HHS Public Access

Author manuscript

Int J Hyg Environ Health. Author manuscript; available in PMC 2022 March 01.

Published in final edited form as:

Int J Hyg Environ Health. 2021 March ; 232: 113686. doi:10.1016/j.ijheh.2020.113686.

Proximity to traffic and exposure to polycyclic aromatic hydrocarbons in relation to Attention Deficit Hyperactivity Disorder and Conduct Disorder in U.S. children

Stephani S. Kim[1,2], **Ann M. Vuong**[1,3], **Kim N. Dietrich**[1], **Aimin Chen**[1,4]

[1]Division of Epidemiology, Department of Environmental Health, University of Cincinnati College of Medicine, Cincinnati, OH

[2]Currently at Department of Anesthesiology & Pain Medicine, Nationwide Children's Hospital, Columbus, OH

[3]Currently at Department of Environmental and Occupational Health, School of Public Health, University of Nevada Las Vegas, Las Vegas, NV

[4]Currently at Department of Biostatistics, Epidemiology and Informatics, Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA

Abstract

Background: Traffic related air pollution (TRAP) and its component polycyclic aromatic hydrocarbons (PAHs) may be neurotoxic in children. There is limited research on postnatal exposure to TRAP and PAHs and child neurodevelopment.

Methods: We linked data from the U.S. NHANES 2001–2004 with the National Highway Planning Network 2005 to examine the proximity to major roads (highway or urban/rural principal arterials), urinary PAH metabolites, and diagnosis of Attention Deficit Hyperactivity Disorder (ADHD) and Conduct Disorder (CD) based on Diagnostic Interview Schedule for Children (C-DISC) in 1253 children aged 8 – 15 years. We calculated odds ratios (ORs) and 95% Confidence Intervals (CIs) for ADHD and CD by traffic proximity and PAH exposures using logistic regression adjusted for confounders.

Results: Higher ADHD prevalence was observed among children living <500 m (9.86%) compared to those ≥500 m (3.84%) from a major road. Prevalence of children with CD was

Corresponding Author: Aimin Chen, MD, PhD, Department of Biostatistics, Epidemiology and Informatics (DBEI), Perelman School of Medicine, University of Pennsylvania, 423 Guardian Dr, Blockley Hall 231, Philadelphia, PA 19104-6021, Tel: 215-746-4272, aimin.chen@pennmedicine.upenn.edu.

Conflicts of Interest: Authors declare no conflicts of interest.

Access to data: The Centers for Disease Control and Prevention (CDC) provided restricted data and merged with the public use dataset for our data analysis in the Research Data Center, National Center for Health Statistics (NCHS). The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the CDC. Use of trade names is for identification only and does not imply endorsement by the CDC, the Public Health Service, or the US Department of Health and Human Services.

comparable (<500 m: 2.51% and ≥500 m: 2.43%). We found little difference in urinary PAH metabolite levels between children living near major roads and those who did not. Children living <500 m from a major road had a non-significant OR of 2.06 (95% CI 0.85–5.03) for ADHD diagnosis. Children living on ≥2 major roads within 500 m of a highway had a non-significant OR of 2.27 (95% CI 0.71–7.26) for ADHD diagnosis. There was no association between proximity to major roads and CD diagnosis.

Conclusion: We found living close to a major road was not associated with increased PAH levels. We did not find statistically significant relation between proximity to a major road or urinary PAH metabolite levels and ADHD or CD diagnosis in this cross-sectional analysis. Prospective studies are needed for the investigation of postnatal TRAP exposure and ADHD and CD diagnosis.

Keywords

traffic related air pollution; polycyclic aromatic hydrocarbons; attention deficit hyperactivity disorder; conduct disorder

Introduction

Polycyclic aromatic hydrocarbons (PAHs) are environmental pollutants mainly from air pollution and dietary intake. Burning fossil fuels, woods, and other wastes produces PAHs. In the U.S., coal-fired power plants and traffic are major contributors of PAH emission in the air. Forest fire, fireplace, grilling food, and exposure to tobacco products also increase exposure to PAHs. It has been shown that PAHs, such as Benzo[a]pyrene (BaP), are carcinogenic and can cause skin, lung, and bladder cancers.[1] Recently, non-carcinogenic effects of PAHs, especially reproductive and developmental toxicity, received more attention as studies in the U.S., Poland, and China suggested potential associations between prenatal PAH exposure and fetal growth restriction, childhood asthma, developmental delays, cognitive deficits, anxiety/depression, attention problems, and DNA methylation alterations.[2–7] It has not been well-studied whether postnatal exposure to PAHs is related to adverse neurobehavioral outcomes in children who are exposed to levels lower than what has been seen in Poland or China. Exploration of the relation between postnatal PAH exposure and its source through traffic-related air pollution (TRAP) is still important as children have direct exposure to PAHs postnatally over a long time of brain maturation. While PAHs can come from ambient air, indoor air, and food sources[8,9], TRAP may affect children's PAH exposure based on the distance to major roads. TRAP exposure increases $PM_{2.5}$ and NOx exposure, but it is not clear whether children living close to highways also have higher biomarkers of PAH metabolites, such as 1-OH pyrene, compared with children living farther away from highways. In urban areas, traffic exposure is hypothesized to be a major contributor to PAH exposure, but research is still lacking whether postnatal traffic exposure is related to air pollutant biomarkers and subsequently, neurobehavioral outcomes.

