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ORIGINAL ARTICLE

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# Oxygen transport in the rat brain cortex at normobaric hyperoxia

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**Abstract** The distribution of oxygen tension ($PO_2$) in microvessels and in the tissues of the rat brain cortex on inhaling air (normoxia) and pure oxygen at atmospheric pressure (normobaric hyperoxia) was studied with the aid of oxygen microelectrodes (diameter = 3–6 μm), under visual control using a contact optic system. At normoxia, the $PO_2$ of arterial blood was shown to decrease from [mean (SE)] 84.1 (1.3) mmHg in the aorta to about 60.9 (3.3) mmHg in the smallest arterioles, due to the permeability of the arteriole walls to oxygen. At normobaric hyperoxia, the $PO_2$ of the arterial blood decreased from 345 (6) mmHg in the aorta to 154 (11) mmHg in the smallest arterioles. In the blood of the smallest venules at normoxia and at normobaric hyperoxia, the differences between $PO_2$ values were smoothed out. Considerable differences between $PO_2$ values at normoxia and at normobaric hyperoxia were found in tissues at a distance of 10–50 μm from the arteriole walls (diameter = 10–30 μm). At hyperbaric hyperoxia these values were greater than at normoxia, by 100–150 mmHg. In the long-run, thorough measurements of $PO_2$ in the blood of the brain microvessels and in the tissues near to the microvessels allowed the elucidation of quantitative changes in the process of oxygen transport from the blood to the tissues after changing over from the inhalation of air to inhaling oxygen. The physiological, and possibly pathological significance of these changes requires further analysis.

**Key words** Hypoxia · Hyperoxia · Microcirculation · Oxygen · Brain

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## Introduction

Terrestrial animals in an adequate habitat are never subjected to partial oxygen pressures ($PO_2$) higher than atmospheric pressure. Hence, inhaling pure oxygen even at the normal barometric pressure (about 760 mmHg) creates unusual conditions for oxygen transport within an organism. It is supposed that under such conditions oxygen can have a toxic impact on tissues (Dedhia and Banks 1994; Visner et al. 1996; Zhang et al. 1993). Nevertheless, the inhalation of pure oxygen is often used in medicine as well as during various kinds of activity in man (e.g., underwater swimming and high-altitude flight). Therefore, there are many studies in which attempts have been made to elucidate the special features of oxygen transport in an organism and its tissues, when the $PO_2$ in the environment is increased (e.g. Leniger-Follert et al. 1975; Metzger et al. 1971; Nair et al. 1975; Schmidt et al. 1996; Shinozuka et al. 1989; Tammela et al. 1996; Torbati et al. 1976). Fairly recently it was shown that arterioles, along with capillaries, are involved in the supply of oxygen to tissues, since their walls are gas permeable (Duling and Berne 1970; Duling et al. 1975; Ivanov et al. 1979b). In addition, we have been able to show that in the brain, up to one-third of all oxygen that the blood gives up to tissues passes to those tissues through the arteriole walls (Ivanov et al. 1982). In this case, the analysis of oxygen transport from the blood to tissues is substantially complicated. A comparison of the efficiency of this process at normoxia and at hyperoxia requires measuring $PO_2$ and other parameters of the oxygen transport function of the blood over the whole length of the vessel bed from the blood in the aorta to that of the main veins. It is also necessary to measure $PO_2$ in the tissues near the microvessels, which also take part in the gas exchange between blood and tissues. Such detailed studies, carried out with the help of very thin oxygen microelectrodes (diameter = 3–6 μm) and a system of contact optics, have been performed in our laboratory for the first time in the history

of studying oxygen transport in the tissues of a living organism. The data obtained from these studies are presented in this work.

