REDUCED AIR RESISTANCE WITH TERRESTRIAL ALTITUDE ALTERS RUN SPRINT PERFORMANCE

TO THE EDITOR: Decades of research in exercise physiology have supported the common view that endurance performance suffers most greatly at altitude because oxidative energy production is limited (4). In contrast, Weyand et al. (5) reported that fit males are capable of running just as fast during “all-out” treadmill efforts of <1 min in hypoxic compared with normoxic conditions (13.00% and 20.93% oxygen, respectively), despite a reduction in the aerobic energy available for sprinting. As underlined by Mounier and Brugniaux (2) in their Counterpoint, it is noteworthy that most of our knowledge on this topic is derived from laboratory-based measurements. When comparing hypobaric and normobaric hypoxia, the effect of air resistance should not be neglected. Indeed, the decrease in air density upon ascent to terrestrial (natural) altitude reduces air resistance, which is likely to decrease the energy cost of running at high velocities, without the detrimental effect of reducing energy availability (3). This may explain—to a large extent—why sprinters generally achieve better performances with exposure to natural altitude. Anecdotally, multiple world records were set in the sprint (i.e. 100, 200, and 400 m) disciplines during the Mexico City Olympics held at an altitude of 2,240 m in 1968, whereas no records were set in the middle- or long-distance running disciplines. By using a mathematical supply-demand model, Arsac (1) calculated improvements in sprinting (i.e. 60, 100 m) times and changes in the components of the energy cost with changes in altitude from 0 to 4,000 m. It was concluded that as the cost of overcoming air resistance decreases with increasing altitude, better performances may be achieved attributable to more energy being available for acceleration. In summary, it should be underlined that the reduced air resistance with terrestrial altitude (hypobaric hypoxia) is likely to induce different responses than exposure to gas mixtures lowering the oxygen fraction (normobaric hypoxia) during running sprints. Of the few studies modeling the effects of natural altitude on the energetics of sprint performance, to date, no study has directly assessed the impact of a reduced air resistance per se, which warrants further research.

REFERENCES


Olivier Girard
Research Scientist
ASPETAR - Qatar Orthopaedic and Sports Medicine Hospital

CORRECT HYPOXIC DOSE AND EXHALED NO CLARIFICATION

TO THE EDITOR: An important consideration for the interpretation of studies that compare normobaric hypoxia (NH) and hypobaric hypoxia (HH) is the correct calculation of hypoxic dose. In many studies, hypoxic doses are calculated based on the ambient PO2 instead of the PiO2, which negates the effect of pH2O (2). This omission creates a different PiO2 in each condition that can lead to spurious findings. Consider the calculations in Table 1: the ambient PO2 is the same, but as a result of the pH2O effect, the PiO2 is different for each condition.

Table 1.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Hypobaric</th>
<th>Normobaric</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patm</td>
<td>430 mmHg</td>
<td>760 mmHg</td>
</tr>
<tr>
<td>PiO2</td>
<td>47 mmHg</td>
<td>47 mmHg</td>
</tr>
<tr>
<td>PiO2</td>
<td>0.209</td>
<td>0.119</td>
</tr>
<tr>
<td>Ambient PO2</td>
<td>(430-0.209 = 90)</td>
<td>(760-0.119 = 90)</td>
</tr>
<tr>
<td>PiO2</td>
<td>(430-47)×0.209 = 80 mmHg</td>
<td>(760-47)×0.119 = 85 mmHg</td>
</tr>
<tr>
<td>pH2O</td>
<td>90</td>
<td>90</td>
</tr>
</tbody>
</table>

To obtain a truly equivalent hypoxic dose across conditions, the ambient PO2 must differ. Thus it is essential to verify the proper calculation of the hypoxic dose when interpreting studies comparing NH and HH.

Second, the rebuttal of Mounier and Brugniaux (6) is correct in stating that some researchers perceived the results of Hemmingsson and Linnarsson (4) as contentious; however, Mounier and Brugniaux (6) misinterpreted the source of the contention. That the partial pressure of exhaled nitric oxide (PENO) differs between NH and HH is actually well supported. For example, several studies have concluded that acute exposure to NH do not decrease the PENO (e.g. 3, 5); furthermore, a decreased PENO in response to HH is a common finding among subjects native to low altitude (e.g., 1, 3). The dispute over the work of Hemmingsson and Linnarsson (4) was largely centered on extrapolations of their data to previous studies of high-altitude natives that employed NO analyzers operating on different technological principles.

