The effect of oxygen on dynamic cerebral autoregulation: critical role of hypocapnia

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1Department of Biomedical Engineering, Toyo University, Saitama; and 2Morinomiya University of Medical Sciences, Osaka, Japan; 3Department of Human Kinetics, Faculty of Health and Social Development, University of British Columbia Okanagan, Kelowna, Canada; and 4Department of Cardiovascular Dynamics, National Cardiovascular Center Research Institute, Osaka, Japan

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Ogoh S, Nakahara H, Ainslie PN, Miyamoto T. The effect of oxygen on dynamic cerebral autoregulation: critical role of hypocapnia. J Appl Physiol 108: 538–543, 2010. First published January 7, 2010; doi:10.1152/japplphysiol.01235.2009.—Hypoxia is known to impair cerebral autoregulation (CA). Previous studies indicate that CA is profoundly affected by cerebrovascular tone, which is largely determined by the partial pressure of arterial O2 and CO2. However, hypoxic-induced hyperventilation via respiratory chemoreflex activation causes hypocapnia, which may influence CA independent of partial pressure of arterial O2. To identify the effect of O2 on dynamic cerebral blood flow regulation, we examined the influence of normoxia, hypocapnia, hypoxia, and hypoxia with consequent hypocapnia on dynamic CA. We measured heart rate, blood pressure, ventilatory parameters, and middle cerebral artery blood velocity (transcranial Doppler). Dynamic CA was assessed (n = 9) during each of four randomly assigned respiratory interventions: 1) normoxia (21% O2); 2) isocapnic hyperoxia (40% O2); 3) isocapnic hypoxia (14% O2); and 4) hypocapnic hypoxia (14% O2). During each condition, the rate of cerebral regulation (RoR), an established index of dynamic CA, was estimated during bilateral thigh cuff-induced transient hypotension. The RoR was unaltered during isocapnic hyperoxia. Isocapnic hypoxia attenuated the RoR (0.202 ± 0.003/s; 27%; P = 0.043), indicating impairment in dynamic CA. In contrast, hypocapnic hypoxia increased RoR (0.444 ± 0.069/s) from normoxia (0.311 ± 0.054/s; +55%; P = 0.041). These findings indicated that hypoxia disrupts dynamic CA, but hypocapnia augments the dynamic CA response. Because hypocapnia is a consequence of hypoxic-induced chemoreflex activation, it may provide a teleological means to effectively maintain dynamic CA in the face of prevailing arterial hypoxemia.

CEREBRAL BLOOD FLOW (CBF) is maintained relatively constant by a number of regulatory mechanisms during fluctuations in cerebral perfusion pressure (1). Although the CBF is regulated through the integration of numerous control mechanisms, cerebral autoregulation (CA) and the reactivity of the cerebral vasculature to changes in arterial blood-gas tensions likely provide the principle inputs of CBF regulation. Arterial Pco2 (Paco2) is a powerful regulator of the cerebral vasculature; hypocapnia stimulates vessel dilation, increasing CBF, but attenuates dynamic CA (CAd), while hypocapnia causes vessel constriction, a decrease in CBF, and improves CAd (1). Hypoxia (10, 12, 35) and hypocxia (15) also influence both the cerebral and the systemic circulation. Acute hypoxia enhances muscle sympathetic discharge, cardiac output, skeletal muscle blood flow, and heart rate (HR), with little or no alteration in arterial blood pressure (ABP) (14). In the brain, isocapnic hypoxia causes cerebral artery dilation mediated by local metabolite production (e.g., adenosine) (36).

