ULTRASTRUCTURE OF THE SYNAPTIC APPARATUS AFTER ADMINISTRATION OF AMPHETAMINE AND HALOPERIDOL

B. V. Vtyurin and V. P. Tumanov

UDC 615.214.31+615.214.22/.015.4:611.8-018.83

The ultrastructure of neurons of the rat cortex was investigated after administration of a single dose of amphetamine and haloperidol. After administration of amphetamine, signs of an increase in functional activity of the neurons were observed: activation of the synaptic apparatus, an increase in the number of pores in the nuclear membrane, dilation of the cavities of the endoplasmic reticulum, swelling of the mitochondria. Under the influence of haloperidol the picture was different: no signs of activation of the synapses were present and the matrix of the mitochondria was condensed.

The object of this investigation was to study the ultrastructure of neurons of the rabbit sensomotor cortex after administration of a single dose of amphetamine, with an excitatory action on the CNS [1], and haloperidol (with the opposite effect) [3]. Particular attention was paid to the state of the synaptic apparatus, changes in which are known to be closely connected with the degree of functional activity of nerve cells [6].

EXPERIMENTAL METHOD

The rats (weighing 180-200 g) of group 1 received a single intraperitoneal injection of amphetamine solution in a dose of 10 mg/kg. The animals were kept in a special box, divided into compartments in which the animal ran for 90 min as a result of the motor excitation induced by amphetamine. The animals of group 2 received a single subcutaneous injection of haloperidol solution in a dose of 9 mg/kg. Before the material was taken, the rats' brain was perfused with 2.5% glutaraldehyde solution in phosphate buffer, pH 7.4. Pieces of tissue were then excised from the sensomotor cortex, from area PA^m, layer V, fixed with OsO_4 and dehydrated in alcohols and acetone. The pieces of tissue were embedded in Araldite and Epon 812. Sections were cut on the LKB ultratome, shadow-cast with uranyl acetate and lead citrate by Reynold's method, and examined in the UEMB-100 V electronmicroscope.

EXPERIMENTAL RESULTS

On investigation of the neurons of the rat sensomotor cortex in the electron microscope after administration of amphetamine, changes were found in the nuclei, endoplasmic reticulum, ribosomes, mitochondria, and synaptic apparatus. The nuclei of the neurons were slightly swollen, with uniformly distributed nucleoplasm, and a compact nucleolus in the center. In some areas of the nuclear membrane, the outer membrane was detached with the formation of enlarged cavities of the perinuclear space and an increase in the number of pores. The number of ribosomes, both free and located on the membranes of the endoplasmic reticulum, in the cytoplasm was reduced. In some neurons the cavities of the endoplasmic reticulum were dilated and had the appearance of vacuoles with uneven edges, on the membranes of which a few ribosomes could be seen. In some cells the mitochondria were swollen and their matrix was translucent, while in others the changes in these organelles were less marked (Fig. 1a).

Laboratory of Electron Microscopy, Department of Pathological Anatomy, A. P. Vishnevskii Institute of Surgery, Academy of Medical Sciences of the USSR, Moscow. (Presented by Academician of the Academy of Medical Sciences of the USSR A. A. Vyshnevskii.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 72, No. 10, pp. 108-110, October, 1971. Original article submitted April 27, 1971.

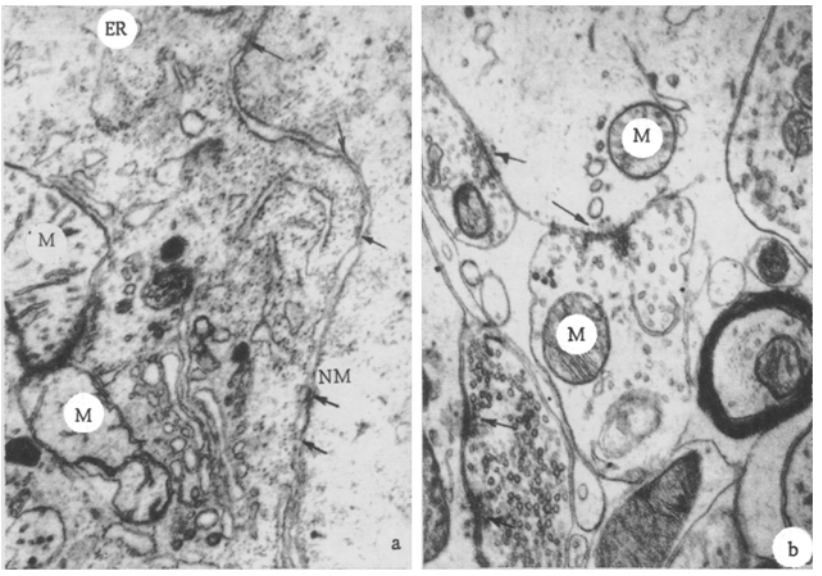

Fig. 1. Neuron of the rat sensomotor cortex after administration of amphetamine: a) translucent matrix of mitochondria (M), increase in size of pores in nuclear membrane (NM) (marked by arrows) and dilatation of tubules of the endoplasmic reticulum (ER); postsynaptic membranes (marked by arrows). Here and in Fig. 2, 28,000 ×.

