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lifetime exposure to traffic-related air pollution and symptoms of depression and anxiety at age 12 years

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Abstract

Background: While air pollution has been associated with depression and anxiety in adults, its impact on childhood mental health is understudied.

Objective: We examined lifetime exposure to traffic-related air pollution (TRAP) and symptoms of depression and anxiety at age 12 years in the Cincinnati Childhood Allergy and Air Pollution Study cohort.

Methods: We estimated exposure to elemental carbon attributable to traffic (ECAT), a surrogate of diesel exhaust, at birth, age 12 years, and average exposure throughout childhood, using a validated land use regression model. We assessed depression and anxiety at age 12 years by parent report with the Behavior Assessment System for Children-2, and by child report with the Child Depression Inventory-2 (CDI-2) and the Spence Children's Anxiety Scale (SCAS). Associations between TRAP at birth, age 12 years, and childhood average and mental health outcomes were estimated using linear regression models adjusting for covariates including parent depression, secondhand smoke exposure, race, household income, and others.

Results: Exposure to ECAT was not significantly associated with parent-reported depression or anxiety. However, exposure to ECAT at birth was associated with increased child-reported depression and anxiety. Each 0.25 $\mu\text{g}/\text{m}^3$ increase in ECAT was associated with a 3.5 point

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Declarations of interest
None.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.envres.2019.03.005.

increase (95% CI 1.6–5.5) in CDI-2 scores and 2.3 point increase (95% CI 0.8–3.9) in SCAS total anxiety scores. We observed similar associations between average childhood ECAT exposures but not for concurrent exposures at age 12.

Conclusions: TRAP exposure during early life and across childhood was significantly associated with self-reported depression and anxiety symptoms in children. The negative impact of air pollution on mental health previously reported among adults may also be present during childhood.

Keywords

Air pollution; Anxiety; Child mental health; Depression; Exposure

1. Introduction

Approximately one-half of all Americans will meet diagnostic criteria for a mental health disorder during their lifetime with initial onset frequently occurring during childhood or adolescence (Kessler et al., 2005; Paus et al., 2008). Adolescence is a particularly important developmental period in which major morphological and functional changes in the brain, combined with hormonal influences, contribute to emotional turmoil (Araín et al., 2013), and these changes are linked with increased incidence of mental health problems (Paus et al., 2008). Depression and anxiety are of particular concern, as these are the most prevalent mental health disorders affecting 14% and 30% of U.S. adolescents, respectively (Caspi et al., 1996; Kessler et al., 2005; Kim-Cohen et al., 2003; Merikangas et al., 2010; Paus et al., 2008; Pollack et al., 1996). Children with mental health problems experience more academic difficulties, are more likely to be engaged in the justice and welfare systems, and are at elevated risk for suicide, the second leading cause of death among adolescents and young adults (Heron, 2016; Liu et al., 2011). The impact of mental health disorders extends beyond childhood as these are associated with lifelong implications including school drop-out, substance use, suicide risk, and recurrent unemployment (Fergusson and Woodward, 2002; Weissman et al., 1999). Recent trends indicate a near doubling in the rate of hospitalization for mental health concerns among children over the last decade demonstrating a significant rise in the prevalence of these disorders during childhood (Plemmons et al., 2018) spurring a need for more research about the etiology and possible prevention of these disorders.

While genetics, family history, socioeconomic status, and medical conditions play an important role in mental health disorders, environmental factors may also influence their development through oxidative stress and neuroinflammatory pathways (Ng et al., 2008; Vogelzangs et al., 2013). Air pollution is a common environmental exposure known to induce systemic inflammation and oxidative stress with adverse health consequences including respiratory and cardiovascular disease (Allen et al., 2017a; Block and Calderón-Garcidueñas, 2009; Block et al., 2012; Campbell et al., 2005; Chen et al., 2008; Chen and Schwartz, 2009; Costa et al., 2014, 2017; Dockery et al., 1993; Dockery, 2009; Dominici et al., 2006; Gauderman et al., 2007; Health Effects Institute, 2010; Lelieveld et al., 2015; Newman et al., 2013; Pope III and Dockery, 2006; Weuve et al., 2012). Recent toxicological studies demonstrate that some air pollutants, including particulate matter and elemental carbon, may affect the central nervous system through multiple mechanisms including

