

Physical Activity and Exercise-Induced Bronchoconstriction in Greek Schoolchildren

Michael B. Anthracopoulos, MD, PhD, FAAP,^{1*} Sotirios Fouzas, MD,¹ Marios Papadopoulos, MD,²
George Antonogeorgos, MD, PhD,³ Anastasios Papadimitriou, MD, PhD,²
Demosthenes B. Panagiotakos, PhD,³ Polyxeni Nicolaidou, MD, PhD,² and Kostas N. Priftis, MD, PhD²

Summary. Objective: To investigate the association between physical activity and exercise-induced bronchoconstriction (EIB) in an urban population sample of schoolchildren, taking into account potential confounders such as asthma symptoms and overweight. Methods: Children aged 10–12 years answered validated questionnaires on physical activity (Physical Activity and Lifestyle Questionnaire) and asthma symptoms (ISAAC questionnaire), and were categorized according to their body mass index (BMI). EIB (FEV₁ decrease from baseline $\geq 13\%$) was assessed by a standardized free running Exercise Challenge Test (ECT). Results: Six hundred seven children completed the ECT. There were no differences among asthma groups (diagnosed asthma, asthma-related symptoms not diagnosed as asthma, no asthma-related symptoms) regarding total daily energy expenditure and time spent in mild (1.1–2.9 metabolic equivalents—METs), moderate (3–6 METs), and vigorous (>6 METs) activities. Only overweight/obese EIB-positive children had shorter duration of vigorous activity as compared to their EIB-negative or non-overweight/obese EIB-positive peers. Total daily energy expenditure and duration of mild- and moderate-intensity activity were negatively associated with EIB independently of BMI status or asthma-related symptoms. Conclusions: Decreased levels of physical activity are associated with EIB irrespectively of BMI status and asthma-related symptoms. Longitudinal studies are needed to confirm the negative impact of sedentary lifestyle on the development of EIB suggested by these findings. **Pediatr Pulmonol.**

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INTRODUCTION

The causes of the increase in asthma prevalence observed in Westernized societies from the 1960s to the mid-1990s remain elusive. Lifestyle changes including physical inactivity and obesity—in addition to allergen exposure, hygiene and diet—have been proposed as potential contributors to the asthma “epidemic.”^{1,2}

Despite important methodological differences among studies, a strong and consistent relationship between asthma and physical inactivity has clearly emerged; however, the direction of causality is disputed.^{3–15} Certain investigators have proposed that asthmatic children experience limitations in physical activity due to their disease.^{3–8} Others, however, have failed to confirm this association, suggesting that poorer fitness is not related to asthma severity but rather to the perceived inability of asthmatic children to participate in physical activities.^{12–14} On the other hand, there is growing evidence that it is actually physical inactivity that predisposes to the development of asthma.¹¹ Along these lines, two longitudinal studies, one in asymptomatic children⁹ and

the other in twin pairs,¹⁰ showed that decreased physical activity in childhood is associated with development

¹Respiratory Unit, Department of Paediatrics, School of Medicine, University of Patras, Rion, Patras, Greece.

²Third Department of Paediatrics, Attikon Hospital, Athens University Medical School, Athens, Greece.

³Department of Nutrition and Dietetics, Harokopion University, Athens, Greece.

Conflicts of interest: None.

*Correspondence to: Michael B. Anthracopoulos, MD, FAAP, Respiratory Unit, Department of Paediatrics, School of Medicine, University of Patras, Rion, Patras 265 04, Greece. E-mail: manthra@otenet.gr

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of asthma later in life. Moreover, the beneficial effect and the safety of regular exercise on asthmatic children (reduced asthma symptoms and physician office visits, improved quality of life) has been convincingly documented.¹⁶

