Traffic-Related Air Pollution and the Incidence of Childhood Central Nervous System Tumors: Texas, 2001–2009

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Background. Due to increasing concerns regarding air pollution and childhood cancer, we conducted a population-based study evaluating the association between traffic-related hazardous air pollutants (1,3-butadiene, benzene, diesel particulate matter [DPM]) and the incidence of childhood central nervous system (CNS) tumors. Additional supporting information may be found in the online version of this article.

INTRODUCTION

Central nervous system (CNS) tumors are the second most common group of childhood cancers in the developed world.[1] While advances in treatment have led to improved survival of children with CNS tumors, such tumors are still the leading cause of pediatric cancer-related deaths in the United States (U.S.).[2] Further, long-term survivors of childhood CNS tumors suffer from adverse health effects in later life including chronic illnesses, neurocognitive impairment, infertility, and early mortality.[3–7] Despite the clinical significance of these malignancies, the only established risk factors for childhood CNS tumors are ionizing radiation and genetic predisposition syndromes, which together account for <5% of all cases.[8,9] One difficulty in conducting epidemiologic studies of CNS tumors is the potential for etiologic heterogeneity among phenotypes (e.g., astrocytomas and medulloblastomas). Therefore, assessments seeking to identify novel risk factors should include the evaluation of associations by phenotype. Furthering our understanding of the risk factors and etiologies of these conditions may inform future prevention efforts.

There is growing concern over the association between air pollution and childhood cancer. Automobile emissions are a major source of ambient air pollution in urban areas and are frequently composed of hazardous air pollutants (HAPs) including 1,3-butadiene, benzene, and diesel particulate matter (DPM), each of which has been classified by the International Agency for Research on Cancer as Group 1 agents, carcinogenic to humans.[10–13] Exposure to traffic-related air pollution has previously been shown to be associated with an increased risk of various cancers in adults, including brain tumors, as well as childhood leukemia.[14,15]

Although air pollution is a common exposure that has been implicated in cancer risk, few studies have examined the relationship between traffic-related air pollution and childhood CNS tumors.[16–18] One study reported a five times increased CNS tumor risk among children <5 years of age living in areas with high traffic density compared to low traffic density.[19] However, other studies found no statistically significant associations between traffic-related air pollution exposure and childhood CNS tumors.[16–18] Previous studies have assessed exposure using measures of residential traffic density and roadway proximity, or relied on criteria pollutant (e.g., nitrogen oxides) measures; however, to our knowledge, no studies have evaluated the associations between HAP exposure and the CNS tumor phenotypes.

We conducted a population-based study to evaluate the associations between ambient air concentrations of 1,3-butadiene, benzene, and diesel particulate matter with childhood CNS tumor incidence in Texas. In this study, we investigated the association between traffic-related air pollution exposure and the incidence of childhood CNS tumors. Traffic-related air pollution exposure was estimated using residential traffic density and roadway proximity measures. The study was conducted in Texas, a state with one of the highest traffic densities in the U.S., and with a large population of children with CNS tumors. The study population included children aged 0–19 years living in rural and urban areas of Texas, and the study period was from 2001 to 2009. The study used a population-based approach to investigate the association between traffic-related air pollution exposure and the incidence of childhood CNS tumors. The study results provide important insights into the potential role of traffic-related air pollution in the development of childhood CNS tumors.
benzene, and DPM and the incidence of juvenile pilocytic astrocytomas (JPAs), other astrocytomas, ependymomas, medulloblastomas, and primitive neuroectodermal tumors (PNET) in children in Texas, a state characterized by a large active cancer registry, as well as high and variable levels of several HAPs.

METHODS

Study Population

We identified 2,019 cases of CNS tumors diagnosed in children <15 years of age and residing in the state of Texas during the period of 2001-2009 from the Texas Cancer Registry (TCR). The TCR is a large population-based registry with gold certification from the North American Association of Central Cancer Registries during the study period. CNS tumor cases included all tumors classified under group III of the International Classification of Childhood Cancer, third edition (ICCC-3).[20] The major CNS tumor phenotypes included: 1) juvenile pilocytic astrocytomas (JPAs) (International Classification of Diseases for Oncology, third edition [ICD-O-3] code 9421); 2) astrocytomas (ICCC-3 group IIIb, excluding JPAs); 3) ependymomas (ICCC-3 group IIIa.1); 4) medulloblastomas (ICCC-3 group IIIc.1); and 5) PNET (ICCC-3 group IIIc.2). Only those children with a CNS tumor as their first malignancy were included as cases. In addition to information on tumor histology, information was obtained for each CNS tumor case from the TCR on the child’s sex, race/ethnicity, and age and residence at the time of diagnosis.