Although prenatal brain development is critical, brain development after birth continues and is intertwined with behavioral processes, such as life experiences, interpersonal relationships, and the home and educational environment, that may be influenced by housing choice (proximity to highways and exposure to traffic pollutants), the community (air

pollution levels), and dietary preparations (charred or grilled food, wood burning for fireplace, etc.)[10]. Because the brain continues to undergo neuronal synapse formation and trimming, myelination, and neurotransmitter regulation after birth, adverse impacts of these processes by neurotoxicant exposure is possible[10]. PAHs are lipophilic and thus can cross the blood brain barrier and may affect brain development[11,12]. Therefore, it is still relevant to understand whether postnatal exposure to PAHs and proximity to a major road pose a threat to neurobehavioral processes in the U.S. general population.

Attention deficit hyperactivity disorder (ADHD) occurs in 7–9% of children aged 4–15 years in the United States.[13] Although, heritability may account for up to a high percentage of cases, epidemiological studies have shown associations with environmental factors, such as lead and environmental tobacco smoke.[14,15] Conduct disorder (CD) is a clinical diagnosis characterized by a repetitive and persistent behavioral pattern of violating the rights of others and social rules. Clinical diagnosis of ADHD and CD has not been studied in a U.S. national sample in relation to postnatal exposure to PAHs and proximity to traffic. Utilizing publicly available and restricted access data, we aimed to determine whether proximity to traffic and urinary PAH metabolite levels are associated with increased odds of ADHD and CD clinical diagnoses using a representative sample of U.S. children.

Methods

The National Health and Nutrition Examination Survey (NHANES) is a stratified multistage probability sample of U.S., consisting of civilian, non-institutionalized individuals. Traffic indicators from the 2005 National Highway Planning Network (NHPN) were linked to 2001–2004 NHANES using residential addresses to assign a distance to the nearest road, identify the number of roads within concentric buffers of a specific radii (100m, 300m, 500m), and obtain an average annual daily traffic measure by the National Center for Health Statistics (NCHS).[16] Of 1,253 children in the NHANES 2001–2004 with an age between 8–15 years and urinary PAH metabolites available, 1,167 (93.1%) had traffic exposure information. We dichotomized the distance to a major road (rural principal arterials, urban principal arterials, and all National Highway System routes) as ≥500 m or <500m, with the latter further categorized into 300–499 m, 100–299 m, and <100 m.[16] Additionally, we categorized the traffic indicator as “No major road within 500 m” (essentially the same as distance to a major road ≥500 m), “1 road within 500 m,” and “≥2 roads within 500 m.” We also used numerical distance in meters in regression models with neurobehavioral outcomes. Because only 43% of children living within a 500 m distance from a major road had average annual daily traffic data available (mostly from urban areas), no further analyses were performed on traffic density data.

The mono-hydroxylated PAHs (OH-PAHs) were measured in urinary samples by the Organic Analytical Toxicology Branch, Division of Laboratory Sciences in the National Center for Environmental Health of the Centers for Disease Control and Prevention using automated liquid-liquid extraction and isotope dilution gas chromatography/high resolution mass spectrometry.[17] The OH-PAHs measured included the metabolites: naphthalene (1-hydroxynaphthalene, 2-hydroxynaphthalene), fluorene (2-hydroxyfluorene, 3-hydroxyfluorene), phenanthrene (1-hydroxyphenanthrene, 2-hydroxyphenanthrene, 3-

hydroxyphenanthrene), and pyrene (1-hydroxypyrene, 1-OHP). The naphthalene, fluorene, and phenanthrene metabolite concentrations were summed as low molecular weight PAH metabolites (sum LMW PAH metabolites) in this analysis while 1-OHP was considered separately as a metabolite from higher molecular weight PAHs.[18] Urinary OH-PAHs were corrected for urinary creatinine concentration to account for urinary dilution, and expressed as ng/g creatinine in the analysis.

The National Institute of Mental Health (NIMH) Computerized-Diagnostic Interview Schedule for Children-Version 4 (C-DISC IV) was used to assess psychiatric diagnosis of children and adolescents of seven disorders in the NHANES study sample; however, for the purposes of the present study only ADHD and CD were analyzed in the study sample.[14,19] The highly structured diagnostic interview questions utilize diagnostic criteria specified in the Diagnostic and Statistical Manual of Mental Disorders-Fourth Edition (DSM-IV) and World Health Organization International Classification of Diseases-Version 10 (ICD-10). Only parent-informant interview (DISC-P) was used to obtain diagnosis of ADHD and CD in the NHANES 2001–2004. Of 1,253 children in the study sample with OH-PAH data, 1,031 (82.3%) children had data for ADHD diagnosis and 1,032 (82.4%) children had data for CD diagnosis.

