Research

Changes in skeletal muscle oxygenation during exercise measured by near-infrared spectroscopy on ascent to altitude

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Abstract

Introduction: We sought to quantify changes in skeletal muscle oxygenation during exercise using near-infrared spectroscopy (NIRS) in healthy volunteers ascending to high altitude.

Methods: Using NIRS, skeletal muscle tissue oxygen saturation (StO₂) was measured in the vastus lateralis of 24 subjects. Measurements were performed at sea level (SL; 75 m), at 3,500 m, on arrival at 5,300 m (5,300 m-a; days 15 to 17) and at 5,300 m again (5,300 m-b; days 69 to 71). Amongst the subjects, nine remained at 5,300 m whilst 14 climbed to a maximum of 8,848 m. Exercise was 3 minutes of unloaded cycling followed by an incremental ramp protocol to exhaustion. The absolute StO₂ at different stages of exercise along with the difference between StO₂ at stages and the rate of change in StO₂ were compared between altitudes. Resting peripheral oxygen saturation was recorded.

Results: NIRS data achieving predefined quality criteria were available for 18 subjects at 75 m, 16 subjects at 3,500 m, 16 subjects on arrival at 5,300 m and 16 subjects on departure from 5,300 m. At SL, mean StO₂ declined from 74.4% at rest to 36.4% after maximal oxygen consumption (P <0.0001) and then rose to 82.3% (P <0.0001) 60 seconds after exercise had ceased. At 3,500 m-a and 5,300 m-b, the pattern was similar to SL but absolute values were approximately 15% lower at all stages. At 5,300 m-a, the resting StO₂ was similar to SL and the change in StO₂ at each exercise stage less marked. At 5,300 m-b, the rate of decline in StO₂ during exercise was more rapid than SL (P = 0.008); here the climbers had a smaller decline in StO₂ during exercise (41.0%) and a slower rate of desaturation (0.08%/second) than those who had remained at 5,300 m (62.9% and 0.127%/second) (P = 0.031 and P = 0.047, respectively).

Conclusion: In most individuals, NIRS can be used to measure exercising skeletal muscle oxygenation in the field. During exercise the patterns of absolute oxygenation are broadly similar at altitude and SL. Following prolonged adaptation to altitude, the rate of muscle desaturation is more rapid than observed at SL but less so in those exposed to extreme hypoxia above 5,300 m.

Introduction

Interindividual tolerance to chronic hypoxaemia is highly varied and may determine survival in the clinical context. Specific mechanisms to explain this heterogeneous response to a sustained reduction in systemic oxygen availability remain unclear. Ascent to high altitude has been suggested as a paradigm for studying human responses to hypoxia in order to probe specific adaptive mechanisms pertinent to critical illness [1]. In combination with exercise, this can provide an effective method of manipulating the balance between oxygen supply and utilisation. In skeletal muscle this equilibrium of tissue oxygen metabolism governs exercise capacity, whilst amongst other organs it is one of the primary determinants of organ function.

The signal from near-infrared spectroscopy (NIRS) can be used to estimate skeletal muscle microcirculatory oxygenation, and principally reflects the venous haemoglobin oxygen status [2,3]. Skeletal muscle oxygenation decreases during exercise and the magnitude of this response is dependent on exercise intensity [4-6]. This desaturation occurs despite an increase in systemic oxygen flux, local vasodilatation leading to enhanced regional blood flow, and increased tissue oxygen extraction. The sustained reduction in exercise capacity, measured by maximal oxygen consumption (VO₂ max), at high altitude is a highly reproducible phenomenon despite adequate acclimatisation [7-10]. The precise mechanism of this persistent decline in exercise capacity remains unclear, but changes in oxygenation of the peripheral circulation detectable by NIRS may help elucidate the phenomenon and further our understanding of the adaptive mechanisms to chronic hypoxaemia in the clinical environment.

