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# Residential exposure to urban traffic is associated with the poorer neurobehavioral health of Ecuadorian schoolchildren

Khalid M. Khan[a,*], M. Margaret Weigel[a,b], Sarah Yonts[a], Diane Rohlman[c], Rodrigo Armijos[a,b]

[a] Department of Environmental and Occupational Health, School of Public Health, Indiana University-Bloomington, USA
[b] Global Environmental Health Research Laboratory, School of Public Health, Indiana University-Bloomington, USA
[c] Department of Occupational and Environmental Health, College of Public Health, The University of Iowa, USA

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ABSTRACT

*Purpose:* We investigated whether chronic traffic-generated air pollution containing fine and ultrafine particulate matter is associated with reduced neurobehavioral performance and behavioral dysfunction in urban Ecuadorian schoolchildren. Also, we examined the effect of child hemoglobin and sociodemographic risk factors on these neurocognitive outcomes.

*Methods:* A convenience sample of healthy children aged 8–14 years attending public schools were recruited in Quito, Ecuador. Child residential proximity to the nearest heavily trafficked road was used as a proxy for traffic-related pollutant exposure. These included high exposure (< 100 m), medium exposure (100–199 m) and low exposure (≥ 200 m) from the nearest heavily trafficked road. The Behavioral Assessment and Research System (BARS), a computerized test battery assessing attention, memory, learning and motor function was used to evaluate child neurobehavioral performance. The Child Behavior Checklist (CBCL/6-18) was used to assess child behavioral dysfunction as reported by mothers. The data were analyzed using multiple linear regression.

*Results:* Children with the highest residential exposure to traffic pollutants (< 100 m) had significantly longer latencies as measured by match to sample ($b = 410.27$; $p = 0.01$) and continuous performance ($b = 37.90$; $p = 0.02$) compared to those living ≥ 200 m away. A similar but non-significant association was observed for reaction time latency. Children living within 100 m of heavy traffic also demonstrated higher scores across all CBCL subscales although only the relationship with thought problems ($p = 0.05$) was statistically significant in the adjusted model.

*Conclusion:* The study findings suggest that children living within 100 m of heavy traffic appear to experience subtle neurobehavioral deficits that may result from fine and ultrafine particulate matter exposure.

## 1. Introduction

Traffic-related air pollution is ranked as a major global environmental health threat (WHO, 2016). It is especially problematic in many low- and middle-income countries where the number of motor vehicles is rapidly increasing and existing environmental regulations are weak or not well enforced. Traffic-generated air pollution consists of a complex mixture of water vapor, gases (e.g., nitrogen oxides, carbon monoxide), volatile organic compounds, and particulate matter (PM) that varies by size, shape, surface area, and heavy metal and other chemical constituents (US-EPA, 2013). Pollutant gases and PM also vary regarding their solubility, toxicity, and inflammatory potential (US-EPA, 2013).

In addition to its well-documented adverse respiratory and cardiovascular health effects, evidence from toxicological and epidemiologic studies suggests that air pollutants generated by traffic and other urban air sources is toxic to the central nervous system of children and adults (Annavarapu and Kathi, 2016; Costa et al., 2017a, b). Fine particulate matter ($PM_{2.5}$) may exert its neurotoxic effects by activating reactive oxygen species and pro-inflammatory pathways leading to central nervous system (CNS) damage (Campbell et al., 2005; Fonken et al., 2011; Win-Shwe et al., 2008, 2012). Ultrafine particulate matter (UFP) also has the capacity to pass through the blood-brain barrier. UFP appears to be capable of activating microglia through a neuroinflammatory pathway resulting in perturbations in CNS functioning (Block and Calderon-Garciduenas, 2009; Costa et al., 2017b; Peters et al., 2006).

Published data reporting on the associations between air pollution

* Corresponding author at: Environmental and Occupational Health, School of Public Health, Indiana University Bloomington, 1025 E 7th Street, Room 029, Bloomington, IN, 47405, USA.
*E-mail address:* kmkhan@indiana.edu (K.M. Khan).

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exposures in children with cognitive and psychomotor performance and with child behavioral problems are limited and their findings vary. Several studies have reported consistent findings showing poorer memory span length (van Kempen et al., 2012) and deficits in working memory (Chiu et al., 2013; Forns et al., 2017; Sunyer et al., 2015; Wang et al., 2009) in children exposed to air pollutants. In addition, prenatal or childhood air pollution exposure was associated with greater behavioral problems including attention (Forns et al., 2016; Fuertes et al., 2016) and delinquent or aggressive behavior (Higa Diez et al., 2016; Yorifuji et al., 2017; Younan et al., 2018).

Conflicting evidence on the associations between air pollution and reduced neuropsychological function or behavioral problems in children was also reported. In a birth cohort study, children with greater residential exposure to $PM_{2.5}$ were more likely to be assessed by classroom teachers (using Behavior Rating Inventory of Executive Function and the Strengths and Difficulties Questionnaires) as having greater problems with behavioral regulation. However, no differences in the same children were identified when parent-reported assessments were used (Harris et al., 2016). Data from six European birth cohorts reported a lack of association between any of the key air pollutants and child cognitive development (Guxens et al., 2014). Finally, an adolescent study in Belgium reported association of distance-weighted traffic density with sustained attention but not with memory or motor speed (Kicinski et al., 2015).

Since children spend significant time at home, long-term residential exposure to pollutants from urban traffic may occur due to the movement of pollutants from outdoors to indoors. However, researchers have not yet examined if long-term residence in close proximity to urban traffic is associated with subtle effects in brain development or other functional behavioral outcomes such as child internalizing and externalizing behaviors as assessed by parents or teachers.