We obtained estimates of the number of residents <15 years of age for each Texas census tract from the 2000 U.S. Census to serve as the at-risk population (i.e., the denominator) in calculating CNS tumor incidence rates.[21] A census tract is a small statistical subdivision of a county, and generally includes approximately 1,200 to 8,000 individuals.[22] There are 4,387 census tracts in the state of Texas. Population estimates were stratified by sex, race/ethnicity (non-Hispanic white, non-Hispanic black, Hispanic, and other), and age categories (0 to <5, 5 to <10, and 10 to <15 years old) for each census tract. CNS tumor cases for each population stratum within each census tract were aggregated. The study protocol was approved by the Institutional Review Boards of the Texas Department of State Health Services, the University of Texas Health Science Center at Houston, and Baylor College of Medicine.

Exposure Assessment

Modeled estimates of ambient 1,3-butadiene, benzene, and DPM concentrations for every Texas census tract were obtained from the 2005 U.S. Environmental Protection Agency’s (EPA) Assessment System for Population Exposure Nationwide (ASPEN).[23] Details on the ASPEN model have been previously described.[24,25] Briefly, ASPEN is a computer simulation model derived from the U.S. EPA’s Industrial Source Complex Long Term model. ASPEN generates estimated annual pollutant concentrations at the census tract level and takes into account several factors including meteorology (e.g., wind speed and direction), location and height of the pollutant source, the rate of release, pollutant deposition, reactive decay, and transformation properties into secondary pollutants.[24] The 2005 U.S. EPA ASPEN estimates are based on the census tract boundaries defined for the 2000 U.S. Census, and therefore population estimates from the 2000 U.S. Census were used to calculate incidence rates.

The exposure assignment was based on the child’s residential census tract at the time of their CNS tumor diagnosis. Information on residence at birth was not available for the current study. HAP exposure was assessed as a categorical variable. Exposure categories were generated based on quartiles of the statewide distributions of ambient 1,3-butadiene, benzene, and DPM census tract-level concentrations. The HAP exposure categories were defined as low (<25th percentile), medium (25th to <50th percentile), medium-high (50th to <75th percentile), and high (≥75th percentile).

Covariates

Potential confounders were selected a priori and included sex, age at diagnosis, race/ethnicity, and socioeconomic status (SES), as these factors are known or suspected to be associated with both childhood CNS tumor incidence and air pollution exposure. [8,9,26–33] As information on SES is not available from the TCR, census tract-level poverty was used as a proxy for SES. Specifically, information on the proportion of households with an income lower than the poverty level for each census tract was obtained from the 2000 U.S. Census.[21]

Statistical Analysis

Frequency distributions were determined for each CNS tumor phenotype by categories of each covariate. Spearman’s rank correlation was used to calculate the correlations between ambient concentrations of 1,3-butadiene, benzene, and DPM. The proportion of HAP concentrations contributed by stationary and mobile sources was estimated by calculating the median and interquartile range (IQR) across all census tracts. We used Poisson regression to assess the association between census tract-level ambient HAP concentrations and childhood CNS tumor incidence rates, generating adjusted incidence rate ratios (aIRR) and 95% confidence intervals (CI). In the case of data over-dispersion, negative binomial regression was used instead of Poisson regression. Regression analyses were repeated to independently evaluate the association between HAP concentrations and each CNS tumor phenotype. All regression models included each of the covariates noted previously.

Statistical significance was defined as P < 0.05. We conducted sensitivity analyses where all adjusted regression models were applied to a restricted dataset that included only cases diagnosed in 2004–2006, the diagnosis period temporally closest to the 2005 HAP concentration estimates. In addition, a sub-analysis was conducted in which the sample was restricted to include only non-Hispanic whites, the largest race/ethnicity group, to assess possible residual confounding by race/ethnicity when assessing the associations between HAPs and astrocytoma incidence rates. Astrocytoma incidence was evaluated because astrocytomas make up one of the largest CNS phenotypic groups and is also where we see an attenuation of the effect estimates in the highest HAP exposure category. Statistical analyses were conducted using Stata 13.1 (StataCorp, College Station, Texas).