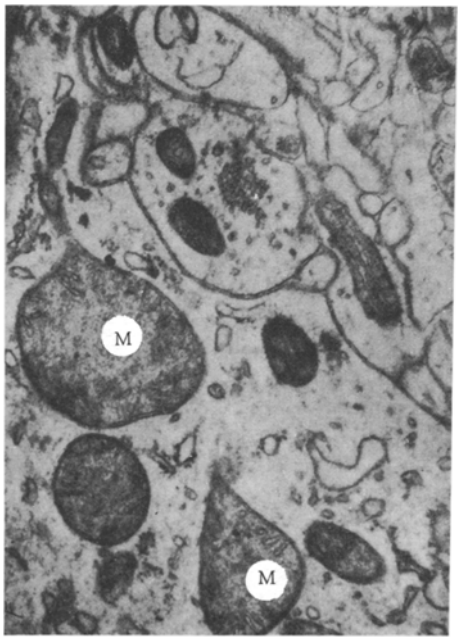

Fig. 2. Localization of synaptic vesicles in center of axon and condensation of matrix in large mitochondria of a neuron in the sensomotor cortex of a rat after administration of haloperidol.

Synapses have several active zones which are responsible for the conduction of the nervous impulse. In the region of the active zones of the axodendritic synapses, thickening of the postsynaptic membranes was observed. The synaptic vesicles were numerous and were arranged all along the axon terminals. Several small mitochondria were found among them. The extent of the active zones of the synapses was considerable, and much of the terminal was covered with spines. Most of the synaptic vesicles were indistinguishable from normal: some were paler, 200-250 Å in diameter, and they occupied the greater part of the plaque, while others were darker and more dense, 300-400 Å in diameter, and lay closer to the presynaptic membrane (Fig. 1b).

Protrusion of the outer nuclear membrane and an increase in the number of pores were observed in the glial cells. The lysosomes in the nerve and glial cells were small and situated near to the Golgi apparatus. An increase in the number of pinocytotic vesicles and loosening and thickening of the basal layer were observed in the endothelial cells of the capillaries in the motor cortex.

After administration of haloperidol, changes different from those described above were observed in the ultrastructure of the neurons in the motor cortex. These changes affected predominantly the mitochondria, which, as a rule, were slightly enlarged and had a dense matrix. In both axons and dendrites, the mitochondria were abnormally long. Most synapses were in a "passive" state: the number of synaptic vesicles in the region of the presynaptic membrane was small, and they were more often concentrated in the center of the terminals (Fig. 2).

As a result of the action of amphetamine and haloperidol, changes were thus observed in the fine structure of the neorons of the rat motor cortex. These changes evidently reflected differences in the degree of excitation and inhibition of the CNS associated with the drugs used.

Increased functional activity after administration of amphetamine was indicated by changes in the synaptic apparatus of the nerve cells such as the appearance of active zones, thickening of the postsynaptic membranes, and the concentration of synaptic vesicles around them. Further evidence was given by an increase in the number of pores of the nuclear membrane and the projection of its outer membrane with the formation of folds. Such changes lead to an increased flow of messenger RNA from nucleus to cytoplasm [4, 7].

The decrease in the number of ribosomes, the increase in size of the cavities of the endoplasmic reticulum, and the translucency of the matrix of the mitochondria also indicate activation of the enzyme systems responsible for increased activity of the nerve cell during excitation. This is in agreement with the effect of psychotonic drugs (caffeine, strychine, etc.) reported in the literature [2, 5, 8].

After administration of haloperidol the changes in the nerve cells were different in character. The synaptic apparatus was inactive. Synaptic vesicles were grouped in the center of the terminals or all over the neuron plaque, while the presynaptic and postsynaptic membranes showed no visible changes. Large and abnormally long mitochondria were observed in the nerve cells and on their processes. The nuclei were increased in size and their nucleoplasm somewhat condensed.

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