ΔStO₂ = difference in tissue oxygen saturation between stage means; NIRS = near-infrared spectroscopy; SL = sea level; SpO₂ = peripheral oxygen saturation; StO₂ = tissue oxygen saturation; StO₂ rate = rate of change in tissue oxygen saturation; VO₂ max = maximal oxygen consumption.
We hypothesised that, when measured at altitude, absolute values of skeletal muscle tissue oxygen saturation ($\text{StO}_2$) measured by NIRS would be lower than those at sea level (SL) both whilst resting and during exercise. We also hypothesised that the difference in $\text{StO}_2$ from rest to maximal exercise would remain unchanged and the rate of desaturation would increase at altitude. We therefore sought to quantify the change in muscle oxygenation using NIRS during exercise on ascent to high altitude.

**Methods**

**Subject selection**

Ethical approval for the present study was obtained from the University College London Committee on the Ethics of Non-NHS Human Research, and all participants gave written informed consent. The subjects were 24 healthy volunteers trekking to the base camp of Mount Everest (5,300 m) in spring 2007; six females and 18 males with a mean age of 35.2 years. This group consisted of two predetermined cohorts. All shared an identical ascent profile to 5,300 m; climbers ($n = 14$) then ascended from 5,300 m to various altitudes, reaching a maximum elevation of 8,848 m, whilst the base-camp team ($n = 10$) remained at 5,300 m for the duration of the study.

**Study settings**

Baseline measurements of exercising skeletal muscle $\text{StO}_2$ were performed at SL (75 m) before departure to high altitude. Further measurements were taken at 3,500 m (days 4 to 6 of the expedition), on arrival at 5,300 m (5,300 m-a; days 15 to 17) and before departure from 5,300 m (5,300 m-b; days 69 to 71). Excessive exercise at altitude has been associated with an increased risk of acute mountain sickness [11]. Any subject suffering symptoms of acute mountain sickness at altitude was therefore not studied. Other exclusion criteria for cardiopulmonary exercise testing were based on the American Thoracic Society/American College of Chest Physicians guidelines for clinical exercise testing [12]; all subjects with an absolute or relative contraindication as defined by these guidelines were excluded from exercise.

**Measurement of skeletal muscle oxygenation**

Measurements were made using the InSpectra™ Tissue Spectrometer (Model 325; Hutchinson Technology Inc., Hutchinson, MN, USA) incorporating a 15 mm probe. The spectrometer calculates $\text{StO}_2$ by applying algorithms to the NIRS signal reflected from tissue below the probe:

$$\text{StO}_2 = \frac{(\text{Oxygenated haemoglobin concentration})}{\text{Total haemoglobin concentration}} \times 100$$

The spectrometer was connected to a laptop computer for the storage of data during exercise. The NIRS probe was placed on the skin of the dominant thigh over the lower third of the vastus lateralis muscle, 10 cm proximal to the knee joint. Once a signal had been confirmed on the spectrometer, the probe was attached firmly with Elastoplast tape. Measurements from the spectrometer were recorded during the predetermined exercise protocol and 60 seconds into the rest period that followed exercise. The InSpectra™ Tissue Spectrometer recorded $\text{StO}_2$ every 3 seconds during standard data collection, and a time-point marker was entered into the computer software to ensure synchronisation of exercise and $\text{StO}_2$ data.

**Exercise protocol**

The subjects performed an incremental ramp test to the limit of tolerance using an electromagnetically braked cycle ergometer (Lode Corival; Lode, Groningen, the Netherlands) and a breath-by-breath cardiopulmonary exercise testing system (Metamax 3b; Cortex, Leipzig, Germany). A full calibration of the breath-by-breath system was performed before each test. Prior to the incremental exercise test, subjects warmed up with a low-intensity 30-minute constant work rate protocol. A ramp slope of 20 to 35 W/minute was chosen depending on the sex, age and physical fitness of the subjects in order to obtain a test duration of approximately 10 to 15 minutes [13]. The ramp slope was kept constant for all subjects throughout the study. Resting measurements were recorded for 3 minutes, followed by 3 minutes of unloaded cycling (ULC) and then the incremental ramped exercise protocol.

