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Environ Res. Author manuscript; available in PMC 2017 July 01.

Published in final edited form as:
Environ Res. 2016 July ; 148: 144–153. doi:10.1016/j.envres.2016.03.035.

Association between prenatal exposure to ambient diesel particulate matter and perchloroethylene with children's 3rd grade standardized test scores

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Abstract

The objective of this research was to determine if prenatal exposure to two common urban air pollutants, diesel and perchloroethylene, affects children's 3rd grade standardized test scores in mathematics and English language arts (ELA). Exposure estimates consisted of annual average ambient concentrations of diesel particulate matter and perchloroethylene obtained from the Environmental Protection Agency's 1996 National Air Toxics Assessment for the residential census tract at birth. Outcome data consisted of linked birth and educational records for 201,559 singleton, non-anomalous children born between 1994-1998 who attended New York City public schools. Quantile regression models were used to estimate the effects of these exposures on multiple points within the continuous distribution of standardized test scores. Modified Poisson regression models were used to calculate risk ratios (RR) and 95% confidence intervals (CI) of failing to meet curricula standards, an indicator derived from test scores. Models were adjusted for a number of maternal, neighborhood and childhood factors. Results showed that math scores were approximately 6% of a standard deviation lower for children exposed to the highest levels of both pollutants as compared to children with low levels of both pollutants. Children exposed to high levels of both pollutants also had the largest risk of failing to meet math test standards when compared to children with low levels of exposure to the pollutants (RR 1.10 95%CI 1.07,1.12 RR high perchloroethylene only 1.03 95%CI 1.00,1.06; RR high diesel PM only 1.02 95%CI 0.99,1.06). There was no association observed between exposure to only one of the pollutants and failing to meet ELA standards. This study provides preliminary evidence of associations between

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Review of Human Subjects Research
The creation of the Longitudinal Study of Early Development and this analysis was reviewed and approved by the New York City Department of Health and Mental Hygiene's Institutional Review Board. Additionally, this analysis was reviewed and approved by the Mount Sinai Institutional Review Board.

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prenatal exposure to urban air pollutants and lower academic outcomes. Additionally, these findings suggest that individual pollutants may additively impact health and point to the need to study the collective effects of air pollutant mixtures. Key Words: air toxics, academic outcomes, urban health, tetrachloroethylene, air pollutant mixtures

Keywords

air toxics; academic outcomes; urban health; tetrachloroethylene; air pollutant mixtures

1. INTRODUCTION

Urban air pollution is a complex mixture of multiple pollutants from a variety of sources. Diesel, itself a mixture of over one hundred distinct components, is one example of a common traffic-related air pollutant (TRAP) within the urban environment.(Krivoshto et al., 2008) Animal research suggests that exposure to diesel can contribute to a variety of adverse developmental effects, including altered brain development and behavior.(Ema et al., 2013) There is growing epidemiologic evidence that prenatal exposure to TRAP is associated with neurodevelopmental and behavioral outcomes in infants and young children(Edwards et al., 2010; Freire et al., 2010; Guxens et al., 2012; Harris et al., 2015; Lin et al., 2014; Perera et al., 2009; Perera et al., 2006), although few studies focused specifically on diesel particulates. Recently, a small cross-sectional study in Texas observed an association between parent-reported grade point averages in elementary school children and living in communities with higher estimates of diesel-associated health risk.(Clark-Reyna et al., 2015)

While much of the literature has focused on TRAP exposures, there are a number of non-traffic related pollutants within the urban environment that have the potential to impact children's neurodevelopment and academic outcomes. Perchloroethylene (also known as tetrachloroethylene or perc) is a solvent primarily used in the dry-cleaning industry.(EPA, 2010) Although a liquid, it evaporates quickly and the majority of the general population is exposed through indoor and outdoor air. Animal research has shown that perchloroethylene can have both neurobehavioral and neuropathological effects in exposed animals, although often at exposure levels much higher than what humans experience in the ambient air.(Bale et al., 2011) Previous epidemiological research has shown association between prenatal exposure to ambient levels of perchloroethylene and autism in children (von Ehrenstein et al., 2014), suggesting the potential for adverse effects from lower levels of exposure.

While previous research suggests that both diesel and perchloroethylene can individually affect neurobehavioral outcomes in children, there has been little work that attempts to estimate how high exposure to both of these commonly co-occurring urban air pollutants could impact children's cognitive health. The goal of this study was to utilize an existing population-based data resource to estimate the effects of prenatal exposure to both diesel particulate matter (PM), a surrogate for total diesel, and perchloroethylene on academic outcomes later in childhood.

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1. METHODS

2.1 Study Population

This project was reviewed and approved by the New York City Department of Health and Mental Hygiene (NYC DOHMH) and the Mount Sinai Institutional Review Boards. The Longitudinal Study of Early Development is a probabilistic data-linkage of administrative registries and databases constructed by the NYC DOHMH.(Pfeiffer et al., 2012) Researchers at the NYC DOHMH used a multi-file linkage methodology to link data for children born between 1994-2004 across five datasets: birth, death and Lead Poisoning Prevention Program registries maintained by the NYC DOHMH and select administrative data from the NYC DOHMH's Early Intervention Program and the New York City Department of Education. Inclusion criteria for this study were that children: (1) had been born in New York City during 1994-1998 to a mother whose primary residence was in New York City; (2) had a successfully geocoded address provided on the birth record; and (3) had been enrolled in 3rd grade in a New York City public elementary school prior to 2008. Children who had been born as part of a multiple birth were excluded, as were those who had congenital anomalies reported on their birth record.

