

Frontal and motor cortex oxygenation during maximal exercise in normoxia and hypoxia

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Subudhi AW, Miramon BR, Granger ME, Roach RC. Frontal and motor cortex oxygenation during maximal exercise in normoxia and hypoxia. *J Appl Physiol* 106: 1153–1158, 2009. First published January 15, 2009; doi:10.1152/jappphysiol.91475.2008.—Reductions in prefrontal oxygenation near maximal exertion may limit exercise performance by impairing executive functions that influence the decision to stop exercising; however, whether deoxygenation also occurs in motor regions that more directly affect central motor drive is unknown. Multichannel near-infrared spectroscopy was used to compare changes in prefrontal, premotor, and motor cortices during exhaustive exercise. Twenty-three subjects performed two sequential, incremental cycle tests (25 W/min ramp) during acute hypoxia [79 Torr inspired P_{O_2} ($P_{I_{O_2}}$)] and normoxia (117 Torr $P_{I_{O_2}}$) in an environmental chamber. Test order was balanced, and subjects were blinded to chamber pressure. In normoxia, bilateral prefrontal oxygenation was maintained during low- and moderate-intensity exercise but dropped $9.0 \pm 10.7\%$ (mean \pm SD, $P < 0.05$) before exhaustion (maximal power = 305 ± 52 W). The pattern and magnitude of deoxygenation were similar in prefrontal, premotor, and motor regions ($R^2 > 0.94$). In hypoxia, prefrontal oxygenation was reduced $11.1 \pm 14.3\%$ at rest ($P < 0.01$) and fell another $26.5 \pm 19.5\%$ ($P < 0.01$) at exhaustion (maximal power = 256 ± 38 W, $P < 0.01$). Correlations between regions were high ($R^2 > 0.61$), but deoxygenation was greater in prefrontal than premotor and motor regions ($P < 0.05$). Prefrontal, premotor, and motor cortex deoxygenation during high-intensity exercise may contribute to an integrative decision to stop exercise. The accelerated rate of cortical deoxygenation in hypoxia may hasten this effect.

altitude; fatigue; near-infrared spectroscopy

REDUCTIONS IN GLOBAL CEREBRAL oxygenation are associated with impairments in central motor drive (1, 17, 22). This effect is poorly understood, and further progress has been limited, because more specific, regional measurements of cerebral blood flow and oxygenation are difficult to obtain during intense exercise. Single-photon emission computed topography and PET studies in conjunction with MRI have shown regional differences in cerebral oxygenation during submaximal exercise (7, 29, 33), yet the temporal resolution of these tools and their intolerance to head motion preclude studies of high-intensity exercise.

Near-infrared spectroscopy (NIRS) allows noninvasive, continuous monitoring of cortical changes in cerebral oxygenation during incremental exercise to maximal exertion. Cerebral NIRS measurements during exhaustive, whole body exercise have been limited to the prefrontal cortex (19). Results have consistently shown that prefrontal oxygenation is maintained or increased slightly during light- to moderate-intensity exercise but decreases near maximal exercise intensity (2, 26, 27,

30). These findings have led to speculation that reductions in prefrontal oxygenation affect executive functions that influence the decision to stop exercising (1, 27). An alternative, yet untested, hypothesis is that deoxygenation occurs across the cortex and, thus, directly affects motor areas that regulate central motor drive.

Acute hypoxic exposure provides a model that stresses oxygen transport systems and amplifies changes in cerebral oxygenation (26). During exercise, prefrontal cortex oxygenation falls precipitously with increasing exercise intensity and, thus, may exert an earlier and larger influence on the drive to continue exercising than under normoxic conditions (1). Although it appears that the degree of hypoxia is associated with the magnitude of change in prefrontal oxygenation (1, 11), such conclusions are limited by inherent errors in baseline measurements resulting from daily variations and inconsistencies in NIRS probe placement between trials. Continuous NIRS recordings spanning normoxic and hypoxic exposures are therefore needed to better quantify differences in oxygenation between conditions.

