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Citation: Ansley, Les, Petersen, David, Thomas, Alan, St Clair Gibson, Alan and Noakes, Timothy (2006) The effect of breathing an ambient low-density, hyperoxic gas on the perceived effort of breathing and maximal exercise performance in well-trained athletes. *British Journal of Sports Medicine*, 41 (1). pp. 2-7. ISSN 0306-3674

Published by: BMJ Publishing Group

URL: <http://dx.doi.org/10.1136/bjism.2006.026989>
<<http://dx.doi.org/10.1136/bjism.2006.026989>>

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Title: The effect of breathing an ambient low-density, hyperoxic gas on the perceived effort of breathing and maximal exercise performance in well-trained athletes

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Keywords: work, fatigue, perception, ventilation, muscle contraction, respiration

Word Count: 3301 words

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ABSTRACT

The role of the perception of breathing effort, in the regulation of maximal exercise performance, remains unclear. This study attempts to determine whether the perceived effort of ventilation is altered through substituting a less dense gas for normal ambient air and whether this substitution affects performance of maximal incremental exercise in trained athletes. Eight highly trained cyclists ($VO_{2max} = 69.9 \pm 7.9 \text{ mL O}_2 \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$) performed two randomised maximal tests in a hyperbaric chamber breathing ambient air composed of either 35% O_2 /65% N_2 (nitrox) or 35% O_2 /65% He (heliox). A ramp protocol was used in which power output was incremented at $0.5 \text{ W} \cdot \text{s}^{-1}$. The trials were separated by at least 48 hours. The perceived effort of breathing was obtained via Borg Category Ratio Scales at 3-min intervals and at fatigue. Oxygen consumption (VO_2) and minute ventilation (VE) were monitored continuously. Breathing heliox did not change the sensation of dyspnoea, there were no differences between trials for the Borg scales at any time point. Exercise performance was not different between the nitrox and heliox trials (Peak PO = $451 \pm 58 \text{ W}$ and $453 \pm 56 \text{ W}$) nor was maximal VO_2 ($4.96 \pm 0.61 \text{ L} \cdot \text{min}^{-1}$ and $4.88 \pm 0.65 \text{ L} \cdot \text{min}^{-1}$) or maximal VE ($157 \pm 24 \text{ L} \cdot \text{min}^{-1}$ and $163 \pm 22 \text{ L} \cdot \text{min}^{-1}$). Between trial variability in peak PO was less than either VO_{2max} or maximal VE. Breathing a less dense gas does not improve maximal exercise performance or reduce the perception of breathing effort in highly trained athletes. Although, an attenuated submaximal tidal volume and VE with a concomitant reduction in VO_2 suggests an improved gas exchange and reduced O_2 cost of ventilation when breathing heliox.

INTRODUCTION

Sensations of respiratory discomfort are consciously monitored during exercise [1] and at higher workloads sensations of dyspnoea are closely related to perceived exertion [2,3]. This evidence indicates a potential role for afferent sensory feedback of ventilatory exertion, from the respiratory muscles, in regulating maximum exercise performance in humans [4]. However, the role of perceived respiratory effort in the regulation of maximal exercise performance remains unclear [5].

Perception of respiratory effort can be manipulated by altering the work of breathing. This effect has traditionally been achieved by either using a pressure assisted ventilation (PAV) device in which a demand valve senses pressure changes at the nose and mouth and reactively assists the breathing [6,7]; or altering the properties of the inspired air so that it is less dense than normal air and therefore reduces the work required to move the air in and out of the lungs [8-10].

A serious limitation to the PAV method is the potential to disrupt the normal breathing pattern of the subjects since the novelty of the task requires subjects to 'train' to breathe on the apparatus before undergoing testing [7]. A further limitation is the delayed response time of the demand valve to pressure changes at the mouth [7]. The result is that the PAV method can only be used effectively during steady STATE exercise and therefore cannot assess the role of ventilatory work or its associated sensations as a factor limiting progressive maximal exercise to exhaustion. Possibly as a result of these limitations, studies have produced mixed results regarding the effects of unloading the work of the respiratory muscles on exercise capacity [6,7].

