EFFECTS OF RESPIRATORY MUSCLE FATIGUE ON EXERCISE PERFORMANCE IN HEALTHY FEMALES

by

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Abstract

The respiratory system has not been traditionally considered a limiting factor in exercise performance however, several studies have demonstrated that respiratory muscle fatigue (RMF) occurs following high-intensity exercise as well as prolonged submaximal exercise. In order to investigate RMF as a limiting factor in exercise performance fatigue was induced in ten healthy female participants (Age = 26.8 ± 2.0 yrs; height = 165.7 ± 4.5 cm; weight = 57.3 ± 7.6 kg; $VO_{2\,max}$ 43.3 ± 4.7 $mL \cdot kg^{-1} \cdot min^{-1}$, range 35.8 to 49.5 $mL \cdot kg^{-1} \cdot min^{-1}$). Subjects were required to visit the lab on six separate occasions. Three test days served as control conditions where RMF was not induced and baseline measures of spirometry and exercise performance were measured. On the remaining three test days, RMF was induced and the subsequent effects on exercise performance were measured. Maximal test of aerobic capacity was performed on two of the six test days and on the remaining 4 test days participants performed tests of endurance performance. Subjects were instructed to breathe at 70% of their maximal voluntary ventilation (MVV) for 15-minutes to induce RMF. Following induction of RMF exercise performance was measured on an electronically braked cycle ergometer. Ventilation during the hyperpnea task equaled 72 to 75% MVV on the three days that RMF was induced. The induction of RMF did not significantly alter maximal aerobic power ($p = 0.111$), although, exercise was ceased at a significantly lower peak heart rate ($p = 0.002$) and peak minute ventilation ($p = 0.013$). Ratings of perceived exertion for the respiratory muscles muscles were significantly increased following the induction of RMF ($p = 0.003$). Endurance performance (time to exhaustion) was reduced from 408.0 ± 84.9 seconds to 320.3 ± 71.5 seconds following the induction of RMF ($p = 0.002$) without any associated changes in

VO_2, heart rate, or minute ventilation. The reduction seen in endurance performance time supports the hypothesis that a decreased time to exhaustion is seen with the induction of RMF. Maximal oxygen consumption did not decrease and therefore cannot support the hypothesis that $VO_{2\,max}$ will be reduced following RMF induction. Respiratory muscle fatigue appears to be a limiting factor in exercise performance in healthy females.

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List of Abbreviations

α	alpha
ANOVA	analysis of variance
B_f	breathing frequency
BPNS	bilateral phrenic nerve stimulation
CMS	cervical magnetic stimulation
DC	duty cycle
DI	dyspnea index
EELV	end-expiratory lung volume
EPT	endurance performance test
FEV_1	forced expiratory volume in 1 second
$FEF_{25-75\%}$	forced expiratory flow at 25% to 75% of FVC
FEF_{max}	maximal forced expiratory flow
FVC	forced vital capacity
HG	hand grip
HR	heart rate
IC	inspiratory capacity
IFR	inspiratory flow rate
IRL	inspiratory resistive loading
MIP	maximal inspiratory mouth pressure
MVV	maximal voluntary ventilation
NS	non-significant
PFT	pulmonary function testing
$P_{di\ max}$	maximal diaphragmatic pressure
$P_{I\ max}$	maximal inspiratory pressure
PO	power output
RER	respiratory exchange ratio
RM	respiratory muscle
RMF	respiratory muscle fatigue
RMT	respiratory muscle training
RPE	rating of perceived exertion
$\%SaO_2$	percent arterial oxyhaemoglobin saturation
SVC	sustained ventilatory capacity
TTE	time to exhaustion
TV	tidal volume
V_E	minute ventilation
VO_2	rate of oxygen consumption
V_E/VO_2	ventilatory equivalent for oxygen
VCO_2	rate of carbon dioxide production
V_E/VCO_2	ventilatory equivalent for carbon dioxide
$VO_{2\ max}$	maximal oxygen consumption
W_{max}	maximal power output

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Introduction

Exercise places many demands on the pulmonary system. The major function of the respiratory system during exercise is to provide the working muscles with oxygen (O_2) and to remove excess carbon dioxide (CO_2) via the circulatory system. During exercise, large volumes of O_2 need to be delivered to and utilized by the working muscles, and during maximal exercise this value can increase up to 20 times normal O_2 uptake. Matching O_2 supply and demand is accomplished in three ways. Firstly, the number of capillaries that are open increases to allow for greater perfusion and gas exchange (Hlasta, 2001). Consequently, at maximal exercise intensities this causes mixed venous PO_2 content to fall below resting values (<20%) and increases mixed venous PCO_2 levels to greater than 80mmHg (Sheel, 2002), therefore placing extreme importance on alveolar to arterial gas exchange. Secondly, an increase in cardiac output helps to achieve oxygen delivery, and allows an increased blood flow through the lungs to pick up more O_2 (Hlasta, 2001). As another challenge to the pulmonary system, this increased cardiac output results in considerably less time for the pulmonary capillaries to accomplish the required gas exchange. Thirdly, in order for a precise regulation of alveolar PO_2 and PCO_2, alveolar ventilation must increase more than 20 times the resting values at maximal exercise (Sheel, 2002). Fortunately, a healthy respiratory system is capable of accomplishing this overwhelming task of force development, but it is crucial that the physiological cost to provide sufficient ventilation not be too great. Breathing pattern and duty cycle must also be precisely controlled. It is imperative that the respiratory and cardiovascular system responses to exercise are coordinated and precisely matched to the increase in metabolic requirements, and required gas exchange.

The potential importance of respiratory muscle fatigue or more specifically

inspiratory (diaphragm) muscle fatigue has become well recognized and for exercise physiologists it has become a concern as a limiting factor in exercise performance. The diaphragm is a highly oxidative, densely capillarized muscle, composed of approximately 55% slow oxidative type I (fatigue resistant) fibres; therefore the human diaphragm is traditionally considered capable of withstanding fatigue. This holds true in most cases, as during exercise to exhaustion at intensities less than or equal to 80% of $VO_{2\,max}$ the diaphragm in normal healthy individuals usually does not fatigue. Respiratory muscle fatigue has been documented to occur at end-exercise following high-intensity endurance exercise, as demonstrated with bilateral phrenic nerve stimulation (Johnson *et al.,* 1993). During high-intensity endurance exercise, high levels of ventilation need to be sustained, the increased diaphragmatic activity required to generate these levels of ventilation could by itself produce diaphragmatic fatigue (Mador *et al.,* 1996). This is cause for concern as the diaphragm is the primary muscle of inspiration as well as the most effective pressure generator for increasing alveolar ventilation. If the diaphragm is subject to fatigue following prolonged submaximal exercise and high-intensity short-term exercise, as it has been demonstrated by many authors (Loke *et al., 1982;* Johnson *et al.,* 1993; Mador and Dahuja, 1996; Ker and Schultz, 1996) it is possibly a limiting factor in exercise performance.

Given the demands on the respiratory system during heavy exercise, competition between respiratory and peripheral locomotor muscles for O_2 delivery may exist, and this hypothesis is supported by demonstration of reduced leg blood flow under conditions of increased respiratory work (Harms *et al.,* 1997). Thus exercise hyperpnea may impose a cost to the balance between central and peripheral oxygen demands, and reduce exercise

performance. The causes of fatigue remain somewhat unclear; they are complex and probably involve simultaneous changes at various sites within both the central nervous system and the muscle itself (Roussos and Moxham, 1985).

Techniques or methods used to induce and/or quantify respiratory muscle fatigue may include having the subject inspire against a resistive load, phrenic nerve stimulation, voluntary hyperpnea, or exercising at a percent of maximal work capacity (VO_2 max) to exhaustion. Mador, Rodis, and Diaz (1996) investigated whether or not diaphragm fatigue could be induced following hyperpnea at levels equal to or greater than 60% of 12-s MVV until task failure. The majority of the subjects demonstrated a 10% or greater reduction in transdiaphragmatic pressure. Mador and coworkers concluded that voluntary hyperpnea to task failure can reliably produce long-lasting fatigue of the diaphragm. Bai and his colleagues (1984) found similar results in their study and concluded that respiratory muscle fatigue induced by prior ventilatory work (short-term near-maximal normocapnic hyperpnea) impaired ventilatory muscle function and may limit endurance at high levels of ventilation.

In order to investigate whether respiratory muscle fatigue is a limiting factor in exercise performance several authors have unloaded the respiratory muscles during exercise and observed the effect on performance. Exercise performance is improved, it may suggest that respiratory muscle fatigue has an effect on exercise performance. Aaron *et al.,* (1985) examined the effect of helium/O_2 breathing on human performance in a group of rowers and found that exercise time increased by 40%. Harms and his colleagues (2000) also unloaded the respiratory muscle in attempt to observe the effects on exercise performance. They also supported the hypothesis that exercise performance

is affected by diaphragm fatigue but at work intensities greater than 90% $VO_{2\,max}$. Through techniques of loading the respiratory muscles (inspiratory resistive breathing) studies have shown that by fatiguing the diaphragm subsequent exercise performance is reduced. Mador and Acevedo (1991) induced diaphragm fatigue in their subjects using a resistive breathing protocol and measured subsequent high-intensity exercise performance. Exercise time was reduced following diaphragm fatigue and the authors concluded that respiratory muscle fatigue does indeed impair exercise performance. Other authors have been interested in the effects of ventilatory work on subsequent exercise, although increased ventilation is one of the most readily observed physiological responses to exercise, it is relatively unclear how severely this hyperpnea stresses the respiratory muscles. Martin, Heinzelman, and Chen (1982) compared short-term maximal running performance in nine subjects with and without prior ventilatory work (150-min sustained maximal ventilation) intended to decrease respiratory muscle endurance. They found that short-term running performance was reduced following the ventilatory work compared to the control group. Studies involving training of the respiratory muscles have provided evidence to support the idea that respiratory muscle fatigue impairs exercise performance, while other studies have shown no effect. Training of the respiratory muscles usually involves resistive training or hyperpnea protocols that result in an increase in respiratory muscle strength and endurance. Boutellier and his coworkers (1992) have demonstrated increases in respiratory muscle strength and endurance as well as modest increases in cycling performance in both healthy sedentary and active subjects. Although still being a controversial area in exercise physiology the results may indicate a respiratory limitation to exercise performance.

Investigation of respiratory muscle fatigue and its effects on subsequent exercise performance is a valid and major concern among exercise physiologists. Voluntary hyperpnea at a level equal to or greater than 60% of MVV represents a non-invasive, reliable method to induce respiratory muscle fatigue and can be demonstrated by a significant decrease in MVV values following the hyperpnea task (Mador *et al.*, 1996). This type of voluntary hyperpnea task mimics the experience of the RM during submaximal exercise, without the entire effects of whole body exercise. The effects of a 15-minute hyperpnea task at >70% MVV on subsequent exercise performance (endurance performance and exercise capacity) has not been investigated previously. Most studies have used small sample sizes, no control group and an inspiratory resistive loading (IRL) protocol to induce fatigue of the respiratory muscles. Results of the proposed study will provide additional knowledge on respiratory muscle fatigue and the implications on exercise performance. If RM fatigue is indeed found to be a limiting factor in exercise performance, implications for respiratory muscle training will be of importance for both athletes as well as in a clinical setting for rehabilitation of patients.

Hypotheses

1. Exercise performances, maximal aerobic power (VO_2max) will decrease following the induction of respiratory muscle fatigue.

2. Endurance performance, defined by time to exhaustion at 80% $VO_{2\,max}$ intensity, will decrease following the induction of respiratory muscle fatigue.

Methodology

Subjects

Ten healthy female subjects were recruited for this study from the University of British Columbia campus and Vancouver recreational and competitive athletic teams. A power calculation based on mean vales of maximal voluntary ventilation before and after a voluntary hyperpnea task from pilot data collected for this study was used to determine the number of subjects required (n=7.4 @ 80% power; α >0.05). A secondary power calculation was also performed (n=10 @ 80% power; α >0.05) using mean vales of endurance performance time before and after the induction of fatigue, provided in a study by Dodd and his colleagues (1989). Subjects were included if they were between the ages of 18 to 35 years, nonsmokers, without a history of pulmonary or respiratory disease and if they were recreationally fit or competitive athletes (VO_2max < 35 $mL \cdot kg^{-1} \cdot min^{-1}$ to >50 $mL \cdot kg^{-1} \cdot min^{-1}$). Subjects were required to perform standard pulmonary function testing to determine lung function. For all testing periods (days), subjects were required to abstain from exhaustive exercise for 24 hours prior to testing, refrain from ingestion of alcohol or caffeine for 12 hours, and food or liquids other than water for 2 hours before the testing period. Subjects received consistent verbal encouragement throughout all exercise tests and the respiratory muscle fatiguing task. Each subject completed a Physical Activity Readiness Questionnaire (Par-Q) prior to testing. Subjects rated their sensations of breathlessness and leg discomfort throughout the testing protocols using the Dyspnea Index (DI) Borg (10-point) scale (please see Appendix E for details). Menstrual phase was recorded for each subject on each test day (for details please see Table 22).

EXPERIMENTAL PROTOCOL

Ethics approval was attained from the University of British Columbia Clinical Ethics Review Board. The subjects were provided with a written description of the testing procedures prior to the first testing session. Following written informed consent, the subjects were asked to complete 6 testing sessions. All testing sessions took place at the Exercise Physiology Laboratory located in the Allan McGavin Sports Medicine Centre at the University of British Columbia. During the first testing session (day 1), descriptive subject data was collected (age, height, weight). Spirometry measures that were performed (Medgraphics CPX-D Metabolic Cart, St. Paul, Minnesota) included: forced vital capacity (FVC), forced expiratory volume in one second (FEV_1), forced expiratory flow at 25% to 75% of FVC ($FEF_{25-75\%}$), and maximal voluntary ventilation (MVV).

Maximal Voluntary Ventilation (MVV)

On test day 1, the subjects became familiarized with the MVV breathing endurance test. The MVV maneuver requires the subject to as best they can breathe as quickly and deeply as possible for a 12-second period, and maximal ventilation ($L \cdot min^{-1}$) is extrapolated. The test was repeated until 3 consistent values within 5% of each other were obtained. The highest maximal ventilation achieved was used to determine the level at which the subjects breathed during the voluntary hyperpnea task.

Maximal Aerobic Power ($VO_{2\,max}$): Day 1(control) and Day 2

Five minutes following the familiarization period the subjects engaged in an incremental exercise test to evaluate VO_2max. For attainment of VO_2max, the subjects warmed-up on an electronically braked cycle ergometer (LODE Excalibur, Groningen, the Netherlands) for 3 minutes at a self-selected power output. All subjects then

performed an exercise test to exhaustion using a ramp protocol beginning at 75-W and increasing by 25-watts·min^{-1} to exhaustion. VO_2 max was accepted upon the basis of reaching three of the four following criteria: (1) ±10% of the age-adjusted maximum heart rate, (2) RER value of 1.1 or greater, and/ or (3) VO_2 plateau (<150 ml·min^{-1z}) with increasing power output and/ or (4) volitional fatigue. Heart rate was monitored during the test and recorded every 15 seconds using a telemetric heart rate monitor (Polar Vantage XL, Finland). During exercise the subjects breathed room air through a low resistance, two-way non-rebreathing valve (Hans Rudolph). Ventilatory parameters were measured for the duration of the test using a 5-L mixing chamber for collection of expired gases. Average ventilatory and gas exchange parameters were recorded every breath and averaged over 15-seconds using a computerized system (Physio-Dyne, Flo II). Inspired ventilation was measured with a flow meter (Physio-Dyne, Flo II). Percent arterial oxyhaemobglobin saturation (%SaO_2) was measured using ear oximetry and reported every 15-seconds (Ohmeda Biox 3740 pulse oximeter). In order to increase ear lobe perfusion, the pinna was rubbed with a vasodilatory nicotine cream (Finalgon, Boehringer Ingelheim). Dyspnea Index scores (leg and respiratory effort) using the Borg scale were recorded once every minute of exercise. Maximal voluntary ventilation was measured at 3- and 5-minutes post-exercise. Following the aerobic fitness test, the subjects had the opportunity to become familiarized with the respiratory muscle fatiguing equipment to be used in the following testing sessions. Please see Figure 2 for flow chart of experimental protocol.

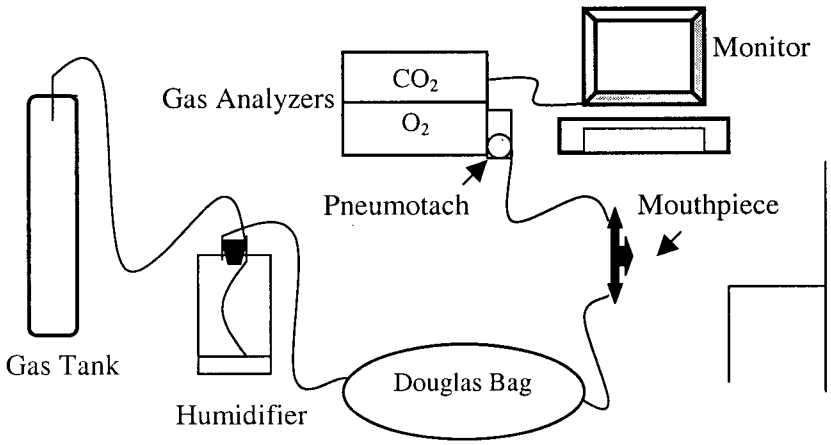
Protocols for the 5 remaining test days were randomly assigned for each participant. Test day 2 (experimental condition) began with the subjects performing a

MVV maneuver, the highest of 3 consistent values (within 5%) was used to calculate 70% MVV used in the respiratory muscle (RM) fatiguing task. Subjects underwent the 15-minute RM fatiguing task (details to follow). In order to ensure the subjects were fully motivated hand grip (HG) strength was measured before and immediately after the induction of RM fatigue. The subjects gripped a hand dynamometer (Lafayette Instrument Co) with maximal strength using their dominant hand for approximately one second. Hand grip strength measurements were repeated twice for each trial to ensure maximal strength was achieved, the highest value was recorded. Immediately following the RM fatiguing task the subject's MVV was measured (@ 1- and 2-minutes post fatigue) to ensure RM fatigue had occurred. After the last MVV measurement the subject immediately underwent a VO_2max test (same as day1). Maximal voluntary ventilation was measured at 3- and 5-minutes post-exercise.

