# MODEL OF CEREBRAL ISCHEMIA IN DOGS WITH PATHOLOGICAL KINKING AND OCCLUSION OF THE CAROTID ARTERIES

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The development and introduction of the latest methods of research aimed at creating an experimental model of cerebral ischemia is a promising aspect for research into the problem of brain ischemia in clinical practice.

Brain tissue is highly sensitive to ischemia. Various factors differing in duration of action and severity may lead to cerebral ischemia. In man at least five ischemic states are distinguished, with the following mechanisms: a) total and permanent ischemia – with the synonym of brain death [7]; b) total transient ischemia, characterized by hypotension (incomplete ischemia) or cardiac arrest (total ischemia), followed by recovery of the circulation to a state of normotension [4]. The clinical outcome may be brain death or survival with transient or permanent disturbances; c) regional arterial ischemia as a result of arterial occlusion, thrombosis, or embolism. The clinical manifestations are usually local neurologic disturbances, sometimes called stroke, which may be transient or permanent [5]; d) regional venous ischemia as a result of occlusion or thrombosis. The clinical manifestations range from headache to unconsciousness [3]; e) arterial ischemia, as a result of severe changes in arteries and arterioles of the brain parenchyma. Tissue changes are manifested as lacunar infarcts [6]. Considering that in each type of ischemia listed above the morphological changes are different, and depend on the severity and duration of the circulatory insuffiency, and also because of the incomplete data in the literature on the particular features of the morphological changes in the brain in the regional type of ischemia, we set out to study morphological changes in the cerebral cortex due to the action of two vascular factors, with a similar mechanism and giving rise to ischemia: occlusion of the internal carotid artery and pathological kinking of the artery which may be unilateral or bilateral.

We could find no experimental research in the accessible literature into the creation of a model of pathological kinking of branches of the arch of the aorta, and in particular, a model of pathological kinking and occlusion of the extracranial branches of the carotid arteries as a result of unilateral or combined bilateral lesions, or the creation of an adequate experimental model of cerebral ischemia in dogs that would correspond to a lesion of these same vessels in man, that would shed light on the morphological substrate of ischemic disturbances of the brain and on some aspects of the pathogenesis of cerebral ischemia.

## EXPERIMENTAL METHOD

The material consisted of the brain of 40 mongrel dogs weighing 10-15 kg, in which various models of a pathological circulation in the bracheocephalic vessels were created under general anesthesia [1, 2]. The experiments of series 1 (16 animals) consisted of the creation of a unilateral lesion of the carotid arteries, and on the basis of angiographic and radioisotope investigations these animals were divided into two groups: those with pathological kinking and those with occlusion of the right internal carotid artery (Fig. 1a, b). The experiments of series 2 (16 animals) consisted of a bilateral combined lesion of the carotid arteries: pathological kinking of the right common

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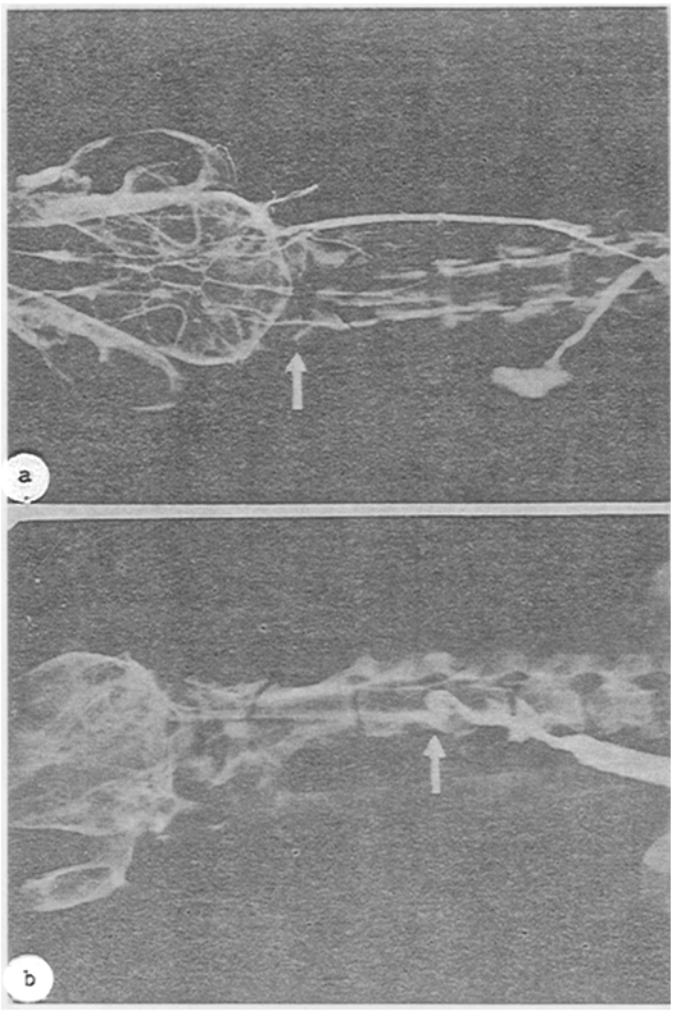