There have been a number of studies examining the influence of hypobaric and normoxic hypoxia on CA. Studies have suggested that there is CA impairment in both newcomers to high altitude (3, 18, 21) and in permanent high-altitude residents living above 4,000 m (19), particularly in the presence of acute mountain sickness (7, 34). During isocapnic hypoxia, studies have suggested that CA is either maintained (2) or impaired (17, 31). Differences in findings may be related to varying degrees of hypoxia (14 vs. 12 vs. 10%) and, importantly, the degree of subsequent hypocapnia. Because hypocapnia improves CAd (1) and is a result of increased hypoxic ventilatory drive via the peripheral chemoreflex, it is difficult to separate the adverse effects of hypoxia per se on CA from the enhancing effects of hypocapnia. Therefore, the purpose of the present study was to examine the influence of hypoxia with and without consequent hypocapnia on both middle cerebral artery blood velocity (MCA V) and CAd. Moreover, while the effects of hypoxia on CA have been partially explored (5, 17, 31), the effects of hyperoxia without concomitant changes in Paco2 are unknown. Although Paco2 has a marked effect on cerebral vascular tone, which defines CAd (1, 24), this response is also influenced by arterial PO2 (PaO2). Therefore, investigation of the effect of hypoxia on CAd will also provide relevant clues regarding the mechanisms by which O2 may affect dynamic CBF regulation. To address these questions, we compared MCA V and CAd during isocapnic hypoxia, hypocapnic hypoxia, and isocapnic hyperoxia to identify the interactions between hypoxia and concomitant influence of hypocapnia on dynamic CBF regulation.

METHODS

Nine healthy, nonathletic men, age 22.7 ± 5.8 yr (mean ± SD), were recruited to participate in the study, as approved by the Human Subjects Committee of Morinomiya University of Medical Sciences (no. 004). Subjects were free of any known cardiovascular and pulmonary disorders and were not using prescribed or over-the-counter medications. Before the experiment, each subject gave informed, written consent and visited the laboratory for familiarization with the techniques and procedures. Subjects were requested to abstain from caffeinated beverages for 12 h and strenuous physical activity and alcohol for at least 24 h before the day of the experiment.
Measurements

All studies were performed at a room temperature between 23 and 24°C with external stimuli minimized. HR was monitored using a lead II electrocardiogram. ABP was monitored with tonometry (BP-608 Evolution II, Omron-Colin, Tokyo, Japan). This system utilizes an state-of-the-art multisensor array technology to detect pulse waves at the radial artery. The ABP system was calibrated from obtained arterial pulse waves by the auscultatory method before each condition. The MCA V was obtained by transcranial Doppler ultrasonography (TCD) (WAKI, Atys Medical, St. Genislaval, France). A 2-MHz Doppler probe was placed on the temporal window and fixed with an adjustable headband and adhesive ultrasonic gel (Tensive, Parker Laboratories, Orange, NJ). Arterial oxygen saturation (SaO2) was assessed at the ear using pulse oximetry (9900-MKII, Kohken Medical, Tokyo, Japan). Ventilatory responses were measured using an open-circuit apparatus. The subjects breathed through a face mask attached to a low-resistance one-way valve with a flowmeter. The valve mechanism allowed subjects to inspire room air or a selected gas mixture from a 200-liter Douglas bag containing 14% O2, 21% O2, or 40% O2 in 0% CO2 with nitrogen (N2) balance. The total instrumental dead space was 200 ml. Respiratory and metabolic data during the experiments were recorded by an automatic breath-by-breath respiratory gas analyzing system, consisting of a differential pressure transducer, sampling tube, filter, suction pump, and mass spectrometer (ARCO2000-MET, Arcosystem, Chiba, Japan). We digitized expired flow, CO2 and O2 concentrations, and derived tidal volume, minute ventilation, end-tidal PO2 (PETO2), and end-tidal PCO2 (PETCO2). Flow signals were computed to single-breath data and matched to gas concentrations identified as single breaths using the peak PETCO2, after accounting for the time delay in gas concentration measurements. The corresponding O2 uptake and CO2 output values for each breath were calculated from inspired-expired gas concentration differences, and by expired ventilation, with inspired ventilation being calculated by N2 correction. During each protocol, HR, ABP, minute ventilation, PETO2, PETCO2, and MCA V were recorded continuously at 200 Hz.

