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EFFECTS OF ALTERED AIRWAY FUNCTION ON EXERCISE VENTILATION IN ASTHMATIC ADULTS

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Abstract

PURPOSE—Variable airway function is a central feature of the asthmatic condition. Thus, habitually active asthmatics are certain to exercise under conditions of variable airway (dys)function. The purpose of this study was to determine the effects of variable pre-exercise airway function on ventilation during whole-body exercise in asthmatic adults.

METHODS—Eight mild asthmatic (age, 26 yrs; $\dot{V}O_2$peak, 49 ml·kg^{-1}·min^{-1}) and nine non-asthmatic (age, 30 yrs; $\dot{V}O_2$peak, 46 ml·kg^{-1}·min^{-1}) adults performed constant workrate cycling exercise-to-exhaustion following four separate interventions: 1) a control trial (CON); 2) inhalation of fast-acting β_2-agonist (BD); 3) eucapnic voluntary hyperpnea challenge (BC); and 4) sham to the hyperpnea (SHAM). Pulmonary function was assessed at baseline and following each intervention. Exercise ventilation and operating lung volumes were compared among the four exercise trials in both control and asthmatic subjects.

RESULTS—Baseline pulmonary function was significantly lower in asthmatic subjects compared with control subjects. In asthmatic subjects, post-intervention (*i.e.*, pre-exercise) forced expiratory volume 1.0 second was significantly different among the four exercise trials (CON, 3.5 ± 0.4; BD, 4.1 ± 0.4; SHAM, 3.6 ± 0.3; BC, 2.8 ± 0.3 L; $p < 0.05$), whereas it was not different in control subjects. There were no differences in exercise ventilation or operating lung volumes during exercise among the four trials either within asthmatic subjects or between control and asthmatic subjects.

CONCLUSION—These findings suggest that the state of airway function – whether bronchodilated or bronchoconstricted – prior to exercise in the mild asthmatic does not affect the exercise ventilatory response. Ventilatory system function in the asthmatic thus appears to be responsive to the acute requirement for increased airflow during whole-body exercise.

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Keywords

Airway caliber; airway mechanics; bronchoconstriction; bronchodilation; exercise-induced bronchodilation; pulmonary mechanics

INTRODUCTION

Variable airway function is a central feature of the asthmatic condition. Asthmatics thus exhibit daily and seasonal variation in airway inflammation, airways hyperresponsiveness (AHR), pulmonary function, and clinical symptoms (8, 14, 17). Exposure to a variety of immunological triggers such as pollens, pet dander, mold, and dustmites instigate airway inflammation, airway smooth muscle contraction, and worsened airway function. Several other non-immunological triggers exist as well, including inhalation of cold/dry air, exposure to environmental pollutants, and whole-body exercise. Importantly, AHR demonstrates seasonal variability and fluctuates with variations in environmental allergen concentrations, and in some asthmatics AHR regularly varies over the course of 24 hours (8, 20). For all of these reasons, habitually active asthmatics are certain to exercise under conditions of variable airway (dys)function. The influences of this variable airway function on the responses to whole-body exercise are not known.

Regular exercise is a generally recommended therapeutic modality in patients with asthma (23, 32, 34). These recommendations are partially informed by studies demonstrating improved aerobic capacity with training and unchanged pulmonary function and exercise-induced bronchoconstriction (EIB) over time with training; pulmonary function and EIB neither worsen nor improve with training (34, 40). Very few studies, however, have examined relationships between baseline airway function and exercise ventilation in the asthmatic. This is an important gap in the literature, as the variable airway function in asthma may interact with the exercise ventilatory response. This contrasts sharply with non-asthmatic persons, in which airway function is consistent on a day-to-day basis. Furthermore, the majority of studies assessing responses to exercise in asthmatic subjects have not included comparisons with non-asthmatic control subjects. In general, the most meaningful insight into the physiological responses to exercise in a patient population can only be gleaned through comparisons with non-diseased control subjects. Improved understanding of the relationships between baseline airway function and exercise ventilation in the asthmatic (and compared with non-asthmatic counterparts) will help to inform exercise recommendations for this large clinical population.

It is reasonable to postulate a relationship between baseline airway function and exercise ventilation in the asthmatic. For example, pre-exercise bronchodilation might be expected to allow for increased exercise ventilation in the asthmatic. However, studies have consistently demonstrated an unchanged exercise ventilation following bronchodilation in asthmatic subjects (11, 18, 35, 36). Conversely, a small number of investigations have experimentally worsened airway function prior to exercise in asthmatic subjects. In one experimental approach, exercise is preceded by induction of airway narrowing *via* osmotic stress, including inhalation of hypertonic saline (5) or voluntary eucapnic hyperpnea (6), or

inhalation of the bronchoconstrictor histamine (13). These studies, however, were not designed to carefully assess the effects of pre-exercise bronchoconstriction on ventilation during exercise, focusing instead on post-exercise airway function in the asthmatic. Thus, the role of pre-exercise bronchoconstriction on ventilation during exercise in the asthmatic remains unknown.

The purpose of this study was to determine the effects of both improved and worsened pre-exercise airway mechanical function on the ventilatory responses to whole-body exercise in asthmatic adults as well as healthy controls. We hypothesized that exercise ventilation would be similar despite variable pre-exercise airway function in asthmatic subjects.

METHODS

Subject selection

Adult male and female asthmatic and non-asthmatic subjects were recruited through advertisements in local newspapers and by flyers posted on the Johnson State College campus and within the local community. Prior to participation, subjects were fully informed of the procedures, risks, and benefits of the study, and written, informed consent was obtained. The experiments described in this proposal were approved by the Johnson State College institutional review board for research involving human subjects.

