# PHYSIOLOGY

# Changes in the Ultrastructure of Axospike Contacts in Human Brain during Normal Aging and in Vascular Disorders

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Light spikes, the majority of which are electron-transparent, are the main structural unit of the axospike contacts in normal brain of aged people (73 and 83 years). Dark spikes and spikes with moderate osmiophilia predominate in the brain of people with vascular disorders at the age of 70-73 years. A "synaptic block", which was morphologically represented by presynaptic terminals with densely packed synaptic vesicles, is revealed in the brain of aged people with vascular disorders. The role of hypoxia in the reorganization of axospike synapses is discussed. It is hypothesized that changes in the structure of axospike contacts in normal aging and vascular disorders are associated with modifications in the ultrastructure of spikes.

**Key Words:** *axospike contact; dendrite spike; spike apparatus; aging; vascular disorders*

Changes in the synapses, which lead to disturbances in the integrative function of the brain, are a cause of functional disorders of the central nervous system during aging or in vascular disorders. Structural modifications of dendritic spikes and axospike contacts (ASC) play a key role in these disorders [1,3, 5,7,9,10].

Changes in the spike apparatus (SA), which is associated and has a similar ultracytochemical organization with the postsynaptic receptor zone, markedly contribute to structural and functional disorders of dendritic spikes [1]. It was suggested that dendritic spikes contain contractile proteins which are associated with the plasma membrane of the spikes and membranes of SA and provide rapid changes in the spike shape [3,7,8].

The ultrastructure of the human brain ASC components, particularly that of postsynaptic zones, under normal and pathological conditions is poorly investigated. Our goal was to study ultrastructural changes occurring in the axospike synapses in normal aging and in vascular disorders.

## MATERIALS AND METHODS

Temporal, frontal, and precentral brain cortex from people died of ischemic heart disease at the age of 70, 72, and 73 years and from people died of vascular disorders at the age of 73 and 83 years was studied by electron microscopy. The material was collected 2.5-4.5 h after death, processed by the standard methods, and embedded into Epon-812. The sections were examined in a Hitachi-H-600 and Hitachi-H-11E electron microscopes.

## RESULTS

The spikes of the dendrites forming the postsynaptic ASC vary in shape and size (Fig. 1). The bulk of

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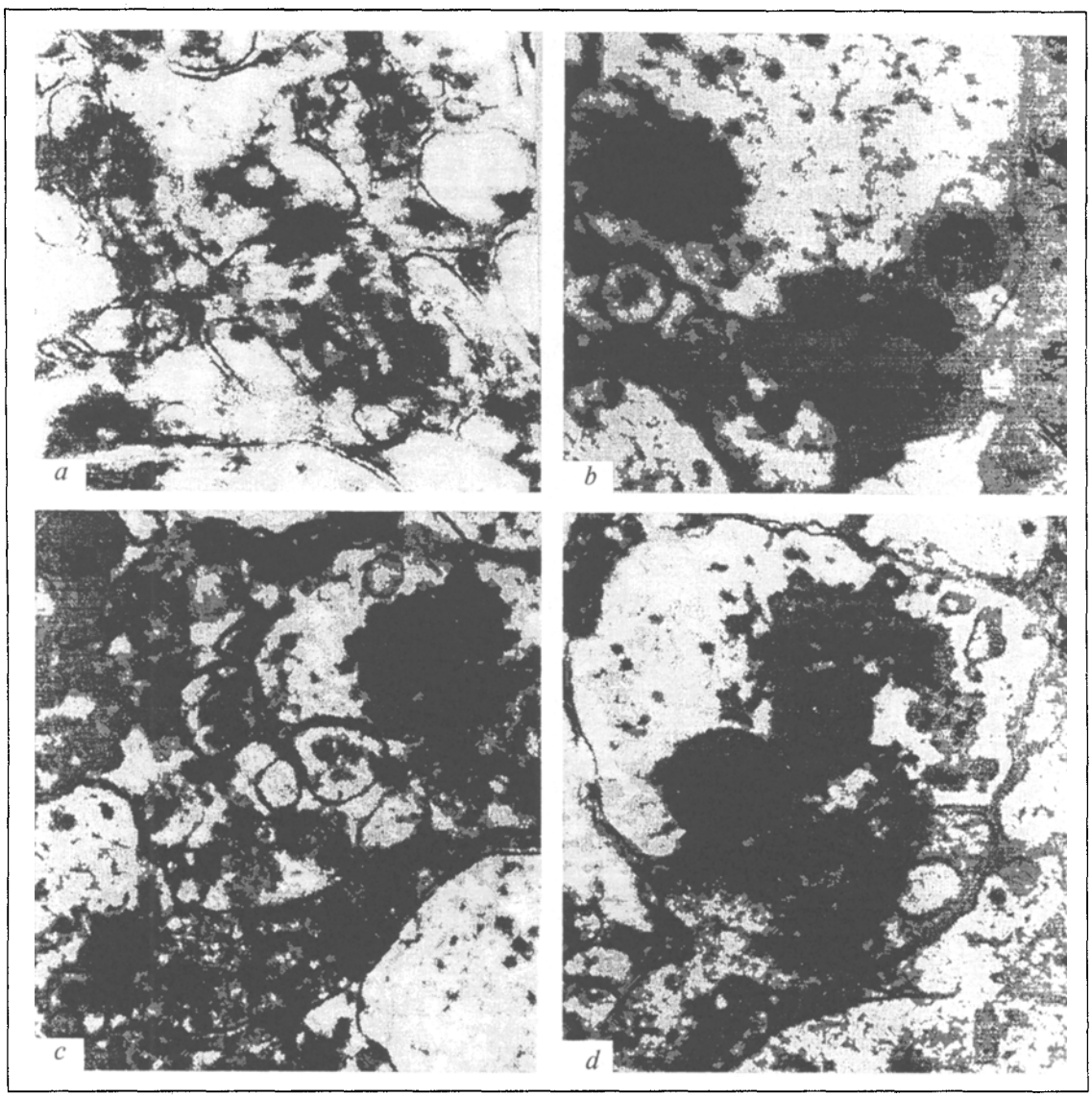


