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The effect of acute hypoxia on local muscle oxygenation during and following submaximal lower and upper body exercise

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Abstract

Background: The effect of hypoxia on VO_{2max} and peak power is attenuated when less muscle mass is involved. Near infrared spectroscopy (NIRS) has been extensively used to investigate local differences in muscle oxygenation during exercise. Muscle oxygenation is reduced in the lower body during exercise in hypoxia, but the effect of hypoxia on muscle oxygenation during upper body exercise is not well known. **Aim:** To investigate the effects of acute hypoxia on local muscle oxygenation during and after submaximal upper and lower body exercise. **Methods:** Nine actively competing male rowers and one cross-country skier (n=10) completed a total of four submaximal exercise protocols at 70% of MAP using a leg-cycle ergometer and an arm-crank ergometer during normoxia and hypoxia: normoxic leg-cycling, hypoxic leg-cycling, normoxic arm-cranking and hypoxic arm-cranking. Local muscle SmO_2 and mVO_2-recovery in the vastus lateralis and biceps brachii were measured, as well as whole body cardiopulmonary variables, lactate, and RPE. **Results:** Hypoxia does not affect SmO_2, tHb, VO_2 or heart rate differently during upper and lower body exercise, but the lactate and ventilation response was more pronounced during leg-cycling than arm-cranking. The post-exercise mVO_2 recovery time constant increased in hypoxia during arm-cranking, but not leg-cycling. **Conclusion:** Exercise intensity was in the anaerobic domain, and too high for significant differences in aerobic metabolism to occur. The effect of hypoxia and exercise mode on the recovery time constant is uncertain due to issues using standardized data analysis. Further research is needed to investigate the effect of hypoxia on local muscle oxygenation during and after aerobic submaximal upper and lower body exercise.

Oppsummering

Bakgrunn: Hypoksi påvirker VO_{2max} og kraftutvikling mindre når mindre muskelmasse er involvert. Nær-infrarød spektroskopi (NIRS) har blitt mye brukt til å undersøke lokale forskjeller i muskulær oksygenmetning under fysisk aktivitet. Hypoksi fører til redusert oksygenmetning i muskelen ved underkroppstrening, men det mangler kunnskap om effekten på oksygenmetning under overkroppstrening. **Mål:** Å undersøke effekten av akutt hypoksi på muskulær oksygenmetning i under- og over-kropp under og etter submaksimal trening. **Metode:** Ni roere og en langrennsløper (N=10) som var aktive utøvere fullførte fire forskjellige submaksimale treningsprotokoller på 70% av maksimal aerob kraft med bein-sykkel og arm-sykkel i normoksi og hypoksi: normoksi bein-sykling, hypoksi bein-sykling, normoksi arm-sykling og hypoksi arm-sykling. Vi målte lokal muskulær oksygenmetning og mVO_2 i vastus lateralis og biceps brachii, samt kardiopulmonære variabler, laktat og RPE. **Resultater:** Hypoksi påvirker ikke SmO_2, tHb, VO_2 eller HR forskjellig i over- og under-kropps-trening, men laktat og ventilasjon økte mer i under-kropps-trening enn over-kropps-trening. Det tok lenger tid å gjenopprette hvile-mVO_2 etter endt aktivitet i overkroppstrening, men ikke underkroppstrening, i hypoksi. **Konklusjon:** Intensiteten var for høy til at signifikante endringer i aerob metabolisme kunne forekomme. Effekten av hypoksi og treningsmodus på Tc er usikker på grunn av problemer med standardisert data-analyse. Mer forskning trengs for å undersøke effekten av akutt hypoksi på lokal muskulær oksygenmetning i under- og over-kropp under og etter submaksimal trening.

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Contents

1. Introduction

Hypoxia, defined as a reduction in the availability of oxygen to tissue, has a profound effect on the physiology of the human body. Hypoxia impairs cardiovascular performance due to reduced oxygen availability caused by a lowered partial pressure of O_2 (1), which leads to an increase in cardiac output at rest and during exercise to compensate for the lowered availability of oxygen (1). The impact of hypoxia on aerobic performance measured as VO_{2max} is relatively linear. The lower the fraction of O_2 in inspired air, the lower the VO_{2max} (2, 3). Well-trained individuals usually experience larger drops in VO_{2max} in hypoxia compared to untrained individuals, likely related to the increase in aerobic metabolism associated with endurance training adaptations (4-7).

The most common form of hypoxia is hypobaric or low-pressure hypoxia, which occurs at higher altitudes where the decreased atmospheric pressure reduces the amount of oxygen molecules present per liter of air. Another form of hypoxia is normobaric or normal pressure hypoxia, where inert gases are added to air to simulate the reduced oxygen content per liter of air of hypobaric hypoxia. Hypoxia can also be divided into acute and chronic hypoxia. Acute exposure to hypoxic conditions at rest causes initial severe hyperventilation, stabilizing to ventilation levels slightly above normoxic conditions after approximately 25-30 minutes (8). Acclimatization performed during exercise can shorten the time required for ventilation to stabilize (9) and is often used in an experimental setting to prevent confounding due to the pulmonary system not being in a steady state. Chronic hypoxia causes cardiovascular adaptations over a period of weeks, but these do not fully compensate for the reduced cardiovascular performance (1).

The effects of hypoxia on different forms of exercise is not uniform. As mentioned earlier, hypoxia has a negative effect on performance in most aerobic sports, whereas performance in many anaerobic sports actually improves during hypobaric hypoxia due to the reduction in drag caused by reduced air pressure and not being impeded by reduced oxygen availability (1). In aerobic sports, the effect of acute hypoxia seems to be related to the amount of muscle mass recruited, with an attenuated effect as the amount of recruited muscle mass is reduced. More practically, this means that exercises that primarily involve the upper body are affected less by hypoxia than exercises that primarily involve the lower body, usually reflected by a less pronounced drop in peak power and VO_{2max} (10, 11). As most studies investigating these differences have only looked at systemic parameters such as power output and whole body

VO_2, little is known about local differences in the upper and lower body during hypoxic exercise. This is due to the difficulty of obtaining localized oxygen consumption measurements during exercise since many of the methods used to investigate muscle tissue *in vivo*, such as muscle biopsies or magnetic resonance spectroscopy, are either invasive, expensive, time-consuming or not usable during exercise.

Near Infrared Spectroscopy (NIRS) is a relatively recent development in research, with small, portable sensors allowing accurate, non-invasive measurements of local changes in tissue oxygenation during exercise. NIRS has been used extensively to investigate local muscle oxygenation and oxygen metabolism at rest and during exercise in both healthy and diseased individuals (12, 13). More relevant to this thesis, it has been used to investigate the effect of hypoxia on lower body deoxygenation during exercise, and it was found that the intensity of the exercise protocol, rather than the type of exercise performed, was important (14-19). In both studies using knee extension protocols (14, 15) and studies using ergometer cycling protocols (16-19), significant differences in deoxygenation between normoxic and hypoxic conditions have been found as long as the intensity was sufficiently high.

Another important variable to consider is the distinction between absolute and relative intensities when comparing hypoxic and normoxic conditions. Due to the reduced VO_2 and peak power in hypoxia, comparing absolute intensities is confounded by being dissimilar metabolically, which can lead to aerobic intensities in normoxic conditions being anaerobic in hypoxic conditions. Conversely, while metabolic intensity is similar when comparing relative intensities, the actual work produced is dissimilar, which could confound the effect of hypoxia on exercise kinetics. However, both intensity modes show significantly increased deoxygenation in hypoxia if the intensity is high enough, with the effect size being bigger when comparing absolute intensities (14, 15, 17-19). Most studies that used NIRS to investigate the effects of hypoxic conditions have investigated the effects on the lower body. In normoxic conditions at the same absolute intensity, upper body deoxygenation tends to be greater than lower body deoxygenation, with a similar rate of decline (20).