All participants were between the ages of 18-45 y, had a negative history for cardiovascular disease and other chronic illness (excepting asthma), were non-smokers, and had an absence of respiratory infection during the 6-weeks prior to participation. Asthmatic subjects were limited to those with mild disease that was controlled or partly controlled, as defined by the Global Initiative for Asthma (12). Asthmatic subjects currently taking inhaled or oral steroids were excluded from participation, as were those who had attended the emergency room for an asthma exacerbation during the previous 3 years. All subjects completed two separate screening studies on different days to determine eligibility for participation as an asthmatic or non-asthmatic subject.

Screening studies

Exercise-induced bronchospasm—All subjects completed an incremental exercise test-to-exhaustion. The inspirate consisted of dry air from a compressed gas tank (FIO_2, .21, balance nitrogen). Pulmonary function was assessed prior to exercise, and at 5, 10, 15, 20, and 30 minutes following exercise.

Bronchodilator reversibility—Following baseline pulmonary function tests (PFT), subjects inhaled 4 actuations of a fast-acting β_2-agonist. For each actuation, subjects exhaled to residual volume, depressed the actuator, inhaled slowly through a chamber (aerovent) to total lung capacity, and held their breath for 3-5 seconds prior to exhaling. Pulmonary function was assessed at several time-points following β_2-agonist inhalation.

Participants meeting at least one of the following two criteria were classified as asthmatic subjects: 1) ≥ 12% decrease in forced expiratory volume 1.0 second ($FEV_{1.0}$) after the

incremental exercise test-to-exhaustion; 2) ≥ 12% increase in $FEV_{1.0}$ after inhalation of the fast-acting β_2-agonist.

Experimental design

All subjects completed four separate exercise studies with four different pre-exercise interventions. The interventions included: 1) four actuations of a fast-acting β_2-agonist to improve airway function; 2) a eucapnic voluntary hyperpnea challenge to worsen airway function; 3) a sham to the hyperpnea; and 4) a control trial. The order of experimental interventions for each subject was randomized, and intervention order was balanced among subjects within the control and asthmatic group. Following each intervention, subjects completed an exercise bout on a magnetized cycle ergometer. Subjects were instructed to refrain from ingesting caffeine for eight hours prior to each study and inhaled β_2-agonist for twelve hours prior to each study.

Experimental interventions

All subjects completed four separate exercise challenges preceded by a different intervention, as follows.

***β_2-agonist* [*bronchodilation (BD)*]—**Following baseline (BL) PFT's, subjects inhaled four actuations of a fast-acting β_2-agonist. Pulmonary function was assessed at 5 and 10 minutes following inhalation [post-intervention, (PI)]. Exercise was commenced at 15 minutes following inhalation, corresponding closely with the time of maximal bronchodilation.

***Eucapnic voluntary hyperpnea* [*bronchoconstriction (BC)*]—**The eucapnic voluntary hyperpnea challenge (EVH) was completed in accordance with the methods described by Anderson and Brannan (2). Briefly, subjects ventilated dry, compressed gas consisting of 21% O_2 and 5% CO_2 at a ventilation rate equal to $FEV_{1.0} \times 30$. Pulmonary function was performed at 5 and 10 minutes following the challenge. Exercise was commenced 15 minutes following EVH, closely corresponding with the time of maximal airway narrowing.

Hyperpnea sham (SHAM)—A sham trial was used to control for subject expectation effects or behavioral responses to the EVH protocol. Utilizing the same apparatus used for the EVH challenge, subjects were instructed to breathe in a normal, relaxed manner. Subjects inhaled room air during this trial; however, they were told that they were breathing air from the tank of compressed gas. The Douglas bag was filled with gas prior to the study, and laboratory personnel mimicked adjustment of a three-way valve and briefly opened the nozzle on the tank occasionally during the experiment. Pulmonary function was assessed at 5 and 10 minutes after the protocol, after which time exercise was commenced.

Control (CON)—Following baseline PFT's, subjects rested in a comfortable, seated position for 10 minutes. Pulmonary function was re-assessed and followed immediately by the exercise test.

Pulmonary function

PFT's were measured with a Medgraphics automated spirometer. All pulmonary function tests were completed in the seated, upright position according to recommendations by the American Thoracic Society and European Respiratory Society (29). During each measurement, subjects completed maximal volitional flow-volume maneuvers for determination of peak expiratory flow, forced vital capacity (FVC), forced expiratory volume 1.0 second ($FEV_{1.0}$), and forced expiratory flow at 50% of FVC ($FEF_{50\%}$). Slow vital capacities were performed for determination of inspiratory capacity (IC). Predicted values are from Quanjer (33).

Exercise apparatus

All exercise was completed on a magnetically braked cycle ergometer (Velotron). Subjects breathed through a two-way, non-rebreathing valve (Hans-Rudolph) with noseclips in place. Compressed gas (21% O_2, balance nitrogen) was used as the inspirate for all exercise studies in both asthmatic and non-asthmatic subjects. Separate pneumotachographs (Hans Rudolph) were used to determine inspiratory and expiratory flowrates. Separate oxygen and carbon dioxide gas analyzers (AEI Technologies) were used to analyze expired gases. A Powerlab 16-channel data acquisition system (ADinstruments) interfaced with a laptop computer was used to collect resting and exercise data.

Exercise protocol

Prior to exercise, subjects performed multiple IC maneuvers and several maximal volitional flow-volume loops. Following resting data collection, subjects completed three minutes of exercise at a workload equal to 70% of the peak workload achieved during the maximal exercise test (WU). Exercise workload was then increased to 85% of peak workload and was continued to volitional exhaustion (prolonged). Inspiratory capacities were performed during WU and at regular intervals during prolonged exercise.

Exercise measurements

Inspired and expired airflow rates and expired gases were used to calculate metabolic oxygen consumption ($\dot{V}O_2$) and carbon dioxide production ($\dot{V}CO_2$), minute ventilation ($\dot{V}_E$), tidal volume (V_T), breathing frequency (fb) and IC. A Polar heart rate monitor (POLAR, USA) was used to record heart rate during exercise. A modified Borg scale (0-10) was used to rate perceived exertion for both breathing and leg discomfort.

