Respiratory Physiology & Neurobiology 189 (2013) 530–536

Contents lists available at ScienceDirect

Respiratory Physiology & Neurobiology

journal homepage: www.elsevier.com/locate/resphysiol

# Sex-related differences in muscle deoxygenation during ramp incremental exercise

Juan M. Murias[a,b], Daniel A. Keir[a,b], Matthew D. Spencer[a,b], Donald H. Paterson[a,b,*]

[a] Canadian Centre for Activity and Aging, The University of Western Ontario, London, ON, Canada
[b] School of Kinesiology, The University of Western Ontario, London, ON, Canada

ARTICLE INFO

*Article history:*
Accepted 17 August 2013

*Keywords:*
Oxygen extraction
Cycling
Near-infrared spectroscopy

ABSTRACT

Sex-specific differences in the temporal profiles of fractional $O_2$ extraction during incremental cycling were examined using changes in near-infrared spectroscopy (NIRS)-derived muscle deoxygenated hemoglobin concentration ($\Delta$[HHb]) and breath-by-breath pulmonary $O_2$ uptake ($\dot{V}_{O_{2p}}$) measurements. Subject's (men: $n = 10$; women: $n = 10$) $\Delta$[HHb] data were normalized to 100% of the response, plotted as a function $\dot{V}_{O_{2p}}$, $\%\dot{V}_{O_{2p}}$, power output (PO), and % PO, and fit with a piecewise double-linear regression model. The slope of the first segment of the double linear model was significantly greater in women compared to men when $\%\Delta$[HHb] was plotted as a function of $\dot{V}_{O_{2p}}$, $\%\dot{V}_{O_{2p}}$ and PO ($p < 0.05$). Both sexes displayed a near-plateau in the $\%\Delta$[HHb] which occurred at an exercise intensity near the respiratory compensation point. Thus, young women display a poorer ability to deliver $O_2$ to the exercising tissue compared to men and oxidative demands must be supplemented by a greater fractional $O_2$ extraction.

## 1. Introduction

At the onset of dynamic exercise, a rapid increase in blood flow to the vascular beds of the exercising tissue is initiated. This hyperemic response results from both an elevation in heart rate and systemic vascular conductance (Rowell et al., 1996). The increase in blood flow is necessary to sustain the metabolic demands of the tissue. As exercise intensity progressively increases (such as during ramp incremental exercise), systemic cardiac output ($\dot{Q}$) must increase in order to deliver sufficient oxygen ($O_2$) to the muscle. A coupling exists between $\dot{Q}$ and whole-body $O_2$ consumption ($\dot{V}_{O_2}$) such that their respective steady-state values during constant load exercise generally display a linear relationship over a range of exercise intensities (~5 L min$^{-1}$ increase in $\dot{Q}$ per 1 L min$^{-1}$ increase in $\dot{V}_{O_2}$) (Rowell, 1986). However, there is variability in the vascular control regulating blood flow to the exercising muscle ($\dot{Q}_m$) and its distribution for $O_2$ delivery to the active fibers.

There is accumulating evidence suggesting that the hyperemic response to exercise may be sex-specific. Young women have been shown to possess an enhanced blood flow response compared to young men during sub-maximal exercise (Parker et al., 2008). This observation may be a result of improved vasodilatory capabilities. Levenson et al. (2001) demonstrated an improved regulation of vascular tone in women in response to shear stress at rest and this sex-specific augmentation has also been observed in response to pharmacologically induced hyperemia (Dietz, 1999). These vasomotor differences at rest may be extended to exercise conditions, as young women have exhibited augmented vasodilatory limb responses to both graded single-leg knee-extension (Parker et al., 2007) and leg cycling exercise (Koch et al., 2005). While augmented vasodilatory capabilities in women seem to improve local blood flow, reduced tonic sympathetic activity (Christou et al., 2005), lower operating mean arterial pressure at rest and during exercise (Gonzales et al., 2007), as well as sex-specific hormonal effects (Rogers and Sheriff, 2004) may also contribute to an improved tissue perfusion in women during dynamic exercise.