Respiratory Muscle Fatiguing Task

On test days 2, 3, and 4 the subjects engaged in a 15-minute hyperpneic RM fatiguing task before engaging the exercise protocols. While wearing a noseclip the subjects breathed through a low resistance 2-way non-rebreathing valve (Hans Rudolph) receiving air from a Douglas Bag with a known gas concentration (21% O_2, 5% CO_2, and balance nitrogen). Gas was warmed and humidified via a 30-L plastic container filled (~2-L) with warm water. The subjects were instructed to breathe at a ventilation level equal to or greater than 70% of their MVV for 15-minutes (see Figure 1). The target ventilation was achieved through visual feedback of ventilation (L·min) on a computer monitor (Physio-Dyne System, Flo II), and encouragement was provided verbally throughout

Figure 1. RM Fatiguing Task Set-up



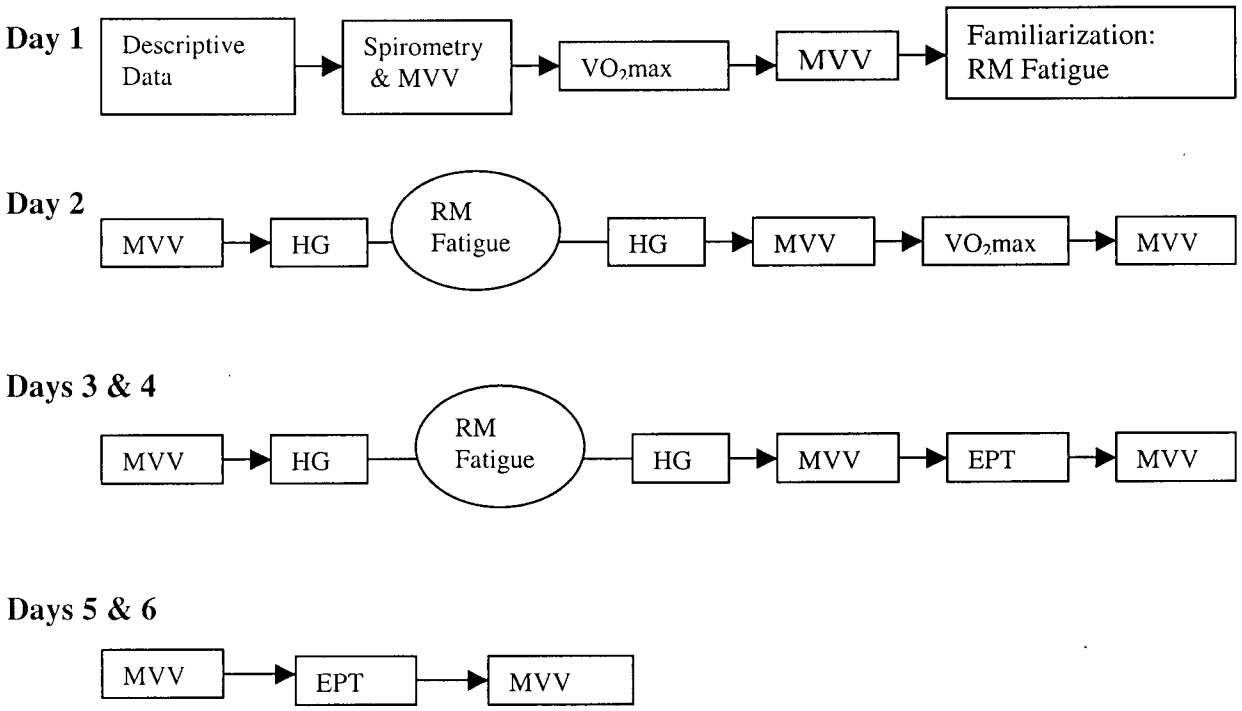
Endurance performance exercise (80% peak power output): Test days 3, 4 (experimental) and days 5, 6 (control)

Experimental test days 3 and 4 proceeded as day 2; measuring MVV and inducing RM fatigue using similar protocol as above. This test was repeated twice in order to reduce intrasubject variability. Hand grip strength was again measured before and immediately following the induction of RM fatigue. Maximal voluntary ventilation was measured post induction of RM fatigue at 1- and 2-minutes, followed immediately by an endurance performance test (EPT). The EPT was conducted at a power output corresponding to the workload at 80% VO_2max obtained on day 1. This test was performed on the same cycle ergometer as day 1 set at a constant workload to exhaustion. During the first minute of exercise the workload was increased incrementally until the 80% VO_2max workload was reached. Heart rate, %SaO_2, ventilation and gas exchange variables were measured. Dyspnea index (DI) and leg discomfort scores were also recorded each minute during exercise. Time to exhaustion (TTE) was recorded at the point at which the subject reached volitional fatigue and ceased exercise, or when the

subject could no longer maintain 40 rpm on the cycle ergometer. Maximal voluntary ventilation was measured at 3- and 5-minutes following exercise.

Test days 5 and 6 were used as control conditions and did not involve the induction of RM fatigue. The subjects were required to do an EPT as described for test 3 and 4. Heart rate, DI and leg discomfort, $\%SaO_2$, ventilation and gas exchange parameters were recorded. Maximal voluntary ventilation was measured previous to exercise and at 3- and 5-minutes post exercise.

Figure 2. Flow Chart of Experimental Protocol



Statistical Analysis

Mean differences in maximal voluntary ventilation (MVV), before and after the induction of respiratory muscle fatigue were analyzed using one-way analysis of variance (ANOVA) with repeated measures; statistical significance was set at $\alpha \leq 0.05$. A

Tukey's HSD post hoc measure was used to make multiple comparisons among the treatment means and to determine where the significant differences exist. A repeated measures paired t-test was performed on aerobic test values from day 1 and day 2; statistical significance was set at $\alpha \leq 0.013$, the Bonferroni correction method was used for the comparison of multiple t-tests; exercise and ventilatory parameters were compared. A repeated measures paired t-test was also used to compare mean differences among the endurance performance tests control versus experimental conditions (days 3, 4, 5, and 6). The best test of endurance performance (TTE) and corresponding exercise and ventilatory parameters of either experimental test day 3 or 4 was used and compared to the best endurance performance test of control day 5 or 6 (the worst endurance performance tests were omitted, i.e. shortest TTE). Statistical significance was set at $\alpha <$ 0.013 using the Bonferroni adjustment. A one-way analysis of variance with repeated measures was used to compare within and between group differences in arterial oxygen desaturation, heart rate, and cardiorespiratory variables during exercise (0%, 25%, 50%, 75%, and 100% of maximum TTE) before and after the induction of RM fatigue. Pairwise comparisons were used to locate where the significant differences existed.

Results

Descriptive characteristics

Ten healthy female participants completed the study. Mean descriptive and baseline spirometry values can be seen in Table 1. Group means for peak maximal cycle ergometer exercise parameters for test days 1 and 2 can be seen in Table 2. Peak constant load (80% of maximum power output) exercise parameters for endurance performance test days 3, 4, 5, and 6 can be seen in Table 3. All individual subject data can be seen in Appendix C.

Table 1. Descriptive characteristics and baseline (resting) spirometry values.

	n = 10
Age, yrs	26.8 ± 2.0
Height, cm	165.7 ± 4.4
Mass, kg	57.2 ± 7.5
FEV_1, litres	3.27 ± 0.56
FVC, litres	3.89 ± 0.56
FEV_1/FVC, percent	83.6 ± 4.1
FEF_{max}, $L \cdot sec^{-1}$	6.68 ± 1.23

Values are mean ± SD; yrs, years; cm, centimeters; kg, kilograms; FEV_1, forced expiratory volume in one second; FVC, forced vital capacity; FEV_1/ FVC, ratio of FEV_1 to FVC; 25- 75%, percent of forced expiratory volume occurring between 25 and 75% of the curve; $FEF_{max,}$ maximal forced expiratory flow in litres per second.

Exercise Parameters

Maximal Aerobic Power ($VO_{2\,max}$): Day 1 (control) versus Day 2 (experimental)

Maximal exercise values from the $VO_{2\,max}$ test on day 1 are shown in Table 2. Subjects demonstrated aerobic capacity values from 1.72 to 3.26 $L \cdot min^{-1}$ (35.8 to 49.5 $mL \cdot kg^{-1} \cdot min^{-1}$), mean values were 2.47 ± 0.41 $L \cdot min^{-1}$ (43.3 ± 4.7 $mL \cdot kg^{-1} \cdot min^{-1}$). This represents a modest range of fitness levels, from low to moderately trained females. The respiratory exchange ratio (RER) during the $VO_{2\,max}$ test exceeded 1.10 in all but two

subjects. Peak heart rate within 10% of predicted (226-age) was achieved in all subjects (McArdle *et al*, 1996). Maximal exercise was indicated by volitional fatigue.

Maximal exercise values from the $VO_{2\ max}$ test on day 2 are also displayed in Table 2. Following the induction of respiratory muscle (RM) fatigue subjects demonstrated aerobic capacity values from 1.68 to 2.96 $L \cdot min^{-1}$ (34.7 to 49.5 $mL \cdot kg^{-1} \cdot min^{-1}$), mean values were 2.33 ± 0.41 $L \cdot min^{-1}$ (40.7 ± 4.7 $mL \cdot kg^{-1} \cdot min^{-1}$). During the $VO_{2\ max}$ test on day 2, 8 of the 10 subjects did not achieve RER values higher than 1.10. A peak heart rate within 10% of predicted (226-age) was achieved in all but 4 subjects.

Table 2. Physiological exercise parameters during a maximal cycle ergometer test to exhaustion.

	Day 1 Non-RMF	**Day 2 RMF**
HR, bpm	185 ± 4.6	179.1 ± 4.7 *
V_E, $L \cdot min^{-1}$	102.1 ± 15.7	92.4 ± 12.3 *
VO_2, $L \cdot min^{-1}$	2.47 ± 0.41	2.43 ± 0.64
VO_2, $mL \cdot kg^{-1} \cdot min^{-1}$	43.3 ± 4.7	40.7 ± 4.7
VCO_2, L/min^{-1}	2.73 ± 0.48	2.46 ± 0.46
RER	1.13 ± 0.06	1.06 ± 0.07 *
IFR, $L \cdot min^{-1}$	2.74 ± 0.51	2.59 ± 0.35
SaO_2, percentage	95.26 ± 3.72	96.33 ± 2.14
V_E/VO_2, $L \cdot min^{-1}$	41.62 ± 6.48	40.3 ± 7.13
V_E/VCO_2, $L \cdot min^{-1}$	36.87 ± 3.67	38.09 ± 5.55

* Denotes a significant different between trials.
Values are mean ± SD; HR, heart rate in beats per minute; V_E, minute ventilation in litres per minute; VO_2, maximal rate of oxygen consumption in litres per minute; $VO_{2\ max}$, maximal rate of oxygen consumption in milliliters per kilogram per minute; VCO_2, rate of carbon dioxide production in litres per minute; RER, respiratory exchange ratio; inspiratory flow rate in litres per minute; arterial oxygen saturation in percentage; oxygen ventilatory equivalent in litres per minute, carbon dioxide ventilatory equivalent in litres per minute.

Pulmonary gas exchange

Ventilatory parameters V_E, VCO_2, VO_2, and RER were measured. A repeated measures paired t-test was performed on aerobic test values from day 1 and day 2. A significant difference was not seen in maximal oxygen consumption (p=0.111). Peak heart rate was significantly different between day 1 and day 2 (185 ± 4.6 versus 179 ± 4.7bpm; p=0.002). Peak minute ventilation was also significantly reduced (p=0.013), from 102.1 ± 15.7 $L \cdot min^{-1}$ on day 1 to 92.3 ± 12.2 $L \cdot min^{1}$ on day 2. Inspiratory flow rate (IFR) was not significantly different between the two test days (p=0.390).

A one-way analysis of variance with repeated measures was used to compare differences in exercise variables between RM fatigue and non-RM fatigue trials throughout maximal exercise; significance was set at $\alpha \leq 0.05$. Heart rate, minute ventilation, carbon dioxide production, oxygen consumption, percent arterial oxygen saturation, and duty cycle during maximal exercise (0%; exercise start, 25%, 50%, 75%, and 100% of maximal exercise time [T_{max}]) were considered. No significant differences were identified for oxygen consumption, carbon dioxide production, duty cycle, or percent arterial oxygen saturation at the start of exercise, throughout exercise or at 100% TTE in the $VO_{2\,max}$ test. A significant interaction effect was identified within the trials for heart rate (p=0.014), and ventilation (p=0.028). A significant reduction was seen in heart rate 100% T_{max} as mentioned previously. Minute ventilation was significantly higher at 50% of T_{max} following the induction of respiratory muscle fatigue (p= 0.047). Mean handgrip strength on day 2 increased from 32.1kg before the hyperpnea task to 32.4kg after the induction of RM fatigue.

Figure 3. Mean values for oxygen consumption during maximal cycle ergometer test ($VO_{2\ max}$ test) with and without prior induction RM fatigue.

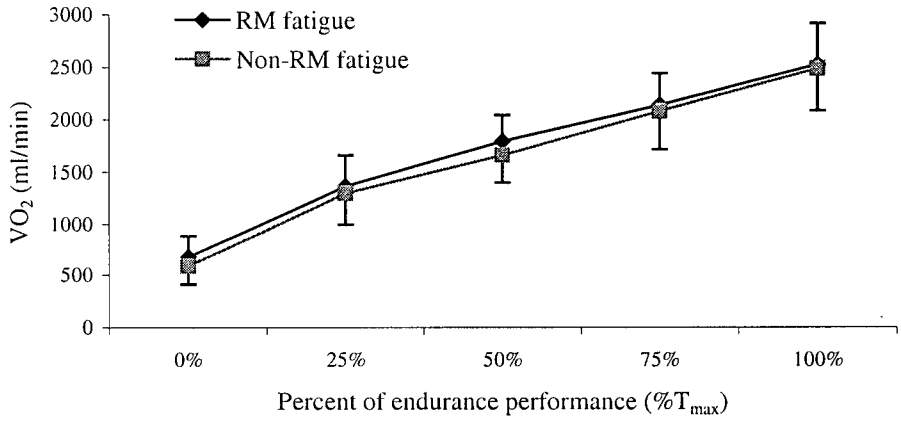
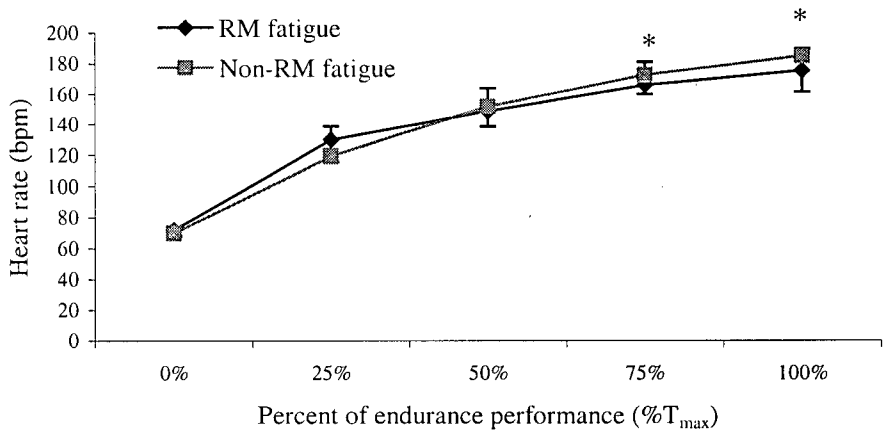
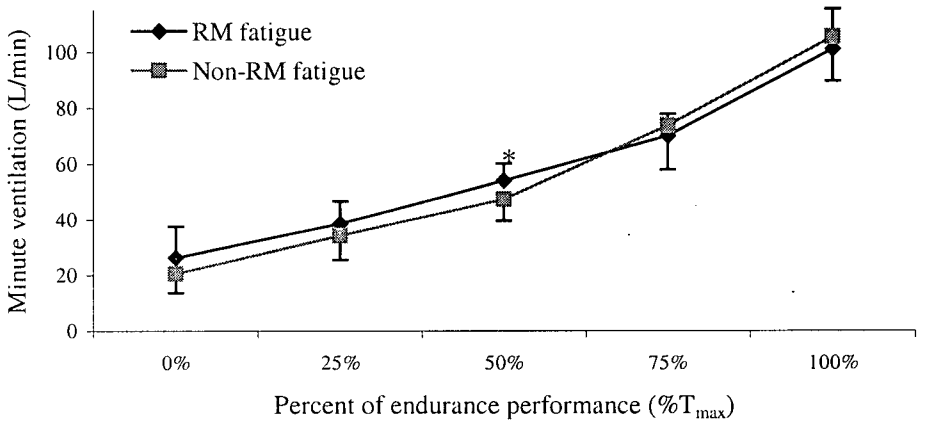


Figure 4. Mean values for heart rate (HR) during maximal exercise ($VO_{2\ max}$ test) with and without prior induction of RM fatigue.



* Denotes a significant difference between groups at corresponding T_{max}.

Figure 5. Mean values of minute ventilation during maximal cycle exercise ($VO_{2\ max}$ test) with and without prior induction of RM fatigue.



* Denotes a significant difference between groups at corresponding T_{max}.

Figure 6. Mean values of carbon dioxide production during maximal cycle exercise ($VO_{2\ max}$ test) with and without prior induction of RM fatigue.

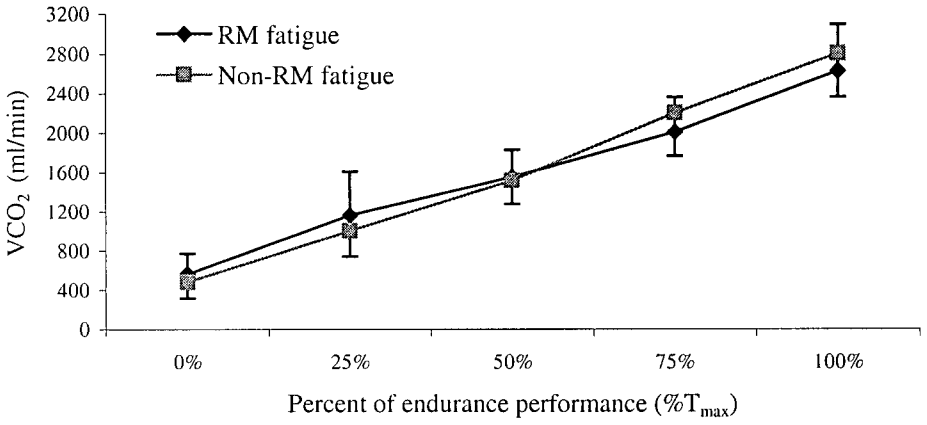


Figure 7. Mean values of percent arterial oxygen saturation (%SaO_2) during maximal cycle exercise ($VO_{2\ max}$ test) with and without prior induction of RM fatigue.

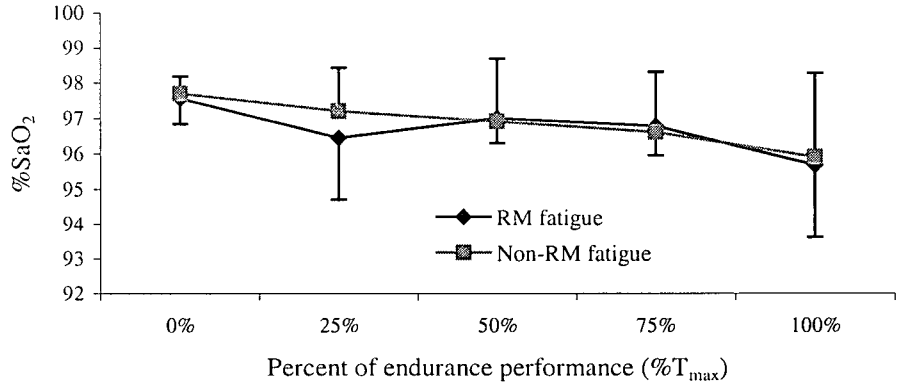
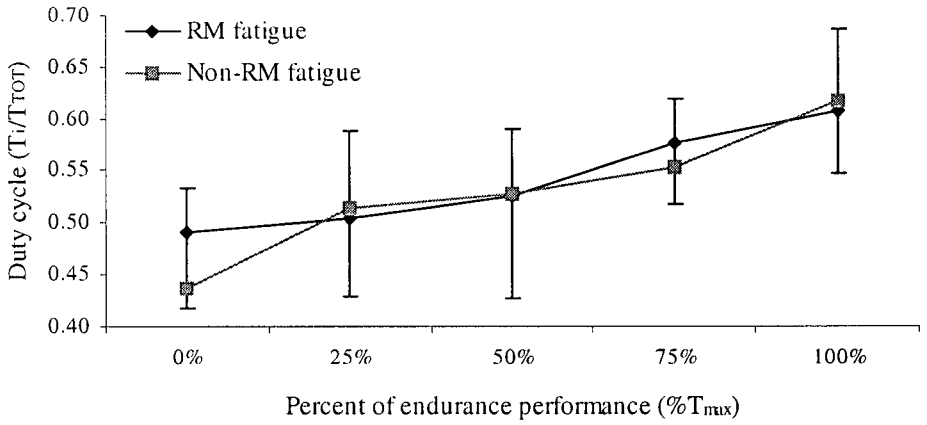


Figure 8. Mean values of duty cycle (T_i/T_{TOT}) during maximal cycle exercise ($VO_{2\ max}$ test) with and without prior induction of RM fatigue.