Bronchial hyperresponsiveness (BHR) is considered to be an objective marker of asthma that is closely related to the underlying mechanisms of the disease and is not influenced by diagnostic fashion.¹⁷ Bronchial response to exercise has been shown to be more specific than airway responsiveness to pharmacological agents for the diagnosis of childhood asthma,¹⁸ while field exercise has been suggested—but not definitively proven—to be more sensitive than laboratory exercise testing when performed under appropriate conditions in elite athletes.¹⁹

Current evidence supports a strong relationship between BHR and physical inactivity.^{7,11,15} However, the association between exercise-induced bronchoconstriction (EIB) and physical activity has not been investigated in a general pediatric population. The aim of the present study was to explore this association by using a field Exercise Challenge Test (ECT) after taking into account potential confounders such as asthma symptoms and body mass, for the first time, in a large urban sample of school-aged children.

METHODS

Participants

Participants were children included in the Physical Activity, Nutrition and Allergies in Children Examined in Athens (PANACEA) study,²⁰ an epidemiological cross-sectional survey designed to evaluate the relationship between the prevalence of asthma symptoms in Greek schoolchildren and their anthropometric and life-style characteristics. The aims and the methods of the PANACEA study have been previously reported.²⁰ A flow diagram of the study is presented in Figure 1. From January to March 2006, 700 children aged 10–12 years (4th to 6th school grade) from 18 randomly selected public schools located in the greater Athens area (Athens, Greece) were enrolled. Information regarding socio-demographic characteristics, asthma symptoms,

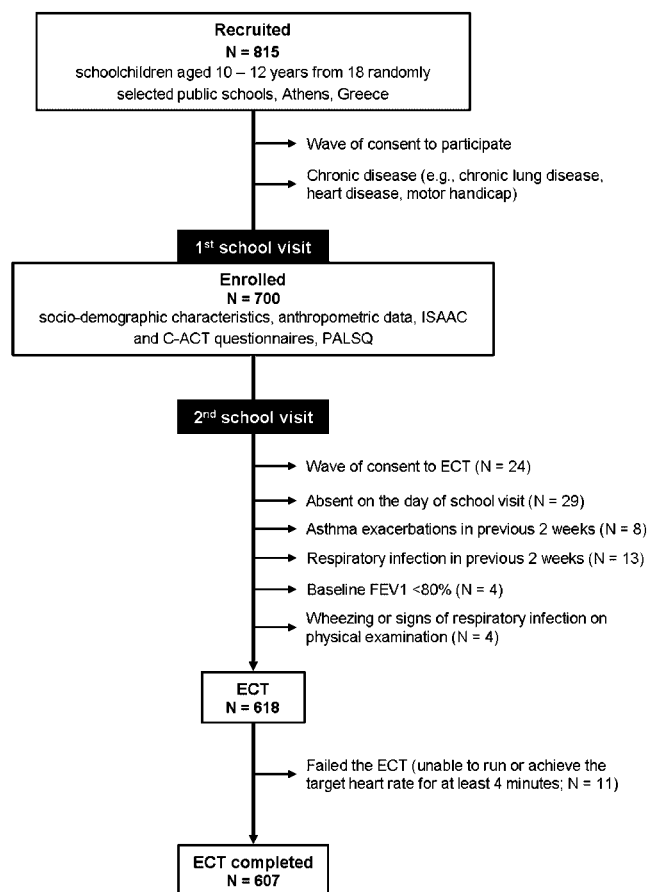


Fig. 1. Flow diagram of the study. ISAAC, The International Study of Asthma and Allergies in Childhood; C-ACT, Childhood Asthma Control Test; PALSQ, Physical Activity and Life Style Questionnaire; ECT, Exercise Challenge Test; ICS, inhaled corticosteroids.

and daily physical activity were obtained during the initial school visit. Two weeks later, eligible children were scheduled to perform an ECT. The field-research team consisted of two pediatricians, one experienced pediatric nurse and one sports science specialist.

The study protocol was approved by the Hellenic Ministry of Education (approval 29712/G7/2006). Participation was on a voluntary basis. Children and their parents provided signed consent after being offered detailed information on the requirements of the ECT protocol and the objectives of the study.

