Effects of acute hypoxia on cerebral and muscle oxygenation during incremental exercise

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Subudhi AW, Dimmen AC, Roach RC. Effects of acute hypoxia on cerebral and muscle oxygenation during incremental exercise. J Appl Physiol 103: 177–183, 2007. First published April 12, 2007; doi:10.1152/japplphysiol.01460.2006.—To determine if fatigue at maximal aerobic power output was associated with a critical decrease in cerebral oxygenation, 13 male cyclists performed incremental maximal exercise tests (25 W/min ramp) under normoxic (Norm: 21% FIO2) and acute hypoxic (Hypox: 12% FIO2) conditions. Near-infrared spectroscopy (NIRS) was used to monitor concentration (μM) changes of oxy- and deoxymethemoglobin (Δ[O2Hb], Δ[HHb]) in the left vastus lateralis muscle and frontal cerebral cortex. Changes in total Hb were calculated (Δ[THb] = Δ[O2Hb] + Δ[HHb]) and used as an index of change in regional blood volume. Repeated-measures ANOVA were performed across treatments and work rates (α = 0.05). During Norm, cerebral oxygenation rose between 25 and 75% peak power output {Powerpeak; increased (inc) Δ[O2Hb], inc. Δ[HHb], inc. Δ[THb]}, but fell from 75 to 100% Powerpeak [decreased (dec) Δ[O2Hb], inc. Δ[HHb], no change Δ[THb]]. In contrast, during Hypox, cerebral oxygenation dropped progressively across all work rates (dec. Δ[O2Hb], inc. Δ[HHb]), whereas Δ[THb] again rose up to 75% Powerpeak and remained constant thereafter. Changes in cerebral oxygenation during Hypox were larger than Norm. In muscle, oxygenation decreased progressively throughout exercise in both Norm and Hypox (dec. Δ[O2Hb], inc. Δ[HHb], inc. Δ[THb]), although Δ[O2Hb] was unchanged between 75 and 100% Powerpeak. Changes in muscle oxygenation were also greater in Hypox compared with Norm. On the basis of these findings, it is unlikely that changes in cerebral oxygenation limit incremental exercise performance in normoxia, yet it is possible that such changes play a more pivotal role in hypoxia.

NIRS measurements have been well correlated with intracellular oxygen tension in muscle (50) and venous oxygen saturation in both muscle (18, 53) and cerebral tissue (22). Several authors have reported that muscle oxygenation decreases progressively with increased exercise intensity, reaching a minimum or plateau near maximal aerobic power output (3–7, 21, 35, 38, 53). Changes in cerebral oxygenation have not been as well defined. In general, cerebral oxygenation has been shown to increase during submaximal exercise, but either remains elevated (24, 25, 32, 39, 41) or decreases at maximal intensity (19, 26, 40). While Gonzalez-Alonso et al. (19) argued that reductions in cerebral oxygenation do not represent a limit to performance, Nielsen et al. (40) reported that administration of supplemental oxygen (FIO2 = 30%) maintains cerebral oxygenation and increases time trial performance without affecting muscle oxygenation, thus supporting a central limitation to exercise. Saito et al. (46) and Imray et al. (25) suggested that cerebral hypoxia may be a limiting factor to exercise under certain environmental conditions, as their subjects exhibited reductions in cerebral oxygenation while performing exercise at high altitudes. More recently, Rasmussen et al. (44) showed that decreased frontal cortex oxygenation was associated with reduced muscle force-generating capacity. Although these studies demonstrated an association between cerebral oxygenation and exercise performance, no studies have determined if a critical level of cerebral deoxygenation limits performance.

A standard model that clearly differentiates between central (central nervous system) and peripheral (muscle) factors associated with fatigue during intense, aerobic exercise has yet to be established. The intent of this study was to use NIRS to monitor changes in both central and peripheral oxygenation during incremental exercise to exhaustion. The study was the first to monitor simultaneous changes in cerebral and muscle oxygenation under both normoxic and hypoxic conditions. We specifically tested the hypothesis that a critical change in cerebral, but not muscle, oxygenation would immediately precede voluntary cessation of exercise.

