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Effects of prenatal community violence and ambient air pollution on childhood wheeze in an urban population

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Abstract

Background: Prenatal exposures to stress and physical toxins influence children's respiratory health, albeit few studies consider these factors together.

Objectives: To concurrently examine effects of prenatal community-level psychosocial (exposure to community violence, ECV) and physical (air pollution) stressors on repeated wheeze in 708 urban children followed to age 2 years.

Methods: Multi-item ECV reported by mothers in pregnancy was summarized into a continuous score using Rasch modeling. Prenatal black carbon (BC) exposure was estimated using land-use regression (LUR) modeling; particulate matter (PM_{2.5}) was estimated using LUR incorporating satellite data. Mothers reported child's wheeze every 3 months. Effects of ECV and air pollutants on repeated wheeze (≥ 2 episodes) were examined using logistic regression. Interactions between ECV and pollutants were examined.

Results: Mothers were primarily Black (29%) and Hispanic (55%) with lower education (62% with ≤ 12 years); 87 children (12%) wheezed repeatedly. In models examining concurrent exposures, ECV [OR=1.95 (95% CI: 1.13-3.36), highest vs. lowest tertile] and BC [OR=1.84 (95% CI: 1.08-3.12), median vs. <median] were independently associated with wheeze adjusting

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for gender, birth season, maternal atopy, education, race, and cockroach antigen. Associations were similar for PM_{2.5} [adjusted-OR=2.02 (95%CI: 1.20-3.40)]. An interaction between ECV with air pollution levels was suggested.

Conclusions: These findings suggest that both prenatal community violence and air pollution may contribute to respiratory health in these urban children. Moreover, place-based psychosocial stressors may impact host resistance such that physical pollutants may have adverse effects, even at relatively lower levels.

Keywords

community violence; prenatal stress; traffic air pollution; particulate matter; repeated wheeze; prenatal exposure

INTRODUCTION

Wheezing respiratory illnesses in infancy account for significant morbidity and healthcare utilization.¹ While the spectrum of childhood wheeze phenotypes are complex, an important step in identifying children at risk for chronic respiratory disorders (e.g., poorer lung function, asthma) is characterizing risk factors that lead to and maintain this early predisposition.

The increased burden of wheezing respiratory illnesses and asthma in lower-socioeconomic status (SES) urban communities may, in part, be related to differential environmental exposures, including psychosocial stressors and physical toxicants, which cluster in more socially disadvantaged communities.^{2,3} Candidate factors receiving increasing attention include community violence and ambient air pollution.

Studies link community violence with increased asthma prevalence,^{4,5} higher asthma hospitalization rates,⁵ more symptom days,⁶ and wheezing in 2-3 year olds.⁷ Higher lifetime community violence exposure was associated with increased childhood asthma risk in a prospective, multi-level analysis adjusted for individual-level factors (e.g., SES, race, smoking) and neighborhood indicators (neighborhood disadvantage, social disorder, collective efficacy).⁸ While various mechanisms may underlie this association, a framework community as leading conceptualizes violence a chronic psychological stressor taxing individuals living in high-risk communities.⁹ Effects of maternal stress on respiratory outcomes may begin in pregnancy,¹⁰ although prenatal community violence has not been studied specifically.

Studies also link ambient pollution to childhood respiratory morbidity including wheeze, asthma, and lung function.¹¹⁻¹³ Evidence suggests a role for particles and other traffic-related components in particular.¹⁴⁻¹⁶ Exposure to environmental toxicants such as air pollution starting *in utero* may alter the normal course of lung morphogenesis and affect both structure and function of the respiratory system.¹⁷ Studies link prenatal air pollution exposure, including fine particulate matter^{18,19} and polycyclic aromatic hydrocarbons,²⁰ with wheeze, respiratory infections, and reduced lung function in children.

Studies including concurrent measures of psychosocial and physical environmental factors that may co-vary in lower-SES urban communities are needed to assess whether they have independent effects on child respiratory health or whether an adverse social environment is confounded by increased physical toxicants (or vice versa).²¹ Moreover, co-occurring psychosocial and physical exposures may combine to influence respiratory health risk. Studies examining interactions between community-level stress and air pollution exposures

in these communities on respiratory health remain sparse and have focused on children or older adolescents.²²⁻²⁴

To begin address these gaps, we examined effects of both prenatal maternal exposure to community violence (ECV), a neighborhood-level stressor, and ambient air pollutants [black carbon (BC), a surrogate of traffic particles, and ambient fine particulate matter (less than 2.5 μm in diameter; $\text{PM}_{2.5}$)] on repeated wheeze risk in urban children, adjusting for sociodemographics, potential confounders, and possible pathway variables (e.g., smoking). We also examined the interactive effects of prenatal ECV and air pollution exposures on wheeze. We hypothesized that there would be independent effects of ECV and ambient pollutants on child wheeze and that those children born to mothers with higher exposure to both ECV and ambient pollutants would be more likely to wheeze compared with children born to mothers with low exposure to both factors.