In low-resource settings, CNS vulnerability may be further increased by the presence of additional poverty-linked stressors such as low-income, poor parental education, overcrowding, and other indicators of a sub-optimal home environment (Hillemeier et al., 2011; Nyman et al., 2017). Child undernutrition manifested as low blood hemoglobin (Hb) or other nutritional anemias is another potential poverty-linked factor that could also be linked to poorer psychomotor and other neurobehavioral (NB) outcomes (Mireku et al., 2015), low IQ (Benton and a.i.s.b.l, 2008; Sungthong et al., 2002), attention problems (Weigel and Armijos, 2018a,b) and aggressive behavior (Su et al., 2016) in children. However, a study conducted by Ai and associates (Ai et al., 2012) found no association between maternal anemia and NB indicators in 6 year-old children.

Traffic-related pollution is a serious environmental health issue for the urban airsheds of many Latin American cities (WHO, 2016). Children of large urban centers in this region are exposed to high levels of $PM_{2.5}$ and other traffic-related air pollutants (Brauer et al., 2012; Fajersztajn et al., 2017). A well-characterized child cohort study investigating the effects of air pollution exposure on cardiorespiratory health, conducted by our research group in Quito, Ecuador (Armijos et al., 2015; Raysoni et al., 2017; Weigel and Armijos, 2018a,b), gave us the opportunity to collect preliminary data to test the hypothesis that living near the heavy urban traffic, a proxy measure for fine and UFP matter exposure, has adverse effects on functional NB outcomes. The residential distance from urban traffic for these children between 8 to 14 years varied (Armijos et al., 2015). This enabled us to identify several exposure groups for comparing NB functions using a computer test battery and parent-reported child behavior checklist (CBCL). Since sociodemographic and nutritional deficiencies are important for child development in low-income communities, the secondary purpose of the study was to assess the relationships of child hemoglobin and other sociodemographic risk factors with multiple NB outcomes.

## 2. Methods

### 2.1. Participants and recruitment

The cross-sectional study was conducted in Quito, the capital city of Ecuador which has a population of 2.6 million residents (INEC, 2017). The city has a significant problem with traffic-generated air pollution where an estimated 488,000 vehicles circulate every year (Romero, 2017). Air quality in many neighborhoods is poor (Armijos et al., 2015; Raysoni et al., 2017). Nearly one-fourth of QMD residents live within 100 m of heavily traveled roads and streets (Arcia et al., 1993).

Eligible participants for the current study were participants in a larger cohort study investigating the association of chronic exposure to urban pollutants on the cardiorespiratory health of children living in three low-income Quito neighborhoods, El Camal (Central Quito), Cotocollao (North Quito) and Alangasi-(Southeast Quito). The recruitment procedure, inclusion and exclusion criteria for the larger cohort study have been previously described elsewhere (Armijos et al., 2015). Briefly, one public elementary school located less than 5 km from the QMD central air monitor in each of the neighborhoods was identified at the beginning of the cohort study. After a meeting with the school teachers, officials, students and their parents about a list of about 100 eligible participants per school was generated. Students within 7–12 years of age, healthy, and living within 5 miles of the QMD central air monitor in the same neighborhood were included. Any child with a recent history of cardiovascular diseases, dyslipidemia, diabetes, or other serious chronic or infectious conditions, an indoor smoker in house, or an eligible sibling in the family was excluded. Data for the current work were collected during final third year of follow-up (2016). A trained research assistant from Indiana University, Bloomington (IUB) collected NB data using parent-reported CBCL and the Behavioral Assessment and Research System (BARS) computer test battery both developed in Spanish. NB assessment continued for a five-week period from June 9 to July 15 of 2016. Healthy children aged 8 to 14 years and their mothers who were participating in other follow-up activities of the cohort study during this specific five-week period were selected for inclusion in this cross-sectional study. Mothers and children who were unavailable to visit their schools for CBCL and BARS data collection activities were excluded from the current study. The trained IUB research assistant was assisted by two local field research assistants who were native (Ecuadorian) Spanish speakers to provide instructions to the children and their mothers and collect CBCL and BARS data.

Children provided oral and written informed assent, mothers gave informed consent for themselves in addition to informed assent for their children. The study protocol was approved by Institutional Review Board of IUB and the University of Central Ecuador Biomedical Ethics institutional review boards. Children received a nutritious refreshment as an incentive for participating in the study.

### 2.2. Exposure assessment

Residential proximity to the nearest heavily trafficked road was used as a proxy measure for child exposure to PM traffic emissions. The unique residential address of each maternal-child participant was physically verified and then geocoded into latitude and longitude coordinates using Google Earth (Mountain View, CA). These coordinates were used to determine the longitude/latitude orientation and straight-line distance (in meters) from each residence to the nearest major traffic artery in each zone following the methodology published in a previous study (Armijos et al., 2015). We identified the major traffic arteries for each residence using traffic volume studies published by the QMD Department of Transportation and Public Works (Empresa Publica Metropolitana de Movilidad y Obras Publicas (EPMMOP), 2011). In this study, heavy traffic was defined as a roadway having a daily volume of $\geq$10,000 vehicles/day. The optimum roadway distance cut-off point was based on our previous study on cardiovascular outcomes in QMD

children (Armijos et al., 2015), which also used the same exposure categories. Multiple studies have also indicated that steep spatial gradients exist for PM and UFP. The highest levels of exposure for these two pollutants are detected in residences < 100 m away from traffic, which gradually declines between 100–400 meters depending on meteorological conditions and local topography (Boothe and Shendell, 2008; HEI, 2013, 2015; Karner et al., 2010). Therefore, residential proximity in this study was defined as < 100, 100–199, and ≥ 200 m from the nearest heavily trafficked road.