Statistical analysis

A three-factor [**GROUP** (asthma *vs.* non-asthma) × **TRIAL** (control, β_2-agonist, hyperpnea, sham) × **TIME** (exercise time)] repeated measures analysis of variance was used to analyze the exercise responses. When significant main effects were found, Bonferroni-corrected multiple pairwise comparisons were employed for post-hoc analysis. Linear regression was used to analyze relationships between selected variables. Tabular data are presented as mean ± standard deviation. Data in figures are presented as mean ± standard error of mean. Significance was set at $\alpha < 0.05$. The statistical software program SYSTAT was used to analyze all data (SYSTAT 12).

RESULTS

Group characteristics

Group descriptive characteristics and results from the screening studies are shown in Table 1. There were no differences in age, height, weight, $\dot{V}O_2$peak, or exercise peak power output between control and asthmatic subjects. Baseline pulmonary function and the change in $FEV_{1.0}$ after both bronchodilator and exercise were significantly different between asthmatic and control subjects. Thus, the two groups were well matched for anthropometric characteristics and exercise capacity, but AHR was only present in asthmatic subjects. Of the eight asthmatic subjects, six were prescribed an inhaled β-agonist on an as needed basis.

Pulmonary function

Group mean results for $FEV_{1.0}$ and $FEF_{50\%}$ at baseline (*i.e.*, upon arrival to lab) and after each intervention (PI) in control and asthmatic subjects are shown in Figure 1. Overall, $FEV_{1.0}$ and $FEF_{50\%}$ were lower in asthmatic compared with control subjects. In asthmatic subjects, EVH caused a decrease of 1.0 ± 0.6 (−27 ± 15%) and 1.7 ± 0.8 (−43 ± 13%) L, in $FEV_{1.0}$ and $FEF_{50\%}$, respectively. Moreover, PI values for $FEV_{1.0}$ and $FEF_{50\%}$ were 1.3 ± 0.8 (+57 ± 47%) and 2.3 ± 0.8 (+209 ± 237%) L higher during BD compared with BC in asthmatic subjects. These differences were not seen in control subjects. Results for peak expiratory flow were very similar to $FEV_{1.0}$ and $FEF_{50\%}$ (data not shown). However, there were no significant differences in FVC between the control and asthmatic group or within either group (data not shown). Thus, airway function was markedly different upon exercise commencement among the four experimental trials in asthmatic subjects.

Exercise workload & time

All subjects in both groups exercised at 70% (WU) and 85% (prolonged) of their individual peak workload attained during a maximal incremental exercise test. Workload during WU (control group, 177 ± 34 watts; asthma group, 180 ± 39 watts) and prolonged exercise (control group, 220 ± 42 watts; asthma group, 225 ± 46 watts) was not different between control and asthmatic subjects. In control subjects, exercise time-to-exhaustion was 8.0 ± 2.9, 7.4 ± 2.7, 7.7 ± 2.0, and 8.3 ± 2.9 min during CON, BD, SHAM, and BC trials, respectively ($p > 0.05$). In asthmatic subjects, time-to-exhaustion was 5.6 ± 1.3, 6.0 ± 2.3, 5.4 ± 1.4, and 5.5 ± 2.5 min during CON, BD, SHAM, and BC, respectively ($p > 0.05$). Group mean exercise time was not different between control and asthmatic subjects among any of the four trials (Bonferroni adjusted p-values: control trial, p=0.177; BD trial, p=1.0; SHAM trial, p=0.214; BC trial, p=0.073).

Exercise ventilation

Results for $\dot{V}_E$, V_T, fb, and the ventilatory equivalent for CO_2 production ($\dot{V}_E/\dot{V}CO_2$) are shown in Figure 2. Within both control and asthmatic subjects, there were no differences among trials for any of the ventilatory variables. Moreover, there were no differences between control and asthmatic subjects for any of the variables among the four experimental trials. Figure 3 depicts the relationship between PI $FEV_{1.0}$ and exercise $\dot{V}_E/\dot{V}CO_2$ in control and asthmatic subjects. In both control and asthmatic subjects, there was no relationship

between PI $FEV_{1.0}$ and exercise $\dot{V}_E/\dot{V}CO_2$. These results highlight the dissociation between baseline airway function and exercise ventilation in control and asthmatic subjects.

Exercise lung volumes

Results for IC and V_T/IC are shown in Figure 4. There were no significant differences in IC or V_T/IC either within or between control and asthmatic subjects. In control subjects, IC exhibited the usual intensity- and time-dependent increase during exercise and exhibited a plateau at the end of exercise. In asthmatic subjects, a significant main effect of exercise trial was found, but bonferroni-corrected pairwise comparisons were not significant. In asthmatic subjects, results for IC were similar during CON, BD, and SHAM, during which IC increased during WU, but thereafter demonstrated a decreasing trend throughout prolonged exercise to approach resting values by end exercise. During BC, IC following intervention was, on average, 0.6 ± 0.3 L lower than the other three trials ($p > 0.05$). During exercise, however, IC increased so that it equaled the other three trials by the end of exercise.

Other exercise responses

In table 2, group mean values for $\dot{V}O_2$, $\dot{V}_E/\dot{V}O_2$, HR, RPE-breath, and RPE-leg are shown for control and asthmatic subjects. In general, values for these variables were not different among the four trials within either subject group. Moreover, there were no significant differences between control and asthmatic subjects for any of the variables at any time point among the four exercise trials.

DISCUSSION

We sought to determine the effects of variable pre-exercise airway function on the ventilatory responses to whole-body exercise in asthmatic adults. Moreover, all studies were completed by a control group of non-asthmatic subjects. We hypothesized that exercise ventilation would be similar despite variable pre-exercise airway function in asthmatic subjects. Indeed, despite markedly different pre-exercise pulmonary function in asthmatic subjects, exercise ventilation was nearly identical among the four trials. Furthermore, there were no differences in exercise ventilation between control and asthmatic subjects among any of the four trials. These results demonstrate a robust pulmonary system in the mild asthmatic; one that is apparently capable of adequately responding to the acute demand for increased airflow necessitated by high-intensity aerobic exercise. From a clinical standpoint, these findings support the idea that regular exercise may be beneficial for the asthmatic (24, 28).