Data on OH-PAHs and covariates were publicly available through the NHANES website; the NHPN and C-DISC data were restricted and access to the linked data was only granted through the NCHS Research Data Center. We compared the traffic indicators and the diagnosis of ADHD or CD by sociodemographic variables using Rao-Scott chi-square tests. We first compared the OH-PAH concentrations by distance to a major road using a linear regression model. We used natural log transformation of OH-PAH concentrations (sum LMW PAH metabolites and 1-OHP), because the data was skewed. We then examined the relation between distance to a major road and the diagnosis of ADHD or CD in separate logistic regression models, using either continuous natural log transformed distance or dichotomous or categorical distances. We adjusted for years of survey, age group, sex, race, maternal age at birth, household reference person education level, poverty income ratio (PIR), maternal smoking during pregnancy, current serum cotinine, current blood lead levels, and U.S. born status to account for potential confounders. Subsequently, we assessed the relation between urinary OH-PAH concentrations with ADHD or CD diagnosis using either continuous natural log transformed OH-PAHs or quartiles of OH-PAHs (LMW PAH metabolites and 1-OHP) in logistic regression models. Complex survey sampling was accounted for in all above-mentioned statistical analyses using SAS survey modules (SURVEYFREQ, SURVEYMEANS, SURVEYREG, SURVEYLOGISTICS) as well as sampling strata and weight. All tests were two-sided, with statistical significance at $p<0.05$. Adjusted odds ratios (ORs) and 95% confidence intervals (CIs) are reported for the diagnosis of ADHD or CD.

Results

The distribution of distance to a major road and ADHD and CD diagnoses by sociodemographic factors, blood lead levels, and serum cotinine levels are shown in Table 1. Among children with available traffic data, the percentages living within a certain distance

from a major road are as follows: 51.1% (>500 m), 15.9% (300–499 m), 23.1% (100–299 m), and 9.9% (<100 m). Additionally, 30.5% of children lived with 1 major road within 500 m, and 18.4% of children lived with 2 or more major roads within 500 m (data not shown in Table 1). Children living in a household with a PIR<1 were more likely to live within 100 m of a major road and have a high ADHD diagnosis percentage ($p<0.01$). In children with C-DISC IV data, 6.5% had a diagnosis of ADHD and 2.9% had a diagnosis of CD. Ascertained ADHD prevalence was significantly higher in boys, children whose mothers smoked during pregnancy, children with higher concurrent blood lead levels, and children born in the U.S. Ascertained CD prevalence was higher in children aged 12–15 years, had higher serum cotinine levels, and those born to mothers who smoked during pregnancy.

Sum LMW PAH metabolite concentrations did not differ by distance to a major road (4,521 ng/g creatinine in ≥500 m group vs. 4,317 ng/g creatinine in <500 m group), neither did concentrations of 1-OHP (72 vs. 67 ng/g creatinine, respectively) (Table 2). Finer subgrouping in the <500 m group (<100 m, 100–299 m, 300–349 m) or by number of roads within 500 m yielded non-significant differences in PAH metabolite levels in the covariate-adjusted regression models. There were no significant differences in specific LMW PAH metabolites by distance to a major road (Supplemental Material Table S1).

After adjusting for potential confounders, ln-distance to a major road was not statistically associated with ADHD diagnosis (adj OR=0.94, 95% CI: 0.72–1.23) (Table 3). Children who lived <500 m had a prevalence of ADHD diagnosis of 9.86%, compared with children who lived ≥500 m from a major road (ADHD prevalence 3.84%), the covariates adjusted OR was 2.06 (95% CI: 0.85–5.03) and not statistically significant. Similarly, children who lived <100 m, 100–299 m, and 300–499 m from a major road all had non-significantly higher odds of having an ADHD diagnosis compared with children who lived ≥500 m from a major road after adjustment for covariates. Children who lived with 1 or ≥2 major road within 500 m also had non-significantly higher odds of being diagnosed with ADHD (adj OR=1.97, 95% CI: 0.83–4.65 and adj OR=2.27, 95% CI 0.71–7.26, respectively). There was no association between urinary PAH metabolites (sum LMW PAH metabolites and 1-OHP) and ADHD diagnosis

The relation between distance to a major road and CD diagnosis was not remarkable, with a null association (Table 3). Sum LMW PAH metabolites did not show a consistent association with CD diagnosis for continuous exposure or quartile analysis. The relation between urinary 1-OHP concentrations and CD diagnosis did not reach statistical significance. We did not observe associations between individual LMW PAH metabolites (naphthalene, fluorene, and phenanthrene) and ADHD and CD diagnoses (Supplemental Material Table S2).

Discussion

In this analysis of a sample of children aged 8 –15 years in the NHANES 2001–2004, we observed that living within 500 m to a major road was not associated with increased PAH levels and not associated with a statistically significant higher odds of ADHD diagnoses in children. There was no association between distance to a major road and the diagnosis of

CD. The findings were adjusted for potential confounders from socioeconomic status to concurrent blood lead and serum cotinine levels.