**Measurement of peripheral oxygen saturation**

Resting peripheral oxygen saturation ($\text{SpO}_2$) was measured using a pulse oximeter (Onyx 9500; Nonin, Plymouth, MN, USA) on the subject’s right index finger.

**Analysis plan**

$\text{VO}_2_{\text{max}}$ was calculated as the average oxygen consumption for the individual breaths taken in the final 20 seconds of the exercise test. The time for $\text{VO}_2_{\text{max}}$ reported was the middle time point of the 20-second time interval. Data were plotted on graphs of $\text{StO}_2$ versus time and were visually assessed for quality and completeness. A number of NIRS plots were rejected from analysis on the grounds that there was little or no change in signal from rest throughout the exercise protocol. These plots represented nonphysiological data, and other authors have adopted a similar quality control technique [14].

The resting $\text{StO}_2$ was calculated as the average of readings during a 30-second rest period before the exercise protocol started. Individual subject $\text{StO}_2$ at each principle stage of the exercise protocol (end of 3 minutes ULC, $\text{VO}_2_{\text{max}}$ and 60 seconds after cessation of exercise) was calculated as the average of three recordings (spanning 9 seconds) around the designated time of occurrence. The mean (confidence interval) of these $\text{StO}_2$ values is reported for each altitude along with differences between stage means ($\Delta\text{StO}_2$). The rate of change in $\text{StO}_2$ ($\text{StO}_2_{\text{rate}}$) between the end of ULC and $\text{VO}_2_{\text{max}}$ was calculated by dividing the difference in $\text{StO}_2$ between stages by the time taken between stages.
Two-tailed paired t tests were used to assess the affect of altitude on StO₂, ΔStO₂ and StO₂ rate. Comparison between groups containing different individuals was by unpaired t test. Correlation between the rate of decline in StO₂ and SpO₂ was by Pearson’s product-moment coefficient, and that between StO₂ and nonparametric data was with Spearman’s rank correlation coefficient. \( P < 0.05 \) was taken to indicate statistical significance in all instances.

**Results**

**Data collection and quality control**

Data collection was incomplete due to a combination of technical difficulties and subjects failing to fulfill the inclusion criteria for exercise testing at altitude. All of the 24 subjects completed the exercise protocol at SL; missing the exercise protocol due to illness were two subjects at 3,500 m, one subject at 5,300 m-a and two subjects at 5,300 m-b. NIRS data were missing due to technical failure for four subjects at SL, for two subjects at 3,500 m, for three subjects at 5,300 m-a and for three subjects at 5,300 m-b. Three subjects (all female) were completely removed from the analysis as part of the quality control screening. NIRS data meeting the predefined quality criteria were available for 18 subjects at SL, for 16 subjects at 3,500 m, for 16 subjects on arrival at 5,300 m and for 16 subjects on departure from 5,300 m. Only six subjects had complete data at each altitude time point, and their individual data can be seen in Figure 1. The data presented are all of the available data at each altitude time point.

**Changes in absolute tissue oxygen saturation during exercise**

The mean StO₂ at rest, at the end of ULC, at VO₂ max and 60 seconds after VO₂ max are presented in Table 1 for each altitude along with the mean weight and resting SpO₂. At SL, the mean StO₂ increased by 6.7% during ULC, from a resting value of 74.4% (68.6 to 80.1) to 81.1% (73.8 to 88.3) \( (P = 0.001) \). The mean StO₂ progressively declined during the incremental workload protocol to a nadir of 36.4% (28.5 to 44.3) at VO₂ max \( (P < 0.0001) \), and then rose rapidly to a level above resting StO₂ (82.3% (76.2 to 88.5); \( P < 0.0001) \).
60 seconds after exercise had ceased. At altitude the incremental exercise protocol resulted in a reproducible pattern of muscle desaturation. Figure 2 shows this pattern of change in mean StO2 at SL and during ascent to altitude. At 3,500 m and 5,300 m-b, the pattern was identical to SL but absolute values were approximately 15% lower at all stages of the exercise protocol. At 5,300 m-a, the resting StO2 was only 4.2% below that observed at SL (not significant) and the pattern of change was considerably flatter than other altitudes, such that the mean StO2 at VO2 max was 16.1% higher than at SL ($P = 0.043$). Figures 3 and 4 show typical NIRS plots (change in StO2 during exercise vs. time) from the same subject at SL and at 5,300 m-b, respectively.

