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Cerebral oxygenation declines at exercise intensities above the respiratory compensation threshold

Yagesh Bhambhani [a,*], Rohit Malik [a], Swapan Mookerjee [b]

[a] *Faculty of Rehabilitation Medicine, University of Alberta, Edmonton, Canada*
[b] *Bloomsburg University, Bloomsburg, Pennsylvania, USA*

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Abstract

During incremental exercise Pa_{CO_2} and PET_{CO_2} begin to decline at the respiratory compensation threshold (RCT-GEX). Since Pa_{CO_2} alters cerebral blood flow it was hypothesized that there would be a systematic decline in cerebral oxygenation (Cox) measured by near infrared spectroscopy above the RCT (RCT-NIRS). Cardiorespiratory and NIRS responses were simultaneously monitored from the left frontal lobe during incremental exercise in 17 men. All subjects showed a decline in Cox above the RCT-GEX with a 20–40 s delay. Significant differences ($P < 0.01$) were observed between the RCT-GEX and RCT-NIRS for time (9.83 versus 10.39 min), power (198 versus 212 W) and oxygen uptake (2.31 versus 2.43 L min^{-1}). Intra-class correlations for power and absolute $\dot{V}O_2$ were 0.97 and 0.98, respectively. Bland–Altman analysis revealed no outliers for any of the variables. The results suggested that the decrease in Cox observed above the RCT was most likely due to a reduction in cerebral blood flow mediated by a decline in Pa_{CO_2} This decline in Cox could reduce neuronal activation thereby limiting maximal exercise capacity in healthy subjects.

Keywords: Brain oxygen saturation; End tidal carbon dioxide; Cycling exercise

1. Introduction

Although the relationship between the metabolic and respiratory gas exchange responses during incremental exercise has been well established, little is known about their effects on cerebral tissue. Middle cerebral artery blood flow and velocity increase systematically during dynamic exercise (Gonzales-Alonso et al., 2004; Jorgensen et al., 2000; Panerai et al., 1999). However, during submaximal exercise continued to exhaustion (Ogoh et al., 2005), cerebral blood velocity decreased significantly and was correlated with arterial carbon dioxide (Pa_{CO_2}) levels. A limitation of these findings is that cerebral blood flow and velocity measurements do not indicate the localized oxygen status of cerebral tissue.

Near infrared spectroscopy (NIRS) is a non-invasive optical technique that is based on the differential absorption properties of chromophores in the near infrared region; i.e. between 700 and 1000 nm (Obrig and Villringer, 1997; Simonson and Piantidosi, 1996). The chromophores that absorb infrared light in cerebral tissue are hemoglobin (Hb) and cytochrome oxidase. At 760 nm, hemoglobin occurs primarily in the deoxygenated form (deoxyHb), whereas at 850 nm it occurs in the oxygenated state (oxyHb). The difference in absorbency between these two wavelengths indicates the relative change in oxyHb saturation at the arterioles, capillaries and venules, whereas the sum of the absorbencies indicates the relative change in localized blood volume. The validity of NIRS in evaluating changes in cerebral oxygenation and blood volume has been established under a variety of experimental conditions including: jugular bulb venous oxygen saturation which is considered an index of mixed cerebral oxygenation (Pollard et al., 1996), blood oxygen level dependent (BOLD) changes measured by functional MRI (Kleinschmidt et al., 1996), and cerebral blood flow measured by transcranial Doppler sonography (Hirth et al., 1997). While several studies have documented the acute changes in cerebral oxygenation and blood volume during submaximal (Ide et al., 1999), maximal (Gonzales-Alonso et al., 2004; Nielsen et al., 1999, 2001; Ogoh et al., 2005) and supramaximal (Shibuya et al., 2004) exercise using NIRS, the relationship between these changes and the metabolic and respiratory gas exchange responses dur-

* Corresponding author at: Room 373 Corbett Hall, Faculty of Rehabilitation Medicine, University of Alberta, Edmonton, Canada T6G 2G4.
Tel.: +1 780 492 7248; fax: +1 780 492 4628.
E-mail address: yagesh.bhambhani@ualberta.ca (Y. Bhambhani).

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ing stepwise incremental exercise has not been systematically evaluated.

It has been well documented that Pa_{CO_2} levels play an important role in regulating cerebral blood flow (Edwards et al., 2002; Madden, 1993; Vovk et al., 2002). An increase in Pa_{CO_2} induces cerebral vasodilation thereby increasing blood flow, while a decrease in Pa_{CO_2} has the opposite effect. During stepwise incremental exercise to voluntary fatigue, Pa_{CO_2} systematically increases until the respiratory compensation threshold (RCT), following which there is a continuous decrease until the $\dot{V}O_{2max}$ is attained (Takano, 2000; Wasserman, 1986). Therefore, it can be hypothesized that during incremental exercise, there will be a systematic decrease in cerebral blood flow at the RCT that would result in concomitant decreases in cerebral blood volume (Cbv) and cerebral oxygenation (Cox) measured by NIRS. To date, this hypothesis has not been tested. Therefore, the purposes of this study were to: (1) examine the acute cardiorespiratory, Cbv and Cox responses during stepwise incremental exercise to voluntary fatigue in healthy subjects, and (2) test whether the decrease in Pa_{CO_2} at the RCT elicits concomitant decreases in the Cbv and Cox responses measured by NIRS.