RESULTS

Of the 2,019 primary CNS tumor cases diagnosed in Texas during the period of 2001–2009 and identified in the TCR, five CNS tumor cases were excluded due to invalid county and census tract code combinations. An additional 65 cases were excluded because they

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had a zero population estimate for their census tract population stratum. Excluded cases (n = 70) had similar frequency distributions across categories of age at diagnosis, sex, and area-level poverty compared to cases eligible for inclusion in our assessment (data not shown). A higher proportion of excluded cases were non-Hispanic black (37.1%) and fewer were non-Hispanic white (17.1%) compared to cases eligible for inclusion in the analysis (P < 0.001).

Of the remaining 1,949 (97%) CNS tumor cases, 1,180 were classified into one of the major CNS tumor phenotypes under evaluation. JPAs and other astrocytomas made up the largest groups (n = 384 [19.7%] and n = 372 [19.1%], respectively), followed by medulloblastomas (n = 235 [12.1%]), ependymomas (n = 142 [7.3%]), and PNETs (n = 47 [2.4%]) (Table I). Approximately half of astrocytoma (non-JPA) (42.7%), ependymoma (47.9%), and PNET (61.7%) cases were diagnosed in children <5 years of age (Table I). In contrast, the largest proportions of JPA (36.5%) and medulloblastoma (43.0%) cases were diagnosed at 5 to 10 years of age. There were more males than females diagnosed with a JPA (54.4% male), ependymoma (59.9% male), or medulloblastoma (64.7% male), whereas PNET cases were more likely to be female (53.2% female). The largest proportions of JPA (36.5%) and astrocytoma (non-JPA) (42.7%), ependymoma (54.4%), and medulloblastoma (55.3%) cases resided in census tracts with low area-level poverty (i.e., <15% of the households within the census tract had an income below the poverty level).

Census tracts categorized with medium, medium-high, and high concentrations of 1,3-butadiene were predominately in and around major metropolitan areas, specifically in the greater Houston, Dallas, Fort Worth, and San Antonio areas (Fig. 1). Similar patterns were observed with benzene (Supplemental Fig. 1) and DPM (Supplemental Fig. 2). The distributions of ambient HAP concentrations across Texas census tracts are presented in Table II. Ambient concentrations of benzene were highly correlated with concentrations of 1,3-butadiene (r = 0.84, P < 0.0001) and of DPM (r = 0.84, P < 0.0001). Similarly, ambient concentrations of 1,3-butadiene were highly correlated with concentrations of DPM (r = 0.86, P < 0.0001).

