INSPIRATORY MUSCLE TRAINING AND ENDURANCE PERFORMANCE IN HYPOXIA

Daniel G. Hursh

Submitted to the faculty of the University Graduate School in partial fulfillment of requirements for the degree

Masters of Science in Kinesiology

in the Department of Kinesiology of School of Public Health

Indiana University

Accepted by the Graduate Faculty, Indiana University, in partial fulfillment of the requirements for the degree of Master of Science.

Master's Thesis Committee

_____

Robert Chapman, Ph.D.

_____

Timothy Mickleborough, Ph.D.

_____

Joel Stager, Ph.D.

ABSTRACT

Ventilation is higher at any submaximal workload in hypoxia as compared to normoxia. Whether or not training the respiratory muscles helps to improve exercise performance in hypoxia is unclear. **Purpose:** To determine if improvements in ventilatory strength with chronic inspiratory muscle training (IMT) improves 20km cycling time trial (TT) performance in hypoxia (F_IO_2 = 16.1%). **Methods:** Thirteen highly-trained men were pair-matched based on pre-exercise values of maximal inspiratory pressure (MIP) and randomly placed into either a sham (n = 5, $\dot{V}O_2max$ = 61.7 ± 2.0 ml·kg^{-1}·min^{-1}) or an IMT (n = 8, $\dot{V}O_2max$ = 63.5 ± 3.4 ml·kg^{-1}·min^{-1}) group. Subjects completed 6 weeks of flow resistive IMT (80% of MIP) or a sham protocol (30% of MIP), with each session consisting of up to 6 sets of 6 MIP maneuvers performed to failure with descending rest intervals 3 times per week. Pre- and post-training, subjects performed tests of pulmonary function, lung volume, MIP, maximal expiratory pressure (MEP), lung diffusion capacity (DLCO), and a 20km cycling TT in hypoxia (FIO_2 = 16.1%). **Results:** After 6 weeks of IMT or sham, the IMT group significantly improved MIP (127.6 ± 13.4 cmH_2O vs 159.0 ± 15.3 cmH_2O, $p < 0.05$), while MIP in the sham group remained unchanged. MEP, DLCO, lung volumes, and pulmonary function values remained unchanged in both groups post-training. 20km TT mean ventilation was significantly higher post-IMT (99.6 ± 5.5 l·min^{-1} vs 110.4 ± 6.8 l·min^{-1}, $p < 0.05$) and unchanged in sham. 20km TT mean breathing frequency was also significantly increased post-IMT (41.4 ± 2.8 b·min^{-1} vs 45.1 ± 2.9 b·min^{-1}, $p < 0.05$) and unchanged in sham. 20km TT mean $\dot{V}O_2$ was significantly increased post-IMT (3.41 ± 0.19 L·min^{-1} vs 3.61 ± 0.21 L·min^{-1}) and unchanged in sham. In the IMT group, 20km TT performance time pre-training was 36.77 ± 1.40 (min) and post-training was 36.28 ± 1.24 (min) (-1.4 ± 1.9%, $p = 0.06$). 20km TT performance time was unchanged in the sham group. 20km TT heart rate and SpO_2 were unchanged in both groups post-training. **Conclusion:** In a small cohort, IMT-induced improvements in respiratory muscle strength which resulted in greater ventilation and oxygen uptake during a 20km time trial in hypoxia. IMT should be explored as a useful strategy for improving the quality of cycle exercise training and/or endurance exercise performance at altitude.

DANIEL G. HURSH

INSPIRATORY MUSCLE TRAINING AND ENDURANCE PERFORMANCE IN HYPOXIA

Table of Contents

Chapter I: Introduction

Athletes competing in a hypoxic environment experience a worsening of exercise performance. One of the main causes is a decline in arterial oxygenation which causes a decline in maximal oxygen consumption. The body compensates for the decline in arterial oxygenation by increasing ventilation, which increases work of breathing. During exercise in normoxia, it is estimated that the inspiratory muscles consume 10 to 15 percent of total body oxygen uptake (1). However, in hypoxia, the oxygen demand of the respiratory muscles increases an additional 20 to 30 percent (2). In response to an increase in work of breathing, the inspiratory muscles increase their oxygen supply by shunting blood away from the working muscle and to the inspiratory muscles (15). Therefore, this causes a decrease in locomotor muscle power production and increases the rate of fatigue.

There have been many different theories and techniques used to attenuate the effects of altitude on exercise performance. Inspiratory muscle training (IMT) has been shown to increase performance during a cycling time trial of 20 km or longer in a normoxic environment (20, 34).

Interestingly, to our knowledge, there has only been one study examining the effects of IMT on performance in hypoxia. In this study by Downey et al., IMT increased oxygen diffusing capacity and arterial oxygen saturation while decreasing ventilation, cardiac output and inspiratory muscle fatigue during a treadmill time to exhaustion test (TTE) in hypoxia (8). Based on these results one would expect exercise performance in hypoxia to benefit from IMT, but there was no significant difference in the time to exhaustion test on a treadmill between the IMT and sham training groups. A lack of significant difference in exercise performance in hypoxia in the Downey et al. study may be due to the specific performance trial used not being robust enough to detect differences. The duration, for the experimental and control group, was 9.7 ± 1.5 min and 7.4 ± 1.2 min, respectively. To our knowledge, in IMT studies using running there has not been a significant performance difference for tests that have a duration of less than 15 minutes (12, 22, 29).

For this study, we used a cycling fixed distance time trial test as our performance variable in place of the treadmill TTE test. TTE has been shown to not be as reliable (28, 43) or as applicable for competition (16) as a time trial. During competitions, cyclists do not cycle at a constant work load thus performing a time trial where they can adjust their work load is a better simulation for competition. Additionally, the length of the performance test used may be a factor in the Downey et al. study failing to show differences in performance after IMT. IMT studies where the mode of exercise is cycling performed in normoxia has shown no significant improvement during a set distance time trial that was only 8 km (38), but when the TT was at least 20 km in length, IMT significantly improved exercise performance (20, 34). Therefore, the purpose of this study was to determine if 6 weeks of IMT improved the performance of highly trained cyclists during a 20 km time trial in hypoxia. We hypothesized that performing IMT for

6 weeks will significantly improve time trial performance in a hypoxic environment for highly trained cyclists compared to a sham training group.

Statement of the Problem

During exercise in hypoxia the body increases ventilation in response to a decrease in arterial oxygenation. An increase in ventilation raises the work of breathing an additional 20 to 30 percent greater than it is in normoxia. IMT has been shown to attenuate the effects of the metaboreflex response, train the respiratory muscles, decrease work of breathing and significantly enhance performance in normoxia. However, it is unclear if IMT can augment performance in a hypoxic environment, where ventilatory output is greater at any given workload.

Purpose of the Study

The purpose of this study was to determine if 6 weeks of inspiratory muscle training improved trained cyclists' 20 km time trial performance at a simulated altitude of 2500 m (8000 ft).

Delimitations

1. Healthy trained male endurance cyclists ($\dot{V}O_{2max} \geq 55$ ml * kg^{-1} * min^{-1}) were recruited for this study.
2. Subjects were recruited from Indiana University via flyers, emails and contact with Little 500 teams.

3. Data collection occurred in a laboratory setting where temperature, humidity and barometric pressure are relatively static.
4. Performance was a fixed 20 km distance cycle time trial.
5. A familiarization was performed to allow the subjects to get accustomed to the equipment, procedure and breathing hypoxic gas.
6. Subjects were asked to wear their preferred cycling clothing and continued to wear the same clothing for each day of testing.
7. Subjects were told they could bring their own cycling shoes and clips and continued to use the same ones for the duration of the study.
8. Subjects were asked to complete a training log citing intensity and duration of each training session.
9. Subjects trained the inspiratory muscles for 6 weeks between the pre- and post- time trial.
10. Inspiratory muscle training was considered successful if the subjects saw an increase in their MIP as a surrogate marker for respiratory muscle strength.
11. The adaptations to inspiratory muscle training were considered successful if the subjects experienced a significant improvement in their 20 km time trial performance in hypoxia.
12. Subjects reported to the laboratory hydrated and 3 hours post-prandial and at least 24 hours after any strenuous exercise.
13. The subjects did not consume alcohol within 24 hours prior to exercise and did not consume caffeine within 6 hours prior to exercise.
14. The subjects performed the testing at the same time of day.

Limitations

1. Subjects were selectively chosen to be highly trained cyclists.

2. Only male subjects were used for the experiment.
3. Subjects were asked to report to the laboratory 3 hours post-prandial, but there was no way to know if they followed those directions.
4. Subjects were asked to refrain from strenuous exercise at least 24 hours prior to entering the laboratory, but there was no way to tell if they followed that direction.
5. Subjects were asked to keep a training log, but there was no way to know if that is accurate.
6. Subjects filled out a questionnaire about previous injury and about training hours per week, but there was no way to know if they were being honest.
7. Subjects were asked to perform to the best of their abilities for every test, but there was no way to tell if they were trying their hardest the whole time.
8. Athletes were asked to breathe through a mask while completing the time trial in the laboratory which feels different than breathing without the mask.
9. The findings in this study can only be attributed to the simulated altitude that the test takes place.
10. We assumed that simulated altitude through breathing hypoxic gas elicits similar effects to actual altitude.
11. Subjects were taught how to properly use the inspiratory muscle trainers, but there was no way to tell if they used them correctly.
12. There was no way of knowing if subjects consumed alcohol within 24 hours of testing or if they consumed caffeine within 6 hours of testing.

Assumptions

1. Subjects accurately represented highly trained cyclists.

2. Subjects followed the guidelines that we provided them for training.
3. The equipment used in the laboratory was reliable.
4. The subjects arrived to the laboratory hydrated, 3 hours post-prandial and have not consumed alcohol or caffeine 24 and 6 hours prior to exercise, respectively.
5. The values received for each test accurately represented the subject's best effort.
6. Motivation to exercise did not change between trials.
7. The familiarization test eliminated the learning curve prior to actual testing.
8. The apparatus used to measure metabolics did not alter the way the subject breathed.
9. Simulated altitude correlated with actual altitude.
10. Subjects are used to performing time trials.

Hypotheses

The study tested the following hypotheses:

1. Inspiratory muscle training will improve highly trained cyclist's 20k time trial performance in hypoxia.
2. Inspiratory muscle training will increase the strength of the inspiratory muscles measured through MIP.
3. Inspiratory muscle training will increase ventilation, breathing frequency and oxygen uptake during the 20k time trial in hypoxia.
4. Inspiratory muscle training will have no effect on lung diffusion capacity.
5. Inspiratory muscle training will have no effect on residual volume or any other static lung volumes.
6. Inspiratory muscle training will decrease dyspnea during the time trial.

7. Inspiratory muscle training will have no effect on RPE during the time trial.

Definition of Terms

Arterial blood oxyhemoglobin saturation (SpO_2) – The percent of hemoglobin that is saturated with oxygen (Turner, 2013).

Diffusing Capacity of the Lung (DLCO) – the diffusing capacity of the lung is measured with carbon monoxide (CO) because CO is limited solely by diffusion. It therefore is the best choice to determine the diffusing capacity of the lung.

Dyspnea – the clinical term for shortness of breath. It is another way to perceive exercise (Eakin, 1995).

Fixed Distance Time Trial (TT) – a set distance that the subjects ride as quickly as possible while control their speed. This experiment with have a 20 kilometer TT.

Frequency of Breathing (f_B) – the number of breaths taken per unit time.

Forced Expiratory Volume of One Second (FEV_1) – The volume of gas that can be exhaled over 1 second from a full inspiration (West, 2012).

Forced Expiratory Flow 25 to 75% (FEF_{25-75}) – the average flow rate measured during the middle 25-75% of expiration (West, 2012).

Fraction of Inspired Oxygen (F_iO_2) – The percent of oxygen in a given environment.

Heart Rate (HR) – the amount of times your heart beats per unit time.

Hypoxia – an environment with a fraction of oxygen less than .2093.

Maximal Flow Volume Loops (MFVL) – The maximum amount of pressure than can be produced through expiration and inspiration (West, 2012)

Maximal Expiratory Pressure (MEP) – The maximal amount of pressure that can be produced during expiration when starting the expiration from total lung capacity (West, 2012).

Maximal Inspiratory Pressure (MIP) – The maximal amount of pressure that can be produced during an inspiration when starting from your residual volume (West, 2012).

Maximal Oxygen Consumption ($\dot{V}O_{2max}$) – maximal volume (L) of oxygen that the body can consume in one minute.

Maximum voluntary Ventilation (MVV) – the maximum volume of air that can be inspired and expired in 6 seconds (Downey, 2006).

Normoxia – an environment with a fractional oxygen content of .2093.

Oxygen Consumption ($\dot{V}O_2$) – the amount of oxygen that the body consumes measured in liters of oxygen per minute.

Rated Perceived Exhaustion (RPE) – a scale that rates from 1 to 20 with 1 being the easiest and 20 your exercise limit that is used to measure exertion in subjects. The subject indicates, by pointing to a number, how exhausting the current exercise is (Borg, 1982).

Residual Volume (RV) – the volume of gas remaining in the lung following maximal expiration (West, 2012).

Respiratory Exchange Ratio (RER) – the ratio between dietary fat and dietary carbohydrates being utilized during exercise (Goedecke, 2000).

Time to Exhaustion Test (TTE) – a fixed workload test where the subjects attempt to maintain a fixed workload for as long as they can. When they can no longer continue at the necessary workload the test is over.

Volume of Carbon Dioxide Expired ($\dot{V}CO_2$) – this is the volume of carbon dioxide that is produced by the body and expired through ventilation in liters per minute (West, 2012).

Ventilation ($\dot{V}\dot{V}E$) – the volume of air that is exhaled and inhaled. It is measured in volume per unit time (West, 2012).

Chapter II: Literature Review

Work of Breathing

Work of breathing is the oxygen demand of the respiratory muscles. Until about 25 years ago it was believed that the work of breathing stayed relatively constant and it did not have an effect on exercise. The respiratory muscles were thought to be non-fatiguing muscles, similar to cardiac muscles. In 1992, Aaron et al. (1) performed a study that indicated that in a normoxic environment the inspiratory muscles consume up to 10 to 15 percent of total body oxygen. Their data indicated that oxygen demand increased proportionally to the increase in ventilation and work throughout exercise (1). It was still believed that the inspiratory muscles did not fatigue so that increase in work of breathing would not hinder the duration of exercise.

Metaboreflex

As cardiac output increases during exercise the blood flow distribution is not equal throughout the body. Blood is shunted away from areas that are deemed less important or non-vital is shunted to areas that are of greater need. There seems to be a hierarchy within the body for blood supply which starts with the brain at the top and moves down to other organs and muscles that the body which are vital for survival.

Harms et al. (15) performed a study examining blood flow distribution during high intensity cycling with ventilatory assistance, ventilatory resistance or normal breathing. The purpose of the study was to determine how ventilatory assistance and resistance affect work of breathing (W_B) and if changing work of breathing has an effect on blood flow distribution. During the study the subjects cycled at a constant power output. The W_B decreased by 36.7 ±

26.6% with ventilatory assistance compared to the control and increased by 128.1 ± 25.2% during ventilatory resistance compared to the control. As W_B increased, the body prioritized the oxygen demand of the respiratory muscles over the leg muscles, by shunting blood away from the leg muscles and to the respiratory muscles through an increase in leg vascular resistance which decreased the percentage of total $\dot{V}O_2$ that was taken up by the leg muscles (15).