Anthropometric Data

Standing height was measured with a height rod (Raven Equipment Ltd., Essex, UK), and body weight with a floor scale (Seca GmbH & Co. Kg, Hamburg, Germany). Overweight and obese children were categorized using the international body mass index (BMI) cut-off points.²¹

ABBREVIATIONS:

BHR	Bronchial hyperresponsiveness
EIB	Exercise-induced bronchoconstriction
PANACEA	Physical Activity Nutrition and Allergies in Children Examined in Athens
ECT	exercise Challenge Test
PALSQ	Physical Activity and Life Style Questionnaire
MET	Metabolic equivalent
BMI	Body mass index

Asthma Symptoms and Categories

Asthma symptoms were evaluated by using the approved Greek version of the International Study for Asthma and Allergies in Childhood (ISAAC) core questionnaire.²² Children were classified into 3 categories: (1) *Diagnosed asthma (group 1)*, which included children with physician diagnosed asthma plus wheeze and/or dry cough at night that was unrelated to respiratory infection in the last 12 months, or use of prophylactic medication for asthma in the last 12 months; (2) *Asthma-related symptoms not diagnosed as asthma (group 2)*, which included children with wheeze and/or dry cough at night in the last 12 months but not physician diagnosed asthma; and (3) *No asthma-related symptoms (group 3)*, which included children without wheeze or dry cough at night in the last 12 months. Control of asthma was evaluated by using the Childhood Asthma Control Test (C-ACT).²³

Physical Activity

The level of physical activity was evaluated by using the Physical Activity and Life Style Questionnaire (PALSQ), an instrument that has been validated against metabolic equivalence in Greek schoolchildren.²⁴ The questions were read to each child by one of the researchers and were completed with the child during the initial school visit. Participants were asked how often and at what level of competitive requirement they participated in various daily activities, including organized sports (such as brisk walking, running, swimming, and cycling), non-sports related activities (such as going out with friends, social visits, going to the cinema), and sedentary activities (reading, watching television, working on computer, playing video games). According to the response to each question, the scoring procedure produces a total of daily energy expenditure ($\text{kcal kg}^{-1} \text{day}^{-1}$),²⁴ and can differentiate the time spent in mild (1.1–2.9 metabolic equivalents—METs), moderate (3–6 METs), and vigorous (>6 METs) activities. According to the total daily energy expenditure reported, participants were classified as active ($\geq 40 \text{ kcal kg}^{-1} \text{day}^{-1}$), moderately active ($37\text{--}39.99 \text{ kcal kg}^{-1} \text{day}^{-1}$), or inactive ($< 37 \text{ kcal kg}^{-1} \text{day}^{-1}$).²⁴

Exercise Challenge Test

ECTs were conducted in the school setting (sports halls or other similar sporting facilities), from 09:00 to 12:00 hr. The relative humidity was 45–60%, and the temperature 12–22°C throughout the study period; these conditions have been evaluated and are considered to be suitable for exercise testing.²⁵ The children were asked to arrive in training clothes and running shoes,

having consumed no more than breakfast; after a detailed demonstration of the ECT protocol, they presented in groups of four to each of the following stations.

Station 1—Eligibility and baseline spirometry

The personal health record booklets were reviewed, and each child underwent detailed physical examination. Children were excluded if they had received bronchodilator medication within 48 hr prior to the ECT, if they had suffered asthma exacerbation or clinically apparent respiratory tract infection in the previous 2 weeks, or had evidence of wheezing or current respiratory infection on physical examination. Children with baseline $\text{FEV}_1 < 80\%$ predicted were also excluded. Baseline spirometry was performed using a portable spirometer (MicroLab, Micro Medical Ltd., Rochester, UK). Three technically acceptable measurements were performed and the highest FEV_1 , FVC, and PEF were recorded as absolute and % predicted values.

