodendritic "junctions," represents a reaction of compensatory adaptation directed at maintaining the function of caudate neurons in the early period of alcohol intoxication. Functionally, the learning of a conditioned reflex motor habit by rats was not appreciably impaired after the first 10-20 days of alcoholization [7].

After the rats had developed alcohol dependence (2-4 months), karyocytolysis with transformation of some neurons into ghost cells was observed in the CN in line with widely distributed degenerative changes in cortical neurons, some of which appeared dead [7]. Changes in the dendritic system of neurons with densely arranged spikes were similar to those seen after days 10 and 20 of alcohol intoxication, although degeneratively changed neurons were also noted, with terminal dendritic branches devoid of spikes, thinned out, and poorly impregnated. Previously, we found that the conditioned-reflex activity of rats is impaired after 4-4.5 months of alcohol intoxication; by this time pathomorphological changes in nerve and glia cells of various brain regions had developed [1].

After 12 months of alcoholization, no marked progression of changes in the intracellular organization of caudate neurons was evident. Staining by the Golgi method showed increased impregnation of vessels and the presence of spherical neurons which had only a few dendrites with widely spaced spikes, the remaining dendrites being without spikes and deformed; the latter dendrites had numerous thinned and weakly stained areas (Fig. 4). Spindle-shaped or