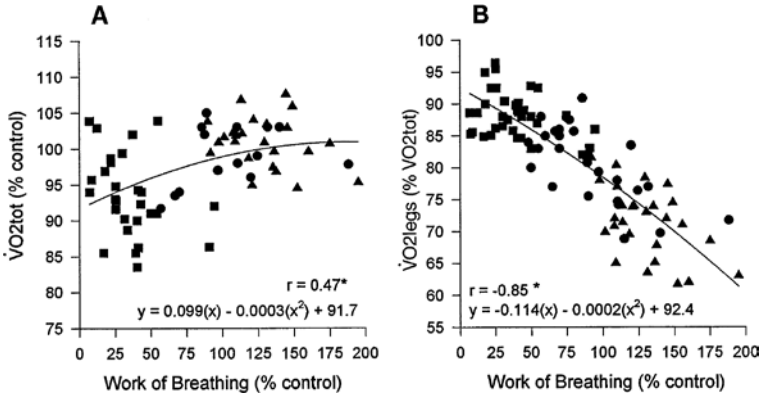

Figure 1: W_B compared to total body $\dot{V}O_2$ and $\dot{V}O_2$ of the legs (15)

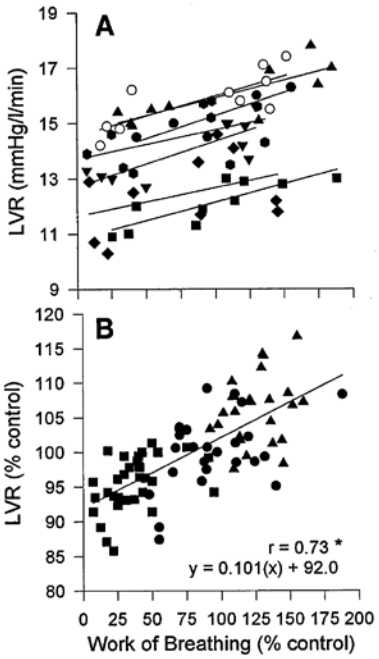

Figure 2: Working of breathing compared to Leg Vascular Resistance (15)

During ventilatory assistance the subjects experienced a decrease in total body $\dot{V}O_2$, compared to the control, even though they were still cycling at the same workload (15). This research indicates that these changes in $\dot{V}O_2$ are directly related to the change in W_B. The power output of the legs for the ventilatory resistance group did not change throughout the study, but they increased their total body $\dot{V}O_2$ and decreased $\dot{V}O_{2legs}$ as a percentage of total body $\dot{V}O_2$. This indicated that the increased $\dot{V}O_2$ was a result of the increase in W_B and the excess oxygen was consumed by the respiratory muscles. Through sympathetic neural drive the body was able to prioritize the respiratory muscles over the working muscles by shunting blood away from the legs and to the respiratory muscles (15).

This decline in percentage of total body $\dot{V}O_2$ to the working muscles during exercise could be detrimental to exercise. In 2000, Harms et al. (13) performed another study on a time to either respiratory unloading, loading or normal breathing during a TTE test. Performing a TTE with respiratory muscle unloading significantly increased cycling duration compared to the control and the ventilatory loading subjects. They experienced a decline in $\dot{V}O_2$, breathing frequency, RPE and dyspnea when compared to the ventilatory resistance group. They increased their ventilation and tidal volume compared to the ventilatory loaded subjects. All of these adaptations are beneficial to exercise, but the problem is that during competition you are unable to compete while using ventilatory assistance. They did not examine $\dot{V}O_{2leg}$, but based on the previous research (15) the changes in $\dot{V}O_2$ were related to the changes in W_B during exercise and the differences in TTE were caused by the differences in W_B between the groups. There was an inverse relationship between W_B and blood flow to the working muscles to the point where the working muscles could no longer be supplied with an adequate supply of oxygen for the given

workload. If there was a way to decrease work of breathing through training it would be beneficial to exercise (6).

Inspiratory Muscle Training

Inspiratory muscle training (IMT) was originally used in the medical field for patients suffering from COPD, heart failure and other various lung problems (6). The objective was to strengthen their inspiratory muscles and decrease the rate of fatigue. The gains from IMT increased linearly until about weeks 4-6 when the inspiratory muscle strength plateaus (8, 20, 26, 34, 44).

There are different ways to perform IMT and not all of them have produced beneficial results. One type of IMT is voluntary isocapnic hyperpnea (VIH) where a subject enters the laboratory 3-5 times per week and breathes for up to 30 minutes at 60-90% of their maximum voluntary ventilation (MVV) (27). During the 30 minutes of ventilation subjects are seated in an upright position allowing the body to rest while the ventilatory muscles mimic high intensity exercise allowing the researchers to isolate only the inspiratory muscles during high intensity exercise. VIH has been shown to increase TTE tests, maximum sustainable ventilatory capacity, vital capacity and MVV, but it does not significantly increase maximal respiratory pressure. The down side with VIH is that it is time consuming and difficult to perform because the subject has to come into the laboratory for every training bout (27).

Inspiratory pressure threshold loading (IPTL) is the most common type of IMT used in research (27). During IPTL an individual is required to produce enough negative force to overcome a threshold load to initiate inspiration. The subjects are required to exhale to residual volume (RV), place their mouth around the training device and inspire maximally against the

pressure resistance to total lung capacity (TLC) in order to complete one repetition. The training protocol is to perform 30-40 repetitions of this maneuver twice a day for 5-7 days a week. In about six weeks of training it has been shown to increase a subject's maximal velocity, maximal rate of shortening, maximal power output, the endurance of their inspiratory muscles and cause diaphragm hypertrophy. The protocol is convenient for subjects to perform because the training can be performed away from the laboratory and without experimenter supervision (8, 27). IPTL has had mixed results during TTE studies, but has had better results during fixed distance time trial studies (20, 34, 35, 38, 41).

Inspiratory flow resistive loading (IFRL) requires individuals to inspire through a 2 mm diameter orifice which provides the resistive load(27). The Test of Incremental Respiratory Endurance (TIRE) technique is used to train the subjects. The TIRE technique uses a 2 mm diameter orifice to produce the resistive load and software that is run through a computer that attaches to an electronic manometer in the device. The subjects are required to perform the training protocol, in which they perform several maximal inspiratory efforts to create a baseline value, then they must inspire 80% of the maximal effort and volume which is called the SMIP and the subject has to achieve this mark 6 times with a break between each effort (29). Completing 6 maximal efforts is considered finishing a stage of training. Once they finish the first stage they receive 1 minute of rest followed by 6 more maximal efforts against 80% resistance. Each time they complete a stage their recovery time decreases by 15 seconds. If they cannot complete a stage then their training bout is complete. Performing the TIRE technique 3 times a week has been shown to increase their inspiratory muscle strength from 18 to 54% and have a small, but statically significant increase in their total lung capacity (27, 29, 40).

Using the TIRE protocol allows subjects to increase the difficulty of their training as their inspiratory muscle strength increases without coming into the laboratory and having the researcher increase the resistance. During IPTL subjects are either unable to increase the resistance or are required to enter the lab periodically to have the resistance adjusted.

IMT on Metaboreflex

Inspiratory muscle training is designed to decrease the W_B which attenuates the metaboreflex response of the inspiratory muscles resulting in increased blood flow to the working muscles allowing the athlete to continue exercising at the same intensity. Until recently, the research was only able to indicate that IMT attenuated muscle fatigue during exercise (8, 11, 14, 34).

The body responds to exercise by increasing heart rate and mean arterial pressures. These are controlled by the sympathetic nervous system and are used to regulate blood flow to the specific areas of the body. After 5 weeks of IMT subjects experienced an attenuated response from their heart rate and mean arterial pressure as compared to their pre-test and the control group during a eucapnic resistive breathing task (44).

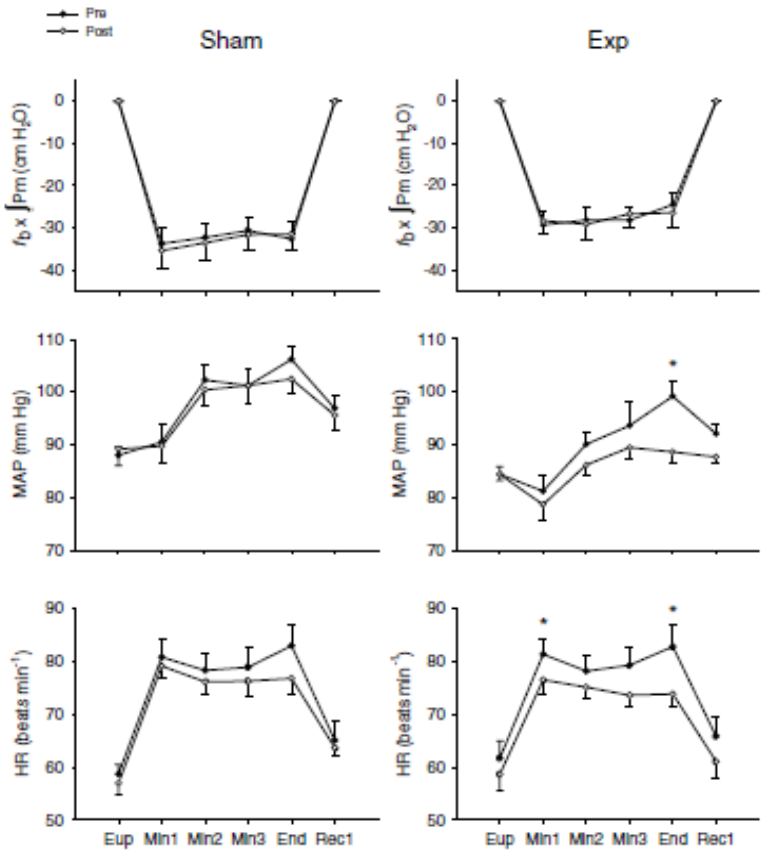

Figure 3: Indicates the attenuation of MAP and HR during exercise for subjects who performed IMT compared to the Sham group(44)

A decrease in mean arterial pressure and heart rate during a eucapnic resistive breathing task indicates that the W_B of the inspiratory muscles decreased allowing the inspiratory muscles to generate the same amount of work with less blood flow (44). This would be advantageous to athletes performing high intensity or long duration aerobic exercise where the working muscles have an increased oxygen demand. This will allow the body to supply the working muscles with a greater quantity of oxygen compared to individuals who have a greater W_B and should increase performance.

IMT and Performance

Inspiratory muscle training has been shown to improve performance during cycling and running time trials (km) (10, 20, 22, 34, 38), but has shown mixed results for TTE tests (8, 42). After IMT the subjects experienced an attenuated decline in MIP after testing, indicating a decrease in inspiratory muscle fatigue (8) and decreased W_B throughout exercise allowing the sympathetic nervous system to lessen the metaboreflex of the inspiratory muscles.

In a study performed by Romer et al. (34) subjects performed 6 weeks of IMT and experienced an increased MIP, maximal inspiratory flow, maximal inspiratory muscle power, optimal pressure and increased maximal rate of pressure development. They also experienced a decrease rate of perceived exhaustion in the respiratory and peripheral muscles (RPE). These physiological and psychological improvements led to a statistically significant improvement in time trial performance of 65 ± 30 seconds and 114 ± 38 seconds for a 20 and 40 km time trial, respectively, when compared to the pre-test. This represented a 3.8 ± 1.7% and 4.6 ± 1.9% improvement during a 20 and 40 km time trial, respectively (34). The majority of the time improvement occurred during the second half of each time trial. Indicating that as the trial progressed that the expected increase in W_B was attenuated by the IMT. Based on these results, IMT attenuates the rate of inspiratory muscle fatigue during endurance exercise which agrees with the results from Witt et al. (44) that had a significantly lower mean arterial pressure post-IMT compared to pre-IMT.

Performance Testing

Time trial and time to exhaustion tests are both considered performance tests, but they do not have the same level of reliability (18, 28). Originally, it was thought that having a subject

exercise at a fixed submaximal workload until exhaustion was the best way to determine performance, but now we know that this is not true. A time to exhaustion test has a significantly greater variance (26.6%) than a fixed distance time trial (3.35%) (18). This variance could be caused by a multitude of reasons, but one of the most likely reasons is motivation (43). A time to exhaustion test is grueling because the subject has to be able to continue until they physically cannot go any farther which brings motivation, mood and experience into play. Some subjects will not want to force their body to go through the necessary pain or they may think that they have reached their limit when, in fact, they have not. If the subjects are not properly familiarized with a time to exhaustion test then they will experience a learning curve (28). This creates a learning effect where it is necessary to do multiple familiarization trials prior to testing. This creates a greater variance between tests compared to a fixed distance time trial.

A study performed by McLellan et al., (28) had their subjects perform 5 TTE tests to analyze the variance from test to test. The subjects performed significantly better during trial 3 than trial 1 and 5 indicating that there was a learning curve between trial 1 and 3, but the difference between trial 3 and 5 was most likely due to motivation. Trial 4 was not statistically significant from trials 3 or 5, but it did fall between the two indicating that the subjects' motivation was decreasing after they reached, what they believed to be, their peak performance. There was also no statistical difference between trial 1 and 5 indicating that the subjects regressed back to their pre-learning ability (28). With this variance throughout five tests it would be difficult to know if you were getting accurate results.

Time trial tests have shown to have high reliability and validity due to the subject knowing that there is a set end point (18). The subject is allowed to control the velocity at which they ride throughout the time trial allowing them to be more applicable for competition than TTE

tests. During TTE tests subjects maintain a fixed velocity throughout the duration of the test, but during competitions cyclists' velocity varies due to pacing strategies (39). During competitions athletes pace themselves by fluctuating their power output throughout the race allowing them to complete the race with an increase in power known as an end spurt. During a time trial subjects are able to fluctuate their power output to mimic the pacing strategy that would be used during competition (9). Unlike a TTE test subjects only need to perform one familiarization test to control for the learning effect (18).

Work of Breathing in Hypoxia

The body attempts to offset the decreased amount of oxygen that is consumed by each breath in hypoxic environments by increasing the rate of ventilation. A reduction in arterial oxygen saturation triggers chemoreceptors in the body to stimulate increased ventilation. It was originally believed that because of the drop in air pressure in hypobaric hypoxia subjects would experience a decrease in W_B, but research now indicates that W_B is greater in hypobaric hypoxia than in normoxia (7). There are a few different reasons as to why this occurs. During exercise in hypoxia the diaphragm has to increase its work output compared to normoxia. The diaphragm produces 20-30% more work during exercise in hypoxia than normoxia because of the increase in breathing frequency and an increase in inspiratory resistive flow rate of 13% during submaximal exercise. At maximal exercise subjects experienced similar levels of minute ventilation and ventilatory work. The W_B is also increased through greater percentages of flow limitation being reached in hypoxia which has been associated with increased oxygen demand of the inspiratory muscles (1, 2).

In hypoxia the arterial oxygenation in the body is reduced compared to normoxia causing a reduction in the quantity of oxygen sent to the inspiratory muscles which increases the rate of fatigue and leads to an increased W_B. In response to the drop in arterial oxygen saturation the diaphragm increases vasodilation of its arteries. In ponies it has been shown that during maximal exercise in hypoxia the oxygen demand of the diaphragm was the same or slightly less than the oxygen supply sent to the working muscles (25). It is still unknown if these same adaptions occur in humans during intense exercise, but, during rest and submaximal exercise, hypoxia stimulates vasodilation. In hypoxia the inspiratory muscles increase their use of their glycogen stores and increase lactate production compared to normoxia which indicates a greater usage of anaerobic pathways during exercise leading to an increased rate of fatigue (2).

A study performed by Loeppky et al. (23) had subjects stay in an environmental chamber for 10 hours on three separate occasions and environments, hypobaric hypoxic, normobaric hypoxic and normoxic hypobaria. During the first hour in the chamber the ventilatory response for the participants was not significantly different between normobaric hypoxia and hypobaric hypoxia, but as the testing continued the ventilation was significantly greater at 3, 6 and 9 hours in normobaric hypoxia compared to hypobaric hypoxia. This significant increase in ventilation at 3, 6 and 9 hours will not affect this study because the 20 km time trial will take highly trained athletes less than an hour to complete. The subjects will have a similar ventilatory response to hypobaric hypoxia while they exercise in normobaric hypoxia (23).

IMT and Hypoxia

Currently, there is a dearth of research on IMT and hypoxia. The small sample of research indicates that IMT is beneficial for athletes competing in hypoxia. IMT has been shown

to attenuate the decline that occurs in arterial saturation as hypoxia increases (24). Subjects performed 4 weeks of IMT prior to having their resting arterial saturation taken at sea level, 1400 m, 4880 m and 5550 m. There was a significant difference between the IMT and control groups for resting arterial saturation at 4880 and 5550 m, but not at 1440 m or at sea level (24). This indicates that there must be a critical point where IMT is able to attenuate the effects of hypoxia on arterial saturation at rest, but this critical point seems to be at a greater elevation for rest than it is for exercise.