Station 2—Exercise challenge

Children, in groups of four, were encouraged to run freely for 6 min in order to achieve a heart rate of 90% of the calculated maximum for age ($0.9 \times [220 - \text{age}]$) for at least 4 min. A sports science specialist coached the children while running in order to motivate them. Heart rate and running time were monitored by a portable heart rate monitor (Polar Electro, Inc., Lake Success, NY). Children who were unable to achieve the target heart rate for at least 4 min were considered as having failed the ECT. Conversely, children who ran for ≤ 6 min but achieved this target were asked to proceed to the next station.

Station 3—Exercise assessment

Each child underwent a careful post-exercise physical examination; signs and symptoms such as wheeze, cough, shortness of breath, and perceived breathlessness were recorded. Spirometry was performed at 5, 10, and 20 min after exercise. On each occasion, three readings were obtained and the highest FEV_1 value was recorded. The ECT response was defined as the greatest drop in FEV_1 , expressed as percentage of the baseline value. EIB was defined as a FEV_1 decrease from baseline of $\geq 13\%$.²⁶ Children who exhibited asthma symptoms were managed with 500 μg of inhaled salbutamol and were re-examined before they returned to class.

Data Analyses

Associations between categorical variables were evaluated using the chi-square test, whereas relationships between continuous variables were tested, after checking

for homoscedasticity, using the one-way analysis of variance (ANOVA) with Bonferroni correction. Overweight and obese children were analyzed as a combined group. The association between body mass and physical activity with EIB was assessed using logistic regression analysis after adjusting for presence of asthma-related symptoms and sex. A posterior statistical power analysis revealed that at least 600 children were adequate to evaluate odds ratios equal to 1.5 at the 0.05 significance level in order to achieve 95% power. Statistical analyses were performed using the SPSS software version 17.0 (SPSS, Inc., Chicago, IL).

RESULTS

Of the 700 children enrolled in the PANACEA study, 607 (86.7%) completed the ECT protocol. The flow diagram of the study is presented in Figure 1. Eleven children failed to complete the ECT: three ran <4 min and eight failed to achieve the target heart rate. Ten of these children (90.9%) were overweight or obese. Twenty-four children (4%) ran <6 min but achieved the target heart rate for at least 4 min. Of these, 20 (83.3%) were overweight or obese; the prevalence of EIB in this group was 4.2% ($n = 1$).

The characteristics of the study population are presented in Table 1. EIB was documented in 63 children (10.4%). Fifty-eight children (92.1%) achieved maximum ECT response at 5 min, and the rest reached their FEV₁ nadir at 10-min post-exercise. Spirometric values normalized after bronchodilator administration in all children.

There were no differences between the 3 symptoms based (ISAAC questionnaire) groups regarding total daily energy expenditure and time spent in mild- or moderate-intensity activities. Children with diagnosed asthma (group 1) or asthma-related symptoms not diagnosed as asthma (group 2), had lower baseline spirometric values and were more likely to exhibit EIB than their asymptomatic counterparts (group 3, Table 2). The prevalence of overweight and obesity was higher among children with asthma-related symptoms not diagnosed as asthma (group 2); this group also reported shorter daily duration of vigorous activities (Table 2). Five children classified in the “no asthma related symptoms” category (group 3) had been diagnosed as asthmatics in the past, but had no asthma-related symptoms and had received no antiasthma medication within the last 12 months; they all had normal baseline spirometry and negative ECTs. The results were not altered when these children were excluded from the analysis.

The prevalence of EIB was higher in participants classified as moderately active or inactive, as compared to their active peers. These children also had lower baseline spirometric values. Increased BMI and asthma-related symptoms not diagnosed as asthma were also

more prevalent among inactive children as compared to their more active peers (Table 3).

There was no statistically significant difference in the prevalence of overweight and obesity between EIB-positive and EIB-negative children (36.5% vs. 29.2%, $P = 0.29$). Irrespective of BMI status, children with EIB showed statistically significant lower daily energy expenditure, shorter time spent in moderate, and longer time spent in mild-intensity activities, as compared to EIB-negative participants. However, the overweight/obese EIB-positive children had shorter duration of vigorous activity, as compared to their EIB-negative or non-overweight/obese EIB-positive peers (Table 4).