In contrast, the performance benefits of breathing a less dense gas have produced more consistent results [8,10-12]. However, the increased breathing resistance imposed by the external gas delivery and collection systems used in these studies, creates a potential difficulty in differentiating between the effects of the lighter gas on the anatomical respiratory tree and the effects on the external respiratory tubing [13,14]. Furthermore, it is possible that altering the properties of the inspired air could result in altered ventilatory dynamics. Although some researchers [15,16] have suggested that a less dense carrier gas might increase the alveolar-arterial pO_2 gradient thereby reducing arterial blood oxygen saturation, Nemery *et al* [17] reported that the physical properties of the inspired gas do not affect ventilatory dynamic. Indeed more recent studies have found that breathing a helium-oxygen mix actually improved arterial saturation [9,18]. Therefore it appears that breathing a less dense gas during high intensity exercise may improve alveolar ventilation or the alveolar-arterial O_2 difference or both, thereby enhancing the oxygen content of arterial blood [5,19].

To fully elucidate any potential role for the perceived effort of breathing in regulating maximal exercise, the confounding effects of breathing a gas, less dense than air, need to be addressed. Conducting a trial of exercise performance in an environment in which the 'lighter' air is substituted for the ambient air will negate the need for external breathing apparatus and hence the confounding effects of unloading the added respiratory resistance caused by such apparatus. Furthermore, any ergogenic benefits derived from improved pulmonary dynamics can be minimised by increasing the fraction of oxygen in the inspired air [19].

Young *et al.* [20] have been able to demonstrate that physically active subjects are able to differentially assess feelings of effort pertaining to the respiratory and cardiovascular systems. Therefore it was the aim of this study to investigate the perceptual and performance effects of breathing a low-density, hyperoxic gas during a graded maximal exercise test to exhaustion in a young, physically fit population. We hypothesised that breathing a less dense gas would attenuated the perceived effort of breathing and improve incremental exercise time to exhaustion.

METHODS

Subjects

Eight highly trained cyclists ($\text{VO}_2\text{max} = 69.9 \pm 7.9 \text{ mL O}_2 \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$) were recruited for this study, which was approved by the university Research and Ethics Committee. This study complied with the Declaration of Helsinki as adopted at the 52nd WMA General Assembly, Edinburgh, October 2000. The nature of the study including the risks associated with exercising in oxygen and helium enriched conditions was clearly explained to the subjects from whom informed consent was obtained prior to the initiation of testing. The mean age, height and weight of the subjects were 20.1 ± 1.2 years, 184.4 ± 5.6 cm and 69.6 ± 5.1 kg respectively. Subjects were excluded from the study if they smoked, suffered from breathing disorders and/or had experienced a respiratory illness within two weeks of the start of the study.

Experimental protocol

Following an habituation trial in normoxic conditions, each subject was required to perform an incremental ramp cycle test to exhaustion on a Lode cycle ergometer (Excalibur, Netherlands) on two separate occasions, while breathing a hyperoxic (nitrox) mixture ($F_{\text{I O}_2}$ of 35% and the balance nitrogen) and a helium (heliox) mixture ($F_{\text{I O}_2}$ of 35% and the balance helium). The tests lasted on average 605 s (437 – 757 s). The hyperoxic concentration of 35% was selected on the basis of previously published literature on heliox breathing [21,22] and the reversal of exercise induced arterial hypoxemia [19].

Consecutive tests were separated by at least two days but were not more than seven days apart. The testing order was randomised and single-blinded since the experimenter but not the cyclist was always aware of the nature of the gas composition in the chamber. The cycle ergometer ramp protocol consisted of a 2 min warm-up ride at 150 W, thereafter the workload of the ramp protocol increased by $0.5 \text{ W}\cdot\text{sec}^{-1}$ to volitional exhaustion [23]. The subjects cycled inside a Multi-place Class “A” 18 000 L hyperbaric chamber of length 3.5 m and diameter 2.5 m built to Lloyd’s and ASME 1 PVHO specifications. There were internal CO_2 scrubbers; O_2 , temperature and humidity were continuously monitored. Oxygen content was maintained at the prescribed concentration for all the trials. Due to the thermal properties of helium, the average temperature and humidity levels tended to be slightly lower in the heliox trials (21°C and 49% vs. 24°C and 63%). The air pressure inside the chamber was maintained at sea-level for all the trials.

The chamber was completely flushed through twice with the relevant ambient gas mixture after the subject and investigator had entered the chamber and the chamber door had been sealed. Talking inside the chamber was not permitted since helium in the air alters the timbre of the human voice and would have been immediately obvious to the experimental subjects. The chamber was not pressurised for either test and a fan maintained continual air movement within the chamber to prevent any gas layering that might occur with a low-density gas mixture. The concentration in the chamber was continuously monitored at the height of the cyclist’s head and any drift away from the required O_2 concentration was corrected by the chamber director who ensured an inflow

of the relevant gas mixture into the chamber until the requisite $F_{I}O_2$ was regained. This ensured that the $F_{I}O_2$ did not differ from the prescribed concentration by more than 1-2%.