The intent of the present study was to address the aforementioned shortcomings by use of multichannel NIRS to obtain uninterrupted measurements of cortical oxygenation during sequential incremental exercise tests in normoxic and hypoxic conditions. Specifically, we tested the null hypothesis that patterns and magnitudes of changes would be similar within prefrontal, premotor, and motor cortices.

METHODS

Subjects. After approval from the Colorado Multiple Institutional Review Board, 25 active, healthy volunteers (23 men and 2 women) from the Denver, CO, metropolitan area (elevation 1,650 m) provided written, informed consent to participate in a larger study investigating the etiology of acute mountain sickness. Physical examinations, including blood and urine tests, were conducted to verify general health before participation. All study procedures followed ethical guidelines established by the Declaration of Helsinki.

Study design. Two incremental exercise tests were performed in an environmental chamber under ambient normobaric [normoxic (Norm), 610 Torr barometric pressure (P_B), 118 Torr inspired P_{O_2} ($P_{I_{O_2}}$)] and hypobaric [hypoxic (Hypox), 425 Torr P_B , 79 Torr $P_{I_{O_2}}$] conditions to assess aerobic fitness for the larger study. Both tests were performed during a single chamber session to allow direct comparisons between Norm and Hypox without introduction of error from sensor placement/replacement. Tests were counterbalanced to control for order using a blinding strategy that varied chamber pressure to elicit similar sounds and changes in ear pressure during standardized 15-min ascent and descent periods. After arrival at the target P_B , 15 min were needed to adjust the cycle ergometer (Velotron Dynafit Pro, Racermate,

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Seattle, WA) and equip subjects with instrumental sensors (see below). Resting data were collected for 2 min before a 5-min warm-up at 50 W. Work rate was then incrementally increased using a 25 W/min ramp protocol to exhaustion. Subjects were blinded to elapsed time, power output, pedal revolutions per minute, and all physiological signals. Cool-down exercise was performed at 50 W for 5 min before chamber pressure was adjusted. After 15 min of ascent/descent and 15 min of rest at the second P_B, the protocol was repeated.

Instrumentation. A multichannel NIRS instrument (Oxyton III, Artinis) emitting continuous wavelengths of 780- and 850-nm light was used to monitor changes in oxygenated (O₂Hb), deoxygenated (HHb), and total (THb) cerebral and muscle heme concentrations. Theoretical and performance details of NIRS have been previously reported (26). Concentration changes in O₂Hb and HHb were calculated using the modified Beer-Lambert law and differential pathlength factors of 5.93 for cerebral and 4.95 for muscle tissue (6, 31). THb was calculated as the sum of O₂Hb and HHb.

Subjects were instrumented with one of two probe configurations based on hair color and thickness. For subjects with dark and/or thick hair, which is known to obstruct NIR light, *configuration 1* was used: probes were placed on the forehead over the left prefrontal cortex ($n = 14$). Specifically, three transmitters (Tx), spaced 4 mm apart, were paired with a single receiver (Rx), placed 40–45 mm from the middle Tx, to illuminate cortical regions associated with standard Fp1 EEG electrode placement (12). For control, a second set of probes (3 Tx and 1 Rx) was placed on the right vastus lateralis (~15 cm proximal and 5 cm lateral from the superior border of the patella). The 3 Tx-1 Rx probe configurations allowed for spatially resolved determinations of tissue saturation indexes (TSI = O₂Hb/THb) using previously determined absorption and scattering coefficients (14). For subjects with no hair or thin hair, which allows NIRS access to the scalp, *configuration 2* was used: 1 Tx-1 Rx optode pairs were placed over four separate regions of the head ($n = 11$). Two pairs were placed bilaterally over the left and right prefrontal cortex (Fp1 and Fp2 EEG electrode sites) as described above. The other two Tx were placed 40 mm rostral and caudal to a single Rx placed at EEG site C1 to span left premotor and motor cortices. Off-center placement was necessary to illuminate cortical tissue without interference from the sagittal sinus. If necessary, the Tx-Rx set was moved <5 mm to obtain strong pulsatile O₂Hb signals, defined as a >0.25 μ M systolic-diastolic difference. All probes were held by a flexible, plastic spacer, which was affixed to the skin/scalp with double-sided adhesive tape and attached to a custom-made headset or held in place with elastic bandages to minimize movement artifact and shield ambient light. NIRS signals were recorded throughout the chamber session at 125 Hz and averaged across 5-s windows. Changes in O₂Hb, HHb, and THb (μ M) were expressed relative to the resting condition in Norm.