Multi-adjusted logistic regression analyses revealed that the total daily energy expenditure and the duration of mild- and moderate-intensity activity were associated with EIB, independently of BMI status or asthma symptoms. The effect of overweight/obesity or that of vigorous activity on EIB was not statistically significant (Table 5).

DISCUSSION

The principle finding of this study is that decreased levels of physical activity of 10- to 12-year-old children

TABLE 1—Characteristics of the Study Population ($n = 607$)

Demographic and anthropometric data	
Age (years)	11.2 $\pm$ 0.6
Male	283 (46.6)
Weight (kg)	44.8 $\pm$ 9.1
Height (cm)	150.0 $\pm$ 8.4
BMI (kg m^{-2})	19.6 $\pm$ 3.2
Overweight	182 (30.0)
Obese	57 (9.4)
Asthma-related history in the last 12 months	
Wheeze	45 (7.4)
Exercise wheeze	30 (4.9)
Night cough	79 (13.0)
Any asthma-related symptom	163 (26.8)
Diagnosed asthma	65 (10.7)
Inhaled corticosteroids	39 (6.4)
Duration of activity (hr/day)	
Mild intensity	13.16 $\pm$ 0.78
Moderate intensity	1.85 $\pm$ 0.43
Vigorous intensity	0.86 $\pm$ 0.35
Total daily energy expenditure ($\text{kcal kg}^{-1} \text{ day}^{-1}$)	40.12 $\pm$ 4.15
Baseline lung function (% predicted)	
FEV ₁	98.1 $\pm$ 4.5
FVC	95.4 $\pm$ 5.8
PEF	91.9 $\pm$ 5.0
Exercise-induced bronchoconstriction	63 (10.4)

BMI, body mass index; FEV₁, forced expiratory volume in 1 sec; FVC, forced expiratory vital capacity; PEF, peak expiratory flow; MET, standard metabolic equivalent.

Intensity of activity: mild 1.1–2.9 METs, moderate 3–6 METs, vigorous > 6 METs.

Data presented as n (%) or mean $\pm$ SD.

TABLE 2—Characteristics of Participating Children According to Asthma Category

	Diagnosed asthma (Group 1), n = 65	Asthma-related symptoms not diagnosed as asthma (Group 2), n = 98	No asthma-related symptoms (Group 3), n = 444
Male	36 (55.4)	51 (52.0)	196 (44.1)
Overweight or obese	22 (33.8)	39 (39.8)*	121 (27.3)
Duration of activity (hr/day)			
Mild intensity	13.18 ± 0.8	13.27 ± 0.79	13.11 ± 0.77
Moderate intensity	1.83 ± 0.45	1.8 ± 0.43	1.86 ± 0.42
Vigorous intensity	0.84 ± 0.36	0.78 ± 0.35*	0.87 ± 0.33
Total daily energy expenditure (kcal kg ⁻¹ day ⁻¹)	40.02 ± 3.34	39.82 ± 3.75	40.2 ± 4.1
C-ACT score	23.4 ± 1.5	—	—
Baseline lung function (% predicted)			
FEV ₁	91.8 ± 4.8 ^{†,‡}	97.3 ± 5.2 [‡]	99.7 ± 4.0
FVC	90.0 ± 5.1 ^{†,‡}	93.0 ± 5.7 [‡]	97.5 ± 5.5
PEF	90.4 ± 5.5 [‡]	91.2 ± 4.7 [‡]	93.1 ± 5.0
Exercise-induced bronchoconstriction	33 (50.8) ^{†,‡}	23 (23.5) [‡]	7 (1.6)

C-ACT, childhood asthma control test; FEV₁, forced expiratory volume in 1 sec; FVC, forced expiratory vital capacity; PEF, peak expiratory flow; MET, standard metabolic equivalent.

