FUNCTIONAL STATE OF CORTICAL BLOOD VESSELS DURING DEVELOPMENT OF PAROXYSMAL ACTIVITY

G. I. Mchedlishvili and D. G. Baramidze UDC 616.8-009.24-07:616.133.33-072.7

An increase in cortical activity in physiological conditions is usually accompanied by a more intensive circulation [4, 8]. However, when the increase of activity is pathological in character, for example when paroxysmal discharges arise on the electroencephalogram, signs of circulatory insufficiency may appear in the cortex [10], the network of blood vessels becomes less dense [12], and the blood flow in the cortex, measured quantitatively, increases only initially, and then begins to diminish progressively, although the paroxysmal activity continues [2].

Since the pial arteries in a focus of paroxysmal activity are dilated [5, 7, 10], it could be assumed that the diminution of the circulation is due to constriction of the smaller vessels of the cortex itself, as preliminary histological investigations showed [6].

In the present investigation an attempt was made to develop a method of quantitative assessment of the state of various parts of the network of blood vessels in the cortex and to determine the width of the cortical vessels during development of paroxysmal activity (only the initial stages of the process—the first 15 min—were investigated).

EXPERIMENTAL METHOD

Because of the impossibility of measuring the width of the vessels in massive organs directly during life, the tissues were fixed supravitally, microscopic preparations were made, and the diameter of the blood vessels in them was measured. By fixing tissue in different stages of the process, the dynamics of the changes in the blood vessels could be recreated in the course of time.

Experiments were carried out on 32 adult rabbits (no general anesthetic was used and the operations were performed under local procaine anesthesia). Preliminary experiments showed that best fixation may be obtained by perfusing the blood vessels without preliminary rinsing out with fluid [1]. The best of the fixing fluids tested was 12% formalin in 0.85% NaCl solution, diluted 1:1 in 96° ethyl alcohol. The brain was perfused through the internal carotid artery (after ligation of the external) under constant pressure (100-120 mm) and blood was withdrawn from the aorta at the same time. After injection of 30-40 ml of fixing solution, the brain was left immersed in it for 24 h, and it was then placed for 3 days in liquid of the same composition but without alcohol. The brain sections began to be investigated on the 4th day.

Investigations were carried out in the temporal, calcarine, occipito-temporal, and occipital regions of the cortex in frontal sections of the brain corresponding to planes D, E, and F of the stereotaxic atlas [11]. To enable most arteries to be examined throughout the thickness of the cortex in the microscopic preparations, as the brain was cut the knife was held perpendicularly to the superior surface, and after insertion of the blade into the brain substance it was gradually and very slightly inclined in a caudal direction. If the brain had been cut incorrectly, subsequent investigations of the cortical vessels were impossible. Sections, 30 μ in thickness, were cut on a freezing microtome. Unstained preparations were investigated: because of differences in their refractive index, all the structural elements of the blood vessel walls could be clearly seen.

In microscopic preparations only those arteries which were visible over a considerable distance, starting from their mouths, were measured by means of an ocular micrometer (magnification 1350 times: 10 × 90 × 1.5). The end of each particular vessel was taken to be the point of its ramification (not where it gave off smaller arteries). The caliber of the vessel was determined from the external diameter of its

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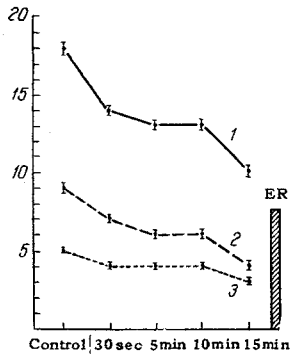

Fig. 1. Progressive constriction of lumen of cortical blood vessels of rabbits during paroxysmal activity caused by local application of strychnine. Abscissa—duration of application of strychnine, ordinate—lumen of vessels (in μ; M ± m). The shaded column on the right represents the mean diameter of the erythrocytes. Here and in Fig. 2: 1) small arteries (20-34 μ); 2) precapillary arterioles (10-19 μ); 3) capillaries (5-9 μ).

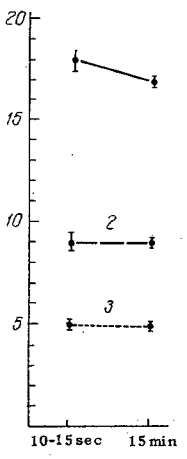

Fig. 2. Absence of marked changes in lumen of cortical vessels after exposure of brain and application of isotonic NaCl solution. Abscissa—duration of exposure of brain, ordinate—lumen of vessels (in μ; M ± m).