**Fig. 1.** Axospike synapses with spikes of various shape and extent of osmiophilia. Electron-transparent spike (*a*), dark spike (*b*), and spike with moderately osmiophilic cytoplasm. Elongated and mushroom-like spikes (*c*, *d*). Temporal brain cortex of a 83-year-old (*a*) and 70-year-old (*b-d*) men. ×32,000.

their population was made of large and medium-sized spikes resembling stalks or mushrooms with or without a short thick stem. There were also elongated spikes without stem and spikes with a round head. We revealed no considerable differences in the shape and size of the spikes in the studied samples.

Light spikes with moderately dense cytoplasm and dark spikes (Fig. 1) were observed. Their ratio was different in normally aging brain and in vascular disorders. In normal brain, light spikes predominantly electron-transparent particularly at the age of 83 years (Fig. 1, *a*) were the main structural units of ASC. In vascular disorders, dark spikes (Fig. 1, *b*) and spikes with moderate osmiophilia (Fig. 1, *c*, *d*) predominated.

In normal aging as well as in vascular disease all spikes lacked SA. Considerable changes were revealed in the fibrillar and vacuolar components of SA (Fig. 2). Vacuolar structures predominated in some spikes (Fig. 2, *a*). Sometimes vacuoles were hypertrophied (Fig. 2, *b*) or reduced (Fig. 2, *c*). In occasional spikes SA consisted of numerous small vacuoles and electron-dense material (Fig. 2, *d*).

Generally, in normal aging (particularly at the age of 83 years) AS is reduced or is represented by several vacuoles. In vascular disorders, SA contains hypertrophied vacuoles and lamellar bodies ("fingerprints") (Fig. 3, *a*). In some spikes with low osmiophilia degenerative changes were observed: destruction of SA, disruption of the spike membrane, fragmentation and degeneration of the spike (Fig. 3, *b*).