To our knowledge only one study has investigated the effect of hypoxic conditions on upper body muscle oxygenation. Jensen-Urstad, Hallback & Sahlin (21) found that submaximal arm exercise at 54% of normoxic VO_{2peak} caused a transient increase in deoxygenation in both hypoxia and normoxia, as well as an estimated 14% increase in blood flow during steady state in the hypoxic condition compared to normoxia.

An increased muscle blood flow measured using Doppler ultrasound was found during low intensity lower body exercise in the hypoxic condition (22, 23). This might indicate that increased blood flow, rather than increased deoxygenation, could be a coping mechanism during low intensity hypoxic exercise. During high intensity lower body exercise, hypoxia reduces aerobic performance, and causes increased muscle deoxygenation in the leg muscles. During upper body exercise, the effect of hypoxia on aerobic performance is less pronounced, while no studies have investigated the effects on muscle oxygenation in the arm muscles during high intensity upper body exercise.

The upper and lower body show different responses to hypoxic conditions during aerobic exercise. In addition, there is a lack of knowledge about these responses locally in muscle tissue. Therefore, the aim of this study was to investigate the effects of acute hypoxia on muscle oxygenation during and following upper and lower body submaximal exercise.

2. Methods and materials

2.1 Participants

Eleven healthy actively competing male participants from the NTNUI rowing (N=10) and cross-country skiing (N=1) clubs volunteered and gave their written, informed consent (Appendix 1) to participate in this study. The study was approved by the regional medical ethical committee. Self-reported exercise amounts and information about competition frequency were collected using a questionnaire (Appendix 2).

2.2 Study design and experimental protocol

Participants were instructed to abstain from exercise and alcohol 24 hours before, caffeine or nicotine 6 hours before, and to not eat a large meal at least 3 hours before the experimental testing. Prior to testing, height was measured, and weight and body composition were recorded by bioelectrical impedance analysis (BIA). Following the pre-test, all participants completed a total of eight tests over four days. Day one consisted of a vascular occlusion technique (VOT) test followed by two leg-cycling exercise (LCE) tests. The first LCE test was a step incremental lactate profile test (LPT), which was followed by a step incremental test to exhaustion. The third test was done on a separate day and consisted of a step incremental arm-cranking exercise (ACE) test to exhaustion. These tests were used to determine exercise-specific maximal aerobic power (MAP) and VO_{2peak}. The submaximal tests were performed under normoxia (N, FiO_2 = 20.9%) and hypoxia (H, FiO_2 15.0%). Combined with the two exercise modes, this resulted in a total of four submaximal tests: LCE-N, LCE-H, ACE-N and ACE-H, performed on two separate days with a minimum of 24 hours between each day. Each day consisted of one LCE test and one ACE test, with the order and condition of the tests randomized.

2.2.1 Vascular occlusion technique test (VOT-test)

Prior to the VOT-test, an inflatable cuff was placed around the leg and the upper arm on the right side of the body. The test started with a three-minute baseline measurement, followed by a one-minute arterial occlusion (AO) for familiarization purposes. After three minutes of recovery, a ten-minute AO was applied, followed by five minutes of recovery. The participants were instructed to refrain from any movements during the occlusion. This occlusion was then used to calculate resting muscle oxygen consumption (mVO_2). Cardiovascular and NIRS variables were continuously measured during the VOT-test.

2.2.2 Incremental tests

Prior to the LPT subjects performed 10 minutes of low intensity warm-up, which was used to estimate the starting intensity. After two minutes of rest, The LPT, which consisted of 25 W · 4min^{-1} steps with 30 second breaks during which lactate was measured, started. The intensity where lactate concentration exceeded 4 mmol · l^{-1} (OBLA) was defined as the lactate threshold (LT), and the test was stopped. Following a 5-minute break, participants performed a 25 W · min^{-1} step incremental test to exhaustion starting at a work rate one step below the final step of the LPT. During both LCE tests, participants were instructed to stay at or above 90 RPM. Prior to the ACE step incremental test participants performed a 10-minute warmup at 50 watts. The ergometer required calibration twice due to heat affecting the friction break, once before the warm-up, and once before the VO_{2peak} test. The initial power of the step incremental test was set to 50 W, with 10 W · min^{-1} steps until exhaustion. Participants were instructed to stay at or above 70 RPM during the test (24, 25). During the incremental tests whole body VO_2 and cardiovascular variables were continuously measured, and lactate and RPE were measured at the end of every test.

2.2.3 Constant power tests

As shown in Figure 1, each submaximal test protocol consisted of a total of three work periods, a warmup period (WU), an acclimatization period (AC) designed to rapidly acclimatize subjects to the hypoxic condition (9), and a submaximal exercise period (SUB). The measurement started with a ten-second AO applied at rest. WU and AC consisted of ten and five minutes of exercise at 30% of MAP respectively, separated by a two-minute break, while the SUB period consisted of 5 minutes of exercise at 70% MAP separated from AC by a one-minute break. For the hypoxic condition tests, subjects were administered a hypoxic gas mixture (15% FiO_2) during AC and SUB by continuously feeding a Douglas bag compressed gas from a cylinder containing hypoxic gas. Immediately following SUB, seven ten-second AOs were applied. Occlusions 2-4 had 20 second pauses, while occlusions 5-8 had 50 second pauses. During the ACE tests the ergometer was calibrated twice, once before WU and once before SUB. During the constant power exercise tests, whole body VO_2, cardiovascular and NIRS variables were continuously measured, and lactate and RPE was measured at the end of every test.

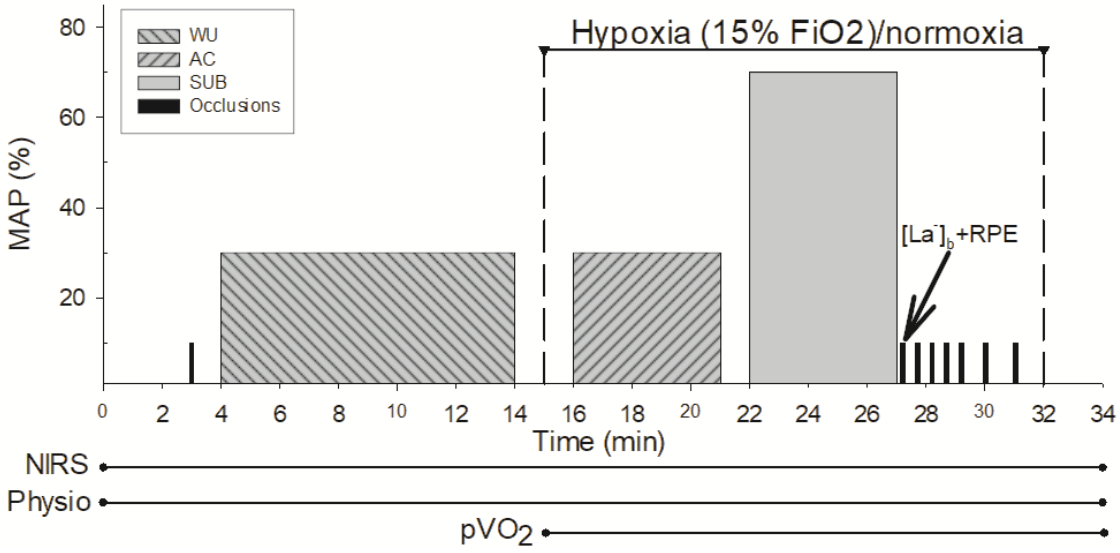

Figure 1. Schematic of the submaximal exercise protocol. MAP = maximal aerobic power, WU1 = Warmup period, AC = acclimatization period, SUB = submaximal period, FiO_2 = fraction of inspired oxygen, $[La^-]_b$ = blood lactate concentration, RPE = rate of perceived exertion.

