Brief Cutting Edge Report
PEDIATRIC OBESITY

Obesity

Secondhand Smoke and Traffic Exhaust Confer Opposing Risks for Asthma in Normal and Overweight Children

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Objective: Exposure to ultrafine particles (UFP) in secondhand smoke (SHS) and traffic-related air pollution (TRAP) may elicit chronic inflammation. It was hypothesized that the association between these exposures would be potentiated in overweight versus normal-weight children.

Methods: Average lifetime exposure to TRAP and SHS and objective, physician-diagnosed asthma were determined for 575 children at age 7. Overweight was defined as having a body mass index (BMI) >85th percentile for age and gender. The association between TRAP and SHS exposure and asthma was examined by logistic regression stratified by BMI.

Results: A total of 131 children were overweight; the prevalence of asthma was 24.4% and 14.2% among overweight and normal-weight children, respectively. Exposure to SHS was significantly associated with asthma among overweight (adjusted odds ratio [adjOR] = 3.0; 95% confidence interval [CI] = 1.2, 7.4) but not normal-weight children (adjOR = 1.1; 95% CI = 0.4, 2.7). In contrast, TRAP was significantly associated with asthma among normal-weight (adjOR = 1.8; 95% CI = 1.0, 3.4) but not overweight children (adjOR = 0.7; 95% CI = 0.4, 2.7).

Conclusions: The association between SHS and TRAP exposure and asthma is modified by children's weight. Children's time-activity patterns, including time spent indoors or outdoors, may vary by weight and play an important role in these UFP exposures.

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Introduction

Environmental exposure to particulate matter (PM), especially ultrafine particles (UFP), regardless of indoor or outdoor sources, likely share common physiological presentations including oxidative stress and enhanced production of IgE and Th2 cytokines resulting in inflammation and increased airway resistance (1-3). UFP, with thousands of affixed chemical constituents, are common components of pollutants including cigarette smoke and traffic related air pollution (TRAP). By number concentration, secondhand smoke (SHS) includes 75% UFP (4), only slightly lower than diesel exhaust particles (DEP), at 92% (5).

Over 60% children are exposed to SHS (6) and 3.7% of the U.S. population (~1.5 million children) live within 150 meters of major highways with high traffic exposures (7). However, these common sources of childhood UFP exposures are often examined individually using cross-sectional study designs. This approach results in insufficient data on the effects of combined lifetime exposures on asthma, especially in potentially susceptible overweight children (8).

Childhood obesity, asthma, and PM exposure have all been linked to the mechanistic pathway of chronic inflammation (9,10). In a study of asthmatic children living near the heavily trafficked US-Mexico border, PM exposure in overweight children was associated with higher levels of exhaled nitric oxide (eNO), a measure of eosinophilic airway inflammation (11). Also, being overweight was shown to increase susceptibility to indoor PM as manifested by respiratory symptoms in asthmatic children (12). Thus, our study

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TABLE 1 Descriptive and exposure characteristics by BMI status

Characteristic	BMI normal ($n = 444$), number (%)	BMI overweight ($n = 131$), number (%)	*P*-value
Health and demographic factors			
Asthma prevalence	63 (14.2)	32 (24.4)	<0.01
Gender			
Male	250 (56.3)	68 (51.9)	0.37
Female	194 (43.7)	63 (48.1)	
Race			
African American	88 (19.8)	42 (32.1)	<0.01
Other[a]	356 (80.2)	89 (67.9)	
Mother education			
>High school ($n = 431$)	352 (81.5)	79 (62.2)	<0.001
≤High school ($n = 128$)	80 (18.5)	48 (37.8)	
Breast fed			
≥ 4 months	245 (55.2)	57 (43.8)	0.02
<4 months	199 (44.8)	73 (56.2)	
Exposure factors			
Household SHS	48 (10.8)	29 (22.1)	<0.001
≥10 cigs/day	396 (89.2)	102 (77.9)	
<10 cigs/day			
Geo.mean cigs/day (95% CI) (birth-7 yr)	7.3 (5.8, 9.2)	9.0 (6.8, 11.8)	
Mean hair cotinine (ng/mg) (SD)[b]	0.13 (28)	0.19 (0.31)	0.09
Average TRAP ($\mu g/m^3$) (birth-7 yr)			
≥0.42 (75th %tile)	117 (26.4)	36 (27.5)	
<0.42 (75th %tile)	327 (73.7)	95 (72.5)	0.80
Geo. mean (95% CI)	0.37 (0.36,0.38)	0.37 (0.35,0.38)	
Day care attendance (birth-1 yr)			
Yes	194 (43.7)	63 (48.1)	0.37
No	250 (56.3)	68 (51.9)	
Dog in home (birth-1 yr)			
Yes	161 (36.3)	40 (30.5)	0.23
No	283 (63.7)	91 (69.5)	
Cat in home (birth-1 yr)			
Yes	106 (23.9)	24 (18.3)	0.18
No	338 (76.1)	107 (81.7)	

