The Acute Response to Sprint Interval Exercise and Moderate Intensity Continuous Exercise in Adults with and without Airway Hyperresponsiveness

By

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ABSTRACT

Introduction: Sprint interval exercise (SIE) has been proposed as a time efficient way to improve physical activity levels; however, SIE has not been studied in adults with airway hyperresponsiveness (AHR). *Methods:* Eight adults with AHR and eight adults without AHR completed both SIE (4x30 second sprints at 7.5% body weight) and moderate intensity continuous exercise (MICE) (20 minutes at 65% peak power output). Spirometry, ventilatory measures, tissue oxygenation, and subjective responses were assessed prior to, during, and following exercise. *Results:* The decline in forced expiratory volume in one second was similar following SIE and MICE. Ventilatory measures, tissue oxygenation, and subjective responses were similar in the AHR group compared to those without AHR. Differences were observed in affect, breathlessness, and exertion between SIE and MICE at the onset of exercise. *Conclusions:* SIE appears to be feasible in adults with AHR; this may have implications for exercise prescription in this population.

Keywords: Sprint interval exercise, Airway Hyperresponsiveness, Lung function, Asthma, Affect

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TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

LIST OF ABBREVIATIONS

ACQ…….. Asthma Control Questionnaire

AHR…….. Airway hyperresponsiveness

ATS……American Thoracic Society

miniAQLQ……mini Asthma Quality of Life Questionnaire

BR……..Breathing reserve

COPD……..…..Chronic obstructive pulmonary disease

EIBC……..Exercise-induced bronchoconstriction

EVH……...Eucapnic voluntary hyperpnea

FEV_1…….. Forced expiratory volume in one second

FS……...Feeling scale/affect

HIIE……...High intensity interval exercise

HR…… Heart rate

MICE…….Moderate intensity continuous exercise

MPO……..Mean power output

MVV……..Maximum voluntary ventilation

NIRS……..Near infrared spectroscopy

O_2……... Oxygen

PACES……..…… Physical Activity Enjoyment Questionnaire

PPO……Peak power output

RPD……...… Rating of perceived dyspnea

RPE……...…… Rating of perceived exertion

RR……..……Respiratory rate

SIE……..… Sprint interval exercise

TSI…….…… Tissue saturation index

T_{Vent}……...… Ventilatory threshold

V_E……...……Expired minute ventilation

V_T…….……..… Tidal volume

VO_2….……...…… Oxygen consumption

W……...… Watts

CHAPTER 1: INTRODUCTION

1.1 THESIS INTRODUCTION

Asthma is a chronic respiratory disease that is characterized by chronic airway inflammation and defined by the variable presence of asthma symptoms including wheezing, shortness of breath, chest tightness and coughing [1]. Asthma symptoms can be triggered by various factors including pollution, change in weather, allergens and exercise [1]. Asthma is also characterized by airway hyperresponsiveness (AHR), which is defined as an over-reaction to constrictor agonists (i.e. allergens and other triggers) in the airways [2]. Individuals without asthma can also have AHR, particularly elite athletes; however, the pathogenesis may be different compared to individuals with classical asthma [3]. The prevalence of asthma is 8.1% in Canada and 4.3% worldwide [4, 5]. However, the worldwide prevalence is likely higher because asthma is often under-diagnosed, particularly in many third world countries [5]. Importantly, up to 90% of adults with asthma experience exercise-induced bronchoconstriction (EIBC) [6, 7]. EIBC may be a barrier to the adoption and maintenance of regular exercise in adults with asthma, as it is associated with coughing, wheezing, shortness of breath and discomfort [8].

In adults with asthma, continuous exercise training has been shown to lead to improvements in aerobic fitness [9-12], number of symptom free days [9, 10], quality of life measures [9, 12], reduced bronchial hyperresponsiveness [12] and reduced number of hospital visits required [13]. The most commonly cited barrier to exercise is lack of time [14]. Sprint interval exercise (SIE) has recently been studied as a time efficient method to improve physical activity levels. SIE involves short, supramaximal bouts of exercise separated by longer recovery periods. Due to the high minute ventilation (V_E) required for SIE, and the association of high V_E with EIBC, it is unclear if SIE would be feasible for individuals with AHR.

1.2 THESIS RESEARCH QUESTIONS

Research Questions

1. Is SIE more asthmogenic than moderate intensity continuous exercise (MICE) in adults with AHR?
2. Is O_2 delivery impaired in the active muscle during exercise due to impaired V_E in adults with AHR?
3. Is the acute ventilatory response to SIE and MICE different in those with and without AHR?
4. Are the subjective responses to SIE and MICE different in adults with AHR compared to those without AHR?

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CHAPTER 2: LITERATURE REVIEW

Literature Review

The following literature review will cover the pathogenesis of exercise-induced bronchoconstriction (EIBC), the airway response to exercise in adults with and without airway hyperresponsiveness (AHR), the benefit of exercise in adults with AHR, and potential role of interval exercise. The review will also explore research related to tissue oxygenation and affect during interval and continuous exercise.

2.1 TERMINOLOGY

Throughout this thesis, several terms are used to describe different aspects of airway disease and exercise. These terms are defined below.

Asthmogenic: This term is used to refer to the overall response related to acute bronchoconstriction. Specifically, it is used when referring to instances where individuals experience a decline in forced expiratory volume in one second (FEV_1) and signs/symptoms associated with airway constriction.

Airway Hyperresponsiveness (AHR): This term is used to reflect an airway that is over reactive to constrictor agonists (i.e. pollution, allergens, and exercise).

Exercise-induced bronchoconstriction (EIBC): This term is used to reflect the physiological event of bronchoconstriction occurring due to an increase in minute ventilation (V_E) associated with exercise.

The naming for different exercise protocols discussed in this thesis is based on the suggestions of Weston et al. and Gibala et al. to standardize terminology [1, 2]. Specifically *high intensity interval training (HIIT)* or *high intensity interval exercise (HIIE)* will refer to protocols where the target intensity is ‘near maximal’ or between 80 and 100% of maximal heart rate. *Sprint interval training (SIT)* or *sprint interval exercise (SIE)* will refer to protocols that involve ‘all out’ or ‘supramaximal’ efforts that are greater than the workload required to elicit 100% of maximal exercise capacity.

2.2 MECHANISMS THAT TRIGGER EXERCISE-INDUCED BRONCHOCONSTRICTION

The mechanisms responsible for EIBC are not completely understood; however, two theories are commonly discussed. These two theories have to do with the thermal and osmotic changes during and immediately following exercise. During and following exercise, high V_E prevents all inspired air from being fully saturated and warmed in the upper airways [3, 4]. Regarding the thermal change, because there is not time to warm air in the upper airway, more energy is expended in the lower airway to warm inspired air. Heat is transferred from the surrounding airway to the inspired air, leading to a lower temperature of the airway during exercise [3]. Following exercise, the rapid rewarming of the airway leads to increased blood flow to capillaries in the airway, possibly intensifying the obstruction [3]. Regarding the osmotic change, as a result of the high V_E associated with exercise, there is an increase in evaporative water loss from the airway, which may stimulate degranulation of mast cells [4]. This in turn leads to increased release of inflammatory mediators such as histamine, leukotrienes, prostaglandin, and platelet activating factors [4]. These mediators then stimulate bronchial smooth muscle contraction [4].

The thermal and osmotic hypotheses act in conjunction with chronic levels of inflammation that occur in individuals with asthma. As a result of EIBC, there may be impairments in the ability for enough gas exchange to occur in the alveoli. This is important to consider because different exercise protocols (eg. variable intensity, continuous vs. interval) have different effects on V_E; thus, certain forms of exercise may be more suitable for individuals with AHR.

2.3 AIRWAY RESPONSE TO EXERCISE IN INDIVIDUALS WITHOUT HYPERRRESPONSIVENESS

In individuals without AHR, little or no change in lung function has been observed from pre to post-exercise [5, 6]. Buono conducted two studies that reported an unchanged FEV_1 and forced expiratory flow in the middle (50%) of expiration following a maximal exercise test [5]. Cordain et al. also saw no changes in FEV_1 following exercise to maximal heart rate and at 85% of maximal heart rate [6]. Since individuals in these studies do not

have AHR, EIBC would not occur; therefore airflow was not limited. Both Buono and Cordain et al. did report an increased residual volume following exercise [5, 6]. It has been speculated that this is due to expiratory muscle fatigue after exercise; therefore, participants are not able to forcefully expire as much air and are left with a greater amount of air trapped in the lungs [6]. Alternatively, Buono proposed that the increased residual volume may be due to slight increases in fluid around the alveoli, decreasing small airway diameter and causing airways to close sooner during forced expiration, trapping more air [5].

Overall, effects on lung function in individuals without AHR are negligible.

2.4 AIRWAY RESPONSE TO EXERCISE IN INDIVIDUALS WITH HYPERRRESPONSIVENESS

In individuals with AHR, many studies have looked at the effects of an aerobic exercise bout on airway constriction. Chhabra & Ojha had adults with AHR exercise on a cycle ergometer for five minutes at 85% of maximum predicted heart rate [7]. Spirometry was then performed at 0, 4, 8, 15, 30, and 60 minutes post-exercise and then hourly for the next 7 hours. All participants showed an "early asthmatic response", observed as a decline in FEV_1 greater than 10%, occurring on average four to six minutes after exercise [7]. In addition to the "early asthmatic response" some participants also showed a "late asthmatic response" between three and eight hours post exercise; however, the significance of this late response is unclear [7].

In a study by Bikoc et al., adults with AHR performed an exercise challenge test on a treadmill. The challenge test was based on a protocol of six to eight minutes at an intensity eliciting 80% to 90% of maximum predicted heart rate; however, the specific intensity or duration was not provided [8]. The exercise challenge caused a significant decline in FEV_1 in 13 of 22 participants ($\geq$10% decline) [8]. This may indicate that not all the adults actually experienced EIBC, since the sample was selected just based on having reversibility following administration of salbutamol (a bronchodilator).

In a third study by Leff et al., individuals (aged: 15 to 45 years) with mild asthma performed an exercise challenge test on a treadmill [9]. The challenge involved running on a treadmill at an intensity eliciting 80% to 90% of predicted maximum heart rate for six

minutes while breathing dry air [9]. On average, participants experienced a decline in FEV_1 between 35% and 40% from pre to post-exercise.

Exercise challenge testing has been used as a diagnostic tool for EIBC. Treadmill and cycle ergometer tests for six to eight minutes are common methods to assess EIBC by maintaining V_E of 40 to 60% of maximum for at least four minutes [10].

All of the studies mentioned above focused on continuous exercise; however, research is lacking on the acute responses to different exercise protocols (i.e. SIE) among individuals with AHR.

2.5 BENEFITS OF EXERCISE IN ADULTS WITH AIRWAY HYPERRRESPONSIVENESS

Due to the discomfort and asthma-related symptoms that often occur as a result of exercise, adults with AHR may not be adequately active. Previous research has reported mixed findings, with some research indicating that adults with asthma are less physically active than their age-matched non-asthmatic peers [11-14], while others have reported no differences between physical activity levels in individuals with and without asthma [15]. Some research has shown that individuals with asthma may have higher physical activity levels than those without asthma [16-19]. Regardless of how adults with asthma compare to those without asthma, physical activity levels are generally suboptimal in Canada. Only 15.4% of Canadians adults are meeting the minimum recommended 150 minutes of moderate to vigorous intensity aerobic exercise per week [20, 21].

Aerobic training has been studied in those with AHR and participants did not experience adverse effects due to the training [22]. Several studies have shown that exercise leads to improvements in aerobic fitness [23-26], number of symptom free days [23, 24], quality of life measures [23, 26], reduced bronchial hyperresponsiveness [26] and reduced number of hospital visits required [27]. Mendes et al. also found decreased inflammatory cell counts in the sputum and decreased exhaled nitric oxide levels after training, both indicating decreased airway inflammation at rest [24]. These training programs all used continuous exercise interventions that ranged in intensity from 60 to

80% maximal oxygen consumption (VO_{2max}) or 80 to 90% maximal heart rate and ran for 6 to 12 weeks. Exercise sessions were either in the pool, on a treadmill or a cycle ergometer.

Clearly, aerobic training is well tolerated in individuals with AHR and provides a number of cardiorespiratory and symptom related benefits. However, it remains unknown as to whether interval training will have similar benefits.

2.6 POTENTIAL BENEFIT OF INTERVAL EXERCISE

In the past ten years, there has been a 'boom' in research related to SIE and HIIE. The main barrier to exercise cited is a lack of time [28]. SIE and HIIE are more time efficient methods of exercise compared to classic aerobic training methods, otherwise known as moderate intensity continuous exercise (MICE). MICE protocols involve a constant workload performed for the entire session. An example of MICE is 40 to 60 minutes of cycling at 65% VO_{2peak} [29]. HIIE involves "near maximal" intervals or between 80 and 100% of maximal heart rate [1]. An example of a HIIE protocol from O'Neill et al. is ten, one minute intervals at 90% peak power output (PPO) with one minute recovery periods at 10% PPO separating each interval [30]. SIE involves short, "supramaximal" or "all out" intervals separated by longer recovery periods [1]. A classic model uses four to six "Wingate" sprints, each separated by four to five minute recovery periods. A "Wingate" is typically performed at 7.5% of body weight resistance on a cycle ergometer for 30 seconds. As an example, in a training study, participants progressed from four to six sprints per session, with sprints at 0.075 kilograms (kg)/kg of body mass, separated by 4.5 minute recovery periods at 30 Watts (W) [31]. A typical SIE or HIIE session lasts 20 minutes with only two minutes of intense exercise for SIE and ten minutes for HIIE. Different modifications have been investigated, specifically to SIE, such as using treadmill running [32], and shortening a session even further down to ten minutes [33]. Interval exercise may be beneficial for adults with AHR as it could allow time for V_E to recover. These recovery periods may allow time for the airway to saturate with water and warm up thus, limiting bronchoconstriction.

A study conducted on soccer players with AHR (aged: 10 to 14 years) implemented high intensity interval training [34]. The children either completed normal aerobic-based practices (control group) or high intensity interval training-based practices for eight weeks.

For the interval-based practices, an approximate ratio of 100 seconds of low intensity exercise to 20 seconds of high intensity exercise was used. Following the intervention, children in the high intensity interval training group had longer distances covered during the six minute walk test and less of a reduction in FEV_1 following this test when compared to themselves at baseline as well as compared to the control group, who saw no improvements in either measure. The results of this study show that interval training may be even more beneficial than aerobic training in individuals with AHR.

In a review of different warm up strategies by Stickland et al., it was reported that EIBC following a subsequent exercise bout is reduced if a variable or high intensity interval warm-up is performed compared to a continuous warm-up [35]. Therefore, HIIE or SIE may be similarly effective in attenuating the decline of FEV_1 following exercise.

In healthy populations, sprint interval training has been shown to have similar benefits to moderate intensity continuous training in regards to skeletal muscle metabolism and cardiorespiratory fitness [1]. Sprint interval training has been done safely by sedentary, overweight/obese men and women [33, 36, 37]. In these populations, improvements in VO_{2peak} [33, 36, 37], resting blood pressure [33, 37], mitochondrial enzyme activity [33], insulin sensitivity index [37], and a lower heart rate and higher stroke volume at the same exercise intensity [36] following training have been observed. Unfortunately, SIE has not been studied in adults with AHR; therefore it remains unknown whether this form of exercise can be implemented within this population.

2.7 HIGH INTENSITY INTERVAL EXERCISE COMPARED TO MODERATE INTENSITY CONTINUOUS EXERCISE

Recent work from our laboratory has shown that MICE (20 minutes at 65% PPO) may be more asthmogenic than HIIE (ten, one minute intervals at 90% PPO separated by one minute recovery periods at 10% PPO) [30]. The decline in FEV_1 following an acute bout of HIIE ($\mathbf{\Delta}FEV_1$=-7.8%) was lower compared to the decline in FEV_1 following an acute bout of MICE ($\mathbf{\Delta}FEV_1$=-14.1%) [30]. It was hypothesized that V_E was able to recover, preventing airway cooling and drying, thus attenuating the symptoms of AHR associated with high V_E.

It appears the HIIE is well tolerated among adults with AHR; however, it is important to examine how different intensities and patterns of exercise impact airway caliber in individuals with AHR. In particular, SIE has not been studied among individuals with AHR. SIE may pose a unique challenge among individuals with AHR due to the high V_E required during sprints, leading to airway drying, desaturation, and airway injury.

2.8 VENTILATORY RESPONSES TO SPRINT INTERVAL EXERCISE

Before a sprint interval training intervention can be implemented, the effects of a single bout of SIE must be examined. Particularly in adults with AHR, where ventilatory responses are important. The acute response to SIE has not been examined in individuals with AHR; however Freese et al. examined V_E in 12 young, recreationally active adults [38]. SIE involved four, 30 second sprints at 8.8% kg/kg fat free mass with four minutes of active recovery between sprints. Oxygen uptake (VO_2), heart rate and V_E all reached levels above 80% of estimated maximal values during the sprint or in the 20 seconds following [38]. Unfortunately, maximal tests were not done in this study to use as a reference; therefore, estimated values had to be used based on the general population. In this study, V_E peaked at a higher level in the second sprint compared to the first sprint. Sprints two, three and four all had a similar peak in V_E. Although not specifically stated, it appears from data presented that V_E returned to near baseline levels within 3 minutes following each sprint [38].

The high levels of V_E observed in the Freese et al. study are important as The American Thoracic Society (ATS) recommends reaching V_E of 40 to 60% of predicted maximum voluntary ventilation (MVV) for six to eight minutes to elicit EIBC during exercise testing [10]. Clearly, V_E higher than 80% of maximum, as observed in the Freese et al. study would be high enough to elicit a response, if maintained. In addition, from pilot work in our laboratory, V_E during sprints reaches levels near the maximum V_E from a maximal exercise test. This high V_E may be enough to cause a clinically significant decline in FEV_1 in adults with AHR. However, since V_E is able to recover between intervals, the bronchoconstriction response may be reduced.

Another factor influencing the amount of bronchoconstriction relates to epinephrine secretion and its role as a bronchodilator. During exercise, epinephrine is

secreted with an increase in secretion occurring at higher intensities [39]. Since SIE is at such a high intensity, epinephrine secretion may help to limit bronchoconstriction. Therefore, research needs to be done to determine if a balance can be found between high V_E leading to bronchoconstriction, and recovery periods and epinephrine secretion possibly preventing it.

2.9 MEASUREMENT OF TISSUE OXYGENATION

Impairments in V_E due to EIBC may lead to impairments in gas exchange between the alveoli and bloodstream. This may cause hemoglobin in the blood to not be fully saturated. During exercise, this may lead to impaired oxygen (O_2) delivery to active muscles and therefore reduced power output compared to if the cardiovascular system were the limiting factor, which is generally the case in healthy populations [40]. A method commonly used to measure O_2 status in the tissue is near-infrared spectroscopy (NIRS). NIRS makes use of light in the near infrared range of the electromagnetic spectrum to gain insight in to the oxygenation status of tissues. Different molecules have unique characteristics regarding the absorption of light in the near-infrared range. Absorption characteristics of hemoglobin, myoglobin and cytochrome oxidase in the near infrared range make it possible to quantify the relative concentrations of the oxygenated and deoxygenated forms of these molecules [41]. The relative contribution of hemoglobin and myoglobin cannot be distinguished with NIRS because their absorbance patterns are so similar in the near-infrared range [42]. Generally the saturation of hemoglobin and myoglobin are grouped together and just referred to as deoxygenated hemoglobin and oxygenated hemoglobin. Cytochrome oxidase also absorbs light in the near infrared range, but the relative concentration of it is much less than that of hemoglobin in vivo and so it is often not discussed when interpreting NIRS signals [43, 44].

