THE ROLE OF EXPIRATORY FLOW LIMITATION IN THE OXYGEN COST OF EXERCISE HYPERPNEA IN HIGHLY-TRAINED DISTANCE RUNNERS

by

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ABSTRACT

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The Role of Expiratory Flow Limitation On the Oxygen Cost of Exercise Hyperpnea in Highly-Trained Distance Runners

There is an upper limitation to the flow rates achievable during exhalation. Once this limitation is reached (expiratory flow limitation; FLexp), such as that observed during intensive exercise, no further increase in expiratory flow is possible. During heavy to maximal exercise, a major consequence of FLexp may be an increased oxygen cost of breathing. To examine the effect of FL_{exp} on respiratory muscle oxygen consumption (VO_{2RM}) during maximal exercise, a sample of highly-trained male distance runners (n=18; $\dot{V}O_2$ max = 74.28 $ml \cdot kg^{-1} \cdot min^{-1}$) completed an incremental exercise test to exhaustion on a treadmill. Based on flow-volume loop analysis, subjects were separated into two groups, flow-limited (FL) and non-flow limited (NFL). During a second visit, runners performed three separate trials of voluntary hyperpnea, matching exercise ventilation ($\dot{V}_E$) at 80%, 90%, and 100% of maximal exercise while standing on the treadmill. Respiratory muscle O2 consumption (VO_{2RM}) was estimated during each voluntary hyperpnea trial. A one-tailed, independent samples t-test detected a significantly greater VO_{2RM} in FL compared to NFL ($P = 0.043$). $\dot{V}_E$ at $\dot{V}O_2$ max was also greater in FL vs. NFL ($P = 0.029$). No differences were found between expiratory reserve volume (ERV), tidal volume (V_T), or breathing frequency (f_b) during maximal exercise. When co-varying for $\dot{V}_E$ at $\dot{V}O_2$ max, there was no significant difference in VO_{2RM} between groups, suggesting that the greater oxygen cost of breathing in flow-limited individuals is a consequence of the greater VE and not due to differences in breathing mechanics associated with flow limitation.

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CHAPTER ONE

INTRODUCTION

During the expiratory phase of the breathing cycle, there is a maximum flow rate that can be achieved. This upper limit to the generation of expiratory flow is caused by airway collapse as a result of extremely high pleural pressure. When flow is plotted versus volume during a forced expiratory maneuver, a boundary for maximal expiratory flow is established. Expiratory flow limitation (FL_{exp}) occurs when the exercise tidal flow-volume loops (FVLs) impinge on the maximal flow-volume envelope. The flow-volume loop method of detecting FL_{exp} describes the extent of flow-limitation as the percentage of tidal volume (V_T) which corresponds to the encroachment of the FVLs on the maximal flow-volume envelope. FL_{exp} has been defined as an impingement of the FVL on the maximal flow-volume envelope which corresponds to 50% of V_T or more (Chapman, Emery, & Stager, 1998).

FL_{exp} occurs as a result of the achievement of maximum flow rates, and healthy individuals who display FL_{exp} are described as having respiratory systems that are highly adapted to endurance exercise. During heavy to maximal exercise, highly-trained athletes are capable of displacing extremely large amounts of ambient gas, and therefore it is not uncommon for these individuals to reach FL_{exp}. In fact, most highly-trained individuals demonstrate a substantial amount of FL_{exp} during maximal exercise, and in some cases, up to 75% of V_T is flow-limited (Johnson, Saupe, & Dempsey, 1992). Is there a price to pay for the attainment of FL_{exp} in highly-trained endurance athletes? Previous investigations on this population have shown that FL_{exp} poses mechanical constraints to exercise ventilation ($\dot{V}_E$) (Johnson, et al., 1992; Chapman, et al., 1998) and masks the expression of ventilatory drive (McClaran, Pegelow, Wetter, & Dempsey, 1999). However, the inability to increase $\dot{V}_E$ in flow-limited athletes during maximal exercise does not apparently constrain pulmonary oxygen delivery (Johnson et al., 1992; Chapman et al., 1998).

During maximal exercise in healthy, untrained individuals, 10% of $\dot{V}O_2$ max is devoted to respiratory muscle oxygen consumption (VO_{2RM}) (Aaron, Johnson, Seow, & Dempsey, 1992), and individuals who utilize a substantial portion of ventilatory reserve during maximal exercise commit 13 to 15% of $\dot{V}O_2$ max to respiration (Aaron et al., 1992). Previous investigations have shown an exponential increase in VO_{2RM} as $\dot{V}_E$ increases with exercise (Aaron et al., 1992; Johnson, et al., 1992; Coast et al, 1993). Although $\dot{V}_E$ at $\dot{V}O_2$ max is not generally regarded as a cause of exercise limitation in healthy, untrained individuals, the superior level of $\dot{V}_E$ at $\dot{V}O_2$ max that is displayed in highly-trained endurance athletes likely requires a substantially greater VO_{2RM} compared to healthy, untrained individuals. The oxygen cost of exercise hyperpnea in elite distance runners has been estimated as 11 to 16% of $\dot{V}O_2$ max without discriminating between the flow-limited and non-flow limited runners. Nevertheless, the high level of $\dot{V}_E$ that is reached in highly-trained athletes during maximal exercise may be considered a potential cause of exercise limitation in that it causes a constraint, or rather, a competition for oxygen supplies between the ventilatory musculature and the metabolically active tissues. It may be that the additional metabolic cost of the elevated $\dot{V}_E$ typical of FL_{exp} imposes an even greater limit on the metabolic capability of the skeletal muscles while exercising at heavy to maximal exercise intensities.

The highly-adapted pulmonary system characteristically demonstrates a superior level of $\dot{V}_E$, and consequentially, FL_{exp} results. This brings into question the potential advantages and disadvantages of the highly-adapted pulmonary system. In general, a greater $\dot{V}_E$ results in greater oxygen delivery to and removal of carbon dioxide from the working muscles. In this case, however, a "point of diminishing returns" may be reached such that the added cost of breathing caused by a greater $\dot{V}_E$ (or FL_{exp}) offsets the expected additional oxygen delivery.

Purpose of the Study

To examine potential differences in $\dot{V}_E$ and VO_{2RM} between flow-limited and non-flow limited, highly-trained distance runners during heavy to maximal exercise.

Significance of the Study

During heavy to maximal exercise, the achievement of FL_{exp} is common in highly-trained endurance athletes. The ability of these individuals to reach FL_{exp} results from the maximal utilization of ventilatory reserve as a strategy to maximize $\dot{V}_E$. However, the ability of the highly-adapted pulmonary system to reach extremely high levels of $\dot{V}_E$ may come with consequences. The increase in airway resistance that is characteristic of FL_{exp} may elevate the oxygen cost of exercise hyperpnea. Previous investigation has shown that 13-15% of total body oxygen consumption during maximal exercise ($\dot{V}O_2$ max) is required by the respiratory muscles in individuals who utilize most of their ventilatory reserve, compared to 10% of $\dot{V}O_2$ max in healthy individuals with less adapted respiratory systems. Furthermore, given that FL_{exp} results from the maximal utilization of ventilatory reserve, it is unknown if $\dot{V}_E$ is greater in flow-limited versus non-flow limited individuals who are highly-trained. The effect of FL_{exp} on the oxygen cost of exercise hyperpnea provides a key step in the elucidation of limitations to exercise capacity in highly-trained endurance athletes. Shedding light on the relationship between FL_{exp} and VO_{2RM} may open doors for further research on the mechanical constraints to $\dot{V}_E$, the work of breathing, and exercise performance in highly-trained endurance athletes.

Limitations

The study was limited by the following:

1. The method of detecting FL_{exp} consisted of placing the average FVL within the maximal flow-volume loop. Correct placement of the average FVL requires inspiratory capacity (IC) maneuvers during exercise. Due to the lack of familiarity of inspiring to total lung capacity (TLC), it is conceivable that not all IC maneuvers were performed correctly during the $\dot{V}O_2$ max test and mimic trials.
2. Individuals who demonstrated FL_{exp} of 5% or less were categorized as non-flow limited, and individuals who demonstrated FL_{exp} of 35% or more were categorized as flow-limited. The arbitrary establishment of the boundaries which define FL_{exp} was set in order to ensure that the extent of FL_{exp} was substantial enough to separate flow-limited and non-flow limited runners.
3. The age range of subjects who participated in the present study was limited to 18 to 30 years. Therefore, the conclusions that are drawn from the present study should not be interpreted to represent individuals outside of this age range.
4. Only white males were recruited to participate in the present study. Therefore, the conclusions drawn from the study should not be interpreted to represent the female or non-white populations.

5. The highly-trained individuals who participated in the study were distance runners. The conclusions drawn from the present study may not represent highly-trained endurance athletes who are trained for other modes of exercise, such as cycling or swimming.

Assumptions

The basic assumptions of the study are as follows:

1. Subjects fasted during the 6 hours preceding each experimental testing session.
2. Resting $\dot{V}O_2$ is the same between standing and voluntary hyperpnea.
3. The difference in total body $\dot{V}O_2$ between standing rest and the corresponding voluntary hyperpnea trials accounts for the work performed by only the muscles that were used for hyperpnea.
4. The muscle groups which are required for $\dot{V}_E$ during voluntary hyperpnea were the same muscle groups used for $\dot{V}_E$ during the $\dot{V}O_2$ max test.
5. Matching breathing frequency (f_b), V_T, and EELV between exercise and voluntary hyperpnea is a valid method for mimicking the work of breathing (Coast et al., 1993).
6. A statistically significant difference in VO_{2RM} between flow-limited and non-flow limited runners is attributed a difference between groups in $\dot{V}_E$, FL_{exp}, or a combination of the two.

Hypotheses

The present study was designed to test the following null hypotheses:

1. FL_{exp} does not vary enough to separate flow-limited and non-flow limited highly-trained distance runners into groups with 35% flow-limitation or more and 5% flow-limitation or less, respectively.

The following null hypotheses were to be tested only if the first null hypothesis was rejected.

2. There are no significant differences in age, height, mass, $\dot{V}O_2$ max, or maximal heart rate (HR max) between flow-limited and non-flow limited subjects.
3. Pulmonary function variables, which include forced vital capacity (FVC), forced expiratory volume in one second (FEV_1), FEV_1 as a percentage of FVC, forced expiratory flow from 25% to 75% of V_T (FEF_{25-75}), and peak expiratory flow rate (PEFR), are not significantly different between flow-limited and non-flow limited runners.
4. $\dot{V}_E$ at maximal exercise is not significantly greater in the flow-limited group compared to the non-flow limited group during maximal exercise.
5. $\dot{V}O_{2RM}$ is not significantly greater in the flow-limited group compared to the non-flow limited group during maximal exercise.
6. When co-varying for $\dot{V}_E$ at $\dot{V}O_2$ max, there is no significant difference in $\dot{V}O_{2RM}$ between flow-limited and non-flow limited subjects.
7. During maximal exercise, expiratory reserve volume (ERV) is not significantly different between flow-limited and non-flow limited groups.

8. During submaximal exercise (80% and 90% of $\dot{V}O_2$ max), there is no significant difference in $\dot{V}_E$ between flow-limited and non-flow limited subjects.
9. During submaximal exercise (80% and 90% of $\dot{V}O_2$ max), there is no significant difference in VO_{2RM} between flow-limited and non-flow limited subjects.