**TABLE I. Demographic Characteristics of CNS Tumor Cases <15 Years of Age Diagnosed in Texas, 2001–2009**

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>All CNS tumors (n = 1,949)</th>
<th>Astrocytomas (n = 372)</th>
<th>JPAs (n = 384)</th>
<th>Ependymomas (n = 142)</th>
<th>Medulloblastomas (n = 235)</th>
<th>PNET (n = 47)</th>
<th>Total TX Population &lt;15 years old* (n = 5,797,483)</th>
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<tbody>
<tr>
<td>Age (years), n (%)</td>
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<tr>
<td>&lt;5</td>
<td>724 (37.2)</td>
<td>159 (42.7)</td>
<td>114 (29.7)</td>
<td>68 (47.9)</td>
<td>79 (33.6)</td>
<td>29 (61.7)</td>
<td>1,926,313 (33.2)</td>
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<tr>
<td>5 to &lt;10</td>
<td>661 (33.9)</td>
<td>119 (32.0)</td>
<td>140 (36.5)</td>
<td>40 (28.2)</td>
<td>101 (43.0)</td>
<td>11 (23.4)</td>
<td>1,960,085 (33.8)</td>
</tr>
<tr>
<td>10 to &lt;15</td>
<td>564 (28.9)</td>
<td>94 (25.3)</td>
<td>130 (33.9)</td>
<td>34 (23.9)</td>
<td>55 (23.4)</td>
<td>7 (14.9)</td>
<td>1,911,085 (33.0)</td>
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<td>Sex, n (%)</td>
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<tr>
<td>Male</td>
<td>1,049 (53.8)</td>
<td>190 (51.1)</td>
<td>209 (54.4)</td>
<td>85 (59.9)</td>
<td>152 (64.7)</td>
<td>22 (44.9)</td>
<td>2,965,931 (51.2)</td>
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<tr>
<td>Female</td>
<td>900 (46.2)</td>
<td>182 (48.9)</td>
<td>175 (45.6)</td>
<td>57 (40.1)</td>
<td>83 (45.3)</td>
<td>25 (55.2)</td>
<td>2,831,552 (48.8)</td>
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<td>Race/ethnicity, n (%)</td>
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<tr>
<td>Non-Hispanic White</td>
<td>903 (46.3)</td>
<td>179 (48.1)</td>
<td>217 (56.5)</td>
<td>57 (40.1)</td>
<td>103 (43.8)</td>
<td>18 (38.3)</td>
<td>2,065,886 (35.6)</td>
</tr>
<tr>
<td>Hispanic</td>
<td>773 (39.7)</td>
<td>130 (35.0)</td>
<td>122 (31.8)</td>
<td>72 (50.7)</td>
<td>104 (44.3)</td>
<td>22 (46.8)</td>
<td>2,021,242 (34.9)</td>
</tr>
<tr>
<td>Othera</td>
<td>273 (14.0)</td>
<td>63 (16.9)</td>
<td>45 (11.7)</td>
<td>13 (9.1)</td>
<td>28 (11.9)</td>
<td>7 (14.9)</td>
<td>1,710,355 (29.5)</td>
</tr>
<tr>
<td>Area-level poverty, n (%)</td>
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<tr>
<td>&lt;15% of households</td>
<td>1,209 (62.0)</td>
<td>254 (68.3)</td>
<td>250 (65.1)</td>
<td>78 (54.9)</td>
<td>130 (55.3)</td>
<td>23 (48.9)</td>
<td>3,065,062 (52.9)</td>
</tr>
<tr>
<td>≥15% of households</td>
<td>740 (38.0)</td>
<td>118 (31.7)</td>
<td>134 (34.9)</td>
<td>64 (45.1)</td>
<td>105 (44.7)</td>
<td>24 (51.1)</td>
<td>2,732,421 (47.1)</td>
</tr>
</tbody>
</table>

CNS, central nervous system; JPA, juvenile pilocytic astrocytoma; PNET, primitive neuroectodermal tumors; TX, Texas. *Source: 2000 U.S. Census, U.S. Census Bureau. †Includes cases that are non-Hispanic black; did not present cases that are non-Hispanic black separately due to small cell sizes to protect subject confidentiality.
Mobile sources of 1,3-butadiene (median [IQR]: 30.3% [9.3–50.1%]) and benzene (median [IQR]: 21.0% [10.2–32.8%]) made up a higher proportion of the overall concentrations across all census tracts compared to stationary sources (median [IQR]: 1 × 10⁻²% [1.1 × 10⁻²–2.1%] and 0.2% [4.4 × 10⁻³–1.1%], respectively). In addition, on road mobile sources (i.e., vehicles on roads and highways) were estimated to contribute to the largest proportion of 1,3-butadiene (median [IQR]: 70.4% [60.4–79.7%]) and benzene (median [IQR]: 67.5% [57.4–77.1%]) concentrations coming from mobile sources. Mobile sources are responsible for 100% of DPM concentrations across all census tracts, with the majority (median [IQR]: 67.7% [54.3–78.0%]) coming from on road mobile sources.

**Astrocytomas**

Compared to census tracts with low HAP concentrations, census tracts with medium and medium-high 1,3-butadiene concentrations had increased astrocytoma incidence rates (Table III). For instance, census tracts with medium and medium-high 1,3-butadiene concentrations had increased astrocytoma incidence rates (aIRR [95%CI]: 1.46 [1.05, 2.01] and 1.69 [1.22, 2.33], respectively) compared to census tracts with low 1,3-butadiene concentrations. Increased astrocytoma incidence rates were not observed when comparing census tracts with high HAP concentrations to low concentrations (aIRR > 1.0). However, when restricting the sample to only include non-Hispanic whites, positive associations were detected in the high exposure categories of 1,3-butadiene, benzene, and DPM and astrocytoma incidence (aIRR [95%CI]: 1.55 [0.90, 2.66]), 1.13 [0.68, 1.86], and 1.29 [0.78, 2.13], respectively), although these associations were not statistically significant (Supplemental Table).