METHODS

Participants were from a pregnancy cohort examining independent and interactive effects of early life psychosocial stress and physical toxins on urban childhood respiratory health.²⁵ In brief, English- or Spanish-speaking pregnant women (≥ 18 years old) receiving care at Brigham & Women's Hospital (BWH), Boston Medical Center (BMC), and affiliated clinics were enrolled mid-to-late pregnancy (28.4 ± 7.9 weeks gestation) between August 2002 and December 2009. Among women approached, 989 of those who were eligible (78.1%) agreed to enroll. There were no significant differences on race/ethnicity, education, and income between women enrolled and those who declined; 955 gave birth to a live born infant and continued follow-up. Procedures were approved by the human studies committees at BWH and BMC. Written consent was obtained.

Exposure to Community Violence (ECV)

Within two weeks of enrollment, mothers completed the My Exposure to Violence questionnaire²⁶ assessing hearing gunshots, witnessing and/or experiencing fights, knife attacks, and/or shootings in their neighborhood. Acceptable internal consistency, test-retest reliability, and validity have been described.^{26,27} Events reported in the past year indicated exposure proximate to and during the pregnancy hereafter termed prenatal ECV. Respondents indicate the event frequency on a scale of 1 (0-1 time), 2 (2-4 times), 3 (5-10 times), or 4 (more than 10 times). The multi-item survey was summarized into a continuous scale using Rasch modeling based on item response theory, as detailed previously.²⁸ The model was generalized to calculate conditional probabilities for each "yes" response given the presumed event severity and accounting for features theoretically influencing severity, including frequency, whether events occurred at home, and whether the respondent knew the victim(s) or perpetrator(s).²⁸ Higher Rasch ECV scores indicate greater severity of violence exposure (e.g., witnessing a knifing or shooting compared to pushing or shoving fights) as well as greater frequency (for more details, see Online Repository and Figure E1).

Air Pollution Levels

Individuals' prenatal exposure to BC was estimated based on residence over the pregnancy (i.e., at enrollment and updated if they moved) using a validated spatio-temporal land-use regression (LUR) model as detailed elsewhere.²⁹ In brief, the BC model was built using data of 24-hr measures of BC based on >6021 pollution measurements from >2079 unique exposure days at 82 monitoring locations in greater Boston. Predictions were based on meteorological and other characteristics (e.g. weekday/weekend of a particular day,

Online Repository Materials

geographic information system (GIS)-based measures [e.g., traffic density within 100 meters, population density, distance to major roadway, percent urbanization]), and BC levels from a central monitor (representing overall area concentration on a particular day). Spline regression methods were used to allow factors to nonlinearly predict exposure and thin-plate splines captured additional spatial variability. Separate models were fit for cold (November-April) and warm (May-October) seasons ($R^2=0.82$ for both seasons). Prenatal BC exposure across the entire pregnancy was calculated by averaging the daily BC levels derived from LUR models for each participant. The monitoring site locations that provided data for the LUR in relation to participant residence locations and their predicted prenatal BC levels, are shown in Figure 1.

Prenatal $PM_{2.5}$ exposure was estimated using a novel spatio-temporal model incorporating Moderate Resolution Imaging Spectroradiometer (MODIS) satellite-derived Aerosol Optical Depth (AOD) measurements at a 10×10 km spatial resolution and layering this remote sensing data with traditional LUR predictors to yield residence-specific estimates of daily $PM_{2.5}$. As the model is based on daily physical measurements of a surrogate for $PM_{2.5}$ concentrations in each grid cell, it benefits both from the spatial resolution of LUR models and the spatio-temporal resolution of satellite models. The model was run using day-specific calibrations of AOD data using ground $PM_{2.5}$ measurements from 78 monitoring stations and LUR and meteorological variables (temperature, wind speed, visibility, elevation, distance to major roads, percent of open space, point emissions and area emissions). The AOD- $PM_{2.5}$ relationship was calibrated for each day using data from grid cells with both monitor and AOD values using mixed models with random slopes for day and nested regions. For days without AOD data (due to cloud coverage, snow, etc.), the model was fit with a smooth function of latitude and longitude and a random intercept for each cell (similar to universal kriging). The “out of sample” ten-fold cross validation R^2 for daily values were 0.83 and 0.81 for days with and without available AOD data, respectively. Individual overall prenatal $PM_{2.5}$ exposure level for each participant was calculated by averaging daily levels throughout pregnancy. Predicted prenatal $PM_{2.5}$ levels at participant’s residence in relation to the 10×10 km grids for which the AOD data are available are shown in Figure 2.