Prior to each test, subjects sat quietly for 10 min in the chamber while breathing the imposed gas mixture to ensure adequate equilibration of the inhaled gas mixtures throughout the body and also complete mixing of the new gas mixture throughout the chamber. The test was followed by a recovery period during which the chamber was flushed through twice with room air to preclude the subjects identifying the nature of the gas mixture that had been present during their trials. Silence was also maintained during the recovery period.

Expired respiratory gas analyses

For the measurement of oxygen consumption (VO_2) and minute ventilation (V_E) during the tests, subjects wore a mask covering the nose and mouth. The expired air passed through an on-line breath-by-breath gas analyser and pneumotach (Cardiovit CS-200 Ergo-Spiro, Schiller, Switzerland) and was averaged over 10-s intervals. Before each test the gas analyser was calibrated by a span gas of known composition and the pneumotach was calibrated with a 2-L syringe. Both the gas analyser and the pneumotach were calibrated *in situ*. Peak VO_2 (VO_{2peak}) and V_E (V_{Epeak}) were defined as the highest 10-s averages measured during the test.

Rating of perceived exertion

Levels of exertion were quantified on two different scales, the Borg 15-point RPE scale (RPE_{15}) and the Borg category-ratio scale (CR_{10}). Printed instructions were provided to familiarise subjects with each scale prior to their first incremental ramp test. Subjects were asked to provide an appropriate single score on the 15-point scale that was

the best representation of their overall level of exertion. No assistance was given by the researcher in translating their feeling into numerical ratings on the RPE scale. The Borg category-ratio exertion scale was used to quantify exertion localised specifically to the effort of breathing. The category -ratio scale was selected to measure localised exertion because the growth of this scale more closely parallels the exponential increase in the ventilation during progressive exercise to exhaustion [24]. Readings were taken at 2 min and then 3-min intervals thereafter.

Statistical analyses

For maximum data variables a paired-samples Student's t-test was performed to identify significant differences. The first 6 minutes of submaximum data were analysed. Repeated measures Analysis of Variance (ANOVA) was used to assess differences between and within the trials for submaximum data. When an ANOVA identified significance condition x time interaction, a Student's t-test *post hoc* was performed. A Bland-Altman was used to identify bias in maximal values between the trials. Significance was accepted at $p < 0.05$. All data are expressed as mean \pm standard error (S.E.).

RESULTS

Maximum values of power output, VO_2 , V_E

Peak power achieved was not significantly different between trials (nitrox = 451 ± 58 W; heliox = 453 ± 56 W; $p = 0.4$). The $\text{VO}_{2\text{max}}$ was also similar for both conditions (nitrox = 4.96 ± 0.61 L.min⁻¹; heliox = 4.88 ± 0.65 L.min⁻¹; $p = 0.6$), as was maximal minute ventilation (nitrox = 157 ± 24 L.min⁻¹; heliox = 163 ± 22 L.min⁻¹; $p = 0.3$). The percentage bias between the means of the nitrox and heliox trials for peak power, VO_2 and V_E are -0.55 ± 1.77 , 1.67 ± 9.19 and -4.02 ± 11.00 , respectively (Figure 1).

Submaximum values of VO_2 and V_E

Figure 2 depicts changes in oxygen consumption and minute ventilation for the first 6 minutes of the exercise test. An ANOVA revealed a significant condition effect for both VO_2 ($p = 0.009$) and V_E ($p = 0.001$) during submaximum workloads. The average for both variables was lower in the heliox condition ($\text{VO}_2 = 2.77 \pm 0.18$ L.min⁻¹; $V_E = 68 \pm 5$ L.min⁻¹) compared with the nitrox condition ($\text{VO}_2 = 3.02 \pm 0.19$ L.min⁻¹; $V_E = 79 \pm 5$ L.min⁻¹). The attenuation in V_E was attained through a reduction in tidal volume, which was significantly lower during the heliox trial compared to the nitrox trial at all submaximal time workloads ($p = 0.011$), while breathing frequency remained unchanged ($p = 0.3$). All submaximal ventilatory variables increased as a function of workload ($p < 0.001$) but there was no condition x time interaction for VO_2 , V_E .