We did not observe consistent associations between PAH exposure and C-DISC based behavioral disorders, ADHD and CD, in this study. A prior study examined urinary PAH metabolites and parent-reported ADHD, learning disability, and special education among children aged 6–15 years in the NHANES 2001–2004 and did not find positive associations with ADHD and learning disability, but identified a positive association with special education for fluorene metabolites.[20] Our study population partially overlapped with this sample, but we only examined C-DISC outcomes that were not available in the public data file. It is possible that one-time PAH metabolite measurements do not capture the exposure profile over time as the half-lives of urinary PAH metabolites are usually <48 hours.[21,22] This is an inherent limitation for cross-sectional analyses of urinary PAH metabolites and health outcomes using NHANES data. A prospective study of African American and Dominican children in New York City identified inverse associations between urinary PAH metabolites at age 5 years and white matter surface measures in the prefrontal region acquired at ages 7–9 years; although, no association with cerebral surface or cortical thickness or ADHD scale scores was found.[23,24] We did not find differences in PAH metabolites by the distance to a major road, suggesting that other exposure routes (e.g., diet) of PAHs may contribute to the concentrations of urinary PAH metabolites. A previous study among a non-occupational study sample conducted by the CDC found that naphthalene exposure was mostly from indoor air inhalation, while other PAHs' route of exposure may likely come from ingestion, particularly pyrene and other higher molecular PAHs.[25] Nevertheless, a Spanish study (Brain Development and Air Pollution Ultrafine Particles in School Children [BREATHE] project) found an inverse association between total air PAHs and BaP measured 1 year before neuroimaging and caudate nucleus volume, but no associations with ADHD scale scores in children at ages 8–12 years.[12] These studies with postnatal urinary PAH metabolite or air PAH measures did not reveal association with parent-reported ADHD diagnosis or ADHD scale scores, however, adverse associations with special education or brain structure and organization were identified. We did not observe associations between urinary PAH metabolite and ADHD diagnosis, maybe due to a) more stringent C-DISC ADHD diagnosis; b) cross-sectional analysis; c) one-time PAH exposure assessment in urine but not repeated measures; d) lack of additional PAH biomarkers (e.g., DNA or albumin adducts) or personal air measures of PAH; and e) PAHs not capturing traffic related air pollution mixture exposure.

We did not identify statistically significant relation between living within 500 m to a major road and C-DISC based ADHD diagnosis. Previously, Saez and colleagues found that children living within 300 m from a motorway or dual carriage way, compared with children living farther away, had an OR of 2.03 (95% CI: 0.94–4.08) for ADHD diagnosis, an estimate close to our research finding.[26] Several studies examining postnatal TRAP (PM_{10}, $PM_{2.5}$, black carbon, elemental carbon) have found positive associations with ADHD diagnosis in India[27] and South Korea,[28] or hyperactivity/inattention scores in Germany[29] and the United States.[30,31] In the Indian study, compared with PM_{10} <120 μg/m^3, PM_{10} 120–139, 140–200, >200 μg/m^3 had an OR of 1.82 (95% CI: 1.07–3.63), 2.20 (95% CI: 1.16–5.03), 2.77 (95% CI: 1.38–5.56), respectively, for DSM-IV based ADHD diagnosis in

children at ages 9–17 years.[27] In the South Korean study, each 1 μg/m^3 increase of PM_{10} was associated with a hazard ratio of 1.18 (95% CI: 1.15–1.21) for ADHD diagnosis up to age 10 years.[28] The German study has shown that each 1 μg/m^3 increase of $PM_{2.5}$ at age 10 or 15 years address was associated with an OR of 1.12 (95% CI: 1.01–1.23) or 1.11 (95% CI: 1.01–1.22) for abnormal/borderline scores in hyperactivity/inattention at age 15 years.[29] In one U.S. study, black carbon during children's lifetime was associated with higher commission errors and slower hit-response time in the Conners' Continuous Performance Test at age 7–14 years, indicating impaired attention.[30] Another U.S. study identified elemental carbon attributable to traffic exposure in the highest tertile was associated with an OR of 1.7 (95% CI: 1.0, 2.7) for hyperactivity score in the "at risk" range.[31] A study in Swedish twins, however, did not identify an association between postnatal PM_{10} exposure at age 1 or 9 years and ADHD diagnosis up to age 12 years.[32] It is also possible that noise is associated with ADHD symptoms while elemental carbon is not, as indicated in the above-mentioned Spanish BREATHE project using exposure assessment at the same time of the outcome assessment.[33] A study in Belgium suggested an association between urinary benzene metabolite trans, trans-muconic acid (t,t-MA), an indicator of traffic exposure, and decreased sustained attention and short-term memory, as well as increased hit-reaction time.[34] Direct comparison of these studies is difficult as they measured different exposure variables, used different ADHD ascertainment or measurement of inattention and hyperactivity, and examined children in different age range. Still, there is increasing evidence suggesting traffic-related exposure is related to ADHD behaviors in children. However, we did not find statistically significant association between proximity to a major road and ADHD diagnosis in this cross-sectional analysis. Socioeconomic and behavioral factors might have explained away the difference in ADHD prevalence by proximity to a major road. With the lack of TRAP exposure or particulate matter measures before the diagnosis, as well as postnatal residential history, our assessment of TRAP was not as precise and temporally relevant to the diagnosis. Despite the availability of the national data, the number of cases with ADHD diagnosis was still small in the analysis for exposure groups. Our biomarker of urinary PAH metabolite levels was only for short-term exposure. Future studies are needed to examine the proximity to major roads and traffic density, with air pollutant measurement and additional biomarkers of traffic-related exposure, in relation to ADHD diagnosis using a prospective study design, as this research question was not fully addressed by existing studies.[35] It is plausible that traffic-related exposure encompasses particulate matter, gaseous pollutants, noise, and may be confounded by housing characteristics associated with living close to major roads; therefore, a comprehensive exposure assessment strategy may be needed, which would include repeated measures during different windows of child development.