Transcranial Doppler (TCD) was used to monitor bilateral middle cerebral artery (MCA) blood flow velocity during exercise. The custom-made NIRS headsets were modified to hold 2-MHz Doppler probes (DWL Multi Dop T2) over the left and right temporal windows to insonate the MCAs. All measurements were optimized at penetration depths between 42 and 48 mm by a single, trained investigator. Continuous traces of the maximal velocity envelope were recorded at 125 Hz and processed offline for determination of beat-by-beat mean velocity (MCA V_{mean}). Because of potential inconsistencies in bilateral MCA anatomy and, thus, TCD insonation angle, values recorded during exercise were expressed in absolute terms as well as percent change from rest.

Mixed expired O₂ and CO₂ concentrations from a 3-liter mixing chamber and expired airflow (TrueOne 2400, ParvoMedics, Sandy, UT) were recorded at 200 Hz on a data acquisition system (Powerlab 16/30, ADInstruments, Colorado Springs, CO) that synchronized TCD, end-tidal Po₂ and Pco₂ (O₂Cap, Oxigraf, Mountain View, CA), ECG (Bioamp, ADInstruments), middle finger O₂ saturation from pulse oximetry (SpO₂; model N-595, Nellcor, Pleasanton, CA), and continuous blood pressure (Nexfin HD) traces. Minute ventilation, O₂

uptake ($\dot{V}O_2$), and CO₂ output were calculated offline using the Haldane transformation in 15-s intervals.

Analyses. Continuous data were collapsed to analyze specific time points of interest corresponding to rest and 25, 50, 75, and 100% of maximal power output (W_{max}). Data were analyzed with 2×5 repeated-measures ANOVA to evaluate effects of trial (Norm and Hypox) across work rates (rest and 25%, 50%, 75%, and 100% W_{max}). Changes at absolute work rates of 100, 150, and 200 W were analyzed similarly. Criterion for significance was set at $P < 0.05$. Post hoc, pairwise comparisons were made using Holm's sequential method to control for type I error. Pearson's product-moment analyses were used to evaluate relationships between optode pairs throughout exercise. Values are means \pm SD.

RESULTS

Subjects. Twenty-three subjects (29 ± 8 yr of age, 73.7 ± 10.0 kg body wt, 181.7 ± 8.0 cm) completed both trials. Two subjects (with NIRS *configuration 1*) completed the Norm trial but were excluded from further study because of nausea and/or paresthesia during the subsequent depressurization period. Metabolic and power responses to both conditions were representative of physically fit, age-matched individuals (Table 1). Hypox reduced maximal $\dot{V}O_2$ and W_{max} by $16 \pm 6\%$ and $21 \pm 12\%$, respectively ($P < 0.01$). Order of trials did not affect the difference in maximal $\dot{V}O_2$ ($P = 0.20$) or W_{max} ($P = 0.95$) between conditions, and 8 of 23 subjects were unable to retrospectively identify the order of testing.