Ratings of perceived exertion

There was no difference in the ratings of perceived exertion for either RPE₁₅ ($p = 0.8$) or CR₁₀ ($p = 0.6$) between trials and both variables increased as a function of workload ($p < 0.001$) (Figure 3).

DISCUSSION

The main finding of this study was that substituting helium for nitrogen in the hyperoxic ambient air did not improve the maximal exercise performance of trained cyclists during an incremental exercise test to exhaustion. This finding is contrary to results from most previous studies that have evaluated the effects of breathing a lighter gas on exercise performance [9,12,25]. Furthermore, the perceived ventilatory effort was not significantly attenuated when subjects breathed heliox. Thus although the work of the respiratory muscles was potentially reduced by breathing a gas with a density of $1/5$ th and a viscosity 1.12 times greater than the nitrox air [26], the sensation of the effort of breathing was not reduced.

Indeed, Babb [25] has previously reported that the work of breathing is not altered when the density of the inspired air is reduced as ventilatory volume was increased at submaximum workloads when heliox was breathed however, in the current study minute ventilation was depressed at submaximum workloads (Figure 2). One likely explanation for this discrepancy is the enormous difference in subject samples between the studies. A prerequisite for inclusion into Babb's study was pathological airflow limitation whereas our subjects were extremely well-trained, healthy individuals. Therefore it is probable that breathing a lighter gas exerts a separate effect in populations that suffer from restricted breathing conditions. It seems logical that in individuals who suffer from airflow limitations, and whom therefore experience an attenuated ventilatory volume, breathing a lighter gas will improve their ventilation towards normal, i.e. the ventilatory volume will increase. Certainly, Puente-Maestu *et al* have demonstrated that a reduction in tidal volume is the limiter to exercise tolerance [27] in patients suffering from COPD.

Indeed Eves *et al* [22] have previously shown that in patients suffering from COPD submaximal tidal volume is increased when patients breathe a heliox gas mixture but does not change when the patients breathe a hyperoxic gas even though both gas mixtures improve exercise tolerance to the same extent. This suggests that the mechanisms through which heliox and hyperoxia improve performance are different; a postulate that is supported by their observation that a hyperoxic-heliox mixture exhibits a performance improvement effect greater than either hyperoxia or normoxic-heliox individually.

In healthy individuals whose ventilation is compromised through hypobaric exposure, the supplementation of helium for nitrogen in the ambient air in hypobaric conditions has a similar effect, to the COPD studies, of increasing submaximal ventilation, towards normobaric values, through an increase in tidal volume [28]. Furthermore Esposito and Ferretti [12] reported that VO_2max and peak power were improved in hypoxic conditions when a heliox gas was inspired; however, they did not find any difference in either VO_2max or peak power when heliox was substituted in normoxic conditions. Interestingly though maximal expired and maximal alveolar ventilation were increased in both hypoxia and normoxia when heliox was substituted for nitrox. In individuals who have no pathological limitations to their ventilation, an effect of inspiring a less dense gas on respiratory work or ventilatory dynamics may be to reduce tidal volume at submaximal workloads. A lower ventilation and oxygen uptake at submaximum workloads, such as that observed in our study, implies superior gas exchange and not altered airway resistance i.e. a lower ventilation is required to deliver oxygen, thus oxygen uptake is lower. Interestingly, the reduction in mean oxygen consumption at submaximum workloads observed during the heliox trial (~8%) is similar

to the oxygen cost that has been determined for breathing normal air during exercise (4.6 – 10%) [29]. Although there was a reduction in submaximal V_E the perceived ventilatory effort remained similar between trials. This can probably be explained by the fact that the reduction in V_E was attained through a reduced tidal volume and not a change in the breathing frequency. A change in the rate of breathing is the respiratory variable that has been associated with the perception of dyspnea [27].