We collected data from the QMD central air monitoring stations to obtain background estimates for annual mean $PM_{10}$ and $PM_{2.5}$ levels for the previous six years (2010–2016). As the child residences and public schools they attended were located within 5 km of the QMD central monitors, we used these data to estimate annual background exposure. Data on annual average concentrations for the 2010 through 2016, provided by the Quito Metropolitan District Department of Environment indicate that the El Camal neighborhood, located in central Quito, had the highest average background concentrations of $PM_{10}$ (43.5 μg/m$^3$) and $PM_{2.5}$ (22.0 μg/m$^3$) for that period. The Cotocollao and Alangasi neighborhoods had substantially lower average background concentrations of $PM_{10}$ (Cotocollao 29.1 μg/m$^3$ and Alangasi 28.9 μg/m$^3$) and $PM_{2.5}$ (Cotocollao 17.0 and Alangasi 16.5 μg/m$^3$). Although the central air monitors do not measure UFP, it is a significant component of urban traffic PM. It has been linked to high near-residential pollutant levels (Fuller et al., 2012; HEI, 2013).

### 2.3. Outcome assessment

#### 2.3.1. Behavioral Assessment and Research System (BARS)

The neurobehavioral health effects of traffic-related air pollution in children, as indicated by redundant residential distance to the nearest heavily trafficked road, were examined using a battery of six computer-based tests that employed the Behavioral Assessment and Research System (BARS). The BARS tests have been previously used for detecting the impact of neurotoxic chemicals on cognitive function for various age groups in different languages including a Spanish version developed for Hispanic children possessing little or no prior computer knowledge (NwETA, 2016; Rodriguez-Barranco et al., 2014; Rohlman et al., 2001, 2007a; Rohlman et al., 2007b).

The specific BARS tests are shown in Table 1. The test administration procedure has been previously described in detail (Butler-Dawson et al., 2016b). Briefly, each of the BARS tests measures specific nervous system functions including attention (Continuous Performance, Reaction Time and Digit Span), response speed and coordination (Finger Tapping), Visual Memory (Match-to-Sample), processing speed (Symbol-Digit) and Working Memory (Digit Span).

In this study, the NB testing sessions were individually conducted with each child participant in a private room in their own public school. The trained local field staff introduced the testing hardware and explained each of the tests prior to the beginning of the testing session following scripts written in Spanish.

#### 2.3.2. Child Behavioral Checklist

The Spanish version of the Child Behavioral Checklist for children 6–18 years (CBCL/6-18) was used to collect data from mothers on reported child psychosocial dysfunction for the past 6-month period (ASEBA, 2001). The CBCL/6-18 has 103 items that are aggregated into eight subscales. The eight empirically validated scales include three subscales from the internalizing domain (anxious/depressed, withdrawn, and somatic complaints), two from the externalizing domain (aggressive and rule-breaking behavior), attention problems, social problems, and thought problems. Participant mothers rated their child on each item as 'not true', 'somewhat or sometimes true' or 'very true or often true'. These responses were respectively scored as 0, 1, and 2, respectively. The scores on these were summed to produce subscale scores. The summed subscale scores were in turn summed to generate the internalizing, externalizing, and total scores. For both the total and subscale-specific scores, the higher the score, the greater the level of specific types or overall behavioral problems.

The psychometric properties of the Spanish-language version CBCL 6–18 are reported to be valid and reliable as a screening tool for assessing psychosocial dysfunction in children from diverse populations (Braet and Ipema, 2011; Wild et al., 2012). In order to confirm the internal validity of the instrument for the urban school-age children in this study, we calculated Cronbach's alpha for each of the eight CBCL subscales. The results revealed that most Cronbach's alpha values were within the range considered acceptable, i.e., between 0.61 and 0.82 although the score for the rule-breaking behavior subscale showed somewhat low reliability (i.e. 0.44). However, the summary scores for internalizing and externalizing behavior showed high Cronbach's alpha values, 0.83 and 0.84 respectively.

### 2.4. Sociodemographic characteristics

Detailed data were collected during face-to-face interviews with participating mothers on the sociodemographic characteristics of the maternal-child dyads, their households, and neighborhoods. These included maternal and child age, gender, ethnicity, and residential history as well as maternal marital status, education and occupation, household size and composition, and monthly *per capita* income.

### 2.5. Child nutritional status

Child participants underwent anthropometric assessments of their

**Table 1**
The BARS tests and neurobehavioral functions measured by the tests.

| Name of BARS Test | Neurobehavioral Function | Description |
|---|---|---|
| Digit Span | Memory and attention | Spoken presentation of number sequences<br>Forward recall only<br>Two chances at each span length |
| Finger Tapping | Response speed and motor coordination | Right and left hand tested<br>Number of taps in 20 seconds duration |
| Match to Sample | Visual memory | 15 stimuli shown for 3 seconds<br>Choose from three choices<br>Delay between presentation/ choice varies from 1 to 8 seconds |
| Continuous Performance | Sustained attention | 75 shapes shown rapidly, 30 targets<br>Pressed key when target (circle) was shown |
| Symbol Digit | Working memory and information processing speed | Nine symbols paired with numbers<br>Match symbols with numbers<br>Completed five trials<br>Not administered to children < 7 years old |
| Simple Reaction Time | Attention and information processing speed | Participants pressed the key as soon as a square appears on the screen. |

weight, height, and arm circumference following a standard protocol by trained study team personnel as described elsewhere (Armijos et al., 2015). Weight and height measurements were used to calculate body mass index (BMI). A 12-hour fasting venous blood sample (7 mL) was obtained for use in the measurement of hemoglobin concentrations. Blood samples were transported to the IUB Global Environmental Health Research Laboratory where they were analyzed using the Modular P-800 chemistry analyzer (Roche Diagnostics, IN). Blood hemoglobin levels were adjusted for the altitude of child residences as the neighborhoods in which they lived ranged from 2613 to 2812 meters above sea level. These adjustments ranged from 15 to 19 g/L depending on residence altitude (WHO, 2011).