Fig. 1. Angiography showing pathological kinking and occlusion of carotid arteries: a) pathological kinking of right common carotid artery of a dog; b) occlusion of right internal carotid artery.

carotid artery and occlusion of the left internal carotid artery. Control experiments were carried out on eight animals, in which no pathological lesion of the carotid arteries was created. The angiographic investigation was carried out on the ARD-2 apparatus with VARKT attachment, and using a remote-controlled automatic syringe of original design for injecting the contrast material. Hemodynamic parameters were recorded on four photographs taken at intervals of 1 sec. The distance from tube to test object was 70 cm, the power of the radiation 50 Ci, and the total number of angiograms was 180.

We have developed an original radiographic technique, consisting of determination of the linear velocity of the blood flow by applying three transducers separately to the heart – brain section; the 1st in the region of the heart, the 2nd in the region of the right cerebral hemisphere, and the 3rd in the region of the left hemisphere (Fig. 2). The radionuclide isotope albumin-$^{131}$I was injected into the dog's right forelimb vein in a dose of 0.066 MBq, diluted in physiological saline, with simultaneous activation of the recorder to determine the graphic amplitude of the linear velocity of blood flow. The brain for morphological investigation was fixed by perfusion with a 5-10% solution of buffered formaldehyde (pH 7.4) with additives. The material for study consisted of frontal serial sections through the frontal, parietal, and occipital regions of the cortex. Paraffin sections were stained by Nissl's method and by hematoxylin and eosin. The electron-microscopic study was carried out on trimmed Araldite blocks, semithin sections being stained with toluidine blue. An (unspecified) electron microscope was used.

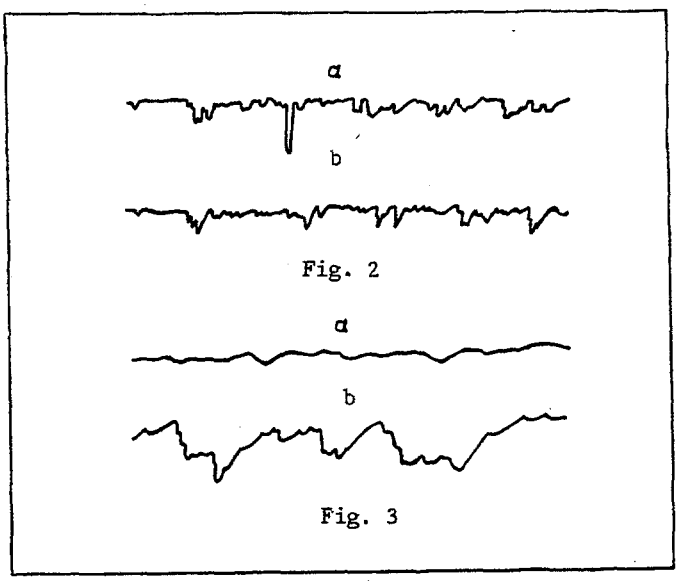


Fig. 2. Graph of linear velocity of carotid arterial blood flow in control animal (investigation with $^{131}I$): a) left carotid artery; b) right carotid artery.

Fig. 3. Graph of linear velocity of blood flow: a) occlusion of left internal carotid artery; b) pathological kinking of right common carotid artery.