Our study differed from other studies that have looked at maximal exercise capacity in healthy subjects breathing a heliox gas [9,12] in two important ways; 1) our subjects were highly trained cyclists and 2) our subjects inspired a hyperoxic gas mixture. Esposito and Ferretti [12] and Powers *et al.*[9] both reported an increase in maximal minute ventilation while breathing a heliox mixture; but, only Powers *et al.* reported a increase in VO_{2max} and workload under normoxic conditions. We have previously alluded that the effects of breathing a heliox gas may be two-fold; an improved ventilatory capacity and improved ventilatory dynamics. With regards to the improved ventilatory capacity, the subjects in our study are accustomed to working at close to their maximal capacity and therefore their respiratory system would be trained to cope with the volume of air that is moved in and out of the lungs at peak workloads. However, in less well-trained individuals the respiratory system would be unaccustomed to the ventilatory volumes especially at the higher workloads (which might explain why Powers *et al.* and Esposito and Ferretti only noted differences in submaximal V_E at higher workloads) and therefore were not able to attain their functional maximal ventilation breathing nitrox gas. However, as in the case with the subjects suffering from restricted breathing heliox allowed them to ventilate closer to their maximal volume.

Additionally, we argue that the effects of the improved pulmonary gas exchange while breathing heliox, evidenced in this study by the lower submaximal ventilation, would have been even more pronounced had the exercise not been conducted in hyperoxic conditions. This argument is indirectly supported by Esposito and Ferretti [12] who observed significantly improved maximal alveolar ventilation when heliox was inspired under hypoxic conditions as compared with normoxic conditions. Although alveolar ventilation did improve in normoxic conditions it was to a lesser extent and not statistically significant. Therefore it would appear that breathing helium may be beneficial to improved work capacity in subjects who have respiratory pathologies or are not habituated to high ventilatory volumes as well as in conditions of low inspired oxygen concentrations.

It is well-documented that exercise-induced arterial hypoxemia occurs at higher exercise intensities in **some** highly trained athletes [30]. Therefore, it could be argued that a compromised oxygen delivery to the working muscles limited the exercise capacity of these subjects before they reached the ventilatory volumes that would terminate exercise. However, it has been demonstrated that the arterial pO_2 is better maintained during severe exercise when a heliox gas is inhaled compared to normal air [9,19]. Furthermore, both Dempsey *et al* [19] and ourselves (Ansley, L. PhD Thesis, 2003) have shown that the arterial desaturation associated with maximal work is completely counteracted when subjects breathe a hyperoxic gas mixture (24 and 30%, respectively) (Table 1). Therefore, it seems unlikely that in this study maximal exercise capacity was limited by arterial desaturation in either condition.

The Bland-Altman plots for peak power, VO_2max and maximal V_E demonstrate the close limits of agreement between the trials for the peak power (-4.0 - 2.9%) compared with both VO_2max (-16.3 – 19.7%) and maximal V_E (-25.6 – 17.5%). These observations are similar to both Laplaud *et al.* [31] who reported an interclass correlation of 1 for peak power utilising a similar protocol and Kuipers *et al.* [32] who showed a co-efficient of variation in peak power and VO_2max of 2.95 - 6.83% and 4.20 – 11.35%, respectively. The greater variability associated with the VO_2max and maximal V_E coupled with the variability previously reported for biological variables [32] it seems doubtful that the termination of the exercise was due to a single physiological correlate but rather due to a multivariable evaluation of integrated afferent feedback that probably includes mechanoreceptors, metaboreceptors and chemoreceptors.

Summary

Conducting this study in hyperoxic conditions controlled for the confounding effect of EIAH during maximal exercise, therefore any effects are attributable directly to the altered density of the inspired gas. Inspiring a less dense hyperoxic ambient gas does not improve short duration maximal exercise capacity of trained athletes and nor does it alter the perceived effort of breathing as measured by the Borg CR_{10} scale. However, submaximal tidal volume was attenuated in the heliox trial, which was manifest in lower submaximal minute ventilation. This was matched by a concomitant reduction in submaximal oxygen uptake. The reduction in both minute ventilation and oxygen consumption suggests an improved gas exchange during the heliox trial. It is also notable that the extent to which the oxygen uptake was reduced is comparable with a reduction in the oxygen cost of ventilation. There does appear to be a potential role for heliox in

improving performance in populations who suffer from impaired respiratory capacity or are unused to high ventilatory volumes as well **as** during maximal work in hypoxic conditions.

ACKNOWLEDGEMENTS

Funding for this study was provided by the Beatrix Waddell Scholarship Fund, the Lowenstein Scholarship Trust and the Harry Crossley Staff Research Fund, all of the University of Cape Town; the National Research Foundation and the Medical Research Council of South Africa; and Discovery Health Pty Ltd.