## Methods

The experiments were carried out on male Wistar rats weighing 220–250 g. The animals were anesthetized with sodium pentobarbital, 50 mg/kg; the anesthesia was maintained by a dose of 15–20 mg · $kg^{-1}$ · $h^{-1}$. The body temperature in the rectum and the brain temperature were maintained at a constant level of 37.5 (0.5)°C with the aid of an external infrared heater. The temperature was measured with thin (diameter = 0.3 mm) copper-constantan thermocouples. Arterial blood pressure was measured with the help of a catheter, inserted into the femoral artery. The $PO_2$ of the blood was determined on a BME-3 (''Radiometer'' gas analyzer, Denmark) gas analyzer. The volume of each of the samples taken was up to 200 $\mu m^3$. The oxygen dissociation curve (ODC) was determined with the help of a Hem-O-Skan device (Aminko, USA). We determined $SO_2$ (the oxygen saturation of hemoglobin, %) and $cO_2$ (the concentration of oxygen in the blood, vol%) from the ODC, the $PO_2$ of the blood, and from the oxygen capacity of the blood, which was on average 20% volume for our animals. The method of determining $SO_2$ and $cO_2$ is given in Fig. 1. To measure $PO_2$ in the blood of brain microvessels and in the tissues surrounding these microvessels, we made a round hole about 8 mm in diameter in the parietal region of the animal's skull. The dura mater was removed. The brain surface was then continuously superfused with a solution of the following composition (mM): NaCl 118; KCl 4.5; $CaCl_2$ 2.5; $KH_2PO_4$ 1.0; $MgSO_4$ 1.0; $NaHCO_3$ 25; glucose 6. The solution was saturated at a temperature of 37°C with a gas mixture of 5% oxygen + 5% carbon dioxide (remaining gas – nitrogen). The pH was 7.40 (0.05). During experiments the animal was allowed to breathe spontaneously. Either air or 98% oxygen was supplied to the animals through a moistened system, regulating valve, and a tracheotomic cannula.

The $PO_2$ was measured by polarographic platinum microelectrodes, insulated with glass, with a tip diameter 3–6 μm (including insulation). The sensitivity of the electrodes was equal to about $3 \times 10^{-12}$ A/mmHg. The drift per hour was about 5%. The electrodes were calibrated with the superfusing solution immediately before and after the experiments (pH 7.3–7.4, temperature 37°C), equilibrated with room air. A necessary correction was made by changing the $NaCl/NaHCO_3$ ratio. The electrodes were practically insensitive to stirring. A more detailed description of the electrode operation has already been reported (Ivanov et al. 1982).

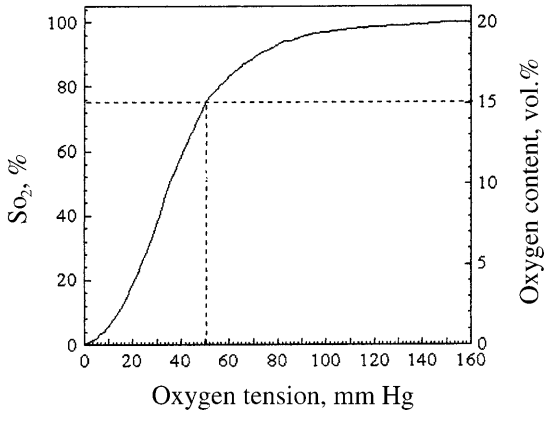


**Fig. 1** The method of determining $SO_2$ (oxyhemoglobin saturation, %) and $cO_2$ (concentration of oxygen in blood, vol%) with the help of an oxygen dissociation curve

The brain microvessels were observed with the aid of a LUMAM-K1 (GOI, Russia) contact microscope, utilizing reflected light, at a total magnification of ×150. The maximal depth of visualization of the brain tissue from the surface was 120 μm. The diameter of the microvessels was measured by an ocular micrometer, with an accuracy of up to 3 μm. The contact of the frontal lens of the epiobjective with the brain surface prevented gas exchange between the superfusion solution and the tissue site under study. The electrodes were introduced into the field of vision and operated there by means of a special micromanipulator that was attached to the microscope. The microelectrode tip was brought, under visual control, to the surface of a microvessel (radial arterioles and venules) using this micromanipulator. In doing so, the tip of the electrode approached the blood stream in the vessel as near as possible without disturbing the blood flow. It has been shown that the $PO_2$ in the lumen of the vessel is equal to the $PO_2$ at its outer surface + the $PO_2$ drop across the vessel wall (Duling et al. 1979); we measured the $PO_2$ on the surface of only very thin arterioles (diameter = 10–30 μm). Furthermore, the electrode tip approached the blood flow in the vessel lumen as close as possible. Hence, in our calculations we made a minimal correction for the $PO_2$ drop across the vessel wall: 0.5 mmHg $PO_2$/1 μm.