Experimental Protocol

On the experimental day, subjects arrived at the laboratory at least 2 h following a light meal. After instrumentation, the subjects were seated in a semirecumbent position (45°) in a reclining seat and 24°C with external stimuli minimized. HR was monitored using a lead II electrocardiogram. ABP was monitored with tonometry (BP-608 Evolution II, Omron-Colin, Tokyo, Japan). This system utilizes an state-of-the-art multisensor array technology to detect pulse waves at the radial artery. The ABP system was calibrated from obtained arterial pulse waves by the auscultatory method before each condition. The MCA V was obtained by transcranial Doppler ultrasonography (TCD) (WAKI, Atys Medical, St. Genislaval, France). A 2-MHz Doppler probe was placed on the temporal window and fixed with an adjustable headband and adhesive ultrasonic gel (Tensive, Parker Laboratories, Orange, NJ). Arterial oxygen saturation (SaO2) was assessed at the ear using pulse oximetry (9900-MKII, Kohken Medical, Tokyo, Japan). Ventilatory responses were measured using an open-circuit apparatus. The subjects breathed through a face mask attached to a low-resistance one-way valve with a flowmeter. The valve mechanism allowed subjects to inspire room air or a selected gas mixture from a 200-liter Douglas bag containing 14% O2, 21% O2, or 40% O2 in 0% CO2 with nitrogen (N2) balance. The total instrumental dead space was 200 ml. Respiratory and metabolic data during the experiments were recorded by an automatic breath-by-breath respiratory gas analyzing system, consisting of a differential pressure transducer, sampling tube, filter, suction pump, and mass spectrometer (ARCO2000-MET, Arcosystem, Chiba, Japan). We digitized expired flow, CO2 and O2 concentrations, and derived tidal volume, minute ventilation, end-tidal PO2 (PETO2), and end-tidal PCO2 (PETCO2). Flow signals were computed to single-breath data and matched to gas concentrations identified as single breaths using the peak PETCO2, after accounting for the time delay in gas concentration measurements. The corresponding O2 uptake and CO2 output values for each breath were calculated from inspired-expired gas concentration differences, and by expired ventilation, with inspired ventilation being calculated by N2 correction. During each protocol, HR, ABP, minute ventilation, PETO2, PETCO2, and MCA V were recorded continuously at 200 Hz.

Experimental Protocol

On the experimental day, subjects arrived at the laboratory at least 2 h following a light meal. After instrumentation, the subjects were seated in a semirecumbent position (~45°) in a reclining seat and rested quietly for ~10 min, while wearing the face mask and breathing room air. After the resting period, each subject performed four randomly assigned respiratory interventions: 1) normoxia (21% O2); 2) hyperoxia (40% O2); 3) hypoxia (14% O2), each with volitionally controlled normal respiratory rate; and 4) hypoxia (14% O2) with hyperventilation. Full recovery was permitted between each intervention. Throughout the experimental interventions (interventions 1–3), subjects were instructed to adjust their resting respiratory pattern (14 breaths/min) to the sound of a metronome and the monitor showing each respiratory cycle, to avoid changes in PETCO2. During intervention 4, subjects were instructed to adjust breath at higher respiratory rate (16 respirations/min) to obtain a lower PETCO2 (29 ± 1 Torr, P < 0.001; Table 1). Eight minutes of baseline data were recorded with the subjects breathing the selected gas mixture with control respiration for each condition. Following the baseline at each condition, the thigh cuffs were inflated to more than the systolic pressure (≥220 mmHg) for 3 min. After the 3 min of cuff inflation, the cuffs were deflated, and measurements were continued 2 min postdeflation to assess the CBF response to a rapid and transient drop in ABP to identify CAa. Previous investigations have indicated that, under resting conditions, the cuff occlusion-induced ischemia does not induce a muscle metaboreflex activation (29). All conditions were randomized and separated by a minimum of 20 min.