## EXPERIMENTAL RESULTS

Hemodynamic investigations of a unilateral model of a carotid arterial lesion (series 1) showed that the linear velocity of the blood flow was reduced by 52% in pathological kinking (group 1) and by 76% in occlusion of the right internal carotid artery (group 2).

In the model of a bilateral combined lesion (series 2) of the carotid arteries, the velocity of the blood flow was reduced by 88.6% (Fig. 3).

Histologic investigation of the dogs of series 1 revealed structural changes in capillaries, ganglion cells, and neuroglia in almost all three regions of the cerebral cortex. This was especially the case with the microcirculatory bed of the cortex. Dilatation and congestion of vessels, ranging from moderately severe to severe, were observed. Structural changes, in the form of chromatolysis, ranging from peripheral to total were found in the ganglion cells in most cases observed. Pathological changes in the nucleus of the neurons predominated: karyorrhexis, karyopycnosis; pycnomorphic neurons were found in the cortex (Fig. 4). More marked pathological changes were concentrated in the parietal lobe. Features of satellitosis and hypertrophy of oligodendrocytes also were noted. Astrocytes were in a state of edema and swelling.

On electron-microscopic study of the zone of involvement of the capillary–astrocyte–neuron system ultrastructural changes were found in the capillary wall: the basal layer was widened, abundant pycnocytosis of the endothelial cells was observed, and the fenestrae were open. Plasmatic astrocytes were swollen, with vacuoles in the cytoplasm, and the fibril-forming astrocytes also were in a state of swelling and edema. Disturbance of the ultrastructure was observed in the cytoplasm of the pycnomorphic neurons: vacuolation, marked osmiophilia of the nucleus and cytoplasm. The cell membranes were fragmented, the cytoplasm became honeycombed in appearance, organelles underwent lysis, and the nuclear chromatin was in a state of condensation.

The same morphological changes as in series 1 were found in the brain in the experiments of series 2. However, structural changes in the capillary–astrocyte–neuron system in animals with a bilateral lesion of the carotid arteries were more severe. In particular, the pathological changes were intensified both in the cells and in the microcirculatory bed of the cerebral cortex (Figs. 5 and 6).

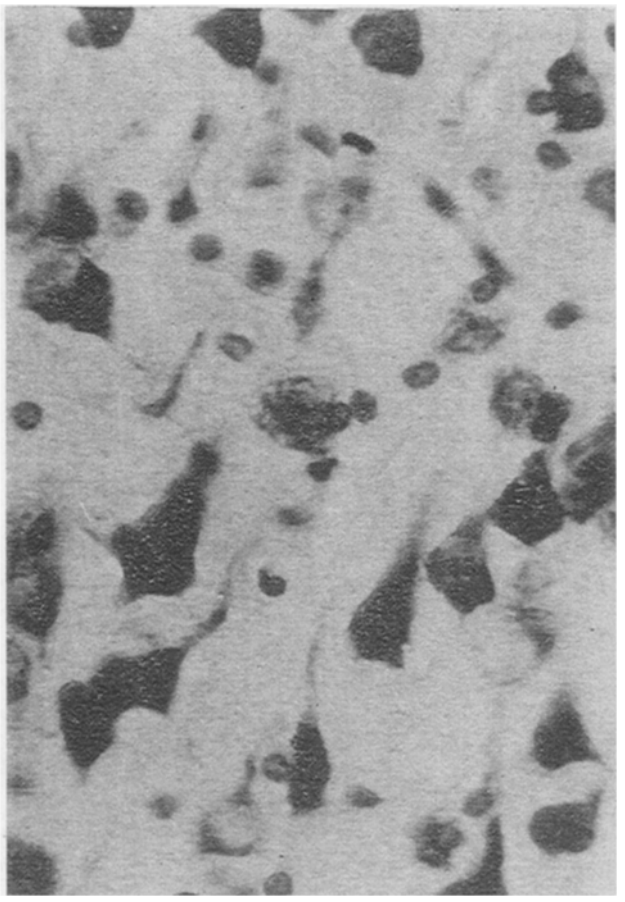

Fig. 4. Hyperchromatosis of ganglion cells and pycnomorphic neuron in cerebral cortex, layer V, parietal region. Nissl's stain, 800×.