2.3 Measurements

Bioelectrical impedance measurements were performed using the InBody 720 (Biospace, Seoul, Korea) following manufacturer instructions. Leg-cycling was done on an electronically braked cycle ergometer (Velotron, Racermate Inc, Washington, USA), while arm-cranking was done using a custom-designed ergometer with a friction break (Computrainer, Racermate Inc, Washington, USA). Cadence and work rate was measured continuously during both exercise modes. Lactate was measured using blood samples taken from the fingertips (Lactate Pro LT-1730, Arkray, Kyoto, Japan). The rate of perceived exertion was measured using the modified Borg scale (26). The MAP for both exercise modes was defined as the work rate of the last whole step completed during the exercise-specific incremental test.

Whole body gas exchange was measured using open circuit spirometry with a mixing chamber (Oxycon Pro, Jaeger GmbH, Höchberg, Germany). The system was calibrated using a gas of known concentration (Riessner-Gase GmbH, Lichtenfels, Germany) and a 3-liter syringe (Hans Rudolph Inc., Kansas City, MO, USA). Inspired air was not measured, and VO_2 + VCO_2 values were calculated using the Haldane transformation for accurate gas exchange measurements during the hypoxic and normoxic exercise periods (27). To check the accuracy of the calculated data, we compared the calculated normoxic test data to the

Jaeger values from the same tests. First expired ventilation (V_E, $l \cdot min^{-1}$) at standard temperature pressure and dry (STPD) was calculated using equation 1:

$$V_E\,(STPD) = V_E\,(BTPS) \cdot \frac{273}{273+T} \cdot \frac{(P_b - PH_2O)}{760} \quad (1)$$

Where V_E (BTPS) is expired ventilation at body temperature and pressure saturated at 100% humidity, T is temperature of gas (assumed to be 37°), P_b is the barometric pressure (mmHg), and PH_2O is the partial pressure of water at T (assumed to be 47.08 mmHg). Inspired ventilation (V_I, $l \cdot min^{-1}$) was then estimated using equation 2:

$$V_I = V_E\ (STPD) \cdot \frac{1-(FeO_2 + FeCO_2)}{1-(FiO_2 + FiCO_2)} \quad (2)$$

Where FeO_2, $FeCO_2$, FiO_2 and $FiCO_2$ are the fractions of expired and inspired O_2 and CO_2, respectively. This formula uses the assumption that nitrogen is equal in inspired and expired air to calculate the ratio of expired to inspired nitrogen, which can then be used to calculate V_I. V_I and V_E are then used to calculate VO_2 using equation 3, and VCO_2 using equation 4.

$$VO_2 = (V_I \cdot FiO_2) - (V_E \cdot FeO_2) \quad (3)$$

$$VCO_2 = (V_I \cdot FiCO_2) - (V_E \cdot FeCO_2) \quad (4)$$

The exercise specific VO_{2peak} was defined as the highest 30 second value reached during the maximal test, while the mean over the last 2 minutes of the submaximal tests was used for comparison purposes for all pulmonary variables. The simplified V-slope method was used to estimate the gas exchange threshold (GET) during the incremental ACE test (28, 29). The V-slope method was not used to estimate the GET in LCE due to the test protocol not fulfilling the intensity criteria required for accurate GET estimations.

Heart rate was measured using signal-morphology impedance cardiology (PhysioFlow Lab1, Manatec Biomedical, Macheren, France), which allows for continuous noninvasive measurements of cardiovascular variables. A total of 6 electrodes (Bluesensor R, Ambu, Denmark) were placed on the torso and neck according to manufacturer instructions and connected to the PhysioFlow device. Blood pressure, required for calculation of cardiovascular variables, was measured using an automatic blood pressure monitor (OSZ 5 easy, Welch Allyn, Jungingen, Germany). Heart rate (HR) and stroke volume (SV) are calculated through the R-R interval and changes in thoracic impedance, respectively (30). These values can then be used to calculate cardiac output. Data were initially sampled at 1

Hz, but this was later lowered to 0.2 Hz due to issues with data loss at rest, and all 1 Hz data was decimated to 0.2 Hz during analysis. The mean over the last two minutes of the submaximal tests was used for comparison purposes for HR. All test protocols included three minutes of baseline measurements and five minutes of recovery measurements, before the first and after the last occlusion or exercise period in the protocol, respectively.

2.3.1 Near infrared spectroscopy (NIRS)

In vivo oxygenation and saturation changes in local tissue were measured using a continuous-wave near-infrared spectrophotometer (Portamon, Artinis Medical Systems, Netherlands). This is possible due to oxyhemoglobin and oxymyoglobin (O_2Hb) absorbing different amounts of light at different wavelengths of light in the near-infrared spectrum compared to deoxyhemoglobin and deoxymyoglobin (HHb). In the present study the wavelengths used were 844 ± 3 nm and 762 ± 1 nm. As it is not possible to differentiate between hemoglobin and myoglobin signals using NIRS, all concentration changes will be reported as hemoglobin changes for the rest of this thesis for simplicity. Using the changes in optical density of reflected light at the different wavelengths, concentration changes in hemoglobin can be calculated using a modified Lambert-Beer law (31). Saturation changes were measured using spatially resolved spectroscopy (SRS), which uses the photon diffusion theory (32) to measure absolute values of hemoglobin. To allow for accurate measurements, the amount of water in tissue is assumed to be constant and corrected for. SmO_2 can then be estimated using the following formula (33):

$$SmO_2(\%) = \left(\frac{O_2Hb^{abs}}{(O_2Hb^{abs} + HHb^{abs})}\right) \cdot 100 \qquad (5)$$

Prior to each measurement, NIRS devices (Oxymon, Artinis Medical Systems, Netherlands) were placed on top of the muscle bellies of the vastus lateralis (VL) and biceps brachii (BB) muscles. The devices were covered with an opaque black cloth to ensure no external light sources interfered with the signals. The device consisted of one receiver and three transmitters, with interoptode distances of 30mm, 35mm and 40mm. The frequency of sampling was 10 Hz. Occlusions were applied by connecting pneumatic cuffs (Hokanson SC12L, Marcom Medical ApS, Denmark) to an automatic inflation system (Hokanson E20 Rapid Cuff, Marcom Medical ApS, Denmark) applying 300mmHg pressure using an external air source. A skinfold caliper (Holtain, Crymych, UK) was used to determine adipose tissue thickness (ATT) by measuring skinfold thickness underneath the NIRS optodes. To ensure

identical placement of the NIRS devices over several days, the placement was marked with a pen and photographed after the first measurement. The raw NIRS data during exercise was filtered using an 8th-order 0.5 Hz low-pass Butterworth filter to reduce movement artifacts. Delta changes in muscle oxygen saturation (ΔSmO_2) and tHb during exercise were calculated using a 30 second baseline at the start of each measurement. Oxygen consumption from AOs were calculated using the initial linear decrease in HBdiff (O_2Hb-HHb) after the start of an occlusion. To calculate mVO_2, concentration changes $\mu M \cdot s^{-1}$ were converted to $ml O_2 \cdot min^{-1} \cdot 100g^{-1}$ using the following formula (34):

$$mVO_2 = Abs\left(\left(\frac{\left[\frac{Hbdiff}{2}\right]Hb \cdot 60}{10} \cdot MD\right) \cdot O_2R\right) \cdot O_2M \,/\, 1000 \qquad (6)$$