All measurements made in the vessels and tissues were made at a depth of 50–60 μm from the brain surface. The experimental procedure was as follows: in the first instance, all of the experiments were performed with the animals breathing air. A microelectrode tip was brought as close to an arteriole or venule wall as possible (until it was just touching the wall). The $PO_2$ was then registered continuously for 3–5 min. At this time we also took blood samples from the femoral artery (100–200 $\mu m^3$) to determine the blood $PO_2$. Then, under visual control, we removed the electrode tip from the wall of a radial arteriole by 7, then by 15, and next in sequence by 35, 50, and then 70–75 μm from the wall, and from the wall of radial venules first by 7, and then by 15 μm. The distances were measured with the help of an ocular micrometer. The electrode was kept at each of these positions in the tissue for 1–2 min. Then, the electrode was returned to its initial position (with the help of the micromanipulator) and the animal was made to breathe oxygen. A new constant $PO_2$ level was set by 1–1.5 min after the start of oxygen inhalation (during this time the animal's blood would have made from 5 to 10 circuits of its body). All of the measurements were then repeated in the same sequence. The time taken to complete all of the measurements on the same vessel and in tissues during air breathing and oxygen breathing was 25–35 min. In separate experiments, with the animals under the same anesthesia, breathing air and then breathing oxygen, blood samples were taken from the sagittal sinus. We used a total of 85 animals.

The data are presented as the mean (SE). The analysis was performed using a software package, ''Statistica 5.0''. We used the Wilcoxon (rank pair test; $P_W$) criterion for the statistical treatment of dependent data from the same animal. The level of statistical significance was set at $P < 0.05$ and $P_W < 0.05$.

## Results

The moment of measuring $PO_2$ at the arteriole wall in the rat brain cortex is given in Fig. 2. The $PO_2$, $SO_2$, and $cO_2$ in various parts of the vessel bed of a rat from the femoral artery to the sagittal sinus during breathing air are given in Table 1A. In the smallest arterioles the $PO_2$ decreases by 23 mmHg compared to the blood in the aorta (we assumed that, according to the listed parameters, the blood from the femoral artery is identical to the blood from the aorta). Since this decrease is in the region of the flat part of the ODC (Fig. 1), it scarcely affects $SO_2$ and $cO_2$. From the smallest arterioles (and, possibly, from the precapillaries) to the

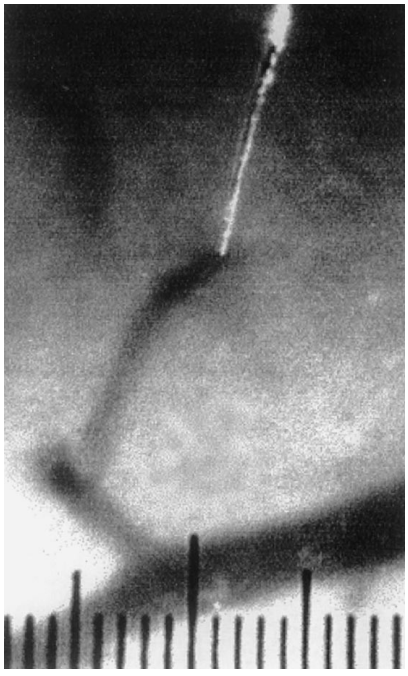

**Fig. 2** Polarographic microelectrode with a tip diameter of 4 μm brought into contact with the wall of a radial arteriole (8 μm in diameter). Scale division = 5 μm

smallest venules the $PO_2$ decreases on average by 30 mmHg. Since a considerable part of the distance between the smallest arterioles and the smallest venules is occupied by the capillaries, this decrease in the $PO_2$ seems to occur over the length of a capillary. The steep part of the ODC comprises such a decrease, which accounts for an abrupt decrease in $SO_2$ and $cO_2$ in the capillary blood. As the blood moves along the venous system to the sagittal sinus the $PO_2$ of the blood increases somewhat. This phenomenon will be discussed below.