neuroinflammation, microglial activation, and altered synaptic plasticity (Block and Calderón-Garcidueñas, 2009; Costa et al., 2014, 2017). Air pollution may also act through oxidative stress mechanisms to induce dopaminergic neurotoxicity (Block and Calderón-Garcidueñas, 2009). Accumulating epidemiologic evidence supports the neurotoxic effects of air pollution with studies reporting associated cognitive deficits and externalizing behaviors in children, and accelerated cognitive decline in adults (Allen et al., 2017a; Block et al., 2012; Campbell et al., 2005; Chen and Schwartz, 2009; Costa et al., 2017; Newman et al., 2013; Weuve et al., 2012).

Less well studied, however, is the impact of air pollution on mental health symptoms, including depression and anxiety. Among adults, reports of air pollution and adverse mental health outcomes, including psychiatric emergency room visits, first appeared in the 1980s (Briere et al., 1983; Bullinger, 1989). Recent studies in the U.S., China, and South Korea, have reported that short-term increases in air pollution are linked to elevated risk for suicide, symptoms of depression and anxiety, and emergency department visits for mental health disorders in adults (Bakian et al., 2015; Chen et al., 2018; Lim et al., 2012; Pun et al., 2016; Szyszkowicz et al., 2009). In European cohorts, associations with long-term exposure to air pollution and depression have been inconsistent but are suggestive of a potentially harmful relationship (Vert et al., 2017; Zijlema et al., 2016).

Research among children and adolescents is sparse, though exposure to various components of air pollution has been associated with increased symptoms of depression and likelihood of depression diagnosis (Roberts et al., 2019) as well as treatment for a mental health disorder (Oudin et al., 2016). In addition, prenatal exposure to polycyclic aromatic hydrocarbons (PAHs) due to the combustion of fossil fuels, including air pollution and other organic materials has been associated with increased depression and anxiety in children at age 6–7 years (Perera et al., 2012).

Given the rising incidence of childhood mental health concerns and the scarcity of research specifically with children, the objective of our study was to examine the association between exposure to traffic-related air pollution (TRAP) across childhood and symptoms of depression and anxiety among children at age 12 years.

2. Methods

2.1. Study population

Study participants were drawn from the Cincinnati Childhood Allergy and Air Pollution Study (CCAAPS), a prospective cohort study of children and their parents residing in the Greater Cincinnati, Ohio region (LeMasters et al., 2006; Ryan et al., 2005). Birth records were obtained from the Ohio and Kentucky Departments of Health from 2001 to 2003. Study eligibility required having a birth record address located less than 400 m (defined as having an average daily truck count > 1000) or more than 1500 m from a major roadway. Eligibility also required having at least one biological parent with atopy confirmed by skin prick testing (LeMasters et al., 2006). Enrolled children and their parents completed clinical evaluations at ages 1, 2, 3, 4, 7, and 12 years that included physical assessments and surveys regarding the participants' health and general wellbeing, housing characteristics, residential

history, and secondhand smoke (SHS) exposure. The focus of the current study is on mental health outcomes, involving assessments of depression and anxiety collected at age 12 years. The study was approved by the Institutional Review Boards of the University of Cincinnati and Cincinnati Children's Hospital Medical Center. Participants and parents provided informed assent and consent, respectively.

2.2. Traffic-related air pollution (TRAP) exposure

We estimated participants' residential exposure to elemental carbon attributable to traffic sources (ECAT) using a previously developed and validated land-use regression (LUR) model (Ryan et al., 2007, 2008). Briefly, PM_{2.5}, elemental carbon (EC), and elemental components of PM_{2.5} were measured at 27 sampling sites operated in the study region from 2001 to 2006 (Ryan et al., 2007). Using chemical mass balance and UNMIX models, the average fraction of elemental carbon in PM_{2.5} from traffic sources (ECAT) was determined for each sampling site and serves as our surrogate marker of the traffic-related air pollution mixture (Hu et al., 2006). We subsequently developed, validated, and applied a LUR model to estimate annual average concentrations of ECAT at participants' homes from birth through 12 years (Ryan et al., 2007, 2008). For this analysis, we estimated: 1) prenatal/early life exposure based on LUR-derived ECAT concentrations at the birth address, 2) current exposure based on the home address at age 12 years, and 3) average childhood exposure based on all reported home addresses from birth through 12 years.