**Medulloblastomas**

Overall, positive associations were observed among census tracts with high concentrations of 1,3-butadiene, benzene, or DPM and medulloblastoma incidence rates (aIRR [95%CI]: 1.09 [0.74, 1.60], 1.16 [0.79, 1.70], and 1.25 [0.83, 1.88], respectively); however, these associations were not statistically significant. Additionally, census tracts with medium DPM concentrations had increased medulloblastoma incidence rates (aIRR [95%CI]: 1.46 [1.01, 2.12]) compared to low DPM concentrations.

**PNET**

Overall, census tracts with medium, medium-high, and high HAP concentrations had increased PNET incidence rates. Although these associations were not statistically significant, the number of cases was small (n = 47) and the effect estimates were relatively high. The strongest associations were observed when evaluating 1,3-butadiene concentrations where census tracts with medium, medium-high, and high concentrations had increased PNET incidence rates (aIRR [95%CI]: 2.60 [0.94, 7.24], 2.76 [0.98, 7.72], and 2.40 [0.83, 6.93], respectively) compared to census tracts with low concentrations.

**JPAs and Ependymomas**

Overall, no associations were observed among HAP concentrations and JPA incidence rates or ependymoma incidence rates. Effect estimates were close to 1.0.

The effect estimates were similar among each of the CNS tumor phenotypes when assessing HAP concentrations and incidence rates using a restricted sample including only CNS tumors diagnosed in 2004–2006 (data not shown).

**DISCUSSION**

Our results suggest that children <15 years of age residing in census tracts with higher concentrations of traffic-related HAPs may have a higher incidence of selected CNS tumor phenotypes compared to those in census tracts with low HAP concentrations. Specifically, the strongest associations were observed with 1) astrocytoma incidence and 1,3-butadiene and DPM, 2) medulloblastoma incidence and DPM, and 3) PNET incidence and 1,3-butadiene, benzene, and DPM. Not all observed associations were statistically significant; however, consistent patterns were typically observed between the three evaluated HAPs and each CNS tumor phenotype, and nearly all of the effect estimates were either close to or greater than 1.0.

For some pollutants, associations were weaker in census tracts with the highest exposure levels. This may be due to exposure misclassification and uncontrolled residual confounding despite the adjustment of several potential confounders in our analysis. In fact, the null effect estimates observed when evaluating high HAP exposure and astrocytoma incidence rates when including all race/ethnicity groups, was not present when assessing non-Hispanic whites alone, indicating that the results in the full group may indeed have been influenced by residual confounding by race/ethnicity. In the U.S., the incidence of CNS tumors is known to be lower in black children compared to white children, and areas with higher HAP concentrations are typically characterized by larger race/ethnicity minority populations, including blacks.[8,29] Although we adjusted for race/ethnicity in our analysis, the association between race/ethnicity and CNS tumors may not have been completely accounted for in census tracts in the highest HAP exposure categories. In
TABLE III. Associations Between HAPs and Incidence Rates of CNS Tumor Phenotypes Among Children <15 years of Age in Texas, 2001–2009