Muscle density (MD) is assumed to be 1.04 $kg \cdot l^{-1}$, the O_2 molar value (O_2M) 22.4 L, and the O_2 to Hb ratio (O_2R) 4. MVO_2-values that were clearly affected by movement artifacts were excluded from subsequent analyses. Figure 2a shows an example occlusion that was included for further analysis, while Figure 2b shows an occlusion excluded due to movement artifacts. Figure 3c gives an example of a curve fit where the first occlusion had to be removed due to movement artifacts. If the two first occlusions had to be removed, the entire test was excluded from subsequent analysis. A 63% recovery time constant was then calculated by fitting the mVO_2 recovery values to a mono-exponential curve (35, 36), with an R-square (R^2) value indicating the fit of the curve.

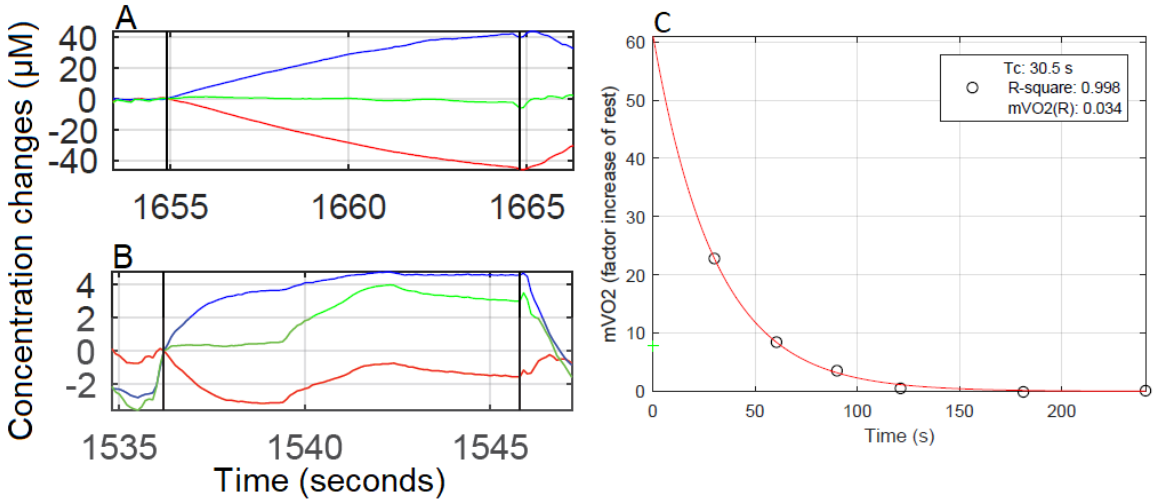

Figure 2. Example good (A) and bad (B) post-exercise occlusions, as well as an example curve fit during hypoxic leg-cycling (C). in (A) and B) red=O_2Hb, blue=HHb, green=tHb, while in (C) the green cross represents an excluded mVO_2-value, Tc = the 63% time constant, R-square indicates the fit of the curve, and mVO_2(R) = resting mVO_2.

2.4 Statistical analysis

All data were checked for normality using a Shapiro-Wilk test, and tested using two-way repeated measures ANOVA (RMANOVA) or paired samples t-tests if parametric, or an equivalent non-parametric test if non-parametric. A one-way RMANOVA was used to test whether incremental test VO_2, MAP and end-exercise lactate differed between exercise mode (2 levels, LCE and ACE), while RPE was tested using a signed rank Wilcoxon test. A two-way RMANOVA was used to test whether submaximal VO_2, ventilation and RPE differed between exercise mode (2 levels, LCE and ACE) and condition (2 levels, normoxia and hypoxia). A Friedman test was used to test for an effect of exercise mode and condition on submaximal lactate and HR. A two-way RMANOVA was used to test whether the difference between hypoxia and normoxia for SmO_2 and tHb (ΔSmO_2-diff and ΔtHb-diff) differed between exercise mode (2 levels, LCE and ACE) and time (11 levels, baseline and every 30 seconds until end of exercise). The Friedman test was used to investigate the effect of exercise mode and condition on time constants. A paired samples t-test was used to check for differences between VL and BB ATT, and the correlation between ATT and resting mVO_2 was tested using either a Pearson's correlation or spearman's rho depending on linearity assessed by a scatterplot. The Greenhouse-Geisser correction was used if the assumption of sphericity was violated. In the case of significant main or interaction effects during the RMANOVA analysis of NIRS-variables, repeated within-subject contrasts with the Bonferroni correction were used to investigate where these differences were located. If the Friedman test was significant, a related samples Wilcoxon Signed Rank test was used to explore the differences. Parametrically tested results are presented as mean±SD, non-parametrically as median±SD. and statistical significance was set to $P<0.05$. Data analysis was performed using Matlab R2017b (MathWorks Inc. Natic, USA), Excel 2016 (Microsoft Inc, Redmond, WA, USA) and SPSS 25 (SPSS, Chicago, USA), while Sigmaplot 14 (Systat Software Inc, USA) was used to create figures.

3. Results

3.1 Descriptives

In total, 10 participants completed all tests. The mean (± SD) age, weight, height and body fat were 23 ± 2 years, 88.3 ± 12.7 kg 185.9 ± 8.1 cm, 9.9 ± 2.2%, respectively. The participants reported 10.3 ± 4.6 hours of exercise per week participated in 6.9 ± 7.9 competitions per year and had been competing for 4 ± 5.1 years. The ATT was 4.9 ± 1.1 mm for the VL and 2.6 ± 1.2 mm for the BB, with a significant mean difference of 2.4 ± 1.2 mm ($p < 0.001$). Four subjects were excluded in the mVO_2-analysis due to poor data quality.

3.2 Pulmonary variables

The Haldane transformation was used to calculate VO_2, and the average values for normoxia were in good agreement with the jaeger values at 99.97 ± 0.10%, 99.1 ± 0.12%, 99.93 ± 0.09, 99.79 ± 0.34% of the Jaeger-provided values for the LCE incremental test, ACE incremental test, LCE-N test and ACE-N test, respectively. The reported accuracy range of the Jaeger Oxycon Pro is 3%, which means that that the calculated differences were still well within the Oxycon pro accuracy range.

3.3 Incremental test results

Table 1 shows that all variables but RPE were significantly higher during LCE than ACE. The mean ACE VO_{2peak} was 72.7 ± 5.4% of the LCE VO_{2peak}.

Table 1: Group mean ± SD values for incremental LCE and ACE test results.