Overall, with NIRS, relative concentrations of oxygenated, deoxygenated, and total hemoglobin can be determined. With certain NIRS systems that incorporate spatially resolved spectroscopy, which makes use of multiple interoptode distances to measure differences in light intensity, an additional measure of tissue saturation index (TSI) can be determined. TSI represents the ratio of oxygenated hemoglobin to total hemoglobin, which indicates the O_2 saturation in the tissue. With the use of NIRS, information regarding O_2

delivery to and utilization by the tissue can be studied. During exercise, sufficient V_E is crucial in order to maintain adequate O_2 delivery to the working muscles. Insufficient O_2 delivery compromises the body's ability to maintain exercise; however, limited research exists on the O_2 delivering capacity in adults with AHR [45]. This will be important to study in adults with AHR, because of the potential ventilatory impairments, muscle fatigue might occur as a result of impaired O_2 delivery.

2.10 TISSUE OXYGENATION DURING INTERVAL EXERCISE

NIRS has been used to study muscle oxygenation changes during SIE and other similar repeated sprint exercises. Buchheit et al. had trained cyclists perform six, 30 second "all out" sprints, each separated by two minutes of passive recovery [46]. In this study, it was found that a) the peak TSI decrease during sprints was an average of -27%, and b) muscle deoxygenation levels and reoxygenation rates increased with sprints (i.e. the tissue was becoming more deoxygenated at the onset of each sprint and was reoxygenated faster following each sprint) [46]. Since there was a decline in power with subsequent sprints but greater deoxygenation, it was suggested that the fatigued muscle may require more energy to produce the same amount of work compared to a non-fatigued muscle [46]. Also, it was found that there was a decrease in the deoxygenation rate with multiple sprints. Since VO_{2peak} did not decrease, it was suggested that O_2 delivery was improved at the onset of the final sprints, indicating a priming effect from previous sprints [46]. Finally, in this study it was observed that TSI returned to baseline levels during the two minute recovery periods. However, previous research has shown that phosphocreatine stores only return to approximately 65% after two minutes of recovery [47]. This may contribute to the observed power declines with multiple sprints, since phosphocreatine is a major contributor to adenosine triphosphate turnover, at least at the onset of a sprint [47].

Two other studies had participants perform ten, ten second sprints at 0.9 Newtons/kg body mass, each separated by 30 seconds of rest. Participants performed these sprints under normoxic (fraction of inspired O_2 =21%) and hypoxic (fraction of inspired O_2=13%) conditions [48, 49]. Interestingly, this could be used as a comparison for individuals with AHR if not enough O_2 can be inspired during EIBC. In the Billaut & Buchheit study, it was observed that under hypoxic conditions, muscle deoxygenation was

12.5% greater than under normoxic conditions [49]. This is in contrast to the previous thought that muscle O_2 extraction reaches a maximum under normoxic conditions during the sprint, because of the plateau in oxygenation level that has been observed [50]. The greater deoxygenation under hypoxia did not impact sprint performance for the first sprints; however total work done was decreased during hypoxia [49]. This suggests that the active muscle still may be able to extract sufficient O_2 under hypoxic conditions and therefore, there may be other factors leading to a decrease in performance. One of the factors suggested in this study was the limited reoxygenation capacity under hypoxic conditions [49]. This indicates that O_2 delivery was not sufficient following exercise in order to adequately reoxygenate the muscle in preparation for the next sprint. Previous studies have suggested that muscle O_2 supply is related to the ability to resynthesize phosphocreatine following exercise, potentially leading to a decrease in subsequent sprint ability [51].

Another factor related to this decreased sprint ability suggested by Smith & Billaut was related to cerebral O_2 delivery [48]. It was observed that cerebral deoxygenation occurred earlier and to a larger extent under hypoxia [48]. This may be related to the impact of O_2 availability on motor neuron activity, and the relationship with mechanisms protecting from muscle fatigue [52]. Regarding muscle oxygenation in this study, there was no difference observed in deoxygenation or reoxygenation changes between the normoxia and hypoxia conditions, which is in contrast to the previously mentioned differences in the Billaut & Buchheit study [48, 49]. It is unclear why these discrepancies may have been observed, since both studies employed the same ten, ten second repeated sprint protocol under the same conditions. Having a longer recovery period than the 30 seconds between sprints used in these studies may allow muscle and cerebral oxygenation changes observed during hypoxia to be limited.

2.11 TISSUE OXYGENATION DURING EXERCISE IN INDIVIDUALS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE

Work in individuals with chronic obstructive pulmonary disease (COPD) has shown that these individuals have slower VO_2 and cardiac output kinetics but faster muscle deoxygenated hemoglobin kinetics compared to age matched controls, indicating a mismatch of O_2 delivery and utilization [53]. Recent studies in patients with COPD have

looked at whether pharmacological or other pulmonary interventions can lead to an improvement in peripheral muscle oxygenation. Bronchodilator use led to reductions in dynamic hyperinflation, slower kinetics and less muscle deoxygenation during subsequent exercise, indicating a better matching of O_2 delivery and utilization at the muscle [54]. The better matching may be due to a redistribution of blood flow to the active muscle away from the respiratory muscles [54]. Another method studied to unload respiratory muscles was proportional assisted ventilation, which implements flow and volume assists [55]. During proportional assisted ventilation, there was less of a decrease in oxygenated hemoglobin, TSI was improved, and total hemoglobin was increased when exercising compared to sham ventilation [55]. This supports the idea that unloading respiratory muscles in patients with COPD can lead to improvements in active muscle blood flow and the delivery and utilization of O_2.

It is not known if a mismatch of O_2 delivery and utilization would occur in individuals with AHR during EIBC. Previous research has shown that dynamic hyperinflation can occur in adults with AHR [56]. Therefore, through the use of bronchodilators it is possible that load could be taken off the respiratory muscles potentially improving muscle oxygenation. However, it remains unclear as to whether this mechanism would be similar among those with AHR as to those with COPD.

2.12 AFFECT DURING INTERVAL EXERCISE

In addition to understanding the physiological response to SIE, it is critical to determine whether adults with AHR enjoy SIE. This is important when considering exercise prescription and long-term adherence to exercise. One way to study this is by looking at affective responses (mood states, perceived enjoyment, feelings during exercise) to exercise. It has been shown that affect during an acute bout of exercise is predictive of future physical activity behaviour [57, 58]. During SIE, affect has been shown to decrease significantly with successive sprints [59]. Saanijoki et al. observed lower affect throughout SIE (four to six, 30 second all out bouts, with four minutes recovery between) compared to MICE (30 to 60 minutes continuous cycling at 60% PPO) among sedentary, middle age adults [60]. Affect scores have been shown to decline throughout both HIIE and MICE but higher affect scores have been observed during HIIE, indicating more enjoyment [61]. In

contrast to this, higher affect scores have been observed during MICE (40% PPO for 20 minutes) compared to HIIE (ten, one minute intervals at 100% PPO separated by one minute intervals at 20% PPO) [62]. This finding is likely due to the MICE session being at a low intensity and the HIIE session being very intense. When participants completed a MICE session at 80% PPO, affect was less than that observed during the HIIE [62]. In the O'Neill et al. study mentioned previously, participants had higher affect scores during HIIE (ten, one minute intervals at 90% PPO separated by one minute recovery periods at 10% PPO) compared to MICE (20 minutes at 65% PPO), indicating they felt better during HIIE [63].

In addition to measuring affect during exercise, perceived enjoyment is an important component in order to ensure future exercise participation. It has been reported that enjoyment was higher for a high intensity interval running bout compared to continuous running [64]. Previous studies have reported higher enjoyment for SIE compared to MICE [65], no significant differences [66, 67], or lower enjoyment [68]. The Astorino et al. study was done in adults with spinal cord injury and used arm ergometry [65]. SIE involved eight, 30 second "all out" bouts separated by two minutes of recovery at 10% PPO, and MICE involved 25 minutes at 45% PPO [65]. Crisp et al. employed a MICE protocol of 30 minutes of cycling at each participants point of maximal fat oxidation [66]. For SIE, they used the same MICE protocol but had participants perform a four second "all out" sprint every two minutes [66]. Sim et al. compared MICE (30 minutes at 60% VO_{2peak}) to SIE (15 seconds at 170% VO_{2peak} alternated with 60 seconds at 32% VO_{2peak}) in sedentary, overweight men [67]. Foster et al. compared MICE (20 minutes at 90% of ventilatory threshold) to SIE (eight intervals of 20 seconds at 170% VO_{2max} alternated with 10 seconds of rest) in untrained, college aged adults [68]. The differences observed in enjoyment are likely due to the different modes of exercise, populations, and specific protocols compared. Our understanding of the affective response to interval exercise in adults with AHR is currently limited; therefore, future research is required.

2.13 GAPS IDENTIFIED

There are a number of areas that have not been addressed in the literature and therefore require further investigation. First, SIE has not been examined in adults with AHR, either as part of a training study, or as an acute session. Due to the impact that V_E has on airway caliber, the degree of bronchoconstriction that occurs as a result of SIE will be important to study. Secondly, EIBC has been observed during exercise; however, it is not known if this would lead to impairments in ventilatory measures or O_2 delivery to the working muscle. Thirdly, while a limited number of studies have examined subjective responses to SIE, none were in individuals with AHR. Since EIBC may occur during exercise in this population, the degree of breathlessness and affect may be influenced. If EIBC occurs during exercise, this could also lead to signs/symptoms typical of asthma (eg. coughing, wheezing, sore throat), which may impact the subjective responses to exercise.

2.14 OBJECTIVES

The overall objective of this research is to determine the acute response to SIE in adults with confirmed AHR. Specifically, the purpose of this research is to determine if:

1. SIE is more asthmogenic than MICE based on the decline in FEV_1 and the presence of signs and/or symptoms of EIBC during and/or following the different exercise protocols.
2. O_2 delivery and utilization is impaired in adults with confirmed AHR during SIE and MICE, based on tissue saturation throughout exercise. Data will be compared between adults with and without AHR to determine if impairments are present.
3. the acute responses to SIE and MICE are different in those with and without AHR, based on changes in FEV_1, V_E during exercise, tissue oxygenation during exercise, and power output.
4. subjective responses and enjoyment are different between SIE and MICE in adults with AHR, and if these responses are different compared to adults without AHR.

2.15 HYPOTHESES

1. It is difficult to hypothesize whether SIE will be well tolerated by adults with AHR given that SIE includes periods of high V_E but also includes recovery periods with low V_E. During exercise there is an increase in epinephrine secretion, which is a known bronchodilator, with greater secretion at higher intensities [39]. However, given that the V_E required for SIE is near maximal, it is expected that this will be sufficient to lead to a clinically significant decline in FEV_1. In addition, it is hypothesized that FEV_1 will decline more following SIE compared to MICE due to the high V_E during and following each sprint.
2. It is hypothesized that TSI in the vastus lateralis during exercise will be impaired, thus decreasing less, in adults with AHR who experience EIBC during SIE sessions.
3. It is hypothesized that FEV_1 will decline more in adults with AHR following both types of exercise compared to adults without AHR. It is also hypothesized that TSI will be impaired and PPO will be lower by the final sprint in adults with AHR who experience EIBC compared to those without AHR due to impairments in V_E and gas exchange in the lung. This may lead to a decrease in O_2 available at the working muscle, thus decreasing performance.
4. It is hypothesized that affect (FS), ratings of perceived dyspnea (RPD), and ratings of perceived exertion (RPE) will be worse during SIE than MICE due to the high peak V_E and maximal effort required in adults with AHR. It is also hypothesized that enjoyment will be lower following SIE again due to the uncomfortable maximal efforts required. Finally, it is hypothesized that subjective responses will be worse in adults with AHR than adults without AHR because of discomfort that may occur as a result of EIBC.

Note: Questionnaires/scales that were created for use in the current study and data collection sheets are available in Appendix A. The signs/symptoms scale (appendix A1), eligibility questionnaire (A2), demographic questionnaire (A3), and late phase asthma symptom questionnaire (A4) have not been assessed for validity or reliability. All other questionnaires/scales used are published elsewhere.

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CHAPTER 3: RESPIRATORY RESPONSES TO SPRINT-INTERVAL EXERCISE IN ADULTS WITH AIRWAY HYPERRESPONSIVENESS

3.1 ABSTRACT

Purpose: Sprint interval exercise (SIE) has gained popularity as a time efficient method for increasing physical activity levels; however, the acute respiratory response has not been studied in individuals with airway hyper-responsiveness (AHR). The purpose of the current study was first, to determine the acute airway response to SIE and moderate intensity continuous exercise (MICE) in adults with AHR, and second, to compare acute ventilatory and oxygen delivery responses in adults with and without AHR. *Methods:* Eight adults (22.3 ± 3.0 years) with AHR and eight adults (22.3 ± 3.0 years) without AHR (comparison group) completed both SIE (4x30 second sprints at 0.075kg/kg of body weight separated by 4.5 minutes of active recovery) and MICE (20 minutes at 65% peak power output) sessions. Spirometry was assessed during exercise and for 20 minutes after SIE and MICE. Ventilatory parameters (expired minute ventilation (V_E), tidal volume (V_T), respiratory rate (RR), and V_E/maximum voluntary ventilation (MVV)) were assessed via expired gas analysis, and tissue saturation index (TSI) was collected continuously throughout SIE and MICE. *Results:* The decline in forced expiratory volume in one second was similar following SIE (8.6 ± 12.6%) and MICE (9.0 ± 9.3%) in adults with AHR. During SIE and MICE there were no significant differences in V_E, V_T, RR, V_E/MVV, and TSI when comparing those with and without AHR. *Conclusions:* These findings suggest that SIE and MICE affect airway responsiveness to a similar extent, and that neither protocol leads to impairment in respiratory measures or oxygen delivery during exercise. These findings have implications for exercise prescription in adults with AHR.

3.2 INTRODUCTION

Airway hyperresponsiveness (AHR) is an over-reaction to constrictor agonists, such as allergens and other triggers (eg. pollution and exercise), in the airways [1]. It is a characteristic feature of asthma. Up to 90% of adults with asthma experience exercise-induced bronchoconstriction (EIBC) [2, 3]. Individuals without asthma may also experience EIBC [4-7]; this is particularly common in athletes.

EIBC is associated with coughing, wheezing, shortness of breath and discomfort in response to exercise [8]. The mechanisms that are responsible for EIBC are not completely understood; however, the osmotic and thermal changes that occur during and following exercise help explain these mechanisms. Specifically, the high minute ventilation (V_E) achieved during exercise prevents inspired air from being fully saturated and warmed in the upper airways [9, 10]. This leads to a lower airway temperature during exercise, with increased blood flow to re-warm the airway following exercise, possibly intensifying the obstruction [9]. In addition, extra evaporative water loss to saturate inspired air may stimulate degranulation of mast cells, releasing inflammatory mediators, thus stimulating bronchial smooth muscle constriction [10]. It is not clear whether *sustained* periods of high V_E are needed to trigger EIBC or whether *short periods of near maximal* V_E are sufficient to trigger EIBC. This is important to consider because different exercise protocols (eg. variable intensity, continuous vs. interval) have different effects on V_E and possibly their ability to trigger EIBC.

Although EIBC typically occurs after exercise, some studies have shown that it can occur during exercise as well [11-13]. In these studies, the exercise protocols varied from a 45 minute cross country skiing race at 90-100% of maximal heart rate [11], to 36 minutes of constant load cycling at 50% of maximal power [12], or 36 minutes of alternating 6 minute periods at 40% and 60% of maximal power [12]. The total volume (duration and intensity) of exercise may be an important factor in determining whether EIBC will occur during exercise. When EIBC does occur during exercise, there may be impairments in gas exchange, thus affecting hemoglobin saturation, and ultimately leading to impairments in oxygen delivery to the working muscle. In individuals with chronic obstructive pulmonary disease (COPD), such mismatch between oxygen delivery and utilization in the working muscle has been reported [14]. It is not known if such a mismatch would occur in

individuals who experience EIBC during exercise and whether a mismatch would be evident among those who have EIBC, but do not experience a decline in forced expiratory volume in one second (FEV_1) until after exercise.

Interval exercise, which allows time during recovery intervals for the airway to saturate with water and to warm up, may limit bronchoconstriction. In fact, a review examining different warm-up strategies found that the decline in lung function was attenuated following a subsequent exercise bout if a variable or high intensity interval warm-up was performed [15]. This suggests that both the intensity and duration of the warm-up may be important for limiting EIBC. In a recent study from our laboratory, a high intensity interval exercise (HIIE) session (alternating 1 minute intervals at 90% peak power output (PPO) and at 10% PPO, for 20 minutes) elicited less of a decline in FEV_1 than a moderate intensity continuous exercise (MICE) time-matched protocol (65% PPO) (-7.1% ± 8.3 vs. -14.8% ± 12.2, for HIIE and MICE, respectively) [16]. V_E was not measured in this study; however, according to heart rate data, the heart rate during MICE reached a higher level after seven minutes and stayed higher for the remainder of exercise compared to the HIIE protocol. Therefore, the ability for heart rate and likely also for V_E to recover during the HIIE session may explain the differences observed in FEV_1 decline.

Another popular form of interval exercise, sprint interval exercise (SIE), involves short, supramaximal sprints separated by longer recovery periods. V_E during or just following a supramaximal sprint is expected to be above 80% of estimated maximal values in individuals without EIBC [17]. The American Thoracic Society (ATS) recommends reaching a V_E of 40 to 60% of predicted maximum voluntary ventilation (MVV) for six to eight minutes to elicit EIBC during an exercise challenge test [18]. Clearly, a V_E higher than 80% of maximum, as observed in the Freese et al. (2013) study, would be high enough to elicit EIBC; but the duration and intermittent recovery of V_E may attenuate the airway response as observed with HIIE [16]. Thus, it is unclear as to whether the short lasting, high peaks in V_E that occur in SIE would still lead to EIBC. The primary purpose of the current study was to determine the acute airway response to SIE and MICE in individuals with AHR. A secondary purpose was to compare acute ventilatory and oxygen delivery responses between those with and without AHR during SIE and MICE. It was hypothesized that the near maximal V_E obtained during SIE would lead to a greater decline in FEV_1

compared to MICE. In individuals who experience EIBC during exercise, it was hypothesized that an impairment in tissue oxygenation would occur. For individuals who do not experience EIBC during exercise, it was hypothesized that there would not be any impairment in tissue oxygenation, and that all respiratory responses would be similar to the healthy controls without AHR.

3.3 METHODS

Participants

Participants were screened for eligibility if they were between the ages of 18-44 years. Adults over 44 years of age were excluded to reduce the possibility of other comorbidities, such as COPD, that would affect measures of interest. Inclusion was further limited to adults engaged in regular physical activity (150 minutes of moderate to vigorous intensity exercise per week) to ensure participants were able to complete the exercise sessions. Participants in the AHR group were required to have self-reported physician diagnosed asthma, a current prescription for a short-acting bronchodilator, and a positive response to the AHR challenge in session 1 (described below). Participants in the comparison group were eligible if they had no previous physician diagnosis of asthma, and a negative response to the AHR challenge. All participants provided written consent prior to beginning the study. The study was approved by the University of Ontario Institute of Technology's Research Ethics Board. A flow diagram representing participants in each group is shown in Figure 1.

Study Design

This was a randomized cross-over study comparing those with and without AHR. All participants completed four sessions, each separated by a minimum of 48 hours to reduce the impact of a refractory period following EIBC. *Session 1* was a eucapnic voluntary hyperpnea (EVH) challenge to confirm AHR, followed by an exercise familiarization session. In *session 2*, participants completed an incremental to maximum exercise test. *Sessions 3 and 4* were the exercise sessions completed in random order.