Exercise workload

The exercise intensity was set at 85% of the peak workrate achieved during an incremental exercise test-to-exhaustion. This demanding exercise workload was both high enough to challenge the capacity of the pulmonary system for generating airflow – reflecting the contractile properties of the respiratory muscles and the airway structural and parenchymal determinants of airflow – but also low enough so that subjects were able to exercise for a duration sufficient to address the purpose of this study. A workload either higher or lower than this would not have met these criteria. Additionally, the exercise workload in this study

is very similar to the workload generally employed in studies evaluating exercise-induced bronchoconstriction.

Pre-exercise pulmonary function

In the current study, pulmonary function was used as an indication of the overall state of airway function prior to exercise. To this end, the decreased forced expiratory flow rates prior to exercise during BC and the increased flow rates during BD indicate markedly different states of airway function prior to the exercise in asthmatic subjects (Figure 1B & 1D). Thus, at the onset of exercise during BC, the capacity for generating airflow was severely compromised. Nonetheless, this markedly disparate pre-exercise airflow generating capacity had no effect on the exercise ventilatory response.

In control subjects, pulmonary function increased slightly following bronchodilator and decreased slightly following EVH. In both cases, the changes from BL were statistically significant. Interestingly, pulmonary function also decreased slightly but significantly between BL and PI during both CON and SHAM trials. Thus, the tendency for pulmonary function to decrease with multiple efforts in asthmatics (*i.e.*, spirometry-induced bronchospasm) may also be the case for non-asthmatic subjects (16). We also note that although the magnitude of decrease in pulmonary function during CON and SHAM was less in nonasthmatics, the greater uniformity of response actually resulted in more statistical significance. These findings exemplify the recurring conundrum of distinguishing between statistical vs. physiological significance in human biology. These findings also highlight the fact that both between- and within-subject variability in pulmonary function – and likely other measures of physiologic functioning – will always be greater in a group of asthmatics compared with nonasthmatic counterparts. Given the variability in airway inflammation, AHR, and lung function in the asthmatic, this is not surprising.

Exercise ventilation

To the best of our knowledge, only one previous study has assessed exercise ventilation following both improved (*via* metaproterenol) and worsened (*via* methacholine) airway mechanical function in asthmatic subjects (26). Mahler and colleagues reported reduced V_T and $\dot{V}_E$ at peak exercise following methacholine challenge compared with a control trial and pre-exercise bronchodilation in adults with reversible obstructive airway disease. In the current study, exercise ventilation was not affected by variable pre-exercise airway mechanical function. There are several differences between the current study and the study by Mahler and colleagues. Most notably, subjects in the study by Mahler were both older and had more severe airways obstruction than our subjects. Secondly, the methods for inducing bronchoconstriction are very different between the two studies; in one case a direct-acting bronchiolar smooth muscle agonist was used (*i.e.*, cholinergic agonist, methacholine) whereas in the current study airway narrowing was induced by the indirect inflammatory effects of dry gas hyperpnea.

Although airway resistance is determined by interactions among several variables, it is most sensitive to changes in airway radius (9). Considering this importance of airway diameter in determining airflow, it is reasonable to posit a relationship between baseline airway function

and exercise ventilation. Evidence that supports this hypothesis, however, is limited. Previous investigations have assessed the effects of pre-exercise bronchodilation on exercise ventilation and exercise capacity in asthmatic adults (11, 18, 35, 36, 37). In all of these studies, pre-exercise bronchodilation had no effect on exercise ventilation as compared with control and placebo conditions. In fact, the airways of asthmatic subjects undergo an initial bronchodilation during whole-body exercise (4, 10, 15, 38). Thus, the natural bronchodilation with exercise may obviate the potential for altered airway function – whether improved or impaired – to influence exercise ventilation. An interesting experiment would be to prevent bronchodilation during exercise in asthmatic subjects. Presumably, this would be difficult, however, as exercise bronchodilation still occurs when the bronchoconstrictors histamine and methacholine are inhaled during exercise in the asthmatic (19, 38). A gradual bronchoconstriction can occur over time during moderate intensity exercise lasting longer than ~10 minutes (4, 21), but the effects of this gradual bronchoconstriction on exercise ventilation and performance have not been studied.

In this study, subjects exercised after six minutes of voluntary eucapnic hyperpnea. Voluntary hyperpnea stimulates the release of inflammatory mediators from resident (*i.e.*, epithelial) and non-resident (*i.e.*, mast cells) airway cells (1, 22). In the asthmatic, this non-specific stimulus causes bronchiolar smooth muscle contraction, plasma exudation, airway wall edema, and mucus secretion into the airways. The stimulus for this inflammatory-based airway narrowing with voluntary hyperpnea is thought to be identical to the osmotically-based stimulus for airway narrowing following whole-body exercise. In this study, subjects began exercise within 15 minutes following the EVH challenge, well before airway narrowing and inflammation had resolved.

A major finding of this study is that exercise ventilation was not affected by the poor airway function prior to exercise. In previous studies, asthmatic subjects have exercised following a variety of procedures that cause airway narrowing, including inhaled histamine, aerosolized hypertonic saline, methacholine, and EVH (5, 6, 13, 25). The purpose of these investigations, however, was to study bronchoconstriction *following* exercise, and analyses of exercise ventilation were minimal. Moreover, exercise was not commenced until pulmonary function had returned, or nearly returned, to baseline values; exercise began between 30 minutes and six hours following the pre-exercise challenge. In the current study, exercise was commenced within 10-15 minutes of the EVH challenge, when $FEV_{1.0}$ was still significantly reduced by the challenge.