A study performed by Downey et al., (8) examined the effects of IMT on a treadmill time to exhaustion test at a simulated altitude of 3000 m (14% O_2). There was no difference in resting arterial saturation between the two groups which indicates that the critical point is at an altitude of greater than 3000 m, but that was not the main objective of this study. They examined the effect of IMT on performance in hypoxia by using a treadmill time to exhaustion test set at 85% of their $\dot{V}O_{2max}$ in normoxia. They also examined the effect of IMT on a multitude of physiological variables. Inspiratory muscle training caused significant hypertrophy in the diaphragm which resulted in an increase in MIP and end-inspiratory pressure. During the treadmill test to exhaustion the IMT group experienced a significant decrease in inspiratory muscle fatigue during exercise in both normoxia and hypoxia as measured by performing a maximal voluntary ventilation test pre- and post-testing.

During the TTE test IMT group experienced a significantly lower $\dot{V}O_2$ (8-12%), ventilation (25 ± 3%) and cardiac output (14 ± 2%) and a significantly greater arterial saturation (4 ± 1) and increased lung diffusing capacity (22 ± 3%). They also reported a lower RPE and dyspnea rating post IMT compared to the control. Based on these results one would expect there to be an improvement in TTE performance, but there was no statistical difference between the

two groups. The decrease in $\dot{V}O_2$, ventilation and cardiac output indicate that there was decreased blood flow to the inspiratory muscles since the subjects were able to perform the same workload. The TTE test on the treadmill was set at 85% of their $\dot{V}O_{2max}$, which was measured in normoxia making the workload even closer to $\dot{V}O_{2max}$ in hypoxia. The test in normoxia lasted 22.0 ± 1.7 minutes (control) and 18.1 ± 1.9 minutes (IMT) which were not significantly different from each other or from their pre-test. There was no change in performance possibly because they used TTE, which has low reliability and validity and mixed results with IMT. It could also have not been significant because the test duration was not long enough to see improvement (8). There have also been mixed results with IMT and running, especially in TTE tests.

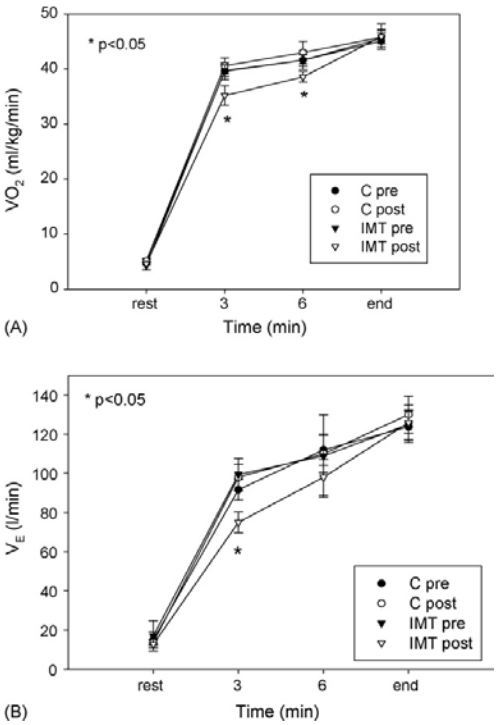

Figure 4: Shows that subjects who perform IMT decrease their ventilation and $\dot{V}O_2$ are decreased

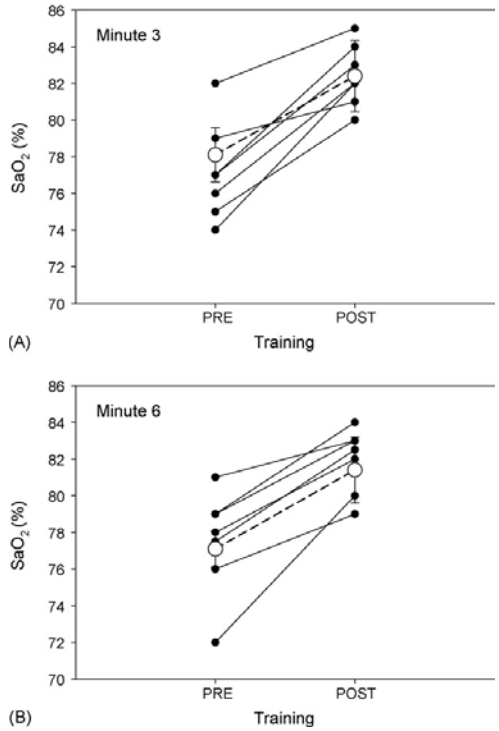

Figure 5: Shows the increase in SaO_2 from pre- to post-IMT

During the TTE in hypoxia the tests lasted 9.7 ± 1.5 min and 7.4 ± 1.2 min for the control and IMT, respectively. There was no statistically significant difference between or within the

groups for duration. The duration of this test was less than half the duration of the TTE in normoxia. Once again the reason for this not being significantly different could be because the duration was too short, they used a TTE test instead of a TT and the subjects performed the test while running instead of cycling. It is most likely a combination of the three that limited the effect of the IMT on the TTE. Based on these results and physiological adaptations that IMT causes we believe that performance should improve (8). That is why during this study we will be using a 20km TT instead of TTE and cycling instead of running. We expect to see the same physiological adaptions, but also see an increase in TT performance.

Chapter III: Methods

The purpose of this study was to determine if 6 weeks of inspiratory muscle training improves trained cyclists' 20 km time trial performance at a simulated altitude of 2500 m (8000 ft).

Subjects

Thirty one male subjects between the ages of 18 and 25 were recruited for this study. Potential subjects were recruited through email or phone calls directly to them or their coach, as well as flyers placed around Bloomington, IN. The subjects were healthy non-smokers with no history of lower limb injury in the past year. They all obtained a maximal oxygen consumption ($\dot{V}O_{2max}$) of greater than 55 ml * min^{-1} * kg^{-1} and were participating in a training regimen to qualify for the study. They were tested at the Indiana University Human Performance Laboratories and were approved by Institutional Review Board for the protection of human subjects. All subjects filled out a medical questionnaire and completed an Indiana University Internal Review Board approved informed consent before any exercise testing was performed.

Study Design

Subjects appeared in the laboratory on four separate occasions. Each occasion the subject arrived at least 3 hours post-prandial, 24 hours post-alcohol consumption, 6 hours post-caffeine consumption and was well hydrated. The initial visit was used to identify which subjects qualified for the study. Immediately upon entering the Indiana University Human Performance laboratory the subjects filed out a medical questionnaire and an informed consent form. After the subjects passed that portion of the qualification, they performed an incremental $\dot{V}O_{2max}$

test(3) and were not allowed to continue in the study if they did not achieve a $\dot{V}O_{2max}$ of at least 55 ml * min^{-1} * kg^{-1}.

The second visit was at least 48 hours after the first visit and was used as a familiarization visit to prevent a learning effect. The subjects arrived to the laboratory as if it were a real test day. They arrived in their cycling gear and were encouraged to bring their own toe clips for the cycle ergometer (Velotron, RacerMate Inc., Seattle, WA). They continued to wear these same clothes and bring the same toe clips for the duration of the study. Upon entering the laboratory their height and weight were taken and then they proceeded to perform a familiarization for maximal flow volume loops (MFVL), static lung volumes (residual volume), lung diffusing capacity (DLCO), maximal inspiratory pressure (MIP) and maximal expiratory pressure (MEP). Following the lung function tests the subjects performed a 20k time trial on a Velotron while breathing hypoxic gas (F_IO_2 = 16.1%). Immediately upon completion of the time trial, the subjects performed a MFVL and MIP test. This same protocol was followed for day 3 and day 4 of testing, separated by a six week IMT or sham training period. Days 1, 2, and 3 of testing were separated by at least 48 hours.

Inspiratory Muscle Training

Subjects were pair matched based on pre-exercise values of MIP and randomly placed into either the control (sham) or the IMT group. They were blinded to which group they were placed in. Subjects in each group were instructed on how to use their inspiratory muscle trainer (PrO2, PrO2 Health, Inc., Smithfield, Rhode Island) which uses flow resistive loading. The device, which is a pressure manometer with a 2mm orifice which provides the resistance, is connected to an app on the subject's phone or iPad through blue tooth. The app is designed to

run the “Test of Incremental Respiratory Endurance” (TIRE) regimen (29). To start the program the subjects perform several maximal inspirations where they initially exhale to RV and then inspire maximally to total lung capacity (TLC). This is used as the baseline and recorded as their sustained maximum inspiratory pressure (SMIP). The program requires them to reach 80 or 30% of their SMIP depending if they are in the IMT or Sham group, respectively. Previous research has shown that having the subjects achieve 30% of their SMIP, while performing the TIRE protocol, does not elicit improvements in inspiratory muscle strength (29). The TIRE protocol consists of 6 levels with each level being made up of 6 breathes with a varying amount of time between each breath. The duration between each subsequent level decreases, but the percent of SMIP needed to continue remains the same.

Level	Recovery Time (seconds)
A	40
B	30
C	20
D	15
E	10
F	5

They continue the protocol until they either complete all 6 levels or fail on a breath two times in a row (30). This training is repeated three times per week for 6 weeks. Compliance was monitored by experimenters throughout the 6 weeks by checking each subject’s results using their login information.

Measurements

Pulmonary Function:

MFVLs were used to determine vital capacity (VC), 1-second forced expiratory volume (FEV_1), and the mean forced expiratory flow between 25% and 75% of forced vital capacity ($FEF_{25-75\%}$) (31). The subjects also underwent residual volume (RV), and DLCO tests which were performed using the metabolic cart (V_{max} Encore Metabolic Cart, CareFusion Corporation, San Diego, CA) in the Indiana University Human Performance Laboratory. These tests were performed following the guidelines provided by the 2005 update of the Standard of Spirometry by the American Thoracic Society (ATS) (31). Each test was performed in triplicate unless the values were greater than a 10% difference in which case the test was performed until three trials were within the acceptable range of 10 percent. The average of the values was recorded. The order by which the tests were performed was:

1. Maximal flow volume loops
2. Static lung volumes (5 minutes between each test)
3. DLCO (5 minutes between each test)
4. MIP
5. MEP

Maximal Inspiratory and Expiratory Pressure

The subject's MIP was determined by having a small leak within the closed mouth-piece (#2700 and #9060, Hans Rudolph, Shawnee, KS) system that allowed a maximum flow of 50 ml * s^{-1} to prevent glottis closure during the maneuvers. The mouth piece was connected, via a side port, to the metabolic cart which was calibrated regularly using a three liter syringe. Subjects

performed a MIP by exhaling to RV, then maximally inhaling to their TLC. They repeated this test until three of the trials were within 10 percent and the average of the trials was recorded.

The MEP was performed using the same equipment. The only difference was that the subjects began the test at TLC and forcefully exhaled to RV. This test was repeated until three of the trials were within 10 percent and the average of the trails.
was recorded.

Arterial Oxygen Saturation (SaO_2) Measurement:

Arterial oxygen saturation was measured indirectly through pulse oximetry. The pulse oximeter (Nellcor N-395 Pulse Oximeter, Medtronic, Minneapolis, MN) was calibrated periodically following the directions in the manufacturer's manual. The forehead sensor was replaced was necessary.

Progressive Maximal Exercise Test:

$\dot{V}O_{2max}$ was determined through a progressive cycle ergometer test and was performed in normoxia. The subjects performed the $\dot{V}O_{2max}$ test on a computer controlled electronically braked cycle ergometer (Dynafit Pro, RacerMate Inc., Seattle, WA). The subjects were allowed to warm up for five minutes at 100 watts (W) on the Velotron cycle ergometer. They were encouraged to cycle around 90RPMs for the $\dot{V}O_{2max}$. After the warm-up the subjects rested for five minutes on the Velotron. After the rest period the test began. The Velotron was loaded with 100 Watts of resistance and increased by 25W each minute until the subject could not maintain the desired workload (Weavil, 2012). $\dot{V}O_{2max}$ was considered achieved if two of the following criteria were achieved:

1. Heart rate $\geq$ 90% of age predicted max
2. Respiratory equivalent ratio (RER) $\geq$ 1.10
3. A plateau ($\leq$150 ml change) in $\dot{V}O_2$ with an increase in workload

Hypoxic Inspirate Delivery System:

During the time trial, subjects breathed from two balloon reservoirs (approximately 850L each) with hypoxic gas produced from a nitrogen generator (CAT-12 model, Colorado Altitude Training, Boulder, CO). The generator pumped air with an F_IO_2 of 16.1% which with a typical barometric pressure in Bloomington, IN gives an inspired PO_2 of 120 mmHg which is equivalent to an altitude of 2500 m / 8000 ft. While in the balloon, the mixed gas has approximately the same humidity and temperature as room air and care was take to prevent any leaks in the system. Two, two way valves were used to allow the rider to breathe from one bag at a time. This made it possible to refill one of the bags while the subject breathed off of the other bag.

20 km Time Trial:

The subjects arrived at the laboratory at the same time of day for each time trial. They arrived 3 hours post-prandial, at least 24 hours post-alcohol consumption, at least 6 hours post-caffeine consumption and were adequately hydrated. They were unable to consume water during the time trial due to the equipment that was worn. A familiarization and two experimental 20 kilometer (km) time trials were performed by each subject. The objective of the familiarization was to decrease the impact of the novelty of a 20km time trial while breathing hypoxic gas.

Prior to the performing the 20km time trial the subjects were able to adjust their saddle and toe clips; they were allowed to bring their own toe clips and saddle. Prior to exercise, the Velotron was set so that 90 RPMs was equivalent to the wattage the subject produced at 70% of their $\dot{V}O_{2max}$. The subject sat on the bike at rest, while breathing hypoxic gas, for 3 minutes prior to exercise while metabolics were recorded. The subjects were allowed to warm up for 5 minutes at 100W followed by 5 minutes of rest. The investigator counted down from 3 and began the time trial (CompuTrainer, RacerMate Inc., Seattle, WA). During the time trial the subjects were able to control the resistance of the Velotron to mimic gearing up or down during competition. The subjects were allowed to know the distance traveled, but everything else was hidden. Every 4km their rate of perceived exertion (RPE) and dyspnea were collected using the Borg's and a modified Borg's scale, respectively. Metabolics were collected every 4km. IC maneuvers were also completed every 4km for the determination of inspiratory flow limitation. Average power output was analyzed every 4km using WKO+ software (Peaksware LLC, Lafayette, Colorado). The test was completed once the subject reached 20km, and completion time was recorded to the tenth of a second. The post-exercise measures of MIP and MVFL were performed beginning within 60s after the completion of the exercise bout and were completed for all subjects within 5 minutes of completed of the exercise bout.

Ventilatory and Metabolic Measurements:

Ventilation and metabolics were measured continuously through a metabolic cart. The program computed the ventilatory and metabolic data breath by breath which was used to determine the average of the last minute of each 4km segment. The metabolic cart was calibrated by using a 3 L syringe to pull gas over the flow ports in the mouth piece within physiological norms. Subjects wore a facemask (Hans Rudolph #7450V2, Kansas City, MO)

which was attached to a two-way non-rebreathing valve with flow sensors inside of the mouth piece that sent the breath by breath reading to the metabolic cart. The metabolic cart took breath by breath measurements of fractional inspired and expired O_2 and CO_2. Heart rate was measured continuously throughout the time trial using a Polar heart rate monitor and a 4km average was recorded.

Flow-Volume Relationships:

Flow-volume loops were determined prior and post exercise. Flow rates were measured using the metabolic cart and used to determine the subject's MFVL, FEV_1, $FEV_{25-75\%}$ and VC. MFVLs were performed by having the subject inhale to TLC then forcefully exhale to RV and inhale to TLC. Subjects were vigorously encouraged during the MFVL and these values were taken in triplicate pre- and post-exercise.

Training Log

Subjects were required to keep a log of their workouts performed between their pre- and post-test. They recorded their intensity, power output or distance (km), and duration, time, for each workout. They were instructed not to increase their intensity and duration throughout the study. They could fluctuate from day to day, but they could not continually increase their intensity and duration throughout the study. This was closely monitored so that the differences from pre- and post-training were caused by the IMT and not training.

Data Analysis

Data were analyzed using IBM SPSS version 22 statistical software. A Shapiro-Wilk test was used to determine normality in all dependent variables. To test the hypothesis that 6 weeks

of IMT will improve performance during a 20k time trial in hypoxia, a 2x2 split-plot repeated measures ANOVA was used with treatment group (IMT vs. SHAM) as a between subjects independent variable and time (Pre- vs. Post-treatment) as a within subjects independent variable. A priori tests of simple main effects was used to determine significant differences in dependent measures, with a Bonferoni correction used to control Type 2 error rate with multiple comparisons. For all comparisons, an alpha level of 0.05 (one-tailed) was used for significance.