Spirometry

Throughout each session, participants completed lung function measurements using a handheld spirometer (EasyOne diagnostic spirometer, ndd Medizintechnik AG,

Switzerland). Lung function measurements assessed were FEV_1, and FEV_1 % predicted based on the Third National Health and Nutrition Examination Survey (NHANES III) reference values [19]. Prior to the first measurement, participants were given verbal instruction as well as a demonstration of a forceful exhale followed by a full inhalation. For baseline measurements, participants performed a minimum of three trials, in accordance with the ATS Guidelines [20]. For measurements during the SIE and MICE sessions and following all sessions, two acceptable trials were performed. During SIE, spirometry was performed 3 minutes following each sprint (minutes 3.5, 8.5, 13.5, and 18.5) and at corresponding time points during MICE to assess the EIBC response during exercise. Following all sessions, spirometry was performed at 1, 5, 10, 15, and 20 minutes post session. The decline in FEV_1 was calculated as follows:

% Fall in FEV_1 = 100 [FEV_1 pre-session – FEV_1 post-session] / FEV_1 pre-session

The highest FEV_1 value at each time point was used for the calculation of FEV_1 decline. The decline in FEV_1 at minutes 3.5, 8.5, 13.5, 18.5 during exercise, and the maximum decline following exercise were used for statistical analysis.

Expired gas analysis

Expired gas was collected through a pneumotachograph and analyzed using an automated gas collection system (Parvo Medics 2400, USA). Data were linearly interpolated to yield second-by-second values and the rate of oxygen consumption (VO_2), rate of carbon dioxide production (VCO_2), V_E, tidal volume (V_T), and respiratory rate (RR) were analyzed. During SIE and MICE, the mouthpiece was removed for minutes 3.5-4.5, 8.5-9.5, 13.5-14.5, and 18.5-20 in order to perform spirometry, therefore corresponding data points were removed from analysis.

MVV was calculated based on ATS Guidelines using 40 times the baseline FEV_1 from the maximal exercise test for the comparison group or from post-bronchodilator FEV_1 for the AHR group [18]. V_E/MVV was calculated throughout exercise in order to assess if the pulmonary system was limited. V_E/MVV is typically ≤80%; however, if the pulmonary system is a limiting factor, a V_E/MVV ratio >80% would be expected [21]. All ventilatory measures were calculated at 0.5, 5.5, 10.5, and 15.5 minutes (corresponding with peak V_E observed at the end of each sprint), by averaging the values of the 5 seconds surrounding each time point. The values at these time points were used for statistical analysis.

Near infrared spectroscopy (NIRS)

A two-wavelength (765 and 855 nm), continuous wave NIRS system using spatially resolved spectroscopy was used to measure tissue saturation index (TSI) (Oxymon MK III, The Netherlands). TSI was monitored continuously throughout the maximal exercise test and both exercise sessions. The NIRS probe was placed over the muscle belly of the vastus lateralis muscle, 12 cm from the knee joint, along vertical axis of thigh. A vinyl sheet was used to cover the probe to limit infrared light from the environment affecting the signal. The probe and vinyl sheet were then secured in place with a tensor bandage. Data was sampled at 50 Hz and then down sampled to yield second-by-second data. The distance between the transmitter and receiver was set at 4.0 cm. The background and details of NIRS is described elsewhere [22]. Briefly, light in the near infrared range is used to determine relative concentrations of oxygenated and deoxygenated hemoglobin, due to their different absorption patterns. TSI represents a ratio of oxygenated hemoglobin to total hemoglobin, which indicates oxygen saturation in the tissue. For MICE, TSI values for each participant were normalized to the average of the 30 to 60 seconds prior to the start of exercise during warm-up, with this baseline value representing 100%. For SIE, baseline 30 to 60 seconds prior to the start of sprint one was again used as 100%. Peak desaturation (the lowest five second period of TSI) at the end of sprint one was used as 0% so that changes observed across sprints could be compared. TSI was calculated at peak desaturation during SIE (approximately 10-15 seconds in to each sprint) based on visual inspection, and at corresponding time points during MICE, by averaging the values of the 5 seconds surrounding each time point. The values at these time points were used for statistical analysis.

Other measurements

During session 1, participants completed the Asthma Control Questionnaire (ACQ). This questionnaire consists of seven questions and is used to measure the level of asthma control in adults. The ACQ has high test-retest reliability (r=0.90) and has been shown to be a valid measure (r=0.73) of asthma control [23]. Power output was collected throughout MICE and during each sprint during SIE using Monark Anaerobic Test Software (Monark Exercise AB, Poland). One participant was excluded from analysis for power output during SIE due to an error with the power collection software during sprint

1. Peak power output during SIE was reported as the highest power output for any sprint (sprint 1 in 10/15 participants). Skinfold thickness of the thigh was measured midway between the proximal border of the patella and the inguinal crease (hip), on the anterior midline of the thigh using calipers (Harpenden skinfold caliper, Baty International, United Kingdom).

Session 1: Eucapnic Voluntary Hyperpnea

Participants were asked to refrain from taking short-acting bronchodilators at least 8 hours prior to testing, and long-acting bronchodilators at least 48 hours prior to testing. The EVH was conducted based on methods previously described by Anderson et al. [24]. Briefly, participants completed baseline lung function measurements using a handheld spirometer followed by six minutes of hyperventilating a dry air mixture (5.0% CO_2, 21.0% O_2, balance N_2) at 25 to 30 times their baseline FEV_1. Spirometry was assessed again at 1, 5, 10, 15, and 20 minutes post-challenge with a positive response to the challenge determined if the greatest decline in FEV_1 was ≥12%. Following the EVH, once FEV_1 returned to near baseline or the participant took their short-acting bronchodilator, participants were familiarized with the cycle ergometer (Monark Ergomedic 894E, Monark Exercise AB, Poland), performing two stages of the maximal exercise test and a sprint that would be done during SIE.

Session 2: Maximal Exercise Test

Participants were asked to refrain from taking short-acting bronchodilators at least 8 hours prior to testing. Following baseline lung function measurements, participants with AHR were instructed to take two puffs of their short-acting bronchodilator. Spirometry was re-assessed to determine reversibility 15 minutes following medication inhalation. Reversibility was defined as a ≥12% and 200 mL increase in FEV_1 from baseline [25].

An incremental to maximum protocol was used with the initial stages occurring for two minutes each at 80, 120, and 160 W and then the workload was increased by 16 W every minute until exhaustion. Participants cycled at 80 rpm for the duration of the test. PPO was recorded as the final stage completed and was used for determining the intensity for the subsequent MICE session. The ventilatory threshold (T_{Vent}) was calculated using the V-slope method and confirmed using ventilatory equivalents [26].

Sessions 3 and 4: Exercise Sessions

Prior to both exercise sessions, participants were asked to refrain from taking short-acting bronchodilators at least 8 hours prior to testing. The SIE and MICE protocols started with a two minute warm-up between 50 and 60 W at 50 to 60 rpm. For the MICE session, following the warm-up, participants cycled at 80 rpm at 65% PPO for 20 minutes. Following the MICE session, participants completed a 5 minute cool down at a self-selected cadence and resistance. For the SIE session, 15 seconds prior to the end of the warm-up, resistance was removed in order to prepare the cycle ergometer for the sprint. Five seconds prior to the end of the warm-up, participants were instructed to cycle as fast as possible with no resistance. Participants then completed the 30 second sprint (at 0.075kg/kg of body weight) with time updates occurring with 20, 10, and 5 seconds remaining in the sprints; no other encouragement was provided during the sprints. Participants completed four sprints with 4.5 minutes of unloaded cycling at 40 to 60 rpm between (20 minutes of total exercise). Following SIE, no additional cool-down was completed, because following the final sprint, the 4.5 minutes of unloaded cycling served as a cool-down. The SIE session was based on previous research using similar protocols [27, 28].

Data Analysis

Means and standard deviations were calculated for all continuous variables to describe the sample. Independent samples t-tests were used to compare descriptive data between groups. Three factor (condition (SIE or MICE) x time (during or following exercise) x AHR status (with AHR or comparison group)) repeated measures analysis of variance tests were used to determine if there were differences within and between exercise protocols for FEV_1, V_E, V_T, RR, V_E/MVV, and TSI. When sphericity had been violated, Greenhouse-Geisser corrections were used. Interactions with $p \leq 0.10$ were examined further to determine where differences occurred using post hoc pairwise comparisons and t-tests. This value, $p \leq 0.10$, was chosen to reduce the likelihood of missing differences since the study was underpowered for secondary variables. All statistics were done in IBM SPSS statistics 23.0 (Armonk, NY) and statistical significance was declared at $p<0.05$. Effect sizes were calculated using G*Power 3.1.10 to report the magnitude of difference between SIE and MICE FEV_1 changes.

Based on effect sizes for the FEV_1 decline (HIIE: 7.1 ± 8.3%; MICE: 14.8 ± 12.2%; d=0.71) calculated from O'Neill et al [16]., a sample size was calculated for an F-test repeated-measures within factors ANOVA using α=0.05, β=0.80, two groups and four repetitions. A total sample size of six was required. Sample size required for between factors was a total of 12 (six per group), we therefore recruited 16 to account for dropouts.

3.4 RESULTS

Group characteristics

Sample characteristics are presented in Table 1. There were no significant differences between the AHR group and the comparison group for any variable presented. Of note, there were six males and two females in both groups, both groups had an average age of 22.3 ± 3.0 years, and VO_{2max} of approximately 41 ml/kg/min. Three of the participants with AHR were also using inhaled corticosteroids (Flovent or Symbicort). All participants with AHR had a prescription for a short-acting bronchodilator.

Pulmonary function

Individual responses of FEV_1 to each session are shown in Table 2, with participant numbers. Mean FEV_1 responses are shown in Figure 2. Participants with AHR experienced a greater decline in FEV_1 following the EVH compared to the comparison group (30.4 ± 17.3 vs. 5.3 ± 2.5, p=0.001). The difference between the decline in FEV_1 following MICE in the AHR compared to the comparison group (9.0 ± 9.3 vs. 2.8 ± 2.0, p=0.087) was approaching significance. There was no statistically significant difference in the decline in FEV_1 between SIE and MICE in the AHR group (p=0.81, d=0.03).

Two participants experienced a clinically significant decline in FEV_1 (≥10%) following SIE, while three others had a ≥9% decline. Two participants also experienced a clinically significant decline in FEV_1 following MICE, with one other experiencing a ≥9% decline. Of the five participants who experienced a ≥9% decline following SIE, four had an ACQ score >1, indicating poorly controlled asthma. Two of the three participants who experienced a ≥9% decline following MICE also experienced a ≥9% decline following SIE. Participants 5 and 7 both experienced bronchodilation or minimal bronchoconstriction following MICE (2.4 and -2.3) and SIE (-0.8 and -8.4), possibly due to the presence of

mild bronchoconstriction prior to exercise during these sessions. The FEV_1 of participant 5 was 5.51 L at baseline for the EVH compared to 4.97 L for MICE and 5.13 L for SIE. FEV_1 for participant 7 was 3.31 L at baseline for the EVH compared to 3.11 L for MICE and 2.99 L for SIE. These participants also did not experience any bronchoconstriction during MICE or SIE.

Only participant 4 experienced a clinically significant level of reversibility (≥12%). This participant also experienced the greatest decline in FEV_1 following the EVH, SIE, and MICE. One participant experienced a clinically significant decline in FEV_1 during SIE. Two other participants also experienced a decline ≥9% during SIE. Only one participant with AHR experienced a clinically significant decline during MICE. All participants with AHR experienced a greater than or equal to decline in FEV_1 during SIE compared to MICE, with the exception of participant 7 who experienced bronchodilation during both; however there was no significant difference ($p=0.11$, $d=0.42$). Since only one participant experienced a ≥10% decline during SIE and MICE, analysis of ventilatory and NIRS data separated by those who experienced EIBC and those who did not, was not performed.

There was no significant three way interaction observed for FEV_1; however, there was a significant two way interaction between time and AHR status ($p=0.044$). The difference between maximum FEV_1 decline following exercise in the AHR compared to the comparison group (8.8 ± 10.7 vs. 3.2 ± 3.9, $p=0.059$) was approaching significance.

Ventilatory measures

Mean ventilatory measures are shown in Figure 3. There were no significant three way interactions for V_E, V_T, RR, or V_E/MVV. Significant two way interactions between condition and time were observed for all ventilatory measures (all $p<0.003$). These interactions were not analyzed further because differences between conditions and time points were expected due to the different protocols of SIE and MICE. The two way interaction between time and AHR status for V_E/MVV ($p=0.082$) was approaching significance. No differences between the AHR and comparison group were identified for any time point.

The maximum V_E from the maximal exercise test was not significantly different between the AHR (135.7 ± 34.4 L/min) and comparison group (124.6 ± 32.7 L/min). V_E at T_{Vent} was also not significantly different between the AHR (67.5 ± 17.7 L/min) and comparison group (60.0 ± 12.8 L/min). For sprints two to four, all participants were above T_{Vent} at peak V_E, with 11/16 participants also above T_{Vent} during sprint one. The average peak V_E for each participant during SIE was 107.1 ± 32.8 L/min. For MICE, all participants were above T_{Vent} from minute 15.5 on, with 13/16 participants above at 10.5 minutes and 8/16 above from 5.5 minutes to the end.

Tissue oxygenation

Representative TSI data is shown in Figure 4. There was no significant three way interaction for TSI ($p=0.371$). There was a significant two way interaction between condition and time ($p<0.001$). There were no significant two way interactions between condition and AHR status ($p=0.523$) or time and AHR status ($p=0.406$).

Power output

There was no significant interaction between time and AHR status ($p=0.306$) for PPO during SIE. There was a statistically significant effect of time ($p<0.001$). Based on pairwise comparisons, sprint one PPO was greater than sprints three ($p=0.034$) and four ($p<0.001$), sprint two PPO was greater than sprint four ($p<0.001$), and sprint three PPO was greater than sprint four ($p=0.013$). No significant differences in PPO were observed between the AHR and comparison group for sprint one (AHR: 758.3 ± 190.9 W vs. Comparison: 665.6 ± 198.9 W, $p=0.37$), sprint two (AHR: 673.8 ± 135.5 W vs. Comparison: 658.2 ± 155.0 W, $p=0.84$), sprint three (AHR: 616.5 ± 140.2 W vs. Comparison: 601.5 ± 129.6 W, $p=0.83$), or sprint four (AHR: 559.3 ± 140.3 W vs. Comparison: 548.4 ± 147.0 W, $p=0.89$). A similar pattern was observed for mean power output (MPO) with no significant differences between the AHR and comparison groups for sprint one (AHR: 550.2 ± 101.9 W vs. Comparison: 493.2 ± 166.0 W, $p=0.43$), sprint two (AHR: 488.3 ± 84.4 W vs. Comparison: 478.1 ± 114.5 W, $p=0.85$), sprint three (AHR: 436.2 ± 91.8 W vs. Comparison: 428.1 ± 103.5 W, $p=0.87$), or sprint four (AHR: 400.7 ± 96.5 W vs. Comparison: 412.5 ± 108.9 W, $p=0.83$). PPO and MPO profiles are shown in Appendix A9.

Power collection did not work during MICE for two participants so results regarding MICE power are based on 14/16 participants (seven in each group). Prescribed power output was 138.3 ± 29.0 W for the AHR group and 150.7 ± 29.7 W for the comparison group. Due to participants not maintaining 80 rpm throughout, actual power was 133.1 ± 23.9 W and 141.5 ± 35.4 W for the AHR and comparison groups, respectively.

3.5 DISCUSSION

We aimed to determine whether the acute FEV_1 response was different following SIE or MICE in adults with AHR, and whether ventilatory parameters would respond differently to such exercise when comparing adults with and without AHR. Our primary finding is that the decline in FEV_1 was similar following SIE (8.6 ± 12.6%) and MICE (9.0 ± 9.3%) in adults with AHR. Clinically relevant responses to the protocols were similar as well. Two participants with AHR had a ≥10% decline in FEV_1 following SIE, while three others had a ≥9% decline. Two participants also had a ≥10% decline in FEV_1 following MICE, while one other had a ≥9% decline. Our secondary finding is that there were no significant differences in V_E, V_T, RR, and V_E/MVV during SIE or MICE when comparing those with and without AHR. These findings suggest that individuals with AHR tolerate SIE and MICE to a similar extent, and that neither protocol leads to impairment in respiratory measures or oxygen delivery during exercise. These findings have implications for exercise prescription in this population.

Pulmonary function

Among those with AHR, the maximum decline in FEV_1 observed following SIE and MICE was similar. Following each exercise protocol, two participants had a clinically significant decline (≥10%); with one participant having a decline following both protocols. Another three participants had a borderline significant decline (≥9%) following SIE and another one following MICE. In addition, four participants had a greater decline following SIE and four had a greater decline after MICE. The decline in FEV_1 following MICE noted in the present study was less (9.0 ± 9.3%) than that observed in a previous study from our laboratory (14.8 ± 12.2%) [16]. This may be because participants in the current study had better asthma control (0.86 ± 0.76 vs. 1.6 ± 0.5) or because they had higher

cardiorespiratory fitness (VO_{2max}=40.4 ± 4.9 ml/kg/min vs. 34.6 ± 8.1 ml/kg/min). The latter is important as research has shown that higher cardiorespiratory fitness is associated with less airway responsiveness [29]. The O'Neill et al. study reported less of a decline in FEV_1 following a HIIE protocol compared to MICE [16]. When considering the results of the current study, that is, SIE and MICE led to a similar decline in FEV_1, it may be that HIIE provides an ideal middle ground for limiting EIBC. This could be because HIIE does not require the same peak V_E as SIE, but still allows recovery periods for V_E.

The similar decline in FEV_1 may also be related to the relatively high intensity of the MICE protocol. During the MICE protocol, all participants were working above T_{Vent} by minute 17.5. Above T_{Vent}, V_E increases at an accelerated rate, possibly leading to faster drying and cooling of the surrounding airway, increasing EIBC [21]. With a lower intensity MICE protocol, EIBC may have been reduced, and differences between SIE and MICE may have been significant. It should also be noted that in the present study, two participants with AHR experienced bronchodilation during SIE and MICE, which may have skewed the means. These participants remained bronchodilated or had minimal bronchoconstriction following both sessions. Both of these participants had lower baseline FEV_1 prior to SIE and MICE than they did for the EVH. This may indicate that these participants had some bronchoconstriction when they arrived in the laboratory, and that exercise improved their airway caliber.

Although there were no statistically significant differences in the decline in FEV_1 following exercise, when comparing the during exercise FEV_1 decline between each participants' SIE and MICE session, seven of the eight participants with AHR experienced a greater decline during SIE than MICE. This decline may be related to the high peak V_E experienced during SIE and subsequent rewarming and saturating of the airways during the recovery period as discussed previously [9, 10]. It is unlikely that this decline is due to participants being out of breath and not performing spirometry properly because V_E was lower during SIE than MICE when spirometry was performed. During MICE, since V_E is constantly elevated there is no time for the airway to rewarm and saturate until following exercise. A clinically significant level of EIBC during exercise may not have occurred in the majority of participants as exercise in this study was just 20 minutes. In studies where EIBC occurred during exercise, exercise protocols of 36 minutes or longer were used [11,

12]. Beck et al. observed a statistically significant decline in FEV_1 (mean of 6%) from baseline after 18 minutes of constant load exercise at 50% of maximal exercise capacity while breathing dry air [12]. It is not clear how many participants experienced a clinically meaningful decline though as the range was 15% to -2% decline [12]. In the Rundell et al. study, participants were cross country skiing in the cold at 90 to 100% maximal heart rate (HR_{Max}) for approximately 42 minutes [11]. The cold weather and high intensity may have contributed to 9 of the 18 participants experiencing ≥10% decline in FEV_1 at some point during exercise [11]. The mechanisms behind EIBC experienced by these individuals may be different as only 4 of the 18 participants had previously been diagnosed with EIBC and all were elite athletes [11].