Note: *P*-values determined by Pearson chi-square test of independence between BMI and subject categories of each characteristic.
[a]Other (431 Caucasians, 1 biracial Hispanic, and 1 biracial Asian).
[b]472/575 had mean hair cotinine levels, 370 normal weight and 102 overweight collected at ages 2 and/or 4.

hypothesis was that lifetime exposure to SHS and TRAP will be associated with asthma in childhood, and this risk is greater among overweight versus normal-weight children.

Methods

Participants

Participants in this study were enrolled in the Cincinnati Childhood Allergy and Air Pollution Study (CCAAPS) cohort. Infants born to atopic parents were identified whose birth address was within 400 m (high TRAP exposure) or beyond 1500 m (low TRAP exposure) from major highways with high truck volumes (13). Children were examined at ages 1, 2, 3, 4, and 7; 95% completed at least four exams. Weight measures were taken on calibrated clinical scales using standardized procedures including removal of shoes, hats, and bulky clothing. Body mass index (BMI) was calculated as weight (kg)/height^2 (m^2) and BMI percentiles for age, gender, and race were determined using Centers for Disease Control and Prevention growth charts. Children were defined as overweight or normal weight based on having a BMI ≥85th percentile or ≤85th percentile, respectively. This study was approved by the University of Cincinnati Institutional Review Board.

Asthma outcomes

Participants underwent spirometry following American Thoracic Society guidelines (14). Predicted values of forced expiratory volume in 1 s (FEV1) were calculated for children ≤8 years (15). Children with either a FEV1 ≤90%, a physician diagnosis of asthma, asthma symptoms in the last 12 months (tight chest or throat, difficulty breathing or wheezing after exercise, wheezing and/or whistling in the chest), or an eNO level of ≥20 ppb received 2.5 mg levalbuterol through a nebulizer followed 15 min afterward by repeat spirometry (16). Children with <12% increase in FEV1 had a methacholine challenge test (MCCT). Children were physician-diagnosed as asthmatic with symptoms of asthma and evidence of bronchial hyper-reactivity (≥12% increase in FEV1 following bronchodilation) or a positive MCCT (PC20 ≤ of 4 mg/ml methacholine concentration) (16) (See Supporting Information for additional details).

Measures of exposures, covariates, and statistical analyses

Air sampling for $PM_{2.5}$ was conducted intermittently at 27 sampling monitors from 2001-2006, and the average daily concentration of elemental carbon attributable to traffic, a marker for the DEP component of TRAP was identified (17). A land-use regression model estimated a time-weighted average lifetime exposure to TRAP, primarily DEP, at all locations where the child spent > 8 h/week from birth to age 7 (13). At the clinical exams, the parent was asked a smoking history for all members living in the child's home. Questions included: "Is that household member a current cigarette smoker?", and if yes, "How many cigarettes does this person smoke?" For those year(s) with missing information the previous year's response was assumed. Also, hair cotinine levels were available for 472 children (see Supporting Information). Other covariates included gender, race (African American (AA) or Non-African American), mother's education, (≤/>high school), breast feeding (</≥ 4 months), dog and/or cat in home through age 1, and attendance at day care through age 1 (yes/no)—that is, defined as wherever the child spent eight or more hours/week outside the home. The odds of childhood asthma were examined by logistic regression stratified by BMI. Continuous covariates were dichotomized for ease of interpreting the modifying effect of BMI. Homogeneity of odds ratios between BMI strata ($P \leq 0.25$) for each potential predictor was evaluated for inclusion as an interaction effect (18). Those predictors meeting the inclusion criteria where shown as two-way interactions in the final multivariate logistic models.