Children’s Repeated Wheeze

At approximately 3-month intervals starting from birth, maternal-reported child wheeze was ascertained up to age 24 months through interviews. Mothers were asked, “*Since we last spoke with you on (date), has your infant/child had wheezing or whistling in the chest? If so, how many times?*”, so that we captured wheeze episodes occurring during each follow-up interval. Two or more episodes constituted repeated wheeze, as in prior studies.^{31,32} Of the 708 children, 449 (63.4%) never wheezed, 172 (24.3%) wheezed once, and 50 (7.1%), 25 (3.5%), 10 (1.4%), and 2 (0.3%) had 2, 3, 4, and 5 wheeze episodes, respectively. Most mothers completed 3 or more follow-up surveys including at 2 years (88%); the percentage of children with repeated wheeze was similar for those completing 3, 4, 5, 6, 7 interviews (16%, 17%, 19%, 22%, and 17%, respectively).

Covariates

Maternal age, race, educational status, history of atopy (ever having clinician-diagnosed asthma, eczema, and/or hay fever), and pre-pregnancy height and weight were ascertained at enrollment; child’s gender, season of birth, and birthweight were reported postnatally. Maternal body mass index (BMI) was calculated as weight divided by height squared (kg/m^2). Given complex patterns of prenatal smoking,³³ we asked about smoking at enrollment and the third trimester; women were classified as prenatal smokers if smoking at either visit. Mothers reported postnatal smoking and whether others smoked in the home at each 3-

month postpartum interview. Lower-SES populations exposed to higher violence and pollution may also be exposed to increased household allergens.³⁴ Settled dust was collected within 2 weeks of enrollment from the mother's bedroom using a standardized protocol.³⁵ Cockroach allergens (*Blatella Germanica*, *Bla g 1* and *Bla g 2*) were analyzed using a monoclonal antibody-based Enzyme-Linked Immunosorbent Assay (Indoor Biotechnologies, Charlottesville, Va). High exposure was defined as *Bla g 1* or *Bla g 2* >2 U/g.³⁵

Exposures to postnatal ECV, postnatal BC, and postnatal PM_{2.5} were also derived. Mothers completed the same questionnaire assessing community violence, as described above, when children were 18-24 months old assessing postnatal ECV from birth. Cumulative average postnatal BC and PM_{2.5} exposure from birth to age 2 years was similarly estimated as prenatal exposures.

Analysis

Those completing two or more postnatal interviews up to 24 months for whom air pollution indicators were derived were included in these analyses ($n=708$). Characteristics of included (maternal age 27 ± 6 years, 62% with high school education, 29% Blacks, 55% Hispanics, 52% boys) versus excluded subjects (maternal age 26 ± 5 years, 64% with high school education, 38% Blacks, 48% Hispanics, 53% boys) were not significantly different. Missingness on covariates was approximately 5%, and thus missing indicators were used in analyses.

The prenatal ECV score (range: -0.68 to 3.53) was categorized as low, medium, and high based on the *a priori* decision to use cutoffs at the 33rd and 67th percentile to address potential non-linearity. Given some tied scores, low ($n=358$), medium ($n=149$), and high ($n=201$) categories were unequal. BC and PM_{2.5} were *a priori* categorized into "high" and "low" groups based on a median split as there is no established health-relevant cutoff.

In primary analyses, independent effects of prenatal ECV and air pollution on child repeated wheeze were examined using multivariate logistic regressions including both in the model and adjusting for child's gender, maternal demographic variables previously correlated with community violence and pollution exposures (e.g., race/ethnicity, maternal education), atopy-related factors (season of birth, maternal atopy), and cockroach exposure. Prenatal BC and PM_{2.5} were considered in separate models as they were moderately correlated (Spearman's $r=0.54$). Variables that may be in the pathway between ECV and/or pollution were considered in secondary analyses, including maternal BMI, pre- and postnatal tobacco smoke exposure, and birth weight adjusting for gestational age.³⁶ To ensure that these results were not affected by the chosen exposure cutpoints, we also explored exposure-response relationships using continuous exposure variables by implementing Generalized Additive Models (GAMs) with smooth penalized spline terms for ECV as well as air pollution indicators that allow model fitting on potential non-linear exposure-response relationships.³⁷

