Respiratory Physiology & Neurobiology 201 (2014) 15–23

Contents lists available at ScienceDirect

Respiratory Physiology & Neurobiology

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

Precise mimicking of exercise hyperpnea to investigate the oxygen cost of breathing

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ARTICLE INFO

Article history:
Accepted 17 June 2014
Available online 27 June 2014

Keywords:
Oxygen consumption of respiratory muscles
Respiratory mechanics
Respiratory muscles
Ventilation
Work of breathing

ABSTRACT

The oxygen cost of exercise hyperpnea ($\dot{V}_{O_2RM}$) has been quantified using a variety of techniques with inconsistent findings. Between-study variation relates to poor control of breathing patterns and lung mechanics. We developed a methodology allowing precise matching of exercising WOB in order to estimate $\dot{V}_{O_2RM}$. Thirteen healthy young subjects (7 male) completed an incremental cycle exercise test, familiarization and experimental days where exercise hyperpnea was mimicked. On experimental days, feedback of exercise flow, volume and the respiratory pressures were provided while end-tidal CO_2 was kept at exercise levels during each 5-min trial. Minute ventilation levels between 50 and 100% maximum were mimicked 3–5 times. The r^2 between exercise and mimic trails was 0.99 for frequency, tidal volume and minute ventilation; 0.86 for esophageal pressure swings and 0.93 for WOB. The coefficient of variation for ($\dot{V}_{O_2}$) averaged 4.3, 4.4 and 5.7% for 50, 75 and 100% ventilation trials. When WOB and other respiratory parameters are tightly controlled, the $\dot{V}_{O_2RM}$ can be consistently estimated.

1. Introduction

With increasing exercise intensity, the higher metabolic demands necessitate a corresponding increase in expired minute ventilation ($\dot{V}_E$). As $\dot{V}_E$ rises, the mechanical work of breathing (WOB) also increases and does so in a hyperbolic fashion (Otis et al., 1950). Work is linearly related to oxygen uptake (Astrand and Rodahl, 1986) therefore, exercise-induced increases in the WOB require a parallel increase in the rate of respiratory muscle oxygen consumption ($\dot{V}_{O_2RM}$). Since the WOB-$\dot{V}_E$ relationship is non-linear (Otis, 1964), it stands to reason that the relation between $\dot{V}_{O_2RM}$-$\dot{V}_E$ would follow a similar function. Thus, in order to fully characterize the oxygen cost of exercise hyperpnea it is necessary to use a wide range of $\dot{V}_E$ values.

There have been numerous attempts to quantify the $\dot{V}_{O_2RM}$ using different methods and the results have varied considerably (Whipp and Pardy, 2011). Not only do the overall techniques vary, but also the duration, level of ventilation and specific population studied (i.e. healthy or clinical) are varied. Not surprisingly, the myriad of methodologies employed has resulted in considerable variation in $\dot{V}_{O_2RM}$ between studies. For example, at a $\dot{V}_E$ of 100 l min^{-1} the reported $\dot{V}_{O_2RM}$ can vary from 50 to 320 ml min^{-1}(Roussos and Campbell, 1986). Some investigators have had subjects breathe at fractions of maximal voluntary ventilation which often results in hyperflation and tachypneic breathing resulting in the WOB being substantially higher (20–300% greater) than what is commonly observed during "natural" breathing patterns (Klas and Dempsey, 1989). The linear work-$\dot{V}_{O_2}$ relationship requires that WOB be controlled, otherwise poor estimates of $\dot{V}_{O_2RM}$ are made (Aaron et al., 1992a). During voluntary hyperpnea, breathing becomes conscious and tidal volume (V_T), breathing frequency (f_R), inspiratory time and respiratory muscle recruitment may differ from patterns observed during spontaneous breathing during exercise (Otis et al., 1950). The potential result from the unstructured conscious breathing is unnatural and inefficient patterns contributing to greater WOB. Thus, in order to accurately assess $\dot{V}_{O_2RM}$ it is crucial that all aspects of exercise hyperpnea are carefully reproduced in order to ensure inspiratory and expiratory work are identical.

Most methods used to estimate $\dot{V}_{O_2RM}$ result in a different end-tidal CO_2 (PET_{CO_2}), compared to what would normally be observed during exercise. Changes in PET_{CO_2} are used as a surrogate for

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http://dx.doi.org/10.1016/j.resp.2014.06.010
1569-9048/

arterial P_{CO_2}, which is known to affect pulmonary and systemic vasculature (Dale and Evans, 1922; Dorrington et al., 2010; Kregenow and Swenson, 2002). As such, voluntary mimicking of exercise hyperpnea with PET_{CO_2} maintained at levels similar to each exercise stage is necessary in order to provide the best estimate of $\dot{V}_{O_2RM}$.

Accordingly, the purpose of this study was to develop an improved methodology for estimating $\dot{V}_{O_2RM}$ by voluntary hyperpnea and to determine its ability to reproduce exercise breathing patterns and mechanics. The current paper describes a new methodology for providing visual on-line feedback of many exercise related parameters and the maintenance of end-tidal gases. We hypothesized that with extensive feedback aimed at accurately mimicking exercise breathing pattern and WOB, we would be able to consistently estimate the $\dot{V}_{O_2RM}$.

2. Methods

2.1. Subject characteristics

Thirteen subjects (7 male) participated after providing written informed consent. All procedures were approved by the Clinical Research Ethics Board at the University of British Columbia. Subjects were healthy nonsmokers, had no history of cardiopulmonary diseases, had normal pulmonary function (all values >90% predicted (Tan et al., 2011)) and regularly engaged in physical activity.