Data presented as n (%) or mean ± SD. Hypothesis testing for significance using chi-square test or one-way ANOVA with Bonferroni adjustment, where appropriate. Intensity of activity: mild 1.1–2.9 METs, moderate 3–6 METs, vigorous >6 METs.

**P* < 0.05 versus no asthma-related symptoms.

[†]*P* < 0.001 versus asthma-related symptoms not diagnosed as asthma.

[‡]*P* < 0.001 versus no asthma-related symptoms.

were consistently associated with EIB, and that this association was independent of BMI status and asthma-related symptoms. This is in agreement with the results of previous studies on the relationship between BHR and physical inactivity.^{7,8,11,15} To the best of our knowledge, no previous report has focused on the relationship between physical activity and EIB assessed by free running challenge in a general population of school-aged children.

Although we cannot prove the direction of causality, our findings suggest that it is the decrease in physical

activity that predisposes to EIB, rather than the opposite. First, if the restriction in the participants' activity were due to EIB, it appears reasonable to expect that such restriction would become more evident during vigorous activity; this was not the case, since increased bronchial responsiveness to exercise was not related to the duration of vigorous activity in our population (Table 5). Instead, it was the increased duration of mild-intensity activities and the decreased duration of moderate-intensity activities—both reflecting a more sedentary lifestyle—that appeared to play a critical role

TABLE 3—Characteristics of Participating Children According to Activity Category

Activity category ¹	Active (n = 308)	Moderately active (n = 194)	Inactive (n = 105)
Male	144 (46.8)	93 (47.9)	46 (43.8)
Overweight or obese	83 (26.9)	52 (26.8)	47 (44.8)*,†
Asthma-related history			
Diagnosed asthma	30 (9.7)	22 (11.3)	13 (12.4)
Asthma-related symptoms not diagnosed as asthma	37 (12.0)	34 (17.5)	27 (25.7)*
Baseline lung function (% predicted)			
FEV ₁	102.1 ± 5.4	95.0 ± 4.7 [‡]	92.1 ± 4.9 ^{‡,§}
FVC	98.3 ± 5.4	93.8 ± 5.6 [‡]	89.8 ± 5.5 ^{‡,§}
PEF	92.3 ± 5.1	91.7 ± 4.6	91.1 ± 4.9
Exercise-induced bronchoconstriction	15 (4.9)	28 (14.4) [‡]	20 (19.0) ^{‡,§}

FEV₁, forced expiratory volume in 1 sec; FVC, forced expiratory vital capacity; PEF, peak expiratory flow.

Data presented as n (%) or mean ± SD. Hypothesis testing was performed using chi-square test or one-way ANOVA with Bonferroni adjustment, where appropriate.

¹Defined according to total energy expenditure (kcal kg⁻¹ day⁻¹) as follows: ≥40 active; 37–39.99 moderately active; <37 inactive.

**P* < 0.01 versus active.

[†]*P* < 0.01 versus moderately active.

[‡]*P* < 0.001 versus active.

[§]*P* < 0.001 versus moderately active.

TABLE 4—Physical Activity Characteristics of Participating Children Stratified by Exercise-Induced Bronchoconstriction and Overweight/Obesity

Group	EIB positive		EIB negative	
	Overweight/obese	Non-overweight/obese	Overweight/obese	Non-overweight/obese
	A (n = 23)	B (n = 40)	C (n = 159)	D (n = 385)
Duration of activity (hr/day)				
Mild intensity	14.0 ± 0.83 [†]	14.06 ± 0.81 [†]	13.10 ± 0.76	13.04 ± 0.78
Moderate intensity	1.21 ± 0.49 [†]	1.32 ± 0.47 [†]	1.86 ± 0.42	1.94 ± 0.39
Vigorous intensity	0.58 ± 0.3 [‡]	0.88 ± 0.31	0.82 ± 0.35	0.88 ± 0.36
Total daily energy expenditure (kcal kg ⁻¹ day ⁻¹)	36.62 ± 3.29 [†]	36.95 ± 3.22 [†]	40.36 ± 3.86	40.56 ± 4.04

EIB, exercise-induced bronchoconstriction; MET, standard metabolic equivalent.