2.2 Assessment of Academic Outcomes

Achievement on 3rd grade standardized tests in math and English language arts (ELA) was used as a measure of academic outcomes. Designed to reflect a child's understanding of the 3rd grade curricula, these tests were administered on an annual basis to all 3rd grade students in New York State until 2013. These tests were used to track students' performance over time as well as compare results across schools. Considered a distal marker of an impact on neurodevelopment and cognition, similar tests have been used as a measure of impairment among childhood cancer survivors.(Harshman et al., 2012) Tests are scored on a continuous scale, ranging from 330 to 770. To compare raw scores across years, scores were standardized using year of birth as a proxy for test-year. The resulting math z-scores have a mean of 0 and a standard deviation of 1. Additionally, each academic-testing year, raw scores were assigned a category score ranging from 1 to 4, which corresponded to the following designations: 1- Way below standards ; 2-Below standards ; 3- Meets standards ; 4- Exceeds standards. For this analysis, the assigned category score was collapsed into a dichotomous variable which divided children into those who scored below the test-based standards and those who met or exceeded the test-based standards.

2.3 Assignment of ambient diesel particulate matter and perchloroethylene exposure

Ambient diesel PM and perchloroethylene exposure levels were assigned using the EPA's National Air Toxics Assessment (NATA) from 1996, the assessment closest in time to the years of birth for children in this study. NATA assessments are periodic, comprehensive evaluations of ambient air toxics in the United States that produce modeled ambient concentrations of air toxics for every census tract in the U.S.(EPA, 2015a) The NATA process includes compiling emissions inventories and applying computer simulation models which account for factors such as the rate and location of release, wind speeds and secondary pollutant formation.(EPA, 2015a) For most air toxics, including perchloroethylene, the NATA primarily relies on the National Emissions Inventory.

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Concentrations of diesel PM, a surrogate for total diesel exhaust, were produced using a PM inventory that was compiled by EPA for regulatory purposes. Both perchloroethylene and diesel PM estimates from the 1996 NATA were assigned an overall confidence rating of medium by the EPA, based on the combined assessment of the certainty and accuracy of the emissions data used in the modeling process and evaluations with monitoring data.(EPA, 2015b)

On average, census tracts are constructed to contain approximately 4,000 people; New York City had 2,217 census tracts during the 1990s. Using the census tract corresponding to the address provided on the birth record, ambient diesel PM and perchloroethylene concentrations were assigned to each child. For each pollutant, concentrations were categorized into quartiles, to account for the highly skewed exposure distributions within this population and avoid overly influential points at the upper tails of the distribution. Common referent-group coding was used to create a single exposure variable with four levels: exposure within the 4^{th} (highest) quartile for both diesel PM and perchloroethylene; exposure within the 4^{th} quartile for diesel PM and exposure to perchloroethylene within the first 3 quartiles; exposure within the 4^{th} quartile for perchloroethylene and exposure to diesel PM within the first 3 quartiles; and exposure within the first 3 quartiles for both diesel PM and perchloroethylene.

2.4 Assessment of Confounders

Potential confounders were identified through review of the literature and directed acyclic graph analysis.(Greenland et al., 1999) The following maternal characteristics were obtained from the birth record and were considered potential confounders: race, age, marital status, nativity, educational attainment, use of tobacco and/or alcohol during the pregnancy and insurance status at the time of delivery as a proxy for early-life socioeconomic status (SES). The following characteristics of the children, obtained from the school record, were considered potential confounders: eligibility for the school lunch program (proxy for current SES) and days absent in 3^{rd} grade. Childhood lead exposure, as represented by the maximum venous blood lead level recorded in the Lead Poisoning Prevention registry, was also considered a potential confounder. Since 1993, New York State has required blood lead level testing for all children at 1 year and 2 years old; therefore, the data was available for this cohort.

In order to control for neighborhood-level factors that can be associated with ambient pollutant concentrations and lower academic outcomes, a neighborhood-deprivation index, defined at the census-tract level, was constructed using a principal components analysis of census data.(Messer et al., 2006) In addition to the 7 variables used to calculate the neighborhood deprivation index in previous air pollution research (percent with college degree, percent unemployment, percent management/professional occupation, percent residential crowding, percent below 200% of the federal poverty line, percent of households receiving public assistance and percent nonwhite race)(Savitz et al., 2014), percent of linguistically isolated households, defined as a household where no one 14 years or older speaks English "very well", was also included in the calculation.

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2.5 Accounting for Missing Data

Although blood lead testing is mandatory in New York State, 22% of children were missing values for venous blood lead levels. Missing maximum blood lead values were imputed using single-chain Markov chain Monte Carlo methodology.(Yuan, 2011) Five imputations were run, and there were 200 burn-in iterations and 20 iterations between imputations. Math score, ELA score, ambient diesel PM concentration estimates, ambient perchloroethylene concentration estimates, all confounders described above and the following auxiliary variables were used in the imputation model: child's sex, year that housing was built, borough of residence, mother's employment status and mother's participation in the Women, Infants and Children supplementary nutrition program. All other variables had less than 5% missing values, and children with missing data on any other confounder were excluded from the analysis.

2.6 Statistical Analysis

For math and ELA scores separately, analyses were performed on each imputation dataset, and then results were pooled using Rubin's rules, which account for the uncertainty associated with imputed values.(Yuan, 2011) Quantile regression was used to estimate the effects of diesel PM and perchloroethylene exposure on multiple points, or quantiles, within the continuous distribution of test scores. As opposed to linear regression, which provides an effect estimate only at the mean of the distribution, quantile regression produces effect estimates at any quantile within the entire outcome distribution.(Koenker and Hallock, 2001) This allows for the exploration of the hypothesis that greater associations with exposure may occur at the tails of the distribution (i.e., among those with very low or very high z-scores).

Due to the large sample size, quantile regression models were fit using an interior point optimization algorithm.(Lustig et al., 1992) Confidence intervals were estimated using bootstrap methods.(Chen, 2005) Interaction was assessed by constructing models with exposure indicator variables for being at or above the 75^{th} centile for each pollutant and then including a product term of the two-indicator variables. Statistical significance of that interaction term was assessed using a Wald test-statistic with an *a priori* alpha level of 0.05. Modified Poisson regression models were constructed to calculate the effect of exposure on a child's risk of failing to meet the curricula standards, as defined by the category score described in section 2.2. This method was extended to include generalized estimation equations to account for the clustering by census tract within the data.(Yelland et al., 2011) All models were adjusted for potential confounders listed above using categorizations presented in Table 1.