2. Methods

2.1. Subjects

Seventeen healthy male volunteers provided written informed consent to participate in this study. The mean ± S.D. for their age, height, body mass and body mass index were: 26.7 ± 8.6 years, 1.78 ± 0.06 m, 77.5 ± 9.3 kg and 24.1 ± 2.5 kg m^{-2}, respectively. The subjects had varying exercise patterns that ranged from no regular physical activity to regular endurance training several times per week (two subjects). Prior to exercise testing, the subjects completed a physical activity readiness questionnaire (Canadian Society for Exercise Physiology, 2002) to identify any contraindications to exercise. Thereafter, each subject completed one exercise session in a laboratory maintained at 21 °C and 40% relative humidity. The Health Research Ethics Board of this institution approved the testing procedures described below.

2.2. Cardiorespiratory and NIRS measurements

After recording age, height and body mass, the subject was prepared for the cardiorespiratory and NIRS measurements while remaining seated on the cycle ergometer (Corival 400, Quinton Instruments, Seattle, WA). The seat height was adjusted so that there was a slight bend in the knee joint when the pedal was at its lowest point. The metabolic cart (Vmax, Sensormedics, CA) was then calibrated using medical grade precision gases (26% oxygen, balance nitrogen; 16% oxygen, 4% carbon dioxide, balance nitrogen). The mass flow sensor was calibrated using a 3 L syringe. Heart rate was recorded continuously with an electrocardiogram that was interfaced with the metabolic cart.

The cerebral NIRS probe (MicroRunman, NIM Inc., Philadelphia, PA) had a separation distance of 4 cm between the light source and the optodes. The probe was placed over the left pre-frontal lobe, approximately 3 cm from the midline and just above the supra-orbital ridge (Kleinschmidt et al., 1996; Obrig et al., 1996). It was secured with a tensor bandage wrapped around the forehead, taking sufficient care to ensure that there was no loss of background light. The metabolic headgear was placed over the probe so as to prevent it from moving. The probe was then calibrated with the NIRCOM software (NIM Inc. Philadelphia, PA) using the following specifications: (1) light intensity between 100 and 120 mV, and (2) moderate penetration which resulted in the light being transmitted to a depth of approximately 2.5 cm from the skin surface. Tissue absorbency measurements were recorded and converted into optical density (OD) units using the modified Beer–Lambert law (Simonson and Piantidosi, 1996). The difference in OD between these two wavelengths was considered an index of Cox, whereas the sum signal reflected the relative change in Cbv. Previous research has indicated that in some instances this probe positioning may not elicit Cbv and Cox measurements (Obrig et al., 1996; Ogoh et al., 2005). In such cases, slight modification of the probe position is required. Therefore, the spectrometer was started prior to the exercise test to ensure that proper NIRS measurements were being recorded. In two instances, the probe position had to be adjusted slightly so as to obtain proper NIRS recordings. A reliability coefficient of 0.88 for the change in oxyHb measurements using this probe placement has been reported (Koike et al., 2004) in heart failure patients during upright cycle exercise.

2.3. Incremental exercise test protocol

After completing the above procedures, the subject rested on the cycle ergometer in an upright position for 2 min to collect baseline cardiorespiratory and NIRS measurements. Thereafter, the power was increased by 30 W every 2 min until voluntary fatigue, or attainment of at least two of the following criteria (American College of Sports Medicine, 2001) for $\dot{V}O_{2max}$: (i) age predicted maximum heart rate calculated as (220 − age), (ii) levelling off or an increase in the oxygen uptake which was <100 ml/min with increasing power, and (iii) a respiratory exchange ratio >1.10. The subject was instructed to maintain an upright posture and avoid gripping the cycle handlebars during the test. Cardiorespiratory responses were continuously monitored using the computerized metabolic measurement cart in the breath-by-breath mode. In this study Pa_{CO_2} was not directly measured. Instead, end tidal carbon dioxide (PET_{CO_2}) values recorded during the breath-by-breath gas exchange responses were used as an index of Pa_{CO_2} (Nielsen et al., 2001; Ogoh et al., 2005). The cardiorespiratory and NIRS measurements were time aligned and averaged over 20 s intervals for subsequent analysis.

2.4. Detection of the respiratory compensation threshold

For each test, an independent evaluator who was experienced in interpreting respiratory gas exchange measurements, but was unaware of the study objectives identified the RCT (RCT-GEX).