Endurance performance exercise (80% peak power output): Day 3, 4 versus 5 (control), 6 (control)

Maximal exercise values from the constant load exercise test on days 3, 4, 5, and 6 are shown in Table 3. Subjects demonstrated group $VO_{2\ max}$ values on days 3, and 4 following the induction of RM fatigue of 2.25 and 2.20 $L \cdot min^{-1}$ (r=0.862), time to

exhaustion on these days was 317.1 and 295.0s (r=0.775), peak heart rate values were 179.3 and 176.8 bpm (r=0.428), peak minute ventilation values were 94.5 and 99.6 $L \cdot min^{-1}$ (r=0.390), respectively. Subjects demonstrated mean aerobic capacity values on days 5 and 6 of 2.26 and 2.47 $L \cdot min^{-1}$ (r=0.633), peak heart rate values 182.0 and 179.8 bpm (r=0.461), and peak ventilation values 98.9 and 96.0 $L \cdot min^{-1}$ (r=0.432), respectively. Subjects demonstrated a group mean endurance performance time on day 5 of 375.0 and 368.9s (r=0.544) on day 6.

Table 3. Endurance Performance Test. Physiological parameters at maximal exercise during constant load (80% of maximum power output) exercise to exhaustion.

	Day 3	**Day 4**	**Day 5**	**Day 6**
	RM Fatigue	**RM Fatigue**	**Non-RM Fatigue**	**Non-RM Fatigue**
TTE, seconds	311.10 ± 75.22	295.30 ± 80.01	375.00 ± 76.66	368.90 ± 13.17
HR, bpm	179.3 ± 3.8	176.8 ± 5.5	182.0 ± 3.1	179.8 ± 4.9
V_E, $L \cdot min^{-1}$	94.5 ± 12.4	99.6 ± 12.5	98.9 ± 9.5	96.0 ± 10.5
VO_2, $L \cdot min^{-1}$	2.25 ± 0.5	2.20 ± 0.3	2.26 ± 0.3	2.47 ± 0.3
VO_2, $mL \cdot kg^{-1} \cdot min^{-1}$	48.25 ± 7.6	48.58 ± 9.0	49.35 ± 10.2	46.20 ± 5.8
VCO_2, $L \cdot min^{-1}$	2.52 ± 0.51	2.55 ± 0.40	2.44 ± 0.49	2.55 ± 0.39
RER	1.06 ± 0.08	1.04 ± 0.08	0.98 ± 0.09	0.99 ± 0.07
IFR, $L \cdot min^{-1}$	2.85 ± 0.42	2.89 ± 0.48	2.89 ± 0.29	2.74 ± 0.33
%SaO_2	96.53 ± 1.68	96.30 ± 1.27	95.51 ± 1.84	93.26 ± 2.85
V_E/VO_2, $L \cdot min^{-1}$	40.22 ± 4.17	40.83 ± 5.32	41.07 ± 4.47	37.97 ± 6.39
V_E/VCO_2, $L \cdot min^{-1}$	38.49 ± 4.51	39.80 ± 5.90	41.86 ± 7.29	38.50 ± 5.90

Values are mean ± SD; TTE, time to exhaustion in seconds; HR, heart rate in beats per minute; V_E, minute ventilation in litres per minute; VO_2, maximal rate of oxygen consumption in litres per minute; $VO_{2\,max}$, maximal rate of oxygen consumption in milliliters per kilogram per minute; VCO_2, rate of carbon dioxide production in litres per minute; RER, respiratory exchange ratio; IFR, inspiratory flow rate in litres per minute; arterial oxygen saturation in percentage; oxygen ventilatory equivalent in litres per minute, carbon dioxide ventilatory equivalent in litres per minute.

Table 4. Best time of Endurance Performance. Physiological parameters at maximal exercise during constant load (80% of maximum power output) exercise to exhaustion.

	Best EPT Day 3/4 RMF	**Best EPT Day 5/6 Non-RM Fatigue**
TTE, seconds	320.30 ± 71.54	408.00 ± 84.90
HR, bpm	178.5 ± 4.5	182.0 ± 2.5
V_E, L/min	96.59 ± 11.21	99.29 ± 8.11
VO_2, L/min	2.28 ± 0.43	2.31 ± 0.28
VO_2, mLkgmin	42.15 ± 5.24	44.20 ± 3.28
VCO_2, L/min	2.54 ± 0.49	2.49 ± 0.43
RER	1.06 ± 0.08	0.98 ± 0.06
IFR	2.91 ± 0.42	2.94 ± 0.30
%SaO_2	96.32 ± 1.46	95.22 ± 2.16
V_E/VO_2, Lmin	10.62 ± 3.97	40.27 ± 4.61
V_E/VCO_2, Lmin	38.68 ± 4.26	40.79 ± 5.26

Values are mean ± SD; TTE, time to exhaustion in seconds; HR, heart rate in beats per minute; V_E, minute ventilation in litres per minute; VO_2, maximal rate of oxygen consumption in litres per minute; $VO_{2\,max}$, maximal rate of oxygen consumption in milliliters per kilogram per minute; VCO_2, rate of carbon dioxide production in litres per minute; RER, respiratory exchange ratio; IFR, inspiratory flow rate in litres per minute; arterial oxygen saturation in percentage; oxygen ventilatory equivalent in litres per minute, carbon dioxide ventilatory equivalent in litres per minute.

A repeated measures paired samples t-test on test days 3, 4, 5, and 6 was performed to identify significant differences among the test days. Statistical comparisons of aerobic test parameters were made between the best endurance performance time of day 3 or 4 and the best TTE achieved on day 5 or 6; significance was set at $\alpha<0.013$, the Bonferroni adjustment method was used for the comparison of multiple t-tests. Subjects performed a mean best TTE of 325.2 ± 75.4s following the induction of RM fatigue and a mean best TTE for day 5 of 408.0 ± 84.9s demonstrating a significant difference between the two test days ($p= 0.002$). A significant difference was not seen in oxygen consumption ($p= 0.066$), peak minute ventilation ($p= 0.267$), peak heart rate ($p= 0.021$),

or mean inspiratory flow rate (p=0.800). Mean HG strength decreased minimally from 32.3kg to 32.2kg following the breathing task.

A repeated measures ANOVA was used to analyze differences among exercise variables throughout exercise with and without the prior induction RM fatigue (RM fatigue versus non-RM fatigue trials). The variables from the best endurance performance times of experimental test days 3 and 4, and control test days 5 and 6 were compared. Heart rate, minute ventilation, carbon dioxide production, oxygen consumption, percent arterial oxygen saturation, and duty cycle during constant load (80% P_{max}) exercise (0%, 25%, 50%, 75%, and 100% of maximal TTE) were considered. No significant changes were seen between the two trials for heart rate, oxygen consumption, duty cycle or percent arterial oxygen saturation at rest or during the exercise test. Minute ventilation was significantly lower (p=0.049) at the start of exercise between the two groups. Carbon dioxide production was also significantly different (p=0.050) at the start of exercise; no significant differences were seen in CO_2 production beyond that time.

Figure 9. Mean values of oxygen consumption during constant load exercise (TTE @ 80% max) with and without prior induction of RM fatigue.

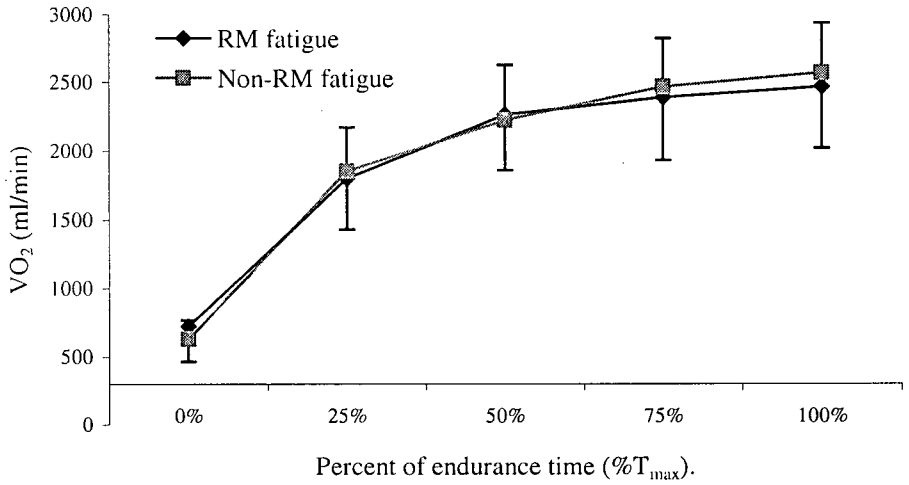


Figure 10. Mean values for heart rate (HR) during constant load exercise (TTE @80% max) with and without prior induction of RM fatigue.

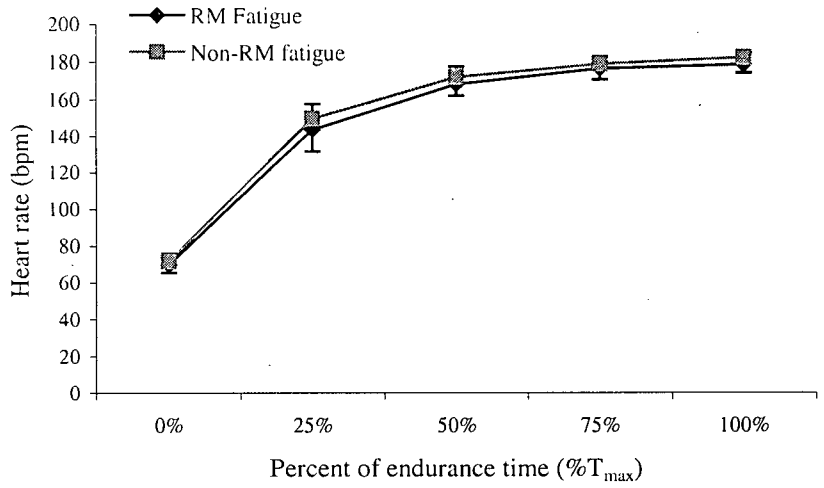
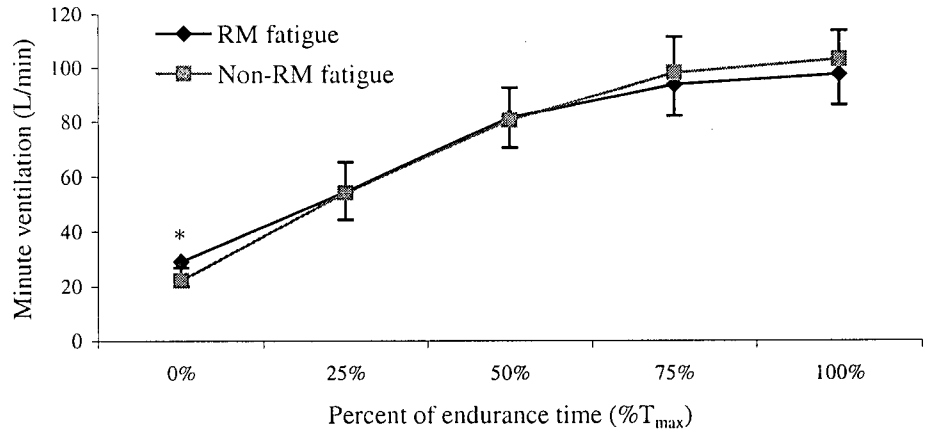


Figure 11. Mean values of minute ventilation during constant load exercise (TTE @ 80% max) with and without prior induction of RM fatigue.



* Denotes a significant difference between groups at corresponding T_{max}.

Figure 12. Mean values of carbon dioxide production during constant load exercise (TTE @ 80% max) with and without prior induction of RM fatigue.

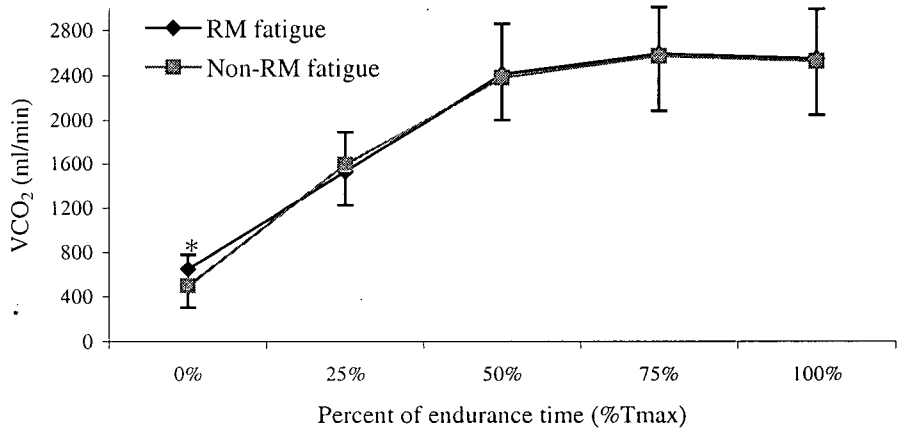


Figure 13. Mean values of percent arterial oxygen saturation during constant load exercise (TTE @ 80% max) with and without prior induction of RM fatigue.

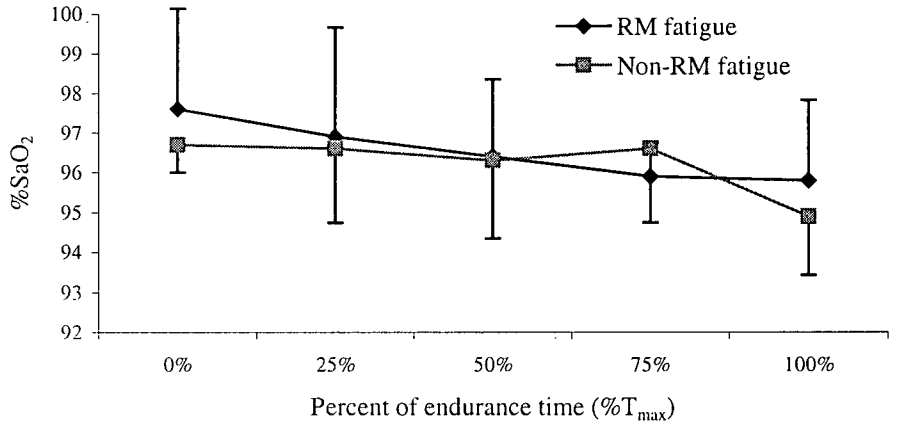
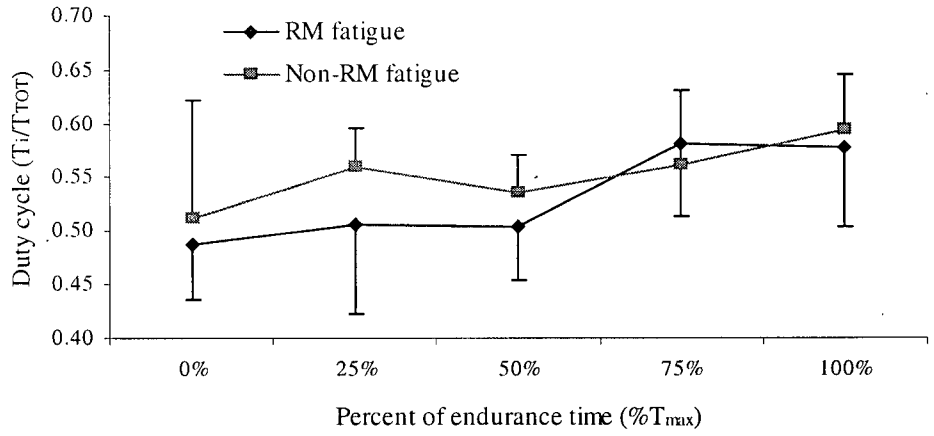


Figure 14. Mean values of duty cycle (T_i/T_{TOT}) during constant load exercise (TTE @ 80% max) with and without prior induction of RM fatigue.



RESPIRATORY MUSCLE FATIGUE

15-minute voluntary hyperpnea task

Throughout the 15-minutes of voluntary hyperpnea (induction of RM fatigue) occurring on test days 2, 3, and 4, mean average ventilation values were equal to 96.63 ± 17.82 $L \cdot min^{-1}$, 96.64 ± 21.46 $L \cdot min^{-1}$, and 93.65 ± 24.17 $L \cdot min^{-1}$, respectively (Table 4). These values correspond to 72.8 ± 6.7%, 74.5 ± 6.0%, and 71.7 ± 11.8% of baseline MVV on test days 2, 3, and 4, respectively.

Maximal voluntary ventilation

Mean maximal voluntary ventilation (MVV) on day 1 before exercise or the voluntary hyperpnea task (baseline) was 128 ± 22 $L \cdot min^{-1}$, 3-minutes following exercise MVV had increased to 133 ± 22 $L \cdot min^{-1}$, and 5-minutes post exercise MVV had nearly returned to baseline (127 ± 22 $L \cdot min^{-1}$). On day 2 of testing, baseline MVV for the group was 132 ± 27 $L \cdot min^{-1}$, 1-minute and 2-minutes following the induction of respiratory

muscle (RM) fatigue MVV had decreased to 114 ± 30 $L \cdot min^{-1}$ and 118 ± 26 $L \cdot min^{-1}$, respectively. MVV was still reduced at 3-minutes post-exercise (125 ± 23 $L \cdot min^{-1}$) and 5-minute post-exercise (125 ± 26 $L \cdot min^{-1}$). Baseline MVV values from day 1 and day 2 proved to be reproducible with an r = 0.841. Mean baseline MVV on day 3 was 131 ± 27 $L \cdot min^{-1}$, at 1- and 2-minutes following the voluntary hyperpnea task MVV decreased to 118 ± 29 $L \cdot min^{-1}$ and 116 ± 27 $L \cdot min^{-1}$, in that order. At 3 and 5-minutes post-exercise MVV was still reduced to 127 ± 28 $L \cdot min^{-1}$ and 125 ± 29 $L \cdot min^{-1}$, respectively. On day 4 MVV baseline values were recorded and provided a group mean of 131 ± 26 $L \cdot min^{-1}$, MVV values decreased by a mean of 14 ± 8 $L \cdot min^{-1}$ and 17 ± 10 $L \cdot min^{-1}$ for the group at 1 and 2-minutes following the induction of RM fatigue. MVV was still reduced at 3 and 5-minutes post-exercise by 7 ± 8 $L \cdot min^{-1}$ and 9 ± 10 $L \cdot min^{-1}$, respectively. MVV values were reproducible for days 3 and 4 at 1-minute (r= 0.957) and 2-minutes (r=0.944) following the induction of RM fatigue. Baseline MVV values for both days 5 and 6 were 132 ± 28 $L \cdot min^{-1}$, this value dropped to 131 ± 26 $L \cdot min^{-1}$ on day 5 and to 128 ± 24 $L \cdot min^{-1}$ on day 6 at 3-minutes post-exercise. At 5-minutes post-exercise MVV values were at 129 ± 27 $L \cdot min^{-1}$ and 127 ± 27 $L \cdot min^{-1}$ on days 5 and 6, respectively.

Table 5. MVV at baseline, following voluntary hyperpnea and exercise. Ventilation during voluntary hyperpnea task.

	Day 2 RM fatigue	Day 3 RM fatigue	Day 4 RM fatigue
MVV (baseline) ($L \cdot min^{-1}$)	132 ± 27	131 ± 27	131 ± 26
MVV 1-minute post-RM fatigue ($L \cdot min^{-1}$)	114 ± 30*	118 ± 29*	117 ± 25*
MVV 2-minute post-RM fatigue ($L \cdot min^{-1}$)	118 ± 26*	116 ± 27*	114 ± 25*
MVV 3-minute post-exercise ($L \cdot min^{-1}$)	125 ± 23	127 ± 28	124 ± 25
MVV 5-minute post-exercise ($L \cdot min^{-1}$)	125 ± 26	125 ± 29	122 ± 26
V_E during 15-minute hyperpnea task ($L \cdot min^{-1}$)	96.6 ± 17.8	96.6 ± 21.5	93.7 ± 24.2
V_E during 15-minute hyperpnea task (%MVV)	72.8 ± 6.7	74.53 ± 6.0	71.7 ± 11.8

* Denotes a significant different difference from baseline MVV.
Values are mean ± SD; MVV in litres per minute; V_E in litres per minute; V_E in percent of baseline MVV.