Differences in tissue oxygenation during Norm and Hypox. During Norm, resting cerebral TSI ($82.9 \pm 27.9\%$) was maintained up to 75% W_{max} but fell by $9.0 \pm 10.7\%$ thereafter ($P = 0.03$) because of large increases in HHb relative to O₂Hb (Fig. 1). In comparison, muscle TSI ($83.1 \pm 14.8\%$) decreased $17.5 \pm 12.3\%$ as work rate increased ($P < 0.01$; Fig. 2). Resting cerebral TSI ($71.9 \pm 25.9\%$) was lower during Hypox than Norm ($P = 0.01$) and was not influenced by trial order ($P = 0.11$). Cerebral TSI fell throughout exercise, exhibiting $26.5 \pm 19.5\%$ decrease from rest ($P < 0.01$). Larger changes in cerebral TSI during Hypox ($P < 0.01$) resulted from greater reductions in O₂Hb ($P = 0.02$, Norm vs. Hypox). In comparison, muscle TSI was not affected by Hypox at rest but decreased $23.5 \pm 15.7\%$ during exercise ($P = 0.02$, Norm vs. Hypox).

Regional differences in cortical oxygenation during exercise. In Norm, bilateral changes in prefrontal oxygenation (O₂Hb, HHb, and THb) were highly correlated throughout exercise ($R^2 = 0.94$ – 1.00 , $P < 0.01$; Fig. 3), although at 100% W_{max} , prefrontal oxygen delivery (increased O₂Hb and THb) was slightly greater in the right than left prefrontal region ($P < 0.05$). Correlations were also strong between left prefrontal, premotor, and motor regions with respect to HHb and THb ($R^2 = 0.94$ – 1.00 , $P < 0.01$), but not O₂Hb ($R^2 = 0.01$ – 0.55), suggesting slight variations in oxygen delivery, particularly within the motor cortex, where reductions in O₂Hb were inversely correlated with prefrontal regions ($R = -0.43$, $P < 0.01$). These differences were not significant at 100% W_{max} .

Hypox decreased resting cerebral oxygenation ($\Delta O_2Hb = -6.5 \pm 6.2 \mu$ M and $\Delta HHb = 4.1 \pm 3.8 \mu$ M, $P < 0.01$) similarly across regions ($P > 0.50$) without affecting cerebral blood volume ($\Delta THb = -2.4 \pm 9.6 \mu$ M, $P > 0.30$). During exercise, patterns of cerebral oxygenation were well correlated between regions ($R^2 = 0.61$ – 1.00 , $P < 0.01$), yet small

Table 1. Metabolic, respiratory, and cerebral blood flow velocity responses to incremental exercise

Variable	Normoxia					Hypoxia				
	Rest	W_{max}				Rest	W_{max}			
		25%	50%	75%	100%†		25%	50%	75%	100%†
Power, W	0±0	110±15	177±27	240±40	305±52	0±0	99±9	151±19	203±28	256±38*
HR, beats/min	73±13	121±11	142±12	162±12	178±10	82±20	130±16	146±15	161±11	172±10*
O ₂ saturation, %	96±2	94±2	93±2	92±2	90±3	85±4*	76±4	73±5	71±6	70±7*
O ₂ uptake, l/min	0.41±0.10	1.69±0.29	2.24±0.43	2.89±0.57	3.49±0.76	0.45±0.23	1.54±0.31	2.04±0.47	2.35±0.42	2.74±0.60*
CO ₂ output, l/min	0.37±0.10	1.53±0.23	2.26±0.35	3.28±0.53	4.49±0.78	0.39±0.17	1.38±0.31	1.91±0.33	2.61±0.47	3.31±0.71*
Minute ventilation, l/min										
BTPS	15.7±5.1	48.8±8.2	68.6±11.6	101.5±20.6	159.6±32.6	18.6±8.2	53.5±11.9	73.9±15.7	105.9±21.6	151.1±32.9
f, breaths/min	14±5	24±4	28±6	37±8	56±11	16±6	25±6	31±8	41±9	57±14
V _T , liters	1.1±0.4	2.0±0.4	2.4±0.5	2.6±0.5	2.7±0.4	1.1±0.4	2.0±0.5	2.3±0.6	2.5±0.6	2.5±0.7
Minute ventilation/O ₂ uptake	38.1±8.0	28.9±2.7	30.7±3.9	35.0±5.2	46.0±8.2	43.3±12.3*	34.8±4.3	37.0±6.6	45.1±6.2	56.0±9.9*
Minute ventilation/CO ₂ output	41.5±5.0	31.7±2.7	30.1±3.1	30.6±4.0	35.3±5.4	48.2±10.5*	39.0±4.9	38.9±5.2	40.9±5.3	46.0±6.1*
End-tidal PO ₂ , Torr	75.8±10.4	74.2±8.2	77.4±7.1	82.9±6.7	91.7±6.5	47.6±7.2*	46.7±4.2	49.6±4.7	54.7±4.6	60.0±5.2*
End-tidal PCO ₂ , Torr	33.8±4.5	37.5±4.6	38.1±4.5	36.2±5.3	28.7±5.4	29.0±4.9*	30.9±4.3	30.3±4.8	27.8±4.2	23.3±4.1*
MCA V_{mean} , cm/s										
Left	53.8±10.0	62.0±12.6	68.0±15.1	70.3±16.0	65.1±14.6	56.6±11.4	68.9±16.2	75.4±14.8	75.2±15.3	70.4±14.7*
Right	56.2±10.2	65.9±11.3	72.0±14.0	74.4±16.0	69.9±15.5	60.0±11.4	74.0±10.5	79.3±12.9	79.3±14.6	76.7±14.4*
MCA V_{mean} , %change										
Left	0±0	15.4±13.1	26.0±16.1	31.0±20.1	21.2±21.4	0±0	25.9±21.1	33.5±24.7	35.1±24.3	26.9±21.0
Right	0±0	18.2±12.0	28.9±13.6	32.7±17.2	24.8±18.3	0±0	25.9±21.1	34.8±25.0	34.2±22.0	30.4±24.9
Mean BP, %change	0±0	16.1±8.9	25.6±8.9	32.2±10.0	38.1±12.8	0±0	16.1±9.4	22.9±9.7	30.4±12.8	36.8±17.2