At 5,300 m-b there were no differences in the absolute StO2 values at any stage of exercise between climbers and the base-camp team, although climbers had a significantly higher SpO2 (86.6% vs. 79.2%, respectively; $P = 0.005$).

**Tissue oxygen saturation differences between exercise stages**

The differences between mean StO2 values at different stages of exercise at SL and at altitude are presented in Table 2. There was no difference in ΔStO2 between rest and VO2 max or between ULC and VO2 max at any altitude except 5,300 m-a, where the difference between rest and VO2 max was 17.5%, compared with 38.0% at SL ($P = 0.018$).

At 5,300 m-b there was a significant difference in the ΔStO2 value between climbers and the base-camp team from ULC to VO2 max; the base-camp team had a desaturation rate of 0.127%/second, compared with only 0.086%/second in the climbers ($P = 0.047$).

Subjects were numerically ranked at each altitude based on their rate of StO2 decline from the end of ULC to VO2 max.

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**Table 1**

| Weight, SpO2 and StO2 during the exercise protocol at different altitude time points |
|---------------------------------|-----------------|-----------------|-----------------|-----------------|
| Altitude                        | Sea level       | 3,500 m         | 5,300 m-a       | 5,300 m-b       |
| Number of subjects              | 18              | 16              | 16              | 16              |
| Weight (kg)                     | 79.1 (72.7 to 85.5) | 78.1 (71.2 to 85.1) | 78.3* (71.9 to 84.6) | 73.3* (69.0 to 77.6) |
| Resting SpO2 (%)                | 97.7 (97.2 to 98.2) | 88.5* (86.8 to 90.2) | 81.8* (79.8 to 82.8) | 84.3* (81.4 to 87.2) |
| Resting StO2 (%)                | 74.4 (68.6 to 80.1) | 58.4* (53.0 to 63.7) | 70.2 (62.3 to 78.0) | 57.5* (49.8 to 65.1) |
| StO2 3-minute ULC (%)           | 81.1† (73.8 to 88.3) | 65.5† (58.2 to 72.8) | 80.3† (73.3 to 87.4) | 69.7†† (63.4 to 76.0) |
| StO2 VO2 max (%)                | 36.4† (28.5 to 44.3) | 24.8† (19.9 to 29.7) | 52.5†† (41.7 to 63.3) | 21.9† (12.0 to 31.7) |
| StO2 60 seconds post-exercise (%) | 82.3† (76.2 to 88.5) | 64.3† (59.4 to 69.2) | 69.8† (63.4 to 76.2) | 63.1†† (54.8 to 71.4) |

Data are presented as mean (95% confidence interval). SpO2, peripheral oxygen saturation; StO2, tissue oxygen saturation; ULC, unloaded cycling; VO2 max, maximal oxygen consumption. *Significantly different from sea level. †Significantly different from the previous exercise stage.