### 2.6. Data analysis

The descriptive data in this study are shown as number with percent or means ± S.D. Participant sociodemographic and nutritional characteristics were compared by the three residential traffic exposure groups: high exposure (< 100 m from the nearest heavily trafficked road), medium exposure (100–199 m from the nearest heavily trafficked road), and low exposure (≥ 200 m from the nearest heavily trafficked road) using one-way analysis of variance (ANOVA) or 2 × 3 and 2 × 4 contingency table analysis with $X^2$, as appropriate.

We constructed simple and multivariable linear regression models to examine the association of residential exposure to traffic, a PM surrogate, as a categorical variable with CBCL subscale summary scores and BARS NB outcome scores using the low exposure category as the reference group, i.e., residence ≥ 200 m from the nearest heavily trafficked road. Since residential proximity to traffic had a skewed distribution this continuous variable was log-transformed before it was used as an exposure variable in additional models. The sociodemographic and nutritional covariates selected for initial inclusion in the statistical models were selected based on the published literature linking these with the neurocognitive effects of air pollutant exposure in healthy children or documented risk factors for poorer child neurocognitive status. These covariates included child age, gender, blood hemoglobin levels, BMI, maternal education, maternal occupation, and *per capita* income. We examined whether these covariates changed the estimated associations between exposure and outcomes. Variables were retained in the models if there was substantial change (i.e. > 10%) in the association of interest. We conducted additional analyses to assess if maternal education was an effect modifier of the risk of neurobehavioral impairment in children exposed to traffic related air pollution at their residence. To perform the tests of effect modification an interaction term for residential proximity and maternal education was included in the linear models.

A total of 176 children participated in the BARS tests. Mothers of two children did not complete the CBCL questionnaire (i.e. less 50% of the questions were answered) and therefore, these children were excluded from the CBCL statistical analyses. The statistical analyses were performed using SAS 9.4 (SAS Institute, Cary NC).Statistical significance was defined as $P < 0.05$ and all hypothesis tests were 2-sided.

## 3. Results

### 3.1. Sample characteristics

As Table 2 shows, the sociodemographic and nutritional characteristics of the child participants from the three residential distance to traffic groups did not differ by age, gender, BMI, blood hemoglobin levels, maternal age, maternal occupation, or household monthly *per capita* income. However, a significantly larger proportion of homes were owned by the parents of the children residing more than 200 m away from the traffic compared to living closer to heavy traffic, i.e., 100–199 meters and < 100 m.

### 3.2. Associations of distance from heavily trafficked road with CBCL summary scores

Table 3 presents the results of the unadjusted regression models analyzing the association of child residential distance to the nearest heavily trafficked road with CBCL summary scores when residential distance to traffic was used as a categorical variable. It also shows the adjusted multivariable regression models that included age, sex, adjusted hemoglobin and maternal education as covariates. The positive beta coefficients in the adjusted regression models indicated that children who resided < 100 m and 100–199 to the nearest heavily trafficked road had higher behavioral problems across all subscales as reported by the mothers compared to those who lived further away, i.e., ≥ 200 m away from the traffic. The difference in the total CBCL scores between the high (< 100 m to the nearest heavy traffic) and reference or low (i.e. ≥ 200 m away from the traffic) exposure groups was marginally significant (b = 6.31; p = 0.06). The high exposure group (< 100 m from traffic) demonstrated significantly higher thought problem (b = 0.77; 95% CI = 0.02, 1.57; p = 0.05), marginally significant higher externalizing behavior (b = 2.14; p = 0.06), and non-significantly higher internalizing behavior subscale scores compared to the reference group. While the moderate exposure group (between 100–199 m from traffic) showed significantly higher internalizing behavior score (b = 3.45; p = 0.02) compared to the reference group.

We also ran regression models using log-transformed residential distance from traffic as a continuous variable and observed similar results produced by the categorical exposure variables. Log-transformed distance from traffic was significantly and inversely associated with thought problem CBCL score (-b = 0.36; p = 0.03). This log-transformed exposure variable demonstrated marginally significant inverse association with total CBCL score (b = -2.42; p = 0.06). Associations of this continuous variable with other CBCL outcomes were non-significant but in the same direction. Overall, we observed a trend of more behavioral problems with decreasing distance to heavy traffic using both categorical and continuous exposure variables.

### 3.3. Association of distance from heavily trafficked road with BARS neurobehavioral performance

Table 3 shows the results of the unadjusted and adjusted analysis regarding the associations between child residential distance to traffic and BARS NB performance outcomes. These indicated significantly worse NB performance in the high exposure group (compared to the low exposure group). For example, the high exposure group children had longer response time (i.e. slower response) in match to sample (p = 0.01), and continuous performance (p = 0.02) tests even after accounting for the model covariates. A positive but marginally significant association was observed for reaction time latency when the high and low exposure groups were compared (p = 0.06). In the continuous performance latency, the adjusted regression coefficient was significantly higher in both the high (b = 37.90) and moderate (b = 35.90) exposure groups resembling somewhat dose-response relationship. In models for other NB outcomes such as finger tapping (alternative hands) and digit span forward count, we observed worse performance indicated by negative associations when high and moderate exposure groups were compared with the low exposure group and these resembled non-significant dose-response associations.