Definitions of Terms

1. End-Expiratory Lung Volume (EELV). The volume of gas remaining in the lungs at the end of expiration, including residual volume (Johnson, Weisman, Zeballos, & Beck, 1999).
2. Exercise hyperpnea. The augmentation of ventilation from rest during exercise (Brooks, Fahey, & Baldwin, 2005, pp. 277-278).
3. Expiratory Flow-Limitation (FL_{exp}). The percentage of V_T that meets or exceeds the expiratory boundary of the maximal flow-volume loop (Johnson et al., 1999).
4. Expiratory Reserve Volume (ERV). The volume of gas remaining in the lungs at the end of expiration, excluding residual volume (Brooks et al., 2005, p. 263).
5. Flow-Volume Loops (FVLs). Lung volume plotted against inspiratory and expiratory flow (Johnson et al, 1999).
6. Inspiratory Capacity (IC) Maneuver. A maximal inspiration during exercise that begins at EELV. This maneuver is used for a) the correction of drift due to slight differences in the measurement of inspiratory and expiratory flow rates and b) the placement of the tidal FVLs within the maximal flow-volume envelope (Johnson et al., 1999).
7. Maximal Oxygen Consumption (VO_2 max). The maximum rate that an individual can consume oxygen (Brooks et al., 2005, pp. 5-6).

8. Respiratory Muscle Oxygen Consumption (VO_{2RM}). Total body $\dot{V}O_2$ while mimicking exercise hyperpnea minus total body $\dot{V}O_2$ at rest. This is considered to be the amount of oxygen consumed by the respiratory muscles for a given intensity of steady state exercise (Aaron, Johnson, Seow, Dempsey, 1992).

CHAPTER TWO

REVIEW OF LITERATURE

Expiratory Flow Limitation: Definition and Mechanics

FL_{exp} is defined as the percent of V_T that meets or exceeds the expiratory boundary of the MFVL (Johnson, Weisman, Zeballos, & Beck, 1999). Respiratory disease patients are typically flow-limited due to either airway inflammation, airway constriction, or a combination of the two (Bousquet, Jeffery, Busse, Johnson, & Vignola, 2000). In healthy, untrained individuals who are free from chronic airflow limitations, FL_{exp} typically is not present during rest to maximal exercise (Aaron, Seow, Johnson, & Dempsey, 1992). However, in most healthy individuals who are highly-trained for endurance competition, FL_{exp} is present during exercise intensities above 85% of $\dot{V}O_2$ max (Johnson et al., 1992).

The onset of FL_{exp} in highly-trained endurance athletes during heavy to maximal exercise is due largely to the extreme amount of expiratory pressure that is generated. When thoracic pressure surrounding the airways exceeds the pressure that is inside the airways, the airways collapse (West, 2008). Due to this phenomenon, termed dynamic airway compression, expiratory flow becomes “effort independent,” which means that an increase in expiratory effort will not result in an increase in flow rate (West, 2008).

Ventilatory Constraints in Respiratory Disease

FL_{exp} is common in individuals with respiratory disease. Understanding the similarities and differences in the physiological nature of FL_{exp} between the diseased and highly-trained populations may provide insight into potential exercise limitations in highly-trained endurance athletes who are flow-limited.

Patients with chronic airflow limitation such as chronic obstructive pulmonary disease (COPD) commonly demonstrate FL_{exp} during low to moderate exercise intensities (O'Donnell, Revill, & Webb, 2001). During incremental exercise to exhaustion, it is typical for these patients to terminate exercise before reaching maximal exercise capacity. The early termination of exercise is associated with a rating of perceived breathlessness, or dyspnea (O'Donnell et al., 2001). The remarkable inability to generate flow during a maximal expiratory maneuver during rest in the diseased population greatly restricts the expansion of V_T with an increase in exercise intensity. At low to moderate exercise intensities, therefore, strategies for expanding V_T in COPD patients differ from those used by healthy individuals who are free from limitations to the generation of expiratory flow. In diseased patients, EELV increases in an attempt to escape the flow-limited portion of expiration, and EILV must also increase in order to expand V_T (Diaz, et al., 2000; Johnson, Scanlon, & Beck, 1995). The increase in EELV above resting levels with exercise, termed dynamic hyperinflation (DH), is significantly correlated with the dyspnea rating in COPD patients during exercise (O'Donnell, Webb, and Lam, 1998). As a result, FL_{exp} and its affect on dynamic lung volumes are limiting factors to exercise capacity in lung disease patients with chronic airflow limitation.

Ventilatory Constraints in Highly-Trained Endurance Athletes

There are key differences in resting pulmonary function between individuals with respiratory disease and highly-trained endurance athletes which allow highly-trained endurance athletes to generate far superior levels of expiratory flow. A major difference between the two populations is the extremely large amount of flow that highly-trained individuals are capable of generating during a maximal expiration. In a study by Johnson, Saupe, and Dempsey (1992) on a group of highly-trained male distance runners (n = 8; $\dot{V}O_2\,max = 73 \pm 1\ ml \cdot kg^{-1} \cdot min^{-1}$), group mean peak expiratory flow rate (PEFR) reached as high as 12 $L \cdot s^{-1}$, group mean forced expiratory flow rate at 50% of VC ($FEF_{50\%}$) was 5.94 $L \cdot s^{-1}$, and group mean forced expiratory volume in one second (FEV_1) was 4.98 L ($\dot{V}O_2$ max = 73 ± 1 $ml \cdot kg^{-1} \cdot min^{-1}$; age = 25 ± 1 yrs). These values can be compared to predicted values of 10.39 $L \cdot s^{-1}$, 4.80 $L \cdot s^{-1}$, and 4.69 $L \cdot s^{-1}$ for PEFR, $FEF_{50\%}$, and FEV_1, respectively (Hankinson, Odenkrantz, & Fedan, 1999). Pulmonary function measurements of 2.98 $L \cdot s^{-1}$, 0.43 $L \cdot s^{-1}$, and 0.94 L, for PEFR, $FEF_{50\%}$, and FEV_1 respectively, were measured in a group of COPD patients (age = 66 ± 8 yrs) (O'Donnell et al., 2001). These pulmonary function values can be compared to 6.96 $L \cdot s^{-1}$, 3.55 $L \cdot s^{-1}$, and 2.85 $L \cdot s^{-1}$ for PEFR, $FEF_{50\%}$, and FEV_1 respectively in a group of age-matched, apparently healthy individuals (age = 63 ± 7) (O'Donnell et al., 2001).

Relative to the healthy sedentary population, highly-trained endurance athletes are capable of generating considerably large flow rates during both inspiration and expiration at heavy to maximal exercise intensities, and in most cases, expiratory flow during maximal exercise is equivalent to a substantial portion of expiratory flow during a resting maximal expiratory maneuver. In some cases up to 75% of the tidal FVL meets or exceeds the expiratory portion of the maximal flow-volume envelope in highly-trained endurance athletes during maximal exercise (Johnson et al., 1992). In healthy, sedentary individuals, the extent of FL_{exp} is much less than in highly-trained athletes. Aaron et al. (1992) measured the amount of FL_{exp} in a group of healthy male individuals (n = 8, $\dot{V}O_2$ max = 51.1 ± 2.6 $ml \cdot kg^{-1} \cdot min^{-1}$). Group mean FL_{exp} was 36.3% of V_T, but the three subjects who qualified as highly-trained reached a mean FL_{exp} of 70% of V_T (Aaron, et al., 1992), indicating a substantially greater constraint to $\dot{V}_E$ in highly-trained athletes compared to healthy sedentary individuals.

Not unlike the diseased population, once a substantial amount of FL_{exp} has been reached in highly-trained individuals, there must be a strategy for increasing $\dot{V}_E$ as the exercise intensity increases. Potential tactics for increasing $\dot{V}_E$ include (1) increasing EELV, which moves the tidal FVL away from the flow-limiting portion of the MFVL, (2) increasing EILV, (3) increasing peak flow at the beginning of expiration, or any combination of the three. In the study by Johnson et al. (1992), six of the eight subjects increased EELV at a constant V_T from heavy to maximal exercise, while the remaining two chose to increase peak flow at the beginning of expiration.

The lung volume response to FL_{exp} was also investigated in a study by McClaran, Wetter, Pegelow, and Dempsey (1999). In their study, a group of trained male cyclists (N = 6; VO_2 max $= 65 \pm 8$ $ml \cdot kg^{-1} \cdot min^{-1}$) performed four separate trials of incremental exercise to exhaustion on a cycle ergometer. With two of the trials, FL_{exp} was reduced by breathing a low density gas mixture (HeO_2). One HeO_2 trial comprised of added dead space (which was used as a ventilatory stimulant), while the other did not. With the remaining two trials, FL_{exp} was superficially increased using a high density gas mixture (N_2O_2), one trial with and one trial without added dead space. In all trials, adding dead space resulted in an increase in exercise $\dot{V}_E$, which was partly explained by an increase in V_T. During heavy to maximal exercise (equal to and above 85% of VO_2 max), adding dead space during the N_2O_2 trial resulted in a significantly greater EELV than when dead space was added during heavy to maximal exercise while breathing HeO_2 ($P < 0.05$), indicating that, when FL_{exp} is present during heavy to maximal exercise, individuals ventilate at higher lung volumes (McClaran et al., 1999).

The elevated EELV during heavy to maximal exercise in flow-limited athletes may be associated with a greater oxygen cost of exercise hyperpnea due to greater elastic work performed by the inspiratory muscles. Collett & Engel (1986) investigated the effect of an elevated EELV on the oxygen cost of exercise hyperpnea in a group of apparently trained, healthy male subjects (N = 5). Two voluntary hyperpnea trials were carried out at a constant V_T, f_b, ratio of inspiratory to total breathing cycle duration, and transpulmonary pressure. One trial consisted of voluntary hyperpnea at an EELV at functional residual capacity (FRC), while the second trial consisted of voluntary hyperpnea with an EELV that was increased to 37% of inspiratory capacity. While ventilating at a high lung volume, VO_{2RM} was 41 ± 11 percent greater than when subjects ventilated with an EELV at FRC ($P < 0.05$). Furthermore, Collett & Engel (1986) found that when the work of breathing at a high lung volume was normalized for the decrease in maximal inspiratory pressure while ventilating with an EELV at FRC, VO_{2RM} was not significantly different between trials ($P > 0.70$). Therefore, the difference in VO_{2RM} between groups was attributed to the difference in EELV during voluntary hyperpnea.

During maximal exercise, FL_{exp} also results in a reduced ventilatory response. The previously mentioned study by McClaran et al. (1999) found that, during maximal exercise while breathing HeO_2, the ventilatory response ($\Delta\dot{V}_E/\Delta P_{ETCO_2}$) to added dead space was 3.1 ± 1.8 $L \cdot mm\ Hg^{-1}$ versus 1.1 ± 1.6 $L \cdot mm\ Hg^{-1}$ during the artificial induction of FL_{exp}. Johnson et al. (1992) investigated the response to a ventilatory stimulus during heavy exercise in a group of competitive male distance runners. Subjects completed two separate, three-minute trials at maximal intensity, as well as two separate three-minute trials at a submaximal intensity (10mph at a 0% grade). Two trials comprised of an inspired fraction of O_2 (F_{IO_2}) of 0.16 during both submaximal and maximal exercise, the third trial included an inspired fraction of CO_2 (F_{ICO_2}) of

0.04 during maximal exercise, and the fourth consisted of an F_{ICO_2} of 0.06 during submaximal exercise. The induced hypoxia trial resulted in a decrease in S_aO_2 from 93 ± 1% to 75 ± 2% during maximal exercise, but $\dot{V}_E$ did not change significantly (167 ± 5 L· min^{-1} while breathing normal air vs. 166 ± 7 L· min^{-1} in hypoxia). Likewise, hypercapnia increased P_{ETCO_2} from 38 ± 1 mm Hg to 61 ± 2 mm Hg, but $\dot{V}_E$ did not change significantly (167 ± 5 L·min^{-1} vs. 168 ± 5 L·min^{-1}). During the submaximal exercise trials, all subjects significantly increased V_E during both the hypercapnia and the hypoxia trials (hypercapnia, 120 ± 5 L·min^{-1}; hypoxia, 99 ± 4 L·min^{-1}; normal air, 73 ± 1 L·min^{-1}), indicating that the substantial extent of FL_{exp} during maximal exercise (61 ± 7% of V_T) results in a decreased ventilatory response.