2.3. Outcome measures

Trained staff collected assessments of depression and anxiety symptoms at age 12 years. Parents completed the Behavior Assessment System for Children-2 (BASC-2) (Reynolds and Kamphaus, 2004) Parent Rating Scales that yields composite scores for Externalizing Problems, Internalizing Problems, Behavioral Symptoms, and Adaptive Skills, and subscale scores of which the Anxiety, Depression, Somatization, and Withdrawal scales were examined. Children completed the short form of the Children's Depression Inventory-2 (CDI-2) (Kovacs, 1992) that assesses symptoms of depression within the past two weeks and yields a total depression score. Children also completed the Spence Children's Anxiety Scale (SCAS) (Spence, 1998) that assesses six domains of anxiety including panic/agoraphobia, social phobia, separation anxiety, obsessive compulsive disorder, physical injury fears, and generalized anxiety, as well as a total anxiety score. All three scales yield age-standardized T-scores with means of 50 and standard deviations of 10.

BASC-2 forms were completed by the parents and were immediately reviewed for completeness. A trained examiner provided standard instructions to the children for completion of the CDI-2 and SCAS and allowed the children to complete the forms on their own. If the children had trouble reading the items or completing the forms, the examiner offered to read the items aloud and assisted with form completion. We used publisher-supplied software to score all instruments. Examiners addressed elevated depression scores, with both children and parents, and offered resources and assistance with referrals for further evaluation as needed.

2.4. Covariates

Parents completed the Beck Depression Inventory-II (BDI-II) (Beck et al., 1996) to assess attitudes and symptoms specific to signs of depression; this assessment was considered in all models examining child depression outcomes. Parents also completed the Parenting Relationship Questionnaire (PRQ) (Kamphaus and Reynolds, 2008) to describe the parent-child relationship from the parent's perspective. The PRQ yields T-scores for Attachment, Communication, Discipline Practices, Involvement, Parenting Confidence, Satisfaction with School, and Relational Frustration; this measure was considered in all models.

Exposure to lead and tobacco smoke have been linked with internalizing symptoms in children (Ashford et al., 2008; Bandiera et al., 2010; Bouchard et al., 2009; Yolton et al., 2008) and were considered in our models. Blood samples collected at age 12 years were analyzed for lead concentrations obtained by ICP-MS at the Laboratory of Inorganic and Nuclear Chemistry at the New York State Department of Health's Wadsworth Center. Hair samples were collected at age 2 and 4 year study visits and analyzed for cotinine by radioimmunoassay at the Hospital for Sick Children (Toronto, Canada). The mean of 2-and 4-year cotinine concentrations was used to estimate early childhood SHS exposure.

2.5. Statistical analysis

Descriptive statistics and graphical plots were used to examine the distribution of all variables, examine potential outliers, and describe the population, exposures, and outcome measures. Means and standard deviations or medians with 25th and 75th percentiles are reported, as appropriate, for the continuous variables; frequencies are reported for categorical variables. Concentrations of hair cotinine below the analytic limit of detection (LOD) were replaced by the LOD divided by the square root of 2 (Hornung and Reed, 1990). Missing hair cotinine concentrations ($n = 58$) were imputed and replaced based on parent report of number of cigarettes smoked by household members (0, 1–10, 11–20, > 20) and available hair cotinine concentrations within each category.