Similar data obtained after converting the animals to inhaling oxygen are given in Table 1B. When the $PO_2$ in the aorta blood increases, on average, to 345 mmHg, hemoglobin appears to be 100% saturated with oxygen. Furthermore, an increase in the $PO_2$ in the arterial blood by 240–260 mmHg compared to the norm increases the $cO_2$ in the blood by about 0.6 ml/100 ml, according to the coefficient of oxygen solubility in the blood plasma under these conditions. As the blood moves along the arterial system the $PO_2$ decreases very abruptly. The $PO_2$ in the blood of the smallest arterioles decreases by about 200 mmHg compared to the blood in the aorta. The $PO_2$ in the smallest arterioles and precapillaries is about 150 mmHg, on average. In the smallest venules the $PO_2$ is about 60 mmHg. Consequently, during oxygen breathing the $PO_2$ over the length of a brain capillary decreases by about 90–95 mmHg, on average. As the $PO_2$ inside a capillary decreases from 150 to ≈100 mmHg, the tissues receive a small amount of oxygen, physically dissolved in the plasma. When the $PO_2$ at any site of a capillary decreases lower than 100 mmHg, oxyhemoglobin begins to dissociate. At this point the flow of oxygen from the capillary blood to the tissues increases abruptly. A decrease in $SO_2$ and $cO_2$ occurs. Both during the inhalation of air and oxygen the $PO_2$ in the blood is somewhat increased as the blood moves from the smallest venules to the sagittal sinus.

**Table 1A, B** Mean (SE) values for $PO_2$ (oxygen tension, mmHg), $SO_2$ (oxyhemoglobin saturation, %), $cO_2$ (oxygen concentration in the blood, vol %) in the blood of the femoral atery, in different brain microvessels, and in the sagittal sinus of rats during inhalation of air (**A**) and during inhalation of oxygen (**B**). For the femoral artery and sagittal sinus, $n$ = the number of animals studied; for the arterioles and venules, $n$ = the number of vessels investigated. The number in parentheses above the mean (SE) values is used to differentiate pairwise statistical comparisons (see Table footnote)

| | Aorta (femoral artery) | Arterioles (diameter) | | Venules (diameter) | | Sagittal sinus |
|---|---|---|---|---|---|---|
| | | 30 μm | 10 μm | 10–15 μm | 30–40 μm | |
| **A** | | | | | | |
| $PO_2$ | (1) | (2) | (3) | (4) | (5) | (6) |
| | 81.1 (1.3) | 72.9 (5.4) | 60.9 (3.3) | 31.5 (3.8) | 42.3 (1.8) | 40.3 (1.5) |
| | $n$ = 36 | $n$ = 5 | $n$ = 10 | $n$ = 8 | $n$ = 9 | $n$ = 11 |
| $SO_2$ | (7) | (8) | (9) | (10) | (11) | (12) |
| | 92 (1) | 87 (2) | 81 (2) | 38 (8) | 59 (2) | 57 (2) |
| | $n$ = 36 | $n$ = 5 | $n$ = 10 | $n$ = 8 | $n$ = 9 | $n$ = 11 |
| $cO_2$ | (13) | (14) | (15) | (16) | (17) | (18) |
| | 18.8 (0.5) | 17.7 (0.5) | 16.6 (0.5) | 7.7 (1.5) | 12.0 (0.5) | 11.4 (0.5) |
| | $n$ = 36 | $n$ = 5 | $n$ = 10 | $n$ = 8 | $n$ = 9 | $n$ = 11 |
| **B** | | | | | | |
| $PO_2$ | (19) | (20) | (21) | (22) | (23) | (24) |
| | 345 (6) | 241 (27) | 154 (11) | 61 (10) | 63 (3) | 69 (3) |
| | $n$ = 36 | $n$ = 5 | $n$ = 10 | $n$ = 8 | $n$ = 9 | $n$ = 12 |
| $SO_2$ | (25) | (26) | (27) | (28) | (29) | (30) |
| | 100 | 100 | 100 | 71 (8) | 73 (2) | 79 (1) |
| | $n$ = 36 | $n$ = 5 | $n$ = 10 | $n$ = 8 | $n$ = 9 | $n$ = 12 |
| $cO_2$ | (31) | (32) | (33) | (34) | (35) | (36) |
| | 20.7 (0.1) | 20.4 (0.2) | 20.2 (0.1) | 14.5 (0.5) | 14.9 (0.5) | 16.1 (0.5) |
| | $n$ = 36 | $n$ = 5 | $n$ = 10 | $n$ = 8 | $n$ = 9 | $n$ = 12 |