A repeated measures ANOVA was used to analyze the effects of the voluntary hyperpnea task on MVV; significance was set at $\alpha \leq 0.05$. On day 2 MVV was significantly reduced from baseline values at 1-minute ($p=0.003$) and 2-minutes ($p=0.000$) following the voluntary hyperpnea task, a significant difference was not seen at 3-minutes ($p=0.115$) and 5-minutes ($p=0.152$) post-exercise ($VO_{2\,max}$ test). At 1- and 2-minutes post-hyperpnea MVV had significantly decreased on day 3 ($p=0.003$ and $p=0.000$, respectively). A significant difference was not found following the constant load exercise (80% P_{max}) at 3- or 5-minutes. Following the induction of RM fatigue on day 4 MVV was significantly reduced from baseline at 1-minute ($p=0.005$) and 2-minutes ($p=0.004$) post-fatigue, whereas a significant difference was not seen at 3-minutes ($p=0.142$) and 5-minutes ($p=0.290$) post-exercise (80% P_{max}). Individual data can be seen in Appendix C.

Figure 15. Absolute change in MVV following 15-minute hyperpnea task on test days 1, 5, and 6.

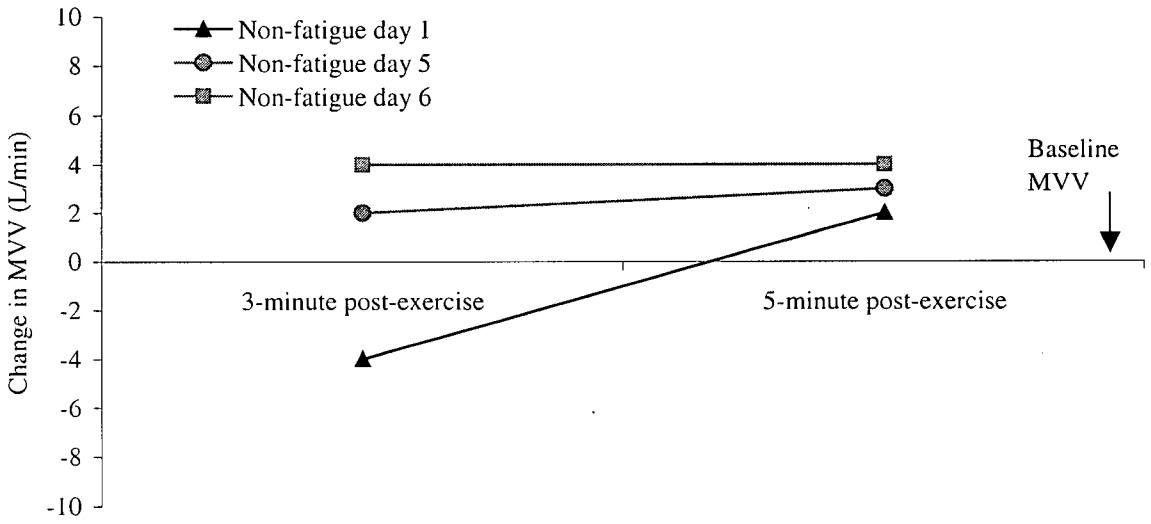
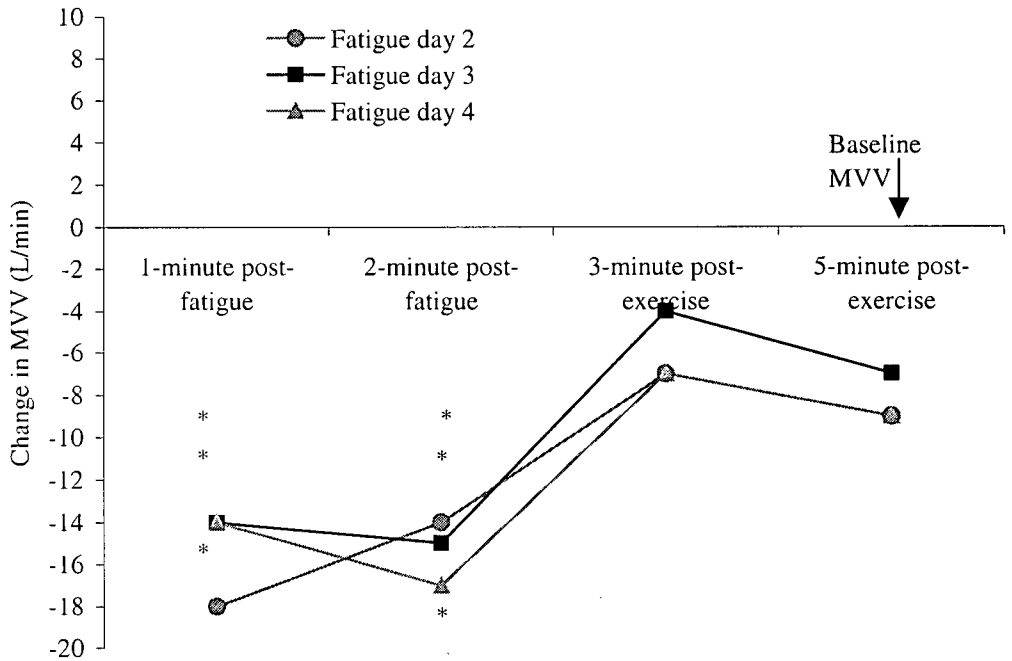


Figure 16. Absolute change in MVV following maximal and constant load exercise on test days 2, 3, and 4.



* Denotes a significant difference from baseline values.

Dyspnea

Subjects rated the level of dyspnea and leg discomfort they felt throughout exercise once every minute and at the end of exercise using the Borg 10-Scale. Following the induction of RM fatigue on test day 2 during $VO_{2\ max}$ test, nine of the ten subjects rated their breathing discomfort, at maximal exercise higher than that on day 1. Leg discomfort was rated higher at maximal exercise following the induction of fatigue in 7 of the ten subjects. Six subjects reported chest tightness and an increased difficulty of breathing throughout exercise especially at maximal exercise following the hyperpnea task, three subjects reported strong sensation of inability of getting enough air into their lungs. Eight of the ten subjects reported increased sensation respiratory effort as the reason for ceasing exercise with prior induction of RM fatigue whereas only one subject stopped exercise because of respiratory related reasons when RM fatigue was not induced prior to the exercise test. The dyspnea index and leg discomfort rating scores were significantly increased following the induction of RMF ($p=0.000$ and $p=0.038$, respectively).

When fatigue was induced prior to the endurance performance test, seven of the ten subjects reported an increased sensation of respiratory effort with the induction of RM fatigue. Eight subjects ceased exercise due to leg discomfort when RM fatigue was not induced, whereas, when RM fatigue was present seven of the ten subjects reported increased respiratory and leg discomfort as the reason to quit the exercise test. Significant differences for the ratings of perceived exertion for neither the legs ($p=1.00$) nor respiratory muscles ($p=0.394$) were found following the induction of respiratory muscle fatigue.

Discussion

The major findings of this research study were as follows: the induction of respiratory muscle fatigue caused (1) a significant decrease in cycle time to exhaustion during the endurance performance test and, (2) significant changes in physiological parameters such as heart rate, minute ventilation at the end of the maximal aerobic capacity assessment. The findings from this study indicate that RM fatigue may impose a limitation on exercise performance in normal healthy females.

Respiratory Muscle Fatigue

A 15-minute voluntary hyperpnea task equal to 70% of the participants MVV was chosen to induce respiratory muscle fatigue. This method of inducing RM fatigue was similar to the method employed by Mador and his associates (1996) who demonstrated that RM fatigue occurred in ten healthy males following a 10-minute hyperpnea task equal to their 60% MVV. Mador *et al.* measured transdiaphragmatic pressure (P_{di}) during bilateral supramaximal phrenic nerve stimulation, a method considered to be the most direct and reliable procedure to assess diaphragm strength. A pilot study conducted in our laboratory identified this hyperpneic method of inducing RM fatigue as significant and reliable [for details please refer to Appendix D]. Hamnegard *et* al. (1996), measured transdiaphragmatic twitch pressure using cervical magnetic stimulation (CMS) following 2-minutes maximal isocapnic ventilation and found a 13% reduction in diaphragm strength. Other authors have stated that maximal sustainable ventilation decreases with time and that ventilation levels equal to 55-80% of MVV can be maintained for approximately 15-minutes. The inability to maintain high levels ventilation is thought to be related to the development of RM fatigue (Fitting, 1991).

Ventilation during the voluntary hyperpnea task on the three different days ranged from 93 to 97 $L \cdot min^{-1}$ or 72 to 75% of MVV. On average, a 10–14% reduction in MVV was seen on all three days in which RM fatigue was induced. The decrease in MVV was found to be significantly different from baseline values, and the reductions were found to be reproducible among the testing days. Therefore we are confident in this method of inducing RM fatigue based on our pilot work and previous research findings. Following exercise only, MVV increased from pre-exercise values by 4% following the maximal aerobic capacity test, and decreased by 1-3% following cycle to exhaustion tests; these changes were insignificant.

The decline in MVV could be attributed to motivational factors, peripheral muscle contractile failure (peripheral fatigue), or a reduction in central motor drive (central fatigue). We made considerable efforts to maintain high levels of motivation by choosing only highly motivated subjects and by continually encouraging the subjects throughout the MVV maneuver.

Exercise Parameters

Test of Maximal Aerobic Power (VO_{2max}): Day 1(control) versus Day 2.

The induction RM fatigue did not significantly alter oxygen consumption during the last minute of maximal exercise, albeit, peak minute ventilation decreased 9.5% and exercise was terminated at an overall lower heart rate. The decrease in peak minute ventilation and heart rate without an associated decrease in $VO_{2\,max}$ may be attributed to the decrease in exercise time. The respiratory quotient at end exercise (1.06 ± 0.07) was significantly reduced following the induction of fatigue compared to the control trial (1.13 ± 0.06), suggesting that skeletal muscle effort was not the same for each trial

Various authors have used mean inspiratory flow as an indicator of respiratory drive (Mador and Acevedo, 1996; Gardner and Meah, 1989). This variable was also not significantly different following the induction of RM fatigue compared to control indicating that the degree of respiratory effort was similar after the induction of RM fatigue, compared to the control trial.

The induction of RM fatigue did not significantly alter $VO_{2\ max}$ even though exercise duration was less following the induction of RM fatigue. An increased sensation of respiratory discomfort is the likely cause of early cessation of exercise. Subjects were asked to rate the level of dyspnea and leg discomfort they felt throughout exercise once every minute and at the end of exercise upon fatigue on scale of 1 to 10 (1= no discomfort at all; 10= maximal discomfort). Dyspneic scores and leg effort scores were significantly increased following the induction of RM fatigue. Six of the ten subjects complained of chest tightness and increased difficulty to breath throughout, as well as at the end of the exercise test following the hyperpnea task. Eight of the ten subjects rated their breathing effort higher than leg effort at the end of exercise following the induction of RM fatigue.

Endurance performance exercise (80% peak power output): Day 3, 4 versus 5 (control), 6 (control).

The results of this study indicate that RM fatigue is a limiting factor in exercise performance. Exercise performance was defined by endurance performance time (EPT) or time to exhaustion (TTE). EPT during the constant load (80% P_{max}) exercise test was reduced by 22% following the induction of RM fatigue, although no significant changes were seen in VO_2, peak heart rate, minute ventilation or inspiratory flow rates during the last minute of exercise. Our findings are in partial agreement with a previous study by

Martin *et al.*, (1982) who observed a 14.5% drop in treadmill run endurance performance time but also found that exercise was ceased at a significantly lower peak minute ventilation, peak oxygen consumption, and peak heart rate following the induction of RM fatigue. In contrast, Dodd and his colleagues found that the induction of RM fatigue via 10-minutes of volitional isocapnic hyperpnea had no effect on 85% peak power output to exhaustion cycle exercise performance or pulmonary function. In response to the latter study, discrepancy between the results it is likely that the ventilation during the volitional hyperpnea task was not sufficient to induce RM fatigue. It was previously stated that at maximal exercise ventilation attains approximately 70% of MVV (Fitting, 1990), whereas, Dodd and his Colleagues had their subjects breathe at a ventilation level equal to only 85% of maximal exercise ventilation, a level possibly insufficient to induce RM fatigue. Mador and Acevedo (1991) found a 23% decrease in exercise performance (90% $VO_{2\,max}$), they also found a significant decline in VO_2, V_E, and heart rate following inspiratory threshold loading when compared to control. It is possible that the different methods of inducing RM fatigue may have caused the discrepancy in our results, although, it is most likely that the higher intensity exercise and therefore shorter exercise duration caused the significant reduction in peak VO_2, V_E, and heart rate. Endurance performance time in the present study lasted considerably longer when compared to the Mador *et al.*, 1991 study performed at 90% $VO_{2\,max}$ exercise. A test of endurance performance at an exercise level equal to 80% $VO_{2\,max}$ exercise was chosen to increase the likelihood that volitional fatigue occurred due to respiratory limitation as well as lower limb fatigue rather than leg fatigue alone, as the legs tend to fatigue rapidly on high intensity cycle tests. We chose the hyperpnea method of inducing RM fatigue, as it more

closely resembles that of the hyperpnea experienced during exercise. Contractile fatigue of the respiratory muscles, namely the diaphragm is a likely explanation for the decrease in exercise performance, as Mador and his colleagues (1996) showed following a volitional hyperpnea task (60% MVV) lasting approximately 8-minutes caused a significant reduction in transdiaphragmatic pressure. The decrease in $P_{di\ max}$ was long lasting and indicative of peripheral contractile fatigue. It is likely that contractile failure is not the sole explanation for the reduction in EPT via the induction of RMF rather it is more likely that a multifactorial process is involved and more research is warranted.

Motivation was an important factor in this study, as mentioned previously only highly motivated subjects were included in this study, equal and consistent verbal encouragement was provided throughout the exercise tests. Verbal encouragement was given on regular time intervals and the same words of encouragement were used on all test days and subjects. Handgrip strength was measured before and after the induction of fatigue to determine if centrally mediated fatigue had occurred and to ensure equal levels of motivation before and following the breathing task. For most subjects handgrip strength increased or remained the same following the breathing task. Mean handgrip strength on day 2 greater following the induction of RM fatigue. On the EPT day mean HG strength decreased slightly following the breathing task. The endurance performance tests were also repeated twice to ensure that maximal effort was achieved in at least one of the test days, the worst performance time for each trial was discarded and the best EP times were analyzed. We feel confident that our subjects were equally motivated to perform exercise all test days we used for our data analysis.

Dyspnea

Eight of the ten subjects tested had an increased sensation of respiratory discomfort during exercise following the induction of RM fatigue, and attributed both leg and respiratory discomfort as the reason for ceasing exercise. Whereas, when fatigue was not induced, only one subject complained of respiratory discomfort as the reason to stop cycling. Eight subjects had higher RPE for the leg muscles and the remaining two subjects had equal ratings for leg and RM discomfort when respiratory muscle fatigue was not induced. Increased sensation of RM discomfort appears to be an important factor in the early cessation of endurance performance exercise following the induction of fatigue.

Conclusion

In summary, these data illustrate that 15-minutes of voluntary hyperpnea has a detrimental effect on exercise performance during constant load exercise in healthy moderately trained females. Exercise performance was reduced from 408.0 ± 84.9 s to 320.0 ± 71.5 s following the induction of fatigue. Maximal oxygen consumption was unaffected with an associated decrease in heart rate and minute ventilation during the last minute of the $\dot{V}O_{2\,max}$ test with the induction of fatigue. The fact that the induction of RM fatigue caused a decrease in exercise performance without an associated decrease in oxygen consumption has important implications to exercise performance and possibly supports research in favor of respiratory muscle training (RMT).

Future Research

According to the results of the present study and various others, the respiratory muscles have proven to be a possible limiting factor in exercise performance, and

therefore support research aimed to improve strength and endurance of the respiratory muscles. The implementation of RMT in athletic training regimes could possibly increase exercise endurance performance by decreasing sensations of respiratory discomfort at maximal exercise via the increase or improvement of respiratory muscle endurance. RMT may also be important for the disease population, such as Chronic Obstructive Pulmonary Disease (COPD) and/or related diseases, by decreasing sensations of breathless and possibly increasing overall quality of life.

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Appendix A: Review of the Literature:

Review of Respiratory Anatomy and Physiology and Exercise

1.0 The Muscles of Respiration

In order to thoroughly discuss the effects of respiratory muscle fatigue on exercise performance it is necessary to review the basic anatomy and physiology of the respiratory muscles. The muscles of respiration serve to change the pressure within the lungs (pleural pressure), thus leading to differences between the pressure within the gas phase of the alveoli and the pressure outside the body (Hlastala and Berger, 2001). These pressure differences result in airflow. The muscles of respiration rely on the central respiratory control system for their rhythmic activation, although they have no inherent rhythm associated with them.

The respiratory muscles are embryologically, morphologically, and functionally skeletal muscles. They are mixed muscles made up of the combinations of the three principle fiber types found in all skeletal muscles. The human diaphragm consists of approximately 55% slow-oxidative (type I) fibres, whereas the remainder of the fibres consist of equal proportions of fast oxidative glycolytic (type IIA) fibres and fast glycolytic (type IIB) fibres (NHLBI Workshop Summary, 1990). Muscles of respiration can be divided into two groups, inspiratory and expiratory muscle groups. The recruitment of these two muscle groups varies greatly between at rest and during exercise conditions.

1.1 Muscles of Inspiration

The mechanical process of pulmonary ventilation is achieved by rhythmically changing the pressure in the thoracic cavity so that it drops slightly below atmospheric pressure and draws air in, then rises slightly above atmospheric pressure and expels this

air (Roussos and Macklem, 1997). Inspiratory muscles are used to elevate (expand) the chest cavity and force the diaphragm downward to increase the thoracic volume (decrease pressure). Inspiration is an active process involving contraction of the inspiratory muscles. The primary muscle of inspiration is the dome-shaped diaphragm, separating the abdominal and thoracic cavities. The overall force length characteristics of the diaphragm depend on its two main components, the costal and crural parts, and how they are linked. The diaphragm attaches to the vertebral column and to the circumference of the lower thoracic cage. The diaphragm bulges towards the thoracic cavity and the contraction of this muscle pulls down the central part, acting like a piston to increase the volume of the thoracic cavity, resulting in an increase in intraabdominal pressure and subsequent expansion of the ribcage. Other muscles of inspiration include the external intercostals; they contract during inspiration to pull the ribs forward and upward, thus increasing thoracic volume. The external intercostals muscles attach adjacent ribs and slope downward and forward. When the respiratory system is pushed to the limits of its reserve (i.e. during intense exercise), accessory muscle recruitment becomes necessary. The accessory muscles of inspiration include the sternocleidomastoid and the scalene muscles, which are attached to the first two ribs and the sternum. Only the diaphragm and external intercostals are active during normal quiet breathing (Mahler and Loke, 1981).

1.2 Muscles of Expiration

The collective purpose of the expiratory muscles is to decrease thoracic volume (which drives up intrapleural pressure) and thereby force gas out of the lungs quickly (Mador and Tobin, 1992). Normal expiration during quiet breathing is an energy-saving

passive process that requires no muscular contraction. It is achieved by the elasticity of the lungs and thoracic cage— the tendency to return to their original dimensions when released from tension (Roussos and Macklem, 1997). When demands are placed on the respiratory system the expiratory muscles must be recruited to reduce the respiratory time and thereby increase the number of breaths per minute (Mahler and Loke, 1981). The expiratory muscles recruited to achieve expiration when there is an increased demand for O_2 uptake and CO_2 removal (i.e. during exercise) includes the rectus abdominus, transverse abdominus, internal obliques, external obliques, and internal intercostals. The rectus abdominus pulls down on the lower ribs while it compresses abdominal contents to push upward on the diaphragm. The internal and external obliques as well as the transverse abdominus are capable of joining in to serve this function as in forced expiration. The internal intercostals pull ribs backward and down, decreasing thoracic volume (Mador and Tobin, 1992).