Despite the shorter duration of exercise in the current study, by minute 17.5 of MICE, participants with AHR were on average above 21 times their baseline FEV_1, the V_E suggested by Parsons et. al for exercise challenge testing to assess EIBC [30]. Participants were also on average at 51.1 ± 5.5% of their MVV at minute 17.5 of MICE, in the 40 to 60% range suggested by the ATS [18]. One participant with AHR and one without were also not able to complete the full 20 minutes of MICE (likely due to lower cardiorespiratory fitness levels) and workload had to be reduced so that these participants still completed 20 minutes of exercise. Another reason we did not see a decline in FEV_1 during exercise could be because exercise was conducted in a normal laboratory environment, that is, participants were not breathing cold-dry air. Future research could utilize cold or dry air breathing to maximize the effect and better determine differences between the protocols.

Exercise ventilation

When examining V_E during SIE and MICE, it was observed that average peak V_E was lowest for sprint one and similar for sprints two, three, and four in both groups. It may be that the two minute warm up protocol used in this study was not sufficient to prepare participants for sprint one. The lower V_E during sprint one may also relate to the lower contribution of the aerobic system during sprint one. Bogdanis reported an increase from 34 ± 2% to 49 ± 2% in aerobic energy contribution between two, 30 second sprints with four minutes of recovery [31]. Repeated sprint exercise has also been shown to cause accumulation of metabolites (such as hydrogen ions (H^+)) leading to metabolic acidosis, and therefore a subsequent increase in V_E for sprints after sprint one [32]. In general, for

all sprints, average peak V_E/MVV was above 45% and average peak V_E was above 70% of maximum V_E from the maximal exercise test, with the exception of the AHR group who were only at 57% of maximum V_E during sprint one. These results differ from Freese et al. who reported V_E values above 80% of predicted maximum [17]. The Freese et al. results were based on an estimate of maximum V_E. Differences may also be related to the specific protocols chosen (8.8% kp/kg of fat free mass vs. 7.5% kg/kg body weight in the current study), or the recovery periods (four minutes vs. 4.5 minutes in the current study).

For MICE, V_E was above T_{Vent} for all participants by minute 17.5 and already above T_{Vent} in 8/16 participants by minute 5.5. An intensity of 46-64% of VO_{2max} has previously been recommended for moderate intensity exercise prescription [33]. In the current study, VO_2 at minute 5.5 during MICE was at 69.4 ± 6.9% and 74.8 ± 9.9% of VO_{2max} for the AHR and comparison groups, respectively. Therefore MICE, in the current study may be considered higher than a typical moderate intensity program. Future research should look at whether there is a certain V_E level, such as above T_{Vent}, important for determining if EIBC will occur in adults with AHR.

There were no significant differences in V_E, V_T, RR, or V_E/MVV between those with AHR and the comparison group. This was unsurprising because only one participant experienced a >10% decline during SIE and MICE, with two others experiencing >8% decline during SIE and/or MICE. Since the majority of participants did not experience significant bronchoconstriction (and some even experienced bronchodilation during exercise), it is not expected that any impairment in ventilation would occur. It has been previously shown that even when individuals with AHR experience bronchoconstriction prior to exercise, ventilatory measures still increase to the same level as when no bronchoconstriction precedes exercise [34]. In contrast to this, another study has shown reduced V_E and V_T at peak exercise when bronchoconstriction precedes exercise compared to a control or bronchodilation condition [35]. The Mahler et al. study was done in older adults and used methacholine as the method of bronchoconstriction which may contribute to the differences observed. Results from the current study support the idea that most individuals with AHR are still able to adequately increase V_E to support demand. It is however unclear if individuals that experience EIBC during exercise would have impairments in V_E or would have a different method of reaching the required V_E. Future

research assessing changes in ventilatory parameters in individuals who do experience EIBC during exercise is needed.

Tissue oxygenation

Tissue saturation data from a representative participant from each group is shown in Figure 4. There were no differences in peak desaturation observed between any of the sprints or when comparing the AHR and comparison groups. This is in contrast to Buchheit et al., who observed a greater decrease in tissue saturation during sprint six compared to sprint one and two [36]. This may be because of the two extra, 30 second sprints performed and only having two minutes compared to four minutes between sprints to recover.

A decrease of TSI was observed across sprints in some participants; however, due to the large inter-individual differences in responses, no significant differences were observed. It is worth noting that only one participant experienced significant EIBC *during* SIE and MICE. It was hypothesized that if participants experienced EIBC, there may be an impairment in hemoglobin saturation in the respiratory system leading to impairments in oxygen extraction in the working muscle. Future research, with larger samples, and using cold or dry air to maximize the airway response should examine if there is an impairment in oxygen extraction when EIBC occurs.

Power output

Most participants reached their highest peak power during the first sprint (n=11). This was as expected. Among those who did not achieve their peak during the first sprint, it is possible that participants were not fully warmed up or despite being familiarized with the protocol, were not sure of how to complete the sprint. Despite this, peak power output decreased from sprint one to sprint four (p.0.001), but there were no significant differences between power output from sprint one to sprint two. A similar pattern was observed for average power output. Sprint one average power was greater than sprint two ($p=0.047$), sprint three ($p<0.001$), and sprint four ($p<0.001$). All participants were able to complete all sprints, with one experiencing mild nausea and six experiencing mild to moderate light headedness.

During MICE, participants were required to maintain 80 rpm in order to maintain the required power output. Participants on average were below the required power output by 2.0% and 3.6% for the AHR and comparison groups, respectively. Given the intensity

of the MICE protocol used, the power output was still sufficient to elicit V_E necessary to cause EIBC.

Strengths and Limitations

There are a number of strengths and limitations that are important to mention. A strength of the current study was the use of a randomized cross over design, allowing participants to act as their own control by completing both SIE and MICE sessions on separate days. Another strength is that the AHR and comparison group were well matched. Specifically, there were an equal numbers of males and females in each group, both groups were the same age, and both groups had the same VO_{2max}. Another strength involves measurement of ventilatory parameters throughout exercise to examine whether differences in V_E between SIE and MICE were related to changes in FEV_1.

Having participants breathe through a mouthpiece, thus forcing mouth breathing, may be a limitation. Previous research has shown that mouth breathing may trigger a greater EIBC response compared to nasal breathing [37]. Participants in the current study therefore may have been more likely to experience EIBC during or following exercise. A second limitation relates to the sample size of eight participants per group. The large effect size for the FEV_1 decline following HIIE and MICE from the O'Neill et al. study used to calculate sample size for the current study may have left us underpowered to detect differences between groups. It also prevented us from doing any sex-based analyses. Previously, sex based differences have been observed for the prevalence of expiratory flow limitation, work of breathing, and airway hyperresponsiveness in women during exercise [38, 39]. Secondly, the results are also limited to young adults who are currently active, and to adults with mild AHR, therefore future research will also need to study the feasibility in individuals of different ages, fitness levels, and asthma severity levels. Thirdly, the EVH test used to confirm airway hyperresponsiveness may be overly sensitive and therefore participants with mild AHR may have been included [40]. This could explain why some participants did not experience EIBC following SIE or MICE and may also contribute to why nine individuals with no history of asthma had a positive response to the EVH. Finally, the MICE protocol used may have been too intense as some participants struggled to complete 20 minutes. A lower intensity MICE protocol would require lower V_E and would be less likely to cause EIBC.

In conclusion, SIE and MICE produced similar airway responses in the AHR group following exercise, despite different patterns of V_E throughout exercise. There were also no differences in ventilatory measures between those with and without AHR during SIE or MICE. Future research is needed to better understand the effect of different intensities and durations of exercise on airway responsiveness among those with different severities of AHR.

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Table 1: Sample characteristics for the AHR and comparison group (mean ± SD)

	AHR Group (n=8)	Comparison Group (n=8)
Sex (# of males)	6	6
Age (years)	22.3 ± 3.0	22.3 ± 3.0
Height (cm)	172.3 ± 6.5	171.1 ± 7.3
Weight at baseline (kg)	79.0 ± 12.6	72.4 ± 12.3
BMI (kg/m^2)	26.5 ± 3.3	24.8 ± 4.5
Waist Circumference (cm)	88.1 ± 9.7	82.3 ± 9.1
Left thigh skinfold (cm)	2.4 ± 1.0	1.8 ± 1.0
VO_{2max} (ml/kg/min)	40.4 ± 4.9	41.7 ± 5.5
Peak Power Output from maximal exercise test (Watts)	222.0 ± 45.6	224.0 ± 48.4
T_{Vent} (% of VO_{2max})	72.2 ± 6.2	69.1 ± 5.2
Peak Power Output from SIE session (Watts)	761.6 ± 187.9	718.7 ± 141.8
%predicted FEV_1	95.6 ± 15.6	103.5 ± 8.7
Long term inhalation of corticosteroid (# of 'yes')	3	N/A

No significant differences were observed between groups

Table 2: Individual participant data for FEV_1 responses to each exercise session

	ACQ score	Baseline FEV_1 (% predicted)	EVH decline (% decline in FEV_1)	Reversibility (% change in FEV_1)	MICE decline (% decline in FEV_1 post-MICE)	SIE decline (% decline in FEV_1 post-SIE)	Decline during MICE (% decline in FEV_1)	Decline during SIE (% decline in FEV_1)
AHR Group								
Participant 1	0	96	13.3 (10)	-2.9	11.9 (1)	9.3 (5)	8.2	9.3
Participant 2	0	101	23.8 (5)	-5.3	9.9 (10)	1.3 (5)	0.5	0.5
Participant 3	1.86	111	45.0 (5)	3.8	4.7 (1)	9.4 (1,5)	3.4	9.9
Participant 4	1.14	96	63.0 (1)	-16.9	29.2 (5)	34.1 (1)	11.2	28.1
Participant 5	0.42	114	13.4 (20)	-2.9	2.4 (20)	-0.8 (15)	-7.0	-2.0
Participant 6	1.14	101	38.7 (1)	-6.9	8.4 (5)	13.7 (10)	1.9	5.0
Participant 7	0.42	78	24.8 (1)	-4.9	-2.3 (1)	-8.4 (10)	-4.2	-8.4
Participant 8	1.86	68	20.9 (5)	-1.2	7.9 (20)	9.8 (1)	4.2	7.4
Average for AHR group	0.86 ± 0.76	95.6 ± 15.6	30.4 ± 17.3	-4.7 ± 5.9	9.0 ± 9.3	8.6 ± 12.6	2.3 ± 6.0	6.2 ± 10.8
Comparison Group								
Participant 9		108	5.4 (15)		1.6 (1,15)	-0.8 (15)	-1.6	-2.5
Participant 10		115	5.6 (5)		5.5 (15)	3.1 (15)	2.9	2.3
Participant 11		112	0 (1)		1.8 (5)	-2.6 (5)	1.3	2.3
Participant 12		101	4.3 (5)		0.4 (15)	13.0 (5)	2.1	2.6

Participant 13		108	6.8 (1)		5.7 (1)	6.6 (20)	2.4	2.3
Participant 14		100	8.7 (5)		1.1 (10)	1.5 (5)	-0.6	-1.1
Participant 15		93	5.7 (1)		3.9 (1)	8.5 (5)	3.9	10.0
Participant 16		91	6.3 (10)		2.8 (1)	-0.8 (5)	0.5	0
Average for comparison group		103.5 ± 8.7	5.3 ± 2.5 *		2.8 ± 2.0**	3.6 ± 5.4	1.4 ± 1.9	2.0 ± 3.7
Effect Size (between groups)		0.62	2.03		0.92	0.52	0.20	0.52

*denotes a difference between those the AHR and the comparison group, $p<0.05$; ** $p<0.10$

Figure 1 – Overview of study design

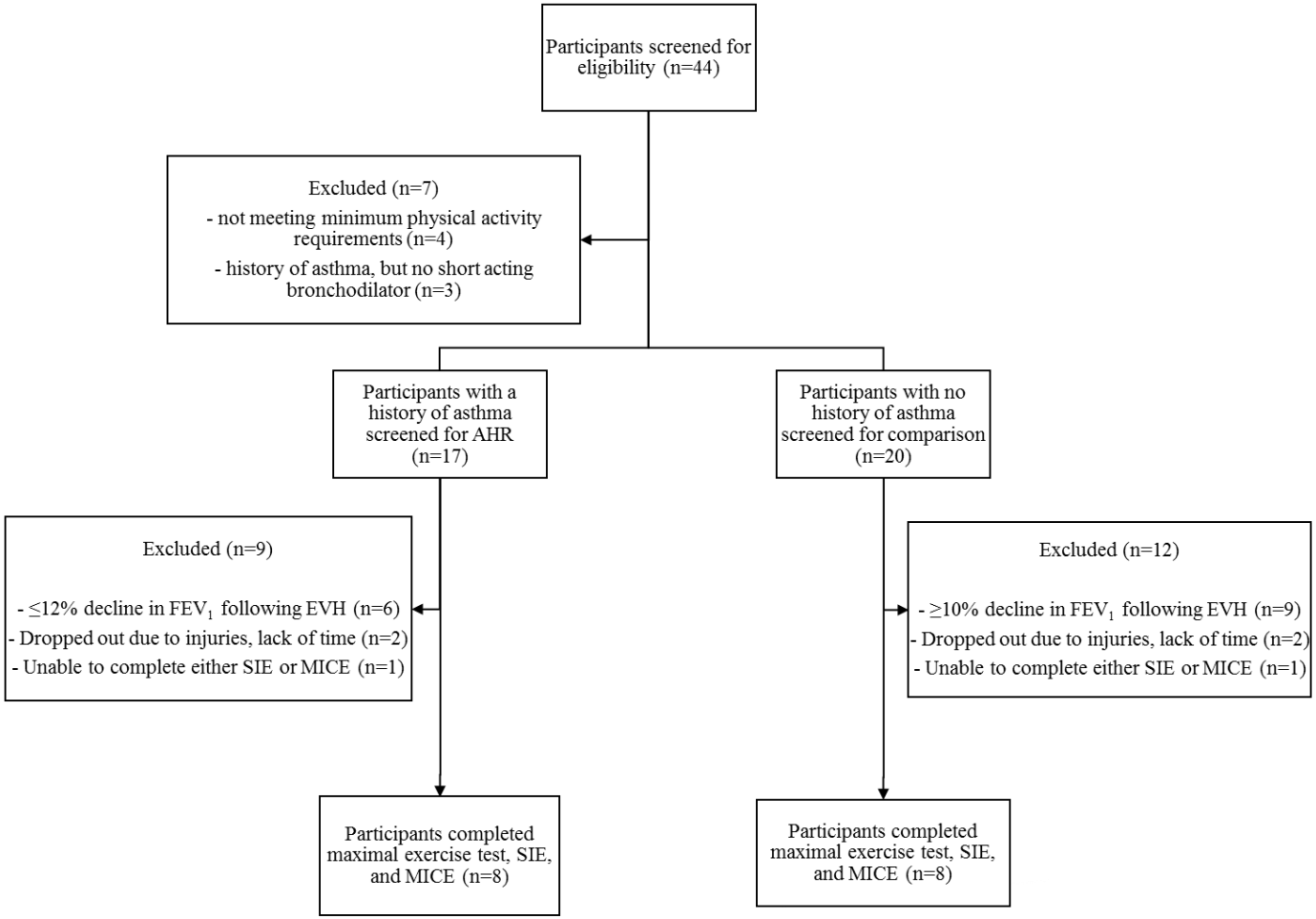
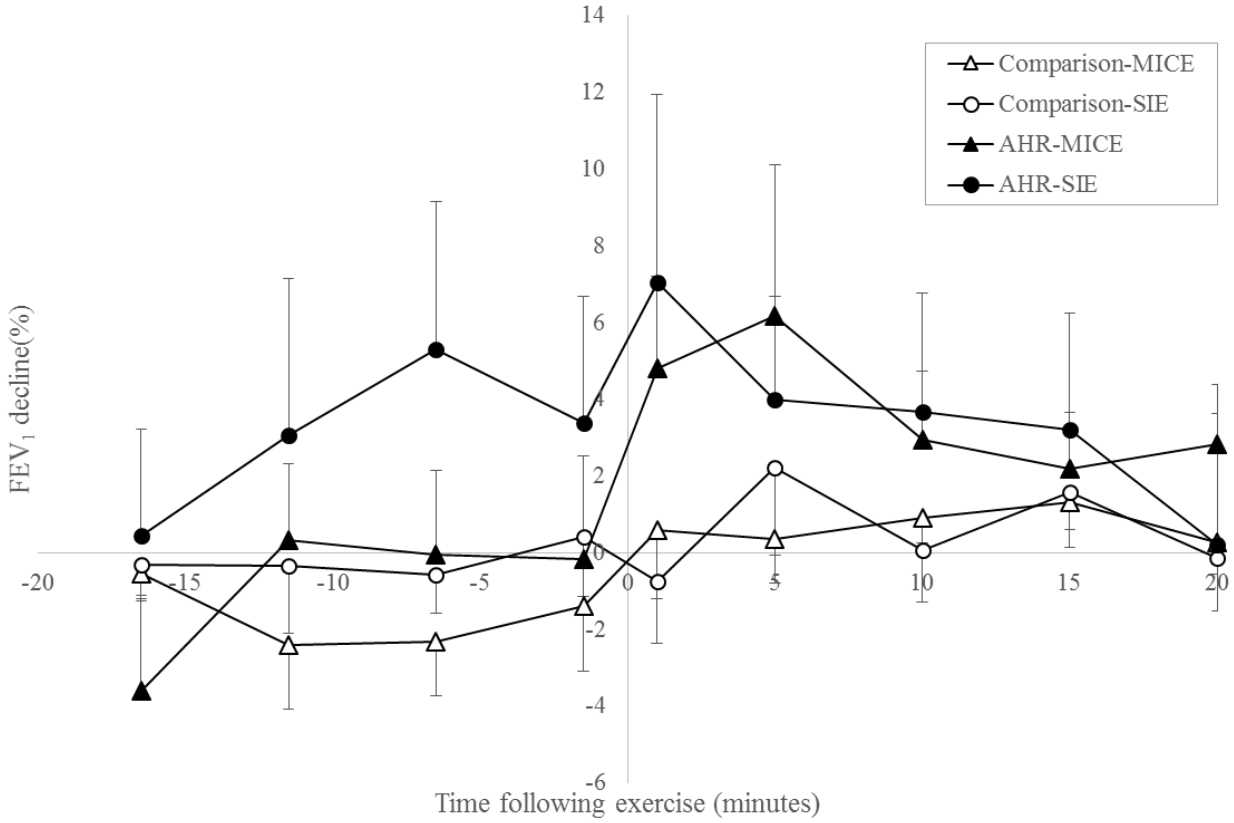


Figure 2 – Changes in FEV_1 during and after SIE and MICE sessions in the AHR (n=8) and Comparison (n=8) Groups

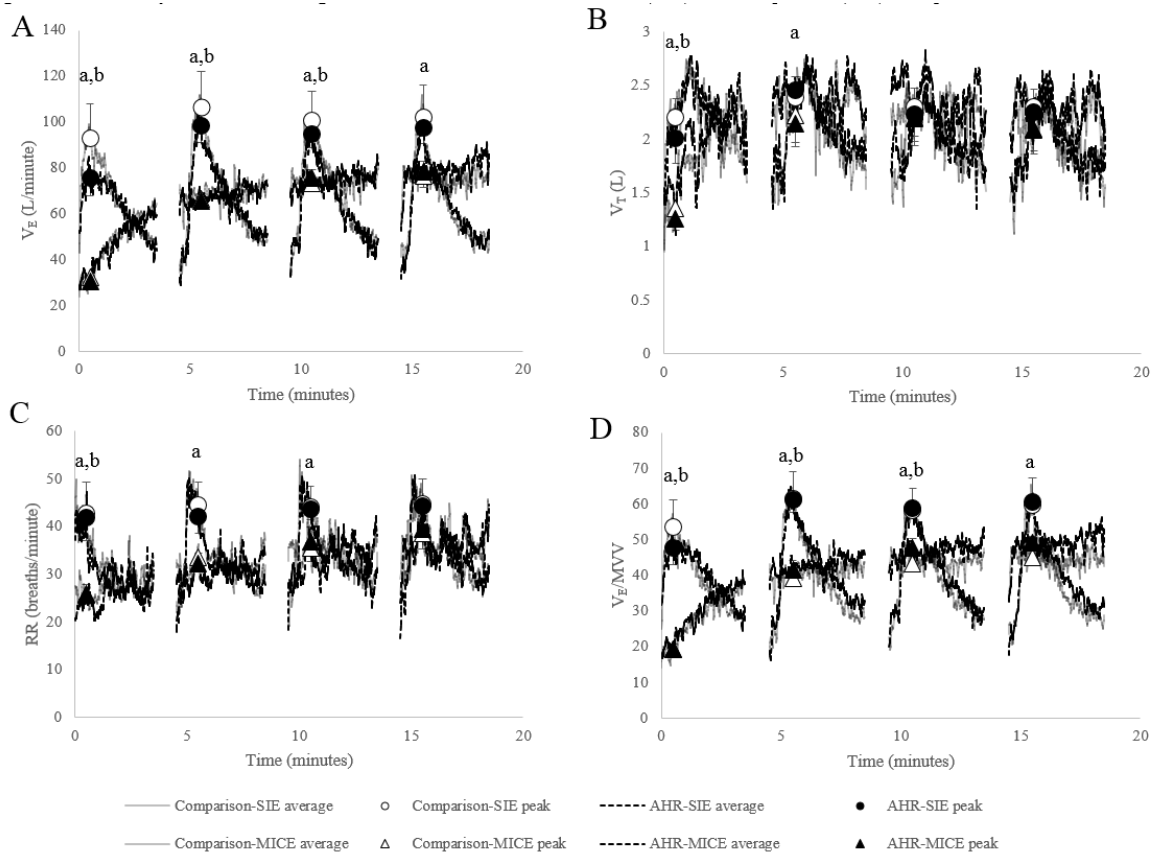


Note: A positive value for FEV_1 indicates a decline from baseline.