Exercise mode	LCE	ACE	Difference	Significance
VO_{2peak} ($ml \cdot kg^{-1} \cdot min^{-1}$)	59.2 ± 4.5	43 ± 3.8	16.2 ± 3.7*	p < 0.001
AT (%VO_{2peak})	80.7 ± 7.4	51.6 ± 8.3	29 ± 12.7*	p < 0.001
MAP (W)	432 ± 57	177 ± 30	255 ± 37*	p < 0.001
$[La^-]_b$ ($mmol \cdot l^{-1}$)	15.4 ± 3.1	13.3 ± 2.1	2.1 ± 2.8*	p = 0.038
RPE[A]	18.5 ± 1.0	17.8 ± 1.2	1.0 ± 1.6	Z = -1.64, p = 0.101

*LCE = leg cycle ergometer, ACE = arm crank ergometer, Difference = difference between exercise modes, AT = anaerobic threshold (LT for LCE, GET for ACE), MAP = maximal aerobic power, $[La^-]_b$= blood lactate concentration, RPE = rate of perceived exertion. * = significant difference between exercise modes, [A] = presented as median.*

3.4 Submaximal work rate and cardiopulmonary variables

There were no differences between normoxic and hypoxic work rates for either exercise mode (Table 2). A two-way RMANOVA was used to analyze VO_2, ventilation, and RPE, while Friedman and Wilcoxon Signed Rank tests were used for HR and lactate. There was a main effect of condition on end-exercise VO_2 (3.9 $ml \cdot kg^{-1} \cdot min^{-1}$ lower in H), indicating

that VO_2 was reduced in hypoxia despite the similar work rates ($F(1,9) = 27.71$, $p = 0.001$). There was no interaction effect between exercise mode and condition ($F(1,9) = 1.09$, $p = 0.325$), indicating that the effect of hypoxia on VO_2 was similar for both exercise modes (Table 2). End-exercise ventilation was higher in hypoxia for both exercise modes (Table 2), with a significant main effect ($F(1,9) = 83.31$, $p < 0.001$). There was also a significant interaction between mode and condition, indicating that hypoxia caused a larger ventilatory response during LCE than during ACE ($F(1,9) = 14.89$, $p = 0.004$), as can be seen in Table 2.

There was an increased end-exercise HR in hypoxia for both exercise modes, and end-exercise HR was also higher during LCE than ACE (Table 2). A Friedman test showed a significant difference between medians for all HR variables ($X_2(3) = 27.720$, $p < 0.001$). Post-hoc analysis using Wilcoxon tests showed that this was mostly due to differences between the exercise modes, as the effect of hypoxia on HR was not significantly different between LCE and ACE ($Z = -1.07$, $p = 0.285$, Table 2). End-exercise lactate increased in hypoxia for both exercise modes (Table 2), and a Friedman test showed that there was a significant difference between medians for lactate ($X_2(3) = 10.742$, $p = 0.013$). Post-hoc analysis showed that hypoxia caused an increase in end-exercise lactate during both LCE ($Z = -2.8$, $p = 0.05$) and ACE ($Z = -2.6$, $p = 0.011$). Table 2 shows that hypoxia had a larger effect on lactate during LCE than ACE ($Z = -2.5$, $p = 0.012$). Hypoxia did not significantly change end-exercise RPE ($F(1,9) = 4.1$, $p = 0.072$), but a combined interaction between hypoxia and exercise mode ($F(1,9) = 11.4$, $p = 0.008$). can be observed (Table 2), as there was a small increase from LCE-N to LCE-H compared to no change from ACE-N to ACE-H.

Table 2. Group mean ± SD values for the last two minutes of submaximal norm and hyp LCE and ACE, as well as mean differences between conditions.

Mode	**LCE**			**ACE**		
Condition	**Norm.**	**Hyp.**	**Diff.**	**Norm.**	**Hyp.**	**Diff.**
Work rate (W)	297.5 ± 0.0	297.5 ± 0.0	0 ± 0.0	125.8 ± 22.3	125.6 ± 21.9	0.2 ± 1.4
VO_2 (ml · kg^{-1} · min^{-1})	47.3 ± 1.6	42.9 ± 2.3	4.4 ± 2.4	29.6 ± 3.6	26.2 ± 4.5	3.4 ± 3
VO_2 (%peak)	80.7 ± 5.7	73.2 ± 6.6	7.5 ± 4	69.4 ± .7.5	61.0 ± 8.2	8.3 ± 7.8
VE (L · min-1)	94 ± 17	116 ± 14	22 ± 3*	74 ± 17	81 ± 17	7 ± 5*
HR (beats · min-1)^A	162 ± 8	169 ± 8	8 ± 4	145 ± 12	155 ± 13	6 ± 7
[La-]b (mmol · l-1)^A	5.4 ± 1.3	11.4 ± 2.6	6.0 ± 1.8*	5.7 ± 1.5	7.6 ± 3.2	1.3 ± 2.2*
RPE	13 ± 1.8	14.8 ± 1.5	1.6 ± 0.9*	13.1 ± 1.7	12.9 ± 1.7	0.2 ± 1.71*

*LCE = Leg cycle ergometer, ACE = Arm crank ergometer, Norm = Normoxia, Hyp = hypoxia, Diff = difference between conditions, EE = end-exercise, VE = pulmonary ventilation (BTPS), HR = heart rate, [La-]b = blood lactate concentration, RPE = Rate of Perceived Exertion. ^{A} = presented as median. * = significantly different from mean difference of other exercise mode*

3.5 Submaximal near infrared spectroscopy (NIRS) variables

3.5.1 Muscle oxygen saturation (ΔSmO_2)

The group responses for ΔSmO_2 during upper and lower body exercise during normoxia and hypoxia are shown in Figure 3. As can be seen in Figure 3a, during LCE ΔSmO_2 decreased rapidly during the first minute of exercise, then stayed relatively constant in both normoxia and hypoxia. Fig 3b shows that during ACE there was also a rapid decrease in ΔSmO_2 in the first minute, with a tendency for a larger decrease in hypoxia as well as an increasing deviation between normoxia and hypoxia towards the end of the test. Figure 3c shows ΔSmO_2-diff for both exercise modes and was used for statistical analysis. Using a two-way RMANOVA, no significant effect of time (F (2.1, 18.9) = 1.95, p = 0.168), exercise mode (F (1,9) = 0.943, p = 0.357) or combined interaction effect between exercise mode and time (F (2.2, 19.5) = 1.07, p = 0.366) on SmO_2-diff was observed.

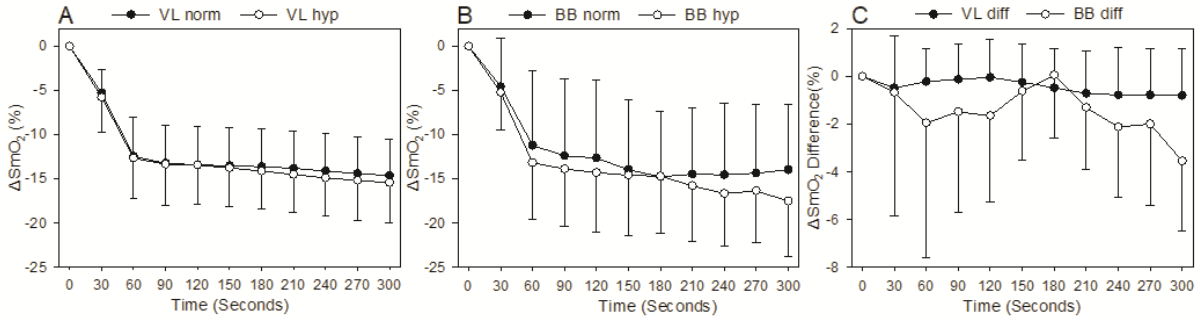

Figure 3. Group mean ± SD ΔSMO_2 changes from baseline for the vastus lateralis (A) and biceps brachii (B) in normoxia and hypoxia, as well as the difference (H-N) between normoxic and hypoxic conditions for both muscles (C).