$P_{1,3} < 0.01$; $P_{3,4} < 0.01$; $P_{4,6} < 0.01$; $P_{7,9} < 0.01$; $P_{10,12} < 0.05$; $P_{13,15} < 0.01$; $P_{16,18} < 0.05$; $P_{19,20} < 0.01$; $P_{20,21} < 0.01$; $P_{21,22} < 0.01$; $P_{22,24} < 0.05$; $P_{28,30} < 0.05$; $P_{31,33} < 0.05$; $P_{33,34} < 0.01$; $P_{34,36} < 0.05$

Of special interest is a comparison of the $PO_2$ in tissues at determined distances from the microvessel walls both during air breathing and during oxygen breathing. Such data were obtained for the first time in these experiments, and are given in Tables 2A and 2B and in Fig. 3. Our data show that as we moved away from the vessel wall the $PO_2$ decreased almost exponentially. The steepest decrease in $PO_2$ occurred at a distance of 10–20 μm from the vessel. However, even at a distance of 60–75 μm from the vessel wall a substantial difference between the $PO_2$ in the tissues in the case of air breathing and in the case of oxygen breathing is retained. Figure 3 demonstrates the effect of increasing distance from an arteriole wall on $PO_2$ during air breathing and during oxygen breathing.

From the point of view of the modern theory of tissue oxygen supply, the role of venules in this process arouses particular interest. The data presented in Table 3 shows that during air breathing most of the venules (diameter 10–40 μm) take part in the supply of oxygen to the tissues. This follows from the fact that the $PO_2$ decreases with distance from the venule walls (i.e., there is a negative $PO_2$ gradient). During air breathing (i.e., the normal condition) the blood from some venules releases oxygen to the tissues. The blood of other venules, on the contrary, "accepts" oxygen from tissues, because the $PO_2$ in the tissues increases with distance from the venule wall (i.e., there is a positive $PO_2$ gradient).

## Discussion

Since A. Krogh, and to the present day there exists a paradigm that when arterial blood reaches the capillaries it has a $PO_2$ that is equal to the $PO_2$ in the aorta blood (i.e., 85–95 mmHg). Such a postulate is also presented in the modern textbooks on physiology (e.g., Schmidt and Thews 1992). Hence, the most important findings of our studies are that on breathing air, when arterial blood reaches the brain capillaries it has a $PO_2$ of about 60 mmHg, and that the differential in $PO_2$ from the smallest arterioles to the smallest venules is, on average, only 30 mmHg. In our recent work (Vovenko and Ivanov 1997), in which we measured $PO_2$ directly, we found that in the capillaries of the rat brain cortex, over a length of 260 (20) μm along the axis of a capillary in the direction from the arterial to the venous end, the $PO_2$ of the blood decreases from 58 (11) to 41 (2) mmHg. As was shown in that same work (Vovenko and Ivanov 1997), the $PO_2$ in the tissues at a distance of 40 μm from the capillary was about 15–35 mmHg. It is interesting that we have also reported the existence of a comparatively small $PO_2$ gradient in the capillaries of skeletal muscle (Vovenko and Ivanov 1990).