We developed separate unadjusted linear regression models to assess associations between early, current, and average childhood TRAP exposures and each outcome. Adjusted linear regression models were subsequently developed for models with significant associations between TRAP exposure and mental health outcomes. Covariates considered for inclusion in adjusted models were selected based on prior literature or their potential roles as confounders of the relationship between TRAP exposure and mental health. These included maternal age at delivery, maternal education, parent marital status and depression (BDI-II); average household income from birth to 12 years, an index of community deprivation based on census-tract level SES data, PRQ scores; child age at study visit, sex, race; early childhood hair cotinine levels, and blood lead measured at 12 years. For each outcome, covariates were included in the adjusted models if significantly ($p < 0.05$) associated with the outcome or if inclusion resulted in a > 10% change in the ECAT parameter estimate. We assessed potential effect modification of ECAT exposure by child sex by including an interaction term in the adjusted models. Any covariate or effect modifier retained in one of the models for the mental health outcomes was included in all final models with the exception of the BDI-II which was only included in analyses of child depression. Given that

the range of estimated ECAT exposures is approximately 0.2–0.9 $\mu\text{g}/\text{m}^3$, effect estimates for ECAT exposure are presented for a 0.25 $\mu\text{g}/\text{m}^3$ change in ECAT exposure. Statistical analyses were performed using SAS® version 9.4 (SAS Institute).

3. Results

3.1. Participant characteristics

A total of 344 children and their parents completed the study visit and were included in the analysis. Five children did not complete the self-report measures (CDI-2 and SCAS) because their visits were completed by mail; these instruments were skipped for mailed visits because we did not have the ability to provide necessary support if scores were elevated. Children were, on average, age 12.2 years, and 44.5% ($n = 153$) were female (Table 1). The majority (75.9%, $n = 261$) of participants were white, reflecting the racial distribution of the greater Cincinnati region. Mothers of participants were, on average, age 30.7 years at the time of the participants' birth, and 78.4% completed high school prior to the age 12 study visit. There were no significant differences between participants who completed the age 12 study visit and those who did not ($n = 419$) with respect to sex, race, maternal education at enrollment, household income at enrollment, or exposure to ECAT at the birth record address (Supplementary Table 1). Average [SD] exposure to ECAT among the participants at the birth record address (0.39 [0.14] $\mu\text{g}/\text{m}^3$) was similar to average exposure at the time of the age 12 study visit (0.37 [0.12] $\mu\text{g}/\text{m}^3$), and average ECAT from birth through the age 12 study visit (0.38 [0.10] $\mu\text{g}/\text{m}^3$) (Table 1). However, individual participant's exposure to ECAT varied throughout childhood due to changes in residential location; the correlation between ECAT exposure at the birth record address and age 1 year was 0.96 while the correlations between ECAT exposure at birth and age 12 years and the average childhood exposure were 0.44 and 0.80, respectively.

3.2. Mental health findings

Mental health outcomes ascertained from the CDI-2, SCAS, and BASC-2 are provided in Table 2. The prevalence of elevated depression scores ($T \geq 65$) is 9.7% in this cohort. The prevalence of elevated SCAS scores ($T \geq 65$) is less than 3% for all anxiety subscales. The prevalence of 'at-risk' BASC-2 scores ($T \geq 60$) range from 8.1% to 14.2%. Correlations between child reported depression and anxiety, assessed by the CDI-2 and SCAS, respectively, and parent-reported child depression and anxiety, assessed by the BASC-2, were low ($r = 0.24$ and $r = 0.35$, respectively).

3.3. TRAP and child-reported internalizing symptoms

Unadjusted analyses of prenatal/early life, current, and average childhood ECAT exposures identified significant associations with child-reported depression and anxiety outcomes (Supplementary Table 3). Prenatal/early life exposure to ECAT was univariately associated with elevated CDI-2 scores for total depression as well as SCAS scores for total anxiety, generalized anxiety, obsessive-compulsive disorders, and panic/agoraphobia (Supplementary Table 3). In addition, a positive association was observed between average childhood ECAT exposure and CDI-2 and SCAS generalized anxiety scores (Supplementary Table 3).