This study has several limitations. The cross-sectional nature of the NHANES makes it difficult to examine temporal associations between exposure and the outcomes. It is likely that children's addresses may have changed before the interview and the urinary PAH metabolites vary over time, thus exposure misclassification is a concern. According to the Census Bureau, about 14% of the U.S. population moved each year in the 2000s.[36] As the linkage between 1999–2008 NHANES and 2005 NHPN was based on addresses at the time of survey, the categorization of proximity to a major road is accurate for the majority of the

study sample except, infrequently, when the road patterns change. However, address(es) a child lived before the interview was not available in the survey. In addition, we did not have traffic density data for all study participants. As mentioned earlier, the onetime measurement of urinary PAH metabolites may not capture the true exposure profile since the typical half-life is <48 hours. This study did not examine biomarker exposure beyond urinary PAH metabolites, and we did not have atmospheric measurements of $PM_{2.5}$, NOx, or other air pollutants. Hence, this study is more exploratory, using existing data to provide preliminary results rather than a confirmatory study with a more thorough exposure assessment.

Despite these limitations, this study had several strengths. We analyzed a population-based representative sample, a major strength compared with other study samples.[26,27,31] We obtained restricted data from CDC, including traffic information and C-DISC based diagnosis of ADHD or CD. Conduct disorder has rarely been studied in environmental epidemiology due to its low prevalence and smaller sample size. We adjusted for multiple potential confounders in the regression, including maternal smoking during pregnancy, current serum cotinine levels for environmental tobacco smoke, and current blood lead level.

In conclusion, in the NHANES 2001–2004 sample of children aged 8–15 years, we did not identify a statistically significant relationship between proximity to a major road (<500 m) and increased risk of ADHD diagnosis. Proximity to a major road was not associated with CD diagnosis. We did not observe associations between urinary PAH metabolite concentrations and ADHD or CD diagnosis, nor did we find associations between proximity to a major road and PAH metabolite concentrations in urine. Using representative NHANES data, the study provides important indications that ADHD and conduct disorder may be more likely associated with prenatal exposure with TRAP, socio-economic indicators and other sources and periods of PAH exposure than from current air pollution. Future research utilizing a more comprehensive exposure assessment that takes into account proximity to a major road, multiple windows of susceptibility, and residential mobility utilizing a prospective study design with better exposure assessment of air pollutants and biomarkers is recommended to examine associations between TRAP as well as PAHs and neurodevelopment in children.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

Sources of financial support: This work was partially supported by grants from the National Institute of Environmental Health Sciences (NIEHS RC4ES019755, R01 ES020349, R01ES028277, P30ES006096).

References

1. ATSDR. Toxicological Profile for Polycyclic Aromatic Hydrocarbons. In: ATSDR, ed. Atlanta, Georgia, 1995.
2. Edwards SC, Jedrychowski W, Butscher M, Camann D, Kieltyka A, Mroz E, Flak E, Li Z, Wang S, Rauh V, Perera F. Prenatal Exposure to Airborne Polycyclic Aromatic Hydrocarbons and Children's

Intelligence at Age 5 in a Prospective Cohort Study in Poland. Environ Health Perspect 2010;118(9):1326–31. [PubMed: 20406721]