In stratified analyses, we examined effect modification on the association between prenatal ECV and children's repeated wheeze by pollutant level. We also fit interaction terms of ECV by median split BC or PM_{2.5} to examine effects on both the multiplicative (by including a product term) and additive scales [by calculating the Relative Excess Risk due to Interaction (RERI; RERI=0 indicates no interaction on an additive scale) and confidence intervals (CIs) using the bootstrap percentile method].³⁸ Sensitivity analyses adjusting for postnatal exposure to ECV, BC and PM_{2.5} were performed. Of note, prenatal and postnatal levels were correlated (Spearman's $r=0.72$ for pre/postnatal ECV, $r=0.96$ for pre/postnatal BC, and $r=0.82$ for pre/postnatal PM_{2.5}; all $p<0.001$). Additional sensitivity analyses were

conducted considering wheeze frequency as a multiple categorical outcome variable (for example, 0-1, 2-3, 4 wheeze episodes) using multinomial logit analyses as well as adjacent-categories logit models (see Online Repository). GAMs and adjacent-categories logit models were implemented using the MGCV and VGAM packages in R (version 2.13.0, Vienna, Austria). SAS (version 9.1.3, SAS Institute Inc., Cary, NC) was used for all other analyses.

RESULTS

Most mothers were ethnic minority (55% Hispanic, 29% African American), low SES (62% having 12 years of education), and nonsmokers (80%); 87 children (12%) had repeated wheeze (Table 1). Spearman's correlations between ECV and pollutants were modest (Table 2).

ECV, Air Pollution, and Wheeze

Table 3 summarizes results from logistic regression. The odds ratios (ORs) for repeated wheeze comparing high and medium to low prenatal ECV groups showed an exposure-response relationship in both the univariate model and when adjusted for prenatal BC or PM_{2.5} levels. Effects of BC and PM_{2.5} were borderline nonsignificant in unadjusted models. In the model adjusting for sociodemographics, atopy, and cockroach exposure, the highest level of prenatal ECV remained significantly associated with repeated wheeze, and higher-level air pollution exposures (both BC and PM_{2.5}) were now significantly related to wheeze. Further inclusion of potential pathway variables (e.g., maternal pre/postnatal smoking, BMI, and gestational-age-adjusted birthweight) did not alter these findings (data not shown). Other significant predictors of repeated wheeze included male gender and maternal atopy. In sensitivity analyses adjusting for postnatal exposure to ECV, the highest level of prenatal ECV remained significant in the fully adjusted BC model (OR=1.9, 95% CI: 1.1-3.3) and the fully adjusted PM_{2.5} model (OR=2.1, 95% CI: 1.2-3.6), respectively. When further adjusting the BC model from Table 3 for postnatal BC exposure, the OR of high prenatal BC was 2.2 (95% CI: 1.1-4.2); when further adjusting the PM_{2.5} model for postnatal PM_{2.5}, the OR of high prenatal PM_{2.5} was 2.5 (95% CI: 1.0-6.5).

Results from the GAMs suggested that the functional form of the exposure-response relationship between wheezing status and each of the three exposures (ECV, BC and PM_{2.5}) were approximately linear on the logit scale (Figure 3). There was some indication of a less steep relationship at the higher exposure levels for each exposure, particularly for ECV.

Finally, sensitivity analyses considering wheeze frequency as a multiple categorical outcome demonstrated that increased exposure to prenatal ECV and/or air pollution indicators was associated with progressively increasing odds of more frequent wheeze (Tables E1 and E2, Online Repository). Thus, these associations were robust to alternative specifications for what constituted repeated wheeze.

Stratified Analyses

In analyses examining effect estimates of ECV exposure stratified by air pollution levels, we observed statistically significant associations between high prenatal ECV and increased repeated wheeze in the low BC (adjusted OR=2.87, 95% CI: 1.33-7.32) and low PM_{2.5} (adjusted OR=3.63, 95% CI: 1.43-9.52) groups, but not in the high BC (adjusted OR=1.31, 95% CI: 0.59-2.93) or high PM_{2.5} (adjusted OR=1.51, 95% CI: 0.71-3.21) groups (Figure 4), albeit multiplicative interactions were not significant ($p>0.20$ for both). The RERI for high ECV by low BC was 0.26 (95% CI: -0.09, 1.83; $p=0.08$), suggesting that the OR for repeated wheeze in those with high ECV and low BC to be 0.26 more than if there were no

interaction on the additive scale. The additive interaction between ECV and PM_{2.5} was not significant ($p=0.33$).