More evidence for a decrease in the ventilatory response to chemical stimuli in highly-trained endurance athletes who are flow-limited during exercise is provided by Derchak et al. (2000), who investigated the relationship between the resting hypoxic ventilatory response (HVR) and arterial oxygen saturation (S_aO_2) during maximal exercise in a group of flow-limited distance runners compared to a group of non-flow limited distance runners (N = 16; VO_2 max = 75.8 ml·kg^{-1}·min^{-1}). A significant relationship between resting HVR and S_aO_2 at maximal exercise (r = 0.92, $P < 0.05$) was found in the athletes who were not flow-limited during maximal exercise (N = 8; VO_2 max = 75.6 ± 4.8 ml·kg^{-1}·min^{-1}), and there was no relationship between the resting HVR and S_aO_2 during maximal exercise (r = 0.49, $P > 0.05$) in the flow-limited athletes (N = 8; VO_2 max = 75.9 ± 4.1 ml·kg^{-1}·min^{-1}). When FL_{exp} was controlled for, the entire group of athletes displayed a significant relationship between resting HVR and S_aO_2 at maximal exercise (r = 0.69, $P = 0.007$), indicating that the ventilatory response to chemical stimuli is masked by FL_{exp}.

In highly-trained endurance athletes, the alveolar to arterial O_2 pressure difference increases 2.5 to 3-fold from rest to maximal exercise (Dempsey, 1986), which is partially compensated by the strong hyperventilatory response. What is the consequence of ventilatory constraints to gas exchange at the level of the lung in flow-limited athletes? Chapman et al. (1998) investigated the ability of highly-trained male distance runners who are flow-limited (N = 5; VO_2 max = 73.5 ± 5.7 $ml \cdot kg^{-1} \cdot min^{-1}$) not only to increase $\dot{V}_E$ during maximal exercise in hypoxia ($F_IO_2 = 0.187$), but also to maintain S_aO_2 between normoxia and hypoxia at maximal exercise compared to a group of non-flow limited individuals at the same fitness level (N = 5; $\dot{V}O_2$ max = 68.1 ± 5.3 $ml \cdot kg^{-1} \cdot min^{-1}$). While the hypoxia trial resulted in a significant increase in $\dot{V}_E$ at maximal exercise in the group of non-flow limited athletes (140.9 ± 13.4 $L \cdot min^{-1}$ in normoxia vs. 154.7 ± 11.9 $L \cdot min^{-1}$ in hypoxia, $P < 0.05$), there was no significant difference in $\dot{V}_E$ at maximal exercise between normoxia and hypoxia in the flow-limited group of athletes (159.5 ± 9.4 $L \cdot min^{-1}$ in normoxia vs. 162.3 ± 6.0 $L \cdot min^{-1}$ in hypoxia). Although it is apparent that FL_{exp} is a source of constraint to increasing $\dot{V}_E$ during maximal exercise, the magnitude of the decline in S_aO_2 from normoxia to hypoxia was not significantly different ($P > 0.05$) between flow-limited and non-flow limited athletes (Chapman, Emery, & Stager, 1998), indicating that there is no consequence to pulmonary oxygen delivery in flow-limited athletes during maximal exercise.

Presently, the literature on highly-trained endurance athletes and FL_{exp} seems to suggest that the work of exercise hyperpnea, and therefore, the oxygen cost of exercise hyperpnea is elevated as a consequence of FL_{exp} during heavy to maximal exercise. Furthermore, it appears that the elevated oxygen cost of exercise hyperpnea may not only be due to the increase in EELV, but it may also be due to amount of expiratory pressure that is generated by the muscles which aide in expiration against an elevated airway resistance. Johnson et al. (1992) measured transpulmonary pressure in their group of highly-trained distance runners, and showed that, while all of the runners reached the maximum level of pressure which contributes to expiratory flow, half of them generated a substantial amount of expiratory pressure beyond that which was necessary to reach FL_{exp}. Therefore, there is likely a considerable amount of work that is performed during the expiratory portion of the breathing cycle that does not result in an increase in flow rate.

The Oxygen Cost of Exercise Hyperpnea in Healthy Individuals

The first study to measure VO_{2RM} during different intensities of exercise by matching the ventilatory mechanics of exercise hyperpnea was the previously mentioned study by Aaron et al. (1992). In their group of eight healthy subjects, VO_{2RM} comprised of 10 ± 0.7 percent of total body $\dot{V}O_2$ max. Out of the eight healthy subjects, however, the three subjects who were considered highly-trained dedicated 13 to 15% of total body $\dot{V}O_2$ to fueling the respiratory muscles during maximal exercise. The study by Aaron et al. (1992) also provided a regression equation describing the relationship between the work of breathing and VO_{2RM}. This equation was used by Johnson et al. (1992) to estimate VO_{2RM} in their group of highly-trained distance runners. In that study, it was estimated, based on the regression equation that was established by Aaron et al.(1992), that the oxygen cost of exercise hyperpnea during maximal exercise comprised of 13% of total body $\dot{V}O_2$ (range 11 to 16%).

The oxygen cost of exercise hyperpnea from a low to maximal exercise intensity depends mainly on exercise $\dot{V}_E$. Martin & Stager (1981) measured VO_{2RM} in a group of endurance trained (N = 8) and non-endurance trained (N = 8) females. In that study, VO_{2RM} was measured by maintaining a $\dot{V}_E$ of 30 L·min^{-1} for four minutes, and $\dot{V}_E$ was increased by 30 L·min^{-1} every four minutes thereafter until a given level of $\dot{V}_E$ could not be sustained for the full four-minute period. It was found that VO_{2RM} was not significantly different between groups over the same range of $\dot{V}_E$. Furthermore, the relationship between $\dot{V}_E$ and VO_{2RM} in the study by Martin and Stager (1981) was nonlinear. As $\dot{V}_E$ increases from rest to maximal exercise, VO_{2RM} increases exponentially. The nonlinear relationship between $\dot{V}_E$ and VO_{2RM} has also been shown in a group of healthy males (Coast, et al., 1993), a group of physically active males (Anholm, Johnson, & Ramanathan, 1987), and in a group of highly-trained male distance runners (Johnson et al., 1992). With the extreme levels of $\dot{V}_E$ that have been measured in highly-trained endurance athletes while exercising at max, it is likely that small differences in exercise hyperpnea during maximal exercise will result in substantial differences in VO_{2RM}. Therefore, it is likely that the superior level of $\dot{V}_E$ that is reached by highly-trained athletes results in a greater VO_{2RM}.

Conclusions

Dynamic airway compression during maximal exercise leads to FL_{exp}, resulting in an increase in airway resistance. Due to the extremely large amount of expiratory pressure that is generated during maximal exercise in highly-trained distance runners, FL_{exp} commonly occurs in this population. While FL_{exp} is also a common occurrence in lung disease patients, the onset of FL_{exp} takes place at a much lower exercise intensity in individuals with obstructive lung disease due to differences in resting pulmonary function values between the two populations. The achievement of FL_{exp} in highly-trained endurance athletes is a result of the ability to maximize the expiratory flow rate.

The mechanical constraints to $\dot{V}_E$ that are imposed by FL_{exp} in highly-trained endurance athletes during heavy to maximal exercise do not appear to confine oxygen delivery at the level of the lung. Strategies for increasing $\dot{V}_E$ during heavy to maximal exercise in flow-limited athletes include increasing dynamic lung volume in order to escape the flow-limited portion of V_T, as well as increasing peak flow at the beginning of expiration. The decrease in lung compliance during inspiration, as well as the increase in expiratory flow against an elevated airway resistance may affect the oxygen cost of exercise hyperpnea.

Healthy, untrained individuals, who typically do not ventilate enough to achieve FL_{exp}, commit 10% of total body $\dot{V}O_2$ to respiratory muscle work during maximal exercise. Highly-trained endurance athletes, however, dedicate upwards of 16% of total body $\dot{V}O_2$ to the respiratory muscles during maximal exercise. The substantially greater VO_{2RM} in the highly-trained population is likely due to the curvilinear relationship between $\dot{V}_E$ and VO_{2RM}.

CHAPTER THREE

METHODS

Subjects

Eighteen highly-trained male distance runners were recruited to participate in the present study. The participants of the study were competitive in events ranging in distances from 800 meters to the marathon. Subjects were recruited from the city of Bloomington, Indiana, and were members of high school, collegiate, and post-collegiate distance running programs, as well as local running clubs. Exclusion criteria comprised of the presence of bronchial asthma, a $\dot{V}O_2$ max of less than 65 ml·kg^{-1}·min^{-1}, and an age outside the range of 18 to 30. All participants gave written informed consent and completed a modified physical readiness questionnaire prior to participating in the study. Each subject was free of cardiopulmonary disease. All testing procedures and informed consent was approved by the Indiana University Human Subjects Institutional Review Board.

Study Design

Subjects were instructed to fast during the six hours prior to each laboratory visit. Experimental testing included two separate visits to the Indiana University Human Performance Laboratory. With the first session, subjects performed a $\dot{V}O_2$ max test on the treadmill. During the second session, subjects voluntarily matched exercise hyperpnea.

Session I. Upon arrival to the laboratory, each subject gave written informed consent and completed a modified physical readiness questionnaire. Body mass and height were then recorded. A warm-up consisting of light jogging was completed prior to testing. The speed, duration, workload, and location of the warm-up were left to the discretion of each individual.

Warm-ups lasted no longer than 15 minutes in duration. Subjects then performed three to six maximal flow-volume maneuvers.

After the collection of pre-exercise MFVLs, subjects were equipped with heart rate monitors (Polar, Inc.) before beginning the $\dot{V}O_2$ max test. Physiological variables were collected throughout, and recorded at the end of each minute for five minutes of standing rest and for each minute of the $\dot{V}O_2$ max test.

Within the five minutes following the $\dot{V}O_2$ max test, each subject removed his heart rate monitor and was allowed a period of recovery while investigators prepared the data acquisition program for the collection of MFVLs. Subjects then performed an additional three to six maximal flow-volume maneuvers. Each subject was encouraged to perform the maximal flow-volume maneuvers as soon as possible following the $\dot{V}O_2$ max test in order to include the effect of exercise-induced bronchodilation.

Session II. Upon arrival to the laboratory for the voluntary hyperpnea trials, body mass was recorded for each subject. Subjects then performed three to six maximal flow-volume maneuvers. Subjects were equipped with a heart rate monitor and physiological variables were measured throughout, and recorded at the end of each minute for five minutes of standing rest.

After five minutes of standing rest, subjects mimicked three separate levels of exercise hyperpnea while standing for four minutes, each level of $\dot{V}_E$ corresponding to 80, 90, and 100 percent of maximal exercise. The voluntary hyperpnea trials were separated by at least five minutes to ensure recovery of the respiratory muscles between trials. The trials were completed in random order. Prior to the first voluntary hyperpnea trial, subjects were allowed at least one minute of familiarization. The extent of familiarization depended how quickly the subject learned to match ventilatory mechanics. Some individuals required more time for familiarization than others.

During the five minutes following the final voluntary hyperpnea trial, each subject removed his heart rate monitor and was allowed a period of recovery while investigators prepared the data acquisition program for the collection of MFVLs. Subjects then performed three to six maximal maneuvers. Each subject was encouraged to perform the maximal maneuvers as soon as possible following the voluntary hyperpnea trials in order to include the effect of bronchodilation. All of the MFVLs were collected within five minutes following the last voluntary hyperpnea trial.

Measurements

Pulmonary Function. The pulmonary function variables were collected and recorded from the computer integration of the inspired and expired flow signals which were provided by a set of pneumotachographs (Series 3800, Hans Rudolph, Kansas City, MO). Pulmonary function measurements included vital capacity (VC), forced expiratory volume in one second (FEV_1), forced expiratory flow from 75 to 25 percent of VC (FEF_{25-75}), and peak-expiratory flow rate (PEFR). These measurements were used 1) as a method of screening to ensure that the subjects were free of pulmonary disease and 2) to detect inherent differences between experimental groups.