.

Chapter IV: Results

Table 1. Subject Characteristics prior to training

	Control (n = 5)	IMT (n = 8)
Age (years)	21.0 ± 0.8	22.4 ± 0.9
Height (cm)	175.9 ± 2.3	178.5 ± 3.1
Mass (kg)	72.6 ± 1.3	75.4 ± 3.6
Body Fat (%)	12.6 ± 1.4	12.7 ± 1.2
TLC (L) (% predicted)	6.50 ± 0.42 (95%)	7.12 ± 0.48 (104%)
RV (L) (% predicted)	1.47 ± 0.28 (87%)	1.25 ± 0.20 (74%)
FVC (L) (% predicted)	5.17 ± 0.14 (102%)	5.97 ± 0.29 (117%)
FEV_1 (L) (% predicted)	4.34 ± 0.25 (105%)	4.70 ± 0.25 (114%)
$FEF_{25-75\%}$ (L/s) (% predicted)	4.78 ± 0.63 (116%)	4.35 ± 0.37 (106%)
PEF (L/s)	10.86 ± 1.12	10.03 ± 0.62
DLCO (ml/min/mmHg)	35.6 ± 1.6	38.3 ± 3.4
MIP (cm H2O)	143.9 ± 7.8	127.6 ± 13.4
MEP (cm H2O)	140.8 ± 16.4	151.9 ± 15.6
$\dot{V}O_{2max}$ (L/min)	4.46 ± 0.19	4.74 ± 0.37
$\dot{V}O_{2max}$ (ml/kg/min)	61.7 ± 2.0	63.5 ± 3.4

Values are mean ± S.E. No signficant differences between groups (P > 0.05); TLC: total lung capacity; RV: residual volume; FVC: functional vital capacity; FEV_1: forced expiratory volume in 1 second; $FEF_{25-75\%}$; forced expiratory flow during 25-75% of vital capacity; PEF: peak expiratory flow; DLCO: lung diffusing capacity; MIP: maximal inspiratory pressure; MEP: maximal expiratory pressure.

Subject characteristics are shown in table 1. There were no significant differences between the sham and IMT group for age, height, mass and body fat percentage. All resting pulmonary function measures were not significantly different between the sham and IMT group and fell within the normal limits for a healthy individual (32). Maximal oxygen consumption, both absolute and relative, were not significantly different between the two groups. Compliance with the IMT, which was performed 3 times a week for 6 weeks, was not significantly different between the groups (IMT = 86.5 ± 3.2%, Sham = 86.7 ± 4.5%). Subjects continued to train at a similar frequency and intensity during the training as they had in the weeks prior based on their

self-reported training log. There were no significant changes in mass (pre-test 74.3 ± 2.2, post-test 74.4 ± 1.7) or body fat percentage (pre-test 12.7 ± 0.9, post-test 13.1 ± 0.8) during the 6 weeks of training.

3.1 Inspiratory Muscle Strength

Table 2 shows MIP for each group before and after 6 weeks of training. The IMT group significantly improved their MIP when compared to their pre-test and to the sham group. This represents a significant increase in inspiratory muscle strength for the IMT group. MIP in the sham group was not different between pre- and post-training.

Table 2. Inspiratory Muscle Strength

		Pre	Post
MIP (cmH_2O)	IMT (n = 8)	127.6 ± 13.4	159.0 ± 15.3*†
	Control (n = 5)	143.9 ± 7.8	150.9 ± 12.5

Values are mean ± S.E.

* Significantly different from pre-training ($p \leq 0.05$)

† Significantly different from control

3.3 Metabolic, ventilatory and TT results

The increase in inspiratory muscle strength did not have a significant effect on average power (figure 2), but average time (figure 1) to completion of the 20km TT is approaching significance ($p = 0.06$). Table 3 shows each group's average over each 4km segment during the time trial. There were no significant differences in any measure between the groups.

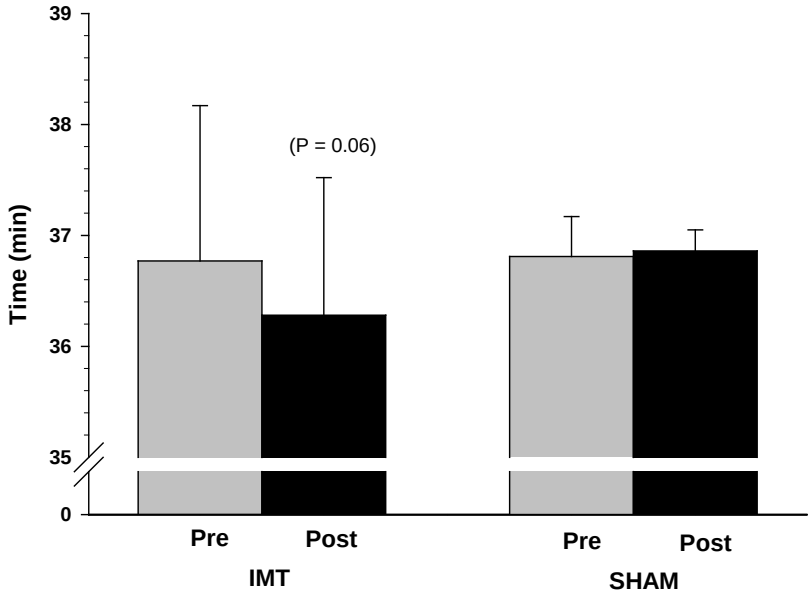

Figure 1. Average time to complete the 20km time trial. Values are mean + SE. * = significantly different from Pre ($p < 0.05$).

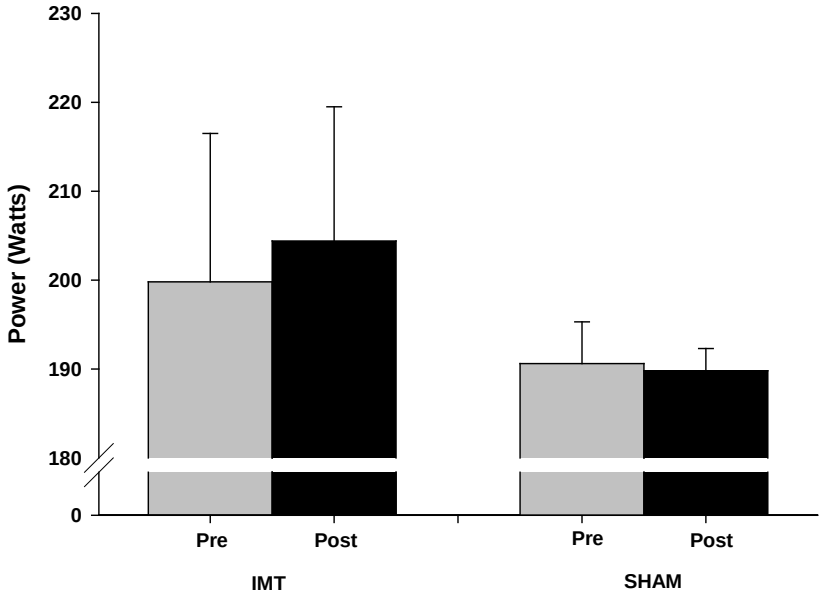

Figure 2. Average power during the 20km time trials. Values are means + SE. * = significantly different from Pre ($p < 0.05$).

Table 3. Time Trial Results

		Pre-train					Post-train				
		4k	8k	12k	16k	20k	4k	8k	12k	16k	20k
Control											
	$\dot{V}O_2$ (L/min)	3.70 ± 0.23	3.66 ± 0.21	3.71 ± 0.24	3.87 ± 0.20	3.97 ± 0.27	3.52 ± 0.22	3.67 ± 0.11	3.68 ± 0.07	3.62 ± 0.15	4.04 ± 0.10
	$\dot{V}O_2$ (ml/kg/min)	50.9 ± 2.4	50.4 ± 2.7	51.2 ± 3.4	53.3 ± 2.8	54.7 ± 3.8	49.1 ± 2.9	51.1 ± 1.4	51.3 ± 1.1	50.5 ± 2.1	56.3 ± 1.2
	$\dot{V}E$ (L/min)	108.9 ± 13.2	105.5 ± 10.6	113.5 ± 12.1	123.3 ± 13.6	138.4 ± 15.6	104.8 ± 10.5	108.0 ± 5.5	110.4 ± 3.8	111.8 ± 8.9	143.5 ± 5.4
	f_R (breaths/min)	46.6 ± 4.7	47.2 ± 4.7	53.7 ± 5.1	57.7 ± 5.6	65.6 ± 5.7	46.5 ± 4.0	51.6 ± 3.4	54.0 ± 2.5	56.7 ± 4.0	66.6 ± 3.5
	SaO2 (%)	89.0 ± 1.2	85.3 ± 3.3	88.0 ± 0.0	90.0 ± 1.0	87.5 ± 0.5	91.5 ± 0.3	90.5 ± 0.9	90.5 ± 0.6	90.3 ± 1.5	88.0 ± 1.1
	HR (bpm)	153.4 ± 4.3	161.3 ± 6.9	165.6 ± 8.8	170.6 ± 8.0	176.4 ± 7.0	151.3 ± 2.0	163.0 ± 3.2	167.1 ± 4.4	167.6 ± 5.9	174.0 ± 4.0
	Dypsnea (Borg 1-10)	4.4 ± 0.7	5.2 ± 0.8	6.2 ± 0.6	7.8 ± 0.4		4.6 ± 0.7	5.4 ± 0.5	6.6 ± 0.4	7.6 ± 0.2	
	RPE (Borg 6-20)	12.6 ± 0.8	12.2 ± 1.5	15.4 ± 0.8	16.4 ± 0.6		13.0 ± 0.7	14.0 ± 0.4	15.6 ± 0.6	16.2 ± 0.7	
	Power (Watts)	175.2 ± 11.1	181.4 ± 5.4	192.8 ± 8.1	196.4 ± 5.8	210.4 ± 7.3	186.6 ± 6.9	193.4 ± 1.7	188.0 ± 4.9	183.2 ± 7.7 *	200.4 ± 4.7
	Duration (min)	7.65 ± 0.22	7.49 ± 0.10	7.32 ± 0.12	7.26 ± 0.08	7.08 ± 0.09	7.46 ± 0.11	7.30 ± 0.02	7.39 ± 0.09	7.49 ± 0.12 *	7.22 ± 0.06
IMT											
	$\dot{V}O_2$ (L/min)	3.43 ± 0.20	3.43 ± 0.22	3.43 ± 0.20	3.39 ± 0.21	3.47 ± 0.20	3.70 ± 0.22*	3.76 ± 0.25*	3.60 ± 0.25	3.59 ± 0.26	4.05 ± 0.24*
	$\dot{V}O_2$ (ml/kg/min)	45.8 ± 2.3	45.8 ± 2.3	46.8 ± 2.1	45.1 ± 2.2	46.6 ± 3.0	48.1 ± 1.9	47.7 ± 1.8	46.8 ± 2.5	46.5 ± 2.5	52.5 ± 2.2
	$\dot{V}E$ (L/min)	100.8 ± 8.0	99.3 ± 6.2	96.5 ± 4.5	95.6 ± 5.5	113.5 ± 6.7	113.4 ± 8.3*	109.8 ± 6.4*	106.2 ± 8.7	107.7 ± 10.3*	137.1 ± 9.7*
	f_R (breaths/min)	39.5 ± 3.8	40.6 ± 2.7	41.6 ± 3.0	41.1 ± 2.3	50.7 ± 2.7	44.9 ± 4.5*	46.1 ± 4.0*	44.1 ± 2.4	44.8 ± 2.0*	53.5 ± 2.7
	SaO2 (%)	88.1 ± 1.3	86.6 ± 1.1	87.4 ± 1.8	87.2 ± 2.0	86.3 ± 2.2	88.1 ± 0.9	87.9 ± 1.0	87.9 ± 1.4	87.4 ± 1.1	87.3 ± 1.1
	HR (bpm)	147.1 ± 4.4	154.8 ± 3.2	154.4 ± 4.0	155.1 ± 5.0	160.8 ± 6.4	151.1 ± 3.7	159.1 ± 4.4	161.3 ± 4.4*	161.8 ± 5.9*	166.9 ± 5.6*
	Dypsnea (Borg 1-10)	4.1 ± 0.5	5.0 ± 0.6	5.3 ± 0.7	5.6 ± 0.8		4.4 ± 0.6	4.9 ± 0.6	5.8 ± 0.6	6.3 ± 0.7*	
	RPE (Borg 6-20)	13.5 ± 0.5	15.3 ± 0.5	15.6 ± 0.6	16.4 ± 0.7		13.6 ± 0.7	14.6 ± 0.6	15.9 ± 0.6	16.6 ± 0.6	
	Power (Watts)	213.9 ± 15.0	198.8 ± 15.8	192.0 ± 15.4	186.8 ± 19.0	209.7 ± 20.9	205.3 ± 19.3	202.9 ± 13.6	197.0 ± 16.3	193.6 ± 18.2*	211.8 ± 17.6
	Duration (min)	7.16 ± 0.24	7.34 ± 0.27	7.44 ± 0.27	7.58 ± 0.36	7.28 ± 0.36	7.05 ± 0.15	7.23 ± 0.21	7.37 ± 0.28	7.45 ± 0.34	7.18 ± 0.29

Values are mean ± S.E.

* Significantly different from pre-training ($p \leq 0.05$)

The absolute oxygen consumption at the 4km, 8km and 20km marks were significantly increased during the post-test compared to the pre-test for the IMT group (figure 3). Ventilation was significantly increased in the IMT group after training during the 4, 8, 16, and 20km segments (figure 4). Subjects in the IMT group also experienced an increase in their heart rate after IMT during the 12, 16 and 20km segments (figure 5). Overall, absolute $\dot{V}O_2$, ventilation and f_B were significantly increased (Table 4) after 6 weeks of IMT.

Table 4. Metabolic and Heart Rate Averages

	IMT		SHAM	
	Pre	Post	Pre	Post
$\dot{V}O_2$ (L/min)	3.41 ± 0.19	3.61 ± 0.21*	3.71 ± 0.18	3.64 ± 0.12
$\dot{V}O_2$ (ml/kg/min)	45.3 ± 2.0	46.9 ± 2.0	51.1 ± 2.3	50.7 ± 1.6
Ventilation (L/min)	99.6 ± 5.5	110.4 ± 6.8*	113.6 ± 10.6	111.0 ± 5.5
f_B (Breaths/min)	41.4 ± 2.8	45.1 ± 2.9*	52.4 ± 4.8	54.3 ± 2.9
Heart Rate (bpm)	151.8 ± 4.4	158.8 ± 4.5	165.4 ± 6.6	164.4 ± 3.3

Values are mean ± S.E

* Significantly different from pre-test ($p < 0.05$)

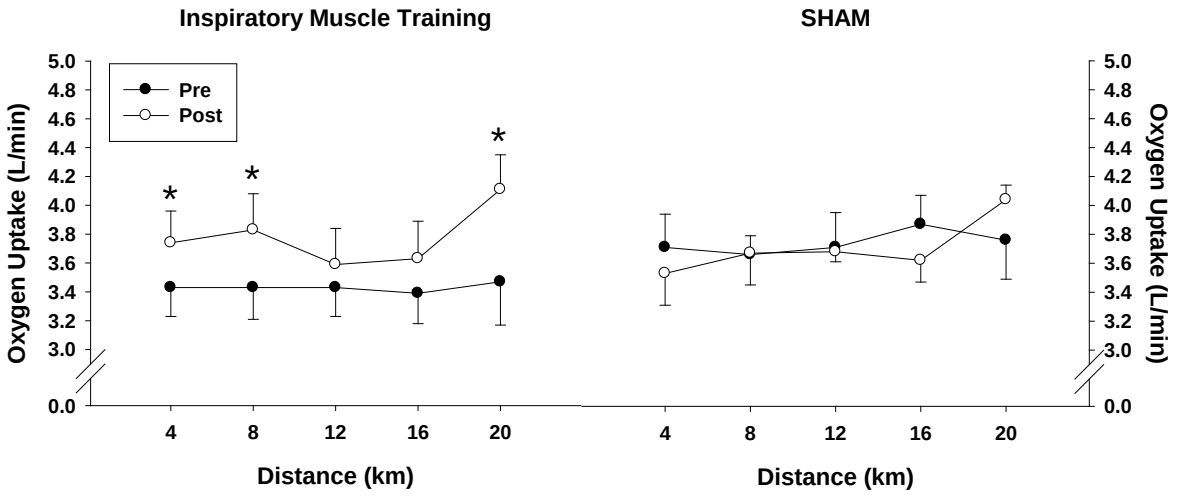

Figure 3. Average $\dot{V}O_2$ (L/min) for each 4km segment. Values are mean + SE. * = significantly different from Pre ($p < 0.05$).

