ULTRASTRUCTURE OF THE CEREBRAL CORTEX AFTER STRYCHNINE APPLICATION

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Application of strychnine to the cerebral cortex leds to ultrastructural changes in the cells and neuropil. Disorganization of the intercellular spaces is observed, with the formation of many marked swellings of the dendrites and glial processes and invagination and tortuosity of the cytoplasmic membranes. The intercellular spaces vary in width (from 50 to 1000 Å or more). Increased consumption of synaptic vesicles and a decrease in the osmiophilia of the synaptic membranes were observed.

In the last decade the selective sensitivity of certain structures of nerve tissue (the synapsis of the glial elements, etc.) to pharmacological agents and structural changes in cortical nerve cells in some pathological states have been described [1-3].

This paper describes a study of the ultrastructure of the surface neuropil of the cerebral cortex following direct application of strychnine.

EXPERIMENTAL METHOD

Eight adult cats were anesthetized by intraperitoneal injection of pentobarbital (40 mg/kg). Strychnine (0.1% solution) was applied in the region of areas 5, 7, and 21 of the right hemisphere by means of filter paper (0.2-0.3 cm in diameter). Brain potentials were recorded on an electroencephalograph (Alvar) and pieces of cortex were taken from the region of application 1.5-2 h after the beginning of the most intensive paroxysmal activity. The application was repeated 40-60 min later. Pieces were taken from the same regions of the brain of intact animals for control purposes. The brain tissue was fixed in 1% osmium tetroxide solution in phosphate buffer, dehydrated in alcohols of increasing concentration, and embedded in Araldite. Thin sections 300-600 Å in thickness were stained by Reynold's method and examined in the JEM-6c electron microscope with an accelerating voltage of 80 kV.

EXPERIMENTAL RESULTS

Changes were found in the nerve and glial cells in the region of application of strychnine. Pale and dark neurons were found, and in the former the Golgi apparatus showed changes, and free ribosomes had almost completely disappeared from the cytoplasm. The cisterns of the Golgi apparatus were more sharply dilated than those of the endoplasmic reticulum. The dark neurons, by contrast with the pale, were shrunken and most of the surface of their soma was covered with swollen glial processes, but the dendrites of the corresponding dark neurons were compact and highly osmiophilic.

In the epileptic cortex disorganization of the intercellular spaces was very noticable; the spaces themselves were irregularly widened (sometime up to 1000 Å or more), but local constrictions also were found (50-150 Å) in small areas. In some places the areas of constriction gave the impression that the opposite

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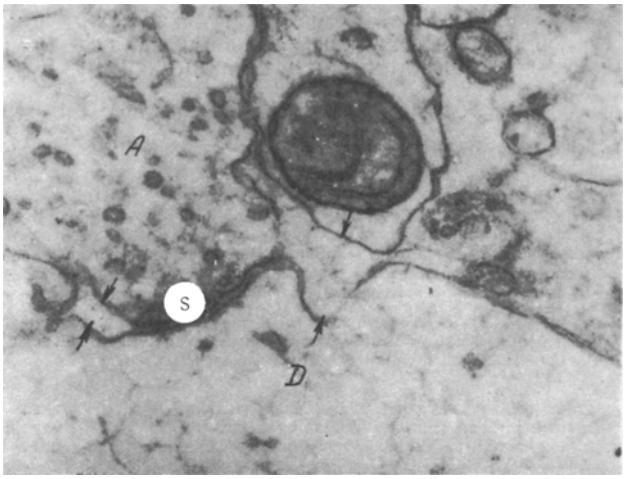

Fig. 1. Enlargement of intercellular space (indicated by arrows), decrease in number of synaptic vesicles in axon terminal (A), swelling of dendrite (D), and tortuosity of synaptic membranes (S). 30,000×.