Data Analysis

Beat-to-beat mean arterial pressure (MAP) and mean MCA V (MCA Vmean) were obtained from each waveform. The cerebrovascular conductance index (CVCi) was calculated by dividing MCA Vmean by MAP and was used as an estimate of changes in cerebrovascular conductance. The derived CVCi during acute hypotension is not directly related to steady-state cerebrovascular conductance, because changes in the vascular compliance affect CBF (1). Control values of MAP, MCA Vmean, and CVCi were defined by calculating their means during the 4 s immediately before thigh-cuff release. Changes in MAP, MCA Vmean, and CVCi during cuff release were determined relative to their concomitant control values. At time 1.0–3.5 s from cuff release, the rate of change in CVCi is directly related to CAa (1). The rate of regulation (RoR) is calculated as an index of CAa (1).

\[ \text{RoR} = \frac{\Delta \text{CVCi}}{\Delta T} / \Delta \text{MAP} \]

where \( \Delta \text{CVCi}/\Delta T \) is the slope of the linear regression between CVCi and time (T); and \( \Delta \text{MAP} \) was calculated by subtracting control MAP from MCA MAP averaged during the interval from 1.0 to 3.5 s (1).

Statistics

Statistical comparison of variables and RoR were made utilizing a repeated-measures one-way analysis of variance. A Student-Newman-Keuls test was employed post hoc when interactions were significant. Statistical significance was set at \( P < 0.05 \), and results are presented as means ± SE. Analyses were conducted using SigmaStat (Jandel Scientific Software, SPSS, Chicago, IL).

Table 1. Steady-state cerebrovascular and cardiorespiratory variables during normoxia, hyperoxia, isocapnic hypoxia, and hypocapnic hypoxia

<table>
<thead>
<tr>
<th></th>
<th>Intervention 1: Normoxia</th>
<th>Intervention 2: Hyperoxia</th>
<th>Intervention 3: Hypoxia</th>
<th>Intervention 4: Hypocapnic Hypoxia</th>
<th>( P )</th>
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<tbody>
<tr>
<td>HR, beats/min</td>
<td>65 ± 3</td>
<td>58 ± 8</td>
<td>68 ± 6</td>
<td>69 ± 3</td>
<td>0.347</td>
</tr>
<tr>
<td>MAP, mmHg</td>
<td>85 ± 3</td>
<td>91 ± 4</td>
<td>85 ± 2</td>
<td>88 ± 5</td>
<td>0.243</td>
</tr>
<tr>
<td>MCA Vmean, cm/s</td>
<td>65 ± 3</td>
<td>62 ± 4</td>
<td>68 ± 4†</td>
<td>54 ± 4‡†</td>
<td>0.001</td>
</tr>
<tr>
<td>PETO2, %</td>
<td>20.7 ± 0.1</td>
<td>40.6 ± 0.1*</td>
<td>13.6 ± 0.1†</td>
<td>13.6 ± 0.1†</td>
<td>0.001</td>
</tr>
<tr>
<td>PETCO2, Torr</td>
<td>104 ± 1</td>
<td>245 ± 2*</td>
<td>58 ± 1‡†</td>
<td>67 ± 2‡†</td>
<td>0.001</td>
</tr>
<tr>
<td>PETCO2, Torr</td>
<td>37 ± 1</td>
<td>36 ± 1</td>
<td>37 ± 1</td>
<td>29 ± 1‡†</td>
<td>0.001</td>
</tr>
<tr>
<td>SaO2, %</td>
<td>97.7 ± 1.3</td>
<td>99.6 ± 0.9*</td>
<td>88.9 ± 1.7‡†</td>
<td>94.2 ± 2.3‡†</td>
<td>0.001</td>
</tr>
<tr>
<td>Vt, l/min</td>
<td>8.8 ± 0.6</td>
<td>9.5 ± 0.5</td>
<td>9.6 ± 0.5</td>
<td>13.1 ± 0.6‡†</td>
<td>0.001</td>
</tr>
<tr>
<td>Vt, ml</td>
<td>647 ± 22</td>
<td>694 ± 41</td>
<td>692 ± 46</td>
<td>843 ± 34‡†</td>
<td>0.001</td>
</tr>
<tr>
<td>RR, breaths/min</td>
<td>13.7 ± 0.8</td>
<td>13.9 ± 0.7*</td>
<td>14.0 ± 0.8</td>
<td>15.6 ± 0.7†</td>
<td>0.001</td>
</tr>
</tbody>
</table>