DISCUSSION

To our knowledge, this is the first prospective study to concurrently assess prenatal exposure to neighborhood-level psychosocial (i.e., community violence) and physical toxins (i.e., ambient pollution) in relationship to early childhood wheeze. Children born to mothers reporting higher community violence exposure prenatally were more likely to have repeated wheeze, even when adjusting for a number of child (i.e., gender, season of birth, birthweight) and maternal (i.e., race, education, BMI, atopic history) factors, as well as other environmental factors (i.e., ambient BC or PM_{2.5}, cockroach allergen, maternal smoking). Moreover, in models considering ECV and air pollution (either BC or PM_{2.5}) together, increased pollution independently predicted repeated wheeze. These findings suggest that both prenatal community violence and increased air pollution contribute to respiratory health in these urban children.

These data add to growing evidence linking community violence to childhood respiratory health. Previous studies have suggested an association between community violence assessed postnatally (i.e., during the child's lifetime) and heightened respiratory morbidity. Berz and colleagues⁷ found an association between witnessing violence and increased repeated wheeze by age 2-3 years, adjusting for gender, maternal asthma, smoking and social support. Increased neighborhood violence exposure was associated with more symptom days among 9-12 year old asthmatics,⁶ elevated asthma prevalence in school-aged children,⁴ and reduced lung function at age 6 years.³⁹ We previously demonstrated a prospective association between higher lifetime community violence exposure and childhood asthma risk adjusting domestic for sociodemographics, smoking, domestic violence, neighborhood disadvantage, social disorder and collective efficacy.⁸ The current study is the first to consider prenatal exposure to community violence in relation to children's respiratory health.

While previous studies link traffic-related air pollution assessed during early childhood (i.e., postnatally) with children's asthmatic symptoms and reduced lung function,¹⁴⁻¹⁶ few studies have focused on prenatal exposures.¹⁸⁻²⁰ Thus, the independent effect of prenatal ambient pollution on early childhood wheeze adjusting for community violence and other covariates is another important finding.

Furthermore, psychosocial and physical pollutants may combine to affect health.^{40,41} A few studies have assessed interactions between stress and traffic-related air pollutants and respiratory health. Notably, findings on interactions have been variable. One study of children aged 5-9 years suggested a stronger association between traffic-related pollution and new onset asthma risk among children of parents reporting higher perceived stress.²⁴ We previously found that postnatal traffic-related nitrogen dioxide (NO₂) interacted with violence exposure to predict increased asthma risk in urban children (mean age 6.8 years); those with both high postnatal NO₂ and high lifetime violence exposures were at greatest risk.²³ On the other hand, another study of asthmatic children aged 9-18 years found that the association between higher family stress and asthma exacerbations was stronger when NO₂ levels were more modest.²² Similar to Chen and colleagues,²² in this study we observed that the association between higher prenatal community violence exposure and repeated wheeze was stronger in children born to mothers with more modest prenatal air pollution exposures. There was also some indication of a negative interaction between air pollution and ECV in our data - the effect estimate of ECV in the high air pollution exposure category was less than that in the lower air pollution category. One possible explanation is that the effect of

higher prenatal traffic-related air pollution exposure on child wheeze might be of significant magnitude to lead to a 'saturation effect' such that the additional risk conferred by prenatal ECV beyond the highest level of air pollution exposure could not be detected (i.e., effects of two factors when the effect of higher-level exposure to factor A reaches the ceiling and masks the effect of factor B). In this case, the effect of factor B on the outcome may be more apparent when the level of exposure to factor A is lower so that the impact on the outcome is not yet 'saturated'. On the other hand, since the two exposures are positively correlated, the results could be due to a less steep relationship for either exposure at higher levels. That is, this may be a result of the less steep relationship with wheeze at higher ECV exposure levels as seen in Figure 3, so that when stratifying by those with high level air pollution and high ECV, an association with wheeze could not be detected due to the nonlinear exposure-response function on this portion of the curve. Finally, the lack of statistical significance when testing interaction terms might be due to chance. It is also notable that the studies mentioned above varied on key aspects [e.g., how and when stress and air pollution were measured, children's developmental stage (prenatal, early childhood, adolescence)], making it challenging to compare results across studies.

Prenatal exposure to psychosocial stress⁴² and ambient pollutants¹¹ may anatomy and/or physiological functioning the and impact of lung interrelated systems. Programming effects may result from toxicant-induced shifts in key regulatory systems including both central and peripheral components of neuroendocrine pathways and autonomic nervous system (ANS) functioning which, in influence the turn, immune system starting *in utero*. Prenatal exposure to air pollutants and stress may permanently organize these systems toward trajectories of enhanced pediatric respiratory disease risk.⁴³ These factors may operate through incompletely overlapping mechanisms described below that thus result in independent as well as cumulative or interactive effects.