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**Figure 2**

Tissue oxygen saturation at specific stages of the work protocol. Mean tissue oxygen saturation (StO2) at specific stages of the work protocol at sea level and different altitude time points. 5300(a), on arrival at 5,300 m (days 15 to 17); 5300(b), before departure from 5,300 m (days 69 to 71); Rest, resting; ULC, after 3 minutes of unloaded cycling; VO2 max, at maximal oxygen consumption; Rec, 60 seconds after exercise has ceased.
Rankings were compared at each altitude by Spearman’s rank correlation coefficient. There was a significant correlation between the subject rank order at SL when compared with 3,500 m (correlation coefficient = 0.780, \( P = 0.002 \)), compared with 5,300 m-a (correlation coefficient = 0.688, \( P = 0.007 \)) and compared with 5,300 m-b (correlation coefficient = 0.41, \( P = 0.041 \)).

Relationship between tissue oxygen saturation and peripheral oxygen saturation
There was no correlation between the resting \( \text{SpO}_2 \) and the resting \( \text{StO}_2 \) at any altitude. There was a correlation, however, between resting \( \text{SpO}_2 \) and \( \text{StO}_2 \) at \( \text{Vo}_2 \text{max} \) at 5,300 m-b (\( r = 0.557, P = 0.019 \)). At 5,300 m-b there was also a negative correlation between the resting \( \text{SpO}_2 \) and
Figures 3 and 4 show typical examples of the change in StO2
exercise, rapidly recovered to a level above the resting value.

On arrival at higher altitude (5,300 m-a),
exercise workload increased. StO2 reached a plateau shortly
before VO2 max was achieved, and then, following cessation of
exercise, rapidly recovered to a level above the resting value.

Discussion
Summary of findings
The present study demonstrated in selected individuals that
NIRS could be used to measure skeletal muscle StO2 in the
vastus lateralis during exhaustive exercise and to generate
reproducible results in the hypoxic environment encountered
at high altitude. Three minutes of unloaded exercise at SL led
to a small rise in StO2 that progressively declined as the
exercise workload increased. StO2 reached a plateau shortly
before VO2 max was achieved, and then, following cessation of
exercise, rapidly recovered to a level above the resting value.

Figures 3 and 4 show typical examples of the change in StO2
during unloaded and loaded exercise at different altitudes. At
3,500 m, the absolute changes in StO2 were similar to those
at SL but values were approximately 15% lower at rest and
throughout exercise. On arrival at higher altitude (5,300 m-a),
the resting StO2 was similar to that at SL and the changes
during exercise (ΔStO2 values) were considerably less
marked than those observed at SL, giving the appearance of
a flattened pattern of StO2 (Figures 1 and 2). By the end of
the expedition (5,300 m-b), days 69 to 71 at altitude, the
pattern was similar to that observed at SL and at 3,500 m
(that is, ΔStO2 unchanged) except that the time-related
decline in StO2 (StO2 rate) during exercise was significantly
more rapid than that at SL (P = 0.008).

At altitude, the maximum exercise capacity was reduced –
leading to a reduction in VO2 max as has been previously
documented [7-10,15] – and the decline in VO2 max was
proportional to elevation.

Study limitations
There were marked interindividual differences in absolute
StO2 values at rest and during exercise (Table 1). One
reason for these differences is related to the fact that near-
infrared light emitted by and received by the spectrometer
probe has an unknown pathlength, and therefore the absolute
StO2 cannot be calculated [16]. Furthermore, significant
heterogeneity in oxygenation has been demonstrated both
within and between specific muscles so probe placement on
the thigh is important and may have a significant effect upon
results [17-19]. StO2 is therefore a value that is specific to
the tissue beneath an individual probe. As a result of this,
comparison of absolute StO2 values between individuals is of
limited value. The relative changes in StO2 as a result of
specific stimuli (ΔStO2), and the rate of change in the
response (StO2 rate), however, may provide valuable insight
into the dynamics of oxygen supply and demand in a subject.