MATERIALS AND METHODS

Subjects

Following institutional review board approval, competitive cyclists were recruited through local cycling clubs. Respondents were screened to select active competitors with recent experience cycling at elevations between 2,500 and 4,300 m. Fifteen male cyclists, meeting the above criteria, gave their written informed consent to participate in the study. Prior to the experimental protocol, all subjects were given
a complete physical examination, including blood tests (complete blood count and metabolic panel), to assess general health. Two subjects were excluded from the study based on the results of baseline examinations (hypertension and recent pneumonia). Thirteen cyclists completed the experimental protocol.

Experimental Design

The study was conducted using a single blinded, cross-over design. Subjects first performed a practice trial of incremental exercise to maximal exertion under ambient conditions (22°C; 15% humidity, 625 mmHg). The testing protocol was repeated on two additional days, spaced at least 1 wk apart, while breathing either normoxic (Norm: $P_{O_2} = 21\%$; $P_{O_2} = 131$ mmHg) or hypoxic (Hypox: $P_{O_2} = 12\%$; $P_{O_2} = 75$ mmHg) mixtures of dry medical grade gas. The order of treatment was randomly assigned and counterbalanced.

Exercise Testing

All testing was performed on a Velotron cycle ergometer (Racermate, Seattle, WA), which was adjusted to each cyclist’s specifications. Prior to testing, subjects were required to warm up for 20 min, under ambient conditions, at a work rate (watts) equaling 1.5 × body weight (kg). Subjects were then instrumented with necessary probes, sensors, and breathing apparatus. To prime the breathing system and analyzers, subjects inhaled experimental gas for no more than 2 min prior to the commencement of exercise. Initial work rate was set at 25 W and increased at a ramped rate of 25 W/min until subjects reached perceived exhaustion, as indicated by volitional cessation of exercise, or failure to maintain a pedal cadence of >50 rpm despite strong verbal encouragement. Following the test, all instrumentation was removed and subjects performed self-paced cool down under ambient conditions.

Instrumentation

NIRS theory. Determination of tissue oxygenation via NIRS is based on the Beer-Lambert Law, which quantifies the attenuation of light due to scattering and absorption by other chromophores. If light intensity, $I$, is the transmitted light intensity, $I_o$ is the incident light intensity, $c$ is the concentration of the chromophore (mM$^{-1}$cm$^{-1}$), $L_o$ is the distance (cm) between light entry and exit, and $\lambda$ is the wavelength of light used.

When applied to biological tissues, the equation is modified to account for light scattering (16): $OD_x = \log(I/I_o) = c\cdot e\cdot L_o$, where $OD_x$ is the medium’s optical density, $I$, is the incident light intensity, $I_o$ is the transmitted light intensity, $e$ is the extinction coefficient of the chromophore (mM$^{-1}$cm$^{-1}$), $c$ is the concentration of the chromophore (mM$^{-1}$), $L_o$ is the distance (cm) between light entry and exit, and $\lambda$ is the wavelength of light used.

$OD_x$ is the change in optical density at a specific wavelength, and $OD_x$ accounts for attenuation due to scattering and absorption by other chromophores. If $OD_x$ is assumed to be constant, one can solve for change in concentration using the formula, $\Delta = \Delta OD / (c\cdot L_o\cdot DPF)$. This equation is valid for a scattering medium with one chromophore. Additional wavelengths of light must be used to differentiate between chromophores in more complex systems.

In biological tissues, NIR light is specifically absorbed by heme groups within hemoglobin (Hb) and myoglobin (Mb); thus NIRS cannot differentiate between the two species. Since Mb is tetrameric and exists in appreciably greater concentrations than the monomeric Hb species, the relative contribution of Hb is substantially greater than that of Mb (53). The ability of NIRS to quantify changes in oxygenation is based on the difference in absorption spectra for oxygenated and deoxygenated heme groups. In light of these facts, it is appropriate to refer to NIRS measurements as indexes of overall tissue oxygenation (51), with the understanding that underlying vascular beds are composed of ~70% venous blood (8).