When we used log-transformed residential distance from traffic as a continuous exposure variable in the regression models we observed similar relationships. Log-transformed distance from traffic was significantly and inversely associated with reaction time latency (b = -34.22; p = 0.05), match to sample latency (b = -194.43; p < 0.001) and continuous performance latency (-13.90; p = 0.02). Associations of this continuous variable with other BARS outcomes were non-significant but in the expected direction. Overall, the effects of residential proximity to traffic (whether it was used as a categorical or continuous

**Table 2**
Comparison of Maternal-Child Dyad Sociodemographic Characteristics by Residential Proximity to Traffic (n = 176).

| Characteristics | Residential proximity to traffic | | |
|---|---|---|---|
| | < 100 m (n = 80) Mean ± SD or No. (%) | 100-199 m (n = 53) Mean ± SD or No. (%) | ≥200 m (n = 43) Mean ± SD or No. (%) |
| Child age (years) | 10.82 ± 1.79 | 11.71 ± 1.81 | 10.88 ± 2.01 |
| Gender (girls) | 49 (61.3) | 29 (54.7) | 19 (44.2) |
| Child BMI (kg/m$^2$) | 16.84 ± 2.41 | 16.72 ± 2.25 | 17.86 ± 2.16 |
| Adjusted blood hemoglobin (g/dl)[1] | 12.15 ± 1.36 | 12.20 ± 0.98 | 12.30 ± 0.97 |
| Maternal age (years) | 35.62 ± 8.87 | 35.40 ± 7.26 | 34.84 ± 7.22 |
| Maternal education (years) | 7.80 ± 3.91 | 7.47 ± 3.41 | 7.44 ± 3.71 |
| Maternal primary occupation | | | |
| Housewife | 35 (43.8) | 23 (43.4) | 18 (41.9) |
| Domestic employee | 7 (8.8) | 9 (17.0) | 9 (20.9) |
| Sales/Business | 15 (18.8) | 16 (30.2) | 9 (20.9) |
| Other | 23 (28.7) | 5 (9.4) | 7 (16.3) |
| *Per capita* income (US$/month) | 121 ± 99 | 129 ± 60 | 132 ± 67 |
| Home ownership[2] (yes) | 28 (35.0) | 28 (52.8) | 31 (72.1) |

[1] Adjusted for altitude of residence (WHO, 2011).
[2] p = 0.02.

variable) on several BARS outcomes were consistent, i.e. lower NB performance in the BARS tests was associated with decreased distance from traffic.

### 3.4. Association of sociodemographic and nutritional covariates with neurobehavioral outcomes

Several sociodemographic and nutritional factors were found to be associated with CBCL subscale scores. For example, child age was positively associated with internalizing (p = 0.001) scores. Adjusted blood hemoglobin was significantly and negatively associated with CBCL thought problem subscale (p = 0.04) and non-significantly but negatively associated with BARS reaction time, match to sample and symbol digit latencies indicating that increased hemoglobin is related to better NB performance. Blood hemoglobin also consistently demonstrated non-significant negative association with other CBCL subscales (Table 4).

Increased age was associated with improved NB performance with respect to all ten BARS outcome variable (all p-values ≤ 0.05) as shown in Table 4. Increased age also had non-significant but positive associations with all CBCL subscales. Girls demonstrated more internalizing behavioral, social and thought problems but less externalizing behavioral and attention problems than the boys although none of these relationships were statistically significant. In finger tapping test, girls demonstrated significantly poorer performance than the boys for both preferred (p = 0.04) and non-preferred (p = 0.03) hands in finger tapping tests and for delayed latency (p = 0.04) in continuous performance test. Also, we observed positive significant associations of maternal education with both internalizing (p = 0.01) and social problem (p = 0.05) and non-significant associations with other CBCL subscale scores. No noticeable or significant associations of maternal education with BARS NB outcomes were observed.

Sensitivity analyses did not reveal any evidence of effect modification by maternal education. For any of the CBCL or BARS outcomes no statistically significant differences in effects were observed across the categories of maternal education (elementary vs middle school vs high school and above).

## 4. Discussion

The present work is one of only a small handful of studies to report on the association of residential exposure to urban traffic with NB performance and behavioral problems in low- and middle-income children in Latin America. The findings identified poorer NB performance and greater child behavioral problems in 8–14 year old children from low-income families in Quito, Ecuador who were living close to (within 100 m) heavily trafficked roads compared to the low exposure group (≥200 m away). Among the associations observed in BARS tests statistically significant results were reported for continuous performance and match to sample latencies indicating poorer sustained attention and visual memory respectively in children living close to traffic. Furthermore, a similar close-to-significance association in the expected direction was observed in reaction time latency. These associations could be the results of exposure to small size particulate matter such as $PM_{2.5}$, and UFP. These species are the dominant types of outdoor air pollutants in Quito originated from diesel exhaust (DE) (Armijos et al., 2015; Raysoni et al., 2017; Weigel and Armijos, 2018a,b). This study has used residential proximity to traffic as surrogate of traffic related PM and UFP exposure in assessing child cognitive performance. The results are consistent with previous epidemiological studies on children exposed to traffic pollution including a study on adolescents in Belgium reporting reduced sustained attention (Kicinski et al., 2015) and a study reporting poorer cognitive performance in Spanish children (Sunyer et al., 2015).