3. Herbstman JB, Tang D, Zhu D, Qu L, Sjodin A, Li Z, Camann D, Perera FP. Prenatal exposure to polycyclic aromatic hydrocarbons, benzo[a]pyrene-DNA adducts, and genomic DNA methylation in cord blood. Environ Health Perspect 2012;120(5):733–8. [PubMed: 22256332]
4. Perera F, Li TY, Lin C, Tang D. Effects of prenatal polycyclic aromatic hydrocarbon exposure and environmental tobacco smoke on child IQ in a Chinese cohort. Environ Res 2012;114:40–6. [PubMed: 22386727]
5. Perera F, Li Z, Whyatt R, Hoepner L, Wang S, Camann D, Rauh V. Prenatal airborne polycyclic aromatic hydrocarbon exposure and child IQ at age 5 years. Pediatrics 2009;124(2):e195–202. [PubMed: 19620194]
6. Perera F, Tang WY, Herbstman J, Tang D, Levin L, Miller R, Ho SM. Relation of DNA methylation of 5'-CpG island of ACSL3 to transplacental exposure to airborne polycyclic aromatic hydrocarbons and childhood asthma. PLoS One 2009;4(2):e4488. [PubMed: 19221603]
7. Perera FP, Tang D, Wang S, Vishnevetsky J, Zhang B, Diaz D, Camann D, Rauh V. Prenatal polycyclic aromatic hydrocarbon (PAH) exposure and child behavior at age 6–7 years. Environmental Health Perspectives 2012;120(6):921–6. [PubMed: 22440811]
8. ATSDR. Toxicological profile for polycyclic aromatic hydrocarbons (PAHs). Atlanta, GA: U.S. Department of Health and Human Services 1995.
9. Zedeck MS. Polycyclic aromatic hydrocarbons: a review. J Environ Pathol Toxicol 1980;3(5–6):537–67. [PubMed: 7441099]
10. American Academy of Pediatrics Council on Environmental Health. Pediatric Environmental Health. 3rd ed Elk Grove Village, IL: American Academy of Pediatrics 2012.
11. Yan T, Chengzhi C, Haiyan Y, Baijie T. Distribution of benzo[a]pyrene in discrete regions of rat brain tissue using light microscopic autoradiography and gamma counting. Toxicol Environ Chem 2010;92:1309–1317.
12. Mortamais M, Pujol J, van Drooge BL, Macia D, Martinez-Vilavella G, Reynes C, Sabatier R, Rivas I, Grimalt J, Forns J, Alvarez-Pedrerol M, Querol X, Sunyer J. Effect of exposure to polycyclic aromatic hydrocarbons on basal ganglia and attention-deficit hyperactivity disorder symptoms in primary school children. Environ Int 2017;105:12–19. [PubMed: 28482185]
13. Danielson ML, Bitsko RH, Ghandour RM, Holbrook JR, Kogan MD, Blumberg SJ. Prevalence of Parent-Reported ADHD Diagnosis and Associated Treatment Among U.S. Children and Adolescents, 2016. J Clin Child Adolesc Psychol 2018;47(2):199–212. [PubMed: 29363986]
14. Braun JM, Froehlich TE, Daniels JL, Dietrich KN, Hornung R, Auinger P, Lanphear BP. Association of environmental toxicants and conduct disorder in U.S. children: NHANES 2001–2004. Environ Health Perspect 2008;116(7):956–62. [PubMed: 18629321]
15. Froehlich TE, Lanphear BP, Auinger P, Hornung R, Epstein JN, Braun J, Kahn RS. Association of tobacco and lead exposures with attention-deficit/hyperactivity disorder. Pediatrics 2009;124(6):e1054–63. [PubMed: 19933729]
16. Parker JD, Kravets N, Nachman K, Sapkota A. Linkage of the 1999–2008 National Health and Nutrition Examination Surveys to traffic indicators from the National Highway Planning Network. Natl Health Stat Report 2012(45):1–16.
17. Li Z, Romanoff LC, Trinidad DA, Hussain N, Jones RS, Porter EN, Patterson DG Jr., Sjodin A. Measurement of urinary monohydroxy polycyclic aromatic hydrocarbons using automated liquid-liquid extraction and gas chromatography/isotope dilution high-resolution mass spectrometry. Anal Chem 2006;78(16):5744–51. [PubMed: 16906719]
18. Alshaarawy O, Zhu M, Ducatman A, Conway B, Andrew ME. Polycyclic aromatic hydrocarbon biomarkers and serum markers of inflammation. A positive association that is more evident in men. Environ Res 2013;126:98–104. [PubMed: 23972896]
19. Merikangas KR, He JP, Brody D, Fisher PW, Bourdon K, Koretz DS. Prevalence and treatment of mental disorders among US children in the 2001–2004 NHANES. Pediatrics 2010;125(1):75–81. [PubMed: 20008426]

20. Abid Z, Roy A, Herbstman JB, Ettinger AS. Urinary polycyclic aromatic hydrocarbon metabolites and attention/deficit hyperactivity disorder, learning disability, and special education in U.S. children aged 6 to 15. J Environ Public Health 2014;2014:628508. [PubMed: 24624143]
21. Motorykin O, Santiago-Delgado L, Rohlman D, Schrlau JE, Harper B, Harris S, Harding A, Kile ML, Massey Simonich SL. Metabolism and excretion rates of parent and hydroxy-PAHs in urine collected after consumption of traditionally smoked salmon for Native American volunteers. Sci Total Environ 2015;514:170–7. [PubMed: 25659315]
22. Li Z, Romanoff L, Bartell S, Pittman EN, Trinidad DA, McClean M, Webster TF, Sjodin A. Excretion profiles and half-lives of ten urinary polycyclic aromatic hydrocarbon metabolites after dietary exposure. Chem Res Toxicol 2012;25(7):1452–61. [PubMed: 22663094]
23. Peterson BS, Rauh VA, Bansal R, Hao X, Toth Z, Nati G, Walsh K, Miller RL, Arias F, Semanek D, Perera F. Effects of prenatal exposure to air pollutants (polycyclic aromatic hydrocarbons) on the development of brain white matter, cognition, and behavior in later childhood. JAMA Psychiatry 2015;72(6):531–40. [PubMed: 25807066]
24. Perera FP, Wheelock K, Wang Y, Tang D, Margolis AE, Badia G, Cowell W, Miller RL, Rauh V, Wang S, Herbstman JB. Combined effects of prenatal exposure to polycyclic aromatic hydrocarbons and material hardship on child ADHD behavior problems. Environ Res 2018;160:506–513. [PubMed: 28987706]
25. Li Z, Mulholland JA, Romanoff LC, Pittman EN, Trinidad DA, Lewin MD, Sjodin A. Assessment of non-occupational exposure to polycyclic aromatic hydrocarbons through personal air sampling and urinary biomonitoring. J Environ Monit 2010;12(5):1110–18. [PubMed: 21491629]
26. Saez M, Barcelo MA, Farrerons M, Lopez-Casasnovas G. The association between exposure to environmental factors and the occurrence of attention-deficit/hyperactivity disorder (ADHD). A population-based retrospective cohort study. Environ Res 2018;166:205–214. [PubMed: 29890425]
27. Siddique S, Banerjee M, Ray MR, Lahiri T. Attention-deficit hyperactivity disorder in children chronically exposed to high level of vehicular pollution. European Journal of Pediatrics 2011;170(7):923–9. [PubMed: 21191614]
28. Min JY, Min KB. Exposure to ambient PM10 and NO2 and the incidence of attention-deficit hyperactivity disorder in childhood. Environ Int 2017;99:221–227. [PubMed: 27939018]
29. Fuertes E, Standl M, Forns J, Berdel D, Garcia-Aymerich J, Markevych I, Schulte-Koerne G, Sugiri D, Schikowski T, Tiesler CM, Heinrich J. Traffic-related air pollution and hyperactivity/inattention, dyslexia and dyscalculia in adolescents of the German GINIplus and LISAplus birth cohorts. Environ Int 2016;97:85–92. [PubMed: 27835751]
30. Chiu YH, Bellinger DC, Coull BA, Anderson S, Barber R, Wright RO, Wright RJ. Associations between traffic-related black carbon exposure and attention in a prospective birth cohort of urban children. Environ Health Perspect 2013;121(7):859–64. [PubMed: 23665743]
31. Newman NC, Ryan P, Lemasters G, Levin L, Bernstein D, Hershey GK, Lockey JE, Villareal M, Reponen T, Grinshpun S, Sucharew H, Dietrich KN. Traffic-related air pollution exposure in the first year of life and behavioral scores at 7 years of age. Environmental Health Perspectives 2013;121(6):731–6. [PubMed: 23694812]
32. Gong T, Almqvist C, Bolte S, Lichtenstein P, Anckarsater H, Lind T, Lundholm C, Pershagen G. Exposure to air pollution from traffic and neurodevelopmental disorders in Swedish twins. Twin Res Hum Genet 2014;17(6):553–62. [PubMed: 25229653]
33. Forns J, Dadvand P, Foraster M, Alvarez-Pedrerol M, Rivas I, Lopez-Vicente M, Suades-Gonzalez E, Garcia-Esteban R, Esnaola M, Cirach M, Grellier J, Basagana X, Querol X, Guxens M, Nieuwenhuijsen MJ, Sunyer J. Traffic-Related Air Pollution, Noise at School, and Behavioral Problems in Barcelona Schoolchildren: A Cross-Sectional Study. Environ Health Perspect 2016;124(4):529–35. [PubMed: 26241036]
34. Kicinski M, Saenen ND, Viaene MK, Den Hond E, Schoeters G, Plusquin M, Nelen V, Bruckers L, Sioen I, Loots I, Baeyens W, Roels HA, Nawrot TS. Urinary t,t-muconic acid as a proxy-biomarker of car exhaust and neurobehavioral performance in 15-year olds. Environ Res 2016;151:521–527. [PubMed: 27569194]
35. Myhre O, Lag M, Villanger GD, Oftedal B, Ovrevik J, Holme JA, Aase H, Paulsen RE, Bal-Price A, Dirven H. Early life exposure to air pollution particulate matter (PM) as risk factor for attention