REFERENCES


Michael S. Koehle
Assistant Professor
Martin J. MacInnis
Normand Richard
School of Kinesiology, University of British Columbia

THE EFFECTS OF NORMOBARIC HYPOXIA AND HYPOBARIC HYPOXIA ON EXERCISE-INDUCED PULMONARY EDEMA

TO THE EDITOR: There is unresolved controversy on whether high-intensity exercise is sufficient to elicit pulmonary edema in humans as detected via different imaging modalities (radiography, MRI, CT). Several recent studies postulated that hypoxic exercise may induce edema to a greater degree than normoxia because of the well known effects of hypoxia on pulmonary vasoconstriction (2–4). Despite a concerted effort and a sound physiological rationale, these studies were unable to demonstrate evidence of lung water accumulation in humans exercising in normobaric hypoxia, despite using sensitive and quantitative imaging techniques (CT and MRI). The present debate raises the question of whether there may be differences in pulmonary edema susceptibility following normobaric vs. hypobaric hypoxic exercise. An examination of previously published imaging studies using different forms of hypoxia suggests that there may be a difference. In contrast to the studies described above, it appears that athletes exercising in hypobaric hypoxia show compelling radiographic evidence of pulmonary edema (1). The physiological basis for this potential difference remains unclear but may be related, in part, to differences in fluid circulation and the trans alveolar-capillary membrane flux, which, as nicely pointed out by Millet et al. (5), may induce greater pulmonary vasoconstriction, thus modifying O₂ diffusion via a decreased pressure gradient. Future lung imaging studies are required to compare pulmonary edema responses in the same subjects exercising under both forms of hypoxia in order fully elucidate this potential physiological difference.

REFERENCES


THE NEUROMUSCULAR FUNCTION IN NORMOBARIC VERSUS HYPOBARIC HYPOXIA

TO THE EDITOR: We would like to address the difference between normobaric (NH) and hypobaric (HH) hypoxia regarding the neuromuscular function, i.e. a critical factor determining exercise performance in hypoxia. Maximal voluntary contraction and muscle contractile properties are generally unchanged in both NH and HH (5). Only a few studies, however, have compared similar hypoxic exposure since NH studies mostly involved acute exposure whereas HH studies generally involved prolonged exposure with intermediate ascent periods to altitude. This potentially leads to acclimatization, fatigue and/or training. Additionally, other factors (e.g., hydration, stress, temperature, etc.) going beyond the strict definition of hypoxia from Mounier and Brugniaux (4) may then modulate the neuromuscular function. Maximal voluntary activation at rest is not modified under NH but remains to be investigated in HH. While increased or unchanged motor cortex excitability has been reported in acute NH, chronic HH induces hypoexcitability of both excitatory and inhibitory cortical circuits (3). Interestingly, this reduction in cortex excitability correlated well with acute mountain sickness (AMS) severity. Hence, more severe AMS in HH as underlined by Millet et al. (1) might be associated with cerebral perturbations (e.g., subedema) that may also affect the motor cortex. Whether such perturbations specific to HH may lead to greater central motor output impairment in HH compared with NH remains hypothetical. At last, NH enhanced both locomotor (2) and respiratory (6) muscle fatigue during dynamic contractions. Regarding the latter, however, reduced air density and work of breathing in HH may result in lesser fatigue at similar ventilatory level.

REFERENCES


Jordan A. Guenette
Postdoctoral Fellow
Michael S. Koehle
Respiratory Investigation Unit, Queen’s University

Stephane Perrey
Senior Scientist
Marc Rupp
Guillaume Y. Millet
HP2 Laboratory (U1042)
Joseph Fourier University and INSERM
Grenoble, France

Samuel Verges
Postdoctoral Fellow
Thomas Rupp
Stephane Perrey
Guillaume Y. Millet
Joseph Fourier University and INSERM
Grenoble, France

Downloaded from http://jap.physiology.org/ by 10.220.33.5 on November 7, 2016
THE ISSUE OF CONFINEMENT WITH CHRONIC NORMOBARIC HYPOXIA

TO THE EDITOR: Millet et al. (4) note differences in performance outcomes between chronic exposure to HH and chronic intermittent exposure to NH may largely depend on the “hypoxic dose” and training content. Our own data confirm that performance changes in endurance athletes after chronic altitude training are dependent on a combination of both erythropoietic and training responses (2, 3).