AHR group: during SIE, n=7 from 5 minutes onwards; during MICE, n=7 from 10 minutes onwards

3 way interaction for time x condition x group was NS.

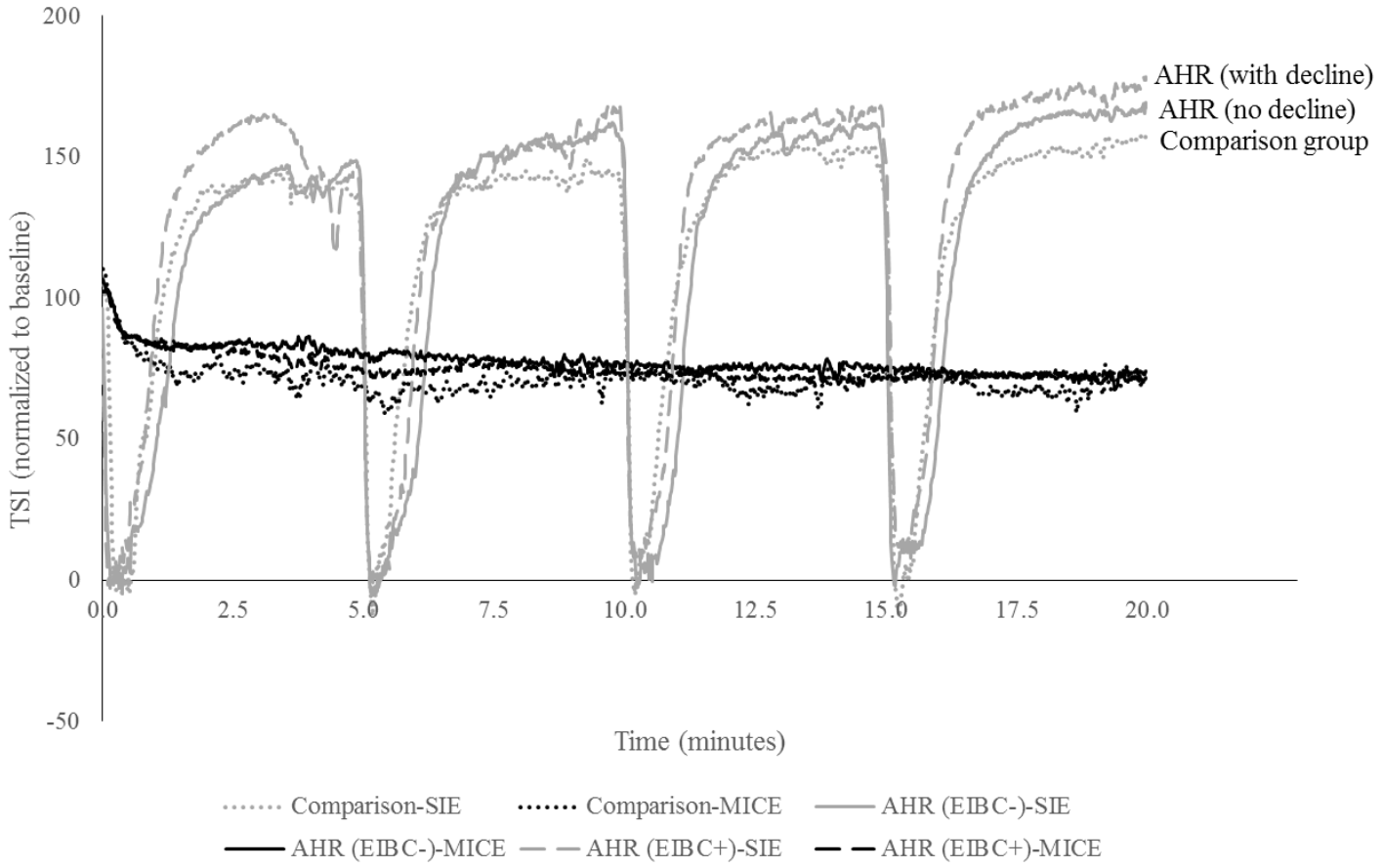
Figure 3 – Ventilatory Parameters during SIE and MICE sessions for the AHR (n=8) and Comparison (n=8) Groups



Note: Time points noted are the times used for statistical analysis where peak V_E occurred during SIE and corresponding points during MICE.

Note: [a] P<0.05 for EIBC: SIE vs. MICE, [b] P<0.05 for Comparison: SIE vs. MICE, [c] P<0.05 for SIE: EIBC vs. comparison, [d] P<0.05 for MICE: EIBC vs. comparison

Figure 4 – Normalized Tissue saturation index (TSI) for a representative participant from the AHR, AHR with decline, and Comparison Groups



Note: There were no significant differences between normalized responses of the AHR and comparison group or across multiple sprints based on the three way interaction

CHAPTER 4: SUBJECTIVE RESPONSES TO SPRINT INTERVAL EXERCISE IN ADULTS WITH AND WITHOUT EXERCISE-INDUCED BRONCHOCONSTRICTION

4.1 ABSTRACT

Objective: Sprint interval exercise (SIE) has gained popularity as a time efficient method for increasing physical activity levels; however, little is known of the subjective response to SIE, particularly in individuals who experience exercise-induced bronchoconstriction (EIBC). Therefore, the purpose of the current study was to compare the subjective response of adults with EIBC between SIE and moderate intensity continuous exercise (MICE), and further to compare responses in adults without EIBC. *Methods:* Eight adults (22.3 ± 3.0 years) with EIBC and eight adults (22.3 ± 3.0 years) without EIBC (comparison group) completed both SIE (4x30 second sprints at 0.075kg/kg of body weight separated by 4.5 minutes of active recovery) and MICE (20 minutes at 65% peak power output) sessions. Affect (FS), perceived breathlessness (RPD), exertion (RPE) were recorded throughout exercise and enjoyment was assessed following exercise. *Results:* There were no significant three way interactions between condition (SIE or MICE) x time during exercise x EIBC status for FS, RPD, or RPE; however, differences between SIE and MICE were observed. Enjoyment was similar for SIE and MICE in the EIBC group (SIE: 72.9 ± 20.0 vs. MICE: 79.5 ± 20.5, p=0.25), and between groups for SIE and MICE. *Conclusions:* Perceived breathlessness may impact affect during the early stages of exercise among those with EIBC. Enjoyment appears to be similar between SIE and MICE for those with and without EIBC. Future research is needed to better understand the relationship between V_E patterns, exercise intensity, and enjoyment of exercise among those with EIBC.

4.2 INTRODUCTION

Asthma is a respiratory disease that is characterized by chronic airway inflammation and is defined by the variable presence of symptoms including wheezing, shortness of breath, chest tightness and coughing [1]. Importantly, up to 90% of adults with asthma experience exercise-induced bronchoconstriction (EIBC) [2, 3]. EIBC is associated with coughing, wheezing, shortness of breath and discomfort as a result of exercise, and therefore may be a barrier to regular physical activity [4]. Improving physical activity levels is important for those with asthma, as studies have shown that exercise leads to improvements in aerobic fitness [5-8], number of symptom free days [5, 6], quality of life measures [5, 8], and number of hospital visits [9].

Enjoyment is an important factor when determining the appropriate type of exercise, as affect during an acute bout of exercise is predictive of future physical activity behaviour [10, 11]. Studies on high intensity interval exercise (HIIE), utilizing alternating 1:1 periods of high and low intensity exercise, have found higher affect during HIIE compared to moderate intensity continuous exercise (MICE) [12, 13]. Enjoyment appears to depend on the relative intensity of exercise, as MICE protocols that are higher in intensity are associated with less enjoyment [13]. Among those with EIBC, interval exercise allows for minute ventilation (V_E) to recover, which may reduce breathlessness and thus improve enjoyment. Previous research from our laboratory found that participants with EIBC had higher affect scores during HIIE (alternating 1 minute intervals at 90% peak power output (PPO) and at 10% PPO) compared to MICE (20 minutes at 65% PPO), but no differences in overall enjoyment [14].

Sprint interval exercise (SIE), which involves short, 'all out' sprints separated by longer recovery periods, is becoming popular as it saves even more time, and provides similar benefits as MICE protocols [15-19]. However, it is not known whether the longer recovery periods during SIE would allow V_E to recover further, thus limiting breathlessness and further increasing affect and enjoyment. Higher affect has been observed during SIE when participants are allowed to listen to music [20] or are given encouragement [21]. Enjoyment has also been shown to be higher for high intensity interval running compared to continuous running [22]. To our knowledge, there are no studies available comparing

affect or enjoyment between SIE and MICE in adults with EIBC. The primary purpose of this study was to compare affect and enjoyment in the context of ventilatory measures during SIE and MICE in adults with EIBC. A secondary purpose was to compare affect and enjoyment between those with EIBC to a healthy comparison group. We hypothesized that perceptions of dyspnea would be greater and affect would be lower during SIE compared to MICE due to the high V_E during SIE. We also hypothesized that individuals with EIBC would experience higher perceptions of dyspnea and lower affect during both SIE and MICE compared to the healthy comparison group.

4.3 METHODS

Participants

The same participants were used for analyses in this manuscript as for the previous manuscript "Respiratory Responses to Sprint-Interval Exercise in Adults with Airway Hyperresponsiveness". Participants were screened for eligibility if they were between the ages of 18-44 years. Adults over 44 years of age were excluded to reduce the possibility of the presence of comorbidities, such as chronic obstructive pulmonary disease (COPD). Inclusion was further limited to adults engaged in regular physical activity (150 minutes of moderate to vigorous intensity exercise per week) to ensure participants were able to complete the sprint session. Participants in the EIBC group were required to have self-reported physician diagnosed asthma, a current prescription for a short-acting bronchodilator, and a positive response to a eucapnic voluntary hyperpnea (EVH) challenge (described elsewhere [23, 24]). Participants in the comparison group were eligible if they had no previous physician diagnosis of asthma, and a negative response to the EVH challenge. All participants provided written consent prior to beginning the study. The study was approved by the University of Ontario Institute of Technology's Research Ethics Board.

Study Design

This was a randomized cross-over study comparing those with and without EIBC. All participants completed three sessions, each separated by a minimum of 48 hours to

reduce the impact of a refractory period following EIBC. In *session 1*, participants completed an incremental to maximal intensity exercise test. *Sessions 2 and 3* were the exercise sessions completed in random order.

Reported Measures

Demographics: Basic demographic information regarding age, sex, and perceived health was collected during the first session through a questionnaire.

Mini Asthma Quality of Life Questionnaire (mini-AQLQ) was completed during session 1. This questionnaire consists of 15 questions regarding symptoms, activities, emotions and environment in relation to overall quality of life. Each question is scored on a scale of 1-7, with higher numbers indicating a better quality of life. The score for each question is averaged yielding a total score, with 7 as the highest possible score. The mini-AQLQ has been shown to have good reliability (Intraclass correlation coefficient=0.83) as well as validity, measured by responsiveness (p=0.0007) [25].

The Physical Activity Enjoyment Questionnaire (PACES) was completed 10 minutes following the completion of the SIE and MICE session. This questionnaire uses 18 questions to assess the enjoyment experienced during exercise and has demonstrated high reliability and validity [26]. This questionnaire was modified by removing the following question "I am very absorbed in this activity – I am not very absorbed in this activity." This was done due to the questionnaire being completed 10 minutes following exercise so the question was irrelevant. Each question is scored on a 7-point bipolar scale with a maximum score of 119. This modified version of the PACES questionnaire has been used previously for HIIE; however, validity and reliability for this modified version have not been assessed [13, 14]. Following the final session, participants were also asked if they preferred SIE or MICE.

Affect: Participants were asked to report on their general affective valence (pleasure/displeasure) based on the One-Item Feelings Scale (FS) [27]. This scale ranges from -5 to +5 (very bad to very good). Participants were instructed "While participating in exercise, it is common to experience changes in mood. For example, one might feel good and bad a number of times during exercise. When asked, please tell me how you feel in the

current moment using the scale.". FS was reported each minute during SIE and MICE. An overview of when each measurements was assessed during SIE and MICE sessions is shown in Figure 1.

Rating of Perceived Dyspnea and Exertion: Participants pointed to a number on a scale of 0 to 10 for their Rating of Perceived Dyspnea (RPD) which corresponds to their perceived feeling of dyspnea (shortness of breath). The RPD has been shown to be a valid and reliable measure [28]. Participants also reported their Borg Rating of Perceived Exertion (RPE) on a scale of 6-20. Participants were asked to think about exertion in their legs because RPD referred specifically to breathlessness. The RPE scale is considered a valid measure of exercise intensity [29]. RPD and RPE were also asked every minute during SIE and MICE.

EIBC symptoms: Participants were asked if they were feeling signs/symptoms typical of EIBC. These included sore throat, coughing, wheezing, light headedness, and phlegm in their throat. If they responded affirmatively that they were feeling a symptom, they were asked to rate this on a scale of 1-5 (from mild to severe) four times throughout SIE and MICE.

Late Phase Asthma Symptom Questionnaire: Only participants in the EIBC group were given this questionnaire. This questionnaire was created to assess any late phase asthma symptoms that may occur as a result of exercise testing up to 48 hours post-exercise. If the participant experienced any of coughing, wheezing, shortness of breath, sore throat, a dry, itchy throat, chest tightness, increased mucus, sleep disturbances or other symptoms they were asked to rate it from 1-5 (mild to severe) and indicate what time point it occurred at.

Physiological measures

Heart Rate: Heart rate (HR) was measured continuously using a Polar heart rate monitor. For statistical analysis, HR was calculated at 0.5, 3.5, 5.5, 8.5, 10.5, 13.5, 15.5, and 18.5 minutes (corresponding with peak HR observed at the end of each sprint, and three minutes following each sprint), by averaging the values of the five seconds surrounding each time point. In cases where peak HR did not occur at the end of the sprint, the average of the five seconds surrounding the true peak HR were used.

Breathing Reserve: Expired gas was collected through a pneumotachograph and analyzed using an automated gas collection system (Parvo Medics 2400, USA). Data were linearly interpolated to yield second-by-second values and V_E was analyzed. Maximum voluntary ventilation (MVV) was calculated based on American Thoracic Society (ATS) guidelines using 40 times the baseline forced expiratory volume in one second (FEV_1) from the maximal exercise test for the comparison group or from post-bronchodilator FEV_1 for the EIBC group [30]. Breathing reserve (BR) was calculated as follows:

$BR = 100 [MVV-V_E] / MVV$

BR is typically ≥ 20% in healthy adults at peak exercise. A BR of <20% may be an indication of a pulmonary disease [31]. BR was calculated at 0.5, 5.5, 10.5, and 15.5 minutes (corresponding with peak V_E observed at the end of each sprint), by averaging the values of the five seconds surrounding each time point.

Methodology

Maximal Exercise Test: An incremental to maximum protocol was used with the initial stages occurring for two minutes each at 80, 120, and 160 Watts (W) and then the workload was increased by 16 W every minute until exhaustion. Participants cycled at 80 rpm for the duration of the test. PPO was recorded as the final stage completed.

Exercise Sessions: Participants were familiarized to the cycle ergometer and all scales prior to completion of SIE and MICE. The SIE and MICE protocols started with a two minute warm-up between 50 and 60 W at 50 to 60 rpm. For the MICE session, following the warm-up, participants cycled at 80 rpm at 65% PPO for 20 minutes. Following the MICE session, participants completed a 5 minute cool down at a self-selected cadence and resistance. For the SIE session, 15 seconds prior to the end of the warm-up, resistance was removed in order to prepare the cycle ergometer for the sprint. Five seconds prior to the end of the warm-up, participants were instructed to cycle as fast as possible with no resistance. Participants then completed the 30 second sprint (at 0.075kg/kg of body weight) with time updates occurring with 20, 10, and 5 seconds left in the sprints. No other encouragement was provided during the sprints. Participants completed four sprints with 4.5 minutes of unloaded cycling at 40 to 60 rpm between sprints (20 minutes of total exercise). Following SIE, no additional cool-down was completed, because following the final sprint the 4.5

minutes of unloaded cycling served as a cool-down. The SIE session was based on previous research using similar protocols [15, 16]. During SIE and MICE protocols, participants reported their RPE, RPD, and FS each minute, starting with the point immediately following the first sprint during SIE (minutes 0.5, 1.5, 2.5, every minute following until the end of SIE and MICE), with the exception of minutes 4.5, 9.5, 14.5, and 19.5, because lung function assessments were being measured at these time points (Figure 1). Four times throughout the protocols (minutes 1.5, 6.5, 11.5, and 16.5), participants were asked if they were feeling any asthma symptoms and their severity.

For statistical analysis of RPE, RPD, and FS, time points corresponding with immediately following and three minutes following each sprint were used.