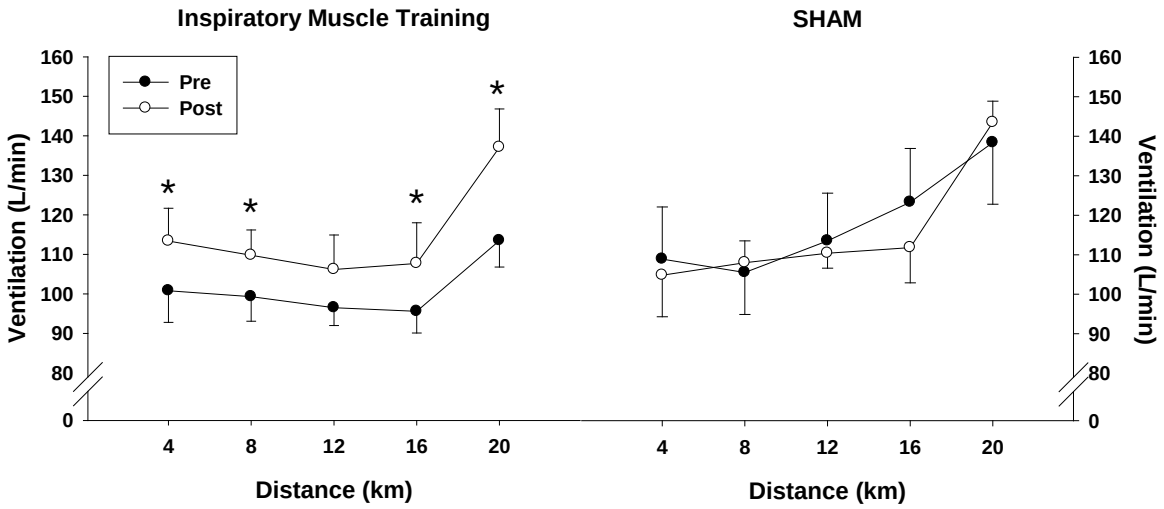

Figure 4. Average V̇E (L/min) for each 4km segment. Values are mean + SE. * = significantly different from Pre ($p < 0.05$).

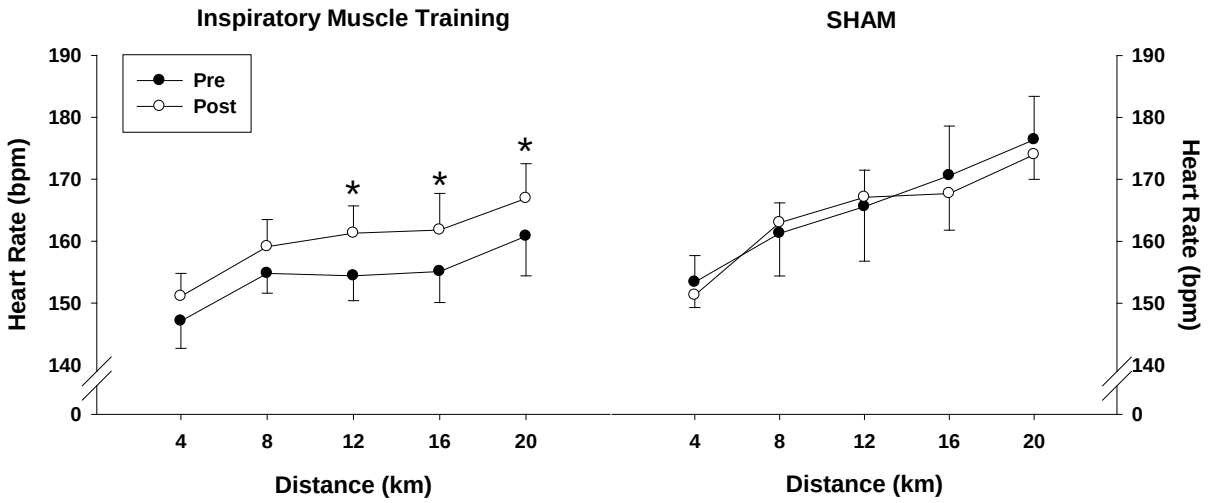

Figure 5. Average HR (bpm) for each 4km segment. Values are mean + SE. * = significantly different from Pre ($p < 0.05$).

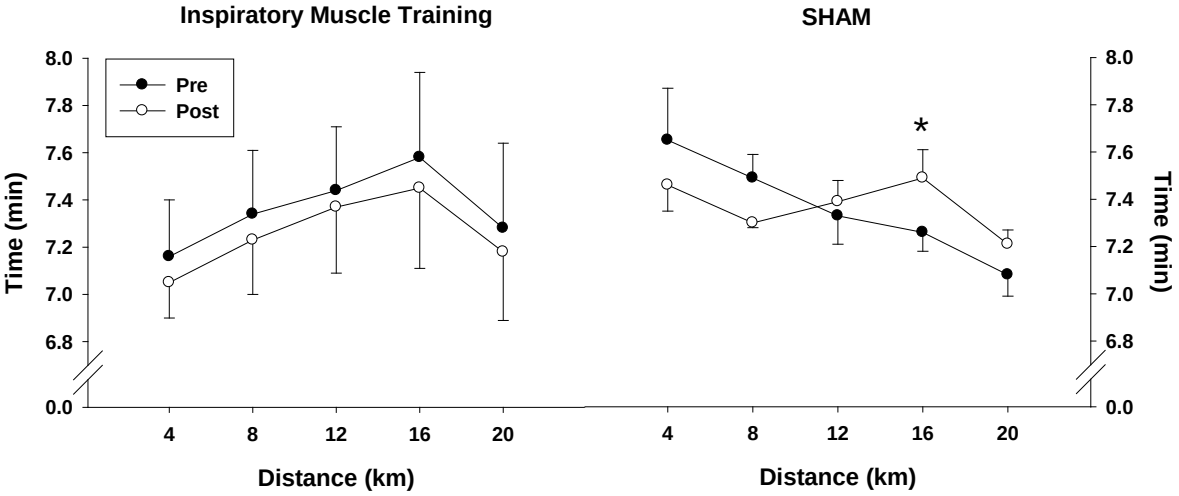

Figure 6. Duration (min) for each 4km segment. Values are mean + SE. * = significantly different from Pre ($p < 0.05$).

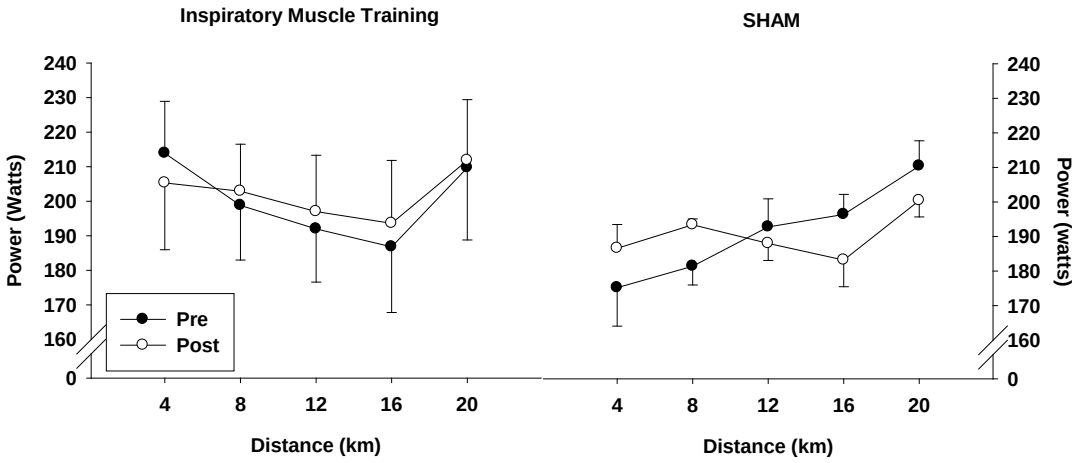

Figure 7. Power (watts) for each 4km segment. Values are mean + SE. * = significantly different from Pre ($p < 0.05$).

As expected both groups experienced a decline in arterial oxygen saturation, but there was no significant difference between groups or within each group at any time point. Inspiratory muscle training had no significant effect on RPE during the time trial. Dyspnea was significantly decreased at the 16km mark in the IMT after training, but not significantly different throughout the test.

Chapter V: Discussion

The major findings of this study were that 6 weeks of inspiratory muscle training significantly improved endurance performance in hypoxia, and increased inspiratory muscle strength, ventilation , frequency of breathing , and $\dot{V}O_2$ during a 20km cycle ergometry time trial in hypoxia. This was the first study, to our knowledge, to examine the effect of inspiratory muscle training on highly trained endurance athletes during a fixed distance time trial in hypoxia. Our results suggest that endurance athletes who are competing acutely at moderate altitude in an event lasting ~30-35 minutes would experience a significant improvement in performance by completing 6 weeks of IMT prior to altitude exposure.

5.1 Time Trial Performance

To date, only one other published study has examined the effects of chronic IMT on exercise performance in hypoxia. Downey et al. (8) performed a similar study using a fixed workload time to exhaustion test (TTE) in hypoxia and saw that IMT did not have an effect on duration. The main difference between this study and ours was our use of a set distance time trial versus a fixed work load TTE trial in the work of Downey et al. During the TTE trial in their study, test subjects experienced a significant decline in ventilation, $\dot{V}O_2$, dyspnea, RPE and an increase in S_aO_2 at the same workload post-IMT, but no change in TTE. The Downey et al. paper concludes that after 6 weeks of IMT, running economy in hypoxia is improved, but performance effects are unclear. We chose to re-examine the concept of IMT effects on hypoxic exercise performance by using a longer fixed distance TT in place of a shorter TTE trial because of the increased reliability (18, 28) and applicability to endurance performance (39). A 20km TT in hypoxia took our subjects approximately 30-40 minutes, compared to the 7-10 minutes that most subjects ran in the TTE trial in Downey et al. Additionally, we selected cycling as the

mode of exercise versus running, as used in Downey et al., because IMT has been shown to have more consistent, positive effects on cycling performance than running performance (20, 34, 42). In contrast to the work of Downey et al., we found that a 20km time trial performance in hypoxia was improved by 1.4% which is approaching significance ($p = 0.06$). Our data indicate that IMT is a useful technique for improving endurance performance with acute exposure to hypoxia.

We hypothesized that there would be greater potential for IMT to affect endurance performance in hypoxia than normoxia, even though several independent studies have clearly documented the ergogenic effects of IMT on normoxic exercise performance. Hypoxia significantly increases work of breathing by an additional 20 to 30 percent (2) during submaximal endurance exercise resulting in an augmentation in the metabolic demand of the respiratory muscles and an increase in dyspnea (36). It has been shown that by unloading the respiratory muscles, in hypoxia, work of breathing is attenuated by 29% during 4 minutes of cycling at 160 watts (21). Decreasing work of breathing attenuates the metabolic demand of the respiratory muscles (15). With the cyclists increasing $\dot{V}E$, $\dot{V}O_2$, and f_b while dyspnea remained unchanged, it can reasonably be assumed that the cyclists improved their breathing tolerance after 6 weeks of IMT.

The performance improvements in our study were not as great as the ones in normoxia where Romer et al. saw a 3.8 ± 1.7% and 4.6 ± 1.9% improvement in during 20km and 40km TT, respectively. Subjects in our study experienced an improvement of 1.4 ± 1.9%. According to Hopkins et al.(17), the smallest amount of variation that significantly enhances an athlete's ability to win an event is about half the variation of the event (17). There is no published research for the variation of a 20km TT in hypoxia, but a study performed by Paton et al. (33) determined that a TT with the duration of about an hour has a ~1% variation. An improvement

of 0.5% would be considered sufficient to increase the athlete's chances of winning. Therefore, the translational application of this work is that after 6 weeks of IMT, an improvement of 1.4 ± 1.9% would likely impact competitive performance in a competitive 20km cycling event at altitude.

5.2 Inspiratory Muscle Strength

Following 6 weeks of training, the IMT group significantly improved their inspiratory muscle strength compared to the control group. Our study used MIP as an indicator of inspiratory muscle strength (20, 35, 38). There are two commonly performed methods of training the inspiratory muscles; inspiratory flow resistive loading (IFRL) and inspiratory pressure threshold loading (IPTL). Both of these methods have been shown to improve MIP (27, 35, 38, 40). In our study, IFRL was performed by both groups with varying degrees of resistance between the groups. Unlike IPTL, where subjects perform 30 maximal breaths 2 times a day for 5 days a week (35), IFRL is performed 3 times per week using the Test of Incremental Respiratory Endurance (TIRE) (30). The TIRE protocol has been used and previously described by Mickleborough et al. and significantly increased inspiratory muscle endurance (43.9%) and strength (26.6%) (29).

One of the major advantages of the TIRE protocol is that the subjects perform the training until failure. The protocols followed in studies that utilize IPTL do not require their subjects to train until failure. By exercising to failure they are maximizing the rate of protein synthesis for up to 24 hours post-training (4). It also allows the inspiratory muscles to have an adequate amount of recovery time.

5.3 Normobaric vs. Hypobaric Hypoxia

This study was performed in normobaric hypoxia, but in practicality, athletes compete in hypobaric hypoxia. Saugy et al. (37) examined the physiological and performance differences between normobaric hypoxia (NH) and hypobaric hypoxia (HH). The duration of the time trial performance in that study was significantly increased during hypobaric hypoxia compared to normobaric hypoxia. The HH condition had a significantly lower S_aO_2 than the NH condition, which probably caused the decrement in performance based on our knowledge that the defense of S_aO_2 during exercise is strongly linked to endurance performance (5). Based on these differences in performance between NH and HH, we speculate, based on our study outcomes, that the effects of IMT on performance in hypobaric hypoxia may be even greater than the improvements seen in our study (37). Further research needs to be performed examining IMT and hypobaric hypoxia to determine how much the effects are enhanced from NH to HH.

5.4 Limitations

As with any training study, there are aspects of subject compliance that can ultimately affect performance outcomes. For example, subjects were asked to self-report their training regimens, abstain from alcohol, caffeine and food prior to testing, but we cannot be completely certain that these requests were actually followed. The subjects were asked to record everything consumed in the 3 hours prior to their pre-test. Prior to their post-test we reminded the subjects of what they consumed and asked them to consume the type and quantity of food and beverage prior to the post-test. It is possible that the subjects did not report everything consumed prior to the pre-test or did not consume everything we told them to consume prior to the post-test. However, we were able to control for hydration status by measuring their urine specific gravity before all performance trials.

The subjects performed the IMT outside of the laboratory without any supervision. Even though we were able to track their results through the app it is possible that they incorrectly performing the IMT. For example, a couple common mistakes are performing the training with a baseline MIP breath that is not a true representation of their MIP, or they might have terminated individual training sessions prior to fatigue. If the training was performed incorrectly it has the capability to skew the data.

Conclusion

The major finding of this study was that 6 weeks of IMT significantly improved endurance exercise performance at a simulated moderate altitude in highly trained subjects. Based on this research, athletes who are competing in an acute hypoxic environment should consider performing 6 weeks of IMT prior to the competition. IMT prior to altitude exposure could also be useful to athletes who are performing altitude training, by maximizing their ability to train at altitude. One of the concerns with altitude training is that athletes are unable to perform the same intensity and duration of training as they would in a normoxic environment, but with 6 weeks of IMT prior to the altitude training they would be able to increase their training load to durations and intensities closer to what they would do in normoxia.