For example, prenatal stress may disrupt maternal physiology [e.g., hypothalamic-pituitary-adrenal axis (HPA), ANS system], which then may potentiate the developing fetal immune system.⁴⁴ Among various stress domains, traumatic stressors such as community violence may be more likely to result in lasting biobehavioral sequelae in the mothers (e.g., psychopathology, neurohormonal disruption) and intergenerational effects⁴⁵. Community violence exposure is an independent predictor of anxiety and depression in urban minority women of childbearing age⁴⁶ as well as disrupted HPA functioning in urban women⁴⁷ and children.⁴⁸ Living in a community with higher crime and violence might alter mothers' health behaviors, such as smoking,⁴⁹ which may subsequently impact childhood wheeze.⁵⁰ Prenatal stress as well as ambient pollution may contribute to poor fetal growth and low birthweight,^{51,52} factors linked to child wheeze.⁵³ Adjusting for birthweight and maternal smoking did not substantially affect our findings, however.

Studies suggested that air pollution may contribute to early airway remodeling through associations with asthma development and consequent effects on lung function.^{11,54,55} In addition, exposure to pollutants may be associated with airway remodeling independent of asthma.^{56,57} Pathways involved in the remodeling process that may be targets of air pollution include xenobiotic metabolism,⁵⁸ mitochondrial biogenesis,⁵⁹ epithelial lung repair and regeneration,⁶⁰ and neural plasticity.⁶¹ Ambient pollutants may also influence HPA axis functioning. HPA axis disruptions have been linked to a host of environmental chemicals (e.g., carbon monoxide, metals).⁶²⁻⁶⁴ Particulate matter and ozone may influence inflammatory cytokine production in the pituitary.⁶⁵ Transplacental exposure to polycyclic aromatic hydrocarbons may lead to disturbances of the pituitary-adrenocortico-placental system in pregnancy and the HPA axis over the life course.⁶⁶

Strengths of this study include the reasonably large lower SES, ethnically mixed, urban prospective cohort, the focus on the prenatal period and available data on confounders and potential pathway variables. In addition, we used advanced methodology (i.e., item response theory) to summarize the multi-item community violence measure. Our findings were consistent across two indicators for prenatal exposure to urban ambient of particulate pollution – BC, a surrogate traffic-related Ppollution, and PM_{2.5}, which also captures other sources. Ambient pollution was estimated using validated, state-of-the-art spatiotemporal LUR models adding satellite-derived AOD data when estimating PM_{2.5}.

We also acknowledge some limitations. Mothers experiencing higher levels of community violence might be less likely to notice their children's wheeze symptoms if overwhelmed by their own stress, or conversely tend to over-report children's symptoms if they are more vigilant overall. It is however reassuring that variables related to wheeze in other studies were associated in the expected direction in our data (i.e., male gender, maternal atopy). Nonetheless, it will be important to examine associations between these exposures and more definitive respiratory outcomes as we follow these children (e.g., physician-diagnosed asthma, lung function) and see if relationships hold. Future studies would also be enhanced by assessing biomarkers of potential mechanisms through which both social and physical environmental stressors might associate with respiratory health (e.g., cortisol disruption, autonomic imbalance, immunomodulation, oxidative stress). In addition, while the stratified analyses suggested significant difference on the associations between ECV and wheeze between low vs. high air pollution groups, the tests for interactions did not reach statistical significance which may be due to the sample size and reduced power to detect interactions. Studies including larger samples may enhance power to detect interactions between community violence and physical environmental factors such as air pollution in the urban environment. While we examined other environmental factors that may co-vary with both ECV and ambient pollutants (e.g., cockroach allergen), we cannot rule out the potential for unmeasured confounding.

In summary, we found independent effects of increased community violence and higher exposure to traffic-related air pollutants in the prenatal period on repeated wheeze in these urban children. This suggests that an adverse psychosocial environment, such as community violence exposure, may not simply be a surrogate of increased exposure to an adverse physical environment at the community level, such as ambient air pollution. Moreover, stratified analyses suggested that place-based psychosocial stressors might impact host resistance such that physical pollutants may have adverse effects, even at relatively lower levels.²¹ Because these factors tend to cluster in the most socially disadvantaged communities, research that considers psychosocial stress and physical environmental toxicants concurrently, including joint effects, may better inform the etiology of respiratory health disparities.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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Abbreviations

AOD	satellite-derived aerosol optical depth
BC	black carbon
<i>Bla g</i>	<i>Blatella Germanica</i>
BMI	body mass index
CI	confidence interval
ECV	exposure to community violence
GAM	Generalized Additive Model
GIS	geographic information system
LUR	land-use regression model
OR	odds ratio
PM_{2.5}	particulate matter with a diameter less than 2.5 µm
RERI	Relative Excess Risk due to Interaction
SES	socioeconomic status

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Key Messages

- These prospective analyses demonstrate independent associations of increased community violence exposure (psychosocial stressor) and higher exposure to urban ambient air pollution (physical toxicants) in the prenatal period with repeated wheeze in urban children.
- These findings indicate that an adverse psychosocial environment, such as community violence exposure, is not simply a surrogate marker of an adverse physical environment such as higher levels of ambient pollution in the urban setting with respect to children's respiratory health.
- Stratified analyses suggest that place-based psychosocial stressors may impact host resistance such that physical pollutants may have adverse effects, even at relatively lower levels.