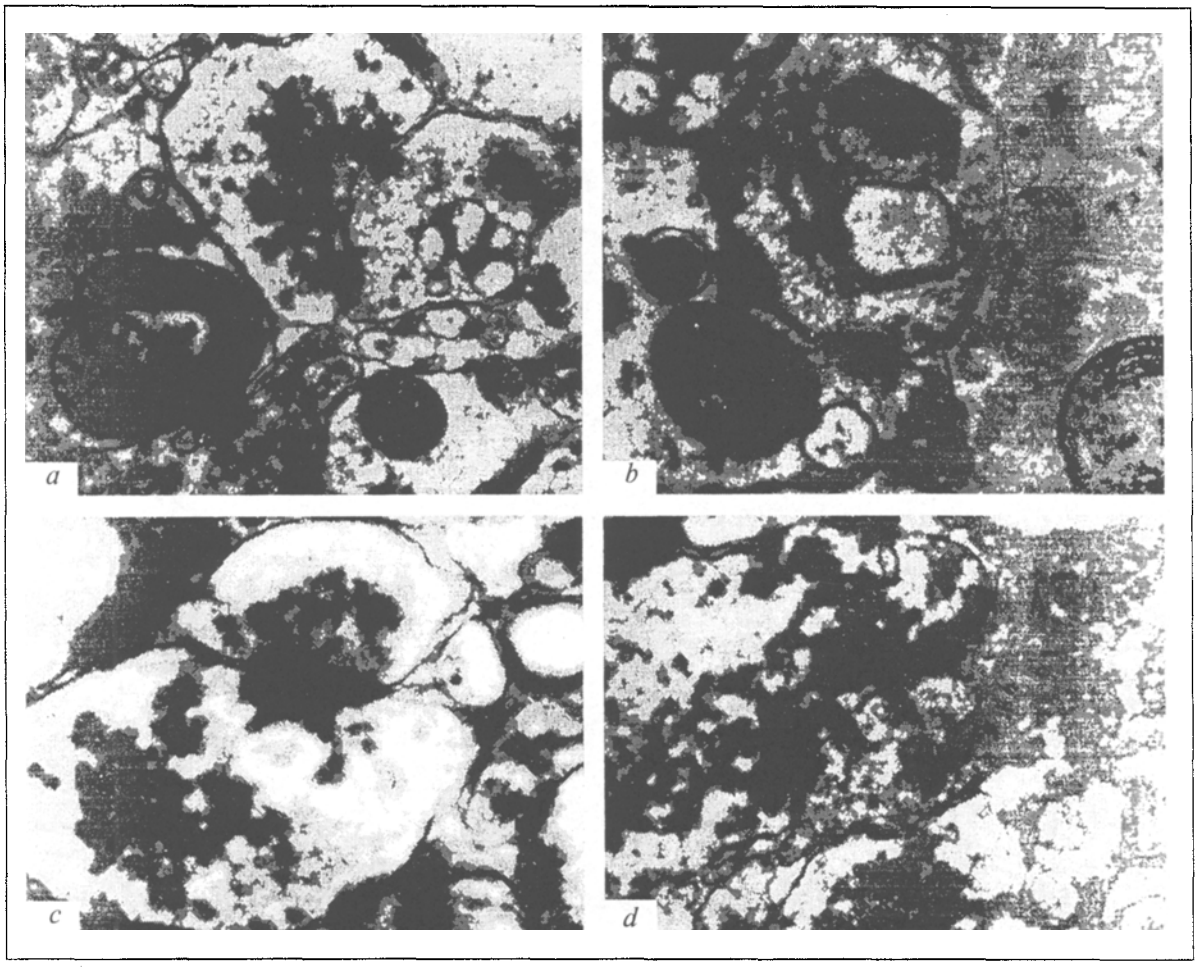


**Fig. 2.** Ultrastructure of spike apparatus. Vacuoles *(a)*, hypertrophy *(b)*, hyperplasia *(c)*, and reduction *(d)* of vacuoles. Temporal *(a, b, d)* cortex of a 70-year-old man and frontal *(c)* cortex of a 72-year-old man. ×32,000.

Dark (degenerating) spikes had no SA or it was represented by hardly discernible vacuoles (Fig. 3, *c*). Small atrophied spikes with an electron-dense matrix and hardly discernible postsynaptic dense areas were observed (Fig. 3, *d*).

Changes in the postsynaptic area of ASC coincided with ultrastructural modifications (occurring predominantly by the light pathway) in the presynaptic area and vacuolation of some terminals (Fig. 3, *e*). Axospike contacts with electron-dense presynaptic terminals due to accumulation of synaptic vesicles were observed in vascular disorders (Fig. 3, *f*).

Thus, we have revealed a number of specific changes in the ultrastructure of pre- and postsynaptic zones of ASC in the brain of aged people with and without vascular disorders. These changes are as follows: moderate osmiophilia of the cytoplasm, degeneration of the spikes by the "dark" pathway, pronounced hypertrophy and structural changes in SA, and the presence of axon terminals with densely packed synaptic vesicles. These modifications resemble those caused by hypoxia; they were observed under various pathological conditions, including brain ischemia [6]. However, the predominance of light spikes, most of which are electron-transparent and contain reduced SA, points to other mechanisms of damage not associated with vascular disorders. This is corroborated by our previous finding that dark neurons predominate in the brain of aged people with vascular disorders, while the occurrence of light neurons is higher in normal aging [2].

Ultrastructural changes in SA that regulates the entry of free intracellular $Ca^{2+}$ into the spike are very important [3,5,9,10]. Destructive changes observed in the brain of aged people with vascular disorders imply that impaired function of a spike results from sustained $Ca^{2+}$ overload of neurons due to hypoxia/ischemia [4]. These changes can be accompanied by synaptic blockade resulting from impaired receptive function of the postsynaptic membrane, which hampers the release of the neurotransmitter. This leads to the formation of a "synaptic block". Morphologically, this block is represented by ASC with presynaptic terminals packed with synaptic vesicles.