VC represents the expired volume (in BTPS), during a forced expiration, from TLC to residual volume (RV). A total of six to twelve measurements of VC were collected during each visit to the laboratory. Of these, the largest expiratory volume was chosen to represent VC.

FEV_1 and $FEF_{25\text{-}75}$ were also measured throughout a series forced expirations. FEV_1 is the expired volume beginning at TLC and ending after one second. $FEF_{25\text{-}75}$ is the flow rate across the range of 75 to 25% of VC.

Maximal Flow-Volume Loops (MFVL). A set of maximum effort ventilatory maneuvers was performed by each subject. Subjects began the maneuvers at RV, performed an inspiration to TLC, and then expired back to RV, each at maximum effort. A graph of flow vs. volume was plotted as a result of these maneuvers.

The MFVL represents the maximal generation of flow that can be generated throughout the duty cycle. The expiratory portion of an MFVL is characterized by a sharp incline in flow, followed by a steady decline as the subject approaches residual volume. As exercise intensity increases, the tidal flow-volume loops approach the MFVL as individuals maximize the generation of flow. The MFVL serves as a boundary through which the exercise tidal flow-volume loops cannot penetrate. As specified below, tidal flow-volume loops are plotted within the MFVL for the determination of expiratory flow limitation (FL_{exp}).

Maximal Oxygen Consumption (VO_2 Max). $\dot{V}O_2$ max was measured during an incremental exercise test to exhaustion on a motorized treadmill (Quinton, Bothell, WA). The treadmill speed remained constant throughout the test. The percent grade was set at zero during the first two minutes of exercise, and increased by two percent every two minutes until volitional exhaustion. The highest recorded $\dot{V}O_2$ was accepted as $\dot{V}O_2$ max if two of the following three criteria were met: 1) A heart rate of equal to or more than 90% of predicted heart rate max, 2) an RER of 1.10 or higher, and 3) an increase in absolute $\dot{V}O_2$ of .15 L/min or less.

Physiological variables were measured using a computer interfaced (DASYlab), indirect calorimetry system. Physiological measurements included $\dot{V}_E$, absolute and relative $\dot{V}O_2$, carbon dioxide production ($\dot{V}CO_2$), and the respiratory exchange ratio (RER). $\dot{V}_E$ was measured by the computer integration of the inspired flow signal which was measured using a pneumotachograph. Dry expired gas was sampled at a rate of 300 ml·min^{-1} from a 5-Liter mixing chamber, and fractional concentrations of O_2 and CO_2 were determined by O_2 and CO_2 analyzers (AEI Technologies, Pittsburgh, PA). The O_2 and CO_2 analyzers were calibrated using commercially available gas mixtures within the physiological range. The fractional contents of the gas mixtures were verified by mass spectroscopy. Absolute $\dot{V}O_2$ was calculated using the equation provided by the Haldane Transformation. Relative $\dot{V}O_2$ was calculated by dividing absolute $\dot{V}O_2$ by body mass in kilograms. $\dot{V}CO_2$ was calculated by subtracting the inspired volume of CO_2 from the expired volume of CO_2. RER was calculated by dividing $\dot{V}CO_2$ by absolute $\dot{V}O_2$. Each subject wore a heart rate monitor (Polar, Inc.) during $\dot{V}O_2$ max testing. Heart rate (beats·min^{-1}) was sampled throughout, and recorded at the end of each minute.

Voluntary Hyperpnea Trials. The matching of exercise hyperpnea for the calculation of VO_{2RM} required subjects to match the mechanics of $\dot{V}_E$. The validity of the methods by which exercise hyperpnea was matched has been established (Coast, et al., 1993).

Isocapnia was maintained by inspiring from a Douglas bag filled with 5% CO_2, 21% O_2, and balance N_2. In addition to the elevated CO_2, a humidifier was added to the inspired side to moisten the inspired air for preventing throat discomfort throughout the voluntary hyperpnea trials. Each subject mimicked three separate levels of exercise hyperpnea, each corresponding to the relative exercise intensities of 80, 90, and 100 percent of $\dot{V}O_2$ max. V_T was matched using a real-time graph of volume changes with time on a computer monitor and f_b was matched using a metronome. Careful attention was made to ensure that mean ERV (as a percent of VC), percent flow limitation, and $\dot{V}_E$ did not differ between exercise and voluntary hyperpnea by more than five percent. Either the third or fourth minute of voluntary hyperpnea was selected for flow-volume loop analysis, depending on which minute more closely matched the mechanics of exercise hyperpnea.

Tidal FVL Analysis. Inspiratory and expiratory flow was measured using a set of pneumotachographs. Inspired and expired volume was calculated by computer integration of the flow signal. Data for each minute was saved in a separate file for subsequent analysis. Tidal FVLs were constructed using a computer program that selects flow and volume at the beginning and end of each breathing cycle and calculates the average FVL from 30 seconds of data collection. The data for the average tidal FVL representing the last half of the minute of interest (80%, 90%, and 100% of $\dot{V}O_2$ max, and the third or fourth minute of voluntary hyperpnea) was plotted within the corresponding MFVL.

FL_{exp} was defined as the percent of V_T that coincided with an impingement of the tidal FVL with the expiratory portion of the MFVL. Individuals with a V_T that was at least 35% flow limited were classified as flow-limited subjects (FL). Those who demonstrated 5% or less flow limitation were grouped into the non-flow limited category (NFL). Although the criteria for inclusion into groups based on the degree of FL_{exp} is arbitrary, the purpose of this method is to ensure that the effect of FL_{exp}, as the independent variable, is clearly present. Individuals who were between 5 and 35 percent flow-limited were omitted from group analysis and used only for correlation analysis.

Estimation of VO_{2RM}. Total body $\dot{V}O_2$ was measured during both standing rest and each voluntary hyperpnea trial. VO_{2RM} was calculated by subtracting total body $\dot{V}O_2$ during standing rest from total body $\dot{V}O_2$ during the third or fourth minute of the voluntary hyperpnea trials.

This calculation is based on the assumption that the only difference between standing rest and mimicking exercise hyperpnea while standing is the work performed by the muscles which aid in pulmonary ventilation.

Statistical Analysis of the Data

Differences in VO_{2RM} and in $\dot{V}_E$ during maximal exercise between FL and NFL were analyzed using a one-tailed, independent samples t-test. Differences in all remaining maximal and submaximal variables were analyzed using a two-tailed, independent samples t-test. The alpha level for all statistical analyses was set at $P \leq 0.05$. The statistical software that was used for analyzing the data was the Statistical Package for the Social Sciences (IBM, Chicago).

CHAPTER FOUR

RESULTS AND DISCUSSION

Subject Characteristics and Pulmonary Function

There were no significant differences ($P > 0.05$) in age, height, weight, and $\dot{V}O_2$ max between FL and NFL (Table 4.1). There was no significant difference ($P > 0.05$) in FEV_1 between groups (FL, 4.55 ± 0.66; NFL, 5.08 ± 0.52) (Table 4.2). However, FEV_1/FVC was significantly greater in NFL compared to FL (89 ± 7.6 vs. 81 ± 6.1, $P = 0.032$). $FEF_{25\text{-}75}$ was also significantly greater in NFL compared to FL (7.06 ± 1.01 vs. 5.13 ± 0.50 $L \cdot s^{-1}$, $P < 0.001$). No significant differences ($P > 0.05$) were detected in VC (FL, 5.68 ± 0.82 L; NFL, 5.74 ± 0.38 L) or in PEFR (FL, 10.47 ± 2.25 $L \cdot s^{-1}$; NFL, 10.75 ± 1.62 $L \cdot s^{-1}$) between groups.

Resting pulmonary function values were compared to predicted resting pulmonary function values (Hankinson, Odencrantz, & Fedan, 1999) and are also presented in Table 4.2. None of the resting pulmonary function variables for FL were significantly different from predicted values ($P > 0.05$) (VC = 101 ± 15.2% of predicted; FEV_1 = 97 ± 15.2% of predicted; FEV_1/FVC = 97 ± 7.1% of predicted; $FEF_{25\text{-}75}$ = 105 ± 12.0% of predicted; PEFR = 103 ± 21.0% of predicted). All pulmonary function variables for NFL were in the normal range of predicted values ($P > 0.05$) except for $FEF_{25\text{-}75}$ (VC = 103 ± 0.5% of predicted; FEV_1 = 110 ± 14% of predicted; FEV_1/FVC = 107 ± 9.1% of predicted; $FEF_{25\text{-}75}$ = 147 ± 26.8% of predicted, $P < 0.001$; PEFR = 107 ± 18.6% of predicted).

The Oxygen Cost of Exercise Hyperpnea and Ventilatory Mechanics During Maximal Exercise

The oxygen cost of exercise hyperpnea and ventilatory mechanics data during maximal exercise are presented in Table 4.3. The degree of FL_{exp} during maximal exercise in FL was 55 ± 11.3% of V_T, and the extent of FL_{exp} during maximal exercise in NFL was 0 ± 1.3% of V_T. VO_{2RM} was significantly greater in the flow-limited subjects compared to the non-flow limited subjects when the values are expressed both as a percent of $\dot{V}O_2$ max and in milliliters per kilogram per minute (19.19 ± 8.44% vs. 13.25 ± 4.89% of $\dot{V}O_2$ max, $P = 0.043$; 14.58 ± 6.66 vs. 9.70 ± 3.64 $ml \cdot kg^{-1} \cdot min^{-1}$, $P = 0.036$). $\dot{V}_E$ at $\dot{V}O_2$ max was also greater in FL compared to NFL (176.47 ± 23.29 $L \cdot min^{-1}$ vs. 157.54 ± 15.31 $L \cdot min^{-1}$, $P = 0.029$). After co-varying for $\dot{V}_E$ at $\dot{V}O_2$ max, there was no significant difference in VO_{2RM} (% of $\dot{V}O_2$ max) between groups ($P = 0.101$).

The ventilatory equivalent for oxygen consumption during maximal exercise was not significantly different between groups ($P > 0.05$) (FL, 34.58 ± 3.01; NFL, 32.67 ± 2.62). Likewise, the ventilatory equivalent for carbon dioxide output during maximal exercise was not significantly different between groups ($P > 0.05$) (FL, 30.52 ± 2.70; NFL, 28.63 ± 1.63).

There were no significant differences ($P > 0.05$) in f_b (FL, 58.50 ± 7.19 $br \cdot min^{-1}$;NFL, 53.56 ± 7.28 $br \cdot min^{-1}$) or in V_T (FL, 3.04 ± 0.41 $L \cdot br^{-1}$; NFL, 2.96 ± 0.25 $L \cdot br^{-1}$) during maximal exercise between flow-limited and non-flow limited subjects. In addition, no significant difference ($P > 0.05$) was detected in ERV during maximal exercise between groups (FL, 36 ± 5.7% of VC; NFL, 35 ± 6.7% of VC).

The Oxygen Cost of Exercise Hyperpnea and Ventilatory Mechanics During Submaximal Exercise

At 80% $\dot{V}O_2$ max, there were no significant differences ($P > 0.05$) in VO_{2RM} between FL and NFL when VO_{2RM} is expressed both as a percentage of total body $\dot{V}O_2$ and in milliliters per kilogram per minute (Table 4.5). At the same exercise intensity, $\dot{V}_E$ was greater in FL compared to NFL (113.67 ± 18.20 vs. 92.84 ± 10.14 $L \cdot min^{-1}$, $P = 0.049$). The ventilatory equivalent for carbon dioxide output at 80% $\dot{V}O_2$ max was also greater in flow-limited versus non-flow limited subjects (29.35 ± 1.97 vs. 25.28 ± 1.81, $P = 0.006$). At 80% $\dot{V}O_2$ max, the ventilatory equivalent for oxygen consumption, ERV, V_T, and f_b were not significantly different between groups ($P > 0.05$).

