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The relationship between body mass index, aerobic performance and asthma in a pre-pubertal, population level cohort

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Abstract

Purpose: To assess the relationship between asthma, body mass index and aerobic performance, as indicated by a shuttle test.

Methods – 20,577 participants (10,413 boys) from the SportsLinx serial cross-sectional study participated.. Parental reports of asthma status and home postcode data were gathered from consent forms. Stature, sitting stature, and body mass were measured and body mass index (BMI), somatic maturity and indices of multiple deprivation scores (IMD) were derived. Performance on the 20m multi-stage shuttle runs test (20mSRT) was used to estimate cardiorespiratory fitness.

Results –Asthma (F (1, 17015) = 82.26, $P < 0.01$) and gender (F (1, 17015) = 678.491, $P < 0.001$) significantly influenced 20mSRT. The addition of BMI, maturity and IMD to the model did not alter these significant effects. There was a significant interaction between 20mSRT and BMI (F (1, 16723) = 132.80, $P < 0.01$), with a significant decrease in 20mSRT from the 50th BMI percentile upwards (t (16699) = 36.88, $P < 0.01$). Binary logistic regression revealed gender and 20mSRT to be significant predictors of asthma occurrence; BMI SDS just reached significance whilst maturity and IMD were not significant contributors to the model.

Conclusions - This study demonstrates the negative influences of low cardiorespiratory fitness and high BMI on the risk of asthma occurrence in pre-pubertal children. Furthermore, it highlights the significant influence of BMI on cardiorespiratory fitness, revealing these effects to be manifest considerably below those BMI percentiles conventionally associated with being overweight or obese.

Keywords: Shuttle run; indices of multiple deprivation; percentiles; cardiorespiratory

Introduction

The incidence of childhood asthma has risen over the past four decades and asthma now represents one of the most common chronic conditions, affecting 1 in 11 children in the UK (UK 2012). A similar rise has been observed in childhood obesity, with nearly 1 in 3 children currently overweight or obese (Ogden et al. 2006; Ogden et al. 2010; Townsend et al. 2013). Consequently, body mass management is considered one of the most serious public health challenges of the 21st century (WHO 2010). These concurrent trends raise concerns about the possibility of an association between asthma and obesity, an association supported by epidemiological studies that show asthmatic children have a higher body-mass index (BMI) than their non-asthmatic counterparts (Chen et al. 2010; Cottrell et al. 2010; Gold et al. 2003; Gilliland et al. 2003).

The mechanisms underlying the co-existence of asthma and obesity are multifaceted and remain to be fully elucidated (Boulet 2013). One potentially influential factor is the level of cardiorespiratory fitness (Lochte et al. 2009; Rasmussen et al. 2000). Although one might postulate that both asthmatic and obese children would be characterised by lower levels of cardiorespiratory fitness, the literature is conflicting. Specifically, whilst some studies showed lower cardiorespiratory fitness in asthmatic and obese children (Dolan et al. 2012; Klungland Torstveit and Sundgot-Borgen 2012; Vahlkvist and Pedersen 2009), others found no difference compared to their healthy counterparts (Berntsen et al. 2009; Pianosi and Davis 2004; Santuz et al. 1997). These equivocal results may be attributable to methodological differences between studies, such as in the exercise tests used to assess cardiorespiratory fitness, the sexual maturity of the study population and the severity of asthma (Dolan et al. 2012; Ferry et al. 2011; Klungland Torstveit and Sundgot-Borgen 2012; Pianosi and Davis

2004; Santos et al. 2010). Furthermore, interpretation of earlier studies is hindered by a failure to account for the potential influence of body size (or mass) on the results as they have predominantly relied on relative peak $\dot{V}O_2$ which penalises those that are heavier as has been extensively addressed elsewhere (Welsman and Armstrong 2000).