NIRS measurements. During all exercise sessions, subjects were instrumented with two pairs of NIRS probes to monitor absorption of light across cerebral and muscle tissue (Oxymon, Artinis, The Netherlands). Headsets were constructed to hold one NIR emitter and detector pair over the left frontal cortex region of the forehead. Spacing between optodes was adjusted to ensure proper placement and signal strength on each individual (range 4.26–4.61 cm). A second emitter and detector pair was affixed over the belly of the left vastus lateralis muscle (~15 cm above the proximal border of the patella and 5 cm lateral to the midline of the thigh). Skinfold measurements were made in the sagittal plane midway between optodes to account for skin and adipose thickness. Probes were held in place by a plastic spacer with fixed optode distance of 5.18 cm and secured to the skin using double-sided tape. Elastic bandages were used to shield the optodes from ambient light. The Beer-Lambert law was used to calculate micromolar changes in tissue oxygenation ($\Delta[O_2Hb]$ and $\Delta[HHb]$) across time using received optical densities from two continuous wavelengths of NIR light (780 and 850 nm) and published DPFs of 4.95 (17) and 5.93 (52) for muscle and cerebral tissue, respectively. Total Hb ($\Delta[THb]$) was calculated as the sum of $\Delta[O_2Hb]$ and $\Delta[HHb]$ and used as an index of change in regional tissue oxygenation (51). Data were recorded at 10 Hz and filtered with a Savitzky-Golay smoothing algorithm prior to analysis. Both cerebral and muscle measurements were normalized to reflect changes from the beginning of the exercise protocol (arbitrarily defined as 0 μM) to express the magnitude of deoxygenation near maximal exercise. A postexercise, leg cuff-ischemia technique to obtain a low-oxygenation reference point was not used because Chance et al. (12) reported little additional deoxygenation (~2%) during suprasystolic cuff occlusion of the vastus lateralis muscle immediately following incremental exercise to maximal exertion.

Absolute measurements of hemoglobin concentration and percent saturation values (analogous to those obtained via pulse oximetry) were unattainable because the exact DPFs were unknown. Thus direct comparisons between the two tissues could not be made due to differences in tissue composition and volumes illuminated.

By definition, $[O_2Hb]$ and $[HHb]$ exist in equilibrium, such that an increase in one results in a stoichiometric decrease in the other. Thus we interpret decreases in $\Delta[O_2Hb]$ and increases in $\Delta[HHb]$ as evidence of relative deoxygenation and, vice versa, as evidence of improved oxygenation. These explanations are only valid if regional blood volume, defined by $\Delta[THb]$, is constant. Since arterial blood is mostly oxygenated, changes in regional arterial flow are reflected by parallel changes in $\Delta[O_2Hb]$ if the rate of oxygen consumption remains constant. Because $\Delta[HHb]$ is closely associated with changes in venous oxygen content and is less sensitive to $\Delta[THb]$ than $\Delta[O_2Hb]$ is, $\Delta[HHb]$ is believed to be a sensitive measure of relative tissue deoxygenation due to oxygen extraction (20).

Cardiopulmonary measurements. Heart rate was measured and recorded with a chest strap and monitor (Polar USA, Irvine, CA). Subjects were instructed to keep their hands and fingers relaxed during exercise testing to obtain strong, pulsatile, finger-tip oximetry signals from either the left index or middle finger (Criticare 503, Waukesha, WI). Experimental gases (Norm = compressed air; Hypox = 12% O2, 88% N2) were administered using a system of plastic tubing and 200 liter Douglas bag reservoir. Subjects’ expired breath was directed through 1.8 m of tubing to a 3.0 liter mixing chamber. Ventilation was measured using a heated pneumotach (Hans Rudolph series 4813, Kansas City, MO). Gas samples from the mixing chamber were analyzed with $O_2$ (Ametek S-3A, AFI Technologies, Pittsburgh, PA) and CO2 (Ametek CD-3A, AEI Technologies) analyzers. Analog data from each instrument were continuously recorded with a PowerLab 16 data-acquisition system (ADInstruments, Colorado Springs, CO), sampling at 100 Hz. Metabolic variables of interest ($V_{O_2}, V_{CO_2}$) were calculated Offline using the Haldane transformation to obtain average values over 20-s periods. Ventilatory threshold (VT) was determined using ventilatory equivalents of $O_2$ and CO2 as previously described (2). Peak power output ($P_{\text{peak}}$) was defined as power output recorded immediately before termination of exercise.
Analyses

Metabolic responses to exercise during Norm and Hypox were evaluated with paired t-tests. All NIRS data were expressed as micromolar concentration change from rest, immediately before the start of exercise (0 μM). Mean values (Δ[O₂Hb], Δ[HHb], and Δ[THb]) were plotted against relative power output to qualitatively describe cerebral and muscle oxygenation patterns during exercise for each treatment. Reliability of NIRS data in response to exercise under normoxic conditions (practice test and Norm) was assessed using the Intraclass Correlation Coefficient (ICC) Alpha. Pearson product moment correlations were used to evaluate relationships between NIRS and pulse oximeter measurements.