At 90% $\dot{V}O_2$ max, there were no significant differences ($P > 0.05$) in VO_{2RM} between FL and NFL when VO_{2RM} is expressed both as a percent of total body $\dot{V}O_2$ and in milliliters per kilogram per minute. $\dot{V}_E$ at 90% $\dot{V}O_2$ max was greater in FL compared to NFL (142.15 ± 19.19 vs. 113.51 ± 12.40 $L \cdot min^{-1}$, $P = 0.019$). The ventilatory equivalent for carbon dioxide output at 90% $\dot{V}O_2$ max was also greater in flow-limited versus non-flow limited subjects (29.88 ± 1.97 vs. 25.35 ± 2.27, $P = 0.006$). In addition, there were no significant differences ($P > 0.05$) in the ventilatory equivalent for oxygen consumption, ERV, V_T, or f_b between groups during exercise at 90% $\dot{V}O_2$ max.

Discussion

The Oxygen Cost of Exercise Hyperpnea During Maximal Exercise

The present study has shown that both VO_{2RM} and $\dot{V}_E$ during maximal exercise are significantly greater in highly-trained distance runners who are flow-limited compared to those who are not flow-limited, rejecting the first two null hypotheses. These findings are consistent with previous research on highly-trained endurance athletes. Aaron et al. (1992) found a 3 to 5% greater oxygen cost of exercise hyperpnea in a group of flow-limited individuals compared to a group of non-flow limited individuals during maximal exercise.

As previously mentioned, it has been established that VO_{2RM} increases exponentially with an increase in $\dot{V}_E$ (Anholm et al., 1987; Coast et al., 1993; Johnson et al., 1992; Martin & Stager, 1981). When co-varying for $\dot{V}_E$ at $\dot{V}O_2$ max, no statistical difference in VO_{2RM} between groups was observed ($P = 0.102$). At maximal exercise, highly-trained endurance athletes operate at extremely high levels of $\dot{V}_E$, and therefore a substantial proportion of total body $\dot{V}O_2$ is devoted to the respiratory muscles. The pulmonary systems of the endurance athletes who participated in the present study are well adapted to high-level endurance training, which results in the maximal utilization of ventilatory reserve, and consequentially, FL_{exp} ensues (Aaron et al., 1992; Johnson et al., 1992). Is the greater VO_{2RM}, as a result of the achievement of mechanical constraints to the generation of expiratory flow due to the superior level of $\dot{V}_E$ at $\dot{V}O_2$ max, or is it a result of the increase in airway resistance that is typical of FL_{exp}? The results of the present study suggest that the difference in VO_{2RM} between groups is explained by the superior level of $\dot{V}_E$ at $\dot{V}O_2$ max that is achieved by flow-limited runners.

Comparisons of the ventilatory equivalents for oxygen consumption and carbon dioxide output during maximal exercise between flow-limited and non-flow limited endurance-trained athletes are consistent with previous studies (Chapman, et al., 1998; Derchak, Stager, Tanner, & Chapman, 2000). Previous work on flow-limited and non-flow limited athletes has shown that there are no significant differences in $\dot{V}_E/\dot{V}O_2$ and in $\dot{V}_E/\dot{V}CO_2$ between flow-limited and non-flow limited athletes during maximal exercise (Chapman, et al., 1998; Derchak, et al., 2000). Furthermore, Derchak et al. showed that a significant relationship existed between resting HVR and S_aO_2 at $\dot{V}O_2$ max in non-flow limited endurance-trained subjects, but there was no relationship between the two in flow-limited endurance-trained subjects during maximal exercise. These results suggest that the expression of ventilatory responsiveness to chemical stimuli is masked by FL_{exp}.

In the present study, the ventilatory equivalent for carbon dioxide output was significantly greater in the flow-limited group compared to the non-flow limited group during exercise at 80% $\dot{V}O_2$ max, as well as 90% $\dot{V}O_2$ max. Without measuring the ventilatory response to chemical stimuli, it is difficult to draw conclusions from these results. Perhaps the significant difference in $\dot{V}_E$ combined with the ventilatory equivalent for carbon dioxide output between groups during submaximal exercise, when there are less mechanical constraints to $\dot{V}_E$, suggests a greater ventilatory drive in flow-limited versus non-flow limited runners, which may partially explain the achievement of FL_{exp} in some highly-trained runners. However, further research is needed to support this conclusion.

Dynamic Lung Volumes in Expiratory Flow Limitation

A link between FL_{exp} and VO_{2RM} may be the increase in EELV at heavy to maximal exercise, which is a strategy that is commonly employed for increasing the expiratory flow rate (McClaran, et al., 1999), and ultimately $\dot{V}_E$ in flow-limited individuals. While increasing $\dot{V}_E$ from heavy to maximal exercise is essential for removing carbon dioxide from the body and for increasing systemic oxygen delivery, it is unknown if a point is reached where the increase in oxygen delivery is offset by the oxygen cost of exercise hyperpnea. Perhaps VO_{2RM} between groups was not explained solely by FL_{exp} in the present study because ERV was not different between groups (Collett & Engel, 1986). In healthy untrained subjects, the strategy for increasing V_T with exercise to max is to decrease EELV while holding EILV constant (Henke, Sharratt, Pegelow, & Dempsey, 1988). However, McClaran et al. (1999) showed that when the degree of FL_{exp} was increased using N_2O_2 in a group of six competitive male cyclists, EELV was significantly elevated. Furthermore, in six of the eight highly-trained male distance runners who participated in the study by Johnson et al. (1992), EELV returned to the equivalence of, or even slightly above resting values during maximal exercise. In the remaining two subjects, however, flow rates were increased by generating high pressures very early during expiration. Although most of the subjects chose to increase EELV back to resting values or higher during maximal exercise, the mean EELV at maximal exercise remained below mean resting EELV. Therefore, it appears that the strategy that is employed for increasing flow rates during heavy to maximal exercise in flow-limited athletes is highly individualized. In the present study, VO_{2RM} between groups appeared to be approaching significance ($P = 0.102$). Perhaps the majority of the flow-limited subjects who participated in the present study “chose” to increase expiratory flow by generating high pressures very early in the expiratory phase rather than “choosing” to increase

EELV, explaining the failure to detect a significant difference in VO_{2RM} during maximal exercise between groups when co-varying $\dot{V}_E$. From an exercise performance standpoint, it is unknown which strategy for increasing expiratory flow is preferred.

The Oxygen Cost of Exercise Hyperpnea During Submaximal Exercise

During submaximal exercise (80% and 90% $\dot{V}O_2$ max), VO_{2RM} was not statistically different between groups. However, $\dot{V}_E$ was significantly greater in FL compared to NFL during exercise at both 80% and 90% $\dot{V}O_2$ max. If $\dot{V}_E$ is significantly different between groups, it is expected based on previous research, that VO_{2RM} would be significantly different as well. Why did this not occur in the present study? One explanation may lie in the unfortunately low number of subjects included in the submaximal exercise portion of the present study due to complications with matching ventilatory mechanics between exercise and voluntary hyperpnea at submaximal exercise intensities. Only six flow-limited, and five non-flow limited subjects were included in the submaximal exercise portion of the present study. From a statistical standpoint, the inherent variation between subjects that comes with measuring VO_{2RM} may necessitate a greater sample size in order to show significance at an alpha level of 0.05 and a statistical power of 0.80.

Another potential explanation for the failure to detect a significant difference in VO_{2RM} in spite of a difference in $\dot{V}_E$ at both 80% and 90% $\dot{V}O_2$ max may be the low level of $\dot{V}_E$ within each group. Perhaps the established slope of the relationship between $\dot{V}_E$ and VO_{2RM} is not steep enough at this level of $\dot{V}_E$ to account for a difference in VO_{2RM}. In the present study, at 80% $\dot{V}O_2$ max, flow-limited subjects had a mean $\dot{V}_E$ of 113.67 $L \cdot min^{-1}$ and a mean VO_{2RM} of 7.35 $ml \cdot kg^{-1} \cdot min^{-1}$. At the same exercise intensity, non-flow limited subjects had a mean $\dot{V}_E$ of 92.84 $L \cdot min^{-1}$ and a mean VO_{2RM} of 3.11 $ml \cdot kg^{-1} \cdot min^{-1}$. Based on the values of $\dot{V}_E$ at 80% $\dot{V}$

O_2 max in the present study, the data presented in the study by Martin and Stager (1981) predicts a VO_{2RM} in our group of flow-limited athletes of 9.6 ml·kg^{-1}·min^{-1}, and a VO_{2RM} in our group of non-flow limited athletes of 7.6 ml·kg^{-1}·min^{-1}. Furthermore, Johnson et al. (1992) estimated VO_{2RM} over a range of $\dot{V}_E$ from resting to $\dot{V}O_2$ max, based on previously published transpulmonary pressure measurements (Aaron, et al., 1992) in their group of elite distance runners. Using the mean values of $\dot{V}_E$ at 80% $\dot{V}O_2$ max in the present study, the data provided by Johnson et al. estimates a VO_{2RM} in our flow-limited subjects of 4.7 ml·kg^{-1}·min^{-1}, and a VO_{2RM} in our non-flow limited subjects of 3.4 ml·kg^{-1}·min^{-1}. Based on the data provided by Martin and Stager (1981), as well as Johnson et al. (1992), it is highly unlikely that their estimates of VO_{2RM} would yield a significant difference in VO_{2RM} between groups at the level of $\dot{V}_E$ that was observed at 80% $\dot{V}O_2$ max in our group of highly-trained athletes, given the standard deviation in the present data.

In the present study, at 90% $\dot{V}O_2$ max, flow-limited subjects demonstrated a mean $\dot{V}_E$ of 142.15 L·min^{-1} and a mean VO_{2RM} of 7.39 ml·kg^{-1}·min^{-1}. At the same exercise intensity, non-flow limited subjects demonstrated a mean $\dot{V}_E$ of 113.51 L·min^{-1} and a mean VO_{2RM} of 4.52 ml·kg^{-1}·min^{-1}. Based on the values of $\dot{V}_E$ at 90% $\dot{V}O_2$ max in the present study, the data presented in the study by Johnson et al. (1992) predicts a VO_{2RM} in the present group of flow-limited subjects of 7.4 ml·kg^{-1}·min^{-1}, and a VO_{2RM} in the present group of non-flow limited subjects of 4.8 ml·kg^{-1}min^{-1}. With the standard deviations that were observed in the measurement of VO_{2RM} in our group of athletes, it is also unlikely that the relationship that was established between $\dot{V}_E$ and VO_{2RM} in the study by Johnson et al. (1992) would predict a significant difference in VO_{2RM} between FL and NFL in the present study. Therefore, although submaximal $\dot{V}_E$ was significantly greater in FL compared to NFL in the present study, previous studies seem to agree with our results, which show that VO_{2RM} is not significantly greater in flow-limited endurance athletes compared to non-flow limited endurance athletes during submaximal exercise. At 80% and 90% $\dot{V}O_2$ max, the slope of the regression line describing the relationship between $\dot{V}_E$ and VO_{2RM} may not be steep enough to explain a difference in VO_{2RM} between the two experimental groups.

Pulmonary Function and Expiratory Flow Limitation

In determining the underlying causes of the presence of FL_{exp} in highly-trained endurance athletes, the data from the present study suggest that submaximal and maximal $\dot{V}_E$ may not be the only contributors to the occurrence of FL_{exp} during maximal exercise. In the present cohort of highly-trained distance runners, FEV_1/FVC was significantly greater in NFL compared to FL (89 vs. 81%). Furthermore, FEF_{25-75} was also significantly greater in NFL (7.06 vs. 5.13 $L \cdot s^{-1}$). These data suggest that, in non-flow limited individuals, there is more room available for the generation of flow across the mid-range of the expiratory portion of the MFVL. By definition, the classification of subjects into the flow-limited category depends highly on the ability to generate maximal expiratory flow. Therefore, the findings of the present study suggest that FL_{exp} during maximal exercise may be partly due to a greater limitation to flow across the mid-range of a maximal expiratory maneuver.