Accurate measurements of $PO_2$, therefore, have shown that in the normal condition (at normoxia), in the brain the oxygen transfer from microvessels to the tissues and oxidation reactions within tissues occur at comparatively low absolute $PO_2$ values. It is believed that such conditions are the result of long-running evolution of aerobic organisms. From the physiological and biochemical points of view, these conditions seem to be optimal for oxygen transport from blood to the tissues and for energy transformations within a cell. This is a very important theoretical problem, but one that cannot be discussed in detail here.

While inhaling oxygen, abrupt changes in the absolute values of $PO_2$ occur in the blood and tissues and in the character of $PO_2$ distribution. It is believed that in man and other animals there are physiological reactions

**Table 2A, B** Mean (SE) values for $PO_2$ (mmHg) on the surface of radial arterioles of rat brain cortex and $PO_2$ in brain tissues at different distances from these vessels during inhalation of air (**A**) and during inhalation of oxygen (**B**). The number in parentheses above the mean (SE) value is used to differentiate pairwise statistical comparisons (see Table footnote)

| Diameter of vessels | Distance from arteriole wall | | | | | |
|---|---|---|---|---|---|---|
| | 0 μm | 7 μm | 15 μm | 35 μm | 50 μm | 70–75 μm |
| **A** | | | | | | |
| 30 μm; $n = 5$ | (1)<br>73 (5) | (2)<br>61 (3) | (3)<br>53 (2) | (4)<br>40 (4) | (5)<br>31 (6) | – |
| 20 μm; $n = 12$ | (6)<br>68 (3) | (7)<br>57 (4) | (8)<br>50 (4) | (9)<br>41 (3) | (10)<br>35 (4) | (11)<br>31 (6) |
| 10 μm; $n = 10$ | (12)<br>61 (3) | (13)<br>51 (2) | (14)<br>46 (3) | (15)<br>37 (4) | (16)<br>29 (6) | (17)<br>32 (4) |
| **B** | | | | | | |
| 30 μm; $n = 5$ | (18)<br>241 (27) | – | (19)<br>190 (22) | (20)<br>158 (18) | (21)<br>140 (14) | (22)<br>121 (10) |
| 20 μm; $n = 12$ | (23)<br>227 (14) | (24)<br>186 (13) | (25)<br>169 (9) | (26)<br>139 (7) | (27)<br>122 (8) | (28)<br>100 (10) |
| 10 μm; $n = 10$ | (29)<br>154 (11) | (30)<br>133 (13) | (31)<br>129 (11) | (32)<br>115 (11) | (33)<br>96 (13) | (34)<br>69 (10) |

$P_{1,12} < 0.01$; $P_{2,13} < 0.05$; $P_{3,14} > 0.05$; $P_{18,29} < 0.01$; $P_{19,31} < 0.05$; $P_{20,32} > 0.05$ Criterion of Wilcoxon (rank pair test; $P_W$): $P_{W1,2} < 0.01$; $P_{W2,3} < 0.01$; $P_{W3,4} < 0.05$; $P_{W4,5} < 0.01$; $P_{W6,7} < 0.01$; $P_{W7,8} < 0.01$; $P_{W8,9} < 0.05$; $P_{W9,10} > 0.05$; $P_{W12,13} < 0.01$; $P_{W\ 13,14} < 0.05$; $P_{W14,15} < 0.01$; $P_{W15,16} < 0.05$; $P_{W16,17} > 0.05$; $P_{W18,19} < 0.01$; $P_{W19,20} < 0.01$; $P_{W20,21} < 0.01$; $P_{W21,22} < 0.01$; $P_{W23,24} < 0.01$; $P_{W24,25} < 0.01$; $P_{W25,26} < 0.01$; $P_{W26,27} < 0.01$; $P_{W27,28} < 0.05$; $P_{W29,30} < 0.01$; $P_{W30,31} < 0.01$; $P_{W31,32} < 0.01$; $P_{W32,33} < 0.01$; $P_{W33,34} < 0.05$