With intermittent exposure to NH, the magnitude of the “normoxic dose” may be just as important as the “hypoxic dose.” Because logistics of NH delivery require a closed environment, the end result is most NH exposures are intermittent in nature. Upon return to a normoxic environment from altitude/hypoxia, circulating erythropoietin (EPO) levels typically fall below baseline levels (2, 3), potentially resulting in a selective hemolysis of the youngest circulating red blood cells—a phenomenon termed neocytolysis (1).

Additionally, the confining nature of a hypoxic tent or room makes it difficult to achieve the same 24-h/full-time exposure to hypoxia as terrestrial altitude living. When the confinement is prolonged enough to deliver an adequate hypoxic dose, it may have unexpected consequences such as the uniform loss of plasma volume observed in both hypoxic and normoxic confined athletes in a recent placebo controlled trial (6). Therefore, if potential differences exist in performance outcomes between HH and NH (4, 5), they may not be due so much to differences in the manner in which hypoxia is achieved, but more from the fact that NH often involves physiological responses to confinement and intermittent exposure to normoxia.

REFERENCES

gases. Particularly in HH, more apneas may arise from arterial CO₂ reduction. Whether the occurrence of more PB and central apneas would be beneficial as shown in our study (5) or deleterious with further SpO₂ reduction during sleep must be elucidated. We suggest that blood gases during sleep are critical regarding the relationship between acute mountain sickness and HH or NH. It is therefore important to further compare HH and NH effects on ventilatory control and blood gases during sleep.

REFERENCES


Hugo Nespoulet
Bernard Wuyam
Renaud Tamisier
Samuel Verges
Patrick Levy
HP2 Laboratory (U1042)
Joseph Fourier University and INSERM
Grenoble, France

PHYSIOLOGICAL RESPONSES TO REDUCTIONS IN AVAILABLE OXYGEN VIA NORMOBARIC VS. HYPOBARIC HYPOXIA: DOES IT REALLY MATTER?

TO THE EDITOR: The diminished availability of oxygen (O₂) (i.e. hypoxia) elicits profound physiological responses. Several of these physiological adaptations are highlighted in the recent Point:Counterpoint about whether hypobaric and normobaric hypoxia induce similar physiological responses (4, 5). Interestingly, vascular responsiveness (aside from pulmonary vasoconstriction) was not addressed by either group of authors. Along these lines, acute exposure to hypoxia tends to elicit vasodilation in several different vascular beds. Specifically, there is significant data demonstrating graded vasodilator responses within skeletal muscle vascular beds under hypoxic conditions at rest and during submaximal exercise (2). Moreover, this skeletal muscle vasodilation has been observed in studies utilizing both hypobaric and normobaric hypoxia (1, 3). Taken together these data would support the argument presented by Mounier and Brugniaux (5) and suggest that it is not necessarily a matter of how hypoxia is achieved (i.e., hypobaric vs. normobaric), but rather the severity of the hypoxic stress and the O₂ sensing capabilities of a given tissue that governs the response. Interestingly, the factors associated with augmenting vasodilation within the skeletal muscle vasculature in response to hypoxia appear to be sensitive to alterations in arterial oxygen content rather than arterial oxygen tension (6). In summary, the mode (hypobaric vs. normobaric) by which hypoxia is achieved is likely less important than the actual changes in arterial oxygen content when discussing the vasodilator response, specifically in the skeletal muscle vasculature.

REFERENCES


Darren P. Casey
Assistant Professor
Mayo Clinic

HYPOBARIC VS. NORMOBARIC HYPOXIA: THE LUNGS MAY BE DIFFERENT

TO THE EDITOR: We read with interest the debate regarding the physiological responses to hypobaric vs. normobaric hypoxia (4, 5).

In agreement with Dr. Millet and colleagues, we believe that the physiological adaptation to hypobaric vs. normobaric hypoxia is different, particularly with regard to lung fluid regulation. Hypobaric and normobaric hypoxia both cause pulmonary vascular constriction, which could elevate capillary pressure sufficiently to initiate fluid flux into the interstitial space. However, although there is abundant evidence that hypobaric hypoxia can cause pulmonary edema (2), it appears that normobaric hypoxia does not elicit a similar response. In sheep, hypobaric but not normobaric hypoxia increases lung lymph flow, an indicator of interstitial edema (3). In healthy humans, we have shown that normobaric hypoxia, even in the setting of an exercise-induced elevation in pulmonary capillary pressure, decreases lung fluid, as shown by a fall in CT-derived lung density and an increase in alveolar-capillary gas conductance (6); so, why the divergence between hypobaric and normobaric hypoxia? Although sympathetic activation, elevated catecholamines, beta-2 adrenergic receptor stimulation, lymphatic dilation, and intrathoracic pressure fluctuations likely enhance fluid removal with both hypobaric and normobaric hypoxia, an increase in pulmonary vascular permeability caused by microemboli (1) and a decrease in interstitial pressure secondary to a reduction in alveolar pressure with hypobaria may increase pulmonary vascular fluid flux into the interstitium to a greater extent than the rate of fluid extrusion. We feel that these data argue...
that the pressure change associated with hypobaria is essential for the formation of hypoxia-induced interstitial edema.