1.3 Respiratory Muscle Bioenergetics

As mentioned previously, at rest, inspiration is an active process whereas expiration is a passive one. Respiratory muscle contraction during moderate and heavy exercise differs significantly than at rest. With exercise, both inspiration and expiration are active processes that require considerable amounts of metabolic work. Elastic work is used for lung expansion during inspiration and elastic recoil via the aid of expiratory muscles overcomes the elastic work done on the chest during expiration. The response to exercise requires coordination of the respiratory and cardiovascular systems. Exercise increases the demand for O_2 and the production of CO_2 by increasing the activity and the demands of skeletal muscle. To supply the increased O_2 and remove excess CO_2, three

primary physiological changes must take place: (1) increased alveolar ventilation, (2) increased cardiac output, and, (3) redistribution of cardiac output to enhance perfusion of exercising muscles (Hlastala, 2001). At rest and during light exercise, the oxygen requirement of breathing is small, averaging 1.9 to 3.1 mL of oxygen per Litre of air breathed, or approximately 2-4% of the total energy expenditure. As breathing rate and tidal volume increase, as in moderate to heavy exercise, the energy cost rises to between 2.1 and 4.5 mL of O_2 per Litre of ventilation (Mahler, Snyder, and Loke, 1980). During exercise that elicits aerobic power (VO_2max), as much as 8 to 11% of the total oxygen uptake is required for respiratory muscle work in untrained individuals and as much as 15 to 16% of VO_2 max and of maximal cardiac output in highly fit individual (Harms *et al.*, 1998; Mahler, Snyder, and Loke, 1980).

In ordinary active individuals, the cardiovascular system limits VO_2max. While overall ventilation can increase by approximately 20-fold during maximal exercise, the heart increases its output by only five times that of its normal resting output. The increase in cardiac output during exercise is due to large increases in heart rate and small increases in stroke volume (Mahler and Loke, 1981). During exercise, redistribution of blood flow is an important adaptive cardiovascular mechanism that increases perfusion of exercising muscles and skin. The blood flow to the respiratory muscles therefore also increases during exercise.

2.0 Respiratory Limitations to Exercise

A major function of the respiratory system during exercise is to provide the working muscles with oxygen via the circulatory system. The respiratory system may fail directly or indirectly in this vital function and thus may limit exercise. Indirect failure

would occur if any additional oxygen provided by an increase in ventilation were taken up by the ventilatory muscles, thus depriving the rest of the body of O_2. A study has recently shown, by unloading the respiratory muscles, that the respiratory muscle work experienced under normal physiological conditions at maximal exercise exerts two types of effects on the cardiovascular response: (1) a substantial percentage of the cardiac output (up to 14-16%) is directed to the respiratory muscles to support their metabolic requirements (Harms *et al.,* 1998) and (2) and blood flow to the working locomotor muscles is decreased due to sympathetically controlled vasoconstriction. Sheel *et al.*, (2001) demonstrated using Doppler ultrasound techniques that leg blood flow decreased and limb vascular resistance increased following fatiguing inspiratory work.

Direct failure would occur if the lung and chest wall were to fail to provide sufficient ventilation to oxygenate the blood adequately or if inefficiency of gas exchange were to lead to arterial hypoxemia (Bye *et al.,* 1984). Lastly, although the ventilation might be temporarily adequate, the onset of respiratory muscle fatigue could eventually cause ventilation insufficiency and arterial hypoxemia.

Past investigation of respiratory factors limiting exercise has been examined in terms of possible limitations arising from the function of pulmonary gas exchange, the energetics of respiratory muscles, the respiratory mechanics, and the development of respiratory muscle fatigue. The purpose of this review and the following review will focus on the development of respiratory muscle fatigue as a limiting factor in exercise performance or capacity.

Appendix B: Respiratory Muscle Fatigue

The National Heart, Lung, and Blood Institute defines muscle fatigue as a condition in which there is a reduction in the force-generating capacity of the muscle, resulting from muscle activity under load that is reversible by rest. Respiratory muscle fatigue occurs at different sites between the brain and the diaphragm and can be divided into three categories: contractile fatigue, transmission fatigue, and central fatigue (Mador, Rodis and Diaz, 1996).

Although several other respiratory muscles are recruited during whole-body exercise (i.e. sternocleidomastoid, external intercostals, and scalene muscles), the diaphragm is the primary inspiratory muscle and the most effective pressure generator for increasing alveolar ventilation and thus provides the best index of respiratory system function. Therefore, respiratory muscle fatigue, when mentioned in this review, will be referring mainly to diaphragmatic fatigue.

According to Roussos *et al.,* (1979), diaphragm fatigue occurs when the diaphragm generates pressure greater than 40% of maximum whereas fatigue of the inspiratory muscles occurs if the pleural pressure developed exceeds 50 to 70% of the maximum pressure. Fatigue also has been determined to occur more readily at low inspired oxygen concentration (Roussos *et al.,* 1979) or when subjects breathe at higher lung volumes (Roussos and Macklem, 1977).

In experimental circumstances, when loading the respiratory muscles, two main determinants of respiratory muscle fatigue are the ratio of pressure developed in inspiratory muscles to their maximal capacity (P/Pmax) and the duty cycle of the inspiratory muscles (Ti/Ttot): fatigue occurs above a certain threshold of intensity and

duration of contraction in the various inspiratory muscles (Roussos and Macklem, 1977). The force generating capacity of the diaphragm decreases at higher lung volumes, indicating end-expiratory lung volume as another important factor in diaphragm fatigue (Smith and Bellemere, 1987). End expiratory lung volume may be actively increased by persistent contraction of the inspiratory muscles, as in asthma. Thus, fatigue occurs with lower inspiratory pressures when end-expiratory lung volume is actively increased (Fitting, 1991). Respiratory muscle fatigue, with respect to energetics, is determined by efficiency, which is determined by the balance between the energy demand and the energy supplied, and by the ratio of external power produced to energy consumption rate (Fitting, 1991). Another possible important determinant of fatigue is the ratio of velocity of muscle shortening to maximal velocity, particularly during unimpeded breathing (Fitting, 1991).

3.0 Measures and/or Detection of Respiratory Muscle Fatigue

The potential importance of respiratory, chiefly inspiratory, muscle fatigue has become well recognized, therefore the importance of reliable measurement techniques to assess respiratory muscle fatigue are also increasingly important. In order to understand fatigue mechanisms, several tests have been developed to measure the change from a non-fatigued, unloaded state to a fatigued state after a load has been applied.

Such tests may include measurements of the pressures generated by the respiratory muscles, these include maximal inspiratory mouth pressure or $P_{I\,max}$, and transdiaphragmatic pressure ($P_{di\,max}$). Unfortunately, when interpreting $P_{I\,max}$, and $P_{di\,max}$, submaximal efforts (poor motivation) cannot be distinguished from central fatigue this may pose a problem with critically ill patients, as well as with healthy normal subjects.

Other tests that are used to assess respiratory muscle fatigue include those that measure diaphragmatic or other inspiratory muscle electrical activity (power spectral analysis and integrated electrical activity and pressure development [E_{di}/P_{di}]). These tests that quantify the electrical activity of such muscles also present some limitations in that they are influenced by changes in spatial relationships between the recording electrodes and the muscle. The cellular mechanisms responsible for the shifts in the power spectrum remain unknown, which casts doubt on the sensitivity and specificity of this technique. The measurement of P_{di} requires the placement of esophageal and gastric balloon catheters and its magnitude is dependent on the geometry of the respiratory system in addition to the contractile state of the diaphragm. To assess fatigue of the diaphragm specifically, supramaximal/bilateral phrenic nerve stimulation (BPNS), i.e. measurement of twitch transdiaphragmatic pressure ($P_{di,\ tw}$) and $P_{di}/\ P_{di\ max}$ frequency curves, is currently regarded as being the most objective measure of diaphragm fatigue. These tests aim to define the capacity of the diaphragm to generate pressure independent of central control mechanisms. Another test used to assess diaphragm fatigue is the twitch-occlusion test. This measures the increase in P_{di} when a twitch is superimposed on the naturally activate diaphragm, to assess the degree of motor unit recruitment through central pathways.

The previous tests mentioned are mostly invasive, uncomfortable for the subject, and impractical for a field setting. Therefore less invasive measures are needed even though a decrease in $P_{di,\ tw}$ is an unequivocal measure of diaphragm fatigue. One noninvasive measure to determine whether respiratory muscle performance is reduced proceeding exercise is to examine the ability of the respiratory muscles to generate

maximum force (strength) through measuring $P_{I\,max}$ and maximal expiratory pressures ($P_{E\,max}$). Another method to evaluate respiratory muscle performance is to carry out short or long term respiratory endurance tasks, for example, maximal voluntary ventilation (MVV) or sustained ventilatory capacity (SVC). The changes in maximal flow tasks can also be investigated, e.g. forced expiratory volume in one second (FEV_1) and forced vital capacity (FVC). Loke and Virgulto (1982) demonstrated that MVV was reduced in some subjects after running a marathon; $P_{I\,max}$ and $P_{E\,max}$ were also reduced post marathon in this study, while other studies reported that MVV remained unchanged after similar endurance competitions (Hill *et al.,* 1991, and Chevrolet *et al.,* 1993). Studies have shown reductions in FEV_1 and mean expiratory flow (Hill *et al.,* 1991, Mahler *et al.,* 1980, and Miles *et al.,* 1983) whereas in other studies these values remained unchanged (Loke *et al.,* 1982, Chevrolet *et al.,* 1993, Maron *et al.,* 1979, and Nava *et al.,* 1992).

3.1 Possible Mechanisms/ Causes of Respiratory Muscle Fatigue

Although a high density of slow twitch fibres makes the diaphragm resistant to fatigue, respiratory muscle fatigue has been demonstrated on volitional tests following both prolonged submaximal exercise (Loke *et al.*, 1982; Ker and Schultz, 1996) and heavy short-term exercise (Johnson *et al.,* 1992). The causes of fatigue are complex and involve simultaneous changes at various sites within both the muscle (peripheral) and the central nervous system (CNS). According to the NHLBI Workshop Summary (1990), fatigue is likely to be the result of a dynamic process in which compensatory mechanisms are overwhelmed in a closed-loop system consisting of central motor drive, peripheral impulse propagation, excitation/contraction coupling, depletion of energy substrates and/or metabolite accumulation, and feedback modulating reflexes.

The condition in which muscle force generation during sustained or repetitive contraction becomes limited due to a decline in motoneuronal output is referred to as "central fatigue". By comparing the forces generated by a truly maximum voluntary to a maximum electrically stimulated contractions, an assessment of central fatigue is possible (Bigland-Ritchie *et al.*, 1979). Although the diaphragm is a skeletal muscle, central control of the diaphragm differs from that of limb skeletal muscles (Luo *et al.*, 2001). McKenzie et al. (1992) showed that central fatigue was more important in the diaphragm than that of limb muscle. McKenzie and his colleagues showed evidence of the development of central diaphragmatic fatigue during repeated maximal and submaximal diaphragmatic contractions. Bellemere and Bigland-Ritchie (1987) found that central fatigue played an important role in the reduced performance of the diaphragm during inspiratory resistive loading (IRL). They also found that motor drive to the diaphragm decreased progressively during repeated maximal breathing efforts. In another study it was found that electromyographic (EMG) amplitude recordings were reduced during IRL trials (Luo *et al.*, 2001). This reduction of the diaphragm EMG responses indicates decreased central respiratory drive because IRL breathing does not cause failure of neuromuscular transmission (Bellemere & Bigland-Ritchie, 1987). Controversy still exists in the literature if central respiratory fatigue actually occurs or if it is a safety mechanism preventing complete contractile failure, further studies are required to fill in the gaps in the literature.

Peripheral fatigue refers to failure at the neuromuscular junction or distal to this structure, and defined to be present when muscle force output or velocity decreases in response to direct electrical stimulation. This type of fatigue can result because of

alterations in the neuromuscular junction (NMJ), changes in propagation of the action potential along the sarcolemmal membrane or the t-tubules, changes of excitation-contraction coupling or due to other alterations in the muscle cell (e.g. alterations in metabolism, changes in contractile proteins). Peripheral fatigue can be further classified as "high" or "low" frequency fatigue. Aldrich (1987) suggested that loss of force at low frequencies represents an impairment of muscle at excitation-contraction coupling, whereas a decline in high frequency force generation is thought to suggest an alteration in NMJ transmission, a reduction in action potential propagation into the t-tubular system, or a reduction in sarcolemmal membrane excitability (Aldrich, 1987; Bazzy and Donelly, 1993). Low frequency fatigue can occur in isolation, whereas high frequency fatigue is always associated with some alterations in muscle force generation at lower frequencies. Force generation in response to high frequency stimulation remains unimpaired in the presence of pure low frequency fatigue, thereby indicating that the contractile proteins are still capable of generating maximal force provided that sufficient calcium is released by the sarcoplasmic reticulum (SR). Therefore, a reduced level of calcium availability due to alterations in SR function or a reduction in calcium sensitivity of the myofilaments at submaximal calcium levels may represent the impaired force generation at low frequencies of stimulation. (American Thoracic Society, 2002) Unfortunately, the explanation for the impaired calcium release by the SR during contractions is not well understood. Low frequency fatigue has been demonstrated in the sternocleidomastoid and diaphragm muscles of normal subjects breathing against high resistive loads (Westerbald *et al.*, 1990; Moxham *et al.*, 1981) and during sustained maximal ventilation for 2-minutes (Wragg *et al.*, 1992).

There are also metabolic factors and chemical changes to consider with the occurrence of muscle fatigue. If the chemical energy available to muscle or the ability of the muscle to utilize this energy becomes impaired, the muscle will fail as a force generator. Babcock et al. (1995) postulated that the effects of locomotor muscle activity, such as competition for blood flow distribution and/or extracellular fluid acidosis, in conjunction with a contracting diaphragm accounted for most of the exercised-induced diaphragm fatigue. Ward and co-workers (1992) concluded that increased diaphragm blood flow improved diaphragmatic function, thereby retarding the development of diaphragmatic fatigue. However, these results also indicate that postponing diaphragmatic fatigue via increased blood flow are through mechanisms independent of O_2 delivery, such as alterations in perfusion pressure, extracellular fluid composition, or capillary surface available for substrate and metabolite exchange. Supinski and colleagues (1987) also support Ward and her co-workers as they reported that increasing blood flow partially reversed the loss of force generating capacity induced by repetitive high-intensity isometric contractions in an isolated diaphragm strip preparation.

It is clear from the numerous studies performed that the precise cause of respiratory muscle fatigue is unknown; rather, it is probably a combination of different causes and may vary between conditions such as exercise intensity, type and duration as well as disease. Future studies and investigations are required to fill the gaps in the literature.

4.0 Methods of Inducing Respiratory Muscle Fatigue

The question of whether or not the respiratory muscles become fatigued during high-intensity exercise and therefore may possibly be a limiting factor in exercise

performance has become a major interest to exercise physiologists. In order to answer these questions techniques to measure and induce respiratory muscle fatigue have been developed and practiced in a laboratory setting. Measurement of respiratory muscle fatigue involves assessment of respiratory muscle strength and endurance as was previously discussed. Techniques or methods used to induce respiratory muscle fatigue may include inspiration against a resistive load, voluntary hyperpnea, or exercising at a percent of maximal work capacity (VO_2 max) to exhaustion.

Induction of respiratory muscle fatigue via loaded breathing involves inspiring against high resistance, or loaded inspiration and unloaded expiration, at a constant duty cycle. The amount of resistance is usually a predetermined percentage of maximal inspiratory pressure ($P_{I\,max}$), or maximal diaphragmatic pressure ($P_{di\,max}$), measured on the same day as the fatigue induction. The subject is normally asked to breath against the resistance until task failure occurs, which is defined as failure to maintain the target pressure for at least 3 to 5 consecutive attempts. A duty cycle will be chosen and the subject will achieve this cycle usually with the aid of a metronome or auditory cue. Yan *et al.,* (1993) induced diaphragmatic fatigue in their subjects by having them breath against an inspiratory resistance requiring 60% maximal transdiaphragmatic pressure with each breath until exhaustion (duty cycle of .60). Similarly Laghi and colleagues (1995) induced diaphragmatic fatigue in their subjects by instructing them to breath against a resistance equal to that of 60% of predetermined $P_{di\,max}$ with the target pressure visually displayed on an oscilloscope at a duty cycle equal to .50. Mador *et al.,* (1991) and Śliwiński *et al.,* (1996) achieved inspiratory muscle fatigue in their subjects by having them breath against an inspiratory threshold load while generating 80% of their

predetermined maximal mouth pressure until they could no longer reach the target pressure.

One of the most readily observed physiological responses to exercise is increased ventilation, although, it is uncertain how severely this hyperpnea stresses the ventilatory muscles. As an approach to answer this question authors have attempted to mimic the hyperpnea experienced during exercise in a laboratory setting. Martin *et al.,* (1982) compared short-term maximal running performance with and without prior ventilatory work designed to reduce ventilatory muscle endurance. The work consisted of 150-minutes of sustained maximum ventilation performed isocapnically while the subjects were seated. The subjects, on average were able to maintain two thirds (68%) of their 12s-MVV. Martin and his colleagues (1982) concluded that reduced ventilatory muscle endurance alone is sufficient to decrease short-term maximal running performance. Bai *et al.,* (1984) demonstrated that ventilatory muscle fatigue may limit endurance at high levels of ventilation. They studied the ventilatory muscle function before, during, and after short-term near-maximal voluntary normocapnic hyperpnea. Mador and associates (1996) had ten male subjects voluntarily breath at minute ventilation equal to or slightly greater than 60% of their 12s-MVV in order to determine whether diaphragmatic fatigue occurred after voluntary hyperpnea to task failure. Prior studies suggest that diaphragmatic fatigue can occur after voluntary hyperpnea at very high ventilatory levels (greater than 70% of MVV) (Bai *et al.,* 1984). With the aid of electromyography diaphragmatic fatigue has been shown in normal subjects hyperventilating above 70% of MVV, a ventilatory level often seen during peak exercise (Fitting, 1991). Mador and his associates (1996) concluded that long-lasting contractile fatigue of the diaphragm reliably

occurs after voluntary hyperpnea at levels sufficient to induce task failure. Hamnegård *et al.*, (1996) investigated the effect of maximal isocapnic ventilation (MIV) on $P_{di,\,TW}$ elicited by cervical magnetic stimulation and concluded that diaphragmatic fatigue may be a limiting factor in maximal ventilation in man.

Many authors have shown that diaphragm fatigue can occur following intense exercise. Johnson and coworkers (1993) found significant diaphragmatic fatigue in subjects measuring $P_{di\,tw}$ using BPNS before and after intense exercise at 85 and 95% of $VO_{2\,max}$. Mador and Dahuja (1996) also measured P_{di} during BPNS before and after subjects exercised at 70 and 75% of their maximal work capacity until volitional exhaustion and reported that diaphragmatic fatigue can be induced by high-intensity constant load exercise. Ker and Schultz (1996) have shown that inspiratory muscles do fatigue with intensive exercise. Loke *et al.*, (1982) measured spirometry and respiratory muscle strength and endurance in runners before and after completion of a marathon race. The results showed no change in forced vital capacity (FVC), inspiratory capacity (IC), or flow rates from pre-race values, whereas, decreases in $P_{I\,max}$, $P_{E\,max}$, $P_{di\,IC}$, and MVV were demonstrated. They concluded that decrements in respiratory muscle strength and endurance suggest development of respiratory muscle fatigue after marathon running.