After adjustment for covariates (Fig. 1), prenatal/early life ECAT was significantly associated with increased CDI-2 T-scores for depression ($\beta = 3.01$, 95% CI 1.03, 4.99 per $0.25 \mu\text{g}/\text{m}^3$ increase in ECAT). Although not statistically significant in adjusted models, CDI-2 T-scores were elevated with increasing average childhood ECAT ($\beta = 2.46$, 95% CI -0.28 , 5.20 , $p = 0.08$).

In the final adjusted models, a $0.25 \mu\text{g}/\text{m}^3$ increase in ECAT exposure in prenatal/early life was significantly associated with a 1.90 point increase (95% CI 0.29, 3.51) in SCAS total anxiety T-score and a 1.64 point increase (95% CI 0.33, 2.95) in generalized anxiety T-score (Fig. 1). Current ECAT exposure was not associated with total anxiety, obsessive compulsive, panic/agoraphobia, fear of physical injury or separation anxiety T-scores, but was associated with increased generalized anxiety ($\beta = 1.90$, 95% CI 0.37, 3.43) and social phobia ($\beta = 1.88$, 95% CI 0.06, 3.70). A similar pattern was observed with average childhood exposure to ECAT with an estimated 2.15 point increase (95% CI 0.35, 3.95) in generalized anxiety T scores per $0.25 \mu\text{g}/\text{m}^3$ increase in average childhood ECAT exposure and an estimated 2.26 point increase (95% CI 0.10, 4.42) in social phobia T scores per $0.25 \mu\text{g}/\text{m}^3$ increase in average childhood ECAT exposure.

3.4. TRAP and parent-reported internalizing behaviors

No significant associations were observed between ECAT exposures during the three time periods and the BASC-2 internalizing composite score or the depression, anxiety, somatization, or withdrawal subscales (Supplementary Table 2). Therefore, we did not conduct additional analyses of parent-reported (BASC-2) behaviors.

4. Discussion

In this longitudinal exposure study, TRAP, assessed through a measure of ECAT, was associated with increased self-reported symptoms of depression and anxiety at age 12 years. Though prior studies have found exposure to air pollution to be associated with cognitive deficits and increased behavior problems in children, and prior studies link air pollution to mental health symptoms in adults, to our knowledge this is the first epidemiologic study to identify associations between childhood exposure to TRAP and elevated depression and anxiety at age 12. The availability of residential addresses throughout childhood allowed us to examine exposures at varying time points, and we observed exposures occurring during early childhood to have the greatest association with depression at age 12. Similarly, exposure to TRAP during early childhood was the only period significantly associated with total anxiety, though nonsignificant trends were evident for TRAP exposure at age 12, as well as average childhood exposure, with total anxiety scores. Notably, increased generalized anxiety was consistently associated with TRAP exposure at all childhood time periods, and for social phobia, associations were positive and significant for current and average childhood exposure.

Our results support the hypothesis that air pollution exposure is associated with adverse mental health outcomes in children and are consistent with previous epidemiologic studies in adult populations (Briere et al., 1983; Bullinger, 1989; Lim et al., 2012; Power et al., 2015; Pun et al., 2016; Szyszkowicz et al., 2009). The majority of studies in adults, however,

examined short-term exposure to air pollution and acute episodes of depression. Szyszkowicz et al. reported a 2–3% increased risk for emergency department visits for depression in the week following elevated ozone exposure across multiple cities in Canada (Szyszkowicz and Kousha, 2016). Similarly, an analysis of daily hospital admissions for mental health disorders in Shanghai, China reported a 1.27% and 1.88% increase in admissions per 10 $\mu\text{g}/\text{m}^3$ increase in 2-day moving average PM_{10} and NO_2 exposure, respectively (Chen et al., 2018). In Salt Lake City, UT the odds of suicide were significantly increased following elevated NO_2 and $\text{PM}_{2.5}$ 1–3 days prior (Bakian et al., 2015).