3.5.2 Total hemoglobin (ΔtHb)

The group responses for tHb during upper and lower body exercise during normoxia and hypoxia are shown in Figure 4. Figure 4a shows that ΔtHb during LCE decreased rapidly at the onset of exercise before staying relatively constant in both hypoxia and normoxia, with a tendency towards increasing in normoxia. ΔtHb during ACE, shown in Figure 4b, decreased rapidly at the onset of exercise with a tendency for a larger reduction in hypoxia, followed by a large increase over time. The differences between exercise modes were larger than those between conditions. Figure 6c shows ΔtHb-diff for both exercise modes and was used for statistical analysis. Using a two-way RMANOVA, no effect of time (F (2.9, 26.2) = 2.17, p = 0.117), exercise mode (F (1,9) = 0.25, p = 0.626), or combined interaction between exercise mode and time (F (2.2, 20.2) = 1.03, p = 0.382) on ΔtHb-diff was observed.

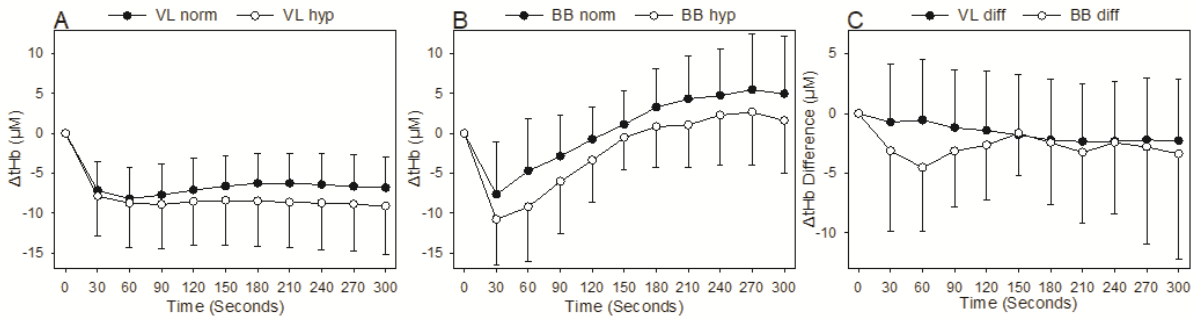

Figure 4. Group mean ± SD ΔtHb changes from baseline for the vastus lateralis (A) and biceps brachii (B) in normoxia and hypoxia, as well as the difference (H-N) between normoxic and hypoxic conditions for both muscles (C).

3.5.3 Muscle oxidative capacity (mVO_2)

Four participants were excluded from the analysis due to movement artifacts during the occlusions. The mean resting mVO_2 values were 0.034 ± 0.005 and 0.071 ± 0.004 ml · min^{-1} · $100g^{-1}$ for the VL and BB respectively and differed significantly between the two muscles ($p < 0.001$). There was a significant correlation found between resting mVO_2 and ATT (r_s (6) = -0.865, $p < 0.001$), using Spearman's rho. Immediately post-exercise, mVO2 in the VL increased by a factor of 18 in N and 12.9 in H (mean difference of 5.1, p = 0.073). BB mVO2 immediately post-exercise increased by a factor of 28.8 in N and 25.6 in H (significant mean difference of 3.2, p = 0.042). Table 3 shows post-exercise time constants, variance and R^2-values. The large variance in LCE-N was due to two outliers who could not be removed due to not fitting our exclusion criteria. A Friedman test showed a significant difference between medians (X^2 (3) = 9.800, p = 0.02). Further analysis using a Wilcoxon test revealed that while Tc was not affected by hypoxia in LCE (Z = -0.105, p = 0.92), there was a significant effect of hypoxia on Tc in ACE (Z = -2.2, p = 0.028).

Table 4. Group median ± SD values, variance and mean R^2 ± SD values for the recovery time constant after submaximal exercise for 6 participants

Test	Time constant (s)	Variance	R^2
LCE-N	30.8 ± 56.5	17.4 – 158.4	0.75 ± 0.36
LCE-H	43.6 ± 7.1	30.5 – 48.5	0.95 ± 0.03
ACE-N	57.7 ± 26.2[1]	22.9 – 95.2	0.90 ± 0.11
ACE-H	71.0 ± 32.6[1]	34.9 – 128.9	0.78 ± 0.13

LCE = Leg-cycling exercise, N = normoxia, H = Hypoxia, ACE = Arm-crank exercise. [1] = significantly different.

4. Discussion

The main findings of this study were that local muscle oxygen saturation and tHb during exercise in hypoxia did not differ significantly between submaximal ACE and LCE at 70% of MAP. The effects of hypoxia on VO_2 and HR were similar in both exercise modes, while the effects of hypoxia on lactate, RPE and ventilation were larger during LCE than ACE. Resting mVO_2 was significantly higher in the BB than the VL, and large differences were found in how hypoxia affected muscle oxidative capacity after exercise between the two exercise modes, with a significantly slower mVO_2 recovery during hypoxia compared to normoxia in ACE, and no significant differences in LCE.

The present study found that in LCE-H compared to LCE-N at the same submaximal intensity, VO_2 was significantly decreased, while VE, heart rate and lactate significantly increased, as expected (1). Due to the reduction in FiO_2, a larger ventilatory exchange and cardiac output is required to transport the same amount of O_2 as during normoxic exercise. The reduction in VO_2 is caused by the reduced aerobic performance in hypoxia, which leads to increased anaerobic energy production and higher lactate due to working at the same absolute intensity with less aerobic energy available. However, contrary to the literature (16-18, 37, 38), we found no significant effects of hypoxia on vastus lateralis SmO_2 during LCE at 70% MAP. A possible reason for this lack of an effect may be the work rate chosen for the submaximal exercise period. In 2012, Spencer et al. reported a breakpoint during ramp incremental exercise after which HHb either plateaus or increases at a slower rate (39). Later studies have found that this breakpoint correlates well with both the maximal lactate steady state (40) and the respiratory compensation point (41-43). In the previously mentioned studies, this breakpoint usually occurred between 76-90% of VO_{2peak}, occurring at a higher $\%VO_{2peak}$ in well trained individuals. In the current study, the mean VO_{2peak} during the last two minutes of exercise was 80.7% for LCE-N and 73.2% for LCE-H (Table 2). Based on this, it seems likely that the intensity chosen for the submaximal exercise period was too high, and at or above the breakpoint at which HHb plateaus. If this was the case, then there would simply be no more O_2 to extract during exercise regardless of the FiO_2 of inspired gas, which could offer an explanation as to why no effect of hypoxia was found on SmO_2 in the vastus lateralis in this study.

Due to the lack of studies investigating ACE, the effects of hypoxia on ACE will mostly be discussed in comparison to the effect of hypoxia on LCE. VO_2 in ACE-H declined similarly to LCE-H, which is in agreement with other studies performed on well trained participants

(11). Lactate in LCE-H nearly doubled compared to normoxia even though the work rates were identical, which clearly illustrates the reduced aerobic performance during lower body exercise in hypoxic conditions. Hypoxia also had a significant, but less pronounced, effect on lactate during ACE. A recent study found that lactate thresholds expressed relative to the FiO_2-specific VO_{2max} do not change due to hypoxia, with the breakpoints simply shifting leftwards compared to normoxia due to the reduction in VO_2 and power output (44). It is also known that peak power declines more in the lower body than in the upper body in hypoxia (11). Based on this and keeping in mind that the absolute work rate was identical for H and N, the differences in end-exercise lactate and ventilatory response to hypoxia between the exercise modes could be explained by the fact that LCE peak power is affected more than ACE peak power by hypoxia, causing the same absolute workload to be higher relative to the hypoxic peak power during LCE than ACE and requiring a larger increase in anaerobic energy production to compensate. This larger increase in anaerobic energy production is then likely to have caused the larger ventilatory response observed during LCE-H compared to ACE-H.