Intensity of activity: mild 1.1–2.9 METs, moderate 3–6 METs, vigorous >6 METs.

Data presented as mean ± SD. Hypothesis testing was performed using one-way ANOVA with Bonferroni adjustment.

[†]*P* < 0.001 versus C and D.

[‡]*P* < 0.001 versus B, C, and D.

in the development of EIB. Second, non-overweight/obese EIB-positive children were characterized by levels of vigorous activity similar to those reported by their EIB-negative peers (Table 4); this should not be the case if increased bronchial responsiveness to exercise was solely the cause of decreased physical activity.

Our findings are in agreement with previous reports, which suggest that BHR may be the result rather than the cause of physical inactivity in asthmatic children.¹¹ There is evidence that asthmatic children, even those

with documented BHR, can achieve levels of exercise performance similar to those of non-asthmatics,¹² provided that they have a comparable level of habitual physical activity.¹⁴ It has also been reported that moderate- or high-intensity physical activity programs are well-tolerated and safe for asthmatic children, and—over the long term—may have a beneficial effect on disease severity.¹⁶ On the other hand, a number of investigators have favored the opposite direction of causality, suggesting that asthmatic children experience limitations in physical activity due to the severity of

TABLE 5—Results From Logistic Regression Models That Evaluated the Association of Overweight and Physical Activity on Exercise-Induced Bronchoconstriction

	Exercise-induced bronchoconstriction				
	Unadjusted model	Adjusted models			
		Model 1	Model 2	Model 3	Model 4
Overweight or obesity vs. normal weight	1.14 (0.58–1.96)	1.02 (0.51–2.03)	1.12 (0.56–2.22)	1.27 (0.78–2.45)	1.08 (0.55–1.91)
Duration of physical activity ¹					
Increased duration of mild-intensity activity (yes vs. no)	5.42 (1.66–15.21)	5.44 (1.65–15.68)	—	—	—
Decreased duration of moderate-intensity activity (yes vs. no)	5.27 (2.04–13.60)	—	5.32 (2.06–13.76)	—	—
Decreased duration of vigorous-intensity activity (yes vs. no)	1.20 (0.62–2.33)	—	—	1.38 (0.86–2.97)	—
Activity category ²					
Active	1.00	—	—	—	1.00
Moderately active	3.62 (1.43–9.16)	—	—	—	3.61 (1.43–9.14)
Inactive	6.50 (2.71–15.59)	—	—	—	6.54 (2.72–15.70)

MET, standard metabolic equivalent.

Results are represented as odds ratios and their corresponding 95% confidence intervals (in parentheses), after adjustment for the presence of asthma-related symptoms and sex. Crude estimates reflect the independent effect of each factor. Combined effects are analyzed using separate models.

¹Dichotomous variable defined by the ability to report higher (increased) or lower (decreased) duration of daily physical activity than the group-specific mean. Intensity of activity: mild 1.1–2.9 METs, moderate 3–6 METs, vigorous >6 METs.

²Defined according to total energy expenditure in kcal kg⁻¹ day⁻¹, as follows: ≥40 active; 37–39.99 moderately active; <37 inactive.

their disease.^{3–8} It should be noted, however, that the most of the later studies are either based exclusively on symptoms related to the disease and have not included an objective appraisal of BHR,^{2–5} or focus on selected populations of children with untreated/uncontrolled asthma.^{6,8} A recent report on a selected population of children at risk for developing asthma showed that in a subsample of the participants the reduction of physical activity was proportional to bronchial responsiveness as assessed by cold air challenge.⁷ Although the investigators of this study suggest that young children experience exercise-induced symptoms in proportion to their BHR, the direction of causality remains unclear.