2.7 Sensitivity Analysis

As part of study protocol, exposure was assigned using only residential census tract at birth. Because children may move within the city and experience different air pollutant levels during early childhood, a sensitivity analysis was performed which repeated all analyses with a study population restricted to children who had the same residential census tract at birth, at the time of lead screening and within Department of Education records. Because these children remained in the same census tract, they would not experience any exposure

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misclassification due to residential mobility after birth. All analyses were performed in SAS v9.2.

2. RESULTS

3.1 Description of Study Population and Exposure Distribution

Demographic characteristics of the study population are presented in Table 1 and reflect the diverse urban population of public-school children that reside in New York City. Children were more likely to be Black or Latino than White or Asian, and slightly more than half of the children were born to foreign-born mothers. Seventy percent of children met or exceeded the test-based standard for math, but only 55.5% met the standard for ELA. Of the full study population, 28% (N=57,025) resided in the same census tract from birth through 3rd grade. These children were more likely to be White or Asian and have mothers with greater educational attainment, and less likely to be eligible for the free school lunch program and to fail to meet the test-based curricula standards than children in the full study population.

Pre-imputation, 4.4% of children had a lead level at or greater than 10 μg/dL. This was similar in the subset of the population that lived in the same census tract through 3rd grade, although the latter group was much less likely to have missing blood lead values. After imputation, the proportion of children in the full study population with a blood lead level greater than 10 μg/dL ranged from 6.0-6.1% within the 5 imputations.

The median diesel PM concentration levels where the study population lived at birth was 7.7 μg/m^3, and the average perchloroethylene concentration was 0.68 μg/m^3. The pollutants were highly correlated with a Spearman correlation coefficient of 0.75. Distributions of pollutants were highly right-skewed. The median value of the high diesel PM category (i.e. exposure within the 4th quartile) was 19.9μg/m^3. However, the estimated ambient concentrations within that category ranged from greater than 9.7μg/m^3 to 140 μg/m^3. The low diesel PM category had a median diesel PM concentration of 6.9 μg/m^3 and a range of 3.9 through 9.7 μg/m^3. The median value of the high perchloroethylene category was 1.13 μg/m^3 and the concentrations ranged from 0.84 μg/m^3 through 9.2 μg/m^3. The low perchloroethylene category had a median estimated ambient concentration of 0.63 μg/m^3 and a range of 0.28 μg/m^3 through 0.84 μg/m^3. There was no difference in the median prenatal exposure levels to diesel PM and perchloroethylene in the full population compared to the children who resided in the same census tract for the entire study period. However, there were slight differences in the percentage of children within the defined exposure categories (Table 1).

3.2 Associations with Continuous Test Scores

Figures 1 through 4 show the adjusted beta coefficients and 95% CIs comparing each exposure category (i.e., exposure within the 4th quartile for both diesel PM and perchloroethylene, within the 4th quartile for diesel PM but not perchloroethylene and within the 4th quartile for perchloroethylene but not diesel PM) to the referent level of children with lower estimated prenatal exposure levels to both diesel PM and perchloroethylene. Coefficients were estimated at every 5th quantile within the math (Figures 1 and 2) and ELA

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test-score distributions (Figures 3 and 4). Figures 1 and 3 show results for the full study population, while figures 2 and 4 are limited to children who did not move out of their census tract after birth. The magnitudes of the beta coefficients represent the proportional change in a standard deviation of the test scores. Crude results were more variable than adjusted and generally showed effect estimates for single pollutants (high diesel or high perchloroethylene) further from the null than adjusted estimates, while estimates for children highly exposed to both pollutants were similar or closer to the null than adjusted estimates (See Supplementary Material, Figures S1-S2, Table S1). Including children with imputed blood lead levels in statistical models brought adjusted results slightly closer to the null than models which excluded children with missing lead data (See Supplementary Material, Table S2, Figures S3-S4).

As shown in Figure 1, children exposed to the highest levels of both diesel PM and perchloroethylene had math scores that were approximately 6% of a standard deviation lower than children with lower levels of exposure for both pollutants. The magnitude of the association is slightly greater at the upper tail of the distribution (i.e., children with higher test scores) and there is no considerable evidence of heterogeneity within the test-score distribution given the width of the confidence intervals (CI). Consistently, children exposed to high levels of both diesel PM and perchloroethylene had the largest decrements in test scores, followed by children exposed to high levels of perchloroethylene only and then children exposed to high levels of diesel PM only. There is no considerable evidence of departure from additivity, as interaction terms were not statistically significant and the individual estimates for exposure to diesel PM and perchloroethylene alone often sum to equal the estimates obtained for children exposed to high levels of both pollutants.

When restricting the analysis to children who did not move from their census tract after birth, those with greater exposure to both diesel PM and perchloroethylene had math scores that were 8-9% of a standard deviation lower than children with lower exposure levels of both pollutants (Figure 2). Similar to results from the full population, the magnitude of the estimates was relatively consistent across the quantiles, although there is evidence that the association is smaller for children in the lower 10% of the test-score distribution. Within this restricted population, estimates were similar for children with higher exposures for diesel PM only or perchloroethylene only. There is some evidence of heterogeneity across the test-score distribution for children with higher exposure to only perchloroethylene, as illustrated in Figure 2 by the estimates at the upper quantiles becoming more negative. Again, there was no evidence of statistically significant departures from additivity.

A different pattern was observed when examining ELA test scores. As seen in Figure 3, there is a small but consistent association between high exposure to only perchloroethylene and lower ELA scores. This estimate is larger in magnitude at the upper quantiles of the distribution, suggesting that perchloroethylene exposure has a larger impact among children with higher scores. Unlike what was observed for math scores, the sum of the coefficients from diesel PM and perchloroethylene is greater than the coefficient for children exposed to both pollutants. However, there was again no evidence of statistically significant interaction between the pollutants.

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We found little evidence of an association between prenatal pollutant exposure and ELA test scores within the subpopulation that did not move. Most effect estimates for the three exposure categories are close to null, except at the upper tail of the distribution, when estimates become negative. This is most apparent for the estimates comparing children with high exposures to only perchloroethylene to children with lower exposures for both pollutants. Similar to the results from the full population, at the 75^{th} quantile and above, children exposed to only high perchloroethylene have 5% lower ELA test scores than children exposed to low levels of both pollutants (Figure 4).