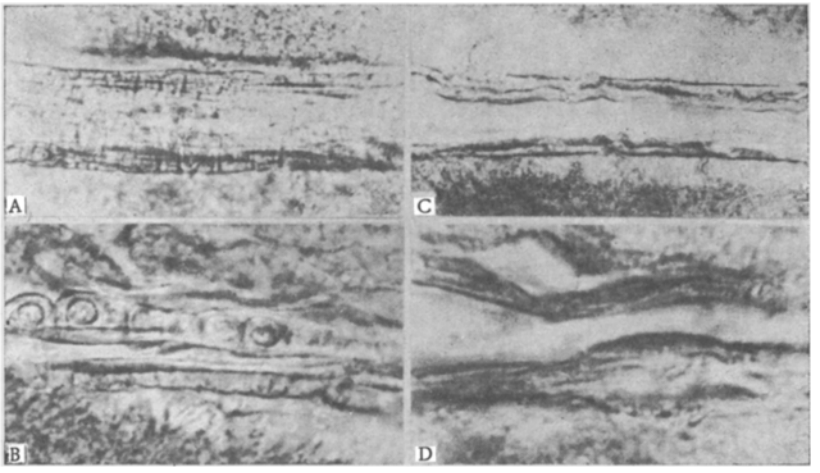

Fig. 3. Histological changes in walls of cortical arteries of rabbits during paroxysmal activity. Photomicrographs of unstained sections. A) Cortical artery in the absence of paroxysmal activity (control), 90× 7; B) swelling of muscle cells and thickening of vessel walls, leading to constriction of lumen, 90 × 10; C) longitudinal separation of muscular coat of a small artery into layers; 90 × 7; D) intramural spaces formed by separation of muscular coat of walls of a cortical artery into layers, 40 × 7.

initial segment, the width of which changed usually very little during the procedures: for the radial arteries this was 20-30 μ after entering the brain, and for their branches 10 μ after leaving the larger arteries. The diameter of the blood vessels was measured throughout their course at intervals of 20 μ, but only in cases when the outlines of their walls were clearly visible and no abrupt morphological changes were present, such as wrinkling of the walls or complete detachment of the vessel from the surrounding tissues. Altogether more than 10,000 measurements of the external and internal diameter of the cortical vessels were made.

EXPERIMENTAL RESULTS

The vascular system in the cerebral cortex of the rabbits was investigated after local application of 0.5% strychnine solution (made up in NaCl to an isotonic concentration) to the corresponding regions of the surface of the hemispheres (see above) for different periods of time. The brain was fixed after 30 sec and 5, 10, and 15 min.

During investigation of three groups of cortical vessels—small arteries (20-34 μ), precapillary arterioles* (10-19 μ), and capillaries (5-9 μ) it was found that they became progressively constricted after the beginning of the action of strychnine. Changes in the cortical vessels were observed only 30 sec after application, before changes in spontaneous electrical activity had usually begun. The external diameter of the cortical vessels changed much less than their internal diameter; constriction of the precapillary arterioles was most marked. The difference in every case was statistically significant (Fig. 1)†.

For control purposes the effect of exposing the brain on the cortical vessels (with application of physiological saline) was studied. Comparison of the diameters of the blood vessels in the rabbits of two control groups in which the brain was fixed 10-15 sec and 15 min later showed that there was no difference or it was many times smaller than with experimental rabbits receiving application of strychnine (Fig. 2).

Histological investigations showed that the blood vessel walls underwent changes at about the same time as the structural elements of the brain [3]—30 sec after application of strychnine to the cortex. Changes appeared in all layers of the vessel walls although they were most marked in the media in the muscular coat. The muscle cells appeared swollen (Fig. 3, A and B) and their layers were thickened. In arteries with a caliber greater than 25 μ, intramural spaces were frequently formed later between the layers of muscle cells (Fig. 3, C and D). This is evidence of changes—in the form of separation into layers—of the connective tissue lying between the layers of muscle cells. In later stages of the action of strychnine, the outlines between the individual layers of muscle cells became indistinct and it was difficult to distinguish the separate structural elements. The well marked swelling of the endothelial cells observed in some places led to a still more marked local constriction of the luman not only of the small vessels, but also of the relatively large arteries of the cortex.

A reduction in the lumen of such narrow vessels, according to the laws of rheology of the blood, may increase its fluidity (and decrease its relative viscosity). However, this is observed only until mechanical obstruction to movement of the particles—in this case erythrocytes—takes place in the narrow lumen of the vessels [9]. As Fig. 1 shows, in a focus of paroxysmal activity the mean diameter of the lumen of the cortical arterioles and capillaries in the rabbit is 3-4 μ, and this must obstruct the flow even of deformed (elongated) erythrocytes. The progressive constriction of the cortical arterioles observed in the course of the present investigation thus explains the diminution of the blood flow, after its initial increase, in the cerebral cortex during paroxysmal activity.

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*The term arterioles is used to describe very small arteries with one layer of muscle cells in their wall.

† The impression is gained that the lumen of the cortical vessels may subsequently be restored, although no special study of this problem was made in the present investigation.

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