Statistical Analysis

Means and standard deviations were calculated for all continuous variables to describe the sample. Three factor (condition (SIE or MICE) x time during or following exercise x EIBC status (with or without EIBC) repeated measures analysis of variance tests were used to determine if there were differences within and between exercise protocols for FS, RPD, RPE, HR, and BR. When sphericity had been violated, Greenhouse-Geisser corrections were used. Interactions with $p \leq 0.10$ were examined further to determine where differences occurred using post hoc pairwise comparisons and t-tests. This value, $p \leq 0.10$, was chosen to reduce the likelihood of missing differences since the study was underpowered for secondary variables. All statistics were done in IBM SPSS statistics 23.0 (Armonk, NY) and statistical significance was declared at $p<0.05$. Effect sizes were calculated in G*Power 3.0.10 to report the magnitude of difference between SIE and MICE enjoyment scores.

4.4 RESULTS

Of eleven eligible participants with EIBC and eleven participants in the comparison group, three from each group were excluded due to an inability to complete SIE and/or MICE, or dropped out due to injuries not related to the study or a lack of time. Sixteen participants completed the study with six males and two females in each group. All participants were meeting minimum physical activity guidelines (>150 minutes of

moderate to vigorous intensity exercise per week) [32]. Additional sample characteristics can be found in Table 1.

Affect

There was no significant three way interaction between condition, time, and EIBC status for FS (p=0.86). There was a significant two way interaction between condition and time (p=0.004). There was no significant two way interactions for time and EIBC status (p=0.14) or condition and EIBC status (p=0.60). The minimum FS reported was similar between the EIBC and comparison group for MICE (-1.8 ± 2.8 vs. 0.0 ± 2.8, p=0.23) and SIE (-2.1 ± 1.9 vs. -0.3 ± 3.1, p=0.16, Figure 2A).When the groups were combined, minimum affect did not differ between SIE and MICE (-1.2 ± 2.6 vs. -0.8 ± 2.8, p=0.71).

Physical activity enjoyment

Enjoyment, as per the PACES questionnaire, was similar for SIE compared to MICE in both the EIBC (72.9 ± 20.0 vs. 79.5 ± 20.5, for SIE and MICE, respectively, p=0.25, d=0.33) and the comparison (81.0 ± 14.7 vs. 86.4 ± 14.2, p=0.07, d=0.37) group. For the combined sample, the difference between enjoyment for SIE compared to MICE was approaching significance (76.9 ± 17.4 vs. 82.9 ± 17.4, p=0.051). In addition, 14/16 participants reported lower enjoyment scores for SIE than MICE (9.0 ± 8.2 lower for SIE). Enjoyment was similar for MICE (p=0.44) and for SIE (p=0.37) when comparing the EIBC and the comparison groups. Ten of the 16 participants (4/8 with EIBC and 6/8 in the control group) reported that they preferred MICE compared to SIE.

Perceived Breathlessness and Exertion

There were no significant three way interactions between condition, time, and EIBC status for RPD (p=0.89) or RPE (p=0.56). As expected, there were significant two way interactions between condition and time (p<0.001 for both RPD and RPE).

For RPD, there were no significant two way interactions between condition and EIBC status (p=0.23) or between time and EIBC status (p=0.27). Peak RPD was similar between the EIBC and comparison group for MICE (6.5 ± 2.4 vs. 6.1 ± 2.4, p=0.76) and SIE (7.9 ± 1.4 vs. 6.6 ± 1.8, p=0.13). Significant differences in RPD between SIE and

MICE in both the EIBC and comparison group were observed at some time points, as shown in Figure 2B.

For RPE, the interaction between time and EIBC status was approaching significance (p=0.080). RPE appeared to start at a higher level for those in the comparison group with values approaching significance or becoming significant at minutes 0.5 (p=0.086), 3.5 (p=0.029), and 5.5 (p=0.069). No differences were observed from minute 8.5 to the end of the session. Participants with EIBC experienced a greater increase in RPE from minute 0.5 to minute 18.5 compared to the comparison group (7.3 ± 5.1 vs. 3.9 ± 5.5, p=0.076). Peak RPE was similar between the EIBC and control groups for MICE (17.4 ± 2.6 vs. 16.9 ± 1.4, p=0.64) and SIE (16.9 ± 2.4 vs. 17.5 ± 2.6, p=0.62, Figure 2C).

Breathing reserve and heart rate

There was no significant three way interaction between condition, time, and EIBC status for BR or HR (p=0.89 and p=0.41). There was a significant two way interaction between condition and time for both (p<0.001 for both). For BR, there was an interaction between time and EIBC status approaching significance (p=0.082); however, no significant differences at any time point were observed between groups. There were no significant interactions between condition and EIBC status for BR (p=0.89) or HR (p=0.91).

Minimum BR was significantly less in the EIBC group during MICE compared to the comparison group (41.5 ± 6.9 vs. 49.0 ± 6.2, p=0.038, Figure 2D). There was no significant difference in minimum BR between the EIBC and comparison groups during SIE (33.5 ± 8.2 vs. 32.4 ± 21.1, p=0.78). Minimum BR was significantly less during SIE than MICE in the comparison group (p=0.029), and approaching significance in the EIBC group (p=0.066). The difference in peak HR between SIE and MICE in the EIBC group (176.6 ± 11.4 vs. 180.1 ± 12.0, p=0.072) was approaching significance.

Peak HR was similar between SIE and MICE in the comparison group (179.3 ± 8.4 vs. 179.3 ± 11.9, p=0.99). Peak HR was also similar between the EIBC and comparison groups for SIE (p=0.60) and MICE (p=0.90).

EIBC symptoms

As per Figure 4A, the comparison group reported a sore throat during MICE (n=3), sore throat during SIE (n=3), coughing during SIE (n=1), and light headedness during SIE (n=3). The EIBC group reported a sore throat during MICE (n=2), sore throat during SIE (n=3), coughing during MICE (n=1), coughing during SIE (n=1), wheezing during MICE (n=1), wheezing during SIE (n=3), light headedness during MICE (n=2), light headedness during SIE (n=3), phlegm in the throat during MICE (n=3), and phlegm in the throat during SIE (n=3). The cumulative frequency for each sign or symptom is shown in Figure 3. When participants with EIBC reported a symptom, the average severity was not significantly different for SIE and MICE (2.0± 0.9 vs. 1.9 ± 1.3, p=0.71).

For both SIE and MICE, for all late phase symptoms, the same number of participants reported experiencing each symptom, with the exception of a sore throat and a dry, itchy throat (two following SIE vs. one following MICE), as shown in Figure 4B. When participants experienced a symptom, the average severity was not significantly different for SIE and MICE (1.8 ± 0.8 vs. 1.5 ± 0.9, p=0.21).

4.5 DISCUSSION

We aimed to determine if perceptions of breathlessness, exertion, affect, and enjoyment were different during SIE and MICE sessions both among those with EIBC and comparing those with EIBC to healthy adults. The primary results of this study indicate that among those with EIBC, breathlessness influences affect during the early stages of exercise; these differences disappear later in exercise, likely due to the relatively high intensity of the MICE protocol chosen in the current study. A secondary finding is that regardless of EIBC status, enjoyment appears to be better for MICE than SIE. These findings have implications for exercise prescription in adults with EIBC.

Affective response during exercise

In general, a decline in affect was observed for both groups during SIE and MICE (Figure 2A). Affect during exercise, measured using the FS, has been reported to decrease as exercise intensity increases [33]. Previous studies have reported a decrease in affect across multiple sprints during SIE; however, these studies did not compare to MICE [20,

21]. In a study by Saanijoket al., lower affect was observed throughout SIE compared to MICE among sedentary, middle-aged men [34]. The study utilized 60% of PPO for the MICE protocol, whereas we used 65% PPO in the current study. Furthermore, the recovery intervals were 30 seconds longer in the present study. In our study, a slight increase in FS was seen three minutes following each sprint during the recovery period compared to the minute immediately following the sprint. Significant differences were observed between SIE and MICE among the EIBC group immediately following sprint one and two, where affect was lower for SIE than MICE. This may be related to the high V_E at the end of each sprint. Exercise above the ventilatory threshold, specifically increasing blood lactate levels, has been shown to be negatively correlated with affect [35, 36]. A few minutes into our MICE protocol, participants were exercising at intensities near or above their ventilatory threshold (as evidenced by HR), thus lactate accumulation may have contributed to the lack of difference observed in affect between SIE and MICE after sprint three and four. Future research should assess protocols using different MICE intensities. A lower intensity MICE protocol may lead to less breathlessness, and better affective responses

Enjoyment of SIE and MICE

Based on previous reports of the strenuous nature of SIE and feelings of light headedness and nausea during SIE, it was hypothesized that enjoyment for SIE would be lower than MICE [37-39]. Our results indicate that enjoyment was similar between the two exercise sessions; however, 14 of the 16 participants reported higher enjoyment following MICE than SIE (9.0 ± 8.2 higher for MICE), and 10 of 16 participants preferred MICE to SIE. Previous research has found that high intensity interval cycling and running may be more enjoyable than MICE [12-14, 22]. However, these studies used near maximal intensity intervals while we utilized supramaximal intervals. Previous studies using supramaximal intervals have reported higher enjoyment for SIE compared to MICE [40], no significant differences [41, 42], or even lower enjoyment [43]. These studies were in different populations, used different modes of exercise, and used different protocols (interval lengths and intensities), which may account for differences observed. Previous studies reporting enjoyment following Wingate-based SIE have not compared to MICE but have compared the effect of music and encouragement on enjoyment. The enjoyment

scores for SIE reported in the current study (76.9 ± 17.4 out of 119) are similar to those reported by Stork et al. (>80 out of 126) and Tritter et al. (72.4 ± 18.0 out of 126 when no encouragement was given) [20, 21]. These results indicate that the specific protocol chosen and other external factors such as music and encouragement may be important in predicting enjoyment.

We also hypothesized that those with EIBC would have lower enjoyment during SIE due to the V_E achieved. Previous research by O'Neill et al. found similar enjoyment between HIIE and MICE protocols in a sample of adults with EIBC [14]. Our enjoyment scores for the MICE session were comparable to those of O'Neill et al. (91.9 ± 17.3 vs. 79.5 ± 20.5, p=0.15) [14]. It is worth noting however, that enjoyment scores in the current study may have been negatively affected as participants were required to breathe through a mouthpiece (forcing mouth breathing), had a small probe pressed against each thigh to assess tissue oxygenation, and were required to perform lung function measurements throughout the exercise sessions. This may have led to a more uncomfortable and less enjoyable experience, particularly as breathing with the mouthpiece can lead to complaints of the air feeling dry. Nevertheless, enjoyment between the different protocols was found to be similar between SIE and MICE in the current study. This indicates that for exercise prescription, SIE and MICE may both be similarly effective for improving exercise adherence. Although, future research is needed to compare SIE to a less intense MICE protocol.

Perceptions of dyspnea and exertion

A similar pattern was observed for RPD, with significantly higher breathlessness observed immediately following sprint one, two, and three in SIE compared to MICE among those with EIBC (Figure 2B) and immediately following sprint one and two in the comparison group. In older adults with COPD, lower dyspnea scores were reported during a high intensity interval exercise program (initially with 30 second intervals of 100% peak work rate alternated with 30 seconds of rest) than continuous exercise (50% peak work rate) [44]. To the best of our knowledge, perceived dyspnea has not been studied using protocols of supramaximal intensity intervals in comparison to continuous exercise in those with EIBC. Previously, V_E has been shown to be a predictor of dyspnea in adults with

asthma during maximal exercise testing [45]. In the current study, BR was significantly lower at the end of each sprint compared to corresponding time points during MICE, potentially contributing to higher RPD (Figure 2D). Even though BR was lower following sprint four during SIE, RPD may not have been higher at this time point because of the sustained V_E required throughout MICE. The minimum BR was also lower in the EIBC group than the comparison group during MICE but not SIE. This highlights the potential importance of the recovery periods during SIE in limiting excess V_E, leading to higher breathlessness.

Similar to perceived dyspnea, RPE was significantly higher immediately following sprints one and two compared to MICE in the EIBC group (Figure 4C). RPE may have been significantly higher during SIE only following sprint one and two because lactate may have accumulated throughout MICE, which has been correlated with RPE [36]. Previously, RPE has been reported to be higher during SIE compared to MICE [34]. As previously mentioned for affect, differences may be due to differences in protocols. It was also observed that RPE was similar between the EIBC and comparison groups for SIE and MICE. This indicates that both groups exerted themselves similarly, so differences in affect or breathlessness would be related to EIBC, not effort. These results indicate that a balance of recovery periods and higher intensity exercise may play an important role in limiting perceptions of breathlessness.

Signs/symptoms during exercise

The forced mouth breathing may have led to participants from both groups experiencing a sore throat during SIE and MICE sessions. A sore throat was experienced more frequently during SIE (21 total reports) than MICE (11 total reports), likely due to high peak V_E achieved during SIE. High peak V_E also likely induced greater symptoms of coughing during SIE (five total reports) than MICE (one total report), wheezing during SIE (ten total reports) than MICE (two total reports), and phlegm in the throat during SIE (ten total reports) than MICE (six total reports). The increased symptoms may be caused by increased drying of the airway associated with high V_E [46]. The increased occurrence of these symptoms may lead to less enjoyment during exercise. Increased light headedness during SIE likely was not related to EIBC as three participants in both the EIBC and

comparison group reported this. Light headedness has been reported previously during SIE [37-39]. Symptoms such as nausea and light headedness may lead to lower enjoyment when compared to MICE or other submaximal interval exercise protocols where these symptoms are not common. Future research should examine if V_E is related to a higher prevalence of symptoms during exercise and if symptoms experienced are related to objective measures of EIBC.

Limitations

There are some limitations to the current study. First, we may have been underpowered to detect differences in enjoyment and affect. A larger sample size would be ideal, however, given the homogeneity within groups, and between groups, the trends observed are informative. Second, participants were wearing a mouthpiece during exercise, and were performing the exercise sessions in a laboratory setting; this may have influenced subjective responses. Finally, sex based differences during SIE and MICE could not be examined as there were only two female participants per group. Previously, breathlessness has been reported to be higher in older women than men during incremental exercise when standardizing V_E [47]. RPE has also been shown to be lower in women [48] or similar [49] to men when comparing the same relative intensity of exercise. It is not known what impact sex differences would have on subjective responses during SIE; therefore this will be important for future research.

In conclusion, SIE and MICE are associated with similar levels of enjoyment and affect among adults with and without EIBC. Future research using larger samples is needed to better understand the relationship between V_E patterns during exercise and the subjective response among those with EIBC.

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Table 1: Sample characteristics for those with EIBC and the Comparison group

	With EIBC (n=8)	Comparison group (n=8)
Sex (# of males)	6	6
Age (years)	22.3 ± 3.0	22.3 ± 3.0
BMI (kg/m^2)	26.5 ± 3.3	24.8 ± 4.5
miniAQLQ	5.6 ± 1.2	N/A

No significant differences were observed between groups

Figure 1 – Timeline of reported measurements assessed during the SIE and MICE sessions

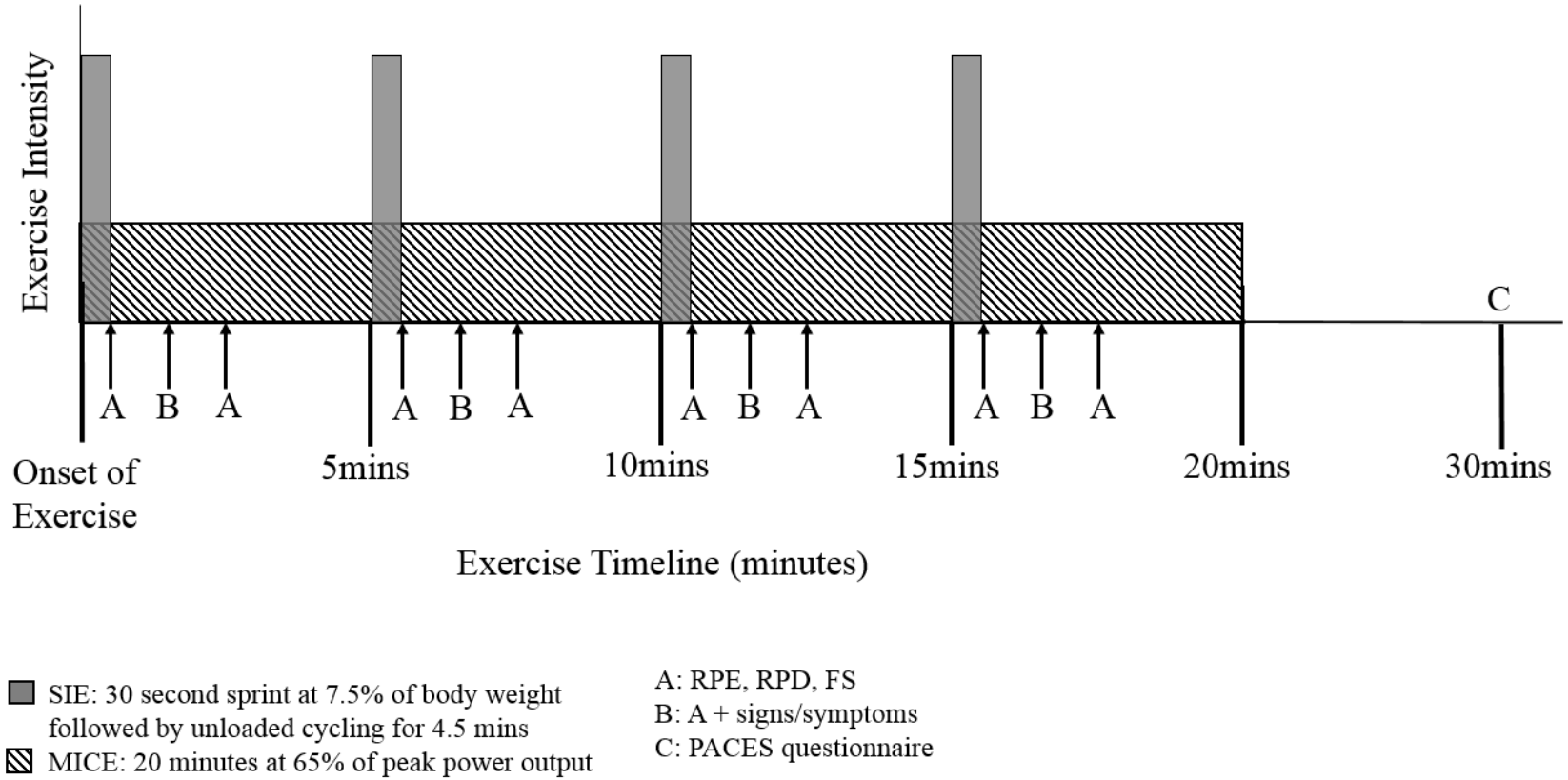
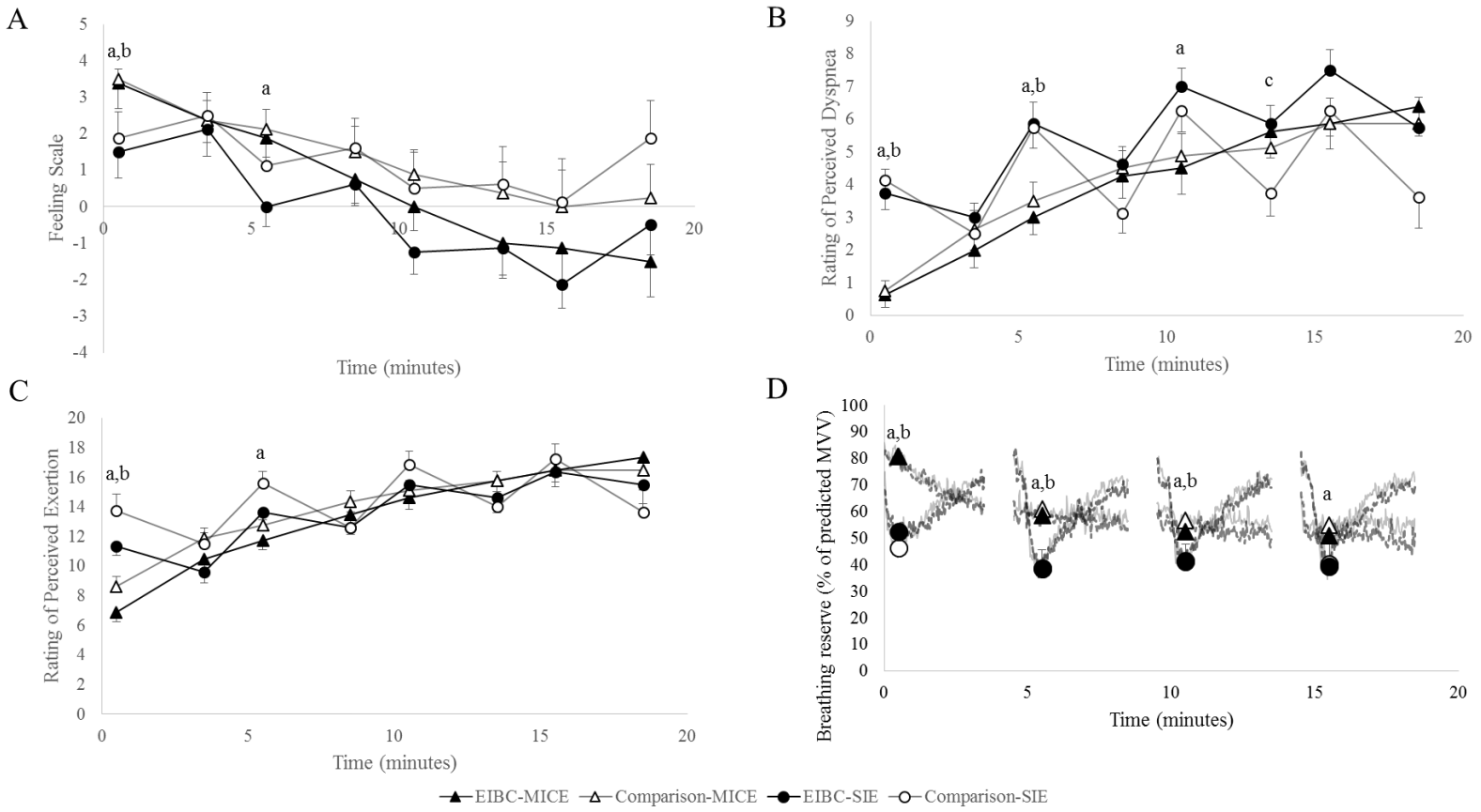