3.3. Association of exposure levels with failing to meet test-based standards

Within the full population, children with high exposures to both diesel PM and perchloroethylene had 1.1 times (95% CI 1.07, 1.12) the risk of failing to meet test-based standards for mathematics as children with lower levels of exposure to both pollutants. This estimate was greater than observed for children with greater exposure to diesel PM only (RR_{diesel} 1.03, 95%CI 0.99, 1.06) or children with greater exposure to perchloroethylene only (RR_{perc} 1.03, 1.00, 1.06). Results were similar within the subpopulation of children who remained in the same census tract after birth. Compared to children with lower levels of exposure for both pollutants, children with high levels of exposure had 1.13 times the risk of failing to meet math standards (95%CI 1.09, 1.18), while children with only high diesel PM exposure had 1.06 times the risk (95%CI 0.99, 1.13) and children with only high perchloroethylene exposure did not have elevated risk(RR 1.01 95%CI 0.95, 1.08).

No associations were observed between pollutant exposures and failing to meet ELA test-based standards, and there was little difference among the exposure categories. Compared to children with lower levels of exposure for both pollutants, children with high exposure to diesel PM and perchloroethylene had 1.03 (95%CI 1.01, 1.04) times the risk of failing to meet test-based standards. Children with only high diesel PM exposure had 1.03 (95%CI 1.00, 1.05) times the risk and children with only perchloroethylene exposure had 1.02 (95%CI 1.00, 1.04) times the risk. Results did not change within the subset of children who remained in the same census tract after birth ($RR_{diesel\ and\ perc}$: 1.02, 95%CI 0.99, 1.05; RR_{perc}: 1.02, 95%CI 0.98, 1.07; RR_{diesel} 1.03, 95%CI 0.98, 1.08).

3. DISCUSSION

This study provides preliminary evidence of inverse associations between prenatal exposure to two common urban air pollutants and academic outcomes. When examining math scores, model-based effect estimates for each of the pollutants were additive, and children with greater prenatal exposure to both diesel PM and perchloroethylene had the greatest decrements in test score and the greatest risk of failing to meet test-based curricula standards. When examining ELA scores, children exposed to higher levels of only perchloroethylene had the greatest decrements in test score, although these decrements were smaller in magnitude than effect estimates for math scores.

Children with greater prenatal exposure to both diesel PM and perchloroethylene had, on average, 6% of a standard deviation lower math scores than children with lower exposure to both pollutants. This effect size was 8-9% when the population was limited to children who

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did not move from the area where their prenatal pollutant exposure was assessed. The decrements in ELA scores among children exposed to perchloroethylene were approximately 5% in the upper quantiles of the distribution. Within the context of the educational intervention literature, effect sizes between 5% and 10% of a standard deviation are considered small, but not trivial.(Hill et al., 2008; Lipsey et al., 2012) In a review of educational interventions, Hill et al. determined that the average effect size of educational interventions when using broad standardized tests to assess academic achievement in elementary schools is 7%.(Hill et al., 2008) Our results suggest that exposure to these pollutants has a similar effect size, though in the opposite direction, of the average intervention aimed at improving elementary school children's educational outcomes.

Larger effect estimates were observed for math scores compared to ELA scores, and there were different patterns of effect estimates for math and ELA scores. It is unclear if there is a real difference in association between pollutants and test results in math and ELA or if there are differences in residual confounding. For example, although all of the children in this analysis were born in the United States and information on maternal nativity was included as a potential confounder, there was no information on language spoken in the home. In NYC, more than half of the children who are considered to have limited English proficiency were born in the United States but live in a home where English is not the primary language.(Stiefel et al., 2003) English proficiency has a greater impact on ELA test scores than math scores(Stiefel et al., 2003), and residual confounding related to household language could overwhelm the relatively smaller impacts of air pollutants on ELA scores.

Models were adjusted for a number of potential confounders. Imputation and adjustment for childhood blood lead levels caused results to be slightly closer to the null and prevented bias due to excluding segments of the population because of missing data. However, residual confounding related to other spatially-varying factors could contribute to our results. Adjusting for the neighborhood deprivation index (Messer et al., 2006) within the models controls for some of the sociodemographic factors that could confound the relationships between common urban air pollutants and children's test scores. Percent of linguistically isolated households was added to the index due to its potential association with test outcomes, but there are other factors, such as stress related to exposure to violence, which may not be wholly controlled for by using the neighborhood deprivation index. Additionally, we do not have any information on early-life home environment and parenting behaviors that are strongly associated with child development and potentially vary by neighborhood.(Ronfani et al., 2015)

There could also be other air pollutants or environmental exposures which co-vary with diesel PM and perchloroethylene that are driving our results. For example, higher levels of black carbon and polycyclic aromatic hydrocarbons, two other common measures of TRAP, have been associated with lower cognitive function in children.(Jedrychowski et al., 2015; Suglia et al., 2008) Additionally, noise exposure co-varies with air pollutant levels in New York City (Kheirbek et al., 2014), and animal research suggests that maternal exposure to noise stress during pregnancy can disturb cognition in offspring. (Barzegar et al., 2015) It is possible that unaccounted for pollutants could lead to our results, which would suggest that diesel PM and perchloroethylene are just proxies for these other pollutants. To fully

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elucidate the impact of ambient air pollution on children's neurodevelopmental and academic outcomes, research methods which account for the large number of correlated air pollutants within the complex mixture of ambient air are needed. For example, there are twenty-three air toxics (including diesel PM and perchloroethylene) suspected to have neurological effects estimated as part of the 1996 NATA.(Windham et al., 2006) These methods also need to produce exposure metrics with clear interpretability for the purposes of research translation, policy development and intervention, an identified limitation of many current methods.(Oakes et al., 2014) Our findings point to the possibility that multiple air toxics can additively impact children's academic outcomes and support the need for methods which can move beyond the investigation of two pollutants to understand the collective effects of the mixture.

