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## **Traffic-Related Air Pollution, Noise at School, and Behavioral Problems in Barcelona Schoolchildren: A Cross-Sectional Study**

Joan Forns,<sup>1,2,3,4</sup> Payam Dadvand,<sup>1,2,3</sup> Maria Foraster,<sup>1,2,3,5,6</sup> Mar Alvarez-Pedrerol,<sup>1,2,3</sup> Ioar Rivas,<sup>1,2,3,7</sup> Mònica López-Vicente,<sup>1,2,3,8</sup> Elisabet Suades-Gonzalez,<sup>1,2,3</sup> Raquel Garcia-Esteban,<sup>1,2,3</sup> Mikel Esnaola,<sup>1,2,3</sup> Marta Cirach,<sup>1,2,3</sup> James Grellier,<sup>1,2,3,9</sup> Xavier Basagaña,<sup>1,2,3</sup> Xavier Querol,<sup>7</sup> Mònica Guxens,<sup>1,2,3,10</sup> Mark J. Nieuwenhuijsen,<sup>1,2,3</sup> and Jordi Sunyer<sup>1,2,3,8</sup>

<sup>1</sup>Centre for Research in Environmental Epidemiology (CREAL), Barcelona, Catalonia, Spain;

<sup>2</sup>Universitat Pompeu Fabra, Barcelona, Catalonia, Spain; <sup>3</sup>CIBER Epidemiologia y Salud Pública (CIBERESP), Barcelona, Catalonia, Spain; <sup>4</sup>Department of Genes and Environment, Division of

Epidemiology, Norwegian Institute of Public Health, Oslo, Norway; <sup>5</sup>Swiss Tropical and Public Health Institute, Basel, Switzerland; <sup>6</sup>University of Basel, Basel, Switzerland; <sup>7</sup>Institute of Environmental Assessment and Water Research (IDAEA-CSIC), Barcelona, Catalonia, Spain;

<sup>8</sup>IMIM (Hospital del Mar Medical Research Institute), Barcelona, Catalonia, Spain; <sup>9</sup>Department of Epidemiology and Biostatistics, Imperial College London, UK; <sup>10</sup>Department of Child and Adolescent Psychiatry/Psychology, Erasmus University Medical Centre–Sophia Children’s Hospital, Rotterdam, the Netherlands

**Address correspondence to** Joan Forns, Centre for Research in Environmental Epidemiology (CREAL), C. Doctor Aiguader 88, 08003 Barcelona, Spain. Telephone: +34 93 214 73 11. E-mail: [jforns@creal.cat](mailto:jforns@creal.cat)

**Short running title:** Air pollution and noise on behavior

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## **ABSTRACT**

**Background:** The available evidence of the effects of air pollution and noise on behavioral development is limited and overlooks exposure at schools where children spend a considerable amount of time.

**Objective:** We aimed to investigate the associations of exposure to traffic-related air pollutants (TRAPs) and noise at school on behavioral development of schoolchildren.

**Methods:** We evaluated children aged 7 to 11 years in Barcelona (Catalonia, Spain) during 2012-2013 within the BREATHE project. Indoor and outdoor concentrations of elemental carbon (EC), black carbon (BC) and NO<sub>2</sub> were measured at schools in two separate one-week campaigns. In one campaign we also measured noise levels inside classrooms. Parents filled out the strengths and difficulties questionnaire (SDQ) to assess child behavioral development, while teachers completed the attention deficit hyperactivity disease criteria of DSM-IV (ADHD-DSM-IV) list to assess specific ADHD symptomatology. Negative binomial mixed effects models were used to estimate associations between the exposures and behavioral development scores.

**Results:** Interquartile range (IQR) increases in indoor and outdoor EC, BC and NO<sub>2</sub> concentrations were positively associated with SDQ total difficulties scores (suggesting more frequent behavioral problems) in adjusted multivariate models, while noise was significantly associated with ADHD-DSM-IV scores.

**Conclusion:** In our study population of 7–11 year old children residing in Barcelona, exposure to TRAPs at school was associated with more behavioral problems in schoolchildren. Noise exposure at school was associated with more ADHD symptoms.

## **INTRODUCTION**

There