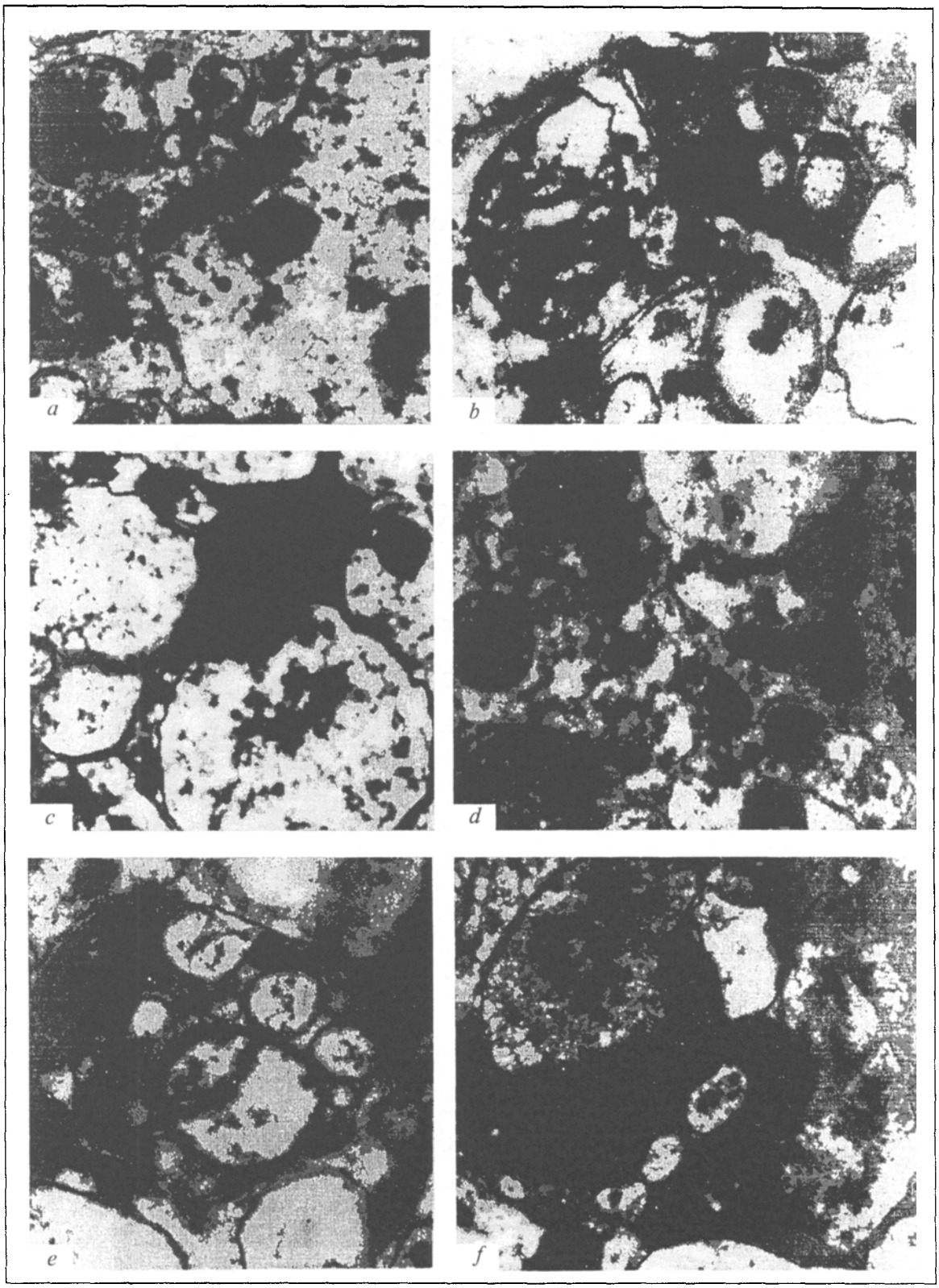


**Fig. 3.** Degenerative changes in the pre- and postsynaptic regions of axospike contacts. Inclusions in spike *(a)*, fragmentation and disintegration of spike (*b*); degeneration of spike by the "dark" pathway and degeneration of axon by the "light" pathway (*c*); atrophy of spike (*d*); vacuolation of the axon terminal (*e*), densely packed synaptic vesicles in the presynaptic terminal ("synaptic block ", *f*). Temporal (*a, b, f*) and precentral (*c, e*) cortex of a 70-year-old man; frontal cortex (*d*) of a 72-year-old man. ×32,000.

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