The depth of tissue beneath the spectrometer probe that
near-infrared light can penetrate is directly related to the
distance between the illumination and detection fibres
(optodes) of the device. The banana-shaped light beam has a
maximum depth of penetration was approximately
7.5 mm. For some individuals this may not represent muscle
tissue oxygenation but overlying adipose tissue or skin. This
factor may further increase the interindividual variation in the
NIRS signal. Most of the NIRS plots that were rejected as a
result of minimal change in oxygenation throughout exercise
were from females; this has been previously noted as a
substantial confounding factor during skeletal muscle NIRS
studies [21]. Other authors also report needing to remove
subjects from the final analysis as a result of poor signal
response due to excessive subcutaneous adipose tissue
[14]. Validated objective criteria for rejection of
nonphysiological NIRS data do not exist. Subjective removal
of data may therefore confound results; however, data
removal was performed without the knowledge of the subject
or altitude identification.

As the NIRS light beam must pass through skin during both
emission and reflection, skin blood flow and oxygenation will
contribute to the overall NIRS signal [22,23]. Ambient
laboratory temperature may therefore have exerted an effect
on results by inducing vasoconstriction within the skin at low
temperature. All studies were performed in purpose-built
insulated temporary laboratories where the average
temperature throughout the 3-month expedition was 24.1°C
at SL, 19.6°C at 3,500 m and 21.5°C at 5,300 m. Diurnal
temperature variation may have resulted in temperatures
considerably lower than these mean values for those tests
performed early in the morning at altitude. The preliminary
warm-up exercise protocol, however, should have provided
sufficient stimulus to negate the effect of cold-induced
vasoconstriction.

Interpretation of results
Although a rarely regarded tissue in the critically ill patient,
early reduction in skeletal muscle StO2 detected by NIRS has
been shown to herald poor outcome by identifying patients at
risk of infectious complications or multiple organ failure [24].
Rather than a quantitative measurement of tissue oxygena-
tion, however, the StO2 value derived from a NIRS signal
reflects the localised equilibrium of oxygen delivery and
utilisation [25] and closely follows regional venous oxygena-
tion [14,26]. Furthermore, correlation between changes in the
continuous-wave NIRS signal and that of 31P magnetic
resonance spectroscopy [25] and of 1H nuclear magnetic
resonance [27] suggests that NIRS can be used effectively in
the evaluation of localised muscle oxidation. As a measure of
oxygen saturation, StO2 could be regarded as a surrogate
marker for tissue oxygen content, therefore indicating crude
alterations in tissue oxygen extraction. Previous work has
demonstrated that acute exposure to hypoxia results in a
greater degree of skeletal muscle deoxygenation during exercise when compared with normoxia [28].

The change in absolute StO₂ observed in the present study at SL has been previously reported by other authors at SL; typically, there is an initial increase in oxygenation followed by a decline until the minimum plateau value at VO₂ max [4,14,29]. The commonly observed plateau of StO₂ shortly before VO₂ max at SL (Figure 3) tended not to be as prominent at 5,300 m-b (Figure 4), although this was difficult to quantify. The significance of this plateau has been suggested as representing the limit of tissue oxygen extraction [14,28]. The relationship between maximal oxygen extraction and VO₂ max may therefore be altered after prolonged exposure to hypoxia and requires more detailed investigation. Similar values for ΔStO₂ at SL, 3,500 m and 5,300 m-b suggest that the overall balance between oxygen delivery and utilisation at these altitude time points were similar. Oxygen delivery exceeded utilisation during ULC, resulting in an increase in StO₂ – but as the work rate increased the situation was reversed, until the peri-VO₂ max plateau when oxygen extraction was maximal and exhaustion was imminent.

The relatively high resting StO₂ and reduced ΔStO₂ between rest and VO₂ max observed at 5,300 m-a (Figures 1 and 2) is not in keeping with the findings at 3,500 m and 5,300 m-b. Identical equipment, protocols and investigators were used on arrival at and departure from 5,300 m, so technical failure or inaccuracy seems unlikely. Limited ability to extract oxygen could account for the reduced ΔStO₂ value; however, the reason for this on arrival at 5,300 m is unclear. One hypothesis is that the small gain in weight observed from 3,500 m to 5,300 m may represent a degree of tissue oedema that could increase oxygen diffusion limitation in muscle tissue. The usual response of ascent to altitude is generally weight loss [30]; the gain in weight observed, or certainly the lack of loss, could therefore be tissue fluid accumulation, frequently observed in those affected detrimentally by high altitude [31].