In one previous study, asthmatic subjects completed an exercise challenge during the midst of a spontaneous asthma attack and also during a late asthmatic reaction to inhaled allergen (10). Exercise ventilation and $\dot{V}O_2$peak were preserved during both exercise conditions. In a different study, exercise ventilation was compared between two exercise bouts in which pulmonary function preceding the second bout was decreased compared with the first (15). Exercise ventilation during the second bout was identical to the first bout. The current findings support and extend these observations.

Exercise lung volumes

There were no statistically significant differences in operating lung volumes in either control or asthmatic subjects. In asthmatic subjects, the average 0.6 L difference in pre-exercise IC between BC and the other three trials, though not statistically significant, is certainly of some physiological significance. This finding is in agreement with other studies demonstrating a decreased IC with bronchoconstriction in asthmatic subjects (31, 39). An increased end-expiratory lung volume (*i.e.*, dynamic hyperinflation) with bronchoconstriction likely represents a compensatory response to increase airway diameter or reduce airway closure, due to interdependence between the airways and lung parenchyma (7). Importantly, the decreased pre-exercise IC during BC was not maintained during exercise, as exercise IC increased progressively to equal the values seen during the other three trials by end exercise. The slight differences in resting V_T/IC between BC and the other trials also disappeared during exercise. Collectively, these results demonstrate a robustly "agile" pulmonary system in the asthmatic, with a wonderful ability to respond to the requirement for increased airflow during exercise.

Perceptual responses during exercise

Despite the differences in pre-exercise airway function among trials in asthmatic subjects, both breathing and leg discomfort were the same during all four exercise trials. Perhaps most interesting is the unchanged RPE-breath following EVH. Intuitively, breathing discomfort would be expected to increase following bronchoconstriction. In asthmatic subjects at rest, however, the relationships between airway function and perception of breathlessness are unclear (30). In one study, pre-exercise bronchoconstriction *via* methacholine did cause an increased intercept for the relationship between exercise workrate and RPE-breath (26). In the same study, however, there were no changes in slope or intercept between RPE-breath and all other exercise variables, including flowrate, mouth pressure, breathing frequency, or tidal volume. Perceptual responses to exercise result from a complicated amalgamation of multiple ascending and descending neurohumerol inputs (27). Further investigation is needed to improve our understanding of the determinants of effort perception during exercise, and how perception of these determinants may be altered in disorders of the pulmonary system.

Generalizability of findings

The findings in this study are limited to asthmatic adults with primarily mild disease. Subjects were able to increase ventilation during exercise no matter how compromised airway function was prior to exercise. In asthmatics with more severely inflamed airways or greater degrees of airflow limitation, the ability to increase ventilation during exercise will likely be more limited.

In the current study, exercise consisted of three minutes at 70% peak power output followed by exercise-to-exhaustion at 85% peak power output. The current findings are thus confined to the high intensity, relatively short duration exercise completed by subjects in this study. There are a variety of bronchodilatory and bronchconstricting factors that interact to determine airway caliber during exercise in the asthmatic (3), and the balance of these factors will vary depending on exercise duration and intensity. For example,

bronchoconstriction can occur during submaximal exercise lasting ten minutes or longer and also during variable intensity exercise when exercise workload is decreased (4, 21). The current findings of unchanged exercise ventilation despite altered pre-exercise airway function should not be generalized to all intensities and durations of aerobic exercise. Further studies will be necessary to determine the relationships among airway function, exercise ventilation, and exercise workload and duration in asthmatic subjects.

Conclusions

We evaluated the effects of both improved and worsened airway function on exercise ventilation in asthmatic adults and compared the results with nonasthmatic control subjects. In a group of mild asthmatics, exercise ventilation was not affected by significant alterations in pre-exercise airway function. Notably, exercise ventilation was nearly indistinguishable between the asthmatic and control subjects. These findings corroborate previous studies demonstrating unchanged exercise ventilation and capacity following pre-exercise bronchodilation in the asthmatic. Moreover, these results demonstrate a remarkable dissociation between pre-exercise airway function and the exercise ventilatory response in the mildly asthmatic adult. These findings also contrast with the general notion that baseline airway function influences exercise ventilation in the asthmatic.

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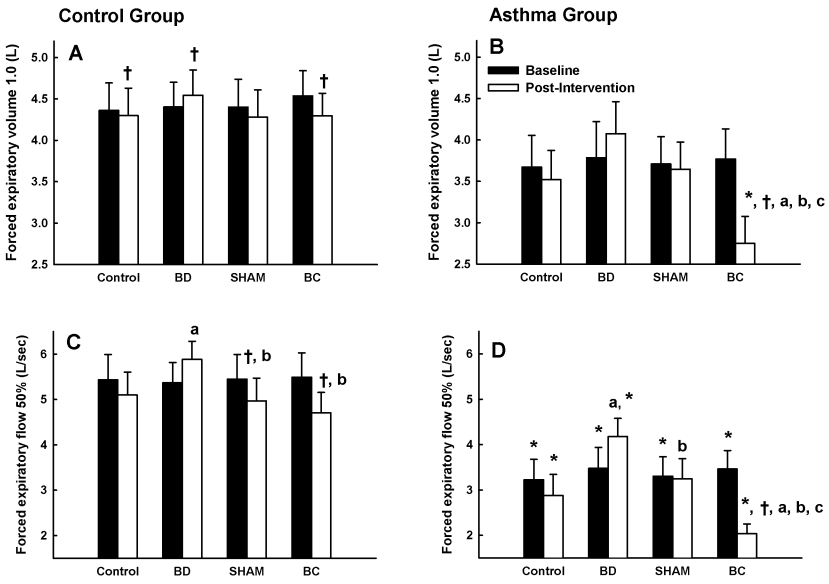

Figure 1.