In addition to the potential for residual confounding due to other pollutants within the mixture of ambient air, there are other limitations which could impact the study's results and their interpretability. Due to concerns regarding privacy, the Longitudinal Study of Early Development does not store school information that can be linked directly to children, and it was not possible to control for the spatial dependence among children within the same school. However, the majority of children in New York City public elementary schools attend their local neighborhood school. Within the modified Poisson models, it was possible to use census tract as a proxy for school and account for that spatial dependence.(Yelland et al., 2011)

There are a number of sources of potential exposure misclassification when using NATA data to assign estimates of prenatal exposure. The only variable used to assign prenatal exposure was the address on the birth record. Previous studies have estimated that 9-32% of mothers may move during pregnancy.(Bell and Belanger, 2012) Although the distances between addresses tend to be small, they may be associated with demographic factors which would lead to confounding of results.(Bell and Belanger, 2012) We also had no information about other locations where the mother may have spent time or how much time was spent outdoors versus indoors. The literature suggests that the difference between using ambient concentrations versus individual exposure estimates often leads to non-differential measurement error and underestimation of health risks associated with air pollutant exposures.(Kioumourtzoglou et al., 2014)

The exposure data represents a single estimate of the annual pollutant concentration in 1996 for a specific census-tract and serves as a proxy for the prenatal exposure of children in the study. Effect estimates were slightly further from the null in later birth years, but the general pattern remained consistent. The lack of temporal variability in the assigned exposure estimates also contributes to error in assigning exposure. Because using an annual estimate fails to account for seasonal fluctuations in pollutant concentrations, we examined the relationship between diesel PM and perchloroethylene exposure and test scores by season of birth. Effect estimates reflecting lower test scores among children exposed to higher levels of both pollutants were consistently observed across the different seasons of birth. However, for children exposed to higher levels of either diesel PM or perchloroethylene, effect estimates were slightly higher among children born in the Fall months (September-November).

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Our findings contribute to a growing literature which suggests an association between prenatal exposure to air pollutants and children's neurodevelopment and potential for academic achievement. Previous work from a longitudinal New York City birth cohort observed associations between biomarkers of prenatal exposure to polycyclic aromatic hydrocarbons and cognitive test scores at age 5 (Lovasi et al., 2014), verbal IQ scores among those with material hardship at age 7 (Vishnevetsky et al., 2015), and ADHD behaviors by age 9 (Perera et al., 2014). Analysis of other birth cohorts has produced similar results when examining air pollutants and children's neurodevelopment.(Chiu et al., 2013; Freire et al., 2010; Guxens et al., 2012; Harris et al., 2015; Jedrychowski et al., 2015; Kim et al., 2014)

There are a number of mechanisms by which prenatal exposure to air pollutants could affect neurodevelopment and academic outcomes later in life. Recent research suggests that possibility that prenatal exposure to air pollutants can directly impact brain development. (Peterson et al., 2015) Additionally, it is possible that the relationship between prenatal exposure to air pollutants and academic outcomes is mediated through adverse birth outcomes. For instance, air pollution exposure is hypothesized to be a causal contributor of decreased gestational age at birth (Stieb et al., 2012), which has been associated with lower academic test scores in previous research (Lipkind et al., 2012). This suggests that gestational age would be on the causal pathway between prenatal air pollutant exposure and academic outcomes in childhood. To examine this possibility, the study population was restricted to include only term-births, and similar associations between exposure to diesel PM and perchloroethylene and 3rd grade test scores were observed (data not shown). This suggests the observed relationship between air pollutant exposure and academic outcomes is not wholly attributable to adverse birth outcomes.

Despite limitations, this study has a number of strengths. This is a large, representative population-based analysis of children born in and attending public school in New York City. It contains a sizable spatial exposure gradient for the pollutants of interest, and the study population contains racial/ethnic and socioeconomic diversity at both the individual and neighborhood levels. Through linkage with the lead monitoring program, the results were adjusted for the effects of elevated blood lead, a well-established neurotoxicant. The use of quantile regression allowed for the exploration of the effect of pollutants on the entire distribution of test scores. This revealed the differences observed between the upper and lower quantiles of the ELA distribution, which would not have been seen using linear regression. Additionally, the results were robust to the sensitivity analysis, which limited the study population to children who lived in the same census tract from birth onward. This suggests the results of this study were not due to the exposure misclassification that results from failing to account for residential mobility later in childhood.

4. CONCLUSION

In summary, this study suggests that prenatal exposure to commonly co-occurring urban air pollutants is inversely associated with measures of academic outcomes later in childhood. These findings are consistent with previous research observing potentially neurotoxic effects of urban air pollution on children, while illustrating the effectiveness of leveraging existing data resources to address important questions related to urban public health. Limitations of

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our study design preclude definitive conclusions on whether the observed results are due to diesel PM and perchloroethylene, or other unaccounted for pollutants. In spite of these limitations, the results suggest at the potential for individual air pollutants within urban air pollutant mixtures to additively impact children's health.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

Funding Source

Dr. Stingone's work was supported by the Elizabeth Mascia Scholarship from the Mount Sinai Children's Environmental Health Center. Additional support was provided by a grant from the National Institute of Environmental Health Sciences (P30ES023515).

Abbreviations

ELA	English Language Arts
NATA	National Air Toxics Assessment
NYC DOHMH	New York City Department of Health and Mental Hygiene
PM	Particulate Matter
SES	Socioeconomic Status
TRAP	Traffic-Related Air Pollutant

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Highlights

- We assessed associations between diesel and perchloroethylene on children's test scores.
- Greater prenatal exposure to both pollutants was associated with lower math scores.
- Combined effects of individual pollutants may additively impact children's health.