The rate of decline in StO₂ during loaded exercise (end of ULC to VO₂ max), as presented in Table 3, is significantly more rapid at 5,300 m-b than at SL. This more rapid rate of decline was not seen on arrival at the same altitude 50 days previous to the departure measurements despite the small rise in mean SpO₂ at 5,300 m-b (P=0.002). Weight loss at altitude results in a greater proportion of lean tissue mass than fat mass [30], which leads to a reduction in the skeletal muscle fibre cross-sectional area [32]. In the group investigated in the present study, mean weight loss during the expedition was 5.8 kg in 72 days (P<0.001).

At 5,300 m-b, those subjects with a lower resting SpO₂ showed a more rapid rate of StO₂ desaturation during exercise. One explanation for this could be that individuals with a low SpO₂ at rest had reduced systemic oxygen availability due either to a blunted hypoxic ventilatory response or to an increased arterial–alveolar oxygen partial pressure difference. Following acclimatisation to high altitude, however, cardiac output remains unchanged from SL values for a given work load throughout exercise [9,33], and the arterial oxygen content remains above SL values [34,35] even at maximal exercise [36]. This implies that systemic oxygen delivery remains similar to that experienced at SL under conditions similar to those experienced by the subjects in this study. More distal mechanisms in the oxygen cascade – such as alterations in regional and/or microcirculatory blood flow, changes in the affinity of oxygen to haemoglobin or diffusion limitation within skeletal muscle tissue – may therefore be responsible for the observed findings.

At the end of the expedition (5,300 m-b) the base-camp team who remained at 5,300 m after ascent were found to have a significantly greater ΔStO₂ and StO₂ rate of decline during exercise than the climbers who ascended above 5,300 m. In the climbing cohort, the exposure to severe hypoxia at altitudes up to 8,848 m is likely to have induced a greater rise in haemoglobin than the base-camp team, thus increasing arterial oxygen content and preventing such a precipitous fall in skeletal muscle oxygenation during exercise. Alternatively, exposure to such hypoxic conditions may trigger a process of hypoxic preconditioning that affords a degree of protection following descent to lower heights.

In the clinical setting, abnormal heterogeneous blood flow in the sublingual microcirculation of critically ill patients [37-39] may account for the imbalance between oxygen delivery and consumption in this pathological state [40]. Reduced sublingual microcirculatory blood flow has been observed in climbers ascending to high altitude [41]. If abnormal blood flow also exists in skeletal muscle microvasculature, one could postulate that it may lead to a reduction in tissue oxygen delivery and hence in StO₂.

**Conclusion**

NIRS is a useful tool for studying thigh skeletal muscle oxygenation during exercise but is limited by the depth of beam penetration in some individuals. The pattern of absolute change in exercising muscle StO₂ on exposure to altitude is similar to that at SL and, despite the reduction in exercise capacity, demonstrates a similar reduction in StO₂ from rest to maximal exertion. The rate of desaturation is more rapid after prolonged exposure to altitude (69 to 71 days), and at this altitude time point a lower resting SpO₂ was associated with a more rapid rate of StO₂ decline during exercise. Exposure to extreme hypoxia above 5,300 m appears to have a protective effect in reducing the degree of muscle desaturation during exercise on return to 5,300 m.

These findings suggest that mechanisms within the peripheral circulation or tissues govern local tissue oxygen flux and utilisation. Alterations at the distal portion of the oxygen cascade may be an important component of adaptation or maladaptation to chronic hypoxia secondary to high altitude.
exposure and disease. The heterogeneity of individual responses to chronic hypoxia may therefore be explained by changes in the peripheral circulation rather than the systemic circulation in both scenarios.

Competing interests
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