<table>
<thead>
<tr>
<th>Pollutant Category</th>
<th>All CNS tumors (n = 1,949)</th>
<th>Astrocytomas, non-JPA (n =372)</th>
<th>JPAs (n = 384)</th>
<th>Ependymomas (n = 142)</th>
<th>Medulloblastomas (n = 235)</th>
<th>PNET (n = 47)</th>
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<tbody>
<tr>
<td>1,3-butadiene</td>
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<tr>
<td>Low (reference)</td>
<td>401</td>
<td>32.1</td>
<td>1.00</td>
<td>57</td>
<td>4.6</td>
<td>1.00</td>
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<td></td>
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<tr>
<td>Medium</td>
<td>590</td>
<td>37.3</td>
<td>1.07 (0.97, 1.25)</td>
<td>117</td>
<td>7.4</td>
<td>1.46 (1.05, 2.01)</td>
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<tr>
<td>Medium-high</td>
<td>550</td>
<td>35.1</td>
<td>1.07 (0.94, 1.23)</td>
<td>132</td>
<td>8.5</td>
<td>1.69 (1.22, 2.33)</td>
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<tr>
<td>High</td>
<td>408</td>
<td>29.0</td>
<td>1.07 (0.83, 1.11)</td>
<td>66</td>
<td>4.7</td>
<td>1.05 (0.73, 1.50)</td>
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<tr>
<td>Benzene</td>
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<tr>
<td>Low (reference)</td>
<td>418</td>
<td>35.1</td>
<td>1.00</td>
<td>75</td>
<td>6.3</td>
<td>1.00</td>
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<tr>
<td>Medium</td>
<td>599</td>
<td>36.8</td>
<td>1.01 (0.89, 1.21)</td>
<td>123</td>
<td>7.6</td>
<td>1.18 (0.88, 1.58)</td>
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<td>Medium-high</td>
<td>529</td>
<td>33.2</td>
<td>1.01 (0.88, 1.15)</td>
<td>105</td>
<td>6.6</td>
<td>1.07 (0.79, 1.45)</td>
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<tr>
<td>High</td>
<td>403</td>
<td>29.1</td>
<td>1.09 (0.84, 1.11)</td>
<td>69</td>
<td>5.0</td>
<td>0.94 (0.67, 1.32)</td>
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<tr>
<td>Diesel particulate matter</td>
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<tr>
<td>Low (reference)</td>
<td>404</td>
<td>32.5</td>
<td>1.00</td>
<td>64</td>
<td>5.2</td>
<td>1.00</td>
</tr>
<tr>
<td>Medium</td>
<td>657</td>
<td>40.6</td>
<td>1.20 (1.06, 1.37)</td>
<td>130</td>
<td>8.0</td>
<td>1.42 (1.05, 1.94)</td>
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<tr>
<td>Medium-high</td>
<td>529</td>
<td>33.5</td>
<td>1.03 (0.90, 1.18)</td>
<td>109</td>
<td>6.9</td>
<td>1.22 (0.89, 1.69)</td>
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<tr>
<td>High</td>
<td>359</td>
<td>26.4</td>
<td>0.90 (0.78, 1.04)</td>
<td>69</td>
<td>5.1</td>
<td>1.07 (0.76, 1.52)</td>
</tr>
</tbody>
</table>

CI, confidence interval; CNS, central nervous system; HAP, hazardous air pollutant; IR, incidence rate; IRR, incidence rate ratio; JPA, juvenile pilocytic astrocytoma; PNET, primitive neuroectodermal tumor. * Per 100,000; aAdjusted for race, sex, age category, and area-level poverty; bPollutant categories: low (<25th percentile), medium (25th to <50th percentile), medium-high (50th to <75th percentile), high (≥75th percentile).
addition, there was typically a small number of cases in the highest exposure category and therefore insufficient power to detect differences.

Childhood CNS tumors are a heterogeneous group of conditions and, due to the rare nature of childhood cancers including CNS tumors, it is challenging to obtain sample sizes that are large enough to independently evaluate the individual phenotypes. Therefore, childhood CNS tumors are often evaluated together as a group. This may explain the inconsistent findings across studies evaluating childhood CNS tumors together as a group, including one study conducted in Denver which reported a five times increased CNS tumor risk in children living in areas with high versus low traffic density, and another study conducted in California which found no association between road and traffic density and childhood CNS tumors.[18,19] Only two studies have evaluated traffic-related air pollution exposure and the risk of individual CNS tumor phenotypes. Overall, both studies reported no statistically significant associations with exposure to criteria pollutants (carbon monoxide, fine particulate matter [PM$_{2.5}$], or nitrogen oxides) or traffic density.[16,17] However, Heck et al. reported positive associations between ependymoma and medulloblastoma risk in children <6 years of age in California (odds ratio [95%CI]: 1.29 [0.72, 2.07] and 1.61 [0.88, 2.95], respectively, per IQR increase in PM$_{2.5}$).[17]

Given the carcinogenic properties of traffic-related HAPs as well as the association of traffic-related air pollution exposure with other CNS disorders, it is biologically plausible that exposure to traffic-related HAPs may be a risk factor for childhood CNS tumors. In fact, both animal and human studies have shown that particulates inhaled from vehicle emissions produce DNA oxidative damage in the brain, which may promote carcinogenesis in the CNS of children and young adults.[36–39]

Our results should be considered in light of several limitations. The ecologic nature of the exposure assessment limits the application of these results to individual-level disease risk.[40] However, biases introduced through data aggregation are likely reduced when using small geographic units, such as census tracts, as well as when the data are stratified into homogeneous sub-populations regarding disease risk.[41] In our analysis, cases and population estimates were stratified by sex, age, and race/ethnicity, as the prevalence of CNS tumors is differential across these demographic groups.[9] Additionally, due to the ecologic nature of this study as well as unavailability of information on the CNS tumor cases and on the underlying population, we were not able to evaluate other factors, such as exposure to ionizing radiation, parental age at birth, or maternal exposures during pregnancy, as potential confounders in our assessment.