5.0 Effects of Respiratory Muscle Fatigue on Exercise Performance

Respiratory muscle fatigue has been documented following loaded breathing, high-intensity exercise to exhaustion, sustained endurance exercise, voluntary hyperpnea to task failure, and of course during acute respiratory failure. Several different approaches have been made to investigate whether or not respiratory muscle fatigue limits exercise performance in healthy, normal individuals at various levels of fitness.

Past studies attempting to answer this question have included respiratory muscle unloading, respiratory muscle loading, exercise-induced respiratory muscle fatigue measures, and respiratory muscle training.

In the past maximal exercise capacity was not usually considered to be limited by ventilation in normal subjects. This theory was supported by the observation that maximal exercise ventilation does not normally exceed 70% of MVV (Olafsson and Hyatt, 1969). This is slightly inaccurate because MVV is usually measured over a 12 to 15s time period and cannot be maintained for much longer. Various other authors have found that the maximal sustainable ventilation decreases with time and that the level that can exceed a 15-minute time period corresponds to 55 to 80% of MVV. Respiratory muscle fatigue most likely explains this inability to sustain MVV for more than 12 to15 seconds (Fitting, 1991).

5.1 Respiratory Muscle Unloading

According to Johnson and his colleagues (1996), the best technique to determine if respiratory muscle affects exercise performance is to first unload the respiratory muscles and second to observe whether or not performance is improved. If performance is in fact improved it may suggest that respiratory muscle fatigue had an effect on exercise performance, on the other hand if no effect is observed, it would be concluded that the degree of fatigue observed was not enough to alter human performance. Methods most commonly used to unload the respiratory muscles involve the use of reduced viscosity gases (helium) or pressure-assist ventilators. The result of unloading the respiratory muscles would be a decrease in whole-body VO_2 secondary to the drop in respiratory VO_2 and an increase in endurance time (Johnson *et al.*, 1996). These results

are based on three theoretical potential effects of unloading the respiratory muscles: (1) decrease in the work of breathing (2) decrease in blood flow demands and competition with locomotor muscles, and (3) decrease in the sensation of dyspnea (Johnson *et al.*, 1996). A previous study performed by Aaron *et al.*, (1985) examined the influence of helium/oxygen breathing on human performance (79% He, 21%O_2) on a group of rowers at 80 and 90 to 95% $VO_{2\,max}$ to exhaustion. At the lower work intensity a significant difference in exercise time and whole-body VO_2 were not observed; however, at the higher work intensity, exercise time increased by 40% while breathing helium. Aaron and colleagues (1985) concluded from the results of this study that respiratory muscle fatigue and/or respiratory load may play a role in limiting human performance at exercise intensities greater than 90 to 95% of $VO_{2\,max}$. Another method of unloading the respiratory muscles is pressure-assist; this method has been investigated by various authors (Gallagher and Younes (1989); and Marciniuk *et al.*, 1994). The device acts as a demand regulator, sensing changes in mouth pressure and responding by partially unloading the respiratory muscles. In the studies mentioned no significant differences were observed in exercise time, whole-body VO_2, ventilation, or perception of effort at work intensities up to 85% of $VO_{2\,max.}$ These results imply that respiratory muscle fatigue or load plays no role in overall performance at exercise intensities less than 85% of VO_{2max}. Harms and coworkers (2000) also unloaded the respiratory muscles using a feedback controlled proportional-assist ventilator (PAV) to reduce the work of the inspiratory muscles during exercise. In their study, respiratory muscle unloading during exercise reduced VO_2, caused hyperventilation, and reduced the rate of change in perceptions of respiratory and limb discomfort throughout the duration of exercise.

Harms and his colleagues concluded that exercise performance at work intensities equal to or greater than 90% VO_2 is influenced by the work of breathing normally incurred at these levels.

5.2 Effects of Ventilatory Work on Respiratory Function

Increased ventilation is a readily observed physiological response to exercise, although it is unclear how much this hyperpnea stresses the respiratory muscles. In order to answer this question many investigators have attempted to mimic this exercise hyperpnea in a laboratory setting and to observe the effects of prior ventilatory work or even respiratory muscle fatigue on subsequent exercise performance.

Martin, Heinzelman, and Chen (1982), approached the previously mentioned question by comparing short-term maximal running performance in nine subjects with and without prior ventilatory work intended to decrease respiratory muscle endurance. This ventilatory work was accomplished with the subjects in a seated position and consisted of 150-minutes of sustained maximal isocapnic breathing. On average the subjects were able to maintain 68% of their 12-s MVV during this sustained long-term breathing test. Short-term maximal running performance following the ventilatory work was reduced compared to the control group (6.5 vs. 7.6 min; $P< 0.01$). Exercise stopped at significantly lower ventilation, and the subjects reached a significantly lower peak O_2 uptake. The results of this study indicate that reduced respiratory muscle endurance by itself is a detriment to short-term exercise performance. Bai and his colleagues (1984) evaluated respiratory muscle function in five normal male subjects prior to, during and following short-term near-maximal voluntary (eucapnic) hyperpnea. Pleural and abdominal pressure measurements and diaphragm EMG during hyperpnea were taken at

76%, 79%, 86% of MVV, and at MVV. Decreases in P_{Imax} and $P_{di\ max}$ were observed post-hyperpnea at 76% and 79% MVV. The decrease in $P_{I\ max}$ indicates that fatigue of other inspiratory muscles in addition to the diaphragm occurred. A decrease in the pressure-frequency curves of the diaphragm and the ratio of high-to-low frequency power of the diaphragm occurred in association with decreases in $P_{di\ max}$, providing further evidence that diaphragm fatigued occurred. In order to attain higher levels of ventilation there was an increasing contribution of the expiratory muscles, as demonstrated by the analysis of the pressure-time product for the inspiratory and expiratory muscles. Bai and his coworkers concluded that respiratory muscle fatigue may limit endurance at high levels of ventilation. A study by Dodd *et al.,* (1989) examined the effects of short-duration, high-intensity ventilatory work on subsequent exercise performance. They tested the hypothesis that 10 minutes of volitional isocapnic (85% of peak exercise ventilation) hyperpnea at a controlled frequency and tidal volume would cause a detriment to subsequent exercise performance because of respiratory muscle fatigue. The study involved 10 healthy, normal male subjects whose pulmonary function values (FVC, FEV_1, FEV_1/FVC) were not significantly altered by the volitional hyperpnea. Ventilation and gas exchange variables (VO_2, V_E, f, end-tidal PO_2 and PCO_2, V_E/VO_2, V_E/VCO_2, $\%SaO_2$) were also insignificantly altered during exercise following the volitional hyperpnea. Exercise time to exhaustion during this study did not change between treatments; therefore these observations indicate that short-term ventilatory work does not affect pulmonary function or subsequent exercise performance. Aaron *et al.,* (1992) addressed two questions in their study (1) does exercise hyperpnea even reach a "critical useful level"? and (2) is the work of breathing at $VO_{2\ max}$ fatiguing to the respiratory

muscles? In attempt to answer these two questions the subjects were required to exercise progressively to a maximal level for as long as they could and the O_2 cost of ventilation was determined. Tidal expiratory flow-volume and transpulmonary pressure-volume loops (Ptp) were also measured. At rest, the participant was then asked to mimic their maximum and moderate exercise Ptp-volume loops, and O_2 cost of hyperpnea and the length of time the subjects could maintain reproduction of their maximum exercise loop was measured. At the maximum level of exercise the O_2 cost of ventilation was found to be 10 ± 1% of the $VO_{2\,max}$, and the O_2 cost of hyperpnea was measured at 9 ± 1%. The length of time the subjects could voluntarily mimic maximum exercise was, on average for all subjects, 3 to 10 times longer than the duration of maximal exercise. Aaron and his coworkers concluded that the work of breathing and O_2 cost of ventilation during maximum exercise are non-fatiguing and sustainable. Hamnegård and colleagues (1996) investigated the effect of maximal isocapnic ventilation (MIV) on $P_{di,\,tw}$ elicited by cervical magnetic stimulation. $P_{di,\,tw}$ was measured in nine normal subjects before and after 2 minutes of MIV. Ventilation decreased by 35% for the nine subjects at 1 minute, $P_{di,\,tw}$ was also reduced (-24%) 10-minutes following MIV. Based on the results of this study it has been demonstrated that diaphragm contractility is reduced following MIV. Hamnegård and coworkers agree that diaphragmatic fatigue may be a limiting factor in maximal ventilation in man. Mador, Rodis and Diaz (1996) attempted to answer whether or not diaphragmatic fatigue occurs after voluntary hyperpnea to task failure. Ten healthy male subjects volunteered for this study, they were asked to breath at minute ventilation equal to or greater than 60% of their 12-s MVV until task failure. Transdiaphragmatic pressure was measured during and 10, 30, 60, and 120-minutes after

hyperpnea during bilateral supramaximal stimulation of the phrenic nerves. During transcutaneous stimulation, 7 of the 10 subjects displayed at least a 10% reduction in P_{di} following the hyperpnea task and a 10% or greater reduction in P_{di} was demonstrated during cervical stimulation in all 10 subjects following hyperpnea. Mador and coworkers concluded from the results of their study that voluntary hypernea to task failure can reliably produce long-lasting contractile fatigue of the diaphragm.

5.3 Respiratory Muscle Loading

Another method used to examine the effects of respiratory muscle fatigue on exercise performance is to load the respiratory muscles. The most common way to load the respiratory (inspiratory) muscle is to have the subject inspire against a threshold load at a certain percentage of maximal inspiratory, as mentioned previously. Mador and Acevedo (1991) induced inspiratory muscle fatigue in ten healthy subjects by having them breath against an inspiratory load while generating 80% of their predetermined maximal mouth pressure until they could no longer reach the target pressure (subjects were able to chose own duty cycle and breathing pattern). On three separate occasions the subjects cycled to volitional exhaustion at 90% of their maximal capacity, once following inspiratory muscle fatigue, the other two occasions served as control trials without prior induction of respiratory muscle fatigue. Oxygen consumption, exercise time, heart rate, breathing pattern, and respiratory effort (using visual analogue scale [VAS]) were measured. Following the induction of fatigue exercise time was reduced compared to the control group (238±69 vs. 311±96s; $P<0.001$). Heart rate and oxygen consumption during the last minute of exercise were also reduced after the induction of fatigue compared to the control group. Effort of breathing reported by the subjects with

the use of VAS was higher after the induction of fatigue compared to the control group. The authors concluded that high-intensity exercise performance is impaired following the induction of inspiratory muscle fatigue. In another study performed by Śliwiński *et al.,* (1996) the effect of induced global inspiratory muscle fatigue on respiratory muscle control during exercise at 30, 60, and 90% of maximal power output (W_{max}) was examined on a cycle ergometer. Inspiratory muscle fatigue was induced in a similar fashion as the previously mentioned study. Six healthy recreationally active males were asked to breath at 80% of a predetermined level of $P_{I\,max}$ until task failure (duty cycle 0.6). When the subject could not reach the target pressure for five consecutive efforts inspiratory muscle fatigue was assumed. The subjects were tested on three separate occasions; the first test was used to determine maximal work capacity, which was accomplished on a cycle ergometer. The second two experimental test days required the subjects to exercise on the same cycle ergometer at the three workloads as a control run, after the induction of global inspiratory muscle fatigue. These tests were performed in random order on two separate days. Perceived breathlessness, breathing pattern, anteroposterior displacement of ribcage and abdomen, and esophageal and gastric pressures were measured. During the mild and moderate exercise bouts (30 and 60% W_{max}) no changes in ventilatory parameters were recorded, however, ventilatory response was altered during heavy exercise; both breathing frequency and minute ventilation were increased with minimal changes in tidal volume. $P_{I\,max}$ and P_{di} were reduced by 23% and 58%, respectively. The authors concluded that global inspiratory muscle fatigue may impair exercise performance in some healthy subjects, for reasons unrelated to extreme breathlessness or other ventilatory factors. The authors concluded that the respiratory

system is remarkably adjustable in maintaining ventilation during exercise in the presence of contractile ventilatory impairment, even though half of the subjects in the study were unable to complete 4-minutes of exercise at 90% of $VO_{2\,max}$ following the induction of global inspiratory muscle fatigue.

5.4 Respiratory Muscle Training

Training the respiratory muscles through resistive training or hyperpnea results in an increase in their strength and endurance and represents another approach to the question of whether or not respiratory muscle fatigue impairs exercise performance. It is well known that during whole-body exercise, the respiratory muscles are required to produce a significant amount of metabolic work, and there is also evidence to suggest the respiratory muscles adapt to exercise training in a similar fashion to the limb (skeletal) muscles. Boutellier *et al.,* (1991) performed a study to examine the respiratory system as a limiting factor to exercise performance. Four healthy, sedentary subjects participated in the study; breathing and cycling endurance as well as physical working capacity were determined before and after a respiratory muscle training protocol. The subjects trained their respiratory system for a four-week period by breathing voluntarily 76-102.5 l/min, 30-minutes daily for five times a week. The subjects were asked to continue with their usual sedentary lifestyle. Both breathing endurance and cycle endurance increased by 268% and 50% respectively. Vital capacity, peak flow, FEV_1, specific airway conductance and MVV did not change significantly following the training regime. Boutellier *et al.,* (1992) performed another similar study with 8 normal, trained subjects. The subjects continued their habitual endurance training, with an additional 30-minutes daily breathing exercise at 85-160 $L \cdot min^{-1}$ for four weeks. The respiratory training

improved breathing endurance, and cycling endurance at the anaerobic threshold. After RMT, minute ventilation for a given exercise intensity was reduced and cycle performance at anaerobic threshold was prolonged. The authors concluded that the results of both studies indicate the respiratory system as a limiting factor in normal trained as well as untrained subjects. Stuessi *et al.,* (2001) investigated the effects of a respiratory training program on exercise performance. The experimental group (E) underwent 15-weeks of 40-sessions breathing at 65-70% of their MVV for 30-minutes each session, whereas a control group (C) performed no respiratory muscle training at all. The thirteen subjects in the experimental group significantly increased their breathing endurance (+632%) whereas the 15 subjects in the control group had a nonsignificant (NS) reduction in their breathing endurance (-2%). The experimental group also significantly increased their cycling time to exhaustion at 70% of maximal work capacity (+24%), whereas the control group had a –4% reduction in exercise performance. The results of this study indicate that RMT does indeed have a positive effect on exercise performance and supports the conclusions of the previous studies mentioned. Other studies performed to investigate the effects of respiratory muscle training on exercise performance have shown contradicting results. Many of these studies consisted of small sample sizes, different respiratory training regimes and different laboratory tests of performance. The training-status of the subjects have been inconsistent so it is hard to compare the results of these different studies (Fairbarn *et al.,* 1991; Voliantis *et al.,* 2001). A study performed by Morgan *et al., (*1987) demonstrated a nonsignificant reduction in cycling performance following respiratory muscle training at 85% MVV 5 days per week for 3-weeks. Although breathing endurance appeared to be improved

significantly (+1575%) cycling performance at 95% $VO_{2\,max}$ to exhaustion displayed 6% reduction. This is an interesting find as respiratory muscle fatigue as been found to occur at this intense level of exercise, and warrants further investigation of respiratory muscle fatigue as a limiting factor in exercise performance.

6.0 Recovery of Respiratory Muscle Fatigue

The rate of recovery of muscle fatigue differs depending on the nature of the fatigue. Skeletal muscle fatigue can develop as a result of high (50-100-Hz) or low (10-30-Hz) rates of nerve activation. It appears that low frequency respiratory muscle fatigue has a slower recovery process compared to that of muscle fatigue occurring as a result of high frequency muscle activation. Previous studies conducted by Aubier and coworkers (1981) investigating diaphragmatic fatigue in healthy subjects, complete recovery of high frequency fatigue occurred within 25-minutes, whereas low-frequency fatigue persisted for at least 30-minutes. Yan and colleagues (1992) showed that low-frequency fatigued persisted one hour following its induction. Laghi et al., (1995) investigated the recovery pattern of diaphragmatic fatigue over 24-hours following IRL at 80% of $P_{Di\,max}$ until task failure. Fatigue was confirmed through the measurement of P_{Di} using BPNS. Diaphragmatic fatigue induced in this experimental protocol resulted in large decreases in diaphragmatic contractility that persisted for at least 24-hours.

7.0 Conclusion

Respiratory muscle fatigue has been shown to be a limiting factor in exercise performance. While controversy still exists in the literature, most authors agree that respiratory muscle fatigue can occur following high-intensity exercise as well as prolonged submaximal exercise, and therefore may be a limiting factor in exercise

performance. Although, due to incomplete and contrasting literature is necessary for further investigation of the respiratory system as a limiting factor in exercise performance. It is still uncertain whether or not diaphragm fatigue impairs exercise performance. Further studies investigating this topic will also provide a clearer picture of the mechanisms behind fatigue as well as any other ventilatory limitations to exercise in both healthy and diseased individuals. If diaphragm fatigue is indeed found to be a limiting factor in exercise performance implications for respiratory muscle training will be of importance for both athletes as well as in a clinical setting for rehabilitation in patients.

Table 6: Summary of the reported effects of respiratory muscle fatigue (RMF) on exercise performance and/or RM strength and endurance.

Study	Subjects	Method of Inducing RMF	Reported changes in RM function	Exercise Load	% change in performance
Harms *et al.*, (2000)	7 male competitive cyclists	E_1: unloaded RM (PAV) E_2: loaded RM (IRL) C: unchanged RM	E_1: Dyspnea and Leg RPE ↓ E_2: Dyspnea and Leg RPE ↑ when compared to controls	Cycle @ 90% VO_2max	E_1: ↑ (EPT) 14 ± 5%, ↓ VO_2 E_2: ↓ EPT 15 ± 3% (both compared to control)
Śliwiński *et al.*, (1996)	6 untrained males	High IRL to exhaustion (80% $P_{I\,max}$; DC @ 0.6)	C: $P_{I\,max}$, P_{di} ↓ from baseline (sig) E: $P_{I\,max}$,(-23%) P_{di} (-58%) from baseline and C (sig), ↑ V_E, f (sig) @ rest	C: 30%,60%, 90% VO_2 max (4-min stages) E: 30%,60%, 90% VO_2 max following RMF cycle ergometer	No diff in VO_2, CO_2 output or HR b/w groups
Hamnegard *et al.*, (1996)	9 males untrained	2-min MIV	$P_{di,\,Tw}$ (-23%) 10-min post; (-13%) 60-min post MIV (sig) During CMS	Exercise not performed	Not applicable
Mador *et al.*, (1996)	7 males	60% MVV to exhaustion	P_{di} BPNS (-10%) in 7/10 subjects (sig) CMS all subjects(-10%) (sig) 60-min post P_{di} sig reduced	Exercise not performed	Not applicable
McConnell *et al.*, (1996)	24 mod-trained males	See exercise Load	$P_{I\,peak}$ (-10%) $P_{average}$ (-8%)	Multi-stage incremental shuttle run to volitional fatigue (10-15-min)	Not applicable; Showed severity of fatigue is related to baseline strength of RM
Ker & Schultz (1996)	10 trained runners (7 males; 3 females)	See exercise load	$P_{I\,max}$ 3 days post-race (NS) $T_{Lim\ IRM}$ (-26.5%) 3 days post-race (sig)	Ultra-marathon (87km)	Not Applicable
Mador *et al.*, (1993)	10 untrained (sedentary) males	See exercise load	$P_{di,\,Tw}$ (-17.5%) @ 10-min post (sig); (-7%) @ 60-min post Ex	80% W_{max} to volitional exhaustion on bicycle erg.	Not Applicable

Johnson *et al.*, (1992)	12 males (range of fitness levels)	See exercise load	E_1: $P_{di, Tw}$ (-8 to -32%); $P_{di\ Tetanic}$ (-21% @ 10-Hz & -13% @ 20-Hz) @ all lung voumes (sig) E_2: $P_{di, Tw}$ (-15%) @ FRC (sig)	E_1: 95% $VO_{2\ max}$; & E_2: 85% $VO_{2\ max}$ to exhaustion Short term run on treadmill	Not Applicable
Mador & Acevedo, (1991)	10 (7males; 3 females)	Inspiratory threshold load @80% $P_{I\ max}$	Not Applicable	90% $VO_{2\ max}$ to exhaustion on cycle ergometer	EPT (-23.5%) (sig) @ last min of exercise VO_2 , HR lower after induction of fatigue (sig)
Hill *et al.*, (1991)	12 trained males	See exercise load	FVC (-7.1%) FEV_1 (-8.4%) $FEF_{25-75\%}$ (-15%) –all sig MVV no change	Endurance triathlon	Not Applicable
Dodd *et al.*, (1989)	10 aerobically trained males	10-min volitional isocapnia hyperpnea (85% exercise V_E)	NS change in ventilation or gas exchange variables	85% peak exercise power output to exhaustion on cycle ergometer	NS in time to exhaustion, PF measures
Martin *et al.*, (1982)	9 (5 females; 4 males)	150-min sustained maximal ventilation (isocapnic)	NS change in MVV, FEV_1, FVC	Treadmill run to exhaustion (self selected running speed; 1%↑incline/min)	EPT -14.5%) sig. exercise ceased @ lower VO_2, V_E, & HR (sig)
Loke *et al.*, (1982)	4 males	See exercise load	P_{di} (-20%) $P_{I\ max}$ (-16.5%) $P_{E\ max}$ (-28%) MVV(-10%) All sig NSD in IC, FVC, flow rates	Marathon race (42.2-km)	Not Applicable

C, Control group; DC, Duty cycle (T_I/ T_{Tot}); E, Experimental group; EPT, Endurance performance time; RPE, Rating of perceived exertion; T_{Lim}, respiratory endurance time.