Capsule Summary

Research that considers psychosocial stress and physical environmental toxicants concurrently, including joint effects, may better inform the etiology of respiratory health disparities given that these factors tend to cluster in the most socially disadvantaged communities in the United States.

Figure 1. Predicted BC levels for ACCESS study participants during pregnancy

This figure demonstrates the predicted BC levels for study participants based on residence during the gestation period. In addition, the locations of monitoring sites used in the model to predict BC levels are presented as black triangles.

Figure 2. Predicted PM_{2.5} levels for ACCESS study participants during pregnancy

This figure demonstrates predicted PM_{2.5} levels for study participants based on residence during the gestation period. The 10km × 10km AOD grid used to predict daily PM_{2.5} levels is also depicted.

Figure 3. Exposure-response relationships of prenatal maternal ECV and prenatal air pollution indicators with children's repeated wheeze

Penalized spline curves using GAMs demonstrating the relationship of (A) prenatal maternal ECV, (B) prenatal BC level ($\mu\text{g}/\text{m}^3$), and (C) prenatal PM_{2.5} level ($\mu\text{g}/\text{m}^3$), with log odds of children's repeated wheeze by age 2 years. Solid lines depict the penalized spline curve while dotted lines indicate the 95% confidence bounds. Models were adjusted for child's gender, season of birth, maternal race, education, atopy, and household cockroach allergens.

Figure 4. Associations between prenatal maternal ECV and children's repeated wheeze in analyses stratified by air pollutant levels

This figure demonstrates ORs and 95% CIs for repeated wheeze comparing medium vs. low ECV groups (squares) and high vs. low ECV groups (diamonds), stratified by (A) BC median level ($0.38 \mu\text{g}/\text{m}^3$) and (B) PM_{2.5} median level ($11.22 \mu\text{g}/\text{m}^3$). The solid markers indicate the ORs for participants exposed to higher levels (median) of air pollution and the hollow markers indicate the ORs for participants exposed to lower levels (<median) of air pollution. Models were adjusted for child's gender, season of birth, maternal race, education, and atopy.

Table 1

Participant characteristics (708 mother-child pairs)

Categorical Variables	n	%
Repeated wheeze until age 2 years ^a		
No	621	87.7
Yes	87	12.3
Child's gender		
Female	343	48.5
Male	365	51.5
Maternal race/ethnicity		
Hispanic	391	55.2
Black	203	28.7
White/Other	104	14.7
Missing	10	1.4
Season of birth		
Winter	190	26.8
Summer	152	21.5
Spring	155	21.9
Fall	211	29.8
Maternal education		
>12 yrs	233	32.9
12 yrs	442	62.4
Missing	33	4.7
Maternal atopy ^b		
No	429	60.6
Yes	243	34.3
Missing	36	5.1
Maternal smoking		
Never smoked	569	80.4
Smoked prenatally, but not postnatally	34	4.8
Did not smoke prenatally, but smoked postnatally	37	5.2
Smoked both pre- and postnatally	68	9.6
Continuous Variables		
Maternal BMI (kg/m ² ; mean, SD)	28.8	6.1
Maternal age at enrollment (years; mean, SD)	27.2	6.0
Gestational age at birth (weeks; mean, SD)	39.0	3.1
Birthweight percentile adjusting for gestational age (mean, SD)	43.7	31.2
Exposure to community violence (ECV) in past 1 year (mean, SD) ^c	0.06	0.90
Prenatal BC level (μg/m ³ ; median, IQR)	0.38	0.30 - 0.50
Prenatal PM_{2.5} level (μg/m ³ ; median, IQR)	11.22	10.25 - 11.89

Categorical Variables	n	%
Bla g 1 (U/g; median, IQR)	0.20	0.20-0.40
Bla g 2 (U/g; median, IQR)	0.50	0.50-0.95

^aRepeated wheeze (≥ 2 episodes) reported by mothers at each 3-month postpartum interview up to age 2 years.

^bEver self-reported doctor-diagnosed asthma, eczema, and/or hay fever.