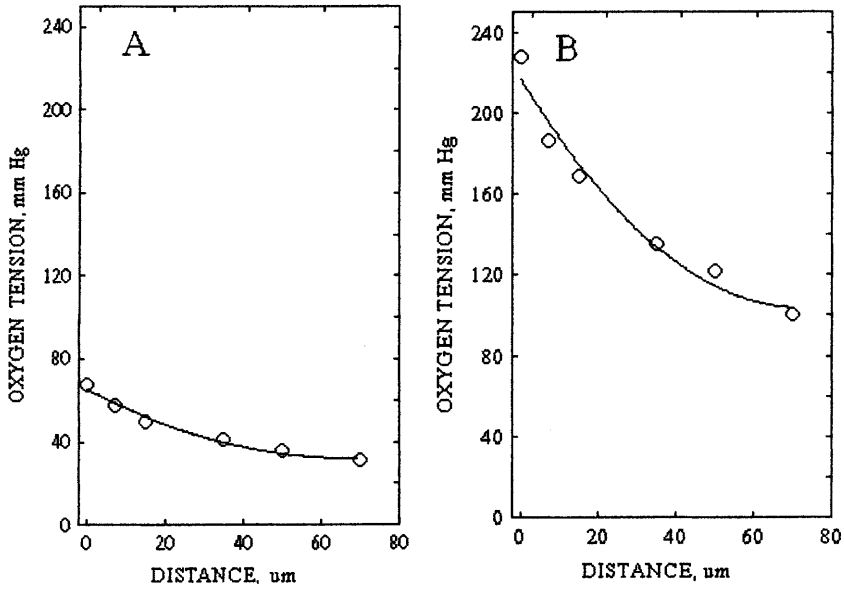


**Fig. 3** Radial profiles of oxygen tension in rat brain cortex tissue in the vicinity of a precortical arteriole (20 μm in diameter) under normoxia (**A**) and hyperoxia (**B**). (*DISTANCE* Distance from the arteriole wall, μm)

**Table 3** Mean (SE) values of $PO_2$ (mmHg) in the brain cortex of rats at various distances from the walls of radial venules under normoxia and hyperoxia. (*1* Venules with a negative $PO_2$ gradient; *2* venules without $PO_2$ gradients, *3* venules with positive $PO_2$ gradients). The numbers in parantheses above the mean (SE) value are used to differentiate pairwise statistical comparisons (see Table footnote)

| | Normoxia Distances from the walls of venules | | | Hyperoxia Distances from the walls of venules | | |
|---|---|---|---|---|---|---|
| | 0 μm | 7 μm | 15 μm | 0 μm | 7 μm | 15 μm |
| 1 | (1)<br>37 (2)<br>$n = 23$ | (2)<br>29 (2)<br>$n = 23$ | (3)<br>25 (2)<br>$n = 23$ | (4)<br>61 (6)<br>$n = 15$ | (5)<br>52 (6)<br>$n = 15$ | (6)<br>49 (7)<br>$n = 15$ |
| 2 | (7)<br>36 (2)<br>$n = 6$ | (8)<br>34 (2)<br>$n = 6$ | (9)<br>36 (4)<br>$n = 6$ | (10)<br>84 (16)<br>$n = 3$ | (11)<br>84 (7)<br>$n = 3$ | (12)<br>82 (12)<br>$n = 3$ |
| 3 | – | – | – | (13)<br>68 (5)<br>$n = 11$ | (14)<br>77 (7)<br>$n = 11$ | (15)<br>83 (7)<br>$n = 11$ |

