differing in the pathways which they follow and the zones of terminal ramifications or projections. There are five types of radial dendrites: 1) ventrolateral, with projection zones in lateral motor nuclei of lamina IX, and also in the ventrolateral funiculus; 2) dorsomedial, for commissural, running into the dorsal part of the ventromedial funiculus or into the anterior commissure; 3) ventromedial with projection zones in the ventromedial nucleus or ventromedial funiculus; 4) ventral with projection zone in the ventral funiculus; 5) dorsal with projection zones in laminae VIII and VII. There is also a sixth type of dendrite, which runs along the spinal cord, in either rostral or caudal directions, and virtually does not go outside the phrenic nucleus.

Penetration of dendrites of the phrenic motoneurons into the ventral, ventrolateral, and ventromedial funiculi, and also into laminae VIII and VII is functionally justified and understandable. Here they obtain information from reticulospinal tracts from the medulla and pons, among which there are respiratory fibers performing different functions [3, 4, 6, 7]. It can be tentatively suggested that dendrites of phrenic motoneurons running into the commissure are responsible for correcting the synchronized working of the phrenic nuclei in the two halves of the spinal cord. The functional significance of the numerous branches of dendrites of the phrenic motoneurons in the ventromedial nucleus, revealed by this investigation, is not yet clear. Ramifications of dendrites of phrenic motoneurons in the region of the lateral motor nuclei are of great interest. They most probably do not begin to function until their supraspinal inhibition is removed under certain conditions. We know, for example that after spinalization of rabbits the rhythm of their respiration follows that of the spinal locomotor generator [9]. Our results are in good agreement with data in [5], although unfortunately bands of dendrites are not described in it.

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## ULTRASTRUCTURAL CHANGES IN DENDRITES DURING AGING


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A detailed study of the response of dendrites during aging is of great theoretical and practical importance in view of their role in the synaptic mechanisms of brain activity as the receptive apparatus of nerve cells that are responsible for integrating information reaching the neuron. During aging in man and animals various changes have been demonstrated (mainly at the light-optical level) in dendrites. A reduction in the number of successive branchings, in the number of branches, and in the total length of both basal and apical dendrites has been noted [6, 8]. In the neocortex of old dogs the horizontal branches and, in some neurons, the basal branches of the dendrites also are lost [2]. A marked decrease in arborization density of the basal dendrites has been found in the auditory cortex of old


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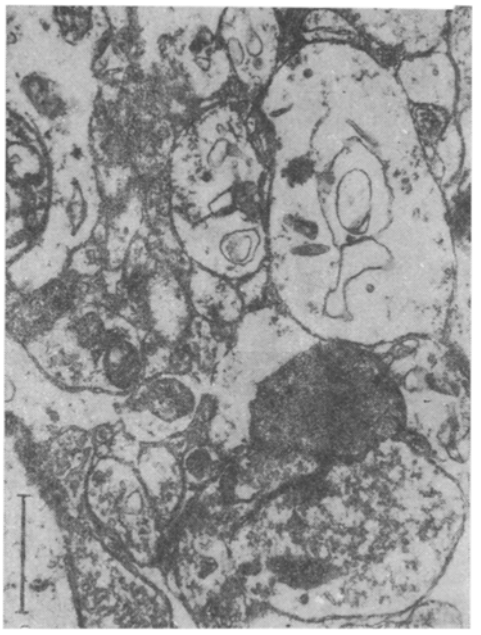

Fig. 1. Ultrastructural changes in dendrites of limbic cortex of an old (30 months) rat. Different vacuoles, membranous structures, destruction of organelles – microtubules, neurofilaments, and mitochrondria – can be seen. Here and in Figs. 2 and 3: scale is 1 μ.

rats, with no change in the extent of the dendritic branches [14]. Besides a reduction in the length of the dendrites, a decrease in their thickness [10, 11], and unevenness of their outlines and varicosities have been found [9, 13]. Some workers consider that accumulation of neurofilaments leads to degeneration of the dendrites [3]. An increase in the number of microtubules and neurofilaments has been demonstrated in dendritic profiles of animals with age [7]. At the ultrastructural level different forms of degeneration of dendrites have been observed. For instance, in the auditory cortex of old cats, electron-dense circular and helical formations and clumps of tubular myelin-like structures, of different shapes and sizes, have been found in the dendrites [4]. A considerable reduction in the number of dendritic spines has been observed with age, and their total disappearance on some dendrites [9, 10, 14]. The study of the various layers of the auditory and visual cortex of old rats has revealed smoothing of the surface of the dendrites and displacement of the spinous apparatus into the dendritic trunk [1].

This paper describes the characteristic ultrastructural changes in dendrites of different parts of the brain in old rats.

## EXPERIMENTAL METHOD

Experiments were carried out on the brain of seven old Wistar albino rats aged 28-30 months. The visual, parietal, sensomotor, and limbic cortex, hippocampus, hypothalamus, locus coerruleus, and reticular formation were studied in the electron microscope. Pieces of brain were processed by the usual method adopted in the Laboratory of Brain Ultrastructure, and embedded in Epon-812. Ultrathin sections were studied in the Hitachi-IIU electron microscope.