Table 1

Measured mean arterial oxygen pressure (p_aO_2) and mean arterial oxygen saturation (s_aO_2) during maximal exercise in a study performed in the same chamber as those in this study (Ansley, L. PhD Thesis, 2003)

Condition	Rest		Peak Exercise	
	p_aO_2 mmHg	s_aO_2 %	p_aO_2 mmHg	s_aO_2 %
21%	111	98.6	94	94
30%	223	99.3	203	98.9

LEGEND TO FIGURES

Figure 1 Bland-Altman plots depicting the percentage bias and individual percentage differences ($\text{mean} \pm 1.96\text{SD}$) for PPO, VO_2 and V_E .

Figure 2 Mean (SEM) data for submaximum oxygen consumption and minute ventilation during incremental exercise performed in a sealed chamber under conditions of 30% O_2 :70% N_2 (nitrox ■) and 30% O_2 :70% He (heliox □).

*Significant trial effect ($p < 0.05$)

Figure 3 Mean (SEM) data for rating of perceived effort for localised respiratory exertion (CR_{10}) and general whole body exertion (RPE_{15}) during maximal incremental exercise performed in a sealed chamber under conditions of 30% O_2 :70% N_2 (nitrox ■) and 30% O_2 :70% He (heliox □).

Figure 1

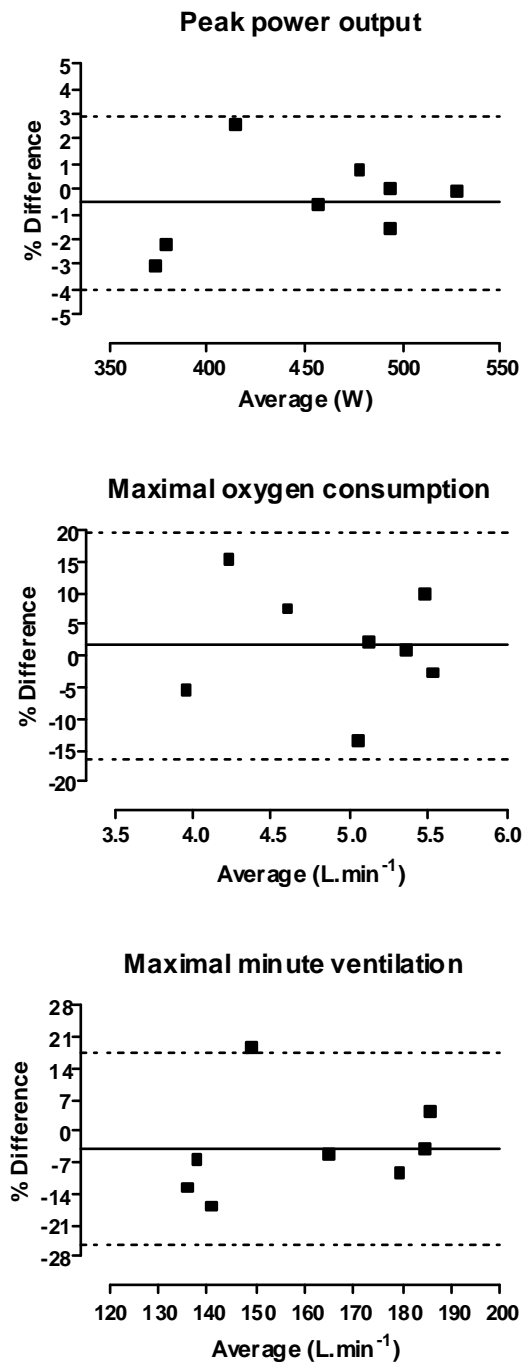


Figure 2

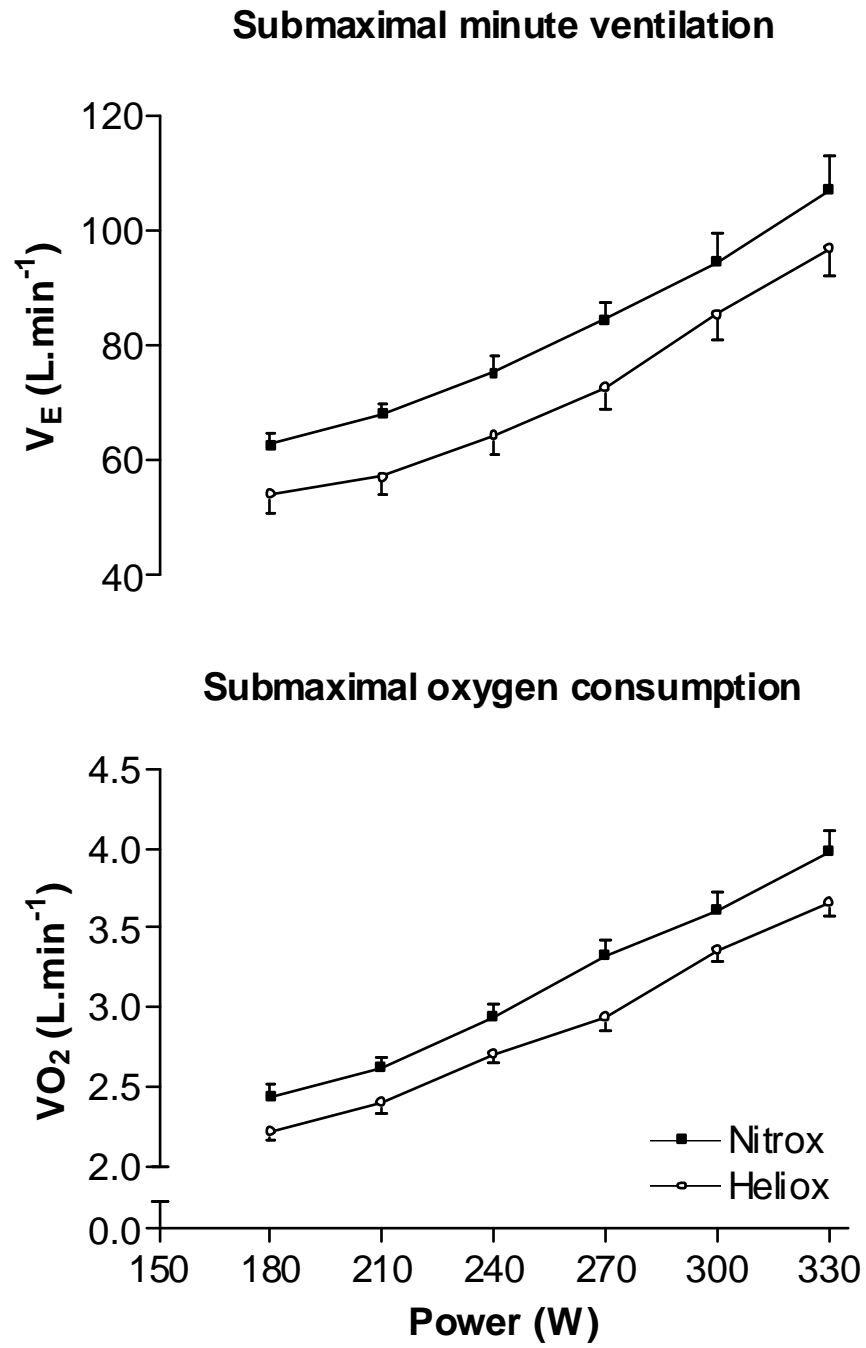
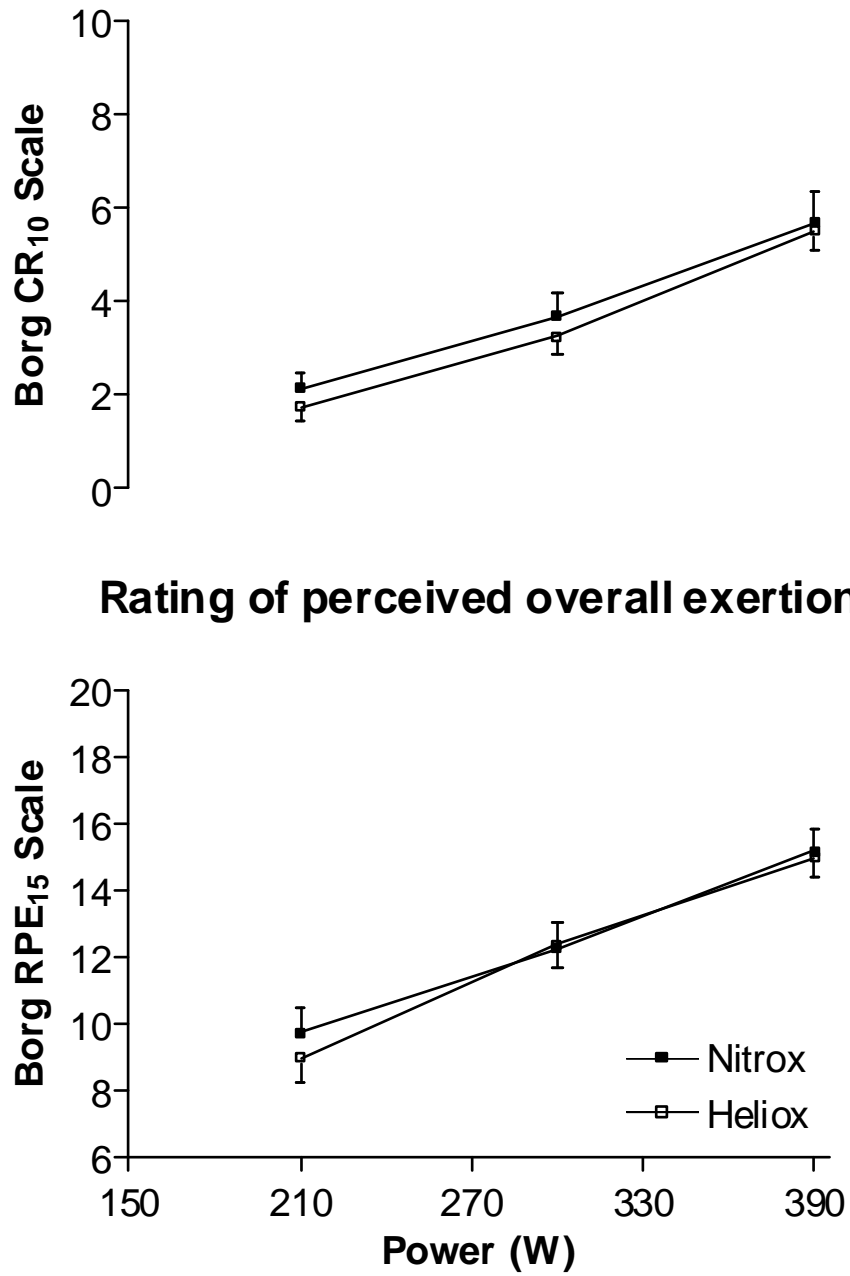
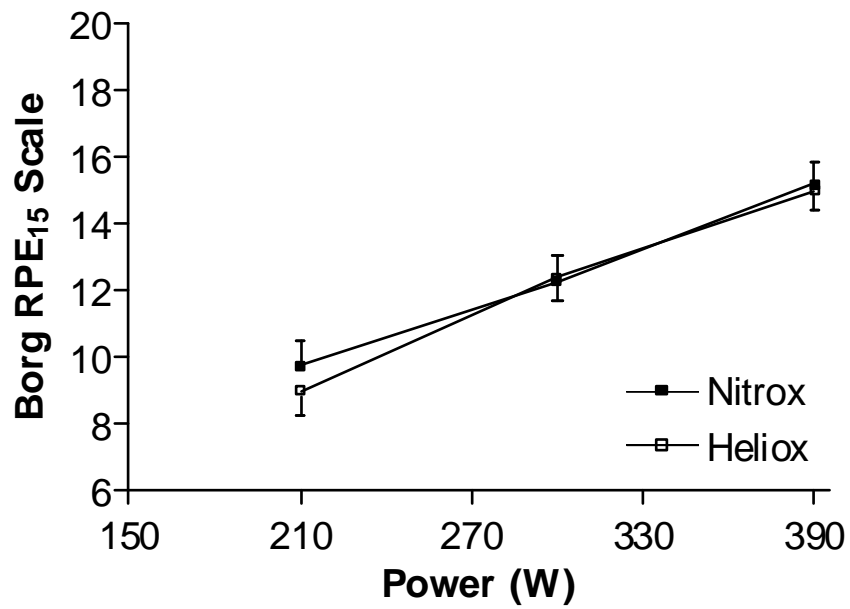


Figure 3

Rating of perceived ventilatory exertion



Rating of perceived overall exertion



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INFORMATION BOX

What is already known on this topic?

Breathing a heliox mixture improves exercise tolerance in hypoxic conditions and in COPD patients. The performance benefits derived from breathing a lighter gas have been associated with both a decrease in the sensation of ventilatory effort as well as an enhancement of arterial blood saturation.

What this study adds

This study indicates that breathing helium does not improve maximal performance when arterial blood saturation is maintained in trained athletes. Also, although submaximal tidal volume is attenuated when breathing heliox, the breathing frequency is maintained and consequently so too is the sensation of respiratory effort.