Values are means ± SD ($n = 23$). HR, heart rate; f, respiratory rate; MCA V_{mean} , middle cerebral artery mean blood flow velocity; BP, blood pressure. O₂ saturation in the middle finger was measured by pulse oximetry. Repeated-measures ANOVA (2 trials × 5 work rates) were performed on each variable. Post hoc paired t -tests were performed on rest and 100% maximal work rate (W_{max}) values only. * $P < 0.05$ vs. normoxia. †All 100% W_{max} values were different from rest ($P < 0.05$).

differences at 100% W_{max} were noted. Perfusion (increased O₂Hb and THb) was greater in the right than left prefrontal region ($P < 0.01$). Deoxygenation (increased HHb) was greater in the prefrontal cortex than premotor and motor regions ($P < 0.01$).

Changes in cerebral blood flow velocity. Resting MCA V_{mean} was similar between hemispheres and was not affected by acute Hypox (Table 1). Throughout exercise, MCA V_{mean} increased slightly during the early stages of exercise but fell from 75 to 100% W_{max} in Norm and Hypox ($P < 0.05$). Small bilateral differences were not significant ($P > 0.20$).

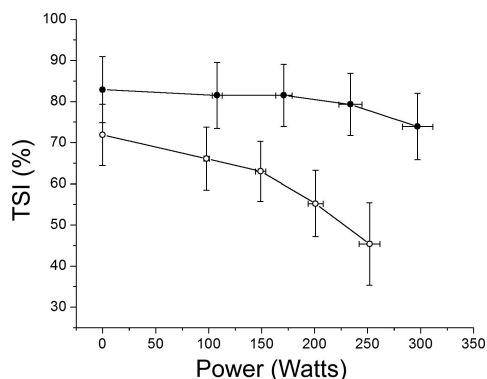


Fig. 1. Cerebral tissue saturation index (TSI) during exercise ($n = 12$). Data points correspond to rest and 25, 50, 75, and 100% maximal power output (W_{max}) in normoxia (Norm, ●) and hypoxia (Hypox, ○). Cerebral TSI is maintained in Norm until 75% W_{max} and declines thereafter ($P < 0.05$). In Hypox, resting TSI is reduced ($P < 0.05$) and continues to fall as exercise intensity increases ($P < 0.01$).