Studies in adults have also reported associations between air pollution and mental health measured through surveys. In Seoul, South Korea, increased symptoms of depression were associated with elevated 3-day moving average exposures to PM_{10} , NO_2 , and ozone (Lim et al., 2012). In a nationwide U.S. cohort of elderly adults, increased $\text{PM}_{2.5}$ was significantly associated with both anxiety and depression, with 180 and 30-day moving averages being the most significant exposure windows (Pun et al., 2016). Three studies have examined longer-term exposure to air pollution and mental health outcomes. In the Nurses' Health Study, significantly increased odds of anxiety symptoms were associated with higher exposure to $\text{PM}_{2.5}$, with exposures occurring less than 1 year before symptoms being more significant than exposures 15 years before symptoms (Power et al., 2015). Long-term exposure to ozone and $\text{PM}_{2.5}$ was also associated with the onset of depression in this study (Kioumourtoglou et al., 2017). In contrast, a study of elderly adults in Boston, MA did not observe significant associations between long-term air pollution exposure and depression symptoms (Wang et al., 2014). These conflicting results may be due to differences in study populations, exposure assessment, and outcome measures.

Research among children and adolescents is meager but suggests exposure to air pollution is associated with increased symptoms of depression, depression diagnosis (Roberts et al., 2019), and treatment for mental health disorders (Oudin et al., 2016). Perera also reported that prenatal exposure to PAHs, that may include TRAP, is associated with increased depression and anxiety in children at age 6–7 years (Perera et al., 2012).

Prior studies have reported links between TRAP and cognition and executive function (Freire et al., 2009; Porta et al., 2016; Sunyer et al., 2015). Other studies, including CCAAPS, have also reported prenatal and childhood TRAP exposure to be significantly associated with behavior problems assessed at school-age including symptoms of attention-deficit hyperactivity disorder (Harris et al., 2016; Min and Min, 2017; Newman et al., 2013). In addition, studies have reported increased odds of autism spectrum disorders with higher prenatal exposures to traffic-related pollutants, $\text{PM}_{2.5}$, and proximal distance to major roadways (Volk et al., 2011, 2013).

Multiple mechanisms by which air pollution may adversely affect the central nervous system and neurobehavior are biologically plausible including the induction of proinflammatory cytokines leading to neuroinflammation in the brain, endothelial dysfunction, disruption of the blood-brain barrier, oxidative stress, and neuronal damage (Block and Calderón-Garcidueñas, 2009; Brockmeyer and D'Angiulli, 2016; Calderón-Garcidueñas et al., 2008, 2016). With respect to depression and anxiety, air pollution may also induce dopaminergic

and/or glutamatergic neurotoxicity. In mice, air pollution provokes behaviors that represent depression and anxiety (Bolton et al., 2013; Davis et al., 2013; Fonken et al., 2011).

While air pollution is a complex mixture of toxic compounds including gases, trace metals, and particulate matter of varying sizes, ultrafine particles (UFPs, particles < 100 nm in diameter) are of particular interest due to their dominant particle concentrations in ambient air, ability to bind toxic compounds to their large surface area, capability to translocate to other organ systems, and potential to directly impact the brain via the olfactory epithelium (Allen et al., 2017a, 2017b; Health Effects Institute, 2010). Experimental evidence in mice also supports the neurotoxicity of UFPs as recent evidence demonstrates UFP exposures lead to inflammation, microglial activation, disruption to white matter development, elevated glutamate, and other pathology (Allen et al., 2017b). The primary contributors to UFPs in ambient air are tailpipe emissions from mobile sources, particularly diesel fuel, and epidemiologic studies examining traffic-specific pollutants including NO₂, black carbon, and ultrafine particles (UFP) are most consistent in their observed associations with adverse cognitive development.

We observed significant associations when examining child self-reported symptoms, but not parent-reported child behaviors. Incongruence between parent and child ratings of psychiatric symptoms have been previously reported in which children and adolescents reported more severe symptoms than their parents, possibly due to parents' unawareness of symptom severity (Moretti et al., 1985; Stanger and Lewis, 1993). Angold and Nauta (Angold et al., 1987; Nauta et al., 2004) reported a discordance in anxiety measures to be greater among children in a non-clinical group than among children with a diagnosed anxiety disorder. By definition, internalizing symptoms are more difficult for others to detect because they project inward. In contrast, externalizing symptoms, including hyperactivity and aggressive behaviors, project outward and are more evident to parents, teachers, and others. The observed low correlation between parent and child report of symptoms of depression and anxiety lends additional support to the possibility that parents may be unaware of their children's experience of these internalizing symptoms.