Studies that have compared ACE and LCE GETs calculated using the simplified V-slope method found that they were not significantly different in untrained individuals, with mean values in both exercise modes ranging from 50-53% of VO_{2peak} (45, 46). A study investigating the ACE-GET in well trained individuals found roughly similar mean VO_{2peak} values of 53-55%, but much higher absolute work rates compared to untrained individuals (47). These values are similar to the ACE GET of 51.6 ± 8.3% of VO_{2peak} found in the present study. Comparing the thresholds of the two exercise modes in the present study is not feasible, due to the different methods used to calculate them.

As for the effect of hypoxia on local muscle oxygenation during ACE, Jensen-Urstad et al. (21) investigated the effect of hypoxia on local muscle oxygenation during a 10-minute submaximal upper body exercise period at 54% VO_{2peak} and found that both conditions caused an initial rapid decrease in oxygenation that was partially reversed over time, with the reversal being slower in hypoxia, as well as an estimated 14% higher blood flow in hypoxia. In the present study no reoxygenation occurs (Figure 3b), but there is an increase in tHb over time that could indicate increased blood flow as the exercise progresses (Figure 4b). Due to the large differences in exercise intensity and training status any further comparisons between Jensen-Urstad et al. and the present study are not very feasible.

Resting mVO_2 in the VL and BB were significantly different. However, earlier studies have found that increased ATT is significantly correlated with reduced resting mVO_2 (34), which is reflected in the present study. Even though the mVO_2 recovery constant results could have interesting implications, there are methodological limitations that make the results less reliable. Earlier studies show that post-exercise mVO_2 can be elevated for long periods of time after high intensity exercise (48), which can significantly affect the Tc due to an increase in mVO_2 directly after exercise ends. A closer inspection of the early regressions (data not shown), indicates that this may be due to the standardized data analysis method, where every occlusion was analyzed using a 3 second period for regression starting 0.2 sec after the occlusion. Almost all occlusions immediately post-exercise showed a linear decrease in HBdiff as the occlusion started. However, the duration and magnitude of this initial linear decrease varied greatly, which indicates that a fixed regression period was not the best fit for our data. Adapting the regression for each individual occlusion to more accurately fit the initial linear reduction would likely have improved the curve fits and reduced the variability of the results, but would also have been far more time-intensive. To investigate the effect of the two outliers in LCE-N on the statistical analysis of the post-exercise time constant, a post-hoc RMANOVA was performed with the outliers excluded. Marginal means showed very similar effects of hypoxia on the time constant during both exercise modes (average increased Tc in hypoxia of 16.7s and 16.3s in LCE and ACE, respectively). However, the small sample size (N=4) means that the statistical significance is uncertain, and any conclusions drawn are risky at best. One final point worth considering here is the oxygen extraction reserve proposed by Inglis et al. (43), who found that an occlusion immediately following the end of a ramp incremental protocol allowed for further deoxygenation beyond the HHb plateau, indicating a possible oxygen extraction reserve that is not used during exercise. In general, visual inspections revealed that the first occlusion plateaued faster during hypoxia than normoxia (data not shown), which could indicate an effect of hypoxia on this proposed oxygen extraction reserve that warrants further research.

Another major methodological limitation in the present study was related to PhysioFlow. There was a large amount of data loss towards the end of the submaximal exercise periods, especially during ACE, likely due to excessive shoulder movements causing movement artifacts and data loss in the HR data collected from the neck electrodes.

In the literature, calibrating NIRS-signals using arterial occlusions has been a method used by some authors to reduce the variability caused by measuring different individuals with

different ATTs at differing measurement sites (13). While calibration by arterial occlusion was not performed in the present study, it is possible that doing so might have reduced the large between-subject variability.

4.1 Conclusion

To conclude, the main finding of this study was that local muscle oxygenation and saturation as well as whole body VO_2 and HR responses to exercise in hypoxia did not differ significantly between submaximal upper and lower body exercise, even though the effect of hypoxia on ventilation and lactate was more pronounced during lower body exercise. The amplified hypoxic lactate response during leg-cycling compared to arm-cranking was likely due to the larger effect of hypoxia on peak power and maximal aerobic power during leg-cycling requiring a more pronounced anaerobic contribution to energy metabolism to compensate for the larger reduction in aerobic capacity. The lack of an effect of hypoxia on muscle oxygen saturation in the vastus lateralis during leg-cycling was unexpected, and a possible mechanism is the HHb plateau that usually occurs at work rates close to or above the lactate threshold. While there were significant differences in the time constant, data issues due to using standardized regression periods during analysis makes it difficult to draw any conclusions, and the usefulness of time constants when investigating high intensity submaximal exercise in hypoxia remains to be investigated. More research is needed to investigate differences in local muscle oxygenation during and following upper and lower body exercise at different aerobic intensities in hypoxia.

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Appendix 1. Consent form

Forespørsel om deltakelse i forskningsprosjektet

" Effekten av simulert høyde på muskulært oksygenforbruk i under- og over-kropps-trening"

Vi søker etter friske mannlige deltakere i alderen 18-40 år som er aktive roere.

Bakgrunn og hensikt

Dette er et spørsmål til deg om å delta i en forskningsstudie for å undersøke effekten av simulert høyde på oksygenforbruk i musklene i løpet av submaksimal aerob under- og over-kroppstrening. Høyde (eller simulert høyde) fører til at kroppen ikke lenger klarer å levere full mengde av oksygen til muskelen (hypoksi). Det er kjent at hypoksi reduserer aerob prestasjonsevne, men studier viser at overkroppen har en mindre reduksjon i prestasjon sammenlignet med underkroppen. Vi vet lite om hvordan hypoksi påvirker muskulært oksygenforbruk i overkroppen. Det er forholdsvis enkelt å måle oksygenforbruket til hele kroppen, men målinger av oksygenforbruk i individuelle muskler er mer komplisert og har først i de siste tiår blitt tilgjengelige for benyttelse i forskning. Vi søker etter friske mannlige deltakere i alderen 18-40 år som er aktive roere. For å kunne delta i prosjektet kan du ikke ha tidligere historie med lunge- eller hjerte-karsykdommer eller ha bevegelsesproblemer problemer som kan forverres på grunn av eksperimentene. Studien gjøres i forbindelse med en mastergradsoppgave ved institutt for nevromedisin og bevegelsesvitenskap, NTNU.

Hva innebærer studien?

Prosjektet er delt opp i fire dager. Den første dagen vil bestå av en bioelektrisk impedansanalyse av kroppssammensetning samt mer informasjon om testene som skal gjennomføres. Deretter kommer de tre testdagene, som vil foregå med noen dagers mellomrom for å sikre fullstendig restitusjon fra treningstestene. Hvis du ønsker å delta i studien må du avstå fra annen trening på dagene da målingene gjennomføres, samt i minst 24 timer før testing. Under de forskjellige testene samles det inn data om oksygenforbruk i hele kroppen, oksygenforbruk i muskulaturen, hjertefrekvens, hjertets minuttvolum og slagvolum, og blodlaktat.