Figure 2 – Acute Subjective and Respiratory Response to SIE and MICE in adults in the EIBC and comparison group



A: 1-item feeling scale, B: Rating of perceived dyspnea, C: Rating of perceived exertion, D: Breathing reserve

Note: [a] P<0.05 for EIBC: SIE vs. MICE, [b] P<0.05 for Comparison: SIE vs. MICE, [c] P<0.05 for SIE: EIBC vs. comparison, [d] P<0.05 for MICE: EIBC vs. comparison

Figure 3 – Frequency of each symptom experienced during SIE and MICE for the EIBC group (A) and the Comparison groups (B)

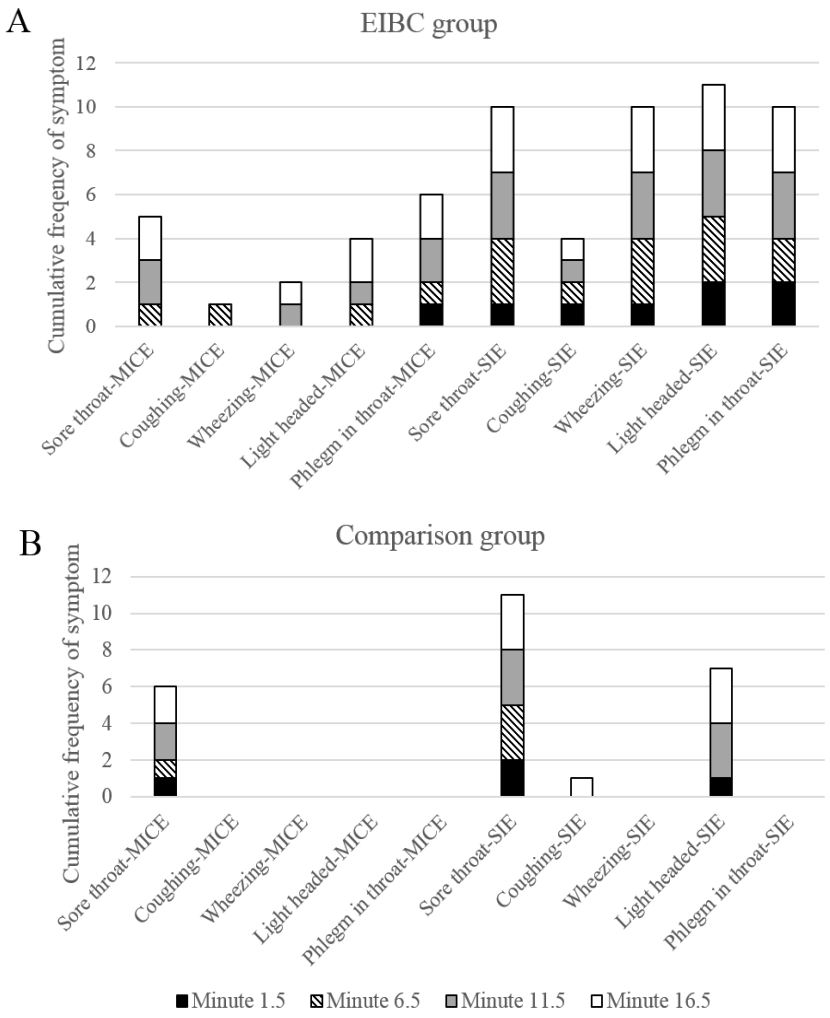
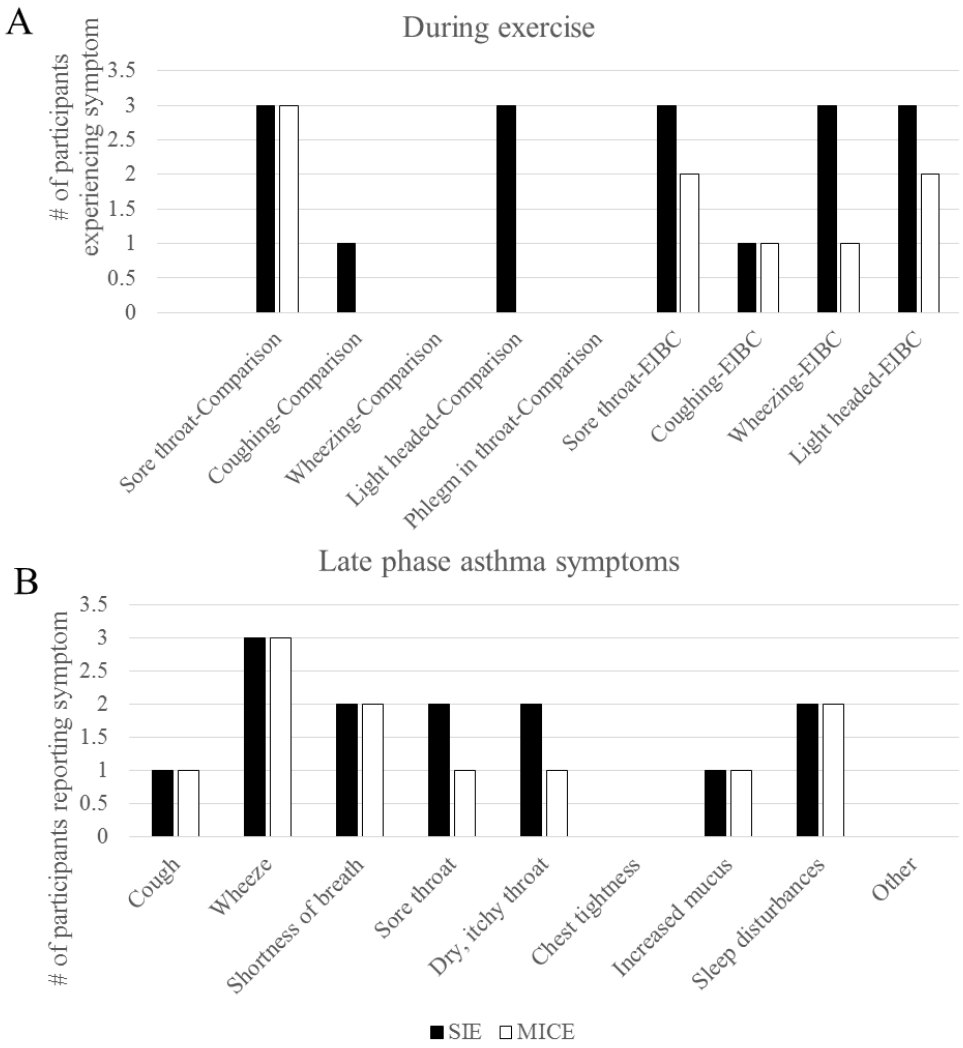


Figure 4 – Symptoms reported by EIBC group during and 48 hours post SIE or MICE



CHAPTER 5: GENERAL DISCUSSION

5.1 OVERVIEW

The purpose of this thesis was to determine if sprint interval exercise (SIE) is more asthmogenic than moderate intensity continuous exercise (MICE) in adults with airway hyperresponsiveness (AHR), to determine if O_2 delivery and utilization are impaired in adults with AHR during SIE and MICE, to compare subjective responses between SIE and MICE and if these responses differ in those with and without AHR, and to determine if the acute response to SIE and MICE, based on forced expiratory volume in one second (FEV_1) decline, ventilation and tissue oxygenation would be different between adults with and without AHR.

We hypothesized that SIE would be more asthmogenic than MICE, that is, would cause a greater decline in FEV_1, due to the high minute ventilation (V_E) required during and following sprints. We found that participants with AHR had a similar decline in FEV_1 *following* SIE (8.6 ± 12.6) compared to MICE (9.0 ± 9.3), as well as *during* SIE (6.2 ± 10.8) compared to MICE (2.3 ± 6.0). Seven of eight participants with AHR, experienced a greater decline in FEV_1 during SIE compared to MICE, and a greater frequency of signs/symptoms was reported during SIE compared to MICE. This may indicate that during exercise, SIE is more asthmogenic than MICE, but following exercise there does not appear to be a difference between the protocols. It is possible that a less intense MICE protocol would have led to greater differences between protocols.

We also hypothesized that O_2 delivery to the working muscle would be impaired during exercise in adults who experienced exercise-induced bronchoconstriction (EIBC). Only one participant experienced a clinically relevant degree of EIBC (≥10%) during SIE and MICE so we were unable to study differences that may occur as a result of EIBC. When comparing the AHR and without AHR groups, we found no difference between the groups in regards to the absolute level of change in tissue oxygenation.

We also hypothesized that FEV_1 would decline more following SIE and MICE in adults with AHR compared to those without AHR. Also, that tissue oxygenation would be impaired and power output would be decreased more by the final sprint in adults with AHR compared to those without AHR. The decline in FEV_1 following MICE (AHR: 9.0 ± 9.3% vs. Comparison group: 2.8 ± 2.0%, p=0.087) was approaching significance. The decline in

FEV_1 following SIE (AHR: 8.6 ± 12.6% vs. Comparison group: 3.6 ± 5.4%, p=0.32) was not statistically significant. Statistical significance likely was not observed for SIE because of the greater variability in FEV_1 decline. Two participants with AHR actually experienced bronchodilation at each time point following SIE compared to baseline and one participant without AHR experienced a 13.0% decline in FEV_1 following SIE. This participant without AHR may have experienced a significant decline because the participant did not give a full effort as five minutes later FEV_1 was only 4.3% below baseline. Regarding tissue oxygenation across sprints, no difference in participants with AHR was observed in tissue oxygenation levels in sprint four compared to sprint one or compared to participants without AHR. In addition, a greater decrease in power output was not observed in the AHR group compared to the comparison group. This is not surprising though, since only one participant experienced EIBC no differences in the groups would be expected.

Our final hypothesis was that subjective responses would be worse during SIE than MICE, that enjoyment would be lower following SIE than MICE, and that subjective responses would be worse in adults with AHR than adults without AHR. We found that affect (FS), perceived dyspnea (RPD), and perceived exertion (RPE) were worse immediately following sprints at the beginning of SIE compared to MICE but differences disappeared by the end of the protocols. We also found enjoyment was similar between SIE and MICE in the AHR and comparison groups; however, when the sample was combined, the difference between enjoyment for SIE compared to MICE was approaching significance (SIE: 76.9 ± 17.4 vs. MICE: 82.9 ± 17.4, p=0.051). Finally, subjective responses were similar between adults with and without AHR for both protocols. Similar to tissue oxygenation, the lack of differences is not surprising since only one participant experienced EIBC during exercise.

5.2 SENSITIVITY OF EUCAPNIC VOLUNTARY HYPERPNEA

The eucapnic voluntary hyperpnea (EVH) challenge is the test currently recommended by the International Olympic Committee-Medical Commission for confirming EIBC and permitting athletes to use β2 agonists [1]. However, a recent systematic review reported a wide range of sensitivity (25 to 90%) and specificity (0 to 71%) values for the EVH. In the current study, of 17 participants with a history of asthma

screened using the EVH, six experienced a ≤10% decline in FEV_1. Of 20 participants with no history of asthma, nine experienced a ≥10% decline in FEV_1. Assuming a previous diagnosis of asthma is correct, sensitivity and specificity values for the EVH in the current study would be 65% and 55%, respectively. The possibility that some participants screened for EVH were previously incorrectly diagnosed with asthma or had asthma despite no previous diagnosis cannot be excluded. In participants without a previous history of asthma and a positive response to the EVH, a different pathogenesis of AHR may be possible. In elite athletes, AHR has been suggested to be a reflection of airway injury related to high V_E while training, especially in cold/dry environments [2].

The test-retest reproducibility of the EVH has also been shown to be unreliable. Price et al. performed EVH tests on 32 recreational athletes on two separate days. It was found that 15 athletes experienced a ≥10% decline in FEV_1 during visit one or two; however, only seven athletes experienced this decline on both days [3]. This suggests that if participants in the current study completed multiple tests, then participants with a history of asthma may have actually experienced EIBC on one of the EVH trials. It also may be that a single test cannot confirm EIBC, particularly in individuals with mild AHR. In our sample, most participants had mild asthma, which may contribute to the variability in results following the EVH. It has been shown that among adults with moderate to severe asthma (≥20% decline in FEV_1), repeatability of the EVH is high [3].

Despite these potential limitations, the EVH appears to be an important screening tool for AHR, particularly in elite athletes where EIBC may limit performance [4, 5].

5.3 REFRACTORY PERIOD DURING SIE

A reason that SIE could lead to less of a decline in lung function following exercise is the potential of a refractory period to occur following one or two sprints, therefore limiting further bronchoconstriction. A review by Stickland et al. reported that EIBC following a subsequent exercise bout is reduced if an interval warm up is performed compared to a continuous warm up [6]. It is possible that an interval warm up would lead to a refractory period, but it has not been studied if interval exercise would have a similar effect. In support of a potential refractory period, six out of eight participants with AHR had less of a decline in FEV_1 following sprint four than sprint three; however, all of these

participants FEV_1 values declined again one minute following exercise. Even among the participant who had the greatest decline in FEV_1 during SIE (28.1%), this participant still experienced a 34.1% decline one minute after SIE. This participant reported that when exercising, if they push through their asthma symptoms, the symptoms generally get better by the end of exercise.

Despite a possible improvement in lung function seen in this study during SIE, it does not appear that refractoriness played a role in reducing EIBC following exercise compared to MICE.

5.4 STRENGTHS

There are a number of strengths of the current study to highlight. First, the randomized cross over design, with all participants completing both SIE and MICE on separate days allowed for participants to act as their own control. Second, the groups were well matched for characteristics such as age (AHR: 22.3 ± 3.0 years, Comparison: 22.3 ± 3.0 years), sex (six males and two females in each group), and aerobic capacity (AHR: 40.4 ± 4.9 ml/kg/min, Comparison: 41.7 ± 5.5 ml/kg/min). Third, the protocol for SIE was standardized with no encouragement given during the sprints and standard recovery periods between sprints. This reduces the potential of encouragement to impact subjective measures and power output, as previously observed [7]. Fourth, by assessing spirometry throughout we were able to assess for EIBC that may have occurred during exercise. This would allow for differentiation between anyone who experienced EIBC during exercise and then had normal lung function following exercise from anyone who did not experience EIBC at all. Finally, ventilation was assessed throughout exercise to allow for any impairments that may occur as a result of EIBC to be studied.

5.5 LIMITATIONS

First, measuring ventilation and assessing spirometry may also be considered a limitation. Breathing through the mouthpiece forces mouth breathing which has been shown to lead to a greater EIBC response than nasal breathing [8]. Therefore, EIBC may be less severe if performing the same exercise protocols without the mouthpiece. By assessing spirometry during exercise, this may have led to less enjoyable experience due

to having to remove the mouthpiece and perform spirometry while still exercising rather than just continuing on unimpeded. Second, temperature and humidity varied between sessions (MICE: 21.8 ± 1.3°C, range 19-24°C, 36.9 ± 14.7% humidity, range 12-67% and SIE: 21.9 ± 0.8°C, range 21-23°C, 29.3 ± 13.6% humidity, range 11-53%). Bolger et al. reported that inspiring warm, humid air limited EIBC in response to exercise compared with cold, dry air [9]. The variation in temperature and humidity may have impacted individual participants' results; however, differences between groups and between SIE and MICE conditions were not significant. Third, some participants may not have understood how to properly perform a Wingate. Only eleven out of sixteen participants recorded their highest peak power during sprint one. Despite completing a familiarization Wingate, some participants may have forgotten the exact protocol, so standardized instructions or playing a video example may ensure a better understanding. Power output was not collected during the familiarization session, which would have been useful for comparison to the sprints during the SIE session. However, it is likely that participants fully exerted themselves since the average heart rate (HR) following sprint four was 93.2% of the maximum HR achieved during the maximal exercise test, and the average RPE of 16.8 following sprint four compared to 18.0 during the final stage of the maximal exercise test. Finally, workload for the MICE session was not able to be set exactly to 65% peak power output (PPO) so participants were required to attempt to maintain 80 rpm. Participants' actual workload for MICE ended up being 62.7 ± 1.7% and 64.2 ± 1.9% PPO for the AHR and comparison groups, respectively. Even at these slightly lower power outputs, V_E was still sufficiently high to elicit EIBC. In addition, two participants were unable to complete MICE at the prescribed workload, so resistance had to be reduced during exercise in order for the participants to complete 20 minutes of exercise. These two participants both had the lowest PPO from the maximal exercise test (160W); however, even this may have been an overestimation because the increase in resistance during the maximal exercise test was from 120 to 160W so the true PPO may have been somewhere in between, thus overestimating 65% PPO for MICE.