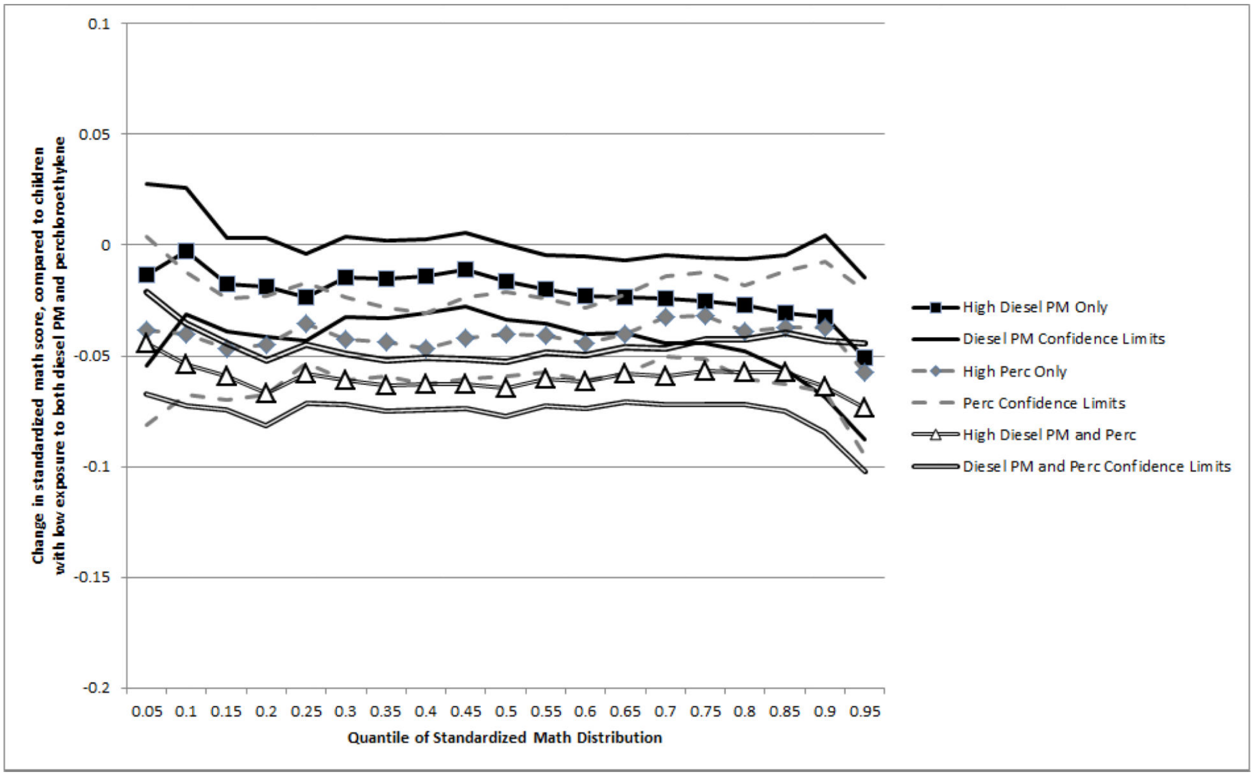

Figure 1.

Adjusted change in standardized math scores and 95% confidence intervals at each quantile within the test-score distribution for children with different combinations of prenatal diesel particulate matter and perchloroethylene exposure compared to children with lower exposures to both pollutants, New York City Longitudinal Study of Early Development, Birth Years 1994-1998 (N=201,124). Models adjusted for maternal factors (race, age, marital status, nativity, educational attainment, use of tobacco and/or alcohol during pregnancy, and primary payor for delivery), eligibility for the school lunch program, days absent from 3rd grade, blood lead level and neighborhood deprivation score.

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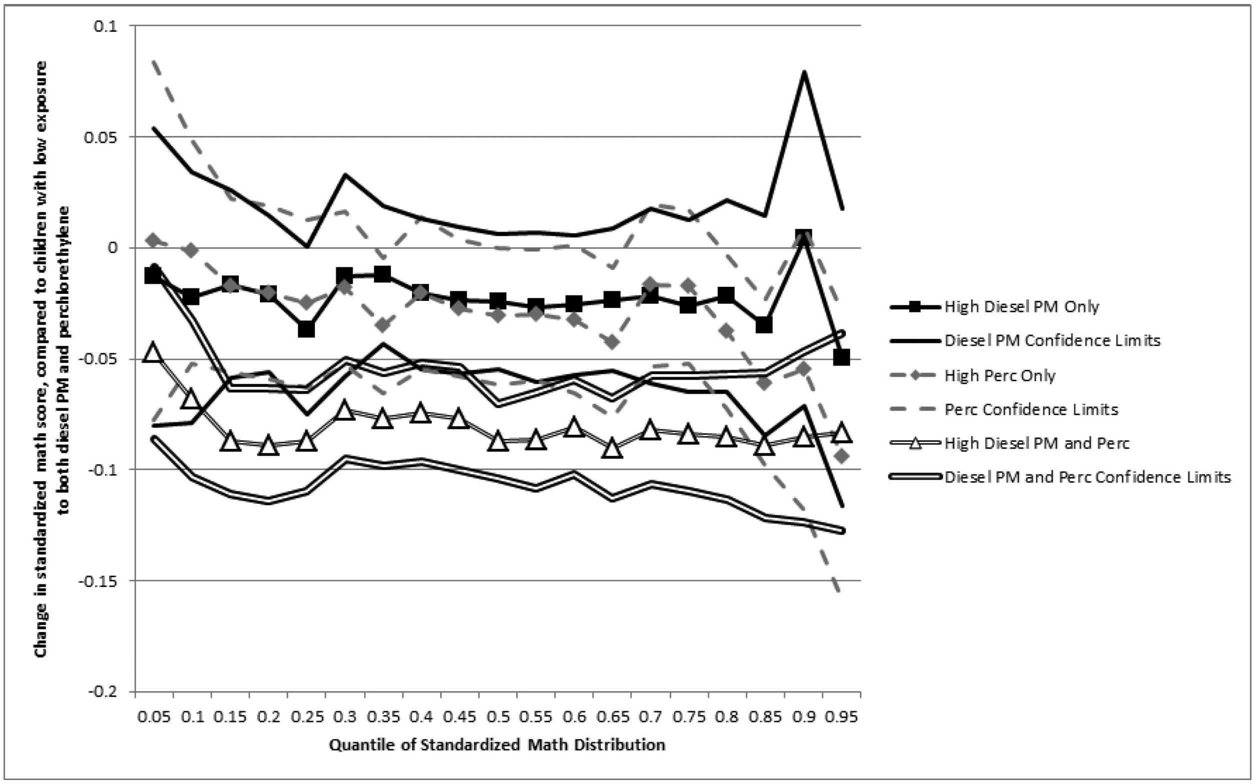

Figure 2.