Forced expiratory volume 1.0 s ($FEV_{1.0}$) and forced expiratory flow at 50% forced vital capacity ($FEF_{50\%}$) in control and asthmatic subjects at baseline and following an intervention during four experimental trials: control; bronchodilation (BD); sham (SHAM); and bronchoconstriction (BC). A) $FEV_{1.0}$ at baseline and following each of four interventions in control subjects; B) $FEV_{1.0}$ at baseline and following each of four interventions in asthmatic subjects; C) $FEF_{50\%}$ at baseline and following each of four interventions in control subjects; D) $FEF_{50\%}$ at baseline and following each of four interventions in asthmatic subjects. Note that $FEV_{1.0}$ and $FEF_{50\%}$ were lower in asthmatic subjects compared with control subjects. Also, note the marked changes in $FEV_{1.0}$ and $FEF_{50\%}$ following BD and BC in asthmatic subjects. *, $p<0.05$ *vs.* control group; †, $p<0.05$ *vs.* baseline; a, $p<0.05$ *vs.* CON trial; b, $p<0.05$ *vs.* BD trial; c, $p<0.05$ *vs.* SHAM trial.

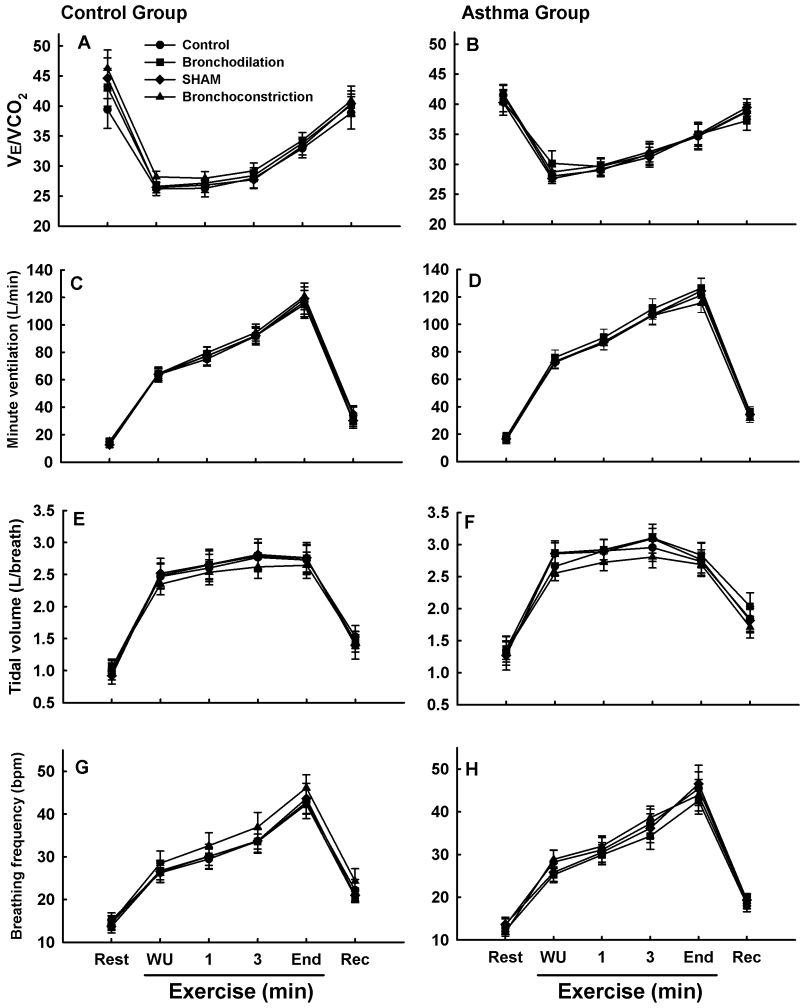

Figure 2.

Ventilatory variables at rest, during warmup exercise (WU), during exercise-to-exhaustion (1 minute, 3 minutes, end exercise), and three minutes after exercise (Rec) in control and asthmatic subjects during four experimental trials. Control group results are shown in A, C, E, and G. Asthma group results are shown in B, D, F, and H. There were no significant differences for any variable within either the control or asthmatic group. Moreover, there were no significant differences between control and asthmatic subjects for any of the variables.

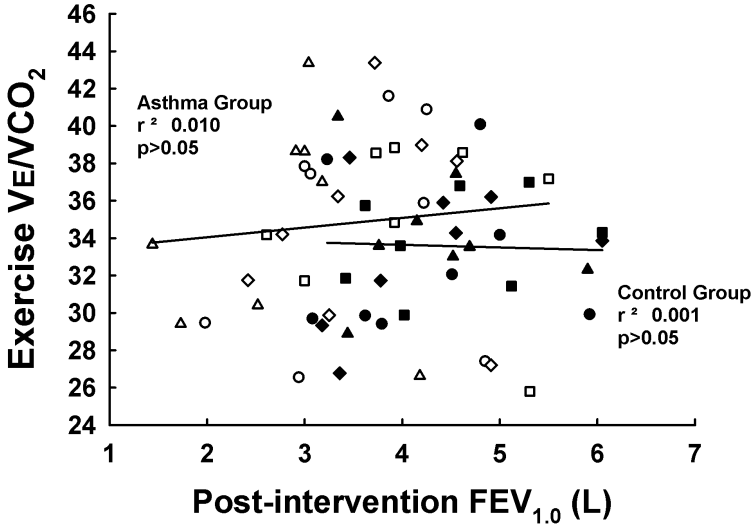

Figure 3.

Correlations between post-intervention forced expiratory volume 1.0 second ($FEV_{1.0}$) and exercise ventilatory equivalent for CO_2 production ($\dot{V}_E/\dot{V}CO_2$) in control (dark symbols) and asthmatic (open symbols) subjects. There was no relationship between post-intervention $FEV_{1.0}$ and $\dot{V}_E/\dot{V}CO_2$ in either control or asthmatic subjects. Circles, control trial; squares, bronchodilation trial; diamonds, sham trial; triangles, bronchoconstriction trial.