While the co-existence of asthma and obesity are well supported in the paediatric literature (Farah and Salome 2012; Rastogi et al. 2012; Lucas and Platts-Mills 2006), the direction of causality remains unclear, not least due to the predominantly cross-sectional nature of previous studies which preclude this issue from being addressed. Indeed, it has been postulated that either: i) asthma may lead to a low level of physical activity, perhaps due to a desire to avoid an exercise-induced exacerbation of the condition, resulting in poor cardiorespiratory fitness and obesity or ii) that obesity may either directly or via a reduced level of physical activity cause asthma (or asthmatic symptoms) to occur. With regard to the latter hypothesis, there are two potential mechanisms by which obesity may be causatively linked to asthma: i) pro-inflammatory adipokines in obese individual's circulation may induce airway inflammation, or increase its severity, thereby contributing to airway hyperresponsiveness or asthma or ii) the pressure of the increased tissue mass in the chest wall and abdomen exerts direct mechanical effects on the lungs, influencing airway hyperresponsiveness or directly increasing symptoms (Farah and Salome 2012).

There are no population level studies in the literature that have attempted to elucidate the relationships between asthma, fitness and obesity over time, neither are there comparative studies of the same factors in asthmatics and non-asthmatics. Therefore, the purpose of this serial cross-sectional study was to assess the relationship between cardiorespiratory fitness, asthma and obesity in a large sample of children. We hypothesised that when potential cofounders, such as age and maturation, are accounted for, those with asthma and obesity would demonstrate the lowest cardiorespiratory fitness, as indicated by the shuttle run performance. Furthermore, we hypothesised that asthma and obesity would demonstrate and interaction to determine cardiorespiratory fitness.

~~low cardiorespiratory fitness would be associated with asthma and high BMI, with the latter exerting a greater influence than the presence of asthma.~~

Methods

After gaining local NHS and institutional ethical approvals, informed parental consent, participant assent and satisfactory medical screening forms 20,577 participants (n = 10,413 boys; 9-12 years), were included in this serial cross sectional project. Data were generated by the SportsLinx project between academic years 2004-2005 and 2010-2011. SportsLinx methods and the reliability of the fitness test battery have been described previously (Boddy et al. 2012; Boddy et al. 2010). Briefly, all primary schools across the Liverpool Local Education Authority were invited to participate in the SportsLinx project each academic year. Prior to participation in a Fitness Fun Day, parents/guardians completed a medical screening form for the participants, which included questions asking parents to confirm if children were asthmatic. ~~Therefore, asthma was diagnosed by a general practitioner and reported by parents.~~ Participants attended a Fitness Fun Day at a local leisure centre, or where facilities permitted, on their school site, and completed a battery of fitness tests adapted from the Eurofit battery, which included the 20m multi-stage shuttle runs test (20mSRT; Eurofit 1993). The 20mSRT has been extensively detailed elsewhere (Riddoch 1990) but, in brief, involves participants running between two markers 20m apart while keeping pace with a pre-recorded audible beep. The speed increases on completion of each level and participants are encouraged to maintain the pace for as long as possible. The test is terminated when the participant fails to reach the marker by the beep on two consecutive occasions. One Senior Fitness Officer led the testing sessions and completed all anthropometric measures.

Stature and sitting stature were measured to the nearest 0.1cm (Seca, Bodycare, Birmingham UK) and body mass was measured to the nearest 0.1kg (Seca, Bodycare, Birmingham, UK), using standard techniques (Lohman et al. 1988). Somatic maturation was estimated using regression equations (Mirwald et al. 2002). Body mass index (BMI) was calculated, and age- and sex-specific BMI percentiles were assigned to each participant (Cole et al. 2000). The total number of completed shuttles from the 20m multi-stage shuttle runs test (20mSRT [Queens University of Belfast protocol] (Lloret-Linares and Oppert 2009) was used to estimate cardiorespiratory fitness (CRF).

An indices of multiple deprivation (IMD) score was assigned to each participant on the basis of home postcode using the National Statistics Postcode Directory database (Census.ac.uk) and the GeoConvert application (Mimas). IMD scores provide an estimate of area deprivation and comprise seven aspects of deprivation (income, employment, health deprivation and disability, education skills and training, barriers to housing and services, crime and living environment). IMD scores are a commonly used method of estimating deprivation in similar studies within the United Kingdom (Fairclough et al. 2009).