DISCUSSION

The major finding of this study was cerebral deoxygenation at maximal exercise across prefrontal, premotor, and motor cortices. Results support previous findings in prefrontal regions (2, 11, 26, 27, 30), yet they provide new evidence to suggest that deoxygenation within the motor cortex may influence central motor drive during exhaustive aerobic exercise. Acute hypoxia increased the rate and magnitude of cortical deoxygenation and, thus, may have hastened the effect on central motor drive, explaining lower W_{max} .

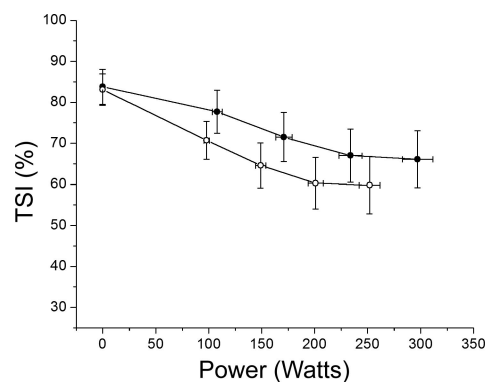


Fig. 2. Muscle TSI during exercise ($n = 12$). Data points correspond to rest and 25, 50, 75, and 100% W_{max} in Norm (●) and Hypox (○). Muscle TSI decreases until 75% W_{max} ($P < 0.05$) and plateaus thereafter. In Hypox, resting TSI is unaffected ($P > 0.75$) and follows a pattern similar to that in Norm during exercise.

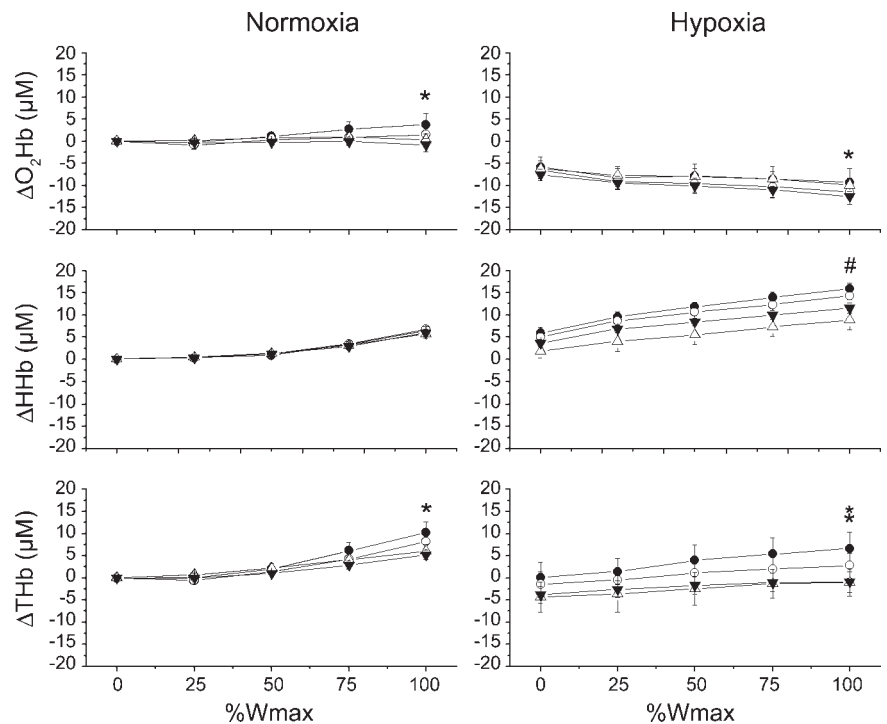


Fig. 3. Regional changes in cerebral oxygenation during incremental exercise ($n = 11$). Continuous recordings obtained across conditions are shown as change from Norm at rest. O_2Hb , oxyhemoglobin; HHb , deoxyhemoglobin; THb , total hemoglobin. Patterns of deoxygenation are similar in right prefrontal (\circ), left prefrontal (\bullet), left premotor (\triangle), and left motor (\blacktriangle) cortices. Extent of deoxygenation is greater in Hypox ($P < 0.05$). Note slight regional differences at 100% W_{max} . * $P < 0.05$, right prefrontal $>$ left prefrontal. # $P < 0.05$, left prefrontal $>$ left premotor and motor.