TABLE 2 Unadjusted asthma odds ratios [95% confidence intervals] by subject characteristics and exposure factors stratified by BMI status

Characteristic	All subjects ($n = 575$)	BMI normal ($n = 444$)	BMI overweight ($n = 131$)	*P*-value, obesity comparisons[a]
Socio-demographic factors				
Gender				
Male	1.3 [0.9, 2.1]	1.3 [0.8, 2.3]	1.5 [0.7, 3.4]	0.78
Female	Ref	Ref	Ref	
Race				0.74
African American	2.4 [1.5, 3.8]	2.3 [1.3, 4.2]	2.0 [0.9, 4.5]	
Other	Ref	Ref	Ref	
Mother education				0.38
$>$ High school	0.3 [0.2, 0.5]	0.4 [0.2, 0.8]	0.3 [0.1, 0.6]	
$\leq$ High school	Ref	Ref	Ref	
Breast fed				
$\geq$ 4 months	0.5 [0.3, 0.8]	0.5 [0.3, 0.9]	0.6 [0.3, 1.4]	0.80
$<$ 4 months	1	1	1	
Environmental exposures				
Household SHS				
$\geq$ 10 cigarettes/day	2.1 [1.2, 3.8]	1.5 [0.7, 3.2]	2.9 [1.2, 7.0]	0.25
$<$ 10 cigarettes/day	Ref	Ref	Ref	
Average TRAP ($\mu g/m^3$)				
$\geq$ 0.42	1.2 [1.1, 2.7]	2.1 (1.2, 3.6]	1.0 [0.4, 2.5]	0.20
$<$ 0.42	Ref	Ref	Ref	
Day care attendance				
Yes	2.2 [1.4, 3.5]	2.8 [1.6, 4.8]	1.3 [0.6, 2.9]	0.13
No	Ref	Ref	Ref	
Dog in home				
Yes	0.6 [0.4, 1.0]	0.6 [0.3, 1.01]	0.7 [0.3, 1.7]	0.68
No	Ref	Ref	Ref	
Cat in home				0.50
Yes	0.5 [0.3, 1.0]	0.6 (0.3, 1.3]	0.4 [0.1, 1.4]	
No	Ref	Ref	Ref	

[a]Breslow-Day test for homogeneity of odds ratios.

Results

There were 762 children enrolled in the CCAAPS cohort and 617 (81%) participated at age 7. Analyses include 575 children having mean age 6.9 (range 6.4–8.7), who had complete data on BMI, PFT and MCCT. There were 131(22.8%) who were overweight (Table 1) and, of these, 59 were obese ($\geq$ 95th percentile). Overweight versus normal-weight children were significantly ($P < 0.05$) more likely to have asthma, be AA, have mothers with lower education and to have been breast fed for less than 4 months (Table 1). Overweight versus normal-weight children were significantly more likely ($P < 0.001$) to have high average lifetime cigarette exposure (22.1% versus 10.8%), respectively. There were no significant differences between BMI groups and TRAP exposure, attendance at day care, and dogs and/or cats in the home (Table 1). However, significantly higher mean levels of eNO in the normal-weight (7.1 ppb) versus the overweight (5.5 ppb) children were observed ($P < 0.01$). The normal-weight versus overweight asthmatic children also had nearly double the eNO levels (10.2 ppb versus 5.5 ppb), respectively ($P < 0.01$).

On the basis of odds ratios (OR) and confidence intervals (CI) shown in Table 2, higher maternal education and longer breast feeding duration significantly reduced the odds of asthma in both BMI groups. Asthma ORs for SHS, TRAP, and day care, although similar in direction, were nonhomogenous between BMI groups ($P \leq 0.25$). High SHS exposure significantly increased the odds of asthma in the BMI overweight group only, whereas high TRAP exposure and day care attendance significantly increased the odds of asthma in the BMI normal-weight group. Thus, in the multivariate analysis the

TABLE 3 Adjusted asthma odds ratios [95% confidence intervals] measuring associations between predictors and asthma including the modifying effects (interactions) of BMI on day care[a], TRAP[a], SHS[a]