Values are means ± SE. HR, heart rate; MAP, mean arterial pressure; MCA Vmean, middle cerebral artery mean blood velocity; PETO2, fraction of inspired oxygen (O2); PETCO2, end-tidal PCO2; PETCO2, end-tidal PCO2; Vt, minute ventilation; Vt, tidal volume; RR, respiratory rate. *\( P < 0.05 \), different from normoxia; †\( P < 0.05 \), different from hyperoxia; ‡\( P < 0.05 \), different from isocapnic hypoxia; ‡‡\( P < 0.05 \), different from hypocapnic hypoxia.
RESULTS

Hyperoxia, Hypoxia, and Hypocapnic Hypoxia

During the four experimental conditions, PETO₂ and PETCO₂ were accurately controlled by the selected mix of inspired gases and control of respiratory pattern (Table 1). During the control intervention (intervention 1; 21% O₂), PETO₂ and PETCO₂ were 104 ± 1 and 37 ± 1 Torr, respectively. In intervention 2 (40% O₂), PETO₂ was elevated to 245 ± 2 Torr (P < 0.001), whereas PETCO₂ was well maintained at preintervention level (36 ± 1 Torr). Likewise, while hypoxia (intervention 3) decreased PETO₂ to 58 ± 1 Torr (P < 0.001 vs. baseline), PETCO₂ was maintained by voluntary control of respiration in the hypoxic (37 ± 1 Torr) condition. During intervention 4 (14% O₂ with hyperventilation), voluntary hyperventilation decreased PETCO₂ from 37 ± 1 to 29 ± 1 Torr. Compared with control, SaO₂ was reduced during both isocapnic and hypocapnic hypoxia; however, the reduction in SaO₂ was greater during the isocapnic hypoxic condition compared with the hypocapnic hypoxia condition (Table 1). During all interventions (interventions 2–4), there were no alterations in HR (P = 0.347) and MAP (P = 0.243). However, the isocapnic hypoxic intervention tended to increase MCA Vₘₑᵃⁿ (4%; P = 0.237). In contrast, controlled hyperventilation during hypoxia decreased MCA Vₘₑᵃⁿ (19%; P < 0.001). The CVCi increased at hypoxia and decreased at hypocapnic hypoxia condition (see Fig. 2).

Thigh Cuff Release During the Experimental Conditions

The release of the thigh cuffs elicited an acute decrease in ABP at all conditions. Changes in MAP with thigh deflation were −27 ± 3% (normoxia; intervention 1), −30 ± 2% (isocapnic hypoxia; 2), −28 ± 2% (isocapnic hypoxia; 3), and −27 ± 4% (hypocapnic hypoxia conditions; 4). There were no differences in the changes in MAP with each condition. As intended, these decreases in ABP were sufficient to evoke a transient decrease in MCA Vₘₑᵃⁿ (1). As a reflection of CA₄, changes in MCA Vₘₑᵃⁿ were smaller (average 23%) from baseline compared with MAP in all conditions, particularly during the hypocapnic hypoxia condition (18 ± 3%, P < 0.001).

The RoR, an index of CA₄, was calculated from the change in CVCi from 1 to 3.5 s (Fig. 1). Compared with normoxia, RoR was not altered with isocapnic hypoxia (0.321 ± 0.028/s; Fig. 2). Isocapnic hypoxia significantly attenuated RoR (0.202 ± 0.003/s; 27%, P = 0.043). In contrast, hypocapnic hypoxia increased RoR (0.444 ± 0.069/s) from normoxia (0.311 ± 0.054/s; +55%, P = 0.041).