References

1. **Aaron EA, Seow KC, Johnson BD, and Dempsey JA**. Oxygen cost of exercise hyperpnea: implications for performance. *J Appl Physiol (1985)* 72: 1818-1825, 1992.
2. **Babcock MA, Johnson BD, Pegelow DF, Suman OE, Griffin D, and Dempsey JA**. Hypoxic effects on exercise-induced diaphragmatic fatigue in normal healthy humans. *J Appl Physiol (1985)* 78: 82-92, 1995.
3. **Buchfuhrer MJ, Hansen JE, Robinson TE, Sue DY, Wasserman K, and Whipp BJ**. Optimizing the exercise protocol for cardiopulmonary assessment. *J Appl Physiol Respir Environ Exerc Physiol* 55: 1558-1564, 1983.
4. **Burd NA, West DW, Staples AW, Atherton PJ, Baker JM, Moore DR, Holwerda AM, Parise G, Rennie MJ, Baker SK, and Phillips SM**. Low-load high volume resistance exercise stimulates muscle protein synthesis more than high-load low volume resistance exercise in young men. *PLoS One* 5: e12033, 2010.
5. **Chapman RF**. The individual response to training and competition at altitude. *Br J Sports Med* 47 Suppl 1: i40-44, 2013.
6. **Chiappa GR, Roseguini BT, Vieira PJ, Alves CN, Tavares A, Winkelmann ER, Ferlin EL, Stein R, and Ribeiro JP**. Inspiratory muscle training improves blood flow to resting and exercising limbs in patients with chronic heart failure. *J Am Coll Cardiol* 51: 1663-1671, 2008.
7. **Cibella F, Cuttitta G, Romano S, Grassi B, Bonsignore G, and Milic-Emili J**. Respiratory energetics during exercise at high altitude. *J Appl Physiol (1985)* 86: 1785-1792, 1999.
8. **Downey AE, Chenoweth LM, Townsend DK, Ranum JD, Ferguson CS, and Harms CA**. Effects of inspiratory muscle training on exercise responses in normoxia and hypoxia. *Respir Physiol Neurobiol* 156: 137-146, 2007.
9. **Doyle JA, and Martinez AL**. Reliability of a protocol for testing endurance performance in runners and cyclists. *Res Q Exerc Sport* 69: 304-307, 1998.
10. **Edwards AM, Wells C, and Butterly R**. Concurrent inspiratory muscle and cardiovascular training differentially improves both perceptions of effort and 5000 m running performance compared with cardiovascular training alone. *Br J Sports Med* 42: 823-827, 2008.
11. **Enright SJ, Unnithan VB, Heward C, Withnall L, and Davies DH**. Effect of high-intensity inspiratory muscle training on lung volumes, diaphragm thickness, and exercise capacity in subjects who are healthy. *Phys Ther* 86: 345-354, 2006.
12. **Hanel B, and Secher NH**. Maximal oxygen uptake and work capacity after inspiratory muscle training: a controlled study. *J Sports Sci* 9: 43-52, 1991.
13. **Harms CA**. Effect of skeletal muscle demand on cardiovascular function. *Med Sci Sports Exerc* 32: 94-99, 2000.
14. **Harms CA**. Insights into the role of the respiratory muscle metaboreflex. *J Physiol* 584: 711, 2007.
15. **Harms CA, Babcock MA, McClaran SR, Pegelow DF, Nickele GA, Nelson WB, and Dempsey JA**. Respiratory muscle work compromises leg blood flow during maximal exercise. *J Appl Physiol (1985)* 82: 1573-1583, 1997.
16. **Hinckson EA, and Hopkins WG**. Reliability of time to exhaustion analyzed with critical-power and log-log modeling. *Med Sci Sports Exerc* 37: 696-701, 2005.

17. **Hopkins WG, Hawley JA, and Burke LM**. Design and analysis of research on sport performance enhancement. *Med Sci Sports Exerc* 31: 472-485, 1999.
18. **Jeukendrup A, Saris WH, Brouns F, and Kester AD**. A new validated endurance performance test. *Med Sci Sports Exerc* 28: 266-270, 1996.
19. **Johnson BD, Saupe KW, and Dempsey JA**. Mechanical constraints on exercise hyperpnea in endurance athletes. *J Appl Physiol (1985)* 73: 874-886, 1992.
20. **Johnson MA, Sharpe GR, and Brown PI**. Inspiratory muscle training improves cycling time-trial performance and anaerobic work capacity but not critical power. *Eur J Appl Physiol* 101: 761-770, 2007.
21. **Kleinsasser A, Von Goedecke A, Hoermann C, Maier S, Schaefer A, Keller C, and Loeckinger A**. Proportional assist ventilation reduces the work of breathing during exercise at moderate altitude. *High Alt Med Biol* 5: 420-428, 2004.
22. **Leddy JJ, Limprasertkul A, Patel S, Modlich F, Buyea C, Pendergast DR, and Lundgren CE**. Isocapnic hyperpnea training improves performance in competitive male runners. *Eur J Appl Physiol* 99: 665-676, 2007.
23. **Loeppky JA, Icenogle M, Scotto P, Robergs R, Hinghofer-Szalkay H, and Roach RC**. Ventilation during simulated altitude, normobaric hypoxia and normoxic hypobaria. *Respir Physiol* 107: 231-239, 1997.
24. **Lomax M**. Inspiratory muscle training, altitude, and arterial oxygen desaturation: a preliminary investigation. *Aviat Space Environ Med* 81: 498-501, 2010.
25. **Manohar M**. Regional brain blood flow and O2 delivery during severe exertion in the pony. *Respir Physiol* 64: 339-349, 1986.
26. **McConnell AK, and Lomax M**. The influence of inspiratory muscle work history and specific inspiratory muscle training upon human limb muscle fatigue. *J Physiol* 577: 445-457, 2006.
27. **McConnell AK, and Romer LM**. Respiratory muscle training in healthy humans: resolving the controversy. *Int J Sports Med* 25: 284-293, 2004.
28. **McLellan TM, Cheung SS, and Jacobs I**. Variability of time to exhaustion during submaximal exercise. *Can J Appl Physiol* 20: 39-51, 1995.
29. **Mickleborough TD, Nichols T, Lindley MR, Chatham K, and Ionescu AA**. Inspiratory flow resistive loading improves respiratory muscle function and endurance capacity in recreational runners. *Scand J Med Sci Sports* 20: 458-468, 2010.
30. **Mickleborough TD, Stager JM, Chatham K, Lindley MR, and Ionescu AA**. Pulmonary adaptations to swim and inspiratory muscle training. *Eur J Appl Physiol* 103: 635-646, 2008.
31. **Miller MR, Hankinson J, Brusasco V, Burgos F, Casaburi R, Coates A, Crapo R, Enright P, van der Grinten CP, Gustafsson P, Jensen R, Johnson DC, MacIntyre N, McKay R, Navajas D, Pedersen OF, Pellegrino R, Viegi G, Wanger J, and Force AET**. Standardisation of spirometry. *Eur Respir J* 26: 319-338, 2005.
32. **Neder JA, Andreoni S, Castelo-Filho A, and Nery LE**. Reference values for lung function tests. I. Static volumes. *Braz J Med Biol Res* 32: 703-717, 1999.
33. **Paton CD, and Hopkins WG**. Tests of cycling performance. *Sports Med* 31: 489-496, 2001.
34. **Romer LM, McConnell AK, and Jones DA**. Effects of inspiratory muscle training on time-trial performance in trained cyclists. *J Sports Sci* 20: 547-562, 2002.

35. **Romer LM, McConnell AK, and Jones DA**. Inspiratory muscle fatigue in trained cyclists: effects of inspiratory muscle training. *Med Sci Sports Exerc* 34: 785-792, 2002.
36. **Roussos C**. Function and fatigue of respiratory muscles. *Chest* 88: 124S-132S, 1985.
37. **Saugy JJ, Rupp T, Faiss R, Lamon A, Bourdillon N, and Millet GP**. Cycling Time Trial Is More Altered in Hypobaric than Normobaric Hypoxia. *Med Sci Sports Exerc* 48: 680-688, 2016.
38. **Sonetti DA, Wetter TJ, Pegelow DF, and Dempsey JA**. Effects of respiratory muscle training versus placebo on endurance exercise performance. *Respir Physiol* 127: 185-199, 2001.
39. **Tucker R, Bester A, Lambert EV, Noakes TD, Vaughan CL, and St Clair Gibson A**. Non-random fluctuations in power output during self-paced exercise. *Br J Sports Med* 40: 912-917; discussion 917, 2006.
40. **Turner LA, Tecklenburg-Lund S, Chapman RF, Stager JM, Duke JW, and Mickleborough TD**. Inspiratory loading and limb locomotor and respiratory muscle deoxygenation during cycling exercise. *Respir Physiol Neurobiol* 185: 506-514, 2013.
41. **Volianitis S, McConnell AK, Koutedakis Y, McNaughton L, Backx K, and Jones DA**. Inspiratory muscle training improves rowing performance. *Med Sci Sports Exerc* 33: 803-809, 2001.
42. **Williams JS, Wongsathikun J, Boon SM, and Acevedo EO**. Inspiratory muscle training fails to improve endurance capacity in athletes. *Med Sci Sports Exerc* 34: 1194-1198, 2002.
43. **Wilmore JH**. Influence of motivation on physical work capacity and performance. *J Appl Physiol* 24: 459-463, 1968.
44. **Witt JD, Guenette JA, Rupert JL, McKenzie DC, and Sheel AW**. Inspiratory muscle training attenuates the human respiratory muscle metaboreflex. *J Physiol* 584: 1019-1028, 2007.

Supplement Material

Appendix I: Variable Key

Group	1 = IMT 2= Sham	8	8km segment
M	$\dot{V}O_{2max}$ test	12	12km segment
1	Pre-test	16	16km segment
2	Post-test	20	20km segment
Pr	Before $\dot{V}O_{2max}$ or time trial	FH	First half average
Po	Post $\dot{V}O_{2max}$ or time trial	SH	Second half average
H	Height	TA	Average for whole 20km TT
W	Weight	Ve	Ventilation
vo2R	Relative $\dot{V}O_2$	BPM	Breaths per minute
vo2A	Absolute $\dot{V}O_2$	t	Time
FL	Percent flow Limited	Sat	Arterial oxygen saturation
FLP	Percent of $\dot{V}O_{2max}$ at which they become FL	Dyp	Dyspnea
FVC	Functional vital capacity	RPE	Rate of perceived exhaustion
FEV	Forced expiratory velocity for 1 second	Pwr	Power
FEF	Forced expiratory flow 25-75%	Compliance	Percent of training sessions completed
PEF	Peak expiratory flow	Pre	Initial training session
BIA	Bioelectrical impedance analysis	Post	Final training session
SG	Urine specific gravity	Fit	Fit score from PrO_2
TLC	Total lung capacity	PC	Power curve from PrO_2
VC	Vital capacity	FiLe	Final level achieved during training session
FRC	Functional residual capacity		
IC	Inspiratory capacity		
RV	Residual Volume		
DLCO	Lung diffusing capacity		
DL/VA	Lung diffusing capacity divided by alveolar volume		
MIP	Maximal inspiratory pressure		
MEP	Maximal expiratory pressure		
Best	Highest MIP average between Pr and Po		
4	4km segment		

Appendix II: Raw Data

Subject	Age	group	HM	WM	vo2RM	vo2MA	FL	FLP	FVCMpr	FEVMpr	FEFMpr	PEFMpr
R1101	27	1	173.30	73.34	59.20	4.34						
R1104	21	1	184.90	83.30	62.10	5.18	48.00	100.00	6.63	5.40	5.59	8.21
R1119	24	1	176.00	76.10	50.40	3.84	no		5.88	4.95	4.97	11.39
R1120	24	1	180.00	74.90	71.00	5.32	no		6.65	4.82	3.63	9.85
R1123	21	1	187.00	73.19	64.90	4.75	no		6.20	4.43	3.48	8.66
R1126	19	1	160.30	50.50	69.00	3.48	no		4.95	3.69	3.03	6.77
R1129	22	1	181.50	80.73	51.80	4.18	no		6.52	5.61	6.16	8.42
R1131	21	1	186.00	86.20	79.20	6.83	no		6.61	5.31	5.23	8.52
R1102	20	2	171.60	67.20	66.80	4.49	44.00	92.00	4.78	3.93	4.06	8.96
R1105	21	2	170.00	70.70	59.30	4.19	44.00	87.00	4.76	3.84	3.58	8.05
R1113	21	2	182.20	72.60	65.00	5.05	no		4.63	4.01	4.39	7.06
R1114	19	2	177.50	74.80	61.90	4.63	38.00	95.00	5.50	4.71	5.10	10.24
R1117	24	2	177.00	71.40	55.40	3.96	23.80	94.04	5.38	4.80	6.40	12.31

Subject	FVCMpo	FEVMpo	FEFMpo	PEFMpo	H1	W1	BIA1	SG1	FVC1pr	FEV1pr	FEF1pr	PEF1pr
R1101					172.20	73.21	19.50	1.01	5.00	4.19	4.87	11.88
R1104	6.42	5.19	5.17	8.35	185.60	85.37	14.20	1.00	6.52	5.25	5.07	9.35
R1119	5.17	4.82	7.13	10.88	177.30	75.50	12.90	1.01	5.76	4.98	5.35	12.84
R1120	6.64	4.79	3.59	9.55	179.30	75.69	11.90	1.01	7.03	5.20	4.11	10.17
R1123	5.98	4.35	3.46	8.76	185.80	74.30	8.00	1.00	6.29	4.56	3.39	9.58
R1126	5.96	5.08	5.27	9.24	160.30	53.71	8.90	1.00	4.61	3.21	2.29	6.95
R1129	4.31	3.30	2.75	7.46	181.50	78.85	12.50	1.01	6.02	4.94	4.78	9.72
R1131					186.00	86.60	13.70	1.02	6.49	5.29	4.96	9.76
R1102	4.74	4.03	4.22	6.41	172.60	68.70	11.50	1.00	4.91	4.03	3.97	9.70
R1105	4.68	3.73	3.47	8.21	170.00	72.80	17.70	1.01	4.77	3.57	2.87	8.26
R1113	4.26	3.75	4.93	7.33	183.60	73.90	10.90	1.02	5.28	4.38	5.24	10.49
R1114	5.40	4.71	5.14	10.12	177.00	76.43	9.70	1.00	5.31	4.74	5.30	10.89
R1117	5.33	4.82	6.48	12.63	176.30	71.25	13.20	1.05	5.57	4.99	6.53	14.96

Subject	TLC1	VC1	FRC1	IC1	RV1	DLCO1	DL/VA	MIP1pr	MEP1pr	FVC1po	FEV1po	FEF1po
R1101	5.68	4.83	2.62	3.05	0.84	28.50	4.79	118.00	126.00	4.92	4.22	5.18
R1104	8.63	6.49	4.27	4.36	2.14	37.10	4.83	174.00	186.50	6.35	5.12	4.84
R1119	6.64	5.86	2.68	3.97	0.79	37.00	5.23	149.33	125.67	5.80	5.18	5.98
R1120	7.93	6.87	2.27	5.67	1.06			108.00	187.00	6.97	5.05	3.77
R1123	8.37	6.49	4.50	3.87	1.88	41.60	5.51	154.00	227.00	6.68	4.79	3.84
R1126	5.47	4.48	2.59	2.88	1.00	29.85	5.29	54.00	93.33	4.37	3.03	2.16
R1129	7.10	6.08	2.98	4.12	1.02	38.50	5.06	100.00	146.00	5.51	4.93	5.63
R1131		5.84		3.87		55.70	6.15	123.00	124.00	6.61	4.32	4.02
R1102	5.96	4.93	2.08	3.87	1.03	34.20	5.59	149.50	156.30	4.50	3.93	4.48
R1105	5.29	4.67	1.63	3.66	0.61	32.90	5.40	127.67	178.33	4.45	3.02	1.93
R1113	6.41	4.53	3.32	3.08	1.88	35.00	6.38	125.00	98.30	5.34	4.57	5.58
R1114	7.27	5.23	3.65	3.62	1.85	33.80		132.00	105.00	4.89	4.77	5.86
R1117	7.58	5.58	3.74	3.84	2.00	41.90	6.11	148.00	166.00	5.71	5.23	6.99