Characteristic	All subjects ($n = 575$)	*P*-value
Sociodemographic factors		
Gender		
Male	1.3 [0.8, 2.0]	0.37
Female	Ref	
Race		
African American	1.5 [0.8, 2.7]	0.20
Other	Ref	
Mother education		
>High school	0.5 [0.3, 0.9]	0.02
≤High school	Ref	
Breast fed		
≥4 months	0.8 [0.5, 1.4]	0.51
<4 months	Ref	
Environmental exposures		
Household SHS[a]	1.8 [0.9, 3.5]	0.08
BMI normal		
≥10 cigarettes/day	1.1 [0.4, 2.7]	0.11
<10 cigarettes/day	Ref	
BMI overweight		
≥10 cigarettes/day	3.0 [1.2, 7.4]	0.02
<10 cigarettes/day	Ref	
Average TRAP ($\mu g/m^3$)[a]	1.8 [1.0, 3.4]	0.06
BMI normal		
≥0.42	1.8 [1.0, 3.5]	0.06
<0.42	Ref	
BMI overweight		
≥0.42	0.7 [0.3, 1.8]	0.46
<0.42	Ref	
Day care[a]	2.6 [1.4, 4.7]	<0.01
BMI normal		
Yes	2.6 [1.5, 4.8]	<0.01
No	Ref	
BMI overweight		
Yes	1.3 [0.5,2.9]	0.60
No	Ref	
Dog in home		
Yes	0.7 [0.4, 1.2]	0.19
No	Ref	
Cat in home		
Yes	0.7 [0.4, 1.3]	0.28
No	Ref	

[a]Interactions of BMI with day care, TRAP, and SHS were modeled, based on $P <= 0.25$ comparing odds ratios between BMI strata (Table 2).

interaction effects of BMI-SHS, BMI-TRAP, and BMI-day care were examined.

High SHS exposure (≥10 cigarettes/day) exhibited a three-fold increase in the odds of asthma in the overweight group, (adjusted (adj) OR = 3.0; 95% CI = 1.2,7.4), but no association was observed among children of normal weight (adjOR = 1.1; 95% CI = 0.4,2.7) (Table 3). In contrast, the BMI normal group indicated that high lifetime TRAP exposure showed almost a twofold increase in the odds of asthma (adjOR = 1.8; 95% CI = 1.0,3.4); no effect was observed in the overweight group (adjOR = 0.7; 95% CI = 0.3,1.8). Attendance at day care also was a significant risk for only those of normal BMI (adjOR = 2.6; 95% CI = 1.5,4.8).

Discussion

To our knowledge, this is the first study to examine objective measures of asthma in normal-weight and overweight children with prospective lifetime exposure estimates for TRAP and SHS. Contrary to the hypothesis, TRAP was significantly associated with asthma only for normal-weight children. We postulate that normal-weight children, compared with those overweight spend more time outdoors with greater chronic exposure to TRAP compounded by increased respiratory rates associated with higher levels of physical activity resulting in chronic airway inflammation (10,19,20). Our data on eNO levels support this hypothesis. Higher average levels of eNO in the normal-weight (7.0 ppb) versus the overweight (5.4 ppb) groups were found ($P < 0.01$), and the normal-weight versus overweight asthmatic children also had significantly ($P < 0.01$) higher eNO levels (10.2 ppb versus 5.7 ppb, respectively, data not shown). If so, the lack of an effect of TRAP on overweight children may be masked by weight-related inflammatory pathways, or by other potential high exposures including SHS. These findings further suggest that the proinflammatory response of weight gain may be different than the orchestration of airway inflammation by UFP or the constituents of TRAP. The association of day care attendance and asthma risk in only the normal-weight children was unexpected and needs further evaluation.

In contrast, SHS exposure had a significant threefold effect on only overweight children. As shown in Table 1, the mean cotinine hair measurements were lower in the normal-weight versus the overweight children ($P = 0.09$). The 23 asthmatic overweight children with hair cotinine measures had the highest values, 0.21 ng/mg (data not shown). Thus, if overweight children engage in less physical activity and spend more time indoors (10), where SHS is near the child's breathing zone, the effect on asthma risk may be greater.

Parental recall of residential history and household smoking history is a study limitation. However, it is unlikely that there is differential bias by BMI status as parents were queried on both before weight measurements and asthma diagnosis.

In conclusion, our findings show a differential effect on asthma risk by type of UFP exposure modified by children's weight status. Interventions targeted for decreasing both outdoor and indoor UFP are needed for children at risk for asthma as they continue lung growth and development until adulthood. O

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