We did not find differences in total daily energy expenditure or time spent in activities of mild and moderate intensity among children with diagnosed asthma (group 1) or asthma-related symptoms not diagnosed as asthma (group 2) and their healthy peers (group 3). Similarly, there was no difference in the prevalence of diagnosed asthma among active, moderately active, and inactive children. The above observations, which are in agreement with previous reports,^{12–14} indicate that asthma symptoms may not be related to the level of physical activity in school-aged children. These results, however, could also be attributed to the efficient treatment and control of the disease. Indeed, diagnosed asthmatics in our study had mild and controlled disease, as evidenced by their C-ACT score and baseline lung function. On the other hand, these children had lower baseline lung function and higher prevalence of EIB as compared to their healthy peers, indicating that the relation between BHR and physical inactivity may be subclinical.

There are several possible mechanisms to explain the relationship between decreased physical activity and BHR. Periodic deep inspirations, as is the case with exercise, have a potent bronchodilatory effect and appear to have an important role in maintaining normal airway tone.²⁷ It has been suggested that the decrease in the frequency of these periodic distensions during sedentary activity may predispose to increased non-specific BHR in children.²⁸ In addition, regular physical activity may downregulate airway and systemic inflammation, thus resulting in a beneficial effect on BHR.²⁹

The interrelations of asthma, decreased physical activity and obesity are complex and only partially understood.² It remains controversial whether decreased physical activity predisposes to increased bronchial responsiveness independently of obesity, or whether obesity creates the conditions that foster the development of EIB irrespective of physical activity. It has been argued that reduced tidal volume and functional residual capacity in obese children may promote airway narrowing, and that obesity per se leads to a state of low-grade inflammation that may act on the lung to

exacerbate asthma.^{30,31} In our analysis, the effect of overweight or obesity on increased bronchial responsiveness was not statistically significant. On the other hand, it was actually the sedentary lifestyle that was associated with the development of EIB, and this relation was independent of BMI. The finding that increased BMI was related to decreased time spent in vigorous activity by children with EIB renders support to the hypothesis that overweight and obesity favor the development of asthma through physical deconditioning. This explanation is strengthened further by the fact that the great majority of the children who failed to complete the ECT due to breathlessness or were unable to run for the total 6 min, but achieved target heart rate for at least 4 min, were overweight or obese.

The findings of the present study should be considered in the context of its potential limitations. First, the use of an interview-administered questionnaire for assessing the level of physical activity may raise reliability concerns. Although the PALSQ has been previously validated in Greek schoolchildren,²⁴ it has been shown that the level of physical activity may be overestimated by using similar instruments.³² Such bias, however, would lead to an underestimation of the association between inactivity and BHR. Moreover, potential misclassifications would be random. The use of standardized interview-administered questionnaires remains a practical method for the assessment of physical activity in epidemiological studies, particularly those which assess large samples of individuals.³³ These instruments are also valuable for the assessment of the setting and the mode of physical activity, two important characteristics which are difficult to be assessed otherwise.³³ Second, although we used a widely applied standardized questionnaire (the ISAAC questionnaire) to classify the participants' asthma, it is difficult to compare our results with those of previous studies due to the variability in the definitions of asthma groups. Third, our study population included only urban schoolchildren, and thus, the study findings may not be applicable to other populations, particularly those with different physical activity patterns. Fourth, the study sample was not adequate to allow for separate analysis of the overweight and obesity groups. Lastly, the cross-sectional design of our study has the inherent limitation of not establishing clear causal relationships. The importance of longitudinal studies in order to assess the direction of causality between decreased physical activity and EIB in the general population should, therefore, be emphasized.

In conclusion, this cross-sectional study showed a strong inverse association between physical activity and bronchial responsiveness due to exercise for the first time in a large urban population of school-aged children. Sedentary lifestyle favored the development of

EIB independently of BMI and asthma-related symptoms. These results underscore the importance of physical activity as an integral part of programs that focus on the primary prevention of childhood asthma.

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