Dag 1 (pretest). På dag en vil deltakerne gå gjennom en bioelektrisk impedansanalyse av kroppssammensetning og få mer informasjon om studien.

Testdag 1. Testdag 1 innebærer måling av vekt, alder og høyde, samt en estimering av kroppens fettprosent gjennom måling av hudfoldtykkelse og omkrets på forskjellige punkter på kroppen. For å måle oksygenforbruket til lår- og arm-muskelen vil en mansjett rundt låret og armen blåses opp i hvile en gang i henholdsvis 1 og 10 minutter som midlertidig klemmer av blodstrømmen (arteriell okklusjon). Det vil også utføres to tester med gradvis økende belastning for å estimere kroppens maksimale evne til å ta opp oksygen i overkropp og underkropp, henholdsvis med armsykkel- og beinsykkel-ergometer. Under sykkeltesten vil det også gjennomføres testing av laktatterskel. De to sykkeltestene vil ta cirka 30 minutter hver å gjennomføre. Det kan forventes å bruke 2 timer på å gjennomføre testene på testdag 1.

Testdag 2 og 3. På begge disse testdagene vil det gjennomføres to submaksimale tester med konstant intensitet. Det vil gjennomføres en armsyklingstest og en beinsyklingstest på begge testdagene. Treningsøktene på en av testdagene vil foregå mens man puster inn en mikstur med lavt innhold av oksygen og på andre dagen mens man puster inn vanlig luft. Rekkefølgen vil bli randomisert, og typen gassmikstur som brukes vil skjules for testpersonen.

Mulige fordeler og ulemper

Denne studien vil kunne framskaffe nyttig kunnskap om forskjellene i oksygenforbruk i over- og under-kropp i hypoksi. Det vil ikke være noen direkte fordeler for den enkelte deltager. Maksimaltestene kan medføre noe ubehag, men de vil bli utført med kyndig personell til stede og etter etablerte prosedyrer. I tillegg kan mansjetten som brukes i studien oppleves som ubehagelig når den er oppblåst, men det er bare under okklusjonen og ingen skader forventes på grunn av dette. Spesielt i starten av okklusjonen kan det være litt vondt. Utover dette vil ikke deltagelse i prosjektet medføre økt risiko eller ubehag utover det som vil oppleves i en normal treningssituasjon.

Hva skjer med testene og informasjonen om deg?

Testene tatt av deg og informasjonen som registreres om deg skal kun brukes slik som beskrevet i hensikten med studien. Alle opplysningene og resultat av tester vil bli behandlet uten navn og fødselsnummer eller andre direkte gjenkjennende opplysninger. I studien vil det

tildeles et deltakernummer som knytter deg til dine opplysninger og resultatene gjennom en navneliste. Vi registrerer ingen direkte personidentifiserbare opplysninger og det vil ikke være mulig å spore deg i resultatene av studien når disse publiseres.

Frivillig deltakelse

Det er frivillig å delta i studien. Du kan når som helst og uten å oppgi noen grunn trekke deg fra prosjektet. Dersom du ønsker å delta, undertegner du samtykkeerklæringen på siste side. Om du nå sier ja til å delta, kan du senere trekke tilbake ditt samtykke. Dersom du senere ønsker å trekke deg eller har spørsmål til studien, kan du kontakte Eirik Kleppe Likvern (tlf. 95 15 38 97, e-mail: eirikkli@stud.ntnu.no) eller prosjektleder Mireille van Beekvelt (tlf. 72 82 08 62, email: mireille.van.beekvelt@ntnu.no). Prosjektet er godkjent av Regional komité for medisinsk og helsefaglig forskningsetikk, Midt-Norge.

Kapittel A- utdypende forklaring av hva studien innebærer

Bakgrunnsinformasjon om studien.
Studien gjennomføres i forbindelse med et mastergradsprosjekt ved institutt for nevromedisin og bevegelsesvitenskap, NTNU.

Undersøkelser deltageren skal gjennomføre

- Som deltager møter du opp tre ganger på bevegelseslaboratoriet i nevro-øst på Øya, samt en gang på forskningsposten.
- Dag 1 (pretest): Informasjon om studiet og måling av kroppssammensetning gjennom bioelektrisk impedans-analyse.
- Testdag 1: Måling av alder, vekt, høyde, oksygenforbruk, hjertefrekvens, minuttvolum, slagvolum blodlaktat, estimering av fettprosent. Samt to tester med gradvis økende intensitet for overkropp og underkropp, henholdsvis armsykling og beinsykling.
- Testdag 2 og 3: Utføring av to submaksimale treningstester. Måling av hjertefrekvens, minuttvolum, slagvolum og oksygenforbruk for hele kroppen og i lår/arm-muskulatur.

Tidsskjema

- Testingen vil foregå i løpet av våren 2018.

Mulige ubehag

- Mansjetten som blåses opp kan oppleves som ubehagelig og noen ganger litt vondt, men det er bare under avklemmingen.
- De fysiske testene kan fremkalle en følelse av ubehag, men dette er ikke forskjellig fra den som kan forventes fra egne treningsaktiviteter.

Kapittel B - Personvern, biobank, økonomi og forsikring

Personvern

Opplysninger som registreres om deg er kjønn, alder, høyde, vekt, omkrets på ulike steder, mål av hudfoldtykkelse på låret, oksygenforbruk i hele kroppen og i bein/arm-muskulatur, kroppssammensetning, minuttvolum, hjertefrekvens og slagvolum. All data samles inn og oppbevares avidentifisert. Bare prosjektmedarbeidere vil ha tilgang til data. NTNU ved dekanus på Det Medisinske Fakultetet (DMF) er databehandlingsansvarlig.

Rett til innsyn og sletting av opplysninger om deg og sletting av prøver

Hvis du sier ja til å delta i studien, har du rett til å få innsyn i hvilke opplysninger som er registrert om deg. Du har videre rett til å få korrigert eventuelle feil i de opplysningene vi har registrert. Dersom du trekker deg fra studien, kan du kreve å få slettet innsamlede prøver og opplysninger, med mindre opplysningene allerede er inngått i analyser eller brukt i vitenskapelige publikasjoner.

Forsikring

Forsøkspersonene i prosjektet er omfattet av pasientskadeloven.

Informasjon om utfallet av studien

Ved endt studie har alle deltakerne rett til å få informasjon på gruppenivå om utfallet/ resultatet av studien.

Samtykke til deltakelse i studien

Jeg er villig til å delta i studien

(Signert av prosjektdeltaker, dato)

Jeg bekrefter å ha gitt informasjon om studien

(Signert, rolle i studien, dato)

Appendix 2. Physical activity questionnaire

Hypoxia study Subject ID: **17HYP**

Questionnaire

Hypoxia Study

Hvilken idrett driver du med? ROING / SKI

Hvor lenge har du drevet med idretten? År

Hvor mange ganger i året konkurrerer du? Ganger

Hvor mange timer i gjennomsnitt i uken trener du:

Utholdenhet: Timer **Styrke:** Timer **Totalt:** Timer

Hvor mange timer i gjennomsnitt i uken trener du:

Underkropp: Timer **Overkropp:** Timer **Begge:** Timer

Body Composition: Skinfold Thickness

	1st	2nd	
Triceps:			mm
Iliac Crest:			mm
Subscapular:			mm
Proximal thigh:			mm
Mid-thigh:			mm
Medial Calf:			mm