Statistical Analysis

Chi-square tests were used to assess the prevalence of asthma over the seven year study period. The influence of asthma on the demographic characteristics and cardiorespiratory fitness of participants was investigated by analysis of variation. Subsequently, analysis of co-variation was used to control for BMI, maturity and IMD with planned contrasts to identify the specific location of significant differences. The association between asthma and cardiorespiratory fitness was assessed by backwards stepwise elimination in binary logistic regression models adjusted for BMI, maturity and IMD. All analyses were conducted using IBM SPSS Statistics 19 (Chicago, Il). All data are presented as mean ± SD. Statistical significance was accepted when $P<0.05$.

Results

Across the entire study period, the prevalence of asthma was 11%; the prevalence varied significantly between study years, ranging from 9.3-11.5% (χ (6, 20777) = 12.90, $P < 0.001$. The trend was characterised by a relatively constant prevalence over the initial 3 years followed by a progressive decline in the subsequent three years. There was a sharp increase in the prevalence in 2010. The prevalence of asthma differed markedly between genders (Boys, 12.2% vs. Girls, 9.1%; χ (1, 20777) = 52.15, $P < 0.001$) and according to BMI-classification (χ (1, 20777) = 30.12, $P < 0.001$). Specifically, 10% of normal weight children had asthma whilst 12.5% of overweight or obese children had asthma.

Participant's anthropometric characteristics are shown in Table 1. The asthmatic and healthy cohorts did not differ in age or stature. There was a significant main effect for asthma (F (1, 20389) = 24.15, $P < 0.01$) and gender (F (1, 20389) = 24.20, $P < 0.01$) on weight, with a significant interaction between these factors (F (1, 20389) = 4.51, $P < 0.05$). BMI was similarly significantly influenced by asthma and gender in both absolute (Ast: F (1, 20375) = 53.55, $P = 0.00$; Gen: F (1, 20375) = 52.75, $P < 0.01$)) and age relative percentile terms (Ast: F (1, 20777) = 39.17, $P < 0.01$; Gen: F (1, 20777) = 15.84, $P < 0.01$)). There was a significant interaction between asthma and gender for both absolute (F (1, 20375) = 5.631, $P < 0.05$) and relative BMI (F (1, 20777) = 4.79, $P < 0.05$).There was a significant main effect of asthma (F (1, 20374) = 6.55, $P < 0.05$) and gender (F (1, 20374) = 7966.26, $P < 0.01$) on years to PHV, but no interaction between asthma and gender. IMD did not differ between asthmatic and healthy children (healthy: 1626 ± 3636 vs. asthma: 1601 ± 3614 ; $P>0.05$).

The results of the shuttle run fitness test is shown in Table 1. There was a significant main effect of asthma (F (1, 17015) = 82.26, $P < 0.01$) and gender (F (1, 17015) = 678.491, $P < 0.001$) on shuttle run performance and a significant interaction between these terms (F (1, 17015) = 5.379, $P < 0.05$). Shuttle run performance varied over the study period, following a 4th order polynomial trend.

When BMI, maturity and IMD were controlled for, the significant main effect of asthma (F (1, 16654) = 56.26, $P < 0.01$) and gender (F (1, 16654) = 545.15, $P < 0.001$) on shuttle run performance remained, as did the interaction between these factors (F (1, 16654) = 10.17, $P < 0.01$). Irrespective of whether the covariates were entered independently or in combination, the only covariate of significance was SDS_BMI (F (1, 16654) = 2854.84, $P < 0.001$). IMD just failed to reach significance (F (1,16654) = 3.80, $P = 0.051$). When maturity was replaced with decimal age, the main effects (asthma: (F (1, 16867) = 56.05, $P < 0.001$; gender: (F (1, 16867) = 823.82, $P < 0.001$; interaction: (F (1, 16867) = 9.44, $P < 0.01$) were not altered but, unlike maturity, age was an additional significant explanatory variable in the model (F (1, 16867) = 58.55, $P < 0.001$). When BMI percentiles were used in the model, the interaction between BMI percentile and asthma failed to reach significance (F (1, 16907) = 1.76, $P = 0.062$).