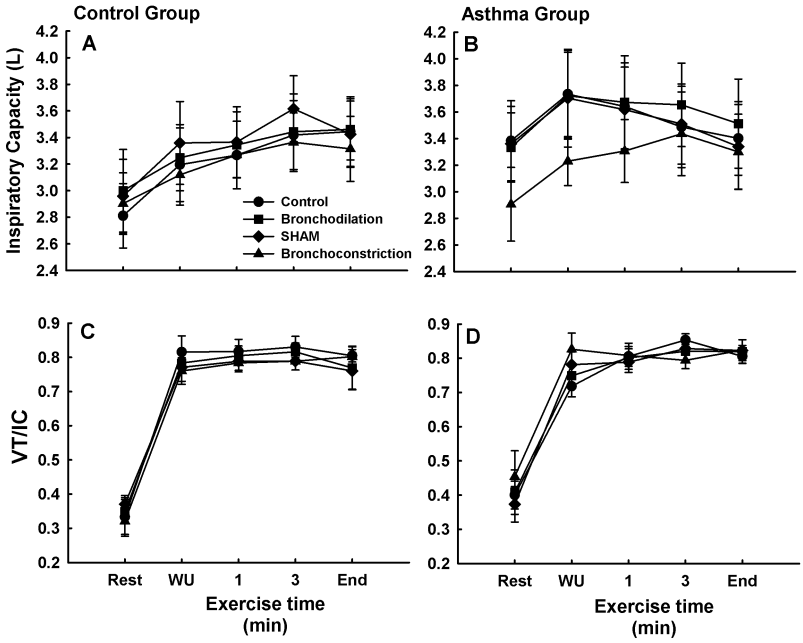

Figure 4.

Inspiratory capacity (IC) and ratio of tidal volume to inspiratory capacity (V_T/IC) at rest, during warmup exercise (WU), and during exercise-to-exhaustion (1 min, 3 min, end) during four experimental trials in control (A and C) and asthmatic (B and D) subjects. In control subjects, IC and V_T/IC exhibited a similar pattern during all four trials. In asthmatic subjects, note the lower IC at rest and early during exercise during the bronchoconstriction trial compared to the other three trials. Also, note that IC decreased during exercise in asthmatic but not in control subjects. There were no significant differences.

Table 1

Descriptive characteristics for control and asthmatic subjects.

	Control Group (*n*=9)	Asthmatic Group (*n*=8)
Male/Female	6/3	5/3
Age, y	25.6 ± 8.8	30.4 ± 8.4
Height, m	1.73 ± 0.1	1.72 ± 0.1
Weight, kg	74.2 ± 11.8	74.4 ± 13.9
Body mass index ($kg \cdot m^2$)	24.7 ± 2.6	25.1 ± 2.7
VO_2peak, $ml^{-1} \cdot kg \cdot^{-1} min^{-1}$	48.5 ± 6.4 (122 ± 0.3)	46.1 ± 6.6 (121 ± 0.3)
FVC, L	5.29 ± 1.07 (115 ± 13)	5.38 ± 1.2 (121 ± 17)
$FEV_{1.0}$, L	4.45 ± .94 (113 ± 11)	3.77 ± 1.1 (99 ± 17)
$FEV_{1.0}$/FVC	0.84 ± 0.07 (105 ± 8.4)	0.70 ± 0.10 (87 ± 13)*
$FEF_{50\%}$, $L \cdot sec^{-1}$	5.27 ± 1.56 (102 ± 24)	3.29 ± 1.3 (65 ± 22)*
PEF, $L \cdot sec^{-1}$	9.35 ± 2.28 (104 ± 13)	7.89 ± 2.2 (91 ± 19)
Peak power output, watts	262 ± 44	275 ± 49
BD reversibility, % change FEV_{10}	+ 5.2 ± 4.1	+ 12.2 ± 7.5*
EIB, % change FEV_{10}	−5.3 ± 3.0	−26.6 ± 15.3*

$\dot{V}O_2$peak, maximal oxygen uptake; FVC, forced vital capacity; $FEV_{1.0}$, forced expiratory volume 1 second; $FEF_{50\%}$, forced expiratory flow at 50% FVC; PEF, peak expiratory flow; BD, bronchodilator; EIB, exercise-induced bronchoconstriction.

*$p<0.05$ *vs.* control group. Percent predicted values in parentheses. Spirometry predicted values from Quanjer (33).

Table 2

Physiological variables measured at baseline, during warmup exercise, and during exercise-to-exhaustion in control and asthmatic subjects.