Adjusted change in standardized math scores and 95% confidence intervals at each quantile within the test-score distribution for children with different combinations of prenatal diesel particulate matter and perchloroethylene exposure compared to children with lower exposures to both pollutants within the subpopulation of children who did not move from their census tract at birth, New York City Longitudinal Study of Early Development, Birth Years 1994-1998 (N=56,931). Models adjusted for maternal factors (race, age, marital status, nativity, educational attainment, use of tobacco and/or alcohol during pregnancy, and primary payor for delivery), eligibility for the school lunch program, days absent from 3rd grade, blood lead level and neighborhood deprivation score.

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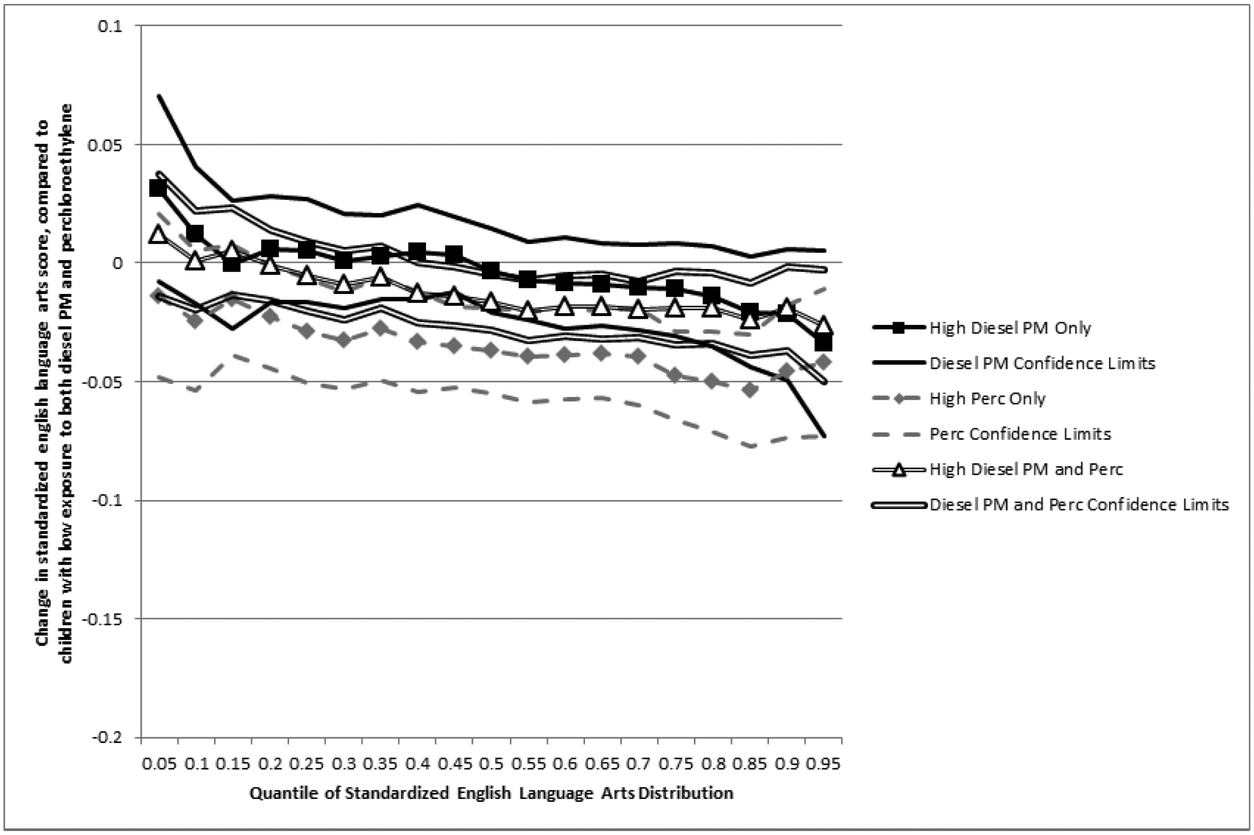

Figure 3.

Adjusted change in standardized English Language Arts (ELA) scores and 95% confidence intervals at each quantile within the test-score distribution for children with different combinations of prenatal diesel particulate matter and perchloroethylene exposure compared to children with lower exposures to both pollutants, New York City Longitudinal Study of Early Development, Birth Years 1994-1998 (N=189,718). Models adjusted for maternal factors (race, age, marital status, nativity, educational attainment, use of tobacco and/or alcohol during pregnancy, and primary payor for delivery), eligibility for the school lunch program, days absent from 3rd grade, blood lead level and neighborhood deprivation score.