deficit/hyperactivity disorder (ADHD): Need for novel strategies for mechanisms and causalities. Toxicol Appl Pharmacol 2018;354:196–214. [PubMed: 29550511]

36. United States Census Bureau. Current Population Survey 1948–2016. Washington, DC: U.S. Department of Commerce, Economics and Statistics Administration, 2016.

Highlights

- Prenatal exposure to traffic-related air pollution associated with neurobehavioral disorders
- Linked 2 databases to see if living near major road was associated with ADHD in children 8–15-years
- The study used U.S. nationally represented datasets with C-DISC based diagnoses
- The relation between proximity to a major road and ADHD and conduct disorder was not statistically significant
- No associations were found between proximity to a major road and urinary PAH metabolites

Table 1.

Traffic exposure and ADHD and CD diagnoses by sociodemographics, behavior, and biomarkers of environmental contaminants

	n	Distance to a major road (%)				Diagnosis (%)	
		≥500 m	300–499 m	100–299 m	<100 m	ADHD	CD
Age group[c]							
8–11 years	463	49.57	17.09	22.57	10.78	7.28	1.73
12–15 years	704	52.66	14.64	23.66	9.04	5.74	4.14
PIR group[a]							
<1	367	35.29	15.53	32.03	17.15	14.22	2.92
1-	280	49.26	14.57	23.20	12.98	1.89	2.34
≥2	467	56.96	16.66	20.10	6.29	5.36	3.25
Race[a]							
White	303	55.53	14.75	21.68	8.04	7.04	2.58
Black	428	48.11	17.09	23.68	11.11	7.46	4.39
Others	436	41.90	17.86	26.36	13.88	4.34	2.97
Sex[b]							
Boy	568	51.11	15.10	24.40	9.38	9.30	2.10
Girl	599	51.11	16.64	21.79	10.45	3.64	3.80
ETS							
Yes	235	50.98	12.72	25.97	10.33	9.83	5.22
No	923	51.19	16.68	22.33	9.80	5.73	2.40
Maternal smoking during pregnancy[b,c]							
Yes	181	53.54	11.90	25.34	9.22	15.01	6.78
No	973	50.06	17.02	22.72	10.20	4.36	1.64
Maternal age at birth (years)							
<25	544	49.75	13.20	25.91	11.14	10.14	4.66
25–29	309	48.63	19.24	21.04	11.09	4.26	1.74
≥30	314	54.95	16.07	21.59	7.39	4.62	2.15
Household reference person education[b]							

