# DISTRIBUTION OF PARTIAL PRESSURE OF OXYGEN IN THE BRAIN OF SPONTANEOUSLY HYPERTENSIVE RATS

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In all forms of arterial hypertension functional and structural components of the vascular resistance to the blood flow are increased. There are several causes of this phenomenon: active vasocontriction of the small resistive vessels [7, 12], narrowing of the lumen of the vessels due to hypertrophy of their wall [9], and also a decrease in the density of the vascular network. In spontaneously hypertensive rats (SHR) the density of the vascular network is reduced in the muscles, mesentery, skin, and other tissues [10, 11, 13]. Vascularization of the brain has also been shown to be reduced in rats with various forms of experimental hypertension [1, 6]. On the basis of this fact it has been suggested that exclusion of some blood vessels from the general microcirculatory system in this disease leads to the formation of regions of local cerebral hypoxia. The appearance of possible zones of hypoxia in arterial hypertension has also been demonstrated by calculations conducted on a model of oxygen transport in nerve cells and the tissue surrounding them, when the intercapillary distance was increased [5, 6]. The presence of these zones in the brain may promote activation of the sympathetic nervous system through a mechanism of cerebral ischemia [8], and in turn, it may lead to a considerable rise of blood pressure (BP). The study of the degree of oxygenation of the brain in spontaneous genetic hypertension is thus of considerable interest as a means of shedding light on the pathogenesis of this disease.

With the introduction of polarographic microelectrodes by means of which direct quantitative measurements of the intercapillary $pO_2$ can be made [4], the way was open for the study of the distribution of $pO_2$ in the brain of hypertensive animals, and the investigation described below was undertaken for this purpose. To detect ischemia of the brain tissue, a morphological method was used.

## EXPERIMENTAL METHOD

Experiments were carried out on six SHR of the Okamoto-Aoki line, aged 9 months, and on

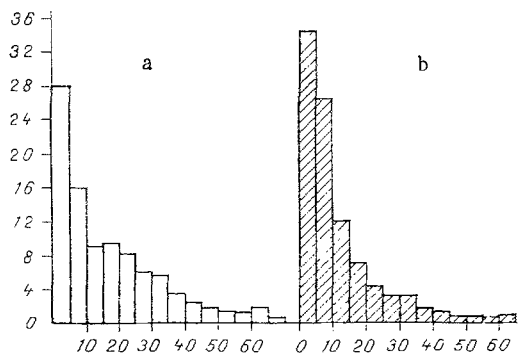


Fig. 1. Histograms of distribution of $pO_2$ in NTR (a) and SHR (b). Abscissa, class of values of $pO_2$ (in mm Hg); ordinate, number of values in each class (in % of total sample).

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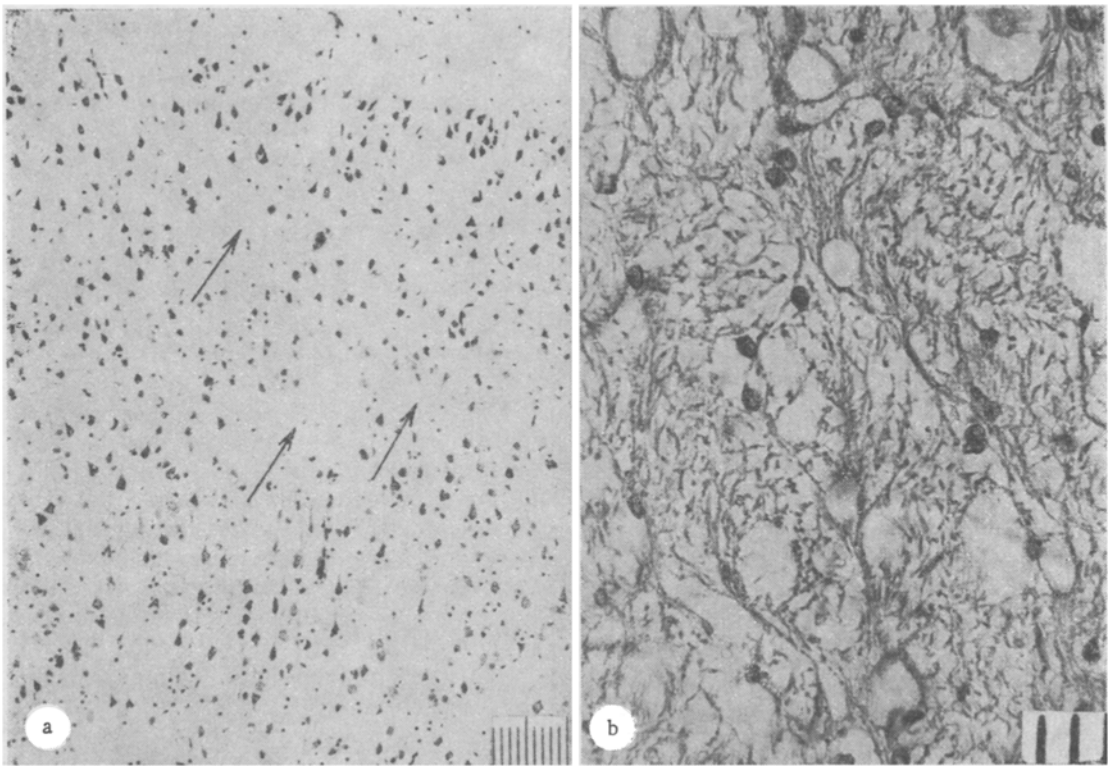