If women have an improved supply of blood to the active muscle during exercise, then this improved $O_2$ delivery would likely reduce the required fractional $O_2$ extraction for a given $\dot{V}_{O_{2p}}$ compared to men. Near-infrared spectroscopy (NIRS) has been used to examine the dynamic balance between local $O_2$ delivery and $O_2$ consumption within the microvasculature. The concentration changes of the NIRS-derived deoxygenated hemoglobin ($\Delta$[HHb]) signal provide insight into the relationship between $\dot{Q}_m$ and muscle $\dot{V}_{O_2}$ and has been used in the past to examine temporal changes in fractional $O_2$ extraction during ramp incremental exercise (Ferreira et al., 2007b; Chin et al., 2011; Spencer et al., 2012). Recently, for example, Boone et al. (2009) demonstrated a rightward shift (based upon a symmetrical sigmoid model) in the $\Delta$[HHb] profile (indicating a lower fractional $O_2$ extraction relative to exercise intensity) in trained versus untrained males during ramp incremental exercise. The rightward shift in the [HHb] profile in the trained group was attributed to a greater muscle perfusion relative to metabolic

---

* Corresponding author at: School of Kinesiology, University of Western Ontario, London, ON, Canada N6A 3K7. Tel.: +1 519 661 1606; fax: +1 519 661 2008.
*E-mail address:* dpaterso@uwo.ca (D.H. Paterson).

1569-9048/$ – see front matter © 2013 Elsevier B.V. All rights reserved.
http://dx.doi.org/10.1016/j.resp.2013.08.011

demand in those subjects. The appropriateness of the sigmoid model for comparative purposes has been challenged recently, and an alternative 'double-linear' model has been proposed (Spencer et al., 2012); using the proposed model, a greater slope in the first component (i.e., $m_1$) indicates a greater reliance on fractional $O_2$ extraction. Furthermore, the second component ($m_2$) has previously been reported to 'level out' indicating an $\Delta$[HHb] breakpoint ($\Delta$[HHb]-*BP*) (Spencer et al., 2012), which may be associated with transitions in exercise intensity domains between moderate, heavy, or very heavy exercise. The purpose of the present study was to examine sex-specific differences in the temporal profiles of microvascular fractional $O_2$ extraction ($\Delta$[HHb]) during ramp incremental exercise. We hypothesized that in women the previously suggested augmented hyperemic (bulk blood flow) exercise response relative to men would be demonstrated as a diminished $m_1$ compared to men when the $\Delta$[HHb] profile was plotted as a function of relative (i.e., % of peak) power output ($PO_{peak}$) or pulmonary $\dot{V}_{O_2}$ ($\dot{V}_{O_{2p}}$), suggesting a reduced reliance on local fractional $O_2$ extraction relative to men during ramp incremental cycling exercise. We further hypothesized that when the $\Delta$[HHb] profile was plotted as a function of absolute PO or $\dot{V}_{O_{2p}}$, women would show a steeper $m_1$ compared to men, reinforcing the idea that changes in the $\Delta$[HHb] signal reflect the relative intensity, and not the absolute energy demand. An additional aim of the study was to characterize the $\Delta$[HHb]-*BP* by comparing it with other 'threshold' indices that manifest during ramp incremental exercise (gas exchange threshold [GET] and respiratory compensation point [RCP]).

## 2. Methods

### 2.1. Subjects

Ten young men (24 ± 5 yr; 82 ± 10 kg; 181 ± 6 cm [mean ± SD]) and 10 young women (22 ± 2 yr; 65 ± 7 kg; 171 ± 8 cm) volunteered and gave written informed consent to participate in the present study. The data presented in this study are part of a larger project designed to also examine central and peripheral adjustments of $\dot{Q}$ and arterial-venous $O_2$ differences (a-$vO_{2diff}$) related to the absolute increments in $\dot{V}_{O_2}$ on a minute-by-minute basis (Murias et al., 2013) without considering sex-related differences. In the present study the normalized $\Delta$[HHb] responses were analyzed on a second-by-second basis for both the absolute and relative PO and $\dot{V}_{O_2}$ in women and men, separately. However, the parameter estimates for the $\Delta$[HHb] fits for the absolute $\dot{V}_{O_2}$ only were reported as descriptive data but not discussed in the mentioned study. The present design allowed us to answer two different research questions while minimizing the unnecessary involvement of separate groups of research participants. The study was conducted according to the Declaration of Helsinki and all procedures were approved by The University of Western Ontario Research Ethics Board for Health Sciences Research Involving Human Subjects. All subjects were recreationally active, non-obese (body mass index $\leq 30\,kg\,m^{-2}$) and non-smokers.