DISCUSSION

The primary finding of the present study is that isocapnic hypoxia impairs CA₄; however, mild hypocapnia counters this to improve CA₄ during hypoxia. These data indicate that, at least acutely, the respiratory chemoreflex may compensate for hypoxic-induced impaired in CA₄ through hyperventilation and consequent hypocapnia. That hypocapnia affected CA₄ even under conditions of hypoxia reinforces the idea that CBF control is influenced to a greater extent by Paco₂ than by Paco₂.

Hypocapnia leads to cerebral vasoconstriction, which attenuates the further fall of brain tissue Pco₂, while hypercapnia causes cerebral vasodilation, limiting elevations in brain tissue Pco₂. Changes in blood-gas concentrations modified dynamic CBF regulation (1, 24). For example, there was a significant inverse relationship between CA₄ and Paco₂, indicating that the response rate of CA₄ is due to cerebral vascular tone as determined by levels of Pco₂ (1). However, while hypoxia is a cerebral vasodilator, reflected in a rise in CBF in proportion to the severity of isocapnic hypoxia (6, 11), under normal conditions the hypoxia-induced activation of peripheral chemoreceptor activity leads to hyperventilatory-induced lowering of Paco₂ and subsequent cerebral vasoconstriction. Thus the cerebrovascular bed receives conflicting signals during exposure to acute hypoxia, which coincides with hypoxic ventilatory response and resultant hypocapnia (4). An important physio-
hyperventilation and subsequent reduction in arterial P CO2 is different from hyperoxia; during acute (5 min) exposure to hypoxia (F IO2 <0.12).

In contrast, another study (31) reported that CAd was impaired, as assessed by using the transfer function (low-frequency gain) in CAd was evident at 17% O2. In contrast, sympathetic nerve activity blockade (25, 37) or hypercapnia (1) impaired CAd. In the present study, hypoxia caused decreased cerebrovascular tone (an increase in CVCi; Fig. 2), accompanied by cerebral vasodilation. In contrast, high cerebrovascular tone, induced via hypercapnia (1), improved CAd. We found that CAd was improved by hyperventilation, even during hypoxia, which causes further cerebral vasodilation. Thus cerebral vascular tone may modify CAd. However, heavy exercise (26), hypertensive patients (16), and orthostatic stress (38) impaired CAd, despite a high cerebral vascular tone.

Comparison with Previous Studies

There are three previous studies to compare our findings. First, Iwasaki et al. (17) found that 5 min of mild hypoxia [inspired O2 fraction (FiO2) = 0.15; inspired Po2 = 105 Torr] impaired CAO2, as assessed by using the transfer function analysis approach. In this study, some impairment (e.g., change in power spectrum density and tendency for increases in low-frequency gain) in CAd was evident at 17% O2. In contrast, Ainslie et al. (5) reported no changes in CAd under more severe hypoxia (FiO2 = 0.12 and 0.10, inspired Po2 = 85 and 70 Torr), assessed using the transfer function analysis approach. In contrast, another study (31) reported that CAd was impaired during acute (5 min) exposure to hypoxia (FiO2 = 0.12). Unfortunately, none of these studies separates the effects of isocapnic vs. poikilocapnic hypoxia; that the cerebral vasculature is highly sensitive to CO2 limits interpretation of these studies with respect to the independent effects of hypoxia. In view of the current findings, differences in the degree of hypoxia and variability in the chemoreflex response and subsequent degree of hypocapnia may explain these inconsistent results. Our findings underscore the critical role of arterial hypocapnia influencing the effects of acute hypoxia on CAd.