Moreover, this relationship between asthma and shuttle run performance persisted within both normal weight (F(1, 11849) = 19.74, $P < 0.01$) and overweight/obese subsets (F(1,

5179) = 5.81, $P < 0.05$). The addition of BMI percentiles to the ANCOVA model resulted in a significant main effect of both asthma ($F(1, 16723) = 41.79$, $P < 0.01$) and BMI percentile ($F(1, 16723) = 132.80$, $P < 0.01$) on shuttle run performance but no interaction between these factors. Specifically, as shown in Figure 1, shuttle run performance was always lower in asthmatic children with a similar influence of increasing BMI irrespective of asthma status. Planned contrasts showed a significant decrease in shuttle run performance from the 50^{th} BMI percentile upwards (t (16699) = 36.88, $P < 0.01$).

Binary logistic regression revealed gender and shuttle run performance to be significant predictors of asthma occurrence; BMI SDS just failed to reach reached significance (P = 0.05) whilst maturity and IMD were not significant contributors to the model (Table 2). Using backwards step regression with IMD and maturity in the second block, BMI_SDS was a significant predictor until both these covariates were removed from the model.

Discussion

This study is novel because it is the first population-based study to address the relationship between asthma and obesity, and its interaction with aerobic fitness, demonstrating a significant relationship between the two primary variables. Specifically, a greater percentage of asthmatic children were overweight than their non-asthmatic counterparts, a relationship that persisted regardless of whether weight status was expressed as absolute mass, BMI or age-relative percentile BMI. Asthma significantly influenced aerobic performance, with asthmatic children completing fewer shuttle runs than their healthy counterparts. Furthermore, a key novelty of the present study was the demonstration that aerobic performance was independently influenced by BMI, with a significant decline in shuttle run performance occurring irrespective of disease status when BMI exceeded the 50^{th} age-relative percentile. Finally, the occurrence of asthma in this large population was found to be ~~predicted~~ influenced by~~by~~ gender, shuttle run performance and standardised BMI, supporting the notion that these factors are not coincidental simultaneous occurrences but may rather be linked through the relationships postulated elsewhere between airways inflammation, obesity and physical inactivity.~~.~~

Obese, asthmatic patients are becoming an increasingly common occurrence (Woodrow 2007), with the high symptom burden and increased morbidity experienced by such patients heightening the necessity for the mechanistic basis of, and thus potential treatment strategies for, the “obese asthma” phenotype to be elucidated. The mean asthma prevalence across the seven years included in the present analysis was 11%, with a higher prevalence evident in boys and overweight/obese participants relative to girls and normal weight participants, respectively. This association between obesity and asthma is in accord with previous studies (Black et al. 2012; Figueroa-Muñoz et al. 2001; Gennuso et al. 1998; Luder et al. 1998), as is the gender difference (Anthracopoulos et al. 2011; Hansen et al. 2013; James et al. 2013). The maturation status of the children is important when comparing studies regarding the prevalence of asthma as the predominance tends to reverse in adolescence and adulthood towards asthma being more prevalent in females (de Marco et al. 2000; Osman et al. 2007). It is therefore suggested that the hormonal changes associated with puberty and their effects on lung growth, along with sex-specific environmental exposures and social/behavioural changes may be implicated in the explanation of these sex-specific patterns (Postma 2007).