^cAssessed using the My Exposure to Violence survey;²⁶ multi-item survey summarized into a continuous score using Rasch modeling.²⁸

Table 2

Spearman's Correlations between prenatal community violence and physical environmental exposures

	Rasch ECV score ^a		BC Level		PM _{2.5} Level		Household <i>Bla g 1</i>	
	<i>r</i>	<i>p</i>	<i>r</i>	<i>p</i>	<i>r</i>	<i>p</i>	<i>r</i>	<i>p</i>
BC Level	0.14	<.001	–	–	–	–	–	–
PM_{2.5} Level	-0.04	0.31	0.54	<.001	–	–	–	–
Household <i>Bla g 1</i>^b	-0.04	0.38	0.17	<.001	0.14	<.001	–	–
Household <i>Bla g 2</i>^c	-0.03	0.54	0.13	<.001	0.06	0.19	0.78	<.001

^a Assessed using the My Exposure to Violence survey;²⁶ multi-item survey summarized into a continuous score using Rasch modeling.²⁸^b Household cockroach allergens (*Bla g 1*)^c Household cockroach allergens (*Bla g 2*)

Table 3

Maternal exposure to community violence and ambient air pollution during pregnancy and repeated wheeze in children: Logistic Regression Models

	Univariate Model ^a			Multivariable-adjusted Model					
				BC Model ^b			PM _{2.5} Model ^c		
Variables	OR	95%CI		OR	95%CI		OR	95%CI	
<u>Community-level stress</u>									
Prenatal community violence									
Low	Ref	–	–	Ref	–	–	Ref	–	–
Medium	1.44	0.79	2.62	1.34	0.71	2.52	1.41	0.75	2.68
High	2.08	1.25	3.46	1.95	1.13	3.36	2.15	1.24	3.71
<u>Ambient air pollution^d</u>									
Prenatal BC exposure									
Low (median)	Ref	–	–	Ref	–	–			
High (>median)	1.61	0.98	2.66	1.84	1.08	3.12			
Prenatal PM_{2.5} exposure									
Low (median)	Ref	–	–				Ref	–	–
High (>median)	1.51	0.95	2.41				2.02	1.20	3.40
<u>Demographic characteristics</u>									
Child's gender									
Female	Ref	–	–	Ref	–	–	Ref	–	–
Male	2.05	1.28	3.28	2.49	1.51	4.12	2.49	1.51	4.13
Maternal race/ethnicity									
Hispanic	Ref	–	–	Ref	–	–	Ref	–	–
Black	1.11	0.66	1.87	0.80	0.45	1.41	0.87	0.49	1.56
White/Other	1.54	0.84	2.83	1.07	0.55	2.12	1.22	0.61	2.43
Maternal Education									
>12 yrs	Ref	–	–	Ref	–	–	Ref	–	–
12 yrs	0.62	0.39	0.98	0.62	0.37	1.04	0.62	0.37	1.04
<u>Atopy related factors</u>									
Season of Birth									
Winter	Ref	–	–	Ref	–	–	Ref	–	–
Spring	1.26	0.64	2.47	1.11	0.55	2.26	1.13	0.56	2.29
Summer	1.13	0.57	2.26	1.07	0.52	2.20	1.20	0.58	2.48
Fall	1.61	0.88	2.95	1.75	0.93	3.29	1.97	1.04	3.74
Maternal atopy ^e									
No	Ref	–	–	Ref	–	–	Ref	–	–
Yes	2.09	1.31	3.34	1.83	1.12	3.00	1.85	1.13	3.04
<u>Household allergens</u>									
Cockroach allergen level^f									
Low (2 U/g)	Ref	–	–	Ref	–	–	Ref	–	–

Variables	Univariate Model ^a			Multivariable-adjusted Model					
	OR	95%CI		BC Model ^b			PM _{2.5} Model ^c		
				OR	95%CI		OR	95%CI	
High (>2 U/g)	0.74	0.33	1.66	0.73	0.30	1.76	0.67	0.28	1.62

^aUnivariate (unadjusted) logistic regressions predicting repeated wheeze. Each variable listed in the table was the independent variable in a separate univariate model.

^bThe BC model included community violence, black carbon, gender, race/ethnicity, maternal education, season of birth, maternal atopy, and cockroach allergen exposure.

^cThe PM_{2.5} model included community violence, PM_{2.5}, gender, race/ethnicity, maternal education, season of birth, maternal atopy and cockroach allergen exposure.

^dBC median=0.38 µg/m³; PM_{2.5} median=11.22 µg/m³

^eEver self-reported doctor-diagnosed asthma, eczema, and/or hay fever.

^fHigh cockroach allergen was defined as *Bla g 1* or *Bla g 2* levels >2 U/g.