Regional changes in cortical oxygenation during maximal exercise. Overall patterns of cortical oxygenation during incremental exercise were similar in prefrontal, premotor, and motor regions (Fig. 3). Bilaterally, O_2Hb and THb were greater in the right than left prefrontal region at maximal exercise intensity in Norm and Hypox. These findings seem to suggest greater right-sided vasodilation during exercise, yet given the similarity in bilateral patterns of HHb (Fig. 2), the discrepancy is more likely explained by variation in arterial and venous contributions of illuminated regions. Specifically, because venous contributions account for $>70\%$ of NIRS signals (4), changes in HHb are more representative of regional changes in oxygenation (8). Thus uniform changes in HHb demonstrate widespread cortical deoxygenation during exhaustive aerobic exercise.

It has been suggested that cerebral deoxygenation during high-intensity exercise is caused by hypocapnia-induced vasoconstriction of pial arteries, thereby reducing oxygen delivery (20). This mechanism cannot adequately explain the changes in oxygenation, since cortical blood volume (THb) rises throughout exercise and is poorly correlated with changes in $MCA V_{mean}$ (27). Increased THb near maximal may be the result of parasympathetically mediated cortical vasodilation in response to relative hypoperfusion (13) and/or larger resistance to venous outflow (25).

Regional influence of cerebral oxygenation on performance. We observed a $9.0 \pm 10.7\%$ reduction in prefrontal cortex tissue saturation (increased HHb relative to O_2Hb) before the cessation of exercise in Norm. Since regional blood flow and oxygenation are directly correlated with neuronal activity, the reduction in prefrontal oxygenation may have, at least in part, influenced the ability to maintain motor output. This hypothesis is supported by the fact that prefrontal oxygenation is directly correlated with maximal handgrip strength and is a strong predictor of motor performance (22). Prefrontal function

is mainly responsible for higher-order cognitive functions but may integrate goal-directed behavior, task-related memory, sensory information, and motivation to plan motor movements (15, 21). In this scenario, it is important to stress that prefrontal oxygenation would be only one of many afferent signals influencing complex regulation of motor drive during high-intensity exercise (24).

Our data are the first to show that deoxygenation also occurs in premotor and motor regions during high-intensity aerobic exercise. We therefore raise the possibility that deoxygenation in motor areas may directly impair motor neuron excitability by altering ion channel and/or neurotransmitter function (10). Alternatively, deoxygenation in motor areas may have had a mediating effect on interneurons connected to basal ganglia, which integrate sensory signals and regulate motor drive (9). In either case, data suggest that motor drive may be influenced by multiple regions of cerebral deoxygenation during high-intensity exercise but do not exclude a role for other physiological (e.g., accumulation of muscle metabolites) and psychological states associated with exhaustion.

Effect of acute hypoxia on maximal aerobic performance. Uninterrupted NIRS recordings were obtained throughout each experiment to assess differences between Norm and Hypox without error from probe placement/replacement. Acute Hypox decreased resting cerebral tissue saturation ($-11 \pm 14\%$, $P < 0.01$) in direct proportion with SpO_2 ($-11 \pm 3\%$, $P < 0.01$). This level of cerebral hypoxia was similar to that at maximal intensity in Norm ($P = 0.71$). This new observation supports the argument that normoxic exercise could not have been limited exclusively by cerebral deoxygenation (1, 26, 27); otherwise, subjects would have been unable to begin exercising in Hypox.

During exercise, a faster rate of deoxygenation led to a larger relative (compared with rest) and absolute (compared with Norm) degree of cerebral hypoxia at maximal effort.