In the present group of non-flow limited runners, the measured values of FEF_{25-75} were significantly greater than the predicted values. Contrary to our findings, Chapman et al. (1998) found that all pulmonary test values (FVC, FEV_1, and MEF_{50}) were within the normal range of predicted values in non-flow limited, highly-trained distance runners. Further contradicting the results of the present study, Chapman et al. (1998) found no significant differences in any of the pulmonary test values between flow-limited and non-flow limited athletes. Further research focusing on pulmonary function variables in flow-limited and non-flow limited endurance athletes is necessary to reconcile the inconsistencies of the present study with previous findings.

Implications for Performance

What is the price to pay for an elevated oxygen cost of exercise hyperpnea during maximal exercise in highly trained endurance athletes? The extremely high levels of respiratory muscle work in highly-trained endurance athletes during maximal exercise require approximately 14% to 16% of total cardiac output (Harms et al., 1998). Due to the substantial amount of blood flow that is required by the respiratory muscles during maximal exercise, competition for blood flow between the working respiratory muscles and the working locomotor muscles may be problematic for exercise performance.

There is evidence that the diaphragmatic muscle fatigue, which normally occurs in highly-trained distance runners at exercise intensities as low as 85% $\dot{V}O_2$ max (Johnson, Babcock, Suman, & Dempsey, 1993), is related to a decrease in exercise performance. There appears to be a sympathetically-mediated reflex in response to diaphragmatic fatigue which causes a decrease in blood flow to the locomotor muscles during exercise. St. Croix, Morgan, Wetter, & Dempsey (2000), found an increase in muscle sympathetic nerve activation as a result of fatiguing the diaphragm during voluntary hyperpnea in a group of seven healthy subjects (Males, N = 3; Females, N = 4). Harms et al. (1997) found a decrease in leg blood flow when the work of exercise hyperpnea was increased during maximal exercise in a group of trained male cyclists (N = 7; VO_2 max = 64.3 ± 5.6 $ml \cdot kg^{-1} \cdot min^{-1}$) along with an increase in norepinephrine spillover, indicating that the decrease in leg blood flow may be due to muscle sympathetic nerve activity (Savard, et al., 1989). In a separate study, Harms, Wetter, St. Croix, Pegelow, and

Dempsey (2000) showed a significant decrease in time to exhaustion at a work rate of 90% $\dot{V}O_2$ max when the respiratory muscle load was increased in a group of trained male cyclists (N = 7; VO_2 max = 63 ± 5 $ml \cdot kg^{-1} \cdot min^{-1}$). The differences in time to exhaustion between control and respiratory muscle loading and unloading was significantly correlated with the differences in both leg rating of perceived exertion and the dyspnea rating between control and respiratory muscle loading and unloading trials (Harms et al., 2000). The decrease in exercise performance during the respiratory loading trials was attributed to the decrease in locomotor muscle blood flow as a result of the increase in respiratory muscle work.

While the work of breathing was not directly measured in the present study, the increase in the oxygen cost of exercise hyperpnea is presumably a result of the increased work of exercise hyperpnea, which occurred due to the elevated level of $\dot{V}_E$ at $\dot{V}O_2$ max in the group of flow-limited athletes who participated in the present study. Based on evidence of diaphragmatic fatigue in highly-trained distance runners while exercising at intensities as low as 85% $\dot{V}O_2$ max (Johnson et al., 1993), it is likely that diaphragm fatigue was present in the current group of highly-trained endurance athletes during maximal exercise. Perhaps the greater amount of work performed by the respiratory muscles in the present group of flow-limited athletes led to vasoconstriction of the leg vasculature. It is unknown whether a sympathetically-mediated reflex activation exists to a greater extent in flow-limited compared to non-flow limited athletes while exercising at heavy to maximal intensities. Future research is required to shed light on this question.

CHAPTER FIVE

SUMMARY, FINDINGS, IMPLEMENTATIONS, AND RECOMMENDATIONS

Summary

The main aim of the present study was to determine the effect of FL_{exp} on the oxygen cost of exercise hyperpnea during heavy to maximal exercise in a group of highly-trained distance runners.

The 18 subjects who participated in the study were highly-trained male distance runners between the ages of 18 and 30 and were recruited from local high school, collegiate, and post-collegiate distance running groups. During the first visit to the Indiana University Human Performance Laboratory, subjects completed a series of pulmonary function tests along with a VO_2 max test. During incremental exercise to max, pulmonary mechanics included V_T, f_b, ERV and percent flow limitation. During a second visit to the laboratory, subjects voluntarily matched the mechanics of exercise hyperpnea during three four-minute trials, each trial consisting of one of three levels of exercise hyperpnea. The levels of exercise hyperpnea that were voluntarily matched corresponded to 80%, 90% and 100% $\dot{V}O_2$ max. VO_{2RM} was the outcome variable of the voluntary hyperpnea trials. Subjects who demonstrated no less than 35 percent of flow limitation during maximal exercise (n = 9) were categorized as flow-limited. Subjects who demonstrated 5 percent or less of flow limitation during maximal exercise (n = 9) were categorized as non-flow limited.

Statistical analysis of the data comprised of a one-tailed independent samples t-test for the detection of differences in VO_{2RM} and $\dot{V}_E$ during maximal exercise between FL and NFL, with an alpha level of 0.05. Differences between groups for all other maximal and submaximal exercise variables, as well as for pulmonary function variables, were analyzed using two-tailed independent samples t-tests with the alpha level set at 0.05.

The analysis of the data revealed the following significant findings:

1. VO_{2RM} was significantly greater in FL compared to NFL during maximal exercise.
2. $\dot{V}_E$ at $\dot{V}O_2$ max was significantly greater in FL compared to NFL.
3. When co-varying for $\dot{V}_E$ at $\dot{V}O_2$ max, there was no significant difference in VO_{2RM} during maximal exercise between FL and NFL.
4. ERV during maximal exercise was not significantly different between FL and NFL.
5. During submaximal exercise (80 and 90% $\dot{V}O_2$ max), $\dot{V}_E$ was significantly greater in FL compared to NFL.
6. During submaximal exercise (80 and 90% $\dot{V}O_2$ max), $\dot{V}_E/\dot{V}CO_2$ was significantly greater in FL compared to NFL.

Conclusions

1. Highly-trained distance runners who demonstrate a substantial amount of flow limitation during maximal exercise commit a greater proportion of total body $\dot{V}O_2$ to fuel the respiratory muscles than individuals of the same aerobic fitness who are not flow-limited.
2. Highly-trained distance runners who are flow-limited during maximal exercise demonstrate a greater level of exercise hyperpnea compared to highly-trained distance runners who are not flow-limited during maximal exercise.

3. The greater oxygen cost of exercise hyperpnea in highly-trained distance runners who are flow-limited compared to those who are not flow-limited during maximal exercise is attributed to the greater $\dot{V}_E$ at $\dot{V}O_2$ max in flow-limited runners.
4. The highly-trained distance runners who are flow-limited during maximal exercise demonstrate a greater drive to ventilate during submaximal exercise than highly-trained distance runners who do not achieve a substantial amount of flow limitation during maximal exercise.

Practical Implications

The findings of the present study may be implemented into endurance training and research in the following ways:

1. FL_{exp} should be considered when training at altitude. Previous studies show that flow-limited athletes are unable to increase $\dot{V}_E$ during maximal exercise. Based on the findings of the present study, flow-limited athletes would be at an advantage when exercising at or near maximal intensity due to their inability to increase $\dot{V}_E$ during maximal exercise in a hypoxic environment. Therefore, it is likely that while exercising at altitude, the oxygen cost of exercise hyperpnea would not be elevated.
2. FL_{exp}, by itself, should no longer be considered a source of an elevated oxygen cost of exercise hyperpnea in highly-trained endurance athletes. Rather, the source of the elevated oxygen cost of exercise hyperpnea in flow-limited athletes is the greater $\dot{V}_E$ during maximal exercise. Therefore, training strategies for decreasing FL_{exp} during heavy to maximal exercise will not decrease the oxygen cost of exercise hyperpnea.

Recommendations for Further Study

The following recommendations are made for further research on highly-trained endurance athletes:

1. The present study should be repeated in highly-trained female endurance athletes. Previous studies show that females consistently have smaller lung volumes and lower maximal expiratory flow rates, even when correcting for height, when compared to men (McClaran, Harms, Pegelow, & Dempsey, 1998). Therefore, there is a much greater prevalence of FL_{exp} in highly-trained female endurance athletes. The effect of FL_{exp} on the oxygen cost of exercise hyperpnea in female endurance athletes is presently unknown.
2. It appears that FL_{exp} is a result of the ability to maximize flow during heavy to maximal exercise in certain individuals. There is also evidence that highly-trained athletes who are flow-limited during heavy to maximal exercise express a greater inherent drive to ventilate. Further research in this area should focus on elucidating the causes of differences in ventilatory drive between individuals.
3. A study should be conducted which tests the effects of reducing flow limitation in highly-trained endurance athletes, who are otherwise flow-limited during maximal exercise, on the oxygen cost of exercise hyperpnea as well as the variables related to ventilatory drive.
4. Further research on the oxygen cost of exercise hyperpnea should focus on training at altitude. More specifically, how does a hypoxic environment affect the oxygen cost of exercise hyperpnea in flow-limited athletes, who are unable to increase $\dot{V}_E$ during

maximal exercise, compared to non-flow limited athletes, who have the potential to increase expiratory flow rates during maximal exercise?

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APPENDIX A

TABLES

Table 4.1 Subject Characteristics

	Flow Limited	Non-Flow Limited	All Subjects
Age (yrs)	22.0 ± 2.7	22.2 ± 4.1	22.1 ± 3.4
Height (cm)	179.8 ± 4.3	179.9 ± 5.1	179.8 ± 4.6
Mass (kg)	67.45 ± 5.44	65.86 ± 5.81	66.66 ± 5.52
VO_2 max ($ml \cdot kg^{-1} \cdot min^{-1}$)	75.72 ± 5.12	73.5 ± 5.61	74.64 ± 5.33
HR max ($beats \cdot min^{-1}$)	190 ± 9.6	192 ± 8.5	191 ± 8.9
Flow Limitation (%V_T)	55.1 ± 11.3	0.3 ± 1.0	-

No significant differences were detected between groups (*P* = 0.05). Definition of terms: VO_2 max, maximal oxygen consumption; HR max, maximal heart rate; Flow Limitation, the percent of tidal volume that was flow limited during maximal exercise. Note: Flow limitation is included in the present table for the purpose of defining the separation of experimental groups. No statistical analysis was carried out on that variable.

Table 4.2 Pulmonary Function Measurements

	Flow Limited	Non-Flow Limited	All Subjects
Vital Capacity (L)	5.68 ± 0.82	5.74 ± 0.38	5.71 ± 0.62
%Predicted	101 ± 15.2	103 ± 0.5	102 ± 12.4
FEV_1 ($L\cdot s^{-1}$)	4.55 ± 0.66	5.08 ± 0.52	4.82 ± 0.63
%Predicted	97 ± 15.2	110 ± 14	104 ± 15.5
FEV_1/FVC (%)	81 ± 6.1	89 ± 7.6*	85 ± 7.8
%Predicted	97 ± 7.1	107 ± 9.1*	102 ± 9.2
FEF_{25-75} ($L\cdot s^{-1}$)	5.13 ± 0.50	7.06 ± 1.01*	6.09 ± 1.30
%Predicted	105 ± 12.0	147 ± 26.8*§	126 ± 29.5
PEFR ($L\cdot s^{-1}$)	10.47 ± 2.25	10.75 ± 1.62	10.61 ±1.11
%Predicted	103 ± 21.0	107 ± 18.6	105 ± 19.4

*Significantly different from FL group ($P < 0.05$). § Actual values are significantly different from predicted values ($P < 0.05$).