### 2.2. Protocol

On two separate days separated by at least 48 h, but not more than 2 weeks, subjects reported to the laboratory to perform a fatigue-limited ramp incremental test (with 4 min at 20 W and then a $20\,W\,min^{-1}$ ramp) on a cycle ergometer (model: Lode Corival 400; Lode B.V., Groningen, Holland). Maximal $\dot{V}_{O_{2p}}$ ($\dot{V}_{O_{2max}}$) and peak PO ($PO_{peak}$) were determined. $\dot{V}_{O_{2max}}$ was defined as the highest 20-s $\dot{V}_{O_{2p}}$ computed from a rolling average and $PO_{peak}$ was identified as the highest PO achieved during the ramp incremental test corresponding to $\dot{V}_{O_{2max}}$.

### 2.3. Measurements

Local muscle deoxygenation ($\Delta$[HHb]) profiles of the quadriceps vastus lateralis muscle were made with NIRS (Hamamatsu NIRO 300, Hamamatsu Photonics, Hamamatsu, Japan) throughout exercise. Briefly, optodes were placed on the belly of the muscle midway between the lateral epicondyle and greater trochanter of the femur. The system consisted of both an emission probe that carries NIR light from the laser diodes and detector probe (interoptode spacing = 5 cm); optodes were housed in an optically dense plastic holder and secured on the skin surface with tape and then covered with an optically dense, black vinyl sheet, thus minimizing the intrusion of extraneous light. The thigh was wrapped with an elastic bandage to minimize movement of the optodes. Four laser diodes ($\lambda$ = 775, 810, 850, and 910 nm) were pulsed in a rapid succession and the light returning from the tissue was detected by the photodiode for online estimation and display of the concentration changes from the resting baseline of $\Delta$[HHb]. Changes in light intensities were recorded continuously at 2 Hz and transferred to a computer for later analysis. The NIRS-derived signal was zero set with the subject sitting at rest on the cycle ergometer prior to the onset of baseline (i.e., 20 W) exercise.

Breath-by-breath gas-exchange measurements similar to those previously described (Babcock et al., 1994) were also made continuously during each exercise protocol. Briefly, inspired and expired flow rates were measured using a low dead space (90 mL) bidirectional turbine (Alpha Technologies VMM 110) which was calibrated before each test using a syringe of known volume. Inspired and expired gases were continuously sampled (50 Hz) at the mouth and analyzed for concentrations of $O_2$, $CO_2$, and $N_2$ by mass spectrometry (Perkin Elmer MGA-1100) after calibration with precision-analyzed gas mixtures. Changes in gas concentrations were aligned with gas volumes by measuring the time delay for a square-wave bolus of gas passing the turbine to the resulting changes in fractional gas concentrations as measured by the mass spectrometer. Data were transferred to a computer, which aligned concentrations with volume information to build a profile of each breath. Breath-by-breath alveolar gas exchange was calculated by using algorithms of Beaver et al. (1981).

### 2.4. Data analysis

$\dot{V}_{O_{2p}}$ data were filtered by removing aberrant data points that lay outside 4 SD of the local mean and then linearly interpolated to 1 s intervals. The second-by-second $\dot{V}_{O_{2p}}$ data from tests one and two were time-aligned and ensemble-averaged to yield a single averaged response for each subject for the ramp incremental exercise protocol; the second-by-second $\Delta$[HHb] data were time-aligned and ensemble-averaged in the same manner. As described by Boone et al. (2010), $\dot{V}_{O_{2p}}$ data were left-shifted by 20-s to account for the circulatory transit delay between muscle and lung; this was undertaken so that changes in "muscle $\dot{V}_{O_2}$" (represented by $\dot{V}_{O_{2p}}$) were aligned with changes in the $\Delta$[HHb] signal. Though this 20-s value may not precisely match the circulatory time lag in all individuals, our laboratory has recently described the limitations and challenges associated with its determination (Murias et al., 2011), and overall, this 20-s value represents a reasonable estimate for the group tested. These averaged and time-aligned $\dot{V}_{O_{2p}}$ and $\Delta$[HHb] responses were then normalized from 0% to 100% such that 0% represented the respective steady-state values observed during 20 W cycling and 100% represented the highest average value observed in any continuous 20 s of exercise.