# Effect of Alveolar Hypoxia on Reactivity of Pial Vessels in Normotensive and Spontaneously Hypertensive Rats

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Intravital television microscopy revealed reduced reactivity of pial arterioles in response to alveolar hypoxia in spontaneously hypertensive rats (SHR) compared to normotensive (WKY) rats, which manifested in decreased number of dilatory reactions and in less prononced vascular dilation.

**Key Words:** *pial arterioles; alveolar hypoxia; spontaneously hypertensive rats; vasodilation; vasoconstriction*

*In vitro* and *in vivo* studies of the effect of hypoxia on cerebral vessels showed that cerebral blood flow increases under conditions of oxygen deficiency due to dilation of pial vessels [6,11,14,15]. The mechanism of the effect of oxygen on the vascular tone is a matter of discussion. There are indirect indications that the effect of oxygen on the formation and maintenance of vascular tone is mediated via modulation of active $Na^+/K^+$ transport and $Na^+/Ca^{2+}$ ion exchange mechanism in smooth muscle cells [13]. There is also evidence that cerebral hyperemia provoked by hypoxia depends on nitric oxide (NO) synthesis [14], although recent data showed that NO and ionic channels contribute to the maintenance of vasodilation during hypoxia via independent routes [6,11]. Probably, these mechanisms operate in various parts of the vascular bed.

The effect of hypoxia on cerebral circulation was usually studied on animals with normal blood pressure (BP). However, the effect of alveolar hypoxia on cerebral vessels under conditions of stable arterial hypertension is little studied. Structural and functional changes in the vascular wall (in particular, in the main cerebral vessels) during systemic hypertension [7,8,12] and changes in active ion transport [5,9,10] accompanied by the corresponding elevation of the vascular tone can modulate reactivity of cerebral arteries and arterioles in hypertensive animals.

Our aim was to compare the responses of pial arterioles to alveolar hypoxia in normotensive (WKY) rats and spontaneously hypertensive rats (SHR).

## MATERIALS AND METHODS

The study was carried out on 10 spontaneously hypertensive (SHR) and 10 normotensive (WKY) rats weighing 240-310 g. In non-narcotized normotensive rats blood pressure in the caudal artery was 120-130 mm Hg, while in spontaneously hypertensive rats it was 180-190 mm Hg. The rats were narcotized with urethane (125 mg/100 g). Hypoxia was modeled by 5-min inhalation of gas mixture with decreased oxygen content (10% $O_2$ in nitrogen). Blood pressure was measured in the carotid artery, $Pco_2$, $Po_2$, and pH in arterial blood were determined.

Dark field microscopy (×630) of brain surface was performed via an opening made in the parietal region of the skull. The diameter of pial arterioles was measured with an accuracy of 2 μ using intravital television microscopy, and the image was fed into a computer for interactive processing.

Vascular reactions were studied in vessels with a diameter of 15-45 μ (155 vessels from SHR and 160 vessels from WKY rats). Arteriolar reactions were assessed by changes in the outer diameter. Vessel images were fed into computer for 30 sec (before stimula-

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**TABLE 1**. Effect of Hypoxia on pH and Blood Gases ($M \pm m$)

| Index | Before hypoxia | | After hypoxia | |
|---|---|---|---|---|
| | WKY | SHR | WKY | SHR |
| pH | 7.377±0.020 | 7.415±0.020 | 7.359±0.020 | 7.433±0.030 |
| $Pco_2$, mm Hg | 25.3±2.1 | 26.03±2.2 | 26.2±2.8 | 24.5±2.7 |
| $Po_2$, mm Hg | 101.03±4.50 | 97.61±7.00 | 55.1±4.6 | 67.6±4.4* |

**Note.** *$p<0.05$ compared to normotensive rats.

tion and on minutes 1 and 5 of hypoxic mixture inhalation) at the rate of 0.25 frames/sec. The mean diameter for 30 sec was taken into analysis.

## RESULTS

Inhalation of hypoxic mixture during 5 min significantly decreased BP in normotensive (by 26.7±3.4%) and hypertensive rats (by 14.5±2.9%), which was accompanied by a drop of $Po_2$ in arterial blood (Table 1).

The examined vascular modules were three-way vessels consisting of one afferent (truncal) arteriole and two efferent first-order branching arterioles [2,4].

In both normotensive and hypertensive rats dilation was the predominant reaction of pial arterioles to hypoxia. Vascular reaction to hypoxia did not significantly differ on minutes 1 and 5 of hypoxia. To the end of hypoxic exposure, 81% truncal arterioles and 77% first-order branches were dilated in WKY rats. The degrees of dilation of truncal vessels and the first-order branches were 44.2±77.9 and 49.1±7.9%, respectively ($p<0.05$). In SHR rats hypoxia produced dilation of only 55% truncal arterioles (dilation degree 19.7±4.2%, $p<0.05$) and 70% first-order branches (dilation degree 26.9±6.7%, $p<0.05$).

Generalized dilation of pial vessel was not observed. Apart from dilated vessels, arterioles with significantly decreased diameter were noted in both SHR (30% truncal arterioles and 15% first-order branches were constricted) and WKY rats (19 and 23%, respectively). The degrees of constriction of truncal arterioles in WKY and SHR rats were 19.01±3.69% and 19.85±5.33%, respectively, while the corresponding values for the first-order branches were 9.2±2.8% and 16.7±4.9%. In SHR, the diameter of some arterioles (15% truncal vessels and the first-order branches) remained unchanged throughout the experiment. Moreover, in contrast to published reports on increased of cerebral blood flow during hypoxia [11,14,15], we observed a pronounced deceleration of cerebral blood flow up to its complete arrest and even reverse blood flow in some rats of both strains. The opposite reactions of cerebral arterioles during hypoxia can be explained by various sensitivity of individual fragments of the vascular bed to the changes in oxygen content in the blood and interstitial fluid [3]. In addition, numerous anastomoses in the pial vessels determine complex blood flow distribution between individual microfragments of pial vascular network. The changes in the velocity and direction of blood flow can result from redistribution of the blood in micromodules of the cerebral vascular bed, which ensures reliable and selective regulation of blood supply under conditions of acute hypoxia.

We also observed less pronounced arteriolar dilation and a lower number of dilated vessels in SHR compared to WKY rats, which is probably related to increased baseline vascular tone due to functional and structural changes in the vascular wall in hypertensive animals [5,9,10].

Our study compares the responsiveness of the vessels in the same module. There is evidence that geometrically different arterioles can demonstrate qualitatively and quantitatively different response to the same stimuli [1,4]. However, in this work hypoxia-induced changes in vessel reactivity in a module were observed only in hypertensive rats. The first-order branches were more frequently dilated than truncal vessels. In hypertensive rats vessel reactivity in a module can change, because the absolute intravascular pressure in a linear arteriole is higher than in curved vessel [1]. This determines more pronounced structural changes of vascular wall in linear vessels and their reduced reactivity in hypertensive rats.

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