Subject	PEF1po	MIP1po	MEP1po	MIPbest1	vo2R14	vo2A14	ve14	BPM14	hr14	pwr14	t14	sat14
R1101	1.15	125.00	114.00	126.00	41.50	3.04	96.41	55.00	130.00	174.00	7.73	95.00
R1104	9.71	176.30	183.67	176.30	52.00	4.44	121.00	47.00	139.00	251.00	6.63	82.00
R1119	12.05	159.00	122.50	159.00	37.46	2.83	72.58	33.00	153.00	131.00	8.55	87.00
R1120	9.87	104.30	175.00	108.00	51.89	3.93	121.83	44.00	140.00	232.00	6.87	88.00
R1123	8.55	158.00	235.70	158.00	41.30	3.07	81.50	27.00	140.00	233.00	6.88	88.00
R1126	6.70	59.67	89.67	59.67	55.17	2.96	88.37	39.00	156.00	203.00	7.19	87.00
R1129	9.15	96.00	179.00	100.00	45.70	3.60	136.40	47.00	169.00	252.00	6.62	87.00
R1131	6.93	132.33	115.67	132.33	41.30	3.58	88.60	24.00	150.00	235.00	6.79	91.00
R1102	9.11	157.00	216.50	157.00	43.30	2.98	69.30	33.00	150.00	133.00	8.48	89.00
R1105	7.69	133.00	154.00	133.00	51.12	3.72	111.26	40.00	164.00	176.00	7.65	91.00
R1113	8.38	129.70	132.30	129.70	49.98	3.69	99.30	47.00	142.00	187.00	7.42	
R1114	9.47	89.00	115.50	132.00	58.30	4.45	151.00	59.00	163.00	197.00	7.27	
R1117	13.55	168.00	152.00	168.00	51.80	3.70	113.70	54.00	148.00	183.00	7.44	87.00

Subject	dyp14	rpe14	vo2R18	vo2A18	ve18	BPM18	hr18	pwr18	t18	sat18	dyp18	rpe18
R1101	3.00	16.00	35.61	2.61	76.41	45.00	137.00	137.00	8.39		3.00	17.00
R1104	5.00	13.00	52.00	4.44	118.10	47.00	151.00	230.00	6.82	81.00	6.00	14.00
R1119	4.00	13.00	40.78	3.02	82.61	38.00	163.00	131.00	8.58	88.00	5.00	15.00
R1120	6.00	14.00	53.90	4.08	120.49	49.00	152.00	222.00	6.92	86.00	7.00	17.00
R1123	4.00	14.00	44.60	3.32	92.30	33.00	150.00	221.00	6.94	86.00	5.00	15.00
R1126	3.00	11.00	52.40	2.81	85.84	45.00	160.00	180.00	7.49	89.00	3.00	13.00
R1129	6.00	14.00	45.70	3.62	117.40	41.00	161.00	217.00	6.96	86.00	7.00	16.00
R1131	2.00	13.00	41.60	3.60	101.10	27.00	164.00	252.00	6.58	90.00	4.00	15.00
R1102	2.00	11.00	50.50	3.47	93.10	34.00	167.00	162.00	7.85	79.00	3.00	12.00
R1105	4.00	12.00	51.13	3.72	113.67	48.00	174.00	181.00	7.48	90.00	4.00	12.00
R1113	6.00	14.00	40.38	2.98	72.00	40.00	142.00	186.00	7.39		7.00	16.00
R1114	5.00	11.00	54.80	4.19	133.90	58.00	175.60	195.00	7.28		5.00	14.00
R1117	5.00	15.00	55.30	3.95	114.60	56.00	148.00	183.00	7.45	87.00	7.00	7.00

Subject	vo2R112	vo2A112	ve112	BPM112	hr112	pwr112	t112	sat112	dyp112	rpe112	vo2R116
R1101	37.31	2.73	78.72	47.00	130.00	118.00	8.90	96.00	3.00	18.00	37.08
R1104	49.30	4.21	106.90	47.00	151.00	215.00	7.01	81.00	6.00	14.00	49.20
R1119	53.77	3.30	92.26	46.00	167.00	148.00	8.12	88.00	7.00	16.00	40.33
R1120	53.99	4.09	115.07	50.00	151.00	210.00	7.08	87.00	7.00	17.00	55.40
R1123	46.40	3.45	96.30	30.00	157.00	234.00	6.78	86.00	6.00	17.00	47.80
R1126	48.80	2.62	79.51	47.00	159.00	164.00	7.78	90.00	3.00	13.00	49.11
R1129	42.60	3.36	102.70	38.00	155.00	209.00	7.07	84.00	7.00	16.00	40.50
R1131	42.40	3.67	100.50	28.00	165.00	238.00	6.74		3.00	14.00	41.50
R1102	55.70	3.83	116.70	47.00	183.00	206.00	7.11	88.00	4.00	14.00	58.60
R1105	53.28	3.88	120.53	49.00	173.00	179.00	7.52		6.00	13.00	51.65
R1113	37.57	2.77	70.40	42.00	146.00	198.00	7.25		7.00	17.00	43.45
R1114	55.10	4.21	145.00	69.00	183.00	212.00	7.07		7.00	16.00	58.10
R1117	54.20	3.87	114.80	62.00	143.00	169.00	7.69	88.00	7.00	17.00	54.80

Subject	vo2A116	ve116	BPM116	hr116	pwr116	t116	sat116	dyp116	rpe116	vo2R120	vo2A120
R1101	2.71	76.20	47.00	126.00	105.00	9.32	96.00	2.00	19.00	37.51	2.75
R1104	4.20	104.90	46.00	148.00	203.00	7.15	81.00	6.00	16.00	37.40	3.19
R1119	3.04	80.00	43.00	161.00	121.00	8.80	87.00	8.00	17.00	48.77	3.68
R1120	4.19	116.10	50.00	153.00	209.00	7.06	86.00	8.00	18.00	58.87	4.46
R1123	3.56	104.30	35.00	163.00	231.00	6.80		7.00	17.00	53.30	3.96
R1126	2.64	78.07	43.00	157.00	157.00	7.95	88.00	3.00	13.00	54.78	2.94
R1129	3.19	96.60	35.00	159.00	211.00	7.04	85.00	7.00	16.00	41.20	3.24
R1131	3.59	109.00	32.00	174.00	257.00	6.53		4.00	15.00	40.60	3.52
R1102	4.02	138.00	57.00	187.00	210.00	7.07	89.00	7.00	15.00	58.30	4.01
R1105	3.76	115.85	20.00	179.00	182.00	7.46		7.00	15.00	55.98	4.05
R1113	3.21	79.86	44.00	156.00	205.00	7.13		8.00	17.00	40.05	2.96
R1114	4.44	162.70	77.00	184.00	202.00	7.19		8.00	17.00	58.50	4.47
R1117	3.91	119.90	62.00	147.00	183.00	7.46	91.00	9.00	18.00	60.90	4.34

Subject	ve120	BPM120	hr120	pwr120	t120	sat120	hr1FH	pwr1FH	t1FH	hr1SH	pwr1SH	t1SH
R1101	85.34	55.00	123.00	100.00	9.52	95.00	133.00	147.00	20.58	126.00	105.00	23.28
R1104	100.80	59.00	154.00	238.00	6.76	81.00	146.00	236.00	16.92	151.00	218.00	17.45
R1119	126.18	59.00	160.00	172.80	7.66	90.00	160.00	132.00	21.30	161.00	148.00	20.41
R1120	128.89	57.00	157.00	219.00	6.97	86.00	147.00	224.00	17.32	154.00	213.00	17.58
R1123	124.40	40.00	168.00	255.00	6.62		147.00		17.21	165.00		16.81
R1126	90.38	48.00	168.00	171.00	7.68	82.00		187.00	18.49		162.00	19.54
R1129	116.80	47.00	171.00	236.00	6.75	84.00		229.00	17.11		220.00	17.33
R1131	135.10	41.00	185.00	286.00	6.26			242.00	16.74		264.00	16.16
R1102	148.30	62.00	188.00	212.00	7.09	87.00	163.00	158.00	19.87	187.00	209.00	17.73
R1105	144.68	61.00	185.00	193.00	7.30		170.00	178.00	18.91	180.00	186.00	18.50
R1113	77.60	49.00	166.00	237.00	6.76		142.00	186.00	18.52	159.00	202.00	6.76
R1114	164.80	74.00	189.00	204.00	7.15		172.00	200.00	18.08	186.00	205.00	17.88
R1117	156.40	82.00	154.00	206.00	7.12	88.00	148.00	179.00	18.77	148.00	190.00	18.39

Subject	Dyp1A	RPE1A	vo2R1TA	vo2A1TA	ve1TA	BPM1TA	hr1TA	pwr1TA	t1TA	H2	W2
R1101	2.75	17.50	38.59	2.83	86.24	50.00	129.00	125.00	43.86	174.00	72.08
R1104	5.75	14.25	49.50	4.23	113.70	48.20	149.00	227.00	34.37	185.00	82.04
R1119	6.00	15.25	40.26	3.04	82.00	40.20	140.00	140.00	41.71	175.00	76.20
R1120	7.00	16.50	53.97	4.09	117.24	48.00	151.00	219.00	34.90	179.00	77.80
R1123	5.50	15.75	45.20	3.36	95.50	31.30	155.00	235.00	34.02	185.00	74.00
R1126	3.00	12.50	50.70	2.72	81.80	43.08	160.00	174.00	38.03	160.30	61.62
R1129	6.75	15.50	43.30	3.41	118.00	41.50	163.00	225.00	34.44	181.50	79.40
R1131	3.25	14.25	41.20	3.57	102.70	29.00	167.60	253.00	32.90	186.00	85.60
R1102	4.00	13.00	51.80	3.56	108.40	44.50	174.00	182.00	37.60	172.10	69.64
R1105	5.25	13.00	51.40	3.74	116.10	47.40	175.00	182.00	37.41	170.50	72.00
R1113	7.00	16.00	42.60	3.15	80.00	42.30	151.00	202.00	35.95	182.60	73.53
R1114	6.25	14.50	55.80	4.27	146.70	66.20	179.00	202.00	35.96	176.50	73.80
R1117	7.00	14.25	54.10	3.85	116.70	61.80	148.00	185.00	37.16	176.80	70.05

Subject	BIA2	SG2	FVC2pr	FEV2pr	FEF2pr	PEF2pr	TLC2	VC2	FRC2	IC2	RV2	DLCO2
R1101	18.00	1.00	4.81	4.14	5.20	12.39	5.39	4.40	2.56	2.83	1.00	
R1104	12.20	1.00	6.73	5.28	4.83	9.87	8.45	6.73	4.47	3.99	1.72	34.60
R1119	14.20	1.01	5.86	4.94	5.07	11.37	5.29	5.72	0.73	4.55	0.00	
R1120	13.40	1.02	7.20	5.24	3.96	10.70	8.86	7.34	3.85	5.01	1.52	43.20
R1123	8.30	1.02	6.71	4.67	3.56	8.31	8.34	6.62	4.57	3.78	1.72	40.90
R1126	8.70	1.01	4.85	3.40	2.47	7.71						
R1129	15.10	1.03	6.10	4.99	4.91	9.12	6.38	5.62	1.61	4.77	0.76	41.00
R1131	13.50	1.01	7.46	5.80	4.97	11.60	8.83	6.58	5.06	3.77	2.26	55.55
R1102	11.50	1.02	4.82	4.03	4.38	8.43	5.14	4.78	1.04	4.11	0.37	27.20
R1105	15.90	1.02	4.93	3.77	3.13	9.13	5.81	4.84	2.15	3.66	0.97	31.60
R1113	12.90	1.01	5.31	4.13	3.51	9.48	5.75	5.29	2.24	3.52	0.47	
R1114	12.10	1.01	5.13	4.53	5.15	9.70	6.23	5.04	2.66	3.82	1.19	29.20
R1117	15.60	1.01	5.53	4.96	6.66	13.25	7.22	5.52	3.61	3.61	1.70	39.50

Subject	DL/VA2	MIP2pr	MEP2pr	FVC2po	FEV2po	FEF2po	PEF2po	MIP2po	MEP2po	MIPbest2	vo2R24	vo2A24
R1101		160.70	165.70	4.86	4.24	4.50	11.92	127.00	127.70	160.70	42.67	3.08
R1104	4.51	213.75	229.67	2.27	5.08	4.88	9.64	218.67	224.33	218.67	54.34	4.46
R1119		188.70	137.30	5.44	4.91	5.59	11.30	176.30	150.30	188.70	44.96	3.43
R1120	4.99	112.70	217.00	7.34	5.37	4.04	11.24	114.00	208.70	114.00	58.00	4.51
R1123	5.43	175.70	213.70	6.52	4.86	4.12	8.48	177.00	227.50	177.00	43.60	3.23
R1126		96.67	92.00	4.31	3.30	2.75	7.46	103.00	99.00	103.00	45.86	3.04
R1129	5.28	101.00	178.33	5.96	5.08	5.27	9.24	97.67	163.33	101.00	45.94	3.65
R1131	6.02	138.33	198.33	6.57	5.80	5.97	10.04	184.00	160.50	184.00	49.30	4.22
R1102	4.62	171.70	243.00	4.51	3.90	4.61	8.12	173.00	222.67	173.00	43.71	3.04
R1105	5.13	105.67	178.33	4.53	3.49	3.06	7.60	122.33	249.00	122.33	50.63	3.65
R1113		139.30	120.30	5.29	4.54	4.57	10.54	139.30	132.70	139.30	41.98	3.09
R1114	4.73	132.30	91.00	4.76	4.43	5.41	9.45	122.67	91.33	132.30	57.85	4.27
R1117	5.75	187.70	191.00	5.58	4.97	7.29	12.02	168.00	188.00	187.70	51.15	3.58

Subject	ve24	BPM24	hr24	pwr24	t24	sat24	dyp24	rpe24	vo2R28	vo2A28	ve28	BPM28
R1101	115.72	71.00	144.00	185.00	7.52	92.00	4.00	17.00	39.38	2.84	100.77	62.00
R1104	121.37	47.00	146.00	239.00	6.74	84.00	4.00	12.00	51.12	4.90	103.08	46.00
R1119	87.17	38.00	163.00	170.00	7.71	86.00	5.00	15.00	46.61	3.55	101.22	50.00
R1120	158.10	51.00	152.00	251.00	6.65	88.00	6.00	13.00	56.30	4.38	148.20	56.00
R1123	88.40	35.00	131.00	200.00	7.22	90.00	2.00	11.00	46.80	3.46	91.70	32.00
R1126	94.48	44.00	155.00	97.00	7.24	90.00	3.00	12.00	46.97	3.11	98.33	51.00
R1129	124.20	44.00	156.00	242.00	6.72	87.00	7.00	15.00	44.63	3.54	114.90	43.00
R1131	117.61	29.00	162.00	258.00	6.58	88.00	4.00	14.00	49.95	4.27	120.09	29.00
R1102	81.23	35.00	150.00	165.00	7.84	91.00	3.00	12.00	51.24	3.57	103.70	43.00
R1105	114.24	41.00	146.00	193.00	7.34	91.00	4.00	11.00	49.87	3.59	102.42	45.00
R1113	85.65	48.00	149.00	176.00	7.60	92.00	4.00	14.00	46.80	3.44	98.97	54.00
R1114	139.60	59.00	157.00	201.00	7.26		5.00	13.00	55.64	4.11	129.62	62.00
R1117	103.20	49.00	154.30	198.00	7.28	92.00	7.00	15.00	51.90	3.63	105.50	54.00

Subject	hr28	pwr28	t28	sat28	dyp28	rpe28	vo2R212	vo2A212	ve212	BPM212	hr212	pwr212
R1101	141.00	135.00	8.42	93.00	4.00	17.00	33.41	2.41	69.23	44.00	139.00	120.00
R1104	146.00	210.00	7.06	84.00	4.00	14.00	51.84	4.25	104.01	43.00	146.00	210.00
R1119	175.00	168.00	7.69	87.00	7.00	17.00	41.71	3.18	85.94	46.00	173.00	138.00
R1120	168.00	226.00	6.87	86.00	7.00	15.00	55.60	4.33	147.10	54.00	171.00	223.00
R1123	148.00	212.00	7.04	91.00	3.00	13.00	51.20	3.79	107.70	41.00	161.00	231.00
R1126	163.00	192.00	7.31	89.00	3.00	12.00	46.94	3.11	100.24	52.00	166.00	187.00
R1129	163.00	218.00	6.95	87.00	7.00	15.00	43.10	3.42	102.50	39.00	163.00	214.00
R1131	169.00	262.00	6.49	86.00	4.00	14.00	50.56	4.33	133.14	33.00	171.00	253.00
R1102	170.00	192.00	7.32	89.00	4.00	13.00	53.23	3.70	116.17	50.00	182.00	201.00
R1105	153.00	189.00	7.36	90.00	5.00	13.00	49.18	3.54	107.46	49.00	155.00	178.00
R1113	158.00	191.00	7.32	90.00	6.00	15.00	48.01	3.53	100.85	52.00	163.00	196.00
R1114	167.00	198.00	7.24		5.00	14.00	53.39	3.94	122.05	61.00	167.00	176.00
R1117	167.00	197.00	7.25	93.00	7.00	15.00	52.92	3.70	105.30	59.00	168.30	189.00