5.6 FUTURE RESEARCH

There are a number of potential areas for future research to be explored. First, using a set up that is more likely to cause EIBC during exercise would allow for impairments in O_2 delivery or ventilatory parameters due to EIBC to be studied. This could be done using inspired cold, dry air rather than room air during exercise, through the use of a bronchoconstricting agent such as methacholine or having participants complete an EVH prior to exercise, similar to Rossman et al. [10]. Another future area of research would be to explore different intensities of MICE. Specifically, if V_E during MICE is at or below the ventilatory threshold (T_{Vent}), then this may have an impact on the severity of EIBC. A final area of future research involves comparing the difference that the breathing apparatus makes on the degree of EIBC. For example, it would be important to compare the work of breathing and the airway response between a mouthpiece (forced mouth breathing), mask (mouth and nose breathing but through a mask), and unobstructed breathing with no mouthpiece or mask. The effect of different breathing apparatus on affective response would also be useful to study to see how comparable laboratory-based exercise would be to a real world "free breathing" setting. Individual responses to SIE and MICE are important to consider as recent research has shown that some individuals may respond to sprint interval training but not continuous training in regards to maximal oxygen consumption (VO_{2max}), T_{Vent}, and submaximal heart rate [11]. The idea of responders and non-responders may cross over to lung function responses to different exercise protocols.

5.7 CONCLUSIONS

In conclusion, the current study indicates that adults with AHR have a similar decline in FEV_1 *following* SIE and MICE. Ventilatory parameters and tissue oxygenation were not impaired in adults with AHR compared to the comparison group. This is not unexpected because only one participant experienced a clinically significant degree of EIBC *during* SIE and MICE. Despite this, seven of the eight participants with AHR experienced a greater decline in FEV_1 *during* SIE than MICE, potentially explaining the larger number of signs/symptoms reported during SIE. If participants in the AHR group were starting to experience EIBC (despite the lack of a statistically significant difference in FEV_1 versus the comparison group) this may explain the higher RPD during the sprint

three recovery period than the comparison group. Differences in subjective responses were observed at the beginning of exercise between SIE and MICE, but became similar by the end of exercise, potentially related to the intense MICE protocol chosen. For the entire sample, participants appeared to report SIE as less enjoyable than MICE.

It appears that SIE may be more asthmogenic during exercise and less enjoyable than MICE, based on 1) greater symptoms reported, 2) the majority of participants with AHR experiencing a larger decline in FEV_1 during SIE than MICE, and 3) a trend towards lower enjoyment following SIE for the entire sample. This may have implications for exercise prescription, specifically if SIE is less enjoyable then exercise adherence may be negatively impacted. Overall, SIE appears to be feasible in adults with AHR.

5.8 REFERENCES

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APPENDIX A: QUESTIONNAIRES AND SCALES

1: Signs/Symptoms Severity Scale

2: Eligibility Questionnaire

3: Demographic Questionnaire

4: Late Phase Asthma Symptom Questionnaire

5: Data Collection Sheet – Session 1

6: Data Collection Sheet – Session 2

7: Data Collection Sheet – Session 3

8: Data Collection Sheet – Session 4

9: Power Output during SIE

A1: SIGNS/SYMPTOMS SEVERITY SCALE

1 – Mild

2

3- Moderate

4

5- Severe

A2: ELIGIBILITY QUESTIONNAIRE

1. Age: _______
2. Has a doctor ever told you that you have asthma or exercise-induced asthma?
    a. Yes
    b. No

    If yes, how old were you when they told you this? _____
3. Do you currently have a rescue/reliever inhaler? (example: Ventolin or Bricanyl, blue puffer)
    a. Yes
    b. No

    If yes, please write the name of the medication here: _____
4. Are you currently taking any prescription or over the counter medications regularly (not previously listed in question 3)?
    a. Yes
    b. No

    If yes, please list the medications here: _____
5. Do you have any injuries that would limit your ability to cycle on a stationary bicycle? (i.e. knee injury)
    a. Yes
    b. No

    If yes, please describe the injury here: _____
6. If you are a female, are you currently pregnant?
    a. Yes
    b. No
7. Have you ever been a regular smoker (at least 1 cigarette per day)?
    a. Yes
    b. No

        If yes, please indicate for how long: _____
8. At any point in the past six months, were you a regular smoker (at least 1 cigarette per day)?
    a. Yes
    b. No
9. In a typical week, please describe the type of physical activity you engage in and how many minutes you engage in (i.e. walking, jogging, cycling):

Type of Activity	**Minutes in a typical week**

A3: DEMOGRAPHIC QUESTIONNAIRE

1) Age:_____

2) Sex:

❑Female ❑Male

3) Education level (check one):

- ❑ Some high school
- ❑ Completed high school
- ❑ Some community college
- ❑ Complete Community College
- ❑ Some university
- ❑ Completed bachelor degree
- ❑ Completed Masters or PhD

4) Perceived Health (check one):

❑ Very Poor

❑ Poor

❑ Average

❑ Good

❑ Very Good

5) What is your current occupation? _____

6) Please list an emergency contact

Name:_____

Relationship: _____

Phone Number:_____

A4: LATE PHASE ASTHMA SYMPTOM QUESTIONNAIRE

Late Phase Asthma Symptom Questionnaire

Please indicate if you experienced any of the following symptoms after your exercise session in the laboratory.

	Please put an "X" if you have experienced any of the following symptoms after your last exercise session. On a scale of 1-5, 1 being mild and 5 being extreme/intense, how would you describe the symptoms you experienced?													
	1-4 hours	Severity	4-8 hours	Severity	8-12 hours	Severity	12-16 hours	Severity	16-20 hours	Severity	20-24 hours	Severity	24-48 hours	Severity
Symptom														
Coughing														
Wheezing														
Shortness of breath														
Sore throat														
Dry, itchy throat														
Chest Tightness														
Increased mucus														
Sleep disturbances														
Other – Please Describe														

Was the occurrence of these symptoms more than what you usually experience? Yes No

Was the occurrence of these symptoms **more severe** than what you usually experience? Yes No

Have you exercised since your last laboratory session? Yes No

If YES, what type of exercise and when? _____

_____

Have you come in to contact with any of your asthma triggers since your last laboratory session? Yes No

If YES, what triggers and when? _____

_____

A5: DATA COLLECTION SHEET – SESSION 1

Data Collection Sheet: Session I

Feasibility of Sprint Interval Exercise in Adults with and without Asthma

Participant ID			
Height (cm)		Weight (kg)	
Resting HR (bpm)		Resting BP (mmHg)	
		Waist Circumference (cm)	
Temperature (°C)		Relative Humidity	
Followed Pre-Session Instructions		Brought Rescue Medication	

Pre-Test Spirometry (0=male, 1=female)

	FEV_1	**FVC**	**FEV % predicted**	**FEV_1/FVC**
Trial 1				
Trial 2				
Trial 3				
Trail 4				
Trial 5				

EVH Protocol

Target Ventilation		Test Notes	

Post-Challenge Spirometry

	FEV_1		**FVC**		**FEV % predicted**		**FEV_1/FVC**	
	Trial 1	Trial 2	Trial 1	Trial 2	Trial 1	Trial 2	Trial 1	Trial 2
Minute 1								
Minute 5								
Minute 10								
Minute 15								
Minute 20								

Drop in FEV_1 from baseline: _____

Maximal Test Familiarization Session

Minutes	Watts	RPE

Wingate Familiarization

Notes on Set-Up:

A6: DATA COLLECTION SHEET – SESSION 2

Data Collection Sheet: Session II

Feasibility of Sprint Interval Exercise in Adults with and without Asthma

Participant ID				
Height (cm)		Weight (kg)		
Resting HR (bpm)		Resting BP (mmHg)		
Followed Pre-Session Instructions		Brought Rescue Medication		
Temperature (°C)		Relative Humidity		
		Thigh Skinfold (cm)	Left	Right

Pre-Test Spirometry (0=male, 1=female)

	FEV_1	**FVC**	**FEV % predicted**	**FEV_1/FVC**
Trial 1				
Trial 2				
Trial 3				
Trail 4				
Trial 5				

Post-Bronchodilator Spirometry (0=male, 1=female)

	FEV_1	**FVC**	**FEV % predicted**	**FEV_1/FVC**
Trial 1				
Trial 2				
Trial 3				
Trail 4				
Trial 5				

Maximal Test Protocol

Minutes	Watts	RPD	RPE	Enjoyment	HR
1	80 (0 kg)				
2	80 (0 kg)				
3	120 (0.5 kg)				
4	120 (0.5 kg)				
5	160 (1.0 kg)				
6	160 (1.0 kg)				
7	176 (1.2 kg)				
8	192 (1.4 kg)				
9	208 (1.6 kg)				
10	224 (1.8 kg)				
11	240 (2.0 kg)				
12	256 (2.2 kg)				
13	272 (2.4 kg)				
14	288 (2.6 kg)				
15	304 (2.8 kg)				
16	320 (3.0 kg)				
17					
18					
19					
20					

Test Notes:

Post-Test Spirometry

	FEV_1		**FVC**		**FEV % predicted**		**FEV_1/FVC**	
	Trial 1	Trial 2	Trial 1	Trial 2	Trial 1	Trial 2	Trial 1	Trial 2
Minute 1								
Minute 5								
Minute 10								
Minute 15								
Minute 20								

Drop in FEV_1 from baseline: _____

A7: DATA COLLECTION SHEET – SESSION 3

Data Collection Sheet: Session III

Feasibility of Sprint Interval Exercise in Adults with and without Asthma

Type of Exercise			
Participant ID			
Height (cm)		Weight (kg)	
Resting HR (bpm)		Resting BP (mmHg)	
Followed Pre-Session Instructions		Brought Rescue Medication	
Temperature (°C)		Relative Humidity	

Pre-Session Spirometry (0=male, 1=female)

	FEV_1	**FVC**	**FEV % predicted**	**FEV_1/FVC**
Trial 1				
Trial 2				
Trial 3				
Trail 4				
Trial 5				

Metabolic Cart Start time	
NIRS Start time	
Wingate Start time	

Exercise Protocol

Minutes	Watts	RPD	RPE	Enjoyment	HR
0.5					
1.5					
2.5					
3.5					
4.5		Pulse Ox:			
5.5					
6.5					
7.5					
8.5					
9.5		Pulse Ox:			
10.5					
11.5					
12.5					
13.5					
14.5		Pulse Ox:			
15.5					
16.5					
17.5					
18.5					
19.5		Pulse Ox:			

Session Notes:

Signs/Symptoms

	Sign/Symptom	Yes/No	Rating
Sprint 1 or Minute 1:30	Sore Throat		
	Cough		
	Wheeze		
	Light Headed		
	Phlegm		
Sprint 2 or Minute 6:30	Sore Throat		
	Cough		
	Wheeze		
	Light Headed		
	Phlegm		
Sprint 3 or Minute 11:30	Sore Throat		
	Cough		
	Wheeze		
	Light Headed		
	Phlegm		
Sprint 4 or Minute 16:30	Sore Throat		
	Cough		
	Wheeze		
	Light Headed		
	Phlegm		

During exercise Spirometry

	FEV_1		**FVC**		**FEV % predicted**		**FEV_1/FVC**	
	Trial 1	Trial 2	Trial 1	Trial 2	Trial 1	Trial 2	Trial 1	Trial 2
3:00 after sprint 1 (minute 3.5)								
3:00 after sprint 2 (minute 8.5)								
3:00 after sprint 3 (minute 13.5)								
3:00 after sprint 4 (minute 18.5)								

Drop in FEV_1 from baseline: _____

Post-Test Spirometry

	FEV_1		**FVC**		**FEV % predicted**		**FEV_1/FVC**	
	Trial 1	Trial 2	Trial 1	Trial 2	Trial 1	Trial 2	Trial 1	Trial 2
Minute 1								
Minute 5								
Minute 10								
Minute 15								
Minute 20								

Drop in FEV_1 from baseline: _____

	Sprint 1/MICE	**Sprint 2**	**Sprint 3**	**Sprint 4**
Peak Power				
Average Power				
Min. Power				
Total Power				

A8: DATA COLLECTION SHEET – SESSION 4

Data Collection Sheet: Session IV

Feasibility of Sprint Interval Exercise in Adults with and without Asthma

Type of Exercise			
Participant ID			
Height (cm)		Weight (kg)	
Resting HR (bpm)		Resting BP (mmHg)	
Followed Pre-Session Instructions		Brought Rescue Medication	
Temperature (°C)		Relative Humidity	

Pre-Session Spirometry (0=male, 1=female)

	FEV_1	**FVC**	**FEV % predicted**	**FEV_1/FVC**
Trial 1				
Trial 2				
Trial 3				
Trail 4				
Trial 5				

Metabolic Cart Start time	
NIRS Start time	
Wingate Start time	

Exercise Protocol

Minutes	Watts	RPD	RPE	Enjoyment	HR
0.5					
1.5					
2.5					
3.5					
4.5		Pulse Ox:			
5.5					
6.5					
7.5					
8.5					
9.5		Pulse Ox:			
10.5					
11.5					
12.5					
13.5					
14.5		Pulse Ox:			
15.5					
16.5					
17.5					
18.5					
19.5		Pulse Ox:			

Session Notes:

Signs/Symptoms

	Sign/Symptom	Yes/No	Rating
Sprint 1 or Minute 1:30	Sore Throat		
	Cough		
	Wheeze		
	Light Headed		
	Phlegm		
Sprint 2 or Minute 6:30	Sore Throat		
	Cough		
	Wheeze		
	Light Headed		
	Phlegm		
Sprint 3 or Minute 11:30	Sore Throat		
	Cough		
	Wheeze		
	Light Headed		
	Phlegm		
Sprint 4 or Minute 16:30	Sore Throat		
	Cough		
	Wheeze		
	Light Headed		
	Phlegm		

During exercise Spirometry

	FEV_1		**FVC**		**FEV % predicted**		**FEV_1/FVC**	
	Trial 1	Trial 2	Trial 1	Trial 2	Trial 1	Trial 2	Trial 1	Trial 2
3:00 after sprint 1 (minute 3.5)								
3:00 after sprint 2 (minute 8.5)								
3:00 after sprint 3 (minute 13.5)								
3:00 after sprint 4 (minute 18.5)								

Drop in FEV_1 from baseline: _____

Post-Test Spirometry

	FEV_1		**FVC**		**FEV % predicted**		**FEV_1/FVC**	
	Trial 1	Trial 2	Trial 1	Trial 2	Trial 1	Trial 2	Trial 1	Trial 2
Minute 1								
Minute 5								
Minute 10								
Minute 15								
Minute 20								

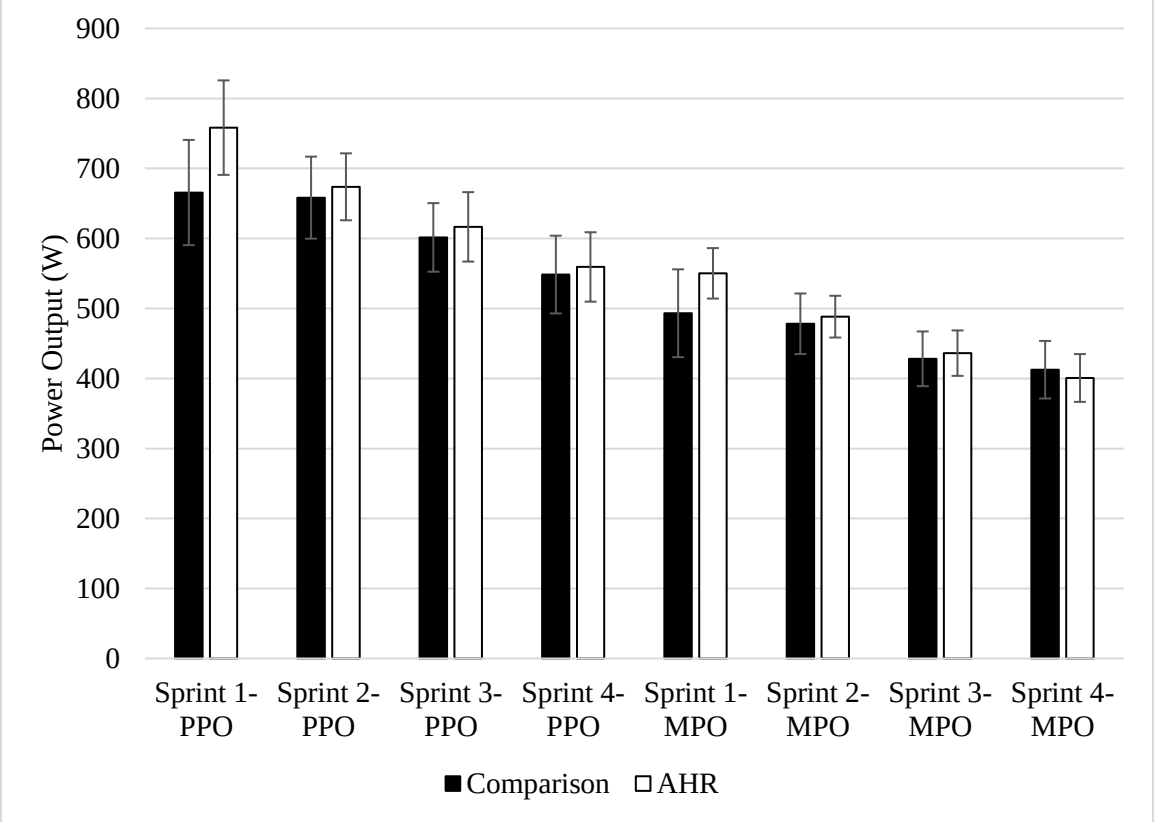
Drop in FEV_1 from baseline: _____

Perception:
Preferred Exercise:_____

	Sprint 1/MICE	**Sprint 2**	**Sprint 3**	**Sprint 4**
Peak Power				
Average Power				
Min. Power				
Total Power				

A9: POWER OUTPUT DURING SIE

Peak Power Output and Mean Power Output during SIE for each sprint for the AHR and Comparison Groups



No significant differences were observed between groups

APPENDIX B: ETHICS APPROVAL LETTER

B1: ETHICS APPROVAL LETTER

Date:	*May 10, 2016*
To:	*Joshua Good*
From:	*Shirley Van Nuland, REB Chair*
REB # & Title:	*(15-117) Feasibility of SIE in Adults with and without Autism*
Decision:	*APPROVED*
Current Expiry:	***May 01, 2017***

Notwithstanding this approval, you are required to obtain/submit, to UOIT's Research Ethics Board, any relevant approvals/permissions required, prior to commencement of this project.

The University of Ontario, Institute of Technology Research Ethics Board (REB) has reviewed and approved the research proposal cited above. This application has been reviewed to ensure compliance with the Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans (TCPS2 (2014)) and the UOIT Research Ethics Policy and Procedures. You are required to adhere to the protocol as last reviewed and approved by the REB.

Continuing Review Requirements (forms can be found on the UOIT website):

- **Renewal Request Form**: All approved projects are subject to an annual renewal process. Projects must be renewed or closed by the expiry date indicated above ("Current Expiry"). Projects not renewed within 30 days of the expiry date will be automatically suspended by the REB; projects not renewed within 60 days of the expiry date will be automatically closed by the REB. Once your file has been formally closed, a new submission will be required to open a new file.
- **Change Request Form**: Any changes or modifications (e.g. adding a Co-PI or a change in methodology) must be approved by the REB through the completion of a change request form before implemented.
- **Adverse or Unexpected Events Form**: Events must be reported to the REB within 72 hours after the event occurred with an indication of how these events affect (in the view of the Principal Investigator) the safety of the participants and the continuation of the protocol (i.e. un-anticipated or un-mitigated physical, social or psychological harm to a participant).
- **Research Project Completion Form**: This form must be completed when the research study is concluded.

Always quote your REB file number (15-117) on future correspondence. We wish you success with your study.

REB Chair
Dr. Shirley Van Nuland
shirley.vannuland@uoit.ca

Ethics and Compliance Officer
researchethics@uoit.ca

NOTE: If you are a student researcher, your supervisor has been copied on this message.