Fig. 2. Ischemic changes in the brain of SHR: a) multiple foci of loss of nerve cells in cerebral cortex. Nissl's stain, 63×; b) of white matter. Van Gieson, 25.2×. One scale division is equivalent to 10 μ.

six normotensive rats (NTR) of the Wistar-Kyoto line of the same age. The systolic BP was measured in the caudal artery by an electroplethysmographic method in conscious animals. Quantitative measurements of $pO_2$ in the intercapillary spaces of the sensomotor cortex and underlying white matter were made with platinum polarographic microelectrodes 1-3 μ in diameter [4]. The animals were anesthetized with Ketalar (8 mg/kg, intramuscularly). The animal's head was securely fixed in a stereotaxic apparatus and the microelectrode was inserted step by step into the brain tissues through a burr-hole in the cranial bones by means of a step motor. To prevent artefacts connected with brain pulsation, the burr-hole was filled with agar, warmed to 37°C. Measurements of $pO_2$ were made with a 50 μ step to a depth of 3000 μ. In each experiment five or six insertions of the electrode were made, so that $pO_2$ could be measured in one animal at 300-400 close-lying points of the brain. To estimate the efficiency of the oxygen supply to the brain histograms of distribution of $pO_2$ in the various regions studied were plotted [4]. The histograms were drawn and the data subjected to statistical analysis with the SM-4 computer. Immediately after the end of the experiments the animals were decapitated and the brain removed and immersed in 10% formalin solution. The histological investigation was carried out on series of brain sections stained with hematoxylin and eosin and by Nissl's and Van Gieson's methods.

## EXPERIMENTAL RESULTS

Measurement of the intercapillary $pO_2$ in the brain by means of microelectrodes showed considerable variability of the values recorded both in SHR (BP 189 ± 12 mm Hg) and in NTR (BP 121 ± 7 mm Hg) within the range from 0 to 70 mm Hg. The histograms in Fig. 1 generalize the results of $pO_2$ measurements in the brain of NTR and SHR. Values of $pO_2$ were distributed over a wide range. The total number of separate values of $pO_2$ did not correspond. In normal and hypertensive animals only solitary values exceeded 65 mm Hg, whereas in SHR values of $pO_2$ above 45 mm Hg were extremely rare. The mean values of $pO_2$ were 20.6 mm Hg in NTR and 13.7 mm Hg in SHR. In most cases values of $pO_2$ in the animals of the two strains lay between 1 and 15 mm Hg. Meanwhile, the total number of values of $pO_2$ within this range in NTR was 52%, but in SHR it was 72%. Consequently, the number of low values of intercapillary $pO_2$ in SHR was increased by 20%. Analysis of the histograms showed that the distribution of

values of $pO_2$ in SHR differed sharply from that in normal animals. The coefficient of asymmetry for SHR was 2.72 and for NTR it was 1.85, which signifies a shift of the most probable values in SHR toward lower levels. The coefficient of excess was 6.53 for SHR and 1.71 for NTR, evidence of the appearance of zones with abnormal $pO_2$ in SHR, The coefficient of variation was 1.25 for SHR and 0.94 for NTR, which indicates that the results for NTR were much more highly reproducible. Thus the distribution of $pO_2$ in the brain of the hypertensive rats showed a considerable shift toward lower values.

The morphological investigation revealed ischemia of the brain tissue in SHR (Fig. 2). Foci of loss of ganglion cells and incomplete necrosis appeared in the cerebral cortex and deep brain formations of SHR, and they alternated with areas of tissue in which the nerve cells were in a state of acute swelling accompanied by varied degrees of chromatolysis and cytolysis. Cerebral edema, a decrease in cell density, and the formation of a wide-looped structure and of small foci of incomplete necrosis were observed in the white matter. Acute and chronic changes were found in the cerebral vessels with a tendency toward anatomical narrowing of the lumen of the arteries (acute swelling of the walls of the small arteries and arterioles, segmental or total permeation of the walls with plasma, and also hypertrophy of the walls of the small arteries).

We know that compensatory changes maintaining the oxygen supply of the brain at a level compatible with its viability develop in SHR: the linear velocity of the blood flow and the oxygen capacity of the blood, etc., increased [2, 3, 14]. However, as this investigation showed, these compensatory changes cannot prevent the formation of ischemia in the brain of SHR with prolonged and severe hypertension.

There are thus grounds for considering that the decrease in density of the microcirculatory bed of the brain [1, 6] and also the functional and anatomical narrowing of the small arteries and arterioles in SHR are the structural basis for disturbance of the $pO_2$ distribution in brain tissue and the development of diffuse and focal ischemia in the brain in arterial hypertension.

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