Subject	t212	sat212	dyp212	rpe212	vo2R216	vo2A216	ve216	BPM216	hr216	pwr216	t216	sat216
R1101	8.83	94.00	4.00	19.00	33.89	2.44	65.80	41.00	127.00	102.00	9.43	92.00
R1104	7.06	84.00	5.00	15.00	49.51	4.06	100.74	45.00	148.00	210.00	7.05	84.00
R1119	8.34	88.00	8.00	17.00	45.10	3.44	96.30	48.00	174.00	139.00	8.29	88.00
R1120	6.92		7.00	15.00	55.70	4.34	152.40	55.00	172.00	219.00	6.97	
R1123	6.80	84.00	5.00	15.00	52.40	3.88	114.50	44.00	167.00	236.00	6.74	84.00
R1126	7.39	91.00	4.00	14.00	41.10	2.72	84.58	48.00	164.00	176.00	7.55	90.00
R1129	7.01	86.00	8.00	17.00	43.08	3.42	101.80	38.00	164.00	212.00	7.03	87.00
R1131	6.58	88.00	5.00	15.00	51.45	4.40	145.39	39.00	178.00	255.00	6.54	87.00
R1102	7.18	89.00	5.00	15.00	54.14	3.77	123.70	54.00	186.00	202.00	7.31	88.00
R1105	7.52	91.00	7.00	14.00	46.32	3.33	98.57	50.00	149.00	156.00	7.95	93.00
R1113	7.25	90.00	7.00	17.00	45.24	3.33	94.15	49.00	168.00	192.00	7.30	90.00
R1114	7.66		7.00	17.00	55.99	4.13	140.82	71.00	169.00	186.00	7.42	
R1117	7.35	92.00	7.00	15.00	50.68	3.55	101.90	59.00	166.30	180.00	7.48	

Subject	dyp216	rpe216	vo2R220	vo2A220	ve220	BPM220	hr220	pwr220	t220	sat220	hr2FH	pwr2FH
R1101	4.00	19.00	41.82	3.01	90.20	52.00	132.00	117.00	8.92	93.00	142.00	152.00
R1104	6.00	15.00	62.76	5.15	172.01	63.00	155.00	246.00	6.67	84.00	146.00	222.00
R1119	9.00	19.00	49.40	3.76	122.80	61.00	175.00	162.00	7.88	87.00	169.00	163.00
R1120	8.00	16.00	57.50	4.47	161.10	57.00	173.00	228.00	6.87		160.00	238.00
R1123	6.00	17.00	56.10	4.15	140.00	54.00	174.00	246.00	6.66	85.00	142.00	210.00
R1126	4.00	14.00	49.81	3.30	114.14	55.00	179.00	207.00	7.10	89.00		193.00
R1129	8.00	17.00	51.09	4.08	136.60	41.00	169.00	220.00	6.93	87.00	160.00	227.00
R1131	5.00	16.00	51.84	4.44	160.01	44.00	178.00	268.00	6.43	86.00		259.00
R1102	7.00	17.00	56.47	3.93	138.05	63.00	187.00	203.00	7.22	89.00	164.00	183.00
R1105	8.00	14.00	56.22	4.05	142.55	64.00	162.00	191.00	7.34	85.00	151.00	189.00
R1113	8.00	18.00	52.23	3.84	130.15	60.00	174.00	209.00	7.08	88.00	155.00	188.00
R1114	8.00	17.00	60.02	4.43	143.55	65.00	171.00	188.00	7.37		162.00	194.00
R1117	7.00	15.00	56.31	3.94	163.10	80.00	176.00	211.00	7.08	90.00	162.00	196.00

Subject	t2FH	hr2SH	pwr2SH	t2SH	Dyp2A	RPE2A	vo2R2TA	vo2A2TA	ve2TA	BPM2TA	hr2TA	pwr2TA
R1101	20.21	110.00	131.00	22.91	4.00	18.00	37.36	2.69	92.82	57.00	138.00	130.00
R1104	17.31	150.00	223.00	17.27	4.75	14.00	52.73	4.32	113.65	48.00	148.00	223.00
R1119	19.55	173.00	147.00	20.36	7.25	17.00	44.40	3.38	93.20	46.00	171.00	155.00
R1120	16.99	172.00	223.00	17.29	7.00	14.75	55.20	4.29	146.60	52.00	167.00	230.00
R1123	17.66	152.00	239.00	16.80	4.00	14.00	47.80	3.54	100.20	36.00	147.00	225.00
R1126	18.24		191.00	18.35	3.50	13.00	45.09	2.99	96.23	49.00	165.40	192.00
R1129	17.17	166.00	215.00	17.47	7.50	16.00	43.85	3.48	112.50	40.00	163.00	221.00
R1131	16.33		259.00	16.29	4.50	14.75	49.14	4.21	128.37	33.00	171.60	259.00
R1102	18.72	185.00	201.00	18.15	4.75	14.25	51.20	3.56	109.64	49.00	173.00	192.00
R1105	18.43	155.00	173.00	19.08	6.00	13.00	49.71	3.58	109.84	50.00	153.00	181.00
R1113	18.52	170.00	199.00	18.03	6.25	16.00	45.31	3.33	95.77	51.00	163.00	193.00
R1114	18.31	170.00	183.00	18.64	6.25	15.25	55.37	4.09	130.10	64.00	167.00	188.00
R1117	18.19	170.30	193.00	18.25	7.00	15.00	52.08	3.64	109.50	58.00	166.20	195.00

Subject	t2TA	Compliance	Fit_pre	PC_pre	MIP_pre	FiLe_pre	Fit_post	PC_post	MIP_post	FiLe_post
R1101	43.12	88.89	58.50	940.00	93.00	26.00				
R1104	34.58	83.33	62.80	1242.00	155.00	31.00	64.40	1321.00	165.00	38.00
R1119	39.91	88.89	85.80	1177.00	127.00	36.00	87.00	1225.00	133.00	39.00
R1120	34.28	83.33			112.00				138.00	
R1123	34.46	100.00			175.00				193.00	
R1126	36.59									
R1129	34.64	88.89	29.30	530.00	87.00	20.00	23.60	459.00	88.00	37.00
R1131	32.62	72.22	89.00	1294.00	124.00	42.00	152.50	1937.00	196.00	28.00
R1102	36.87	77.78	29.00	602.00	99.00	19.00	30.60	652.00	95.00	26.00
R1105	37.51	83.33	40.30	814.00	134.00	42.00	20.50	643.00	142.00	41.00
R1113	36.55	100.00	16.00	439.00	86.00	42.00	20.70	601.00	135.00	40.00
R1114	36.95	77.78	24.30	564.00	109.00	42.00	21.00	595.00	116.00	22.00
R1117	36.44	94.44	44.70	810.00	149.00	41.00	38.70	741.00	143.00	42.00

Appendix III: General Study Questionnaire

General Study Questionnaire

Name	**Date**

Do you consider yourself to be a highly endurance trained individual?	**(Circle one) YES NO**
On average, how many days per week do you typically complete a cycle workout?	
On average, how many minutes do you cycle in a typical week?	

Participant Signature	**Date**

Appendix IV: PAR-Q

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 not do 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. (Researcher will complete) Measure height and weight to determine BMI:
Height:_____
Weight:_____

Participant Signature	**Date**

INDIANA UNIVERSITY INFORMED CONSENT STATEMENT FOR

The Effect of Inspiratory Muscle Training on Exercise Performance in Hypoxia

You are invited to participate in a research study that will help determine if inspiratory muscle training (training the breathing muscles) can help improve exercise performance in hypoxia (low oxygen content of the air). You were selected as a possible subject because of your status as a highly trained cyclist. We ask that you read this form and ask any questions you may have before agreeing to be in the study.

Disclaimer: It is possible that after completing the study questionnaires and the initial exercise test that you will not qualify for the study.

The study is being conducted by Robert F. Chapman, Ph.D. (Principal Investigator), and co-investigators Daniel Hursh and Timothy Mickleborough, Ph.D. in the Department of Kinesiology at Indiana University-Bloomington.

STUDY PURPOSE

The purpose of the proposed study is to investigate if inspiratory muscle training (breathing in against a resistance) will help to improve exercise performance in a low oxygen environment, like what exists at altitude.

NUMBER OF PEOPLE TAKING PART IN THE STUDY:

If you agree to participate, you will be one of approximately 24 subjects who will be participating in this research.

PROCEDURES FOR THE STUDY:

If you agree to be in the study, the following items are included:

An invitation will be extended to visit the Human Performance laboratory on four occasions at a previously agreed-upon time. Each visit will last approximately 60 minutes. You will also be asked to complete a “real” or “fake” inspiratory muscle training protocol in your home on three days a week, over the course of six weeks. These home inspiratory muscle training sessions will last approximately 8-15 minutes. Finally, you will be asked to complete an online training log of your cycling workouts, which will take approximately 2 minutes each day.

The initial laboratory testing session (Session 1) includes completion of two written questionnaires, measures of your height and weight, measure of your body composition (fat and lean weight), and a maximal exercise test on a cycle ergometer (a stationary bike). A maximal exercise test is where you exercise at efforts become harder each minute, until you become too tired to continue. The remaining three laboratory sessions (Sessions 2, 3, and 4) include measures of your resting pulmonary function (breathing tests) and a 20km (about 12.5 mile) all out time trial on a cycle ergometer.

Each of these tests is described below.

Height and weight measures. Height will be measured by asking you to stand against a wall and a device will be lowered until it touches the top of your head. Weight will be measured by having you sit on a chair, which is placed on a scale. This test will be completed in both visits to the lab.

Body composition measures. You will be asked to stand on a scale in bare feet and hold two handles connected to the scale. A small, electrical current which you will not be able to feel will pass through your body for about two seconds. The scale will calculate an estimate of the percent of your weight that is lean weight and the percent that is fat weight. This test will be completed only on the first visit to the lab.

Resting pulmonary function (breathing tests). You will be asked to sit in a chair and rest comfortably for 10 minutes. You will be asked to put nose clips on your nose and breathe through a plastic mouthpiece. The nose clips are cleaned in detergent and an antibacterial solution after each use, and the plastic mouthpiece is new for each subject. While sitting in the chair, you will be asked to complete various breathing tests which measure the size of your lungs, how fast you can move air in and out of your lungs, the ability of your lungs to transfer gas to the blood, and the ability of your lungs to generate pressure.

Cycle Tests. These exercise tests will be completed on a cycle ergometer. One test is a maximal exercise test and the other is a 20km time trial. For all cycle tests, you will be allowed to warm up on the cycle ergometer for 10 minutes at any pedaling rate and resistance you would like to select. A strap will be placed around your chest which will measure your heart rate. A small sensor will be placed on your forehead that measures the amount of oxygen in your blood. Another sensor will be placed on your thigh and secured with an elastic bandage. You will be asked to complete the cycle tests while breathing through a face mask which covers your nose and mouth. Air will flow into and out of your lungs as you breathe through the face mask. The face mask, forehead sensor, thigh sensor, and heart rate monitor are cleansed in a detergent and antibacterial solution following each use.

For the maximal exercise test, the initial workload will be set at 100W, and you will be asked to maintain a pedaling rate between 80 and 110 RPMs throughout the test. Every minute, the workload will increased by 25W until you become so tired that you need to stop, or your cadence drops below 70 RPM for three seconds. The goal is to pedal for as long as you can, with a typical test lasting between 10 and 15 minutes.

For the 20km time trials, you can pedal at any pedaling rate you like and set the resistance / gearing at any level you like. The goal is for you to complete a 20km ride in as short of a time as possible. You will be given real time feedback of the distance you have completed on a video

monitor, as well as verbal feedback of distance completed every 4km. For these 20km time trials, the air you breathe in will have a reduced amount of oxygen, which is equivalent to an altitude of 2500m or 8000ft.

Inspiratory muscle training. Between Sessions 3 and 4, you will be asked to complete breathing exercises called inspiratory muscle training (abbreviated as IMT below). You will be placed into either: a) a "fake" inspiratory muscle training group that completes breathing exercises at a low effort that does not cause the breathing muscles to get stronger, or b) a "real" inspiratory muscle training group that completes breathing exercises at an effort which causes the breathing muscles to get stronger. Half of the subjects who agree to participate in the study will be placed randomly in each group, and you will not be told which group you are placed.

For both groups, you will be asked to complete six weeks of real or fake IMT. You will be asked to complete three IMT sessions a week, with at least 48 hours between sessions. You will be given a handheld IMT device to take home and you will be asked to download a smartphone app which pairs via Bluetooth with the IMT device. The daily IMT procedure starts with three maximal effort inspirations against a resistance for about 12-15 seconds. From these maximal inspirations, the smartphone app will draw a graph on the screen which shows a target inspiratory pressure to try and meet during the remainder of the training session. You will then be asked to complete the day's training by inspiring against a set amount of resistance in an attempt to match the graph displayed on the app. The resistance will be set to either 80% (real IMT group) or 15% (fake IMT group) of your maximal inspiratory pressure, and you will not be told which level of resistance is set on the IMT device. After a rest period of between 15 and 60 seconds, you will be asked to complete additional inspiratory repetitions until the app indicates that you were unable to inspire within 10% of the required pressure. A typical IMT session includes 6-18 inhalations and takes between 8 and 15 minutes. Before you leave the lab with the device for the first time, an investigator from our study will teach you how to use the device correctly and follow the procedures listed above. You will have an opportunity to practice this in the lab, and investigators from our study can monitor how well you are doing remotely through the smartphone app.

Cycle training log. You will be given a link to an online training log, where we will ask you to record the number of minutes cycled each day and a subjective rating of the effort of the training session. It is estimated that this will take approximately 2 minutes per day.

RISKS OF TAKING PART IN THE STUDY:

While in the study, the risks are:

Submaximal (low and moderate effort) and maximal (all-out effort) exercise tests of healthy individuals, as described by the American College of Sports Medicine, present little risk to the subject and do not require medical clearance for subjects under the age of 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. One death occurs for roughly every 880,000 man hours of submaximal exercise in apparently healthy individuals. 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.

All face masks will be cleaned in detergent and antibacterial solution after each use, minimizing the risk of virus transmission between subjects.

When breathing the low oxygen gas, you may feel lightheaded, which can be quickly reversed by removing the face mask and breathing room air. The low oxygen gas does not have substantial moisture, and may dry out and irritate your throat.

There are no known risks of completing inspiratory muscle training using the IMT device.

There is a potential risk of loss of confidentiality.

BENEFITS OF TAKING PART IN THE STUDY:

The benefits to participation that are reasonable to expect are information regarding your 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 the study upon request.

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 IU 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

Should you qualify for the study, you will be paid a $50 gift card for completing the entire study. Should you quality for the study then withdraw from the study for any reason, you will be paid a $20 gift card. Payment is made via a gift card, which will be given to you at the end of your final testing session.

COMPENSATION FOR INJURY

In the event of physical injury resulting from your participation in this research, necessary medical treatment will be provided to you at your own expense. 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, by signing this form 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. If you cannot reach the researcher during regular business hours (i.e. 8:00AM-5:00PM), please call the IU Human Subjects Office at (812) 856-4242 or (800) 696-2949.

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 IU Human Subjects Office at (812) 856-4242 or (800) 696-2949.

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 investigators or Indiana University.

Your participation may be terminated by the investigator without regard to your consent in the following circumstances: an abnormal response to exercise testing or an inability to complete the exercise tests.

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 Name: _____

Signature of Person Obtaining Consent: _____
Date: _____