## EXPERIMENTAL RESULTS

During normal aging in rats various forms of disturbances of dendritic ultrastructure were observed. The ultrastructural changes were well marked in dendrites of large and medium caliber, whereas the small terminal ramifications remained more completely preserved. This tendency was characteristic of all cortical and subcortical brain formations studied. The commonest and most widespread change in the dendrites during physiological aging was vacuolation, which was observed in virtually all dendrites and was distinguished by considerable

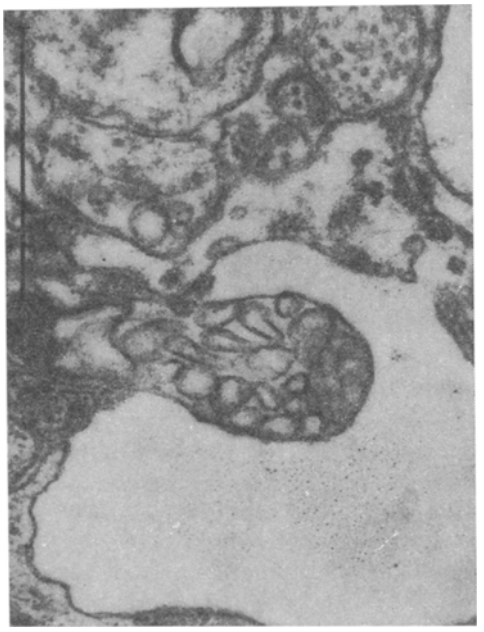

Fig. 2

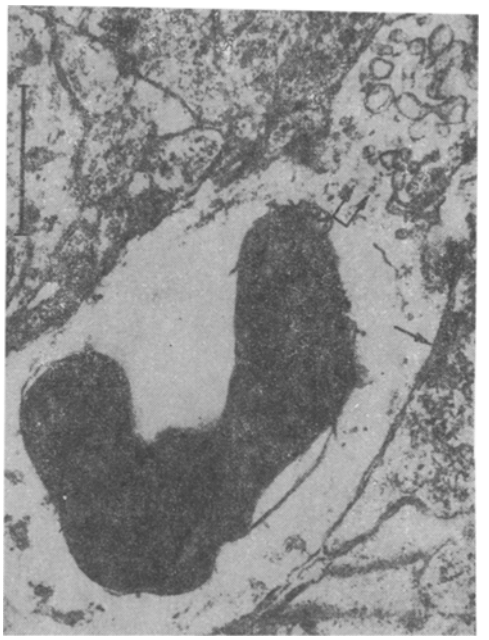

Fig. 3

Fig. 2. Invagination of adjacent axon into a large dendrite. Dendrite appears optically empty, and in the invaginated axon swelling and destruction of synaptic vesicles can be seen. Hypothalamus of a rat aged 30 months.

Fig. 3. Abnormal dark formation in large dendrite of sensomotor cortex of an old (30 months) rat. Preserved synapse (arrow) and destroyed synapse (doube arrow) can be seen on surface of dendrite.

polymorphism for size, shape, internal content, and source of origin. Some vacuoles were optically empty, others were filled with osmiophilic material or had various inclusions inside the cavity (Fig. 1). The vacuoles were surrounded by a single or double membrane, with a complex and curious shape in most cases. The source of origin of the vacuoles could be mitochondria, cisterns of the endoplasmic reticulum, the intracellular reticular complex and swollen fragments of microtubules, with which different vacuoles could often be seen to be connected. Some vacuoles were formed by invagination of the limiting membrane of the dendrite and of areas of adjacent profiles within the dendrite. In grossly disintegrated dendrites swollen vesicles and pinocytotic vesicles could be observed. The phenomenon of vacuolation was observed both in dendrites with intact organelles and in those with destructive changes in their organelles.

Dendrites of large and medium caliber were characterized by various ultrastructural changes. These took the form of disturbance of the orientation of the microtubules and neurofilaments, and their swelling, fragmentation, or total disappearance. The changes observed were both focal and diffuse in character. Fragmentation and disorientation of the microtubules in the large dendrites was often accompanied by destruction of other organelles. Changes in the dendrites described did not disturb their shape, and their outlines remained smooth.

Pathological changes of another type in dendrites mainly of large caliber consisted of swelling, characterized by edema of the dendroplasm and destruction of the organelles for their complete disappearnace, and disturbance of the outlines of the dendrites. The swelling was focal or total in character. The outer membrane of the dendrites became uneven, curiously shaped, and twisted, and in some places it was destroyed. It was in dendrites such as these that invagination of regions of adjacent structures of nerve tissue could be observed: axons, dendrites, synaptic endings (Fig. 2). Invasion of adjacent structures by dendrites also has been observed by other workers under different conditions: hypoxia, acute experimental anoxia, food deprivation, direct electrical destruction of the cortex, the action of various narcotic drugs, and in an epileptic focus [2, 3, 5]. The functional importance of this phenomenon has not yet been fully explained. Some workers regard it as a compensatory function of the neurons, as making good a deficiency of nutrients, the

supply of which from the body of the nerve cell has been disturbed due to disorganization of microtubules [3, 5]. Abnormal inclusions may often be observed in swollen, optically empty dendrites: dark homogeneous formations, and complex membranes and myelin-like structures (Fig. 3). The ultrastructural disturbances observed in dendrites correspond to varicose and bead-shaped changes in dendrites discovered by many investigators at the light-optical level [12]. We also observed these abnormal formations in ultrastructurally better preserved dendrites.

Incidentally, different forms of ultrastructural lesions could often be observed in dendrites located alongside one another, evidence that the changes are not synchronized even in the same structure. In all parts of the brain studied, dark degeneratively changed dendrites were found, often surrounded by glial processes.

The results of these investigations are evidence of the heterogeneity of ultrastructural changes in the dendrites during aging and of the greater severity of changes in the large dendrites compared with small. The greater vulnerability of large dendrites in some pathological processes and under some experimental conditions has been reported by other workers also [3]. This may be connected with the fact that destructive processes begin from the body of neurons, in which dystrophic changes take place in all cytoplasmic organelles, but primarily, the protein-synthesizing and energy-producing apparatus, leading to depression of metabolic function and gradual death of the cells. At the same time, this may also be connected with the greater vulnerability of synapses on large dendritic trunks compared with small [9, 10] and, consequently their greater degree of deafferentation.

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