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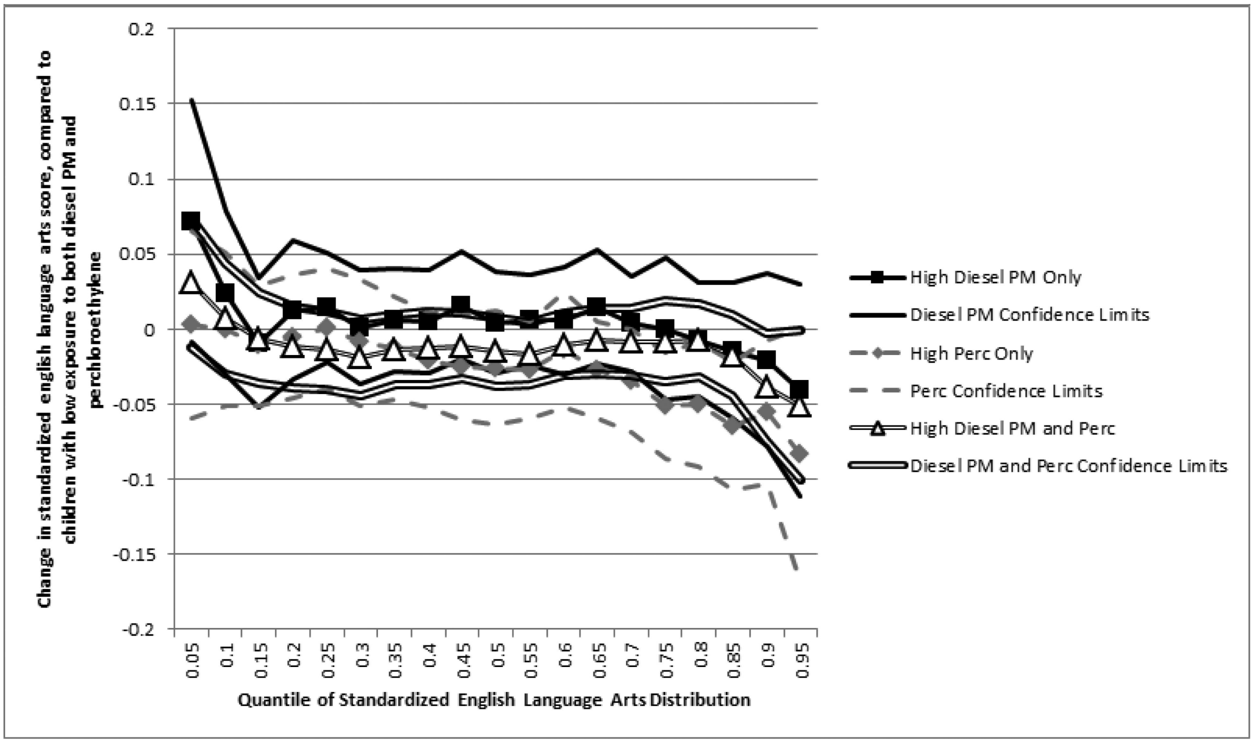

Figure 4.

Adjusted change in standardized English Language Arts (ELA) scores and 95% confidence intervals at each quantile within the test-score distribution for children with different combinations of prenatal diesel particulate matter and perchloroethylene exposure compared to children with lower exposures to both pollutants within the subpopulation of children who did not move from their census tract at birth, New York City Longitudinal Study of Early Development, Birth Years 1994-1998 (N=54,030). Models adjusted for maternal factors (race, age, marital status, nativity, educational attainment, use of tobacco and/or alcohol during pregnancy, and primary payor for delivery), eligibility for the school lunch program, days absent from 3rd grade, blood lead level and neighborhood deprivation score.

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Table 1

Demographic characteristics, test-score outcomes and exposure levels for the study population, New York City Longitudinal Study of Early Development Birth Years 1994-1998.

Demographic Characteristic	Full Study Population		Subset Living in same Census Tract after Birth	
	N	%	N	%
N	201,559		57,025	
Child's Sex				
Female	101,054	50.1	28,512	50.0
Male	100,505	49.9	28,513	50.0
Borough of Residence at Birth				
Manhattan	30,137	15.0	9,481	16.6
Bronx	41,540	20.6	11,372	19.9
Brooklyn	71,076	35.3	18,628	32.7
Queens	48,503	24.1	13,675	24.0
Staten Island	10,303	5.1	3,869	6.8
Maternal age at birth, mean (sd)	27.2 (6.4)		28.8 (6.4)	
Maternal Race/Ethnicity				
black, non-Hispanic	64,353	31.9	16,577	29.1
white, non-Hispanic	32,730	16.2	11,253	19.7
Hispanic	81,716	40.5	22,284	39.1
Asian/PI	21,757	10.8	6,614	11.6
Other	1,003	0.5	297	0.5
Maternal Nativity				
Mother Foreign Born	103,685	51.4	28,934	50.7
Maternal Marital Status Married	83,693	41.5	28,429	49.9
Maternal Education				
0-8 years	20,233	10.0	5,435	9.5
9-11 years	49,630	24.6	11,717	20.5
12 years, High School Graduate	77,735	38.6	22,011	38.6
13-15 years, Some College	32,900	16.3	10,185	17.9
16 years+, Completed college or beyond	21,061	10.4	7,677	13.5
Primary Payor of Delivery				
Medicaid	131,295	65.1	33,219	58.3
HMO	18,728	9.3	6,500	11.4
Other 3rd Party	41,768	20.7	15,023	26.3
Self	9,768	4.8	2,283	4.0
Reported Tobacco Use during Pregnancy	11,154	5.5	2,522	4.4
Reported Alcohol Use during Pregnancy	1,107	0.5	208	0.4
Child's Lead Level (pre-imputation)				
Missing	44,317	22.0	4,172	7.3
<5mcg/dL	96,134	47.7	34,119	59.8
5mcg/dL-<10mcg/dL	52,299	25.9	16,276	28.5

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Demographic Characteristic	Full Study Population		Subset Living in same Census Tract after Birth	
	N	%	N	%
10mcg/dL or greater	8,809	4.4	2,458	4.3
Days absent in 3rd grade mean (sd)	10.1 (10.5)		8.6 (9.3)	
Eligible for school lunch	172,155	85.4	46,547	81.6
Met Math Standard on 3rd grade standardized test	142,230	70.7	42,614	74.9
Met ELA Standard on 3rd grade standardized test	105,224	55.5	31,941	59.1
Median Diesel Particulate Matter Exposure, μg/m median (sd)	7.7 (8.6)		7.7 (9.6)	
Median Perchloroethylene Exposure, μg/m^3 median(sd)	0.68 (0.38)		0.68 (0.39)	
Exposure Categories*				
Low Diesel PM, Low Perc	136,830	67.9	38,034	66.7
High Diesel PM, Low Perc	14,445	7.2	3,824	6.7
Low Diesel PM, High Perc	14,466	7.2	4,239	7.4
High Diesel PM, High Perc	35,818	17.8	10,928	19.2

*Diesel PM exposure dichotomized low/high at 9.7 μg/m^3; Perchloroethylene (Perc) exposure dichotomized low/high at 0.84 μg/m^3