	n	Distance to a major road (%)				Diagnosis (%)	
		≥500 m	300–499 m	100–299 m	<100 m	ADHD	CD
< High school	391	47.63	15.29	25.04	12.05	3.30	1.93
High school	303	43.46	15.17	29.25	12.11	11.28	2.51
Some college or above	436	57.19	15.65	18.91	8.24	5.12	3.50
Blood lead levels[b]							
<1 ug/dL	400	54.30	16.62	20.13	8.95	3.52	2.41
1- ug/dL	462	50.99	12.93	23.69	12.39	9.34	3.70
≥2 ug/dL	202	39.27	22.31	30.10	8.32	10.69	3.66
Survey years[c]							
2001–2002	615	49.33	15.44	25.20	10.03	7.99	1.52
2003–2004	552	53.01	16.32	20.88	9.79	4.95	4.43
US born[b]							
Yes	1050	51.64	15.34	22.90	10.11	6.79	3.05
No	117	43.46	23.39	26.16	6.99	1.07	0.75
Serum cotinine levels[c]							
<0.1 ng/mL	565	49.74	16.98	23.61	9.68	4.68	1.31
0.1- ng/mL	315	56.47	15.59	19.52	8.42	7.44	4.80
≥1 ng/mL	157	45.80	12.17	27.43	14.60	13.21	7.00

a: $p<0.05$ for distance from a major road

b: $p<0.05$ for ADHD diagnosis

c: $p<0.05$ for CD diagnosis

Table 2.

Urinary PAH metabolite levels (ng/g creatinine) by traffic exposure

	N	Sum LMW PAHs GM (IQR) ng/g creatinine	1-OH pyrene GM (IQR) ng/g creatinine	Adj difference (95% CI) of Ln(Sum LMW PAHs)	Adj difference (95% CI) of Ln (1-OH Pyrene)
Distance to major roads					
≥500 m	551	4521 (2629–6300)	72 (39–137)	ref	ref
<500 m	616	4317 (2574–6319)	67 (36–107)	−0.09 (−0.23, 0.05)	−0.04 (−0.21, 0.14)
<100 m	135	4013 (2201–5957)	67 (36–105)	−0.19 (−0.41, 0.03)	−0.09 (−0.26, 0.09)
100–299 m	285	4470 (2762–6377)	65 (36–102)	−0.05 (−0.21, 0.12)	−0.03 (−0.25, 0.20)
300–499 m	196	4303 (2417–6062)	69 (36–109)	−0.11 (−0.31, 0.09)	−0.02 (−0.24, 0.19)
1 road within 500 m	359	4252 (2510–5941)	68 (38–108)	−0.10 (−0.25, 0.05)	−0.02 (−0.21, 0.17)
≥2 roads within 500 m	257	4429 (2651–6794)	65 (35–104)	−0.09 (−0.29, 0.12)	−0.07 (−0.26, 0.12)

GM: Geometric mean; IQR: Interquartile range

Adjusted for survey years, age group, sex, race, maternal age at birth, household reference education level, poverty income ratio, current serum cotinine, US born status

Table 3.

Prevalence and adjusted odds ratio and 95% confidence intervals of C-DISC ADHD and CD diagnosis by proximity to traffic and PAH exposure

	N	% ADHD	Adj OR (95% CI)	% CD	Adj OR (95% CI)
Distance to major road (Ln)			0.94 (0.72–1.23)		0.99 (0.69–1.40)
≥500 m	461	3.84	Ref	2.43	Ref
<500 m	501	9.86	2.06 (0.85–5.03)	2.51	1.32 (0.40–4.36)
<100 m	108	8.47	1.84 (0.39–8.64)	3.02	1.55 (0.30–7.89)
100–299 m	226	12.93	2.26 (0.75–6.82)	0.92	0.44 (0.07–2.75)
300–499 m	167	6.50	1.90 (0.70–5.22)	4.39	2.75 (0.53–14.26)
1 road within 500 m	301	10.44	1.97 (0.83–4.65)	3.13	1.54 (0.41–5.86)
≥2 roads within 500 m	200	8.80	2.27 (0.71–7.26)	1.40	0.83 (0.16–4.19)
Sum LMW PAHs (Ln)			0.90 (0.60–1.35)		1.54 (0.80–2.98)
Quartile 1 (<2625 ng/g Cr)	245	4.00	Ref	2.12	Ref
Quartile 2 (2625–4073 ng/g Cr)	254	8.56	1.75 (0.58–5.25)	4.68	1.77 (0.33–9.46)
Quartile 3 (4074–6466 ng/g Cr)	234	7.97	2.38 (0.83–6.78)	0.72	0.24 (0.05–1.03)
Quartile 4 (≥6467 ng/g Cr)	243	6.33	1.41 (0.44–4.51)	3.72	1.41 (0.29–6.72)
1-OH-pyrene (Ln)			0.94 (0.54–1.64)		1.36 (0.68–2.73)
Quartile 1 (<39 ng/g Cr)	294	5.53	Ref	1.02	Ref
Quartile 2 (39–67 ng/g Cr)	267	7.46	0.83 (0.27–2.56)	3.85	3.86 (0.57–26.18)
Quartile 3 (68–123 ng/g Cr)	230	7.28	1.04 (0.32–3.40)	4.28	4.09 (0.61–27.29)
Quartile 4 (≥124 ng/g Cr)	227	5.86	0.57 (0.16–2.09)	2.75	2.91 (0.52–16.19)

Adjusted for survey years, age group, sex, race, maternal age at birth, household reference education level, poverty income ratio, maternal smoking during pregnancy, current serum cotinine, current blood lead levels, US born status