Given that obesity has been implicated in airway inflammation, ~~T~~the present findings showing a higher proportion of asthma in overweight/obese children than their normal-weight counterparts provides support for the contention that the simultaneous occurrence of these conditions is not coincidental but rather a reflection of an underlying, causative association (Farah and Salome 2012). The nature of this association is an area of considerable debate, with even the direction of causality remaining equivocal. It has been suggested that obesity may precede the development of asthma, with surgical and diet-induced weight-loss in adults associated with improvements in lung function and asthma symptoms (Aaron et al. 2004; Hakala et al. 2000; Maniscalco et al. 2008). There are two potential mechanisms by which obesity may be causatively linked to asthma: i) pro-inflammatory adipokines in obese individual's circulation may induce airway inflammation, or increase its severity, thereby contributing to airway hyperresponsiveness or asthma or ii) the pressure of the increased tissue mass in the chest wall and abdomen exerts direct mechanical effects on the lungs, influencing airway hyperresponsiveness or directly increasing symptoms (Farah and Salome 2012). Alternatively, asthmatic patients may be prone to avoiding exercise that may trigger their asthma symptoms and are thus at an increased risk of becoming obese (Battilani et al. 2004; Hallstrand et al. 2000). Although Pianosi and colleagues (Pianosi and Davis 2004) suggested that the greatest determinant of cardiorespiratory fitness is not asthma severity but the patients' perception of their ability, the present findings, and those of others (Basso et al. 2010; Lochte et al. 2009; Rastogi et al. 2012), suggest a significant negative relationship between asthma and cardiorespiratory fitness. These findings agree with those showing children with asthma to be less physically active (Firrincieli et al. 2005; Glazebrook et al. 2006; Vahlkvist and Pedersen 2009), although it is important to highlight that physical activity was not measured in the present study and that others have found no difference in physical activity between healthy and asthmatic children. Indeed, it is important to highlight the third potential explanation for the associations found in the present study between obesity and asthma; specifically, that both these conditions are independently attributable to a third factor, namely, physical inactivity, and are thus of no consequential relation to each other.

The absence of physical activity data and the cross-sectional nature of this study circumvent further interpretation of these relationships of their causalities, however.

The present findings also suggest that, in addition to the interactions between asthma occurrence, obesity and cardiorespiratory fitness, obesity and cardiorespiratory fitness may independently interact, as evidenced by the significant decline in CRF above the 50^{th} percentile of BMI, irrespective of asthma status. This finding provides the first quantitative evidence regarding the tipping point in the relationship between BMI and cardiorespiratory fitness and highlights that detrimental effects are evident considerably below those percentiles attributed to overweight and obesity. This finding has worrying implications for the health and well-being of many pre-pubertal children and highlights the importance of cardiorespiratory fitness across the body mass spectrum and not just for those traditionally perceived as being “at risk”. It therefore remains to be elucidated how asthma occurrence, obesity and cardiorespiratory fitness interact in pre-pubertal children.

This is the first study to investigate the relationship between asthma and obesity and its interaction with cardiorespiratory fitness in a large population of pre-pubertal children. Whilst the considerable sample size of the present population allows confidence in the conclusions drawn, the study is not without its limitations, not least of which are those inherent to its cross-sectional design and the indirect assessment of cardiorespiratory fitness employed. Equivocal findings to date may, at least in part, be attributable to variations in the definition of asthma used (Pearce et al. 1999) or, as in the present study, a lack of account for the influence of asthma severity on the relationships observed (Farah and Salome 2012). An issue commonly identified in population based studies such as this is the potential for mis-diagnosis on the basis of poor fitness. Unfortunately, interpretation of the present study is also hindered by a lack of information on participants' respiratory function and physical activity levels. Finally, it is pertinent to note that direct measures of cardiorespiratory fitness were not obtained in the present study. Nonetheless, the estimates of cardiorespiratory fitness were derived from field-based tests validated in this population (Ortega et al. 2008; Ruiz et al. 2011). Future studies should seek to address these variables to preclude such limitations.

In summary, this study demonstrates the association between asthma and obesity in determining an individual's cardiorespiratory fitness. Specifically, this study suggests a negative, independent interaction between obesity and cardiorespiratory fitness that appears to become evident considerably below those percentiles typically associated with being overweight or obese. This study therefore further highlights the serious health consequences associated with poor cardiorespiratory fitness occurring simultaneously with obesity and asthma. The interactions and direction of causality between these factors remains to be elucidated, with factors such as maturation and sex accounted for given their modulatory influences on both obesity and cardiorespiratory fitness.

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