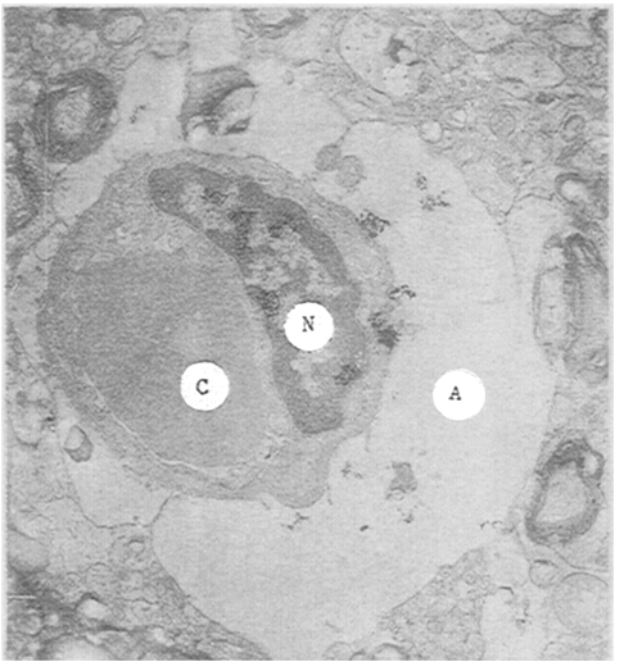


Fig. 5. Edema of cytoplasmic astrocyte (A) enveloping brain capillary (C), widening of basal layer and swelling of nucleus (N) of an endothelial cell. 25,000×.

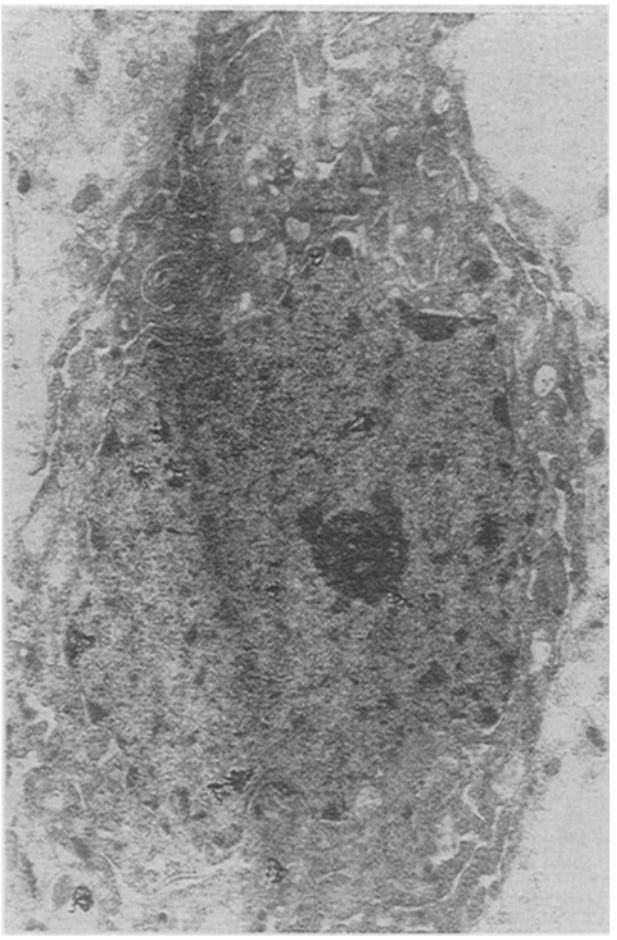

Fig. 6. Pycnomorphic neuron from layer V of cerebral cortex. Nuclear chromatin condensed osmiophilia of organelles in cytoplasm. 30,000×.

The morphologic picture of the cortex reflected the severe hypoxic changes of the ganglion cells, capillaries, and glial cells and approximated to the morphologic picture of an ischemic brain infarct. The cytoarchitectonics of the cortex was disturbed in all three regions studied. This tendency can be explained by the deficient blood flow of the cortex.

On the basis of the pathophysiological data and the pathological changes in the brain of the experimental animals it can accordingly be concluded that significant pathological changes arise after a unilateral lesion of the carotid arteries. In such a situation the conditions are optimal for preventive surgical correction of the blood flow, whereas a bilateral lesion of the brachiocephalic vessels gives rise to a critical state of the brain tissue and requires operative treatment without delay.

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