Our study has some important strengths including its longitudinal design and collection of complete childhood address histories allowing us to estimate exposures from birth through age 12 years. Our findings suggest early life exposure, as estimated at the birth record address, represents the most relevant period of exposure with respect to depression outcomes, and was also significantly associated with anxiety symptoms. Though we did not capture residential mobility during the entire pregnancy, due to temporal proximity it is likely that TRAP exposure estimated at the birth record address is highly correlated with TRAP exposures during the third trimester, a previously identified period of enhanced vulnerability to the neurotoxic effects of air pollution (Allen et al., 2017b). The comprehensive assessment of multiple covariates, including SHS exposure, maternal depression, and the parent-child relationship, is another strength of the study.

Our assessment of depression and anxiety at age 12 years is also an important component to our design given that adolescence is a developmental period during which the incidence of mental health problems increases (Paus et al., 2008). The prevalence of depression among

adolescents has been estimated at rates of 5–14% (Birmaher et al., 1996; Jellinek and Snyder, 1998; Merikangas et al., 2010), and anxiety has been estimated at 32% (Merikangas et al., 2010). These rates appear to be increasing from generation to generation, with earlier onset ages (Gershon et al., 1987; Gotlib and Hammen, 2014). While multiple factors influence an individual's risk for adverse mental health outcomes, environmental factors contributing to depression and anxiety in children are poorly understood. Identifying and intervening on modifiable environmental exposures, including air pollution, associated with childhood depression and anxiety is a significant public health challenge given that childhood mental health disorders often persist into adulthood, leading to continued depressive and anxiety disorders, suicidal behavior and psychiatric hospitalization as well as academic failure, recurrent unemployment, and relationship difficulties. Like adults, children with psychiatric disorders are often undertreated; 70–80% of depressed children receive no treatment (Cicchetti and Toth, 1998). Identification of air pollution as a contributor to the increased prevalence of these disorders during childhood may provide additional leverage to inform policy around air quality.

It is important to note that the observed increase in reported symptoms in our cohort of typically developing children is relatively small, 3-points and 2-points, for depression and total anxiety, respectively. These are equivalent to one-third to one-fourth of a standard deviation in the T-scores, respectively, and are not likely to result in a clinical diagnosis of a mental health disorder in a low-risk sample like ours. However, even small effects of exposure may have a substantial impact at the population level by shifting the population distribution and resulting in increased risk of poor outcomes (Bellinger, 2012).

The study is not without limitations. We acknowledge attrition of the cohort over time, which is common in longitudinal research, but we did not find significant differences between those who completed the study at 12 and those who did not. We estimated TRAP exposure at the homes of study participants, and therefore there may be some exposure misclassification due to time spent away from the home. However, we expect this exposure misclassification to be non-differential, and therefore bias is toward the null. Future studies may also consider underlying genetic susceptibility or modifying factors that may increase susceptibility to air pollution including stress and APOE4 gene variants (Calderón-Garcidueñas et al., 2018; Cooney, 2011). Additional limitations include the potential for residual confounding due to unmeasured covariates that may affect neurobehavior and the use of a single pollutant (ECAT) as our air pollution exposure metric. However, previous studies support the hypothesis that air pollutants emitted from traffic, including elemental and black carbon, NO₂, and UFPs are most consistently linked to adverse neurobehavioral outcomes.