$P_{W1,2} < 0.01$; $P_{W2,3} < 0.05$; $P_{W4,5} < 0.01$; $P_{W5,6} > 0.05$; $P_{W7,8} > 0.05$; $P_{W8,9} > 0.05$; $P_{W10,11} > 0.05$; $P_{W11,12} > 0.05$; $P_{W13,15} < 0.01$; $P_{W13,14} < 0.01$; $P_{W14,15} > 0.05$

that can hamper an increase in $PO_2$ in the blood during oxygen inhalation: a decrease in respiration frequency, or a contraction of the vessels in the lungs. Nevertheless, in arterial blood the $PO_2$ increases. According to our data from the arterial blood of rats, the $PO_2$ increases from 84.1 (1.3) to 345 (6) mmHg (Tables 1A and 1B). There is, however, a second "line of protection" of the tissues from an increased $PO_2$: the high permeability of the arteriole walls to oxygen. Because of this property, most of the oxygen, which is under an increased pressure in the plasma, passes to the tissues long before the blood reaches the capillaries. The $PO_2$ decreases by 200 mmHg from the blood in the aorta to the blood in the smallest arterioles (and, evidently, in precapillaries, Tables 1A and 1B). It should be noted that the $PO_2$ in the tissues near the arterioles, nevertheless, exceeds the corresponding values obtained during air breathing, by 100–150 mmHg (Tables 2A and 2B, Fig. 3).

However, oxygen transport during oxygen inhalation is not limited by the difference in the $PO_2$. On breathing air, the arterioles are an important source of oxygen for tissues. As shown in this study (Table 1A), from every 100 ml of blood flowing along the arterioles, about 2.2 ml of oxygen (or even a little more) pass into the tissues before reaching the capillaries. During oxygen inhalation, the arterioles almost lose this important function. Under these conditions, from every 100 ml of blood flowing through the arterioles only ≈0.5 ml of the oxygen that is dissolved in the plasma passes to the tissues before reaching the capillaries (Table 1B).

According to our data, during oxygen breathing the $PO_2$ of the blood reaching the brain capillaries is close to 150 mmHg. In the smallest venules, the $PO_2$ decreases to 71 mmHg. The neurons of the brain cortex receive oxygen mostly from the capillaries that are located in the immediate vicinity of a neuron or are tight against the body of a neuron. Hence, the $PO_2$ on the surface of a neuron is almost equal to the $PO_2$ in the blood of the capillary (Ivanov et al. 1979a). It should be noted that during oxygen breathing the $PO_2$ in capillary blood appears to be essentially lower than in the aorta. Of course, this reduces the effect of a high $PO_2$ on a neuron.

Nevertheless, we emphasize that the $PO_2$ gradient between the smallest arterioles and the smallest venules is 83 mmHg (Table 1B) during oxygen breathing, which exceeds that observed during air breathing by a factor of more than 2.5. Therefore, we can suggest that during oxygen breathing an elevated $PO_2$ does affect neurons.

During oxygen inhalation, some physiological changes in the oxygen transport system also occur. Let us consider only one of them, which is of interest with respect to both normoxia and normobaric hyperoxia: the increase in $PO_2$ in the blood of the sagittal sinus compared to that in the blood of the smallest radial venules of the rat brain cortex (Tables 1A and 1B). At normoxia, in the sagittal sinus the $PO_2$ increases by 9–11 mmHg, which increases the $cO_2$ in the blood by 3–4% vol. For normoxia, the origin of this phenomenon remains obscure. One suggestion regarding the functions of a tissue arterial-venous shunt (Lubbers et al. 1968; Piiper 1998; Popel 1982) is not corroborated by our data. Some other mechanisms can exist here; for example, the functioning of direct vascular arterial-venous anastomoses. It is also possible that deeper brain venules carry blood that is more saturated with oxygen to the sagittal sinus. However, during oxygen breathing the existence and functioning of an arterial-venous oxygen tissue shunt is directly corroborated by our data (Table 3).

The aim of the work presented here was to determine and compare the $PO_2$ at various sites of the vascular system from the aorta to the sagittal sinus and in the tissues in the vicinity of the microvessels of the brain cortex (in which gas exchange between the blood and tissues occurs) in rats breathing air and breathing oxygen. We obtained a large amount of precise numerical data which, to the best of our knowledge, has not been presented in modern scientific literature before. These data can serve as a basis for elucidating the toxic action of oxygen on the nervous tissue. They can also be used for the physiological analysis of positive effects of inhaling oxygen during various kinds of oxygen deficiency. These are quite special problems that require further investigation.

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