We found a statistically significant association between residential proximity (high exposure or < 100 m from traffic) and one behavioral problem subscale (i.e. thought problems). Additionally, the data showed a trend of consistent positive but non-significant associations for other CBCL subscales after adjusting for covariates. These findings are similar to several other child studies reporting associations of black carbon or suspended total particulate matter in outdoor air with other behavioral problems such as hyperactivity (Newman et al., 2013), delinquent or aggressive behavior (Yorifuji et al., 2017) and inhibition and impulsive behavior (Yorifuji et al., 2016).

The findings from several experimental studies support those of epidemiological studies. Exposure to high levels of diesel exhaust *in utero* resulted in the alteration of motor activity and coordination along with altered impulsive behavior in male mice (Suzuki et al., 2010; Yokota et al., 2013). Postnatal exposure to PM and UFP also have been shown to impair memory and impulsive behavior in the same species (Allen et al., 2014a, b). How the specific traffic-related pollutant induces damages to the central nervous system and underlying molecular mechanisms of such damages in humans still needs further research. Several biological effects of PM on CNS such as oxidative stress and neuroinflammation have been noted (Block and Calderon-Garciduenas, 2009). Pregnant mother exposed to PM can pass the particles to the placenta inducing brain inflammation, blood-brain barrier breakdown, or neuronal and glial damage (Calderon-Garciduenas et al., 2015, 2014). Neuroinflammation during pregnancy may affect neuroapoptosis, myelination, as well as the synaptic pruning and maturation of the ventral tegmental area (VTA) leading to disruption of functions of frontal and prefrontal cortex responsible for cognitive function (Chiu

**Table 3**
Unadjusted and adjusted analyses of the association of residential distance from traffic with child CBCL and BARS NB outcomes (n = 174).

| Outcome Variables for Child Behavior or NB Performance | < 100 m b (95% CI) | 100-199 m b (95% CI) | ≥200 m b (95% CI) |
|---|---|---|---|
| *Positive coefficients (b) indicates higher behavioral problems with decreasing residential distance from traffic* | | | |
| Total CBCL Score | | | |
| Unadjusted Model | 6.34[a] (−0.50, 13.20) | 5.74 (−1.69, 13.17) | Reference Category |
| Adjusted Model | 6.31[a] (−0.55, 13.18) | 5.72 (−1.64, 13.11) | Reference Category |
| Externalizing Behavior CBCL Score | | | |
| Unadjusted Model | 1.94 (−0.39, 4.28) | 0.75 (−1.73, 3.28) | Reference Category |
| Adjusted Model | 2.14[a] (0.11, 4.47) | 0.86 (−1.65, 3.38) | Reference Category |
| Internalizing Behavior CBCL Score | | | |
| Unadjusted Model | 2.14 (−0.56, 4.84) | 3.49[b] (0.57, 6.42) | Reference Category |
| Adjusted Model | 2.09 (−0.60, 4.78) | 3.45[b] (0.56, 6.34) | Reference Category |
| Attention Problems CBCL Score | | | |
| Unadjusted Model | 0.57 (−0.82, 1.95) | 0.80 (−0.70, 2.30) | Reference Category |
| Adjusted Model | 0.64 (−0.80, 2.02) | 0.81 (−0.69, 2.33) | Reference Category |
| Social Problems CBCL Score | | | |
| Unadjusted Model | 0.84 (−0.28, 1.95) | 0.26 (−0.94, 1.47) | Reference Category |
| Adjusted Model | 0.70 (−0.42, 1.83) | 0.21 (−0.99, 1.42) | Reference Category |
| Thought CBCL Problems Score | | | |
| Unadjusted Model | 0.85 (0.06, 1.65) | 0.43 (−0.42, 1.29) | Reference Category |
| Adjusted Model | 0.77[c] (0.02, 1.57) | 0.39 (−0.46, 1.24) | Reference Category |
| *Positive coefficients (b) indicates lower NB performance with decreasing residential distance from traffic* | | | |
| Reaction Time Average Latency (ms) | | | |
| Unadjusted Model | 109.65[d] (5.76, 213.55) | 82.98 (−29.79, 195.74) | Reference Category |
| Adjusted Model | 81.83[a] (−7.31, 171.33) | 76.18 (−20.00, 172.35) | Reference Category |
| Symbol Digit Latency (ms) | | | |
| Unadjusted Model | 327.73 (−87.66, 743.33) | 22.82 (−428.27, 473.92) | Reference Category |
| Adjusted Model | 317.92 (−51.37, 687.21) | −26.19 (−422.93, 370.54) | Reference Category |
| Match to Sample Latency (ms) | | | |
| Unadjusted Model | 415.59[e] (154.59, 676.59) | 246.40 (−36.88, 529.70) | Reference Category |
| Adjusted Model | 410.27[b] (151.80, 670.00) | 226.44 (−53.38, 506.27) | Reference Category |
| Continuous Performance latency (ms) | | | |
| Unadjusted Model | 44.77[f] (11.32, 78.21) | 42.40[b] (6.10, 78.70) | Reference Category |
| Adjusted Model | 37.90[b] (5.77, 70.00) | 35.91[d] (1.40, 70.45) | Reference Category |
| *Negative coefficients (b) indicates lower NB performance with decreasing residential distance from traffic* | | | |
| Number of Taps (preferred hand) | | | |
| Unadjusted Model | −8.58[a] (−17.48, 0.32) | −0.61 (−10.26, 9.06) | Reference Category |
| Adjusted Model | −6.17 (−14.85, 2.53) | 1.05 (−8.28, 10.38) | Reference Category |
| Number of Taps (Non-preferred hand) | | | |
| Unadjusted Model | −5.41 (−13.33, 2.49) | −0.86 (−9.44, 7.72) | Reference Category |
| Adjusted Model | −3.31 (−10.61, 4.39) | 0.78 (−7.27, 8.84) | Reference Category |
| Number of Taps (Alternative hands) | | | |
| Unadjusted Model | −4.30 (−9.87, 1.25) | −2.43 (−8.47, 3.60) | Reference Category |
| Adjusted Model | −3.68 (−9.31, 1.93) | −1.96 (−8.00, 4.08) | Reference Category |
| Digit Span Forward (count) | | | |
| Unadjusted Model | 0.26 (−0.22, 0.75) | −0.08 (−0.60, 0.45) | Reference Category |
| Adjusted Model | 0.25 (−0.21, 0.72) | −0.07 (−0.57, 0.43) | Reference Category |
| Digit Span Backward (count) | | | |
| Unadjusted Model | 0.49 (−0.15, 1.15) | 0.38 (−0.32, 1.09) | Reference Category |
| Adjusted Model | 0.48 (−0.15, 1.13) | 0.42 (−0.26, 1.11) | Reference Category |
| Match to Sample (correct count) | | | |
| Unadjusted Model | −0.26 (−1.26, 0.72) | −0.61 (−1.68, 0.46) | Reference Category |
| Adjusted Model | −0.16 (−1.11, 0.79) | −0.48 (−1.51, 0.54) | Reference Category |
| Continuous Performance (fraction correct) | | | |
| Unadjusted Model | −0.04 (−0.09, 0.02) | 0.01 (−0.06, 0.0.09) | Reference Category |
| Adjusted Model | −0.03 (−0.10, 0.0.04) | 0.01 (−0.05, 0.0.08) | Reference Category |