Table 4.3 O_2 Cost of Hyperpnea and Ventilatory Mechanics During Maximal Exercise

	Flow Limited	Non-Flow Limited	All Subjects
VO_{2RM} (%VO_2 max)	19.19 ± 8.44	13.25 ± 4.89*	16.22 ± 7.35
VO_{2RM} (ml·kg^{-1}·min^{-1})	14.58 ± 6.66	9.70 ± 3.64*	12.14 ± 5.78
V_E max (L·min^{-1})	176.47 ± 23.29	157.54 ± 15.31*	167.01 ± 21.46
V_E/VO_2 max	34.58 ± 3.01	32.67 ± 2.62	33.62 ± 2.91
V_E/VCO_2 max	30.52 ± 2.70	28.63 ± 1.63	29.57 ± 2.37
ERV (%VC)	36 ± 5.7	35 ± 6.7	36 ± 6.1
V_T max (L·breath^{-1})	3.04 ± 0.41	2.96 ± 0.25	3.00 ± 0.33
f_b max (breaths·min^{-1})	58.50 ± 7.19	53.56 ± 7.28	56.03 ± 7.47

* Significantly different from FL ($P < 0.05$). Definition of terms: VO_{2RM}, respiratory muscle oxygen consumption; V_E max, ventilation at maximal exercise; ERV, expiratory reserve volume; V_T max, average tidal volume at maximal exercise; fb max, breathing frequency at maximal exercise.

Table 4.4 O_2 Cost of Hyperpnea and Ventilatory Mechanics During Submaximal Exercise

		Flow Limited	Non-Flow Limited	All Subjects
90% of VO_2 max				
	VO_2RM (%VO_2)	10.30 ± 7.97	7.01 ± 3.74	8.81 ± 6.35
	VO_2RM (ml·kg^{-1}·min^{-1})	7.39 ± 5.96	4.52 ± 2.32	4.95 ± 5.07
	VE (L·min^{-1})	142.15 ± 19.19	113.51 ± 12.40*	129.13 ± 21.66
	VE/VO_2	30.51 ± 2.90	26.15 ± 3.96	28.53 ± 3.96
	VE/VCO_2	29.88 ± 1.97	25.35 ± 2.27*	27.82 ± 3.10
	ERV (%VC)	33 ± 7.3	32 ± 8.2	33 ± 7.3
	V_T (L·breath^{-1})	2.99 ± 0.66	2.68 ± 0.25	2.99 ± 0.56
	f_b (breaths·min^{-1})	49.25 ± 11.64	42.60 ± 5.50	43.27 ± 9.89
	Flow Limitation (%V_T)	39 ± 23.6	0 ± 0	-
80% of VO_2 max				
	VO_2RM (%VO_2)	11.95 ± 8.47	5.39 ± 3.89	8.97 ± 7.32
	VO_2RM (ml·kg^{-1}·min^{-1})	7.35 ± 5.03	3.11 ± 2.23	5.42 ± 4.42
	VE (L·min^{-1})	113.67 ± 18.20	92.84 ± 10.14*	104.20 ± 18.03
	VE/VO_2	27.61 ± 2.65	23.87 ± 3.32	25.91 ± 3.43
	VE/VCO_2	29.35 ± 1.97	25.28 ± 1.81*	27.50 ± 2.79
	ERV (%VC)	32 ± 8.1	40 ± 7.7	36 ± 8.4
	V_T (L·breath^{-1})	3.00 ± 0.61	2.48 ± 0.22	2.76 ± 0.53
	f_b (breaths·min^{-1})	39.00 ± 8.85	37.70 ± 5.38	38.41 ± 7.16
	Flow Limitation (%V_T)	6 ± 13.9	0 ± 0	-

* Significantly different from FL ($P < 0.05$). Definition of terms: VO_{2RM}, respiratory muscle oxygen consumption; V_E, exercise ventilation;

ERV (%VC), expiratory reserve volume expressed as a percentage of vital capacity; V_T, tidal volume; f_b, breathing frequency. FL, n = 6; NFL, n = 5.

Table 4.5 Difference in Ventilatory Mechanics Between Exercise and Voluntary Hyperpnea

	Flow Limited	**Non-Flow Limited**	**All Subjects**
% ΔV_E ($L \cdot min^{-1}$)	3.8 ± 2.7[a]	1.4 ± 11.1	1.2 ± 8.3[a]
ΔERV (%VC)	1.4 ± 6.0	0.5 ± 3.4	0.4 ± 4.8
ΔFL (%V_T)	1.7 ± 9.2	4.9 ± 8.8	3.3 ± 8.9

[a] Exercise hyperpnea values are greater than voluntary hyperpnea values. Definition of terms: % ΔV_E, percent difference in V_E between exercise and voluntary hyperpnea; ΔERV, difference in expiratory reserve volume between exercise and voluntary hyperpnea expressed as a percent of vital capacity; ΔFL, difference in flow limitation between exercise and voluntary hyperpnea expressed as a percent of tidal volume.

APPENDIX B

DATA COLLECTION SHEETS

Data Collection - VO2max

Name

Post Cal

Age

Mass

Height

Pbar

RH

Speed

	Minute	Grade %	HR	VO2	%VO2max	ERV	BF	TV	VE	%EFL

Data Collection - Voluntary Hyperpnea

Name
Age
Mass
Height
Pbar
RH

80%	Minute	VO2	VE	HR	ERV	%EFL

VE =
TV =
BF =
ERV =
%FL =

90%	Minute	VO2	VE	HR	ERV	%EFL

VE =
TV =
BF =
ERV =
%FL =

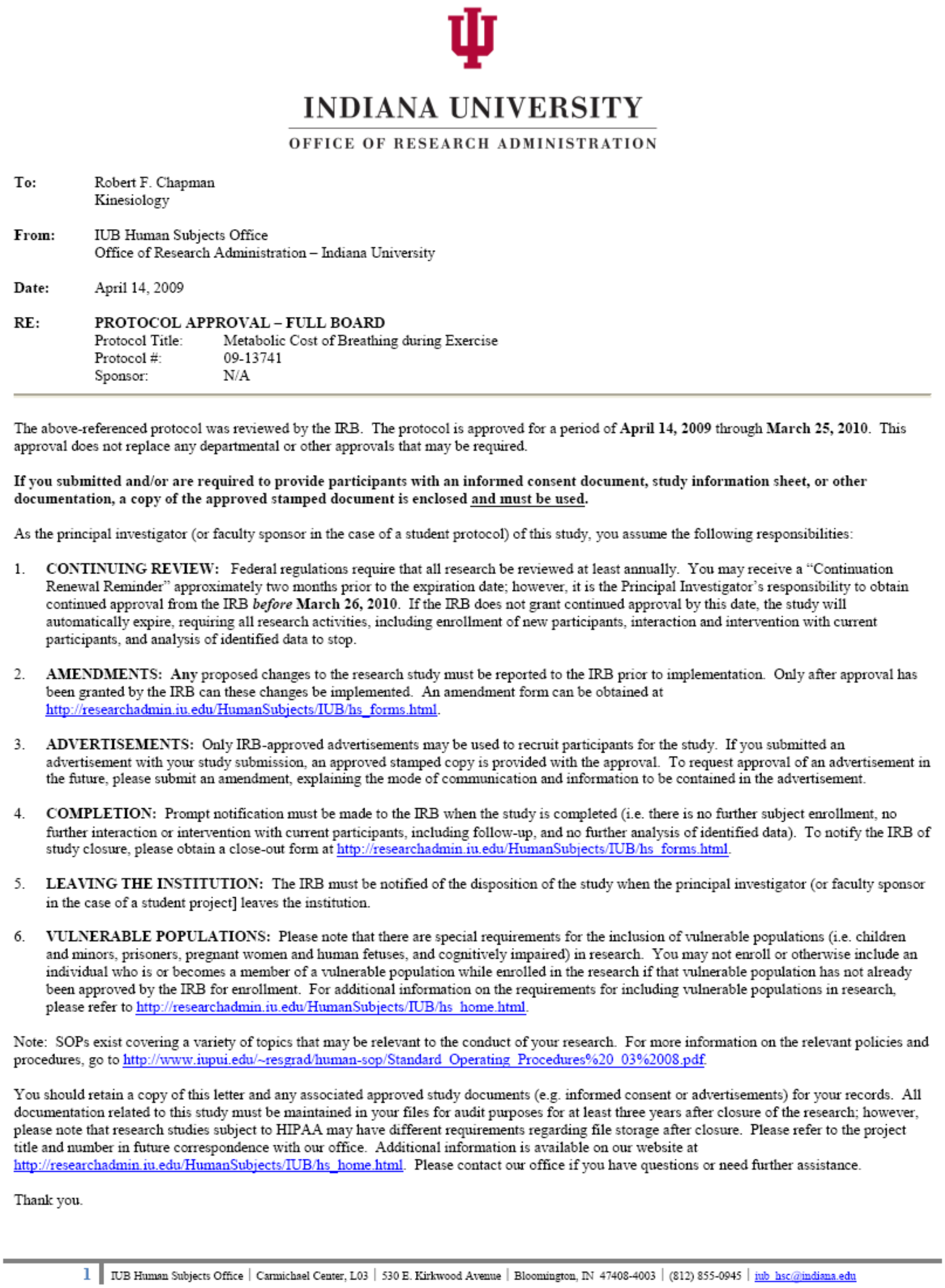
MAX	Minute	VO2	VE	HR	ERV	%EFL

VE =
TV =
BF =
ERV =
%FL =

Post Cal =

APPENDIX C

IRB Approval



INDIANA UNIVERSITY
OFFICE OF RESEARCH ADMINISTRATION

To: Robert F. Chapman
Kinesiology

From: IUB Human Subjects Office
Office of Research Administration – Indiana University

Date: April 14, 2009

RE: **PROTOCOL APPROVAL – FULL BOARD**
Protocol Title: Metabolic Cost of Breathing during Exercise
Protocol #: 09-13741
Sponsor: N/A

The above-referenced protocol was reviewed by the IRB. The protocol is approved for a period of **April 14, 2009** through **March 25, 2010**. This approval does not replace any departmental or other approvals that may be required.

If you submitted and/or are required to provide participants with an informed consent document, study information sheet, or other documentation, a copy of the approved stamped document is enclosed and must be used.

As the principal investigator (or faculty sponsor in the case of a student protocol) of this study, you assume the following responsibilities:

1. **CONTINUING REVIEW:** Federal regulations require that all research be reviewed at least annually. You may receive a "Continuation Renewal Reminder" approximately two months prior to the expiration date; however, it is the Principal Investigator's responsibility to obtain continued approval from the IRB ***before*** **March 26, 2010**. If the IRB does not grant continued approval by this date, the study will automatically expire, requiring all research activities, including enrollment of new participants, interaction and intervention with current participants, and analysis of identified data to stop.

2. **AMENDMENTS:** **Any** proposed changes to the research study must be reported to the IRB prior to implementation. Only after approval has been granted by the IRB can these changes be implemented. An amendment form can be obtained at http://researchadmin.iu.edu/HumanSubjects/IUB/hs_forms.html.

3. **ADVERTISEMENTS:** Only IRB-approved advertisements may be used to recruit participants for the study. If you submitted an advertisement with your study submission, an approved stamped copy is provided with the approval. To request approval of an advertisement in the future, please submit an amendment, explaining the mode of communication and information to be contained in the advertisement.

4. **COMPLETION:** Prompt notification must be made to the IRB when the study is completed (i.e. there is no further subject enrollment, no further interaction or intervention with current participants, including follow-up, and no further analysis of identified data). To notify the IRB of study closure, please obtain a close-out form at http://researchadmin.iu.edu/HumanSubjects/IUB/hs_forms.html.

5. **LEAVING THE INSTITUTION:** The IRB must be notified of the disposition of the study when the principal investigator (or faculty sponsor in the case of a student project] leaves the institution.