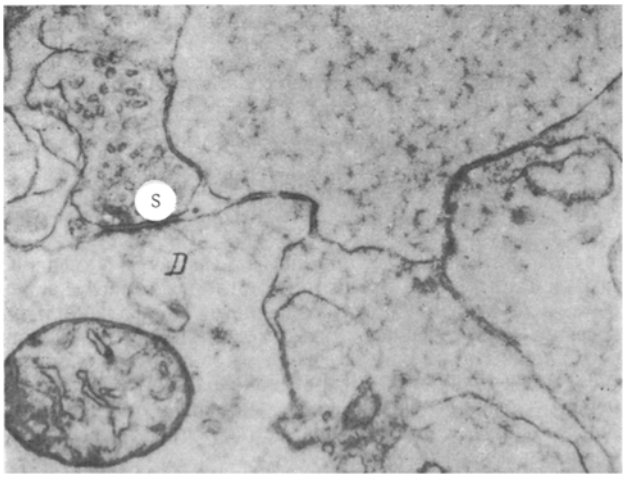

Fig. 2. Marked swelling of dendrite (D) and low osmiophilia of synaptic membranes (S). 21,000×.

cytoplasmic membranes were in direct contact. The widenings of the intercellular spaces were particularly large in the region where three different structures met (Fig. 1). Membranes of the terminal branches of axons and dendrites were extremely tortuous, their cross sections had lost their normal round configuration, and they formed frequent invaginations of varied depth and width (Fig. 2). Similar invaginations could be formed anywhere in the body or along the processes of the neuron.

The dendritic terminals, unlike the axonal, were greatly swollen, sometimes by several times, their cytoplasm was loose in texture, their organelles were scattered, their mitochondria also were swollen and often had a pale matrix (Fig. 3), while mitochondria with a dark matrix were less frequent, and the cristae of the internal membrane were reduced in number (Fig. 3). Grossly swollen dendritic terminals still had synaptic contacts of the normal size with axonal terminals (Fig. 3).

The synaptic spaces were more or less intact and their width was about 200-250 Å. However, in the immediate neighborhood of the active synaptic zones, their membranes were highly tortuous. The tortuosity of the membrane was widespread in character, and in some cases it extended also to the synaptic membranes (Fig. 1). Neither in the control experiment nor in response to direct electrical stimulation of the cortex, was tortuosity of the membranes of this type observed [4].

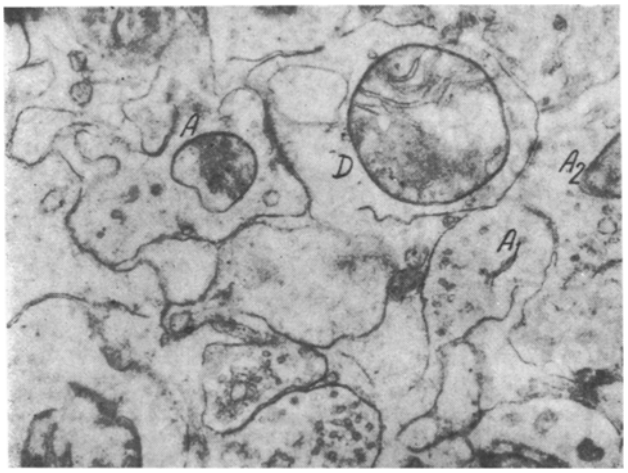

Fig. 3. Deformation of axon terminal (A), decrease in number of synaptic vesicles in terminals A, Al, A2, and widening of intercellular spaces. 17,000 ×.

Synaptic contacts with a large osmiophilic mass were very rare, and in the overwhelming majority of cases the synaptic membranes and spaces were clearly distinguishable (Figs. 1, 2, and 3) for the degree of osmiophilia of the synaptic membranes was low. A marked decrease in the number of synaptic vesicles was noted, and often only a few synaptic vesicles were present on the presynaptic membrane (Figs. 1 and 3). There were comparatively many synaptic vesicles in axon terminals in contact with the denser dendrites. In these cases more vesicles than in the control cases were concentrated on the presynaptic membrane. The presence of these more or less normal synapses is evidence that the application of strychnine affects all synaptic contacts equally. All the changed axon terminals had irregular outlines with invaginations and evaginations of the membrane.

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