Analyses adjusted for child age, gender, blood hemoglobin levels, and maternal education.
[a] p = 0.06.
[b] p = 0.02.
[c] p = 0.05.
[d] p = 0.04.
[e] p = 0.002.
[f] p = 0.01.

et al., 2016; Donev and Thome, 2010; Gillies et al., 2014). PM and UFP can also affect microglia, the resident macrophages in the developing brain (Chiu et al., 2016). Therefore, our findings from the study identifying cognitive and behavioral effects of PM exposure due to close proximity to traffic in older children is biologically plausible. What we do not know is whether these effects have occurred due to maternal exposure during pregnancy or due to chronic exposure at the residences of the children throughout the childhood.

Among the covariates used in our study, age and sex showed associations with the NB outcomes in expected directions. Girls demonstrated higher internalizing, social and thought problems than the boys. Similar findings were observed in previous studies conducted across multicultural settings (Achenbach et al., 2008; McKelvey et al., 1999). In contrast, higher externalizing behavior and attention problems were demonstrated by boys which were similar to the findings of several studies (Bird et al., 1988; McKelvey et al., 1999; Rescorla et al., 2007).

**Table 4**
Model covariates and neurobehavioral outcomes-CBCL (n = 174).

| Outcome Variables | Hemoglobin (g/dl) b (95% CI) | Age b (95% CI) | Sex (girls vs boys) b (95% CI) | Maternal Education (yrs) b (95% CI) |
|---|---|---|---|---|
| *Positive coefficients [b] indicate that behavior/NB performance is worse with increasing exposure* | | | | |
| *Externalizing Behavior Score** | −0.22 (−1.04, 0.61) | 0.32 (−0.20, 0.84) | −1.15 (−3.34, 0.74) | 0.21 (−0.03, 0.47) |
| *Internalizing Behavior Score** | −0.10 (−1.04, 0.85) | 0.20 (−0.39, 0.79) | 0.32 (−1.84, 2.49) | 0.40[a] (0.12, 0.69) |
| *Attention Problems Score** | −0.21 (−0.71, 0.28) | 0.10 (−0.21, 0.41) | −0.42 (−1.55, 0.72) | 0.10 (−0.-6, 0.24) |
| *Social Problems Score** | −0.10 (−0.50, 0.29) | 0.15 (−0.10, 0.40) | 0.62 (−0.28, 1.53) | 0.11[b] (0.01, 0.22) |
| *Thought Problems Score** | −0.30[c] (−0.57, -0.01) | 0.12 (−0.05, 0.30) | 0.30 (−0.34, 0.94) | 0.06 (−0.03, 0.14) |
| Reaction Time Average Latency (ms)* | −16.19 (−47.80, 15.41) | −26.40[a] (−46.11, -6.70) | 7.85 (−64.30, 80.0) | −2.33 (−11.92, 7.24) |
| Symbol Digit Latency (ms)* | −27.26 (−103.12, 157.65) | −301.15[e] (−380.46, -219.85) | 10.25 (−287.37, 307.90) | 16.38 (−23.13, 55.90) |
| Match to Sample Latency (ms)* | −52.10 (−144.07, 39.86) | −68.74[a] (−120.10, -11.40) | 31.51 (−176.41, 241.45) | −3.36 (−31.23, 24.51) |
| Continuous Performance latency (ms)* | 1.87 (−9.47, 13.23) | −11.10[e] (−18.16, -5.00) | 45.84[e] (19.93, 70.76) | −0.16 (−3.60, 3.28) |
| *Negative coefficients [b] indicate that behavior/NB performance is worse with increasing exposure* | | | | |
| Number of Taps (preferred hand) # | −0.20 (−3.27, 2.85) | 2.14[d] (0.22, 4.04)) | −12.44[e] (−19.44, -5.44) | −0.13 (−1.06, 0.80) |
| Number of Taps (Non-preferred hand) # | 0.03 (−2.68, 2.62) | 3.11[d] (1.46, 4.76) | −10.61[d] (−16.66, -4.56) | −0.27 (−1.05, 0.53) |
| Number of Taps (Alternative hands) # | −0.02 (−2.01, 1.97) | 1.22[b] (0.02, 2.46) | −2.54 (−7.07, 1.99) | −0.14 (−0.73, 0.46) |
| Digit Span Forward (count) # | 0.13 (−0.03, 0.30) | 0.17[e] (0.08, 0.27) | 0.31 (−0.07, 0.68) | −0.07[a] (−0.11, −0.02) |
| Digit Span Backward (count) # | 0.03 (−0.20, 0.25) | 0.29[e] (0.14, 0.43) | 0.10 -0.41, 0.62) | 0.01 (−0.06, 0.07) |
| Match to Sample (correct count) # | −0.10 (−0.43, 0.23) | 0.48[e] (0.27, 0.69) | −0.52 (−1.29, 0.24) | −0.02 (−0.12, 0.09) |