Quantitative differences in cerebral and muscle NIRS measurements were analyzed with multivariate (Wilks’s Lambda), repeated-measures ANOVA to evaluate effects of treatment (Norm and Hypox) across both relative work rates (25%, 50%, 75%, and 100% Peak Powerpeak) and absolute work rates (100 and 200 W). Criterion for significance was set at P < 0.05. Post hoc, pairwise comparisons were made using the Holm’s sequential method to control for type I error.

RESULTS

Subject Characteristics

Subjects were competitive, amateur cyclists who resided at altitudes between 1,585 and 1,890 m and reported weekly training volumes of 11 ± 3 h during the testing period (January-April). Those completing all experimental trials (n = 13) were 30 ± 7 yr old, 182 ± 6 cm tall, weighed 78 ± 9 kg, and had thigh skinfold thickness of 8 ± 3 mm. Average Hb concentration and hematocrit were 16.2 ± 0.7 g/dl and 47 ± 2%.

Metabolic Measurements

Average metabolic responses to exercise trials are shown in Table 1. VO₂peak (ml·kg⁻¹·min⁻¹) and Powerpeak (W) were reduced 37 and 29% under Hypox compared with Norm (P < 0.05). Hypox resulted in relative hyperventilation at absolute work rates, but ventilation at the point of exhaustion was lower than Norm (Table 1). VO₂ and Power at VT were 33% lower during Hypox (P < 0.05), but, in relative terms, were not different from Norm (70 ± 5% VO₂peak and 63 ± 5% Powerpeak during Norm vs. 74 ± 8% VO₂peak and 59 ± 7% Powerpeak during Hypox). All but two subjects were able to correctly identify the order of treatment; however, no subjects reported adverse side effects of hypoxia (dizziness, headache, or nausea) during or following exercise.

<table>
<thead>
<tr>
<th>Table 1.</th>
<th>Metabolic responses to incremental exercise tests</th>
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</thead>
<tbody>
<tr>
<td>Variable</td>
<td>VT</td>
</tr>
<tr>
<td>V̇E, l/min</td>
<td>85.8 ± 10.3</td>
</tr>
<tr>
<td>VO₂, ml·kg⁻¹·min⁻¹</td>
<td>42.6 ± 5.0</td>
</tr>
<tr>
<td>V̇O₂/VO₂</td>
<td>25.6 ± 2.4</td>
</tr>
<tr>
<td>V̇CO₂/Pco₂</td>
<td>27.1 ± 2.3</td>
</tr>
<tr>
<td>Power, W</td>
<td>256 ± 30</td>
</tr>
<tr>
<td>SpO₂, %</td>
<td>92 ± 3</td>
</tr>
<tr>
<td>HR, beats/min</td>
<td>150 ± 13</td>
</tr>
</tbody>
</table>

Values are means ± SD; n = 13, VT, ventilatory threshold. *Different from normoxia (P < 0.05).

Near-Infrared Measurements

Reliability of NIRS measurements was evaluated using data collected during practice and Norm trials. ICC Alpha was high for cerebral (0.98 to 0.99) and muscle (0.97 to 0.98) Δ[O₂Hb], Δ[HHb], and Δ[THb] across all work rates. Cerebral and muscle NIRS measurements were correlated (P < 0.001) with pulse oximeter readings during exercise in Norm (r = 0.62 to 0.90) and Hypox (r = 0.94 to 0.96). Average concentration changes in cerebral and muscle NIRS signals were graphed for all subjects across relative work rates during Norm and Hypox (Fig. 1).

Cerebral analysis. During Norm, regional cerebral oxygenation was unchanged from rest to 25% Powerpeak. NIRS signals increased from 25 to 75% Powerpeak (↑Δ[O₂Hb], ↑Δ[HHb], and ↑Δ[THb]), suggesting regional cerebral vasodilation during moderate intensity exercise, yet displayed evidence of decreased oxygenation between 75 and 100% Powerpeak while regional blood volume remained constant (↓Δ[O₂Hb], ↑Δ[HHb], →Δ[THb]; Table 2). During Hypox, regional cerebral oxygenation decreased progressively from the start of exercise to the point of maximal exertion (↓Δ[O₂Hb], ↑Δ[HHb]), whereas regional blood volume again increased, but reached a plateau after 75% Powerpeak. Changes in Δ[O₂Hb] and Δ[HHb] were greater in Hypox compared with Norm at all relative and absolute work rates (Tables 2 and 3).