		Exercise-to-exhaustion				
	Baseline	**Warmup**	**1 min**	**3 min**	**End**	**Recovery**
Control Group (n=9)						
VO_2, L·min^{-1}						
Control trial	0.42 ± 0.1	2.7 ± 0.6	3.1 ± 0.6	3.3 ± 0.6	3.6 ± 0.9	0.67 ± 0.2
BD trial	0.40 ± 0.1	2.6 ± 0.5	3.0 ± 0.6	3.2 ± 0.6	3.4 ± 0.7	0.65 ± 0.2
SHAM trial	0.40 ± 0.1	2.6 ± 0.4	3.0 ± 0.7	3.2 ± 0.7	3.5 ± 0.9	0.63 ± 0.2
BC trial	0.40 ± 0.1	2.6 ± 0.5	3.0 ± 0.7	3.2 ± 0.7	3.6 ± 0.9	0.77 ± 0.3
V_E/VO_2						
Control trial	35.0 ± 16.3	24.9 ± 4.8	26.1 ± 5.8	29.5 ± 6.4	34.1 ± 7.7	47.3 ± 14.9
BD trial	36.5 ± 10.0	25.2 ± 4.4	26.7 ± 4.2	29.3 ± 4.9	34.3 ± 6.0	45.9 ± 8.4
SHAM trial	36.3 ± 9.4	25.3 ± 4.6	26.8 ± 5.0	29.3 ± 5.0	34.5 ± 5.5	47.3 ± 8.5
BC trial	39.6 ± 11.1	25.3 ± 3.3	27.2 ± 4.3	29.9 ± 4.4	34.5 ± 5.5	45.6 ± 5.5
HR, BPM						
Control trial	71.7 ± 9	140.2 ± 14	156.9 ± 12	167.7 ± 11	177.0 ± 8	113.1 ± 9
BD trial	80.4 ± 13	144.0 ± 12	158.7 ± 12	169.1 ± 8	177.6 ± 8	113.0 ± 11
SHAM trial	73.8 ± 7	144.1 ± 12	158.8 ± 12	168.6 ± 11	178.1 ± 12	113.7 ± 17
BC trial	72.0 ± 6	139.8 ± 11	157.4 ± 9	167.8 ± 9	177.4 ± 11	111.2 ± 13
RPE, Breath						
Control trial	0.28 ± 0.44	1.39 ± 1.02	2.78 ± 1.09	4.78 ± 1.20	7.44 ± 1.59	3.33 ± 1.98
BD trial	0.17 ± 0.35	1.17 ± 0.71	2.50 ± 1.00	4.89 ± 1.27	7.67 ± 1.94	3.78 ± 1.92
SHAM trial	0.33 ± 0.71	1.56 ± 0.98	3.22 ± 0.83	5.00 ± 1.12	8.33 ± 1.73	4.22 ± 2.22
BC trial	0.22 ± 0.44	1.33 ± 0.97	3.44 ± 1.01	4.89 ± 1.83	8.22 ± 1.39	3.33 ± 1.66
RPE, Legs						
Control trial	0.17 ± 0.25	2.17 ± 1.52	4.44 ± 1.67	6.00 ± 1.22	9.44 ± 0.73	5.28 ± 2.41
BD trial	0.17 ± 0.25	2.39 ± 2.00	3.78 ± 1.92	6.06 ± 1.51	8.89 ± 1.05	5.00 ± 2.12
SHAM trial	0.17 ± 0.35	2.22 ± 1.37	4.11 ± 1.45	6.11 ± 1.17	9.22 ± 1.09	5.33 ± 2.65
BC trial	0.06 ± 0.17	2.56 ± 1.51	4.56 ± 0.88	6.44 ± 1.33	9.22 ± 1.30	5.00 ± 2.00
Asthma Group (n=8)						
VO_2, L·min^{-1}						
Control trial	0.40 ± 0.1	2.6 ± 0.4	2.8 ± 0.6	3.1 ± 0.6	3.3 ± 0.7	0.71 ± 0.2
BD trial	0.50 ± 0.2	2.7 ± 0.4	2.8 ± 0.5	3.1 ± 0.7	3.4 ± 0.6	0.81 ± 0.2
SHAM trial	0.50 ± 0.2	2.5 ± 0.6	2.7 ± 0.6	3.0 ± 0.7	3.3 ± 0.8	0.69 ± 0.2
BC trial	0.40 ± 0.1	2.5 ± 0.5	2.8 ± 0.5	3.1 ± 0.7	3.2 ± 0.7	0.69 ± 0.2
V_E/VO_2						
Control trial	39.4 ± 7.8	28.2 ± 3.3	30.9 ± 3.5	35.0 ± 5.6	37.6 ± 7.6	48.7 ± 5.0
BD trial	35.0 ± 10.1	27.7 ± 4.5	30.5 ± 6.1	33.1 ± 7.2	36.0 ± 6.6	42.5 ± 9.2

	Exercise-to-exhaustion					
	Baseline	**Warmup**	**1 min**	**3 min**	**End**	**Recovery**
SHAM trial	36.1 ± 12.2	28.5 ± 4.0	31.9 ± 5.2	32.7 ± 4.2	38.4 ± 7.1	50.0 ± 4.3
BC trial	37.2 ± 8.0	29.2 ± 3.1	31.4 ± 3.5	33.4 ± 4.9	36.8 ± 6.3	46.7 ± 6.2
HR, BPM						
Control trial	74.0 ± 13	136.5 ± 14	151.8 ± 11	165.0 ± 13	173.3 ± 12	110.8 ± 17
BD trial	81.1 ± 16	142.1 ± 15	156.9 ± 13	167.1 ± 13	173.6 ± 13	117.3 ± 18
SHAM trial	72.3 ± 9	139.4 ± 16	154.9 ± 14	165.9 ± 14	172.3 ± 13	112.8 ± 19
BC trial	75.3 ± 13	139.6 ± 14	154.4 ± 13	164.7 ± 13	168.4 ± 13	114.1 ± 28
RPE, Breath						
Control trial	0.25 ± 0.27	1.50 ± 1.28	3.00 ± 1.85	5.13 ± 2.46	7.88 ± 1.96	3.31 ± 2.69
BD trial	0.19 ± 0.26	2.50 ± 1.41	4.13 ± 2.10	5.57 ± 2.70	7.81 ± 3.21	3.19 ± 2.00
SHAM trial	0.31 ± 0.70	2.19 ± 1.13[a]	3.56 ± 1.45	5.50 ± 1.93	7.63 ± 2.13	3.00 ± 1.77
BC trial	0.69 ± 1.36	2.13 ± 1.55	4.00 ± 2.14	5.38 ± 2.67	7.31 ± 3.08	3.88 ± 3.04
RPE, Legs						
Control trial	0.19 ± 0.26	2.19 ± 1.46	3.88 ± 1.64	6.50 ± 2.00	8.63 ± 1.51	3.14 ± 2.12
BD trial	0.13 ± 0.23	2.88 ± 1.73	4.81 ± 2.10	6.31 ± 2.22	8.13 ± 1.64	2.71 ± 2.48
SHAM trial	0.13 ± 0.23	2.94 ± 1.43	4.25 ± 1.58	6.25 ± 1.89	8.00 ± 2.27	2.75 ± 1.16
BC trial	0.13 ± 0.23	2.50 ± 1.77	4.56 ± 2.38	5.69 ± 2.52	8.38 ± 1.69	3.50 ± 1.93

VO_2, oxygen consumption; V_E/VO_2, ventilatory equivalent for oxygen consumption; RPE, rating of perceived exertion. a, $p<0.05$ *vs.* control trial