[a] p = 0.01.
[b] p = 0.05.
[c] p = 0.04.
[d] p = 0.03.
[e] p < 0.001.

However, it must be noted that the effects of sex on NB performance are inconsistent and results vary across populations. Several factors such as differences in exposure during childhood, outcome measures or instrument, social influences and statistical analyses can explain these inconsistencies (Mergler, 2012). It is difficult to explain which specific factor was associated with poorer NB performance in girls than the boys in our study. For all NB outcomes, our findings support the hypothesis that NB performance improves with age. This finding has been already reported in Hispanic children in the U.S. (Rohlman et al., 2007a, 2008).

The distribution of BARS neurobehavioral outcome variables are comparable to several child studies that have used batteries consisting of several tests used in the current study. For instance, a recent study on slightly younger Latino children in Oregon demonstrated similar distribution of BARS outcome variables although we observed slightly better mean NB performance in our sample since the range and mean for participants' age in our study sample were higher (range 8–14 vs 5–13 years; mean age 10.8 vs 8.4 years) (Butler-Dawson et al., 2016a).

Micronutrient deficiency is a major public health concern for low-income community children. Since iron is important for the synthesis of neurotransmitters and myelination of neurons, deficiency of iron and low levels of hemoglobin may affect NB performance, as shown in previous child studies (Kordas et al., 2004; Lozoff et al., 2006). Our study present similar evidence as we observed significantly negative relationships of serum hemoglobin, a marker of iron deficiency with one CBCL subscale and two NB outcomes of attention, information processing and visual memory (i.e. outcomes of reaction time and match to sample tests).

There are several strengths of the study. First, it used culturally adaptable and valid instruments to measure multiple functional outcomes of subtle NB effects. The Spanish version of the BARS was previously validated on sample of families who migrated from South American countries (Rohlman et al., 2001, 2007a). Second, the results demonstrated consistent evidence of PM-induced neurotoxicity across various functional domains such as visual memory, information processing speed, attention and behavior. Third, this is the only child study examining the effects of residential proximity to heavy traffic as proxy of traffic related air pollution on behavioral and cognitive outcomes. The use of adjusted blood hemoglobin as a potential covariate allowed us to measure the associations after controlling for an important micronutrient that plays vital roles in development and maturation of the brain.

Our study results may have limited "geographic generalizability" since our sample may not be representative of other low-income Ecuadorian communities. The findings may not be generalizable to children from other populations where PM levels are low. The cross-sectional design reduces our ability to examine causality inferences about the relationships between an air pollutant and multiple neurodevelopmental outcomes. Also, the current study did not consider measurement of individual level particulate matter exposure. Due to the absence of individual exposure data the possibility of exposure misclassification exists. It is known that distance from traffic is inversely correlated with road traffic noise levels. Epidemiological studies in various age groups of children have already reported associations of road and aircraft noise with sleep problems (Weyde et al., 2017a) and cognitive performance such as complex switching attention (van Kempen et al., 2010), inattention (Weyde et al., 2017b), memory and reading (Stansfeld and Clark, 2015). Traffic noise exposure was not measured in the present study, therefore, any potential confounding effect of traffic noise remained unknown. Future studies examining the impact of traffic distance on child neurobehavioral outcomes should therefore consider measurement of residential noise exposure. Furthermore, some other unmeasured nutritional and sociodemographic variables could have affected exposure-outcome relationships in the current study as reported in our prior study (Armijos et al., 2015).

The two BARS outcomes that were found significantly associated with residential proximity to traffic are measures of latency that may not be substantial enough to argue that both sustained attention and visual memory were simultaneously affected. However, a previous study on the characteristics of the BARS indicated that continuous performance and match to sample test latencies could reflect impairment of sustained attention and visual memory respectively (Rohlman et al., 2003). The other outcome measures of these two tests including continuous performance hit fraction and match to sample correct count also demonstrated non-significant associations with residential proximity to traffic indicating that both of neurobehavioral functions might have been affected by residential PM and UFP exposure. It is also possible that the differences in two latency outcomes may be due to reduced motor function in high and medium exposure groups as revealed by the non-significantly lower finger tapping test scores in the highest exposure group. Further investigations with larger samples are

needed to confirm the associations of PM and UFP exposures due to residential proximity to traffic with various domains of neurobehavioral functions reported in the current study.

## 5. Conclusion

This preliminary study presented associations of residential proximity to heavy traffic with worse neurobehavioral outcomes as measured by mother-reported CBCL and a computer NB test battery. Despite a relatively small sample size, the present study supports the hypothesis that living close to heavily trafficked roadways is detrimental to brain development in children. Future prospective studies with a larger sample size, long-term follow-up and residential PM assessment may help us confirm the findings, which may eventually help improve the current clean air policies.

## Transparency document

The Transparency document associated with this article can be found in the online version.

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