DISCUSSION

The major finding in this study was that hypoxia profoundly affected the pattern of frontal cerebral cortex oxygenation during incremental exercise. Results demonstrated that incremental exercise to maximal exertion elicited a larger degree of cerebral deoxygenation in hypoxia compared with normoxia. This study was the first to monitor simultaneous changes in cerebral and muscle oxygenation during incremental exercise to maximal exertion under both normoxic and acute hypoxic conditions. We tested the hypothesis that a critical change in cerebral oxygenation would immediately precede voluntary cessation of exercise. Under normoxic conditions, we detected a drop in cerebral, but not muscle, oxygenation during late-stage, high-intensity exercise; however, during acute hypoxia, a similar decrease in cerebral oxygenation was observed during low-intensity exercise, long before the point of exhaustion. Thus we conclude that it is unlikely that frontal cortex oxy-
Cerebral and muscle oxygenation during exercise in normoxia (○) and hypoxia (○). All values are expressed relative to the peak power output achieved in normoxia.

**Technical Considerations**

**Influence of skin blood flow.** Because NIRS probes are typically placed on the skin surface, the relative contribution of skin blood flow to NIRS tissue signals has been questioned (10, 14). The influence of skin blood flow has been estimated to account for ~15 to 23% of NIR light attenuation (31, 49), thus underlying tissues are the primary determinants of resulting NIRS measurements. Owen-Reece et al. (43) and Kirkpatrick et al. (29) demonstrated that occlusion of scalp blood flow does not affect underlying cerebral NIRS measurements when optode distance is sufficient. Since NIR light follows an arc-shaped path through tissues and penetrates to a depth of approximately one-half of the distance between emitter and detector, wider optode spacing decreases the relative contribution from skin. We used an optode distance comparable to that of Owen-Reece et al. (43) to minimize the effect of skin blood flow. Nevertheless, if our $\Delta$[O$_2$Hb] and $\Delta$[THb] measurements were elevated as a result of augmented skin blood flow during exercise, our results would underestimate the relative extent of tissue deoxygenation and not alter our conclusions.

**Reliability of NIRS measurements.** While oxygenation is not homogeneous across skeletal muscle beds (36), we minimized potential errors introduced by probe placement/replacement by measuring and tracing the final location of the probes with an indelible marker. The cerebral NIRS probe was placed ipsilaterally on the forehead, just lateral to the midline. The location and distance between emitter and detector was adjusted for each individual to obtain strong, pulsatile NIRS signals on first placement. Handmade headsets, which held NIRS probes firmly, were customized for each individual to avoid movement artifact during exercise and minimize errors in sequential placements. NIRS measurements were limited to the frontal cortex, yet frontal lobe oxygenation has been associated with global changes in cerebral blood flow (9), metabolic rate (37), and muscle force (44) during hypoxia.

**Table 2. NIRS concentration changes across relative work rates**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Normoxia</th>
<th>Hypoxia</th>
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<tbody>
<tr>
<td></td>
<td>25%</td>
<td>50%</td>
</tr>
<tr>
<td>$\Delta$[O$_2$Hb]</td>
<td>$-1.6\pm0.8$</td>
<td>$1.6\pm1.5$†</td>
</tr>
<tr>
<td>$\Delta$[HHb]</td>
<td>$1.0\pm0.3$</td>
<td>$1.3\pm0.6$</td>
</tr>
<tr>
<td>$\Delta$[THb]</td>
<td>$-0.6\pm0.8$</td>
<td>$2.9\pm1.2$†</td>
</tr>
</tbody>
</table>

Muscle concentrations, $\mu$M

<table>
<thead>
<tr>
<th>Variable</th>
<th>Normoxia</th>
<th>Hypoxia</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>25%</td>
<td>50%</td>
</tr>
<tr>
<td>$\Delta$[O$_2$Hb]</td>
<td>$-10.8\pm2.3$</td>
<td>$-18.4\pm2.8$†</td>
</tr>
<tr>
<td>$\Delta$[HHb]</td>
<td>$9.9\pm2.7$</td>
<td>$23.8\pm2.8$†</td>
</tr>
<tr>
<td>$\Delta$[THb]</td>
<td>$-0.9\pm1.9$</td>
<td>$5.4\pm1.6$†</td>
</tr>
</tbody>
</table>

Values are micromolar changes from resting conditions (means ± SE); $n = 13$. NIRS, near-infrared spectrometry; O$_2$Hb, oxyhemoglobin; HHb, deoxyhemoglobin; THb, total hemoglobin. Brackets indicate concentration. Different from *normoxia, †25%; ‡50%; §75%; $P < 0.05$. 