5. Conclusions

Our results demonstrate that early life exposure to TRAP is associated with self-reported symptoms of depression and anxiety at age 12 years when controlling for relevant covariates. In addition, current exposure to TRAP at age 12 years, and average exposure across childhood, is associated with self-reported symptoms of generalized anxiety and social phobia when controlling for relevant covariates. To our knowledge, these findings are

the first to demonstrate that childhood exposure to TRAP is associated with mental health symptoms during adolescence and adds to the growing body of epidemiologic evidence for the role of air pollution in neurobehavioral and mental health disorders.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Abbreviations:

BASC-2	Behavior Assessment System for Children-2
BDI-II	Beck Depression Inventory-II
CCAAPS	Cincinnati Childhood Allergy and Air Pollution Study
CDI-2	Child Depression Inventory-2
ECAT	elemental carbon attributable to traffic
LOD	limit of detection
LUR	land-use regression
NO₂	nitrogen dioxide
PM	particulate matter
PRQ	Parenting Relationship Questionnaire
SCAS	Spence Children's Anxiety Scale
SD	standard deviation
SHS	secondhand smoke
TRAP	Traffic-related air pollution
UFP	ultrafine particle

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Fig. 1. Adjusted* Parameter Estimates (per 0.25 $\mu\text{g}/\text{m}^3$ increase) for the Association between Early, Current, and Average Childhood ECAT Exposure and Child-Reported Symptoms of Depression and Anxiety. *Adjusted for maternal age at delivery, average household income birth to 12 y study visit, maternal BDI-II scores, PRQ Relational Frustration T-score, child race, average hair cotinine from samples collected at ages 2 and 4 years.

Table 1

Child, Maternal, and Household Characteristics of CCAAPS Participants (n = 344).

Characteristic	Mean/n	SD/%
<i>Child characteristics</i>		
Age at 12 y Study Visit (y)	12.2	0.8
Female	153	44.5%
Race/Ethnicity		
White	261	75.9%
Black/More than One Race	83	24.1%
<i>Maternal characteristics</i>		
IQ (Wechsler Abbreviated Scale of Intelligence (WASI-2))	105.2	13.3
Depression (BDI-II)	6.4	4.0
Age at Study Enrollment (years)	30.7	5.9
Maternal Education at 12 y Study Visit		
High School	72	21.6%
Some College or Trade School	94	28.1%
College Degree	168	50.3%
<i>Household/Parenting characteristics</i>		
Household Income at enrollment		
< \$20,000	58	17.4%
\$20,000 to < \$ 40,000	54	16.2%
\$40,000 to < \$70,000	96	28.8%
\$70,000 to < \$90,000	89	26.7%
> \$90,000	36	10.8%
Parent Relationship Questionnaire (PRQ) T-scores		
Attachment	52.2	9.6
Communication	50.7	10.1
Discipline Practices	48.3	10.4
Involvement	52.3	11.3
Parenting Confidence	51.4	9.5
Relational Frustration	48.2	9.5
<i>ECAT exposure measures</i>		
Early Life ECAT at Birth Record Address ($\mu\text{g}/\text{m}^3$)	0.39	0.14
Current ECAT at 12 y Study Visit ($\mu\text{g}/\text{m}^3$)	0.37	0.12
Average Childhood ECAT; Birth to 12 y Study Visit ($\mu\text{g}/\text{m}^3$)	0.38	0.10

Table 2

Summary of Child and Parent Reported Measures of Depression and Anxiety.

Responder	Assessment	Index	n ^a	Mean (SD)	n (%) > 65
Child Reported	CDI-2	Total Depression	339	52.7 (10.2)	33 (9.7)
		Total Anxiety	339	44.2 (8.2)	3 (0.9)
	SCAS	Generalized Anxiety	339	46.4 (6.6)	1 (0.3)
		Obsessive Compulsive Disorder	339	46.0 (7.5)	9 (2.6)
		Panic/Agoraphobia	339	46.9 (7.4)	7 (2.1)
		Fear of Physical Injury	339	49.5 (8.2)	9 (2.6)
		Separation Anxiety	339	45.4 (6.5)	4 (1.2)
		Social Phobia	339	46.7 (8.0)	5 (1.5)
Parent Reported	BASC-2	Internalizing Composite	344	50.6 (11.1)	31 (9.0)
		Depression Subscale	344	49.9 (10.2)	28 (8.1)
		Anxiety Subscale	344	52.1 (12.0)	49 (14.2)
		Somatization Subscale	344	49.4 (11.4)	30 (8.7)
		Withdrawal Subscale	344	50.0 (11.0)	34 (9.9)

^aNumber of participants with completed assessments