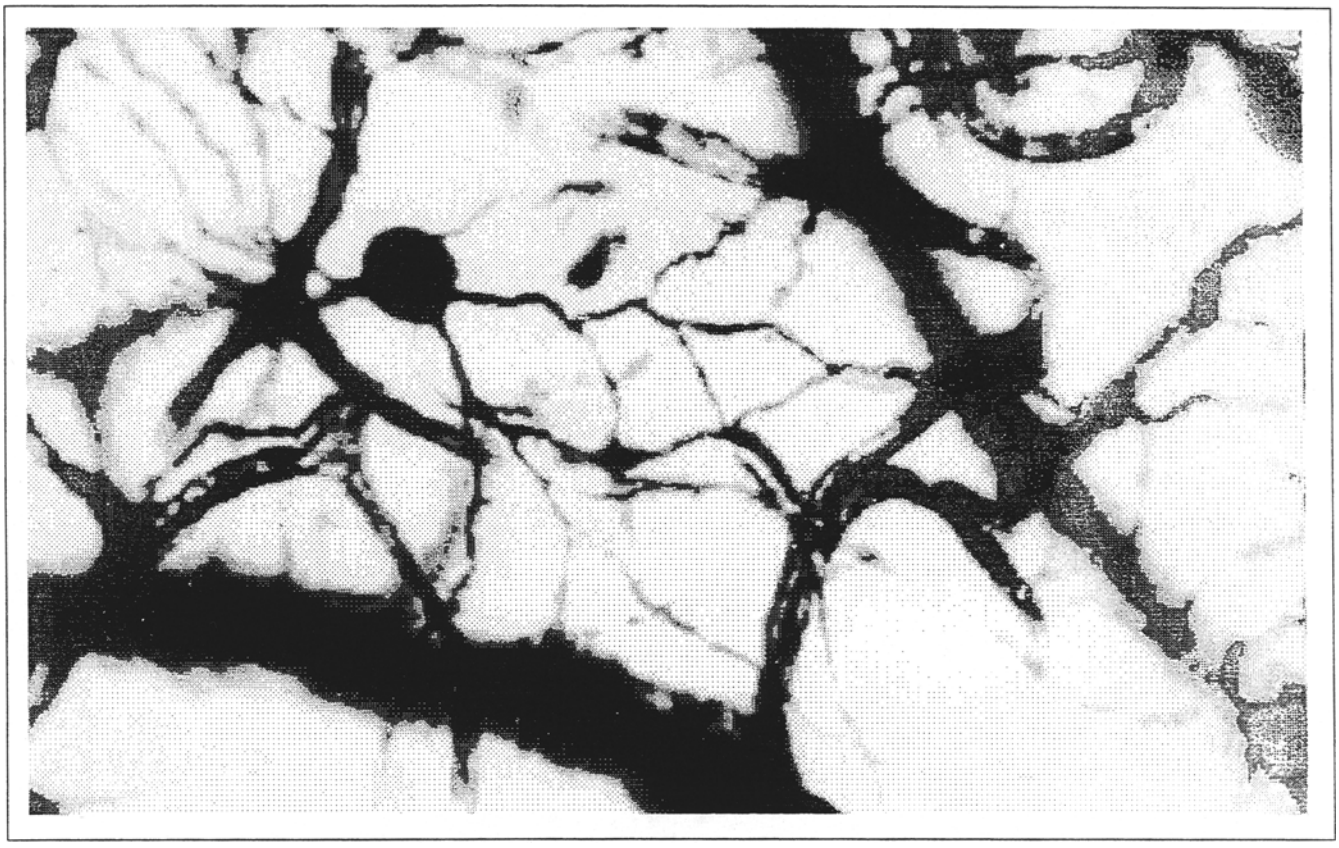

Fig. 4. Dendrites of a caudate neuron from a rat alcoholized for 12 months. Golgi method, magnification 300.

varicose dilatations typical of neocortical dendrites in various diseases [8] were not observed. Morphophysiological study with the use of mathematical modeling [10] showed that the addition of several constrictions to the swelling on a neurite lowers the amplitude of action potential, which results in conduction blockade. The presence of similar dendritic changes in CN of rats alcoholized for 12 months is probably a manifestation of functional insufficiency of the CN. In such rats, an increase in convulsive activity was detected on the EEG and behavioral manifestations of this increase were observed [1].

Experimental chronic alcoholization leads to morphofunctional disorganization of the CN, which adversely affects higher integrative functions of the brain.

REFERENCES

1. T. M. Vorob'eva, Zh. P. Gordienko, and L. N. Paikova, *Zh. Nevropatol. Psikhiatr.*, **90**, No. 2, 77-84 (1990).
2. T. M. Vorob'eva and L. N. Paikova, *Zh. Nevropatol. Psikhiatr.*, **93**, No. 5, 85-90 (1993).
3. L. Sh. Galeeva, "Forensic medical evaluation of morphological changes in the brain and selected viscera in alcohol intoxication," Author's Synopsis of Dissertation [in Russian], Karaganda (1973).
4. L. S. Kaminskii, *Statistical Processing of Laboratory and Clinical Data* [in Russian], Moscow (1964).
5. G. N. Krivitskaya, V. B. Gel'fand, and E. N. Popova, *Destructive and Reparative Processes in Focal Lesions of the Brain* [in Russian], Moscow (1980).
6. V. A. Otellin and E. B. Arashunyan, *The Nigrostriatonigral System* [in Russian], Moscow (1989).
7. E. N. Popova, V. B. Polyanskii, K. A. Nikol'skaya, *et al.*, *The Brain and Alcohol* [in Russian], Moscow (1984).
8. S. A. Sarkisov, *Essays on Structure and Function of the Brain* [in Russian], Moscow (1964).
9. O. S. Sotnikov, *Structural Dynamics of the Living Neuron* [in Russian], Leningrad (1985).
10. N. F. Suvorov, *Fiziol. Zh.*, **80**, No. 1, 3-13 (1994).
11. B. F. Tolkunov, K. B. Shipovalova, and S. V. Afanas'ev, *Zh. Vyssh. Nervn. Deyat.*, **40**, No. 6, 1027-1038 (1990).
12. O. G. Chivilyaeva, in: *The Striatal System in Health and Disease* [in Russian], Leningrad (1988), pp. 130-132.
13. V. T. Shuvaev, *Fiziol. Zh.*, **79**, No. 5, 138-148 (1993).