2.2. Overview

Subjects visited the laboratory on four occasions (Days 1–4). The second testing day occurred a minimum of 48 h after the first testing day, while the other visits were separated by 24 h to 1 week. Baseline pulmonary function tests and a graded maximal exercise test on a cycle ergometer were completed on Day 1. The second day served to familiarize the subjects with the voluntary hyperpnea protocol. On Days 3 and 4 subjects mimicked their exercise breathing patterns while resting in their cycling position. Subjects were instrumented with esophageal and gastric balloon catheters on the 1st, 3rd and 4th testing day.

2.3. Maximal exercise test (Day 1)

Subjects completed an incremental cycle exercise test to exhaustion using a stepwise protocol on an electromagnetically braked cycle ergometer (Excalibur Sport, Lode, the Netherlands). Prior to the maximal test, the bike and handle bars were adjusted and a 10 min self-selected warm-up was completed. Exercise started at 80 W for women and 120 W for men, and both increased in 20 W increments every 2 min. The test was terminated when the subjects could no longer maintain a cadence of >60 rpm despite verbal encouragement.

2.4. Data acquisition

During all tests, raw data (flow, pressures, end-tidal, inspired gas fractions and mixed-expired gases) were recorded continuously at 200 Hz using a 16-channel analog-to-digital data acquisition system (PowerLab/16SP model ML 795, ADInstruments, Colorado Springs, CO, USA) and stored on a computer for subsequent analysis.

Ventilatory and mixed expired metabolic parameters were gathered using a customized metabolic cart consisting of independent inspired and expired pneumotachographs (model 3818, Hans Rudolph, Kansas City, MO, USA), and two pairs of independently calibrated O_2 and CO_2 analyzers (SA/II and CD-3A respectively; Applied Electrochemistry, Pittsburgh, PA, USA). Inspired fractions of O_2 (FI_{O_2}) and CO_2 (FI_{CO_2}) were determined by sampling gas on the inspired circuit immediately before the inspired pneumotachograph and expired gas fractions were determined by sampling from a mixing chamber distal to the expired pneumotachograph (Fig. 1). During exercise (Day 1) subjects inspired room air. End-tidal CO_2 was sampled at the mouth through a port in the mouthpiece of a two-way non-rebreathing valve (Hans Rudolph 2700B, Hans Rudolph, Kansas City, MO, USA) and connected to a calibrated CO_2 analyzer (Vacumed model 17630, Ventura, CA). The inspiratory and expiratory portions of the two-way non-rebreathing valve were connected to the pneumotachographs via wide bore tubing. At the highest relevant flows ($\sim 9\,l\,s^{-1}$) the difference in apparatus resistance between the exercise trials and hyperpnea trials was $0.1\,cm\,H_2O\,l^{-1}\,s^{-1}$.

Mouth pressure (PM) was sampled through a second port in the mouthpiece while esophageal (PES) and gastric (PGA) pressures were measured by balloon-tipped catheters (no. 47-9005, Ackrad Laboratory, Cranford, NJ, USA). The balloon catheters were placed after application of a topical anesthetic and were passed through the nose and positioned according to previously described techniques (Milic-Emili et al., 1964). Pressures were measured by a piezoelectric pressure transducer (Raytech Instruments, Vancouver, BC, CA), and calibrated by a digital manometer. Transdiaphragmatic pressure (PDI) and transpulmonary pressure (PTP) were calculated from the difference of PGA and PES, and PES and PM, respectively.

Operational lung volumes were determined at rest, each exercise stage and each hyperpnea trial by inspiratory capacity (IC) maneuver. If the IC maneuver was not performed adequately, another IC maneuver was prompted before the end of the stage or trial. End expiratory lung volume (EELV) was calculated by subtracting the IC volume from the forced vital capacity (FVC) volume. End-inspiratory lung volume (EILV) was calculated as the sum of V_T and EELV. Maximal expiratory flow-volume curves were developed using pre and post exercise FVCs (to account for bronchodilation) and with different efforts (to account for thoracic gas compression) while the subject was seated in cycling position on the bicycle ergometer; methods for collection have been described previously (Dominelli et al., 2011; Guenette et al., 2010).

A heart-rate monitor (S610i, Polar Electro, Kempele, Finland) was worn on the chest, and heart rate was recorded every minute. Blood pressure was obtained with an automated blood pressure cuff (UA-767, Life Source).

2.5. Exercise analysis

Cardio-respiratory parameters were averaged over the last 30 s of each exercise stage and at maximal intensity. Composite average flow-volume and pressure-volume loops were constructed by signal averaging the breaths within the 30 s average. Errant breaths or erroneous noise such as coughing or swallowing were individually excluded before the breaths were averaged. At every stage, flow-volume loops were placed within the maximal expiratory flow-volume curve according to EELV as determined by the IC maneuver. Using the composite average pressure-volume loops we determined the energetic WOB and divided the work into the constituent elastic and resistive components using modified Campbell diagrams (Dominelli and Sheel, 2012). All analysis was performed using customized software (GNAR^{x}, developed with LabView 2013, National Instruments, Austin, TX, USA)

2.6. Familiarization visit (Day 2)

Day 2 served to familiarize the subjects with the mimicking procedures and the extensive feedback provided (see Section 2.7). Between 2 and 5 trials of each workload were performed to allow