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Fig. 1. Near-infrared spectroscopy (NIRS) concentration changes (means ± SE) during incremental exercise in normoxia (○) and hypoxia (○). All values are expressed relative to the peak power output achieved in normoxia.
Table 3. NIRS concentration changes across absolute work rates

<table>
<thead>
<tr>
<th>Variable</th>
<th>Normoxia</th>
<th>Hypoxia</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>100 W</td>
<td>200 W</td>
</tr>
<tr>
<td>Cerebral concentrations, µM</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Δ[O2Hb]</td>
<td>-0.9±0.8</td>
<td>1.3±1.7</td>
</tr>
<tr>
<td>Δ[Hb]</td>
<td>0.7±0.3</td>
<td>1.7±0.6</td>
</tr>
<tr>
<td>Δ[THb]</td>
<td>-0.2±0.7</td>
<td>2.9±1.4</td>
</tr>
<tr>
<td>Muscle concentrations, µM</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Δ[O2Hb]</td>
<td>-12.8±3.2</td>
<td>-20.2±2.5†</td>
</tr>
<tr>
<td>Δ[Hb]</td>
<td>11.5±2.3</td>
<td>25.7±2.9†</td>
</tr>
<tr>
<td>Δ[THb]</td>
<td>-1.3±1.9</td>
<td>5.5±1.7†</td>
</tr>
</tbody>
</table>

Values are micromolar changes from resting conditions (means ± SE); n = 13. Different from *normoxia, †100 W (P < 0.01).

Our test retest validation of NIRS changes during normoxic exercise trials shows a high degree of reliability for changes in tissue oxygenation across all work rates (ICC range: 0.97–0.99). These findings are in agreement with those of Kishi et al. (30) and Kolb et al. (33), who reported 8–9.4% day-to-day variation in NIRS measurements of cerebral oxygenation.

Cerebral Oxygenation During Incremental Exercise

We observed that regional cerebral oxygenation and blood volume were maintained during low-intensity exercise up to 25% Powerpeak and increased between 25 and 75% Powerpeak (Δ[O2Hb], Δ[Hb], and Δ[THb]). These findings are in agreement with the theory that cerebral perfusion increases to maintain oxygen delivery during submaximal exercise (24–26, 32, 39). At higher exercise intensities (75 to 100% Powerpeak), cerebral oxygenation fell in all subjects. Specifically, from 75 to 100% Powerpeak, a progressive decrease in Δ[O2Hb] and reciprocal increase in Δ[Hb] was observed while Δ[THb] remained unchanged. These results are in accord with others who reported decreased cerebral oxygenation during maximal (40) and supramaximal (47) exercise protocols. Such high exercise intensities are associated with hyperventilation-induced reductions in arterial CO2 tension, which results in cerebral vasoconstriction and diminished cerebral blood flow (25, 40). Gonzalez-Alonso et al. (19) suggested that the fall in cerebral oxygenation near exhaustion during constant work rate tests is due to a small decrease in cerebral blood flow paired with a relatively larger increase in cerebral O2 uptake. Our data support a similar conclusion for incremental exercise tests. Near maximal exercise intensity, the rate of change in cerebral blood volume was reduced (from Δ[THb] to Δ[THb]), whereas the rate of oxygen extraction was accelerated (Δ[O2Hb] and Δ[Hb]).

Does Cerebral Oxygenation Limit Incremental Exercise Performance?

We questioned whether the observed drop in cerebral oxygenation near maximal exercise intensity in normoxia triggered the cessation of exercise. To test this hypothesis, we compared the patterns of change in cerebral oxygenation obtained during normoxia and acute hypoxia. We hypothesized that a similar drop in cerebral oxygenation would be observed at a lower work rate during acute hypoxia and would also immediately precede the termination of exercise.