Appendix C. Tables: Individual Subject Data

Table 7. Participant Characteristics.

Subject (n=10)	Age (yrs)	Height (cm)	Mass (kg)
1	25	168.1	69.0
2	26	164.3	55.5
3	28	172.5	66.5
4	26	166.7	63.4
5	29	165.6	57.5
6	31	164.0	54.4
7	26	173.0	58.7
8	26	160.8	52.5
9	24	162.3	51.6
10	27	160.0	43.6
Mean	**26.8**	**165.7**	**57.3**
SD	**2.0**	**4.5**	**7.6**

yrs, years; cm, centimeters; kg, kilograms.

Table 8. Resting lung volumes of participants.

Subject	FVC (L)	FEV_1 (L)	FEV_1/FVC (%)	25-75%	FEF_{max} ($L \cdot sec^{-1}$)	FEV_1 %Pred	FVC %Pred
1	4.12	3.19	77.51	2.70	7.53	96.65	106.23
2	4.07	3.67	90.17	4.50	6.2	116.88	111.2
3	4.44	3.75	84.46	3.90	6.48	111.28	111.28
4	3.53	2.73	77.34	2.40	5.05	84.78	93.63
5	3.35	2.73	81.49	3.67	6.57	87.22	91.28
6	4.25	3.78	87.06	4.60	7.24	124.75	119.38
7	4.55	3.88	85.27	3.86	6.02	114.58	112.59
8	3.53	2.96	83.85	2.97	6.04	98.01	100.57
9	4.24	3.71	87.50	4.11	9.59	119.29	117.45
10	2.81	2.31	82.20	2.51	6.07	77.52	81.45
Mean	**3.89**	**3.27**	**83.69**	**3.52**	**6.68**	**103.10**	**104.51**
SD	**0.56**	**0.56**	**4.17**	**0.82**	**1.23**	**16.43**	**12.42**

FVC, forced vital capacity; FEV_1, forced expiratory volume; FEV_1/FVC, ratio of FEV_1 to FVC; $FEF_{25-75\%}$, percent of forced expiratory volume occurring between 25 and 75% of the curve; FEF_{max}, maximal forced expiratory flow in litres per second, FEV_1 pred, percent of predicted FEV_1 actually achieved; FVC % pred, percent of predicted FVC actually achieved.

Table 9. Ventilatory parameters at peak exercise. Individual subject data. Day 1.

Subject	$V_{E\ (BTPS)}$	VCO_2	V_E/VO_2	V_E/VCO_2	RER
1	119.07	32.43	34.28	32.08	1.13
2	124.40	45.18	54.84	47.35	1.24
3	92.86	37.40	36.59	40.66	1.04
4	94.18	37.76	33.26	33.98	1.05
5	95.00	31.43	36.92	34.20	1.11
6	118.80	37.16	38.51	34.25	1.19
7	104.84	36.67	35.80	34.13	1.10
8	91.14	36.71	39.03	36.10	1.11
9	106.65	36.18	50.29	46.35	1.17
10	73.73	37.82	43.48	41.84	1.14
Mean	**102.07**	**36.87**	**40.30**	**38.09**	**1.13**
SD	**15.69**	**3.67**	**7.13**	**5.55**	**0.06**

V_E, minute ventilation in litres per minute; VO_2, O_2 consumption in litres per minute; VCO_2, CO_2 production in litres per minute; V_E/VO_2 and V_E/VCO_2, ventilatory equivalents for O_2 and CO_2, respectively; RER, respiratory exchange ratio.

Table 10. Ventilatory parameters at peak exercise. Individual subject data. Day 2.

Subject	$V_{E\ (BTPS)}$	VCO_2	V_E/VO_2	V_E/VCO_2	RER
1	101.51	3.16	34.28	32.08	1.07
2	114.43	2.41	54.84	47.35	1.16
3	85.90	2.11	36.59	40.66	0.90
4	80.34	2.36	33.26	33.98	0.98
5	105.32	3.08	36.92	34.20	1.08
6	95.49	2.78	38.51	34.25	1.13
7	88.22	2.58	35.80	34.13	1.05
8	88.09	2.44	39.03	36.10	1.08
9	90.13	1.94	50.29	46.35	1.09
10	73.34	1.75	43.48	41.84	1.02
Mean	**92.28**	**2.46**	**40.30**	**38.09**	**1.06**
SD	**12.19**	**0.46**	**7.13**	**5.55**	**0.07**

V_E, minute ventilation in litres per minute; VO_2, O_2 consumption in litres per minute; VCO_2, CO_2 production in litres per minute; V_E/VO_2 and V_E/VCO_2, ventilatory equivalents for O_2 and CO_2, respectively; RER, respiratory exchange ratio.

Table 11. Ventilatory parameters at peak exercise. Individual subject data. Day 3.

Subject	$V_{E\ (BTPS)}$	VCO_2	V_E/VO_2	V_E/VCO_2	RER
1	117.79	3.44	39.06	34.24	1.14
2	84.49	1.73	50.23	48.85	1.03
3	101.08	2.79	37.68	36.16	1.05
4	95.85	2.38	40.15	40.20	1.00
5	103.82	2.89	37.13	35.92	1.04
6	*	*	*	*	*
7	98.02	2.64	35.96	37.15	0.95
8	88.00	2.25	38.49	39.50	0.98
9	83.01	2.58	39.02	34.34	1.14
10	78.14	1.99	44.23	40.06	1.17
Mean	**94.47**	**2.52**	**40.22**	**38.49**	**1.06**
SD	**12.39**	**0.51**	**4.17**	**4.51**	**0.08**

* Denotes missing data

V_E, minute ventilation in litres per minute; VO_2, O_2 consumption in litres per minute; VCO_2, CO_2 production in litres per minute; V_E/VO_2 and V_E/VCO_2, ventilatory equivalents for O_2 and CO_2, respectively; RER, respiratory exchange ratio.

Table 12. Ventilatory parameters at peak exercise. Individual subject data. Day 4.

Subject	$V_{E\ (BTPS)}$	VCO_2	V_E/VO_2	V_E/VCO_2	RER
1	102.13	3.24	33.90	31.57	1.08
2	120.32	2.22	55.01	54.25	1.00
3	100.28	2.54	39.51	41.36	0.96
4	101.35	2.67	37.76	37.91	1.00
5	109.52	2.88	37.01	38.09	0.97
6	103.30	2.57	41.83	40.16	1.04
7	100.50	2.53	39.58	39.58	1.06
8	90.84	2.29	39.45	39.70	1.00
9	95.45	2.76	41.46	34.60	1.20
10	71.92	1.78	42.77	40.74	1.06
Mean	**99.56**	**2.55**	**40.83**	**39.80**	**1.04**
SD	**12.53**	**0.40**	**5.32**	**5.90**	**0.07**

V_E, minute ventilation in litres per minute; VO_2, O_2 consumption in litres per minute; VCO_2, CO_2 production in litres per minute; V_E/VO_2 and V_E/VCO_2, ventilatory equivalents for O_2 and CO_2, respectively; RER, respiratory exchange ratio.

Table 13. Ventilatory parameters at peak exercise. Individual subject data. Day 5.

Subject	$V_{E\ (BTPS)}$	VCO_2	V_E/VO_2	V_E/VCO_2	RER
1	116.48	3.38	36.58	34.44	1.06
2	102.50	2.18	45.99	46.99	1.02
3	108.18	2.58	41.21	41.99	0.98
4	95.21	1.70	42.33	55.95	0.76
5	94.45	2.74	34.15	35.20	0.90
6	104.27	2.67	45.14	39.10	1.02
7	86.46	2.50	35.18	34.59	1.02
8	93.54	2.49	39.59	37.54	1.06
9	101.15	2.40	42.29	42.26	1.00
10	86.80	1.75	48.24	50.53	0.98
Mean	**98.90**	**2.44**	**41.07**	**41.86**	**0.98**
SD	**9.46**	**0.49**	**4.47**	**7.29**	**0.09**

V_E, minute ventilation in litres per minute; VO_2, O_2 consumption in litres per minute; VCO_2, CO_2 production in litres per minute; V_E/VO_2 and V_E/VCO_2, ventilatory equivalents for O_2 and CO_2, respectively; RER, respiratory exchange ratio.

Table 14. Ventilatory parameters at peak exercise. Individual subject data. Day 6.

Subject	$V_{E\ (BTPS)}$	VCO_2	V_E/VO_2	V_E/VCO_2	RER
1	98.65	3.12	33.33	31.66	1.05
2	114.85	2.28	53.27	50.42	1.06
3	100.09	2.26	38.00	44.39	0.88
4	95.51	2.64	36.01	36.22	0.99
5	98.81	2.86	36.00	34.62	1.04
6	94.50	2.54	37.00	37.50	1.00
7	100.23	2.50	36.60	40.07	0.91
8	91.41	2.37	39.66	38.67	1.03
9	93.49	3.05	27.13	30.72	0.89
10	72.25	1.85	42.69	40.77	1.04
Mean	**95.98**	**2.55**	**37.97**	**38.50**	**0.99**
SD	**10.53**	**0.39**	**6.39**	**5.90**	**0.07**

V_E, minute ventilation in litres per minute; VO_2, O_2 consumption in litres per minute; VCO_2, CO_2 production in litres per minute; V_E/VO_2 and V_E/VCO_2, ventilatory equivalents for O_2 and CO_2, respectively; RER, respiratory exchange ratio.

Table 15. Performance at peak exercise. Individual subject data. Day 1.

Subject	HR (bpm)	Dyspnea Borg 10-point Scale		$VO_{2\,max}$ ($mL \cdot kg^{-1} \cdot min^{-1}$)	$VO_{2\,max}$ ($L \cdot min^{-1}$)
		Leg discomfort	Breathlessness		
1	193	maximal (10)	very, very strong (9)	47.28	3.26
2	187	very, very strong (9)	very strong (7)	38.73	2.14
3	186	strong (5)	strong (5)	35.83	2.31
4	184	strong (5)	strong (5)	39.53	2.51
5	187	maximal (10)	very, very strong (9)	46.63	2.69
6	175	very strong (7)	strong (5)	49.48	2.69
7	187	very, very strong (9)	very strong (8)	44.38	2.60
8	182	maximal (10)	strong (5)	42.65	2.25
9	183	very strong (8)	strong (6)	48.65	2.52
10	186	very strong (8)	strong (6)	39.48	1.72
Mean	**185.00**			**43.26**	**2.47**
SD	**4.62**			**4.72**	**0.41**

HR, heart rate in beats per minute; Dyspnea, amount of leg discomfort and breathlessness at point volitional fatigue; $VO_{2\,max}$, maximum oxygen consumption in litres per minute and milliliters per kilogram of body mass per minute.

Table 16. Performance at peak exercise. Individual data. Day 2.

Subject	HR (bpm)	Dyspnea Borg 10-point Scale		$VO_{2\,max}$ ($mL \cdot kg^{-1} \cdot min^{-1}$)	$VO_{2\,max}$ ($L \cdot min^{-1}$)
		Leg discomfort	Breathlessness		
1	183	maximal (10)	maximal (10)	42.95	2.96
2	174	maximal (10)	very, very strong (9)	37.70	2.09
3	179	maximal (10)	very, very strong (9)	35.28	2.35
4	178	very, very strong (9)	very, very strong (9)	38.03	2.42
5	190	maximal (10)	maximal (10)	49.53	2.85
6	174	maximal (10)	very, very strong (9)	45.40	2.47
7	180	very strong (8)	very strong (7)	42.08	2.47
8	179	maximal (10)	very strong (7)	42.88	2.25
9	177	maximal (10)	very, very strong (9)	34.65	1.79
10	177	very, very strong (9)	very strong (7)	38.63	1.68
Mean	**179.10**			**40.71**	**2.33**
SD	**4.68**			**4.69**	**0.41**

HR, heart rate in beats per minute; Dyspnea, amount of leg discomfort and breathlessness at point volitional fatigue; $VO_{2\,max}$, maximum oxygen consumption in litres per minute and milliliters per kilogram of body mass per minute.

Table 17. Performance at peak exercise. Individual data. Day 3.

Subject	HR (bpm)	Dyspnea Borg 10-point Scale		$VO_{2\ max}$ ($mL \cdot kg^{-1} \cdot min^{-1}$)	$VO_{2\ max}$ ($L \cdot min^{-1}$)
		Leg discomfort	Breathlessness		
1	176	very strong (9)	very strong (8)	43.78	3.02
2	177	maximal (10)	very, very strong (9)	30.40	1.68
3	177	maximal (10)	maximal (10)	40.23	2.68
4	177	very, very strong (9)	very, very strong (9)	37.63	2.39
5	184	very, very strong (9)	very strong (8)	48.53	2.80
6	*	maximal (10)	very, very strong (9)	*	*
7	186	maximal (10)	maximal (10)	46.60	2.73
8	181	maximal (10)	very, very strong (9)	43.93	2.31
9	175	maximal (10)	very, very strong (9)	41.90	2.17
10	181	very strong (7)	very, very strong (9)	40.58	1.77
Mean	**179.33**			**41.51**	**2.25**
SD	**3.84**			**5.33**	**0.47**

* Denotes missing data.

HR, heart rate in beats per minute; Dyspnea, amount of leg discomfort and breathlessness at point volitional fatigue; $VO_{2\ max}$, maximum oxygen consumption in litres per minute and milliliters per kilogram of body mass per minute.

Table 18. Performance at peak exercise. Individual data. Day 4.

Subject	HR (bpm)	Dyspnea Borg 10-point Scale		$VO_{2\ max}$ ($mL \cdot kg^{-1} \cdot min^{-1}$)	$VO_{2\ max}$ ($L \cdot min^{-1}$)
		Leg discomfort	Breathlessness		
1	169	very strong (7)	strong (5)	43.70	3.01
2	178	very, very strong (9)	maximal (10)	40.13	2.22
3	172	maximal (10)	maximal (10)	38.08	2.54
4	182	very strong (7)	very strong (7)	42.78	2.69
5	186	maximal (10)	very, very strong (9)	51.38	2.96
6	171	very, very strong (9)	very strong (8)	45.35	2.47
7	175	maximal (10)	very, very strong (9)	42.30	2.53
8	183	maximal (10)	maximal (10)	43.78	2.30
9	175	maximal (10)	maximal (10)	44.50	2.30
10	177	very strong (8)	very strong (8)	38.70	1.68
Mean	**176.80**			**43.07**	**2.20**
SD	**5.53**			**3.81**	**0.28**

HR, heart rate in beats per minute; Dyspnea, amount of leg discomfort and breathlessness at point volitional fatigue; $VO_{2\ max}$, maximum oxygen consumption in litres per minute and milliliters per kilogram of body mass per minute.

Table 19. Performance at peak exercise. Individual data. Day 5.

Subject	HR (bpm)	Dyspnea Borg 10-point Scale		$VO_{2\,max}$ ($mL \cdot kg^{-1} \cdot min^{-1}$)	$VO_{2\,max}$ ($L \cdot min^{-1}$)
		Leg discomfort	Breathlessness		
1	180	maximal (10)	very strong (8)	46.03	3.17
2	180	maximal (10)	very strong (8)	40.35	2.23
3	179	very strong (7)	very strong (7)	39.38	2.63
4	187	very, very strong (9)	very strong (8)	35.43	2.25
5	181	very, very strong (9)	maximal (10)	49.05	2.82
6	177	maximal (10)	very strong (8)	47.08	2.56
7	183	very, very strong (9)	very, very strong (9)	41.98	2.50
8	184	maximal (10)	very, very strong (9)	44.93	2.36
9	185	maximal (10)	maximal (10)	46.25	2.39
10	184	very strong (7)	very strong (7)	41.35	1.80
Mean	**182**			**43.2**	**2.26**
SD	**3.09**			**4.18**	**0.33**

HR, heart rate in beats per minute; Dyspnea, amount of leg discomfort and breathlessness at point volitional fatigue; $VO_{2\,max}$, maximum oxygen consumption in litres per minute and milliliters per kilogram of body mass per minute.

Table 20. Performance at peak exercise. Individual data. Day 6.

Subject	HR (bpm)	Dyspnea		$VO_{2\,max}$ ($mL \cdot kg^{-1} \cdot min^{-1}$)	$VO_{2\,max}$ ($L \cdot min^{-1}$)
		Leg discomfort	Breathlessness		
1	173	very strong (8)	very strong (8)	42.93	2.96
2	173	maximal (10)	very, very strong (9)	38.98	2.16
3	182	very, very strong (9)	very, very strong (9)	39.55	2.64
4	183	very strong (8)	very, very strong (9)	41.78	2.65
5	188	very, very strong (9)	very, very strong (9)	47.65	2.75
6	173	maximal (10)	very strong (8)	46.95	2.55
7	183	maximal (10)	very, very strong (9)	46.80	2.74
8	185	maximal (10)	very, very strong (9)	43.80	2.31
9	177	maximal (10)	very strong (7)	66.60	3.44
10	181	very strong (7)	very strong (8)	40.45	1.37
Mean	**180**			**45.55**	**2.47**
SD	**5.45**			**8.03**	**0.25**

HR, heart rate in beats per minute; Dyspnea, amount of leg discomfort and breathlessness at point volitional fatigue; $VO_{2\,max}$, maximum oxygen consumption in litres per minute and milliliters per kilogram of body mass per minute.

Table 21. Ventilation in Litres per minute during the 15-minute voluntary hyperpnea task. Individual subject data.

	Day 2 RM fatigue $VO_{2\ max}$ test		Day 3 RM fatigue TTE test		Day 4 RM fatigue TTE test	
Subject	$V_{E\ (BTPS)}$	**Percent of baseline MVV (%)**	$V_{E\ (BTPS)}$	**Percent of baseline MVV (%)**	$V_{E\ (BTPS)}$	**Percent of baseline MVV (%)**
1	110.0	75.7	98.3	78.1	69.6	48.3
2	115.5	72.2	109.8	77.3	130.9	81.3
3	74.0	67.3	95.3	80.8	78.4	69.4
4	81.8	73.0	79.8	70.0	65.7	58.7
5	100.9	78.8	94.9	75.9	101.4	83.1
6	114.8	70.4	139.8	83.7	122.6	78.1
7	105.0	86.1	100.6	74.0	109.3	85.3
8	97.5	73.3	83.6	74.0	88.1	78.0
9	103.7	61.2	106.8	64.0	107.2	64.5
10	63.1	70.1	57.5	67.6	63.3	70.3
Mean	**96.63**	**72.81**	**96.64**	**74.53**	**93.65**	**71.70**
SD	**17.82**	**6.67**	**21.46**	**6.01**	**24.17**	**11.84**

V_E, average minute ventilation throughout hyperpnea task, in litres per minute. Percent of baseline MVV, average percentage of baseline MVV achieved throughout hyperpnea task.