The Mechanisms of Action

The mechanism of changes in CAd seems to be associated with cerebral vascular tone. Reductions in cerebral vascular tone via sympathetic nerve activity blockade (25, 37) or hypocapnia (1) impaired CAd. In the present study, hypoxia caused decreased cerebrovascular tone (an increase in CVCi; Fig. 2), accompanied by cerebral vasodilation. In contrast, high cerebrovascular tone, induced via hypercapnia (1), improved CAd. We found that CAd was improved by hyperventilation, even during hypoxia, which causes further cerebral vasodilation. Thus cerebral vascular tone may modify CAd. However, heavy exercise (26), hypertensive patients (16), and orthostatic stress (38) impaired CAd, despite a high cerebral vascular tone.

Implications

High altitude. There have been a number of studies that have examined the influence of high altitude on CA. Studies indicate an impairment in CA (3, 18, 21) in both newcomers to high altitude and in permanent high-altitude residents living above 4,000 m (19), especially in the presence of acute mountain sickness (7, 34). These studies reported impairment in CAd, despite the presence of marked hypocapnia, which is in contrast with those from the present study, where CAd was improved with the addition of hypocapnia. Differences in the experimental protocol (i.e., length of hypoxic exposure), severity, and type of hypoxic exposure (i.e., simulated vs. high altitude) may underpin these different findings. Nevertheless, the possibility that those with a more vigorous hypoxic ventilatory responses at high altitude (and, therefore, greater degree of hypocapnia) may benefit from a better maintained CAd and, therefore, protection against acute mountain sickness (7, 34) warrants further study.

Pathology. Arterial hypoxemia is a common consequence of chronic lung and cardiac diseases. Little is known with respect to how CA and CBF may be regulated in these disorders (4). However, transient drops in PacO2 are known to occur in a range of physiological (e.g., postural change, exercise) and pathophysiological (e.g., asthma, sleep apnea, congestive heart failure, anxiety attacks) situations. The possibility that such hypocapnia is of teleological relevance to offset hypoxic-induced impairment in CAd warrants further research.

Methodological considerations. A potential limitation of estimating MCA V using TCD is that changes in the diameter of the insonated vessels could modulate MCA V independently of flow. Numerous studies support the validity of MCA V as an index of regional CBF (9, 23, 27, 30, 32, 33). Moreover, studies have shown that MCA diameter is relatively unchanged in the range of 23–60 Torr for PacO2 (13, 30, 33). However, evidence of unchanged MCA diameter during hypoxia is still less clear. Nevertheless, it is noteworthy that the observed MCA V response during isocapnic hypoxia was comparable to
findings by Noth et al. (22), who have previously assessed the CBF response to isocapnic hypoxia using MRI (22). Consistent with this report, earlier studies (28) have used the Doppler power signal as an index of the cross-sectional area of the MCA diameter and have also reported that the diameter is unchanged during comparable hypoxia conditions. Collectively, these findings support the use of MCA V as a valid measure of CBF. In addition, TCD-determined blood flow velocity in large basal cerebral arteries (i.e., MCA) is widely used as an index of CBF and can identify a transient change in CBF (24).

A consequence of the hypoxic hypocapnia condition was that the hyperventilation caused a small rise in PETO2 (~9 Torr) and, therefore, SaO2. Nevertheless, alterations in CAq occur at 15% O2; some changes were also evident at 17% O2 (17). Moreover, because of the alveolar-to-arterial PO2 gradient [normally = <5–8 Torr (5, 20)], PAO2 would likely be <50 Torr. Thus it would seem unlikely that the small increase in PETO2 and, therefore, vasodilatory stimulus would alter our findings.

In summary, isocapnic hypoxia impairs CAq, whereas it is unchanged under conditions of isocapnic hyperoxia. In addition, hyperventilation-induced mild hypocapnia acts to improve CAq, even during hypoxic conditions. It seems likely that, at least acutely, respiratory chemoreflex may compensate for hypoxia-induced impairment in CAq.

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DISCLOSURES

No conflicts of interest are declared by the author(s).

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