The decrease in cerebral oxygenation from the start of exercise to 25% Powerpeak in hypoxia was similar to that seen near maximal exercise intensity in normoxia. If our hypotheses were correct, subjects would have stopped exercising in hypoxia at only ~25% of their actual Powerpeak. In reality, subjects continued to perform at progressively higher work rates in the face of continual reductions in cerebral oxygenation. The extent of deoxygenation (Δ[O2Hb], Δ[Hb]) was, therefore, greater in hypoxia throughout exercise, despite minimal changes in regional blood volume (Δ[THb]) at comparable work rates.

These findings demonstrate a large tolerance for change in cerebral oxygenation during exercise and refute the thought that smaller changes seen during normoxia limited performance. Our results do not discount the possibility that cerebral oxygenation is an important variable in the integrative decision to stop exercise or that such large changes in cerebral oxygenation may limit exercise performance in hypoxia (1, 25, 44). Further tests with more severe hypoxia or that rapidly alter cerebral oxygenation but maintain systemic normoxia are necessary to test this hypothesis. Additionally, investigations with chronic exposures to hypoxia are necessary to determine the effect of acclimatization on cerebral oxygenation during exercise.

Muscle Oxygenation During Incremental Exercise

Vastus lateralis oxygenation decreased linearly up to 75% Powerpeak, despite increased regional blood volume (Δ[O2Hb], Δ[Hb], and Δ[THb]). At higher exercise intensities, the rate of deoxygenation decreased as all values reached plateaus above 90% Powerpeak. While some authors have reported that a rightward shift (Bohr effect) in the oxyhemoglobin dissociation curve accelerates the rate of deoxygenation at or near lactate or ventilatory thresholds (3, 21, 36), our results appeared more linear at these exercise intensities. NIRS measurements have been correlated with changes in intracellular oxygen tension (50) and venous oxygen saturation (18, 53), thus plateaus in oxygenation have been interpreted as evidence of maximal oxygen extraction (18, 48, 53), in accordance with the theory that diffusion rate of oxygen across myocyte membranes is limited at exercise intensities >50% Powerpeak (45). Since NIRS cannot distinguish between hemo- and myoglobin, we cannot make specific claims about the rate of oxygen transfer between blood and muscle. We contend that plateaus in oxygenation observed in the present study simply imply a balance between overall oxygen delivery and extraction/consumption over progressively higher work rates. Because subjects were able to continue exercising at greater intensities after the appearance of the plateau, it is unlikely that observed levels of tissue deoxygenation were directly responsible for the termination of exercise during normoxic conditions. Our assessment is supported by the findings of Nielsen et al. (40), who showed that supplemental oxygen did not affect the pattern of muscle deoxygenation during exercise despite a significant improvement in performance.
Effect of Acute Hypoxia on Muscle Oxygenation

During hypoxia, patterns of change in muscle oxygenation were similar to normoxia up to 75% Power_peak, but differed thereafter. Further inspection of individual data revealed that only 6 of the 13 subjects demonstrated plateaus in oxygenation near maximal exercise intensity. Cyclists who demonstrated plateaus tended to achieve significantly greater maximal power output during normoxia ($P = 0.06$), but displayed larger reductions in maximal power output between normoxia and hypoxia ($P = 0.04$) than the athletes who continued to deoxygenate throughout exercise. We detected no other physiological differences between groups, but note that these post hoc observations were limited by low statistical power. Thus future studies are warranted to explain individual differences in muscle oxygenation patterns during acute hypoxia and test their association with fatigue.

The extent of tissue deoxygenation during hypoxia was greater at all relative and absolute work rates. These results are similar to those who report larger levels of deoxygenation during constant work rate tests under hypoxic conditions (13, 23, 35) and add support to our claim that tissues maintain their functional ability under a wide range of oxygenation. Our findings are in contrast to those who report minimal changes in tissue oxygenation between normoxic and hypoxic trials at a given absolute work rate (15), potentially highlighting differences in patterns of oxygenation between incremental and constant work rate tests.

In conclusion, the results of this NIRS study demonstrate that incremental exercise performance under normoxic conditions is not likely to be limited by changes in cerebral oxygenation, at least in athletic residents of moderate altitude. However, these findings do not discount potential moderating effects that tissue oxygenation may play in a complex, integrative model of fatigue. Future studies should investigate the effects of varied and more severe levels of hypoxia with innovative methods that independently alter cerebral and muscle oxygenation during exercise to gain further insight into the role that tissue oxygenation may play in fatigue.

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