Greater deoxygenation in Hypox was primarily caused by reduced availability of oxygen (reduced O₂Hb), resulting from reduced Sp_{O₂}, but was exacerbated by greater oxygen extraction (increased HHb). Severe hypoxia increases the relative influence of cerebral hypoxia on motor drive and perception of effort (1, 22, 23) and, thus, may have hastened the decision to stop exercising, explaining lower W_{max}. Whether the extent of cerebral deoxygenation at maximal intensity in severely hypoxic conditions approaches a critical absolute limit remains to be resolved but could be determined using a similar design if exercise with progressively greater levels of hypoxia is stopped at comparable levels of cerebral oxygenation.

Overall, the increase in cerebral blood volume (THb) during incremental exercise was lower in Hypox. This may reflect diversion of blood from cortical regions to protect deeper structures, such as the basal ganglia and thalamus (3, 5), from severe hypoxia. Although patterns of deoxygenation were similar between prefrontal, premotor, and motor regions, the extent of deoxygenation (HHb) was largest in prefrontal areas ($P < 0.05$). Hypoxic impairment of prefrontal processing (32) may thus have played a more dominant role in the decision to stop exercise during Hypox.

Differences between cerebral and muscle tissue oxygenation: potential for steal? In Norm, cerebral and muscle tissue saturations exhibited varied responses to exercise. Near maximal intensity, reductions in end-tidal PCO₂, MCA V_{mean}, and cerebral oxygenation were concurrent with a plateau in muscle oxygenation (Table 1, Figs. 1 and 2). It is possible that hypocapnia-induced cerebral vasoconstriction allowed for a greater percentage of cardiac output to be diverted toward working muscle, effectively maintaining the balance between leg oxygen delivery and demand from 75 and 100% W_{max}. A similar steal-like mechanism may have also occurred during Hypox, since resting reductions in Sp_{O₂} and cerebral oxygenation were associated with preservation of muscle oxygenation (18). To test a cerebral steal hypothesis, future studies that maintain arterial PCO₂, and thus cerebral blood flow, during high-intensity exercise are needed.

Limitations. The four regions monitored during this study represent a large cross section of cortical tissue. Illuminated volumes spanned areas associated with cognitive and motor performance but were unable to discriminate between specific functional areas that are active during gross motor movements (16, 28). Additional channels of NIRS (Tx-Rx pairs) would permit higher-resolution cortical mapping of neuronal activity during exhaustive exercise. Such functional NIRS (NIRS) assessments would significantly advance our understanding of cerebral contributions to whole body fatigue but are not without limitations.

Penetration depths of NIRS are limited to superficial layers (2–3 mm deep) of the cerebrum, which are sufficient to illuminate cortical gray matter. However, deeper structures associated with motor, respiratory, cardiovascular, and temperature regulation, such as the basal ganglia, brain stem, and cerebellum, remain inaccessible by NIRS. Additionally, NIRS accurately monitors relative changes in O₂Hb and HHb, but mathematical assumptions needed to obtain absolute concentration values (i.e., absorption and scattering coefficients) introduce error in tissue saturation estimates. During pilot work, even slight variance in probe placement was noted to introduce significant discrepancies in cerebral TSI values. This was

likely due to heterogeneity of arterial and venous composition of illuminated volumes, as previously discussed, and accounts for large variance between subjects. In general, TSI measurements were greater than would be expected in mixed venous blood (14). For this reason, we designed the protocol to collect all necessary data from each individual during a single session in which NIRS probes were left in place. We also restricted our interpretations to relative changes in NIRS values across conditions and exercise. We encourage others using NIRS to follow similar precautions in designing and interpreting results to directly address limitations of the technology.

Conclusions. Cortical deoxygenation during high-intensity exercise is not restricted to prefrontal regions of the brain. Deoxygenation in premotor and motor cortices may contribute to fatigue and/or decisions to stop exercising. Acute hypoxia exacerbates cortical deoxygenation and, thus, may hasten these effects. Future functional NIRS studies are needed to expand our understanding of the role of cerebral activity in exhaustive whole body exercise.

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GRANTS

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