REFERENCES

**DIFFERENCES IN RESPIRATORY MUSCLE METABOLIC COST BETWEEN NORMOBARIC AND HYPOBARIC HYPOXIA**

**TO THE EDITOR:** Both resting and exercise minute ventilation (VE) have been shown to be higher during exposure to normobaric hypoxia (NH) compared with hypobaric hypoxia (HH) (2, 4). The exact mechanism for this ventilatory difference is not completely understood, but the physiological consequence can be estimated.

The metabolic cost of breathing is dependent upon a number of variables, including ventilation rate and the density of inspired air. Using a submaximal exercise ventilation of 130 l/min in HH (corresponding to a workload of approximately 85% V̇O₂max in highly trained endurance athletes), a 10% higher VE in NH (1), and a regression equation developed from previously published data (1), we calculated a 17–19% difference in the oxygen cost of exercise hyperpnea between HH and NH based solely on VE differences, given equal air densities. However, at an altitude of 3,000 m the density of air is 69% that of air in normobaric hypoxia (equivalent PIO2), making the work of breathing approximately 1.3 times greater in NH than HH based upon air density alone (6). The combined higher costs from VE and air density result in an estimated overall respiratory muscle cost that is 72% (153 ml O₂/min) greater in NH compared with HH during moderately hard exercise. This difference would likely widen further with increases in altitude and/or exercise intensity.

Ultimately, increased respiratory muscle V̇O₂ may compromise locomotor muscle blood flow (3), negatively impacting endurance training and exercise performance. The interchangeability of NH and HH (1, 5) may then depend on the respiratory muscle cost.

REFERENCES

**COMMENTARY FOR POINT:COUNTERPOINT: HYPOBARIC HYPOXIA INDUCES/DOES NOT INDUCE DIFFERENT RESPONSES FROM NORMOBARIC HYPOXIA**

**TO THE EDITOR:** I agree with evidence presented by Millet et al. (3) favoring more severe AMS in HH than NH at equal PIO2. Responses may be qualitatively similar (4) but are more pronounced in HH. Also, limited observations on mountains indicate that increased PB speeds AMS recovery from that achieved with oxygen alone (2), but more measurements are needed. AMS study results vary because: 1) AMS “measurements” are subjective and debated (e.g., headache or not?), 2) susceptibility varies greatly, and 3) study times are too variable (30 min to 12 h). Differences in AMS-related physiology between HH and NH should be studied in the same highly susceptible subjects.

Many studies show that a greater SaO2 decrease within the first hour after decreased PIO2 is associated with greater subsequent AMS. This early SaO2 decrease is greater in HH and usually attributed to pressure effects on ventilation (6). However, different fluid balance, circulatory, and autonomic responses to HH and NH should also be considered in association with AMS. The contribution of PB differences per se to hypoxia-induced AMS is still undefined.

In nature humans live in HH, but not NH (except with lung disease) or hypobaric normoxia, so genetic adaptations are not comparable in these conditions. A clue to response differences may be available from genetic studies of plants grown in HH and NH (1, 5), where distinct gene expression responses to HH and NH may be available from genetic studies of plants grown in HH.

REFERENCES
HYPOBARIC HYPOXIA: A COMPLEX AND MULTITUDE OF STIMULI

TO THE EDITOR: The Point:Counterpoint article on hypoxia highlights one of the most important pathophysiological stimuli under two different conditions [normobaric (NH) and hypobaric (HH)] hypoxia (4, 5). Clinically, conditions such as pulmonary artery hypertension (PAH), sleep disorders, and cancer hypoxia are found in both types of hypoxia, and the molecular pathways triggered by hypoxia might not discriminate on normobaric vs. hypobaric hypoxia.