Table 22. MVV at rest, following hyperpnea task and exercise of all participants.

Subject	Baseline MVV	MVV Post-RMF (1-min)	MVV Post-RMF (2-min)	MVV Post-Exercise (3-min)	MVV Post-Exercise (5-min)
Test Day 2 ($VO_{2\ max}$: RM fatigue)					
1	126	99	103	120	124
2	160	146	144	151	160
3	110	99	104	107	108
4	112	71	92	99	99
5	128	106	109	120	118
6	163	140	146	146	151
7	133	126	124	125	116
8	133	126	124	125	116
9	170	155	157	165	165
10	85	68	77	95	89
Test Day 3 (EPT: RM fatigue)					
1	126	106	104	117	113
2	161	142	136	152	148
3	118	104	103	101	106
4	114	92	99	112	111
5	125	118	119	135	131
6	167	153	151	161	159
7	136	128	120	133	130
8	113	114	106	104	103
9	168	157	157	172	170
10	85	62	66	87	76
Test Day 4 (EPT: RM fatigue)					
1	144	113	109	129	125
2	161	136	130	145	140
3	113	107	101	114	110
4	112	93	94	96	89
5	122	108	110	122	119
6	157	150	147	150	151
7	128	122	120	116	123
8	113	103	88	107	97
9	168	157	157	172	170
10	90	77	82	92	92

MVV, litres per minute; EPT, endurance performance test.

Table 23. Individual subject data, menstrual cycles (day).

Subject	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6
1	3	23	19	10	28	6
2	3	9	24	4	23	18
3	20	16	4	13	13	22
4	23	8	26	25	12	11
5	14	9	20	23	8	5
6	4	8	3	14	3	11
7	12	13	9	27	5	16
8	2	6	27	20	9	12
9	28	1	22	7	17	1
10	14	7	3	20	5	26

Number represents menstrual day within 28-day cycle for each testing day.

Table 24. Individual subject data, handgrip strength before and after the induction of RM fatigue.

Subject	HG strength (kg)					
	Day 2:VO2max RM Fatigue		Day 3: EPT RM Fatigue		Day 4: EPT RM Fatigue	
	Pre	Post	Pre	Post	Pre	Post
1	32.0	33.5	30.5	30.5	35.0	36.0
2	31.5	31.0	30.0	31.0	31.5	28.0
3	32.0	33.0	31.0	33.0	33.0	32.0
4	32.0	31.0	28.0	28.5	29.0	29.0
5	30.0	29.0	31.0	33.0	30.5	29.0
6	35.0	35.0	35.0	37.0	34.0	33.0
7	35.0	37.0	37.0	39.0	36.0	38.0
8	30.0	33.0	34.0	33.0	33.0	33.0
9	32.0	31.0	33.0	34.0	31.5	32.0
10	31.0	30.0	30.0	29.5	27.0	29.0
Mean	**32.1**	**32.4**	**32.0**	**32.9**	**32.1**	**31.9**
SD	**1.7**	**2.4**	**2.7**	**3.3**	**2.7**	**3.3**

HG, hand grip strength in kilograms.

Appendix D: Pilot Data Summary

Seven healthy female subjects with various fitness levels were tested in order to assess MVV as an indicator of respiratory muscle fatigue. The study took place in the exercise physiology lab at Allan McGavin Sports Medicine Center. Briefly, the subjects were required to come into the lab and perform testing to ensure normal pulmonary function. Spirometry measures were performed with the same device mentioned previously, FEV_1, FVC, and $FEF_{25-75\%}$ were measured along with MVV. MVV was measured until 3 consecutive measures were obtained within 5% of each other. The largest of these 3 values was used in order to calculate 70% MVV. Each subject was then asked to breathe at 70% MVV (hyperpnea RM fatiguing-task) for 15 minutes (See Figure 1 for setup). FEV_1, FVC, $FEF_{25-75\%}$ were measured immediately following the RM fatiguing task to ensure bronchoconstriction was not the cause for post-RM fatigue drop in MVV. MVV was measured following the RM fatiguing task at 0, 2, 3, 5, 10 and 15-minutes post RM fatigue. The percent drop in post-fatigue MVV was calculated. The subjects were tested on two different days separated by at least 48 hours to ensure reliability of the measures. Subjects were asked to refrain from exhaustive exercise, caffeine consumption for 12 hours prior to testing, and food and liquid consumption (excluding water) for 2 hours prior to testing.

Results

All subjects showed a reduction in MVV immediately (0-min) following the 15-minute RM fatiguing task except one subject who showed an increase in MVV from measured baseline values. The mean percent fall in MVV (SD) at 0-minutes post-RM fatigue was 12.3% (6.6), -16.1% (6.2) at 2-min, - 16% (5.2) at 3-min, -17.1% (6.8) at 5-

min, -13.5% (6.3) at 10-min, and –12.5% (6.8) at 15-minutes post RM fatigue (See Table 3). Statistical analysis using one-way ANOVA, with repeated measures, demonstrated a significant F-ratio ($\alpha < 0.01$) at all times measured post-fatigue. The results indicate that MVV was still significantly reduced from baseline values at 15-minutes post-fatigue. A Tukey's HSD was applied post-hoc and the greatest difference in MVV was observed at 5-minutes post-fatigue. The subjects were required to visit the lab on two separate occasions with a minimum of 42-hours rest in order to test the reliability of the tests. Reliability was determined between days for MVV at 5-minutes post fatigue with a correlation coefficient of $r = 0.962$.

Conclusion

The results of this experiment indicate that the 15-minute hyperpnea task at ≥70% MVV can consistently result in respiratory muscle fatigue in healthy female subjects, when using percent drop in MVV as an indicator of fatigue. As a group the percent mean fall in FEV_1 was 4.4%, indicating that bronchoconstriction was not a factor in causing the reduction seen in MVV post-hyperpnea. The results indicate that this type of fatiguing task produces a longer-lasting low-frequency type of respiratory muscle fatigue as MVV was still significantly reduced 15-minutes post-hyperpnea. In a study performed by Mador *et al.*, (1996) the subjects were required to breathe at minute ventilation equal to or greater than 60% of their MVV until task failure. Twitch transdiaphragmatic pressure ($P_{di, Tw}$) was measured before and after the breathing task. At 10-minutes post hyperpnea $P_{di, Tw}$ was significantly reduced from baseline values in all subjects and remained significantly reduced for 1-hour post hyperpnea. Mador and his associates (1996)

concluded that long-lasting fatigue of the diaphragm reliably occurs after voluntary hyperpnea at levels sufficient to induce task failure.

Pilot Data: Raw Data

Maximal Voluntary Ventilation as an Indicator of Respiratory Muscle Fatigue Following 15-minutes of Voluntary Hyperpnea.

Table 25. Age, height, mass, individual subject data.

Subject	Age (yrs)	Weight (kg)	Height (cm)
1	26	62.6	174.3
2	29	57.0	167.0
3	31	53.0	165.0
4	26	45.0	156.0
5	25	69.0	169.7
6	26	57.7	164.9
7	28	64.5	165.5
Mean	**27.3**	**58.4**	**166.1**
SD	**2.0**	**7.4**	**5.2**

yrs, years; cm, centimeters; kg, kilograms.

Table 26. Resting lung volumes before and after 15-minute the hyperpnea task, individual subject data.

Subject	Test Day	Pre-hyperpnea FEV_1	Post-hyperpnea FEV_1	Pre-hyperpnea FVC	Post-hyperpnea FVC
1	Day 1	3.62	3.54	4.55	4.53
1	Day 2	3.55	3.46	4.51	4.48
2	Day 1	2.43	2.43	3.05	3.04
2	Day 2	2.93	2.84	3.67	3.56
3	Day 1	3.00	2.96	3.76	3.69
3	Day 2	2.98	3.16	3.74	3.96
4	Day 1	3.23	3.42	4.02	4.25
4	Day 2	3.45	3.36	4.37	4.02
5	Day 1	2.39	2.40	2.80	2.83
5	Day 2	2.89	2.29	3.40	2.65
6	Day 1	3.18	3.00	4.36	4.17
6	Day 2	3.21	3.23	4.14	4.23
7	Day 1	3.79	3.67	4.25	3.83
7	Day 2	3.84	3.84	4.33	4.36
	Mean	**3.18**	**3.11**	**3.93**	**3.83**
	SD	**0.45**	**0.49**	**0.55**	**0.61**

FVC, forced vital capacity, litres per minute; FEV_1, forced expiratory volume, litres per minute.

Table 27. Maximal voluntary ventilation before and after the 15-minute hyperpnea task, individual subject data.

Subject	Test Day	Pre MVV	Pre MVV	Pre MVV	V_E @ 70% MVV	Average V_E (% MVV)	Post MVV 0-min	Post MVV 2-min	Post MVV 3-min	Post MVV 5-min	Post MVV 10-min	Post MVV 15-min
1	1	128	134	131	**94.0**	**63.0**	114	114	118	119	122	123
1	2	135	138	133	**96.6**	**73.0**	116	113	116	110	122	120
2	1	129	123	122	**86.1**	**66.7**	115	109	105	106	104	109
2	2	121	114	114	**79.8**	**78.5**	110	104	104	101	109	108
3	1	145	146	148	**103.6**	**69.8**	152	137	134	139	142	145
3	2	159	150	150	**111.3**	**71.0**	145	140	140	138	144	153
4	1	131	127	135	**94.5**	**87.3**	123	118	109	102	107	117
4	2	114	106	102	**79.8**	**118.0**	102	81	81	80	100	84
5	1	83	86	89	**62.3**	**78.4**	84	78	80	82	90	91
5	2	94	86	86	**65.8**	**90.0**	65	67	78	70	70	82
6	1	126	124	131	**91.7**	**73.6**	115	112	108	108	110	114
6	2	134	135	137	**95.9**	**86.2**	123	118	117	110	119	112
7	1	156	163	162	**114.0**	**81.3**	141	136	133	136	137	145
7	2	164	168	163	**117.6**	**93.6**	145	138	135	140	144	151
Mean		129.9	128.6	128.8	**92.4**	**70.0**	117.9	111.8	111.3	110.1	115.7	118.1
SD		22.9	24.9	24.2	**16.6**	**5.3**	24.0	23.1	20.7	22.8	21.7	23.6

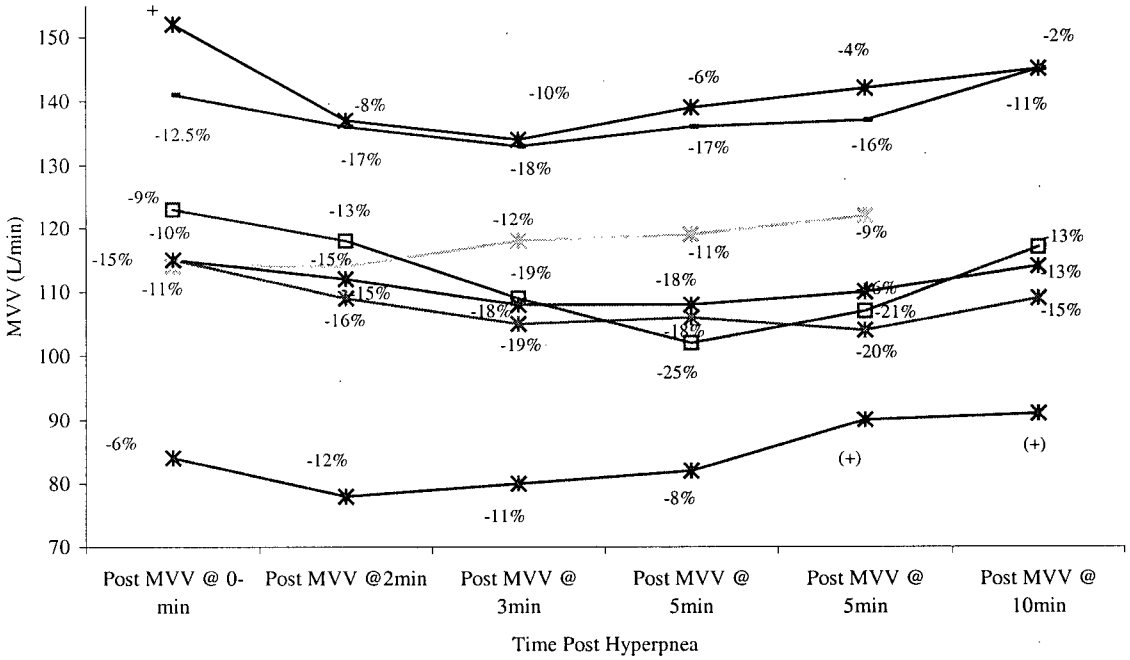
MVV, maximal voluntary ventilation, in litres per minute; V_E, average minute ventilation throughout hyperpnea task, in litres per minute. Percent of baseline MVV, average percentage of baseline MVV achieved throughout hyperpnea task.

Table 28. Percent drop in MVV, FEV_1, and FVC following 15-minute hyperpnea task, individual subject data.

Subject	Test Day	FEV_1 (%)	FVC (%)	Post MVV 0-min (%)	Post MVV 2-min (%)	Post MVV 3-min (%)	Post MVV 5-min (%)	Post MVV 10-min (%)	Post MVV 15-min (%)
1	1	2	1	15	15	12	11	9	8
1	2	(+)	(+)	16	18	16	20	12	13
2	1	0	0	11	16	19	18	20	15
2	2	3	3	4	9	9	12	4	5
3	1	1	2	(+)	8	10	6	4	2
3	2	(+)	(+)	9	12	12	13	10	4
4	1	(+)	(+)	9	13	19	25	21	13
4	2	3	8	11	29	29	30	12	26
5	1	(+)	(+)	6	12	11	8	(+)	(+)
5	2	21	22	31	29	17	26	26	19
6	1	6	4	12	15	18	18	16	13
6	2	(+)	(+)	10	14	15	20	13	18
7	1	3	10	13	17	18	17	16	11
7	2	0	(+)	14	18	20	17	14	10
Mean		**4**	**6**	**12**	**16**	**16**	**17**	**14**	**12**
SD		**6**	**7**	**7**	**6**	**5**	**7**	**6**	**7**

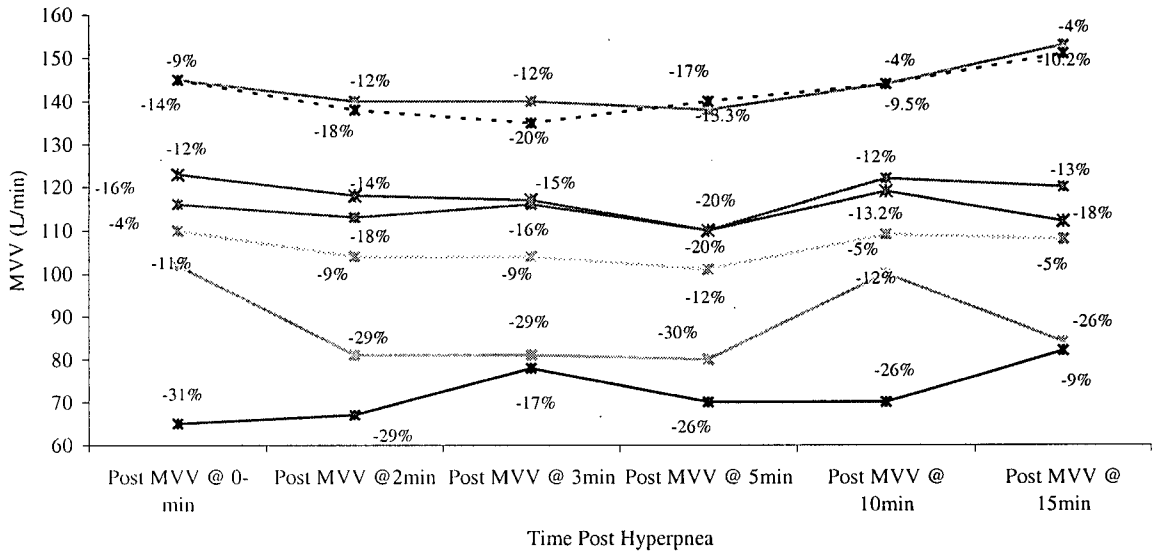
(+) Represents an increase

Figure 15. Absolute change in MVV following 15-minute hyperpnea task, individual subject data. Day 1.



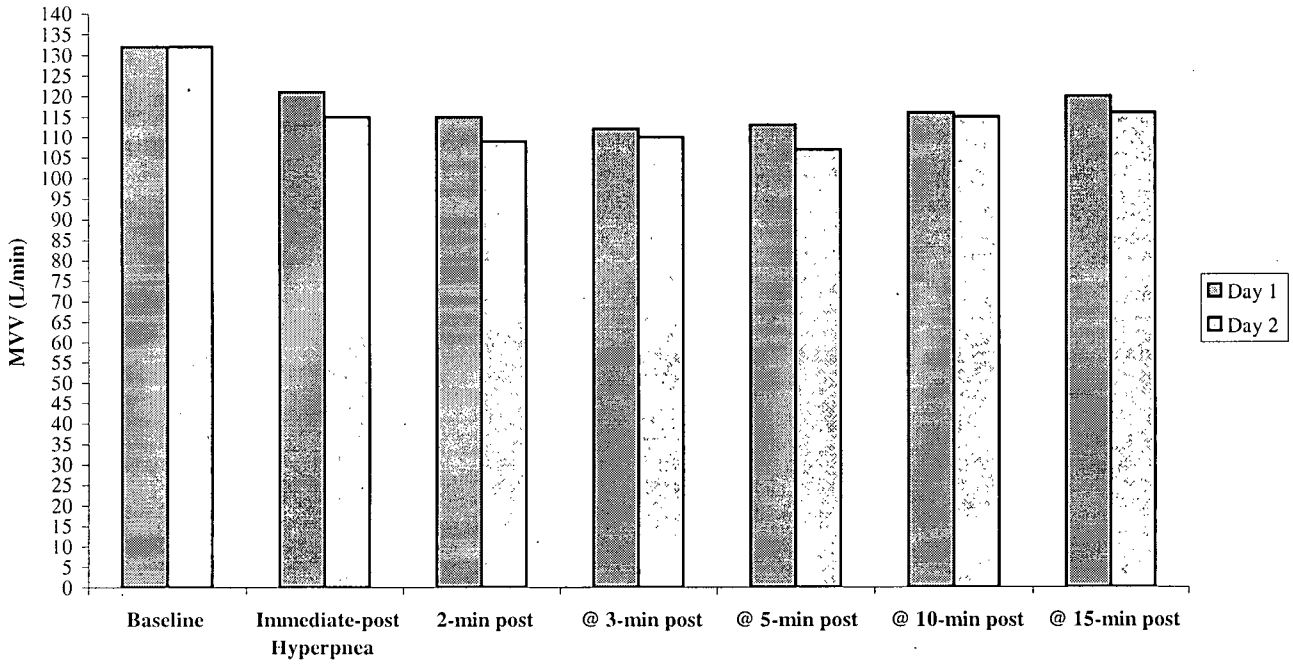
Note: Each line represents individual subject data.

Figure 16. Absolute change in MVV following 15-minute hyperpnea task, individual subject data. Day 2.



Note: Each line represents individual subject data.

Figure 17. Comparison of change in MVV following 15-minute hyperpnea task between Test Days 1 and 2.



Appendix E: Borg 10-point Scale for ratings of perceived exertion.

0 Nothing at all

0.5 Very, very easy
1 Very easy
2 Easy
3 Moderately hard
4 Somewhat hard
5 Hard
6
7 Very hard
8
9
10 Very, very hard