6. **VULNERABLE POPULATIONS:** Please note that there are special requirements for the inclusion of vulnerable populations (i.e. children and minors, prisoners, pregnant women and human fetuses, and cognitively impaired) in research. You may not enroll or otherwise include an individual who is or becomes a member of a vulnerable population while enrolled in the research if that vulnerable population has not already been approved by the IRB for enrollment. For additional information on the requirements for including vulnerable populations in research, please refer to http://researchadmin.iu.edu/HumanSubjects/IUB/hs_home.html.

Note: SOPs exist covering a variety of topics that may be relevant to the conduct of your research. For more information on the relevant policies and procedures, go to http://www.iupui.edu/~resgrad/human-sop/Standard_Operating_Procedures%20_03%2008.pdf.

You should retain a copy of this letter and any associated approved study documents (e.g. informed consent or advertisements) for your records. All documentation related to this study must be maintained in your files for audit purposes for at least three years after closure of the research; however, please note that research studies subject to HIPAA may have different requirements regarding file storage after closure. Please refer to the project title and number in future correspondence with our office. Additional information is available on our website at http://researchadmin.iu.edu/HumanSubjects/IUB/hs_home.html. Please contact our office if you have questions or need further assistance.

Thank you.

APPENDIX D

INFORMED CONSENT, PAR-Q

IRB Study #09-13741

INDIANA UNIVERSITY BLOOMINGTON

INFORMED CONSENT STATEMENT

Metabolic cost of breathing during exercise

You are invited to participate in a research study of the role that breathing plays during exercise. You were selected as a possible subject because of your expressed interest in being a subject. We ask that you read this form and ask any questions you may have before agreeing to be in the study.

The study is being conducted by Dr. Robert Chapman with the Department of Kinesiology at Indiana University – Bloomington.

STUDY PURPOSE

The purpose of this study is to determine how much oxygen the respiratory muscles consume during maximal exercise.

NUMBER OF PEOPLE TAKING PART IN THE STUDY:

If you agree to participate, you will be one of approximately 50 subjects who will be participating in this research.

PROCEDURES FOR THE STUDY:

If you agree to be in the study, you will complete the testing procedures listed below, conducted on two separate days. All tests will take place in the Human Performance Laboratories in the Health, Physical Education, and Recreation (HPER) building on the Indiana University Bloomington campus.

On Day #1 of testing, you will complete a medical questionnaire, a breathing function test and a maximal aerobic capacity exercise test. On Day #2 of testing, you will complete a voluntary hyperventilation test.

Medical Questionnaire: You will be asked to complete a short questionnaire about your medical history, which should take less than 10 minutes. After completing the questionnaire, certain answers may cause you to be ineligible for further participation in the study.

Breathing Function Tests: Tests of breathing function are performed as described by the American Thoracic Society. These tests include the measurement of total lung capacity (the volume of air your lungs can hold), vital capacity (the volume of air you can push out with one maximal breath), residual volume (the volume of air remaining in your lungs after you breathe out as much as possible), your FEV_1 (the volume of air you can forcefully breathe out in one second), maximal voluntary ventilation (the maximal volume of air you can breathe in 12 seconds), and lung diffusion capacity (the ease at which oxygen can move from your lungs into your blood). For all of these procedures, you must wear nose clips and breathe through a disposable mouthpiece. These procedures will require 15 minutes total.

Maximal Aerobic Capacity Exercise Tests: These tests measure your maximal oxygen consumption capacity (your highest exercise capacity). The test will utilize either treadmill running or stationary bicycle exercise. You will be given an opportunity to warm up and familiarize yourself with the treadmill or stationary bicycle device before the test begins. The investigators will help you with necessary adjustments to assure your comfort. You will be fitted with a rubber mouthpiece and nose clip. Rubber mouthpieces are cleansed in a detergent solution and submerged in an antibacterial solution following each use. You will wear a heart rate monitor to measure heart rate. The aerobic capacity test will begin with five minutes of rest while you sit quietly while breathing through the mouthpiece and wearing the nose clip. At the completion of the exercise portion of the aerobic capacity test, an additional two minutes of recovery data will be collected before you can remove the mouthpiece and nose clip. Each of these individual tests described below takes approximately 60 minutes.

Treadmill Running

At the end of the five-minute rest period, the treadmill speed will then be increased to a running speed that is comfortable for you (usually between 6 and 8 mph). You will run for two minutes with the treadmill flat. The treadmill slope will then be raised every two minutes, similar to running up a hill, until you no longer wish to continue running.

Stationary Bicycle

For this test, we utilize a stationary bicycle. At the end of the five-minute rest period, you will begin pedaling at 70 revolutions per minute (70 rpm) at a light workload. To help you maintain 70 rpm, there will either be a visual meter showing your pedal revolutions or signal that you can hear will beep with the pedaling rate to be maintained. At the end of each two-minute period, additional resistance will be added to the bike making it harder to pedal. The test will end when you are no longer able to maintain 70 rpm or you no longer wish to continue.

Flow-Volume Loops: During a maximal exercise test (listed above), the speed at which you breathe air in and out and the volume of air you breathe in and out will be measured. Approximately every 30 seconds during the exercise test, you will be prompted to breathe in completely, filling your lungs, then you will return to normal breathing. Before and after the exercise test, while at rest, you will be prompted to perform 3 breathing tests, where you complete a maximal inhalation (filling your lungs completely) followed by a complete exhalation (where you breathe out all the air that you can). Rubber mouthpieces are utilized during this procedure which will be cleansed in a detergent solution and submerged in an antibacterial solution following each use. This test adds approximately 15 minutes to the time required for the maximal exercise test.

Voluntary Hyperventilation Test

For this test, you will be fitted with a rubber mouthpiece and nose clip. Rubber mouthpieces are cleansed in a detergent solution and submerged in an antibacterial solution following each use. While sitting on a stool, you will be instructed to breathe deeply and rapidly at rest. You will be able to view a computer monitor that will display your breathing rate, and the investigator will give you a target value which you will try to maintain. The air you breathe will come from a large balloon, which is filled with normal room air with additional CO_2 added. This will allow you to breathe heavily at rest and not become light headed. You will breathe at the target breathing rate for 5 minutes. This test, including set up, will take approximately 30 minutes to complete.

RISKS OF TAKING PART IN THE STUDY:

While on the study, the risks, side effects, and/or discomforts are:

Breathing Function Tests: A slight risk of headache, temporary light-headedness, throat dryness or fainting does exist with breathing function testing. As you will be sitting comfortably and carefully monitored, fainting is not likely to occur. You are free to indicate any discomfort and discontinue participation at any time.

Maximal Aerobic Capacity Exercise Tests: Both maximal and moderate level exercise tests of healthy individuals, as described by the American College of Sports Medicine, presents little risk to the subject and does not require medical clearance for subjects under 40. Potential risks and/or discomforts can include episodes of temporary light-headedness, chest discomfort, leg cramps, occasional irregular heartbeats, and abnormal blood pressure responses. The risk of heart attack, although minor, (approximately 1 to 2 in 10,000) does exist. During the test you will be closely monitored for any abnormal changes in heart rate or breathing. You are free to indicate any discomfort and discontinue participation at any time.

Flow-Volume Loops: There are no anticipated risks associated with this measurement. You are free to indicate any discomfort and discontinue participation at any time.

Voluntary Hyperventilation Test

The voluntary hyperventilation test involves a slight risk of headache, throat dryness, and breathing muscle fatigue. With 5% CO_2 added to the inspired air, the risk of light headedness and fainting during this procedure is low. You are free to indicate any discomfort and discontinue participation at any time.

Additional risks for all testing include the possible loss of confidentiality.

BENEFITS OF TAKING PART IN THE STUDY:

The benefits to participation that are reasonable to expect are information regarding breathing function and overall level of fitness. Other than this information, you will gain little benefit. All subjects will be provided with feedback concerning their own results and the general findings of their study upon request.

ALTERNATIVES TO TAKING PART IN THE STUDY:

An alternative to participating in the study is to choose not to participate.

CONFIDENTIALITY

Efforts will be made to keep your personal information confidential. Data will be stored on password protected computers in locked rooms with limited public access. We cannot guarantee absolute confidentiality. Your personal information may be disclosed if required by law. Your identity will be held in confidence in reports in which the study may be published and databases in which results may be stored.

Organizations that may inspect and/or copy your research records for quality assurance and data analysis include groups such as the study investigator and his/her research associates, the IUB Institutional Review Board or its designees, and (as allowed by law) state or federal agencies, specifically the Office for Human Research Protections (OHRP) who may need to access the collected medical and/or research data.

PAYMENT

You will not receive payment for taking part in this study.

COMPENSATION FOR INJURY

In the event of physical injury resulting from your participation in this research, necessary medical treatment will be provided to you and billed as part of your medical expenses. Costs not covered by your health care insurer will be your responsibility. Also, it is your responsibility to determine the extent of your health care coverage. There is no program in place for other monetary compensation for such injuries. However, you are not giving up any legal rights or benefits to which you are otherwise entitled.

CONTACTS FOR QUESTIONS OR PROBLEMS

For questions about the study or a research-related injury, contact the researcher Robert Chapman, Ph.D. at (812) 856-2452 or rfchapma@indiana.edu

For questions about your rights as a research participant or to discuss problems, complaints or concerns about a research study, or to obtain information, or offer input, contact the IUB Human Subjects office, 530 E Kirkwood Ave, Carmichael Center, L03, Bloomington IN 47408, 812-855-3067 or by email at iub_hsc@indiana.edu

VOLUNTARY NATURE OF STUDY

Taking part in this study is voluntary. You may choose not to take part or may leave the study at any time. Leaving the study will not result in any penalty or loss of benefits to which you are entitled. Your decision whether or not to participate in this study will not affect your current or future relations with the investigator(s).

SUBJECT'S CONSENT

In consideration of all of the above, I give my consent to participate in this research study.

I will be given a copy of this informed consent document to keep for my records. I agree to take part in this study.

Subject's Printed Name:____

Subject's Signature:____**Date:**________________
(must be dated by the subject)

Printed Name of Person Obtaining Consent:____________________________

Signature of Person Obtaining Consent:______________________________**Date:**________________

IRB Approval Date: APR 14 2009

Continuing Review Date: MAR 26 2010

Modified Physical Activity Readiness Questionnaire (PAR-Q)

Name			**Date**
DOB	**Age**	**Home Phone**	**Work Phone**

Regular exercise is associated with many health benefits, yet any change of activity may increase the risk of injury.
Please read each question carefully and answer every question honestly:

Yes	**No**	**1. Has your doctor ever said that you have a heart condition and that you should only do physical activity recommended by a doctor?**
Yes	**No**	**2. Do you feel pain in your chest when you do physical activity?**
Yes	**No**	3. **In the past month, have you had chest pain when you were not doing physical activity?**
Yes	**No**	**4. Do you lose your balance because of dizziness or do you ever lose consciousness?**
Yes	**No**	**5. Do you have a bone or joint problem that could be made worse by a change in your physical activity?**
Yes	**No**	**6. Is your doctor currently prescribing drugs (for example, water pills) for your blood pressure or heart condition?**
Yes	**No**	**7. Do you know of any other reason you should to physical activity?**
Yes	**No**	**8. Has your doctor ever told you that you have diabetes?**
Yes	**No**	**9. Has your doctor ever told you that you have high blood pressure?**
Yes	**No**	**10. Has your doctor ever told you that you have high cholesterol?**
Yes	**No**	**11. Has your doctor ever told you that you have high blood sugar?**
Yes	**No**	**12. Do you smoke?**
Yes	**No**	**13. Are you currently inactive?**
Yes	**No**	**14. Do you have a father, brother or son with heart disease before the age of 55 years old or a mother, sister or daughter with heart disease before the age of 65 years old?**
15. Measure height and weight to determine BMI: **Height:________** **Weight:________**		

Participant Signature	**Date**

Note to ParQ Reader:

A "yes" to any Question 1-8 will eliminate the individual from participation.

A "yes" to 2 or more of Questions 9-14 indicates > low risk.

#15: If over 30 kg/m^2, the individual may have the risk factor of obesity.