The findings from well-controlled NH studies have not always been reproduced in field settings of HH. The outcome from an elegantly conducted and rigorous study showing a decrease hypoxic PAH with Acetazolamide (6) was not reproduced in a large clinical trial in the Himalayas (1). There could be arguments about various confounding factors in the field, which preclude the possibility of making direct comparisons between HH and NH, as highlighted by Millet et al. (4). The complex nature of HH can be further highlighted from the sleep studies, where PaCO2 or hypoxic ventilatory response did not provide an accurate prediction of central sleep apnea (CSA), a common condition of HH at high altitude (3). Conversely, a study with obstructive sleep apnea (OSA) patients under NH has generated exciting results (2). The study conducted by Burgess et al. at a simulated altitude of 2,750 m in a normobaric hypoxic chamber found OSA completely resolved and replaced with CSA. The observation from these studies point toward HH having a complex and multitude of stimuli compared with NH.

REFERENCES

Matiram Pun
Graduate Student (of Prof. Dr. Marc J. Poulin)
Mountain Medicine and High Altitude Physiology
Dept. of Physiology and Pharmacology
University of Calgary

NO CLINICALLY RELEVANT DIFFERENCE BETWEEN NORMOBARIC AND HYPOBARIC HYPOXIA

TO THE EDITOR: Millet et al. (3) suggest that severity and prevalence of acute mountain sickness (AMS) are higher in hypobaric (HH) vs. normobaric hypoxia (NH). The cited study (5) examined the effect of hypobaria on AMS in a proper design and lasted 9 h only. AMS is, however, most prominent after the first night spent at a particular altitude (2). Therefore, we compared prevalence and scores of AMS after an overnight exposure of 18 h in NH (PO2 = 0.12) (1) with the data obtained in a field study after an overnight stay, i.e. 18 h after arrival at 4,559 m (6). The AMS incidence was 50 vs. 58%, the Lake Louise Score 8.0 ± 1.9 vs. 8.1 ± 2.9 (means ± SD) and the AMS-C score 1.42 ± 0.74 vs. 1.72 ± 0.87 in NH and HH, respectively. It appears that a significant effect of hypobaria cannot be detected anymore after an overnight exposure in NH and HH at a comparable ambient PO2 (91 mmHg). Furthermore, the three studies cited by Millet et al. do not allow the conclusion that repeated hypobaric but not normobaric exposures to hypoxia prevent AMS because of relevant differences in the time of exposure, the level of exposure (2,600, 3,460, and 4,300 m on average) and the study design (uncontrolled vs. placebo-controlled single or double-blind) between these studies. Thus, although there are slight differences in ventilation and fluid balance between NH and HH, we agree with Mounier and Brugniaux (4) that these do not result in a persistent, clinically relevant difference in severity and prevalence of AMS.

REFERENCES

Kai Schommer
Peter Bartsch
Medical Clinic, Division of Sports Medicine
University Hospital Heidelberg
NUANCES IN THE PHYSIOLOGICAL RESPONSES DURING HYPOBARIC HYPOXIA AND NORMOBARIC HYPOXIA

TO THE EDITOR: Hypoxia is a potent modulator of approximately 1% of genes of human genome (1) and is known to cause plethora of cardiorespiratory symptoms. Although hypoxia is a severe stressor, hypobaria associated at high altitudes plays an important role in causing physiological disturbances. Authors (5) factor out low pressure in addressing them, whereas their critics (6) equate physiological responses of hypobaric hypoxia (HH) and normobaric hypoxia (NH). This comment supports the view that the physiological responses in a normal healthy individual are different during HH and NH. Although such a stand requires thorough experimental evidence, at least few strong reasons can be given as follows: 1) the arterial blood oxygen concentration is low in HH than in NH. This is due to a deleterious effect of hypobaria on pulmonary capillary permeability and gas exchange efficiency (3). It is also reported that hypobaria enhances the water and sodium retention effect of hypoxia.

2) Another reason for this difference between arterial blood oxygen concentration in HH and NH is greater activation of the sympathetic nervous system. In humans, hypobaric hypoxia, but not always normobaric hypoxia, is associated with increased circulating norepinephrine (4).

3) Last, a report (2) has shown a relationship between seasonal periods of low atmospheric pressure and associated high abdominal aortic aneurysm rupture. It is intuitive to say that normal oxygenated pressure is indispensable for well being. The parameter of pressure is crucial in the physiological assessment of hypoxia.

REFERENCES


Mary C. Vagula
Asst. Professor
Charles F. Nelatury
Gannon University