Annual ambient HAP concentration estimates for 2005 were used as the exposure measurement in this assessment. The U.S. EPA recommends against using multiple years of ASPEN estimates simultaneously in one assessment,[23] therefore, we relied on the 2005 estimates, which corresponds to the midpoint of the diagnosis period. Hence, it is possible that some exposure misclassification exists in our assessment; however, ASPEN estimates have been used extensively in other assessments of HAPs and rare disease outcomes assessed over an extended time period.[42–44] While HAP levels have been declining over time, previous studies suggest that the relative ranking of census tracts regarding HAP exposure have remained the same.[45] Furthermore, we found similar results to those presented in this report when restricting our assessment to CNS tumor cases diagnosed in 2004–2006. Lastly, ASPEN estimates of 1,3-butadiene and benzene in Texas census tracts have been previously shown to have good agreement with nearby monitors.[46]

In this assessment, we relied on population estimates from the 2000 U.S. Census to determine CNS tumor incidence rates; we used the 2000 estimates because the ASPEN HAP estimates from 2005 were based on the census tract boundaries used in the 2000 U.S. Census. There is potential for census tract-level population fluctuations throughout the study period, 2001–2009, which may introduce bias into the incidence rate estimates and should be considered when interpreting these results (i.e., incidence rates may have been over- or under-estimated). Census tract boundaries change between the decennial census, and although cross-walk resources are available to estimate annual population changes while taking into account census tract boundary changes between each census, there is no counterpart for estimating HAP concentrations with changing census tract boundaries. However, while it is possible that there are population changes within census tracts over our study period, according to the 2010 U.S. Census, there was only a slight change in the overall Texas population <15 years of age (1% decrease) compared to the 2000 U.S. Census.[47]

Exposure was assigned based on the census tract of residence at the time of cancer diagnosis. The critical period of exposure is unknown for childhood CNS tumors, and previous studies evaluating air pollution exposure and childhood CNS tumor risk have reported exposures based on home address in utero, at birth, or at the time of diagnosis.[16,18,19] Of these previous studies, a statistically significant positive association between traffic-related air pollution exposure and CNS tumor risk was reported only when exposure was based on the child’s home address at diagnosis.[19] Home address at diagnosis has been extensively used for exposure assignment in other assessments of air pollution exposure and childhood cancer.[44,48–50] Additionally, a recent meta-analysis on traffic-related air pollution exposure and childhood leukemia reported that postnatal exposure was positively associated with leukemia risk whereas no association was observed when evaluating prenatal exposure.[14] However, depending on the critical window of exposure, it is possible that residential mobility between the time of birth and diagnosis may have resulted in exposure misclassification. For instance, a previous report estimated that 66% of children with leukemia had moved to a different residence between birth and diagnosis.[51] To further elucidate the relevant period of exposure for CNS tumors, the utilization of complete residential histories in future assessments of environmental exposure and CNS tumor risk is warranted.

Our study has several important strengths. This population-based assessment included the entire state of Texas and a large sample of childhood CNS tumor cases; we identified approximately 2,000 CNS tumor cases from which 1,180 cases were classified into one of the major CNS tumor phenotypic groups. The large sample of cases allowed for the independent evaluation of the childhood CNS tumor phenotypes, including the rare PNET group. In addition to its large cancer registry, Texas is composed of areas with variable levels of traffic-related HAPs allowing for a comprehensive assessment of HAP exposure. Furthermore, the demographic makeup (i.e., sex, race/ethnicity, and area-level poverty) of our sample of childhood CNS tumors was similar to that of childhood CNS tumors throughout the U.S.[8]

To our knowledge, this is the first report to suggest that traffic-related HAPs may be potentially associated with higher incidence
of astrocytomas and medulloblastomas in children <15 years of age. The upsurge of people living in urban areas with dense networks of roadways and high levels of traffic-related air pollution in conjunction with the steady increase of childhood CNS tumor incidence in the past few decades presents an important public health concern.\[1,13\] In addition, HAPs are not as well-regulated or monitored as criteria pollutants, further highlighting the need for more research in understanding the health impact of exposure to these pollutants. In light of our results, future studies are needed to evaluate etiologic hypotheses regarding traffic-related air pollution exposure and the various childhood CNS tumor phenotypes. Identifying risk factors for childhood CNS tumors and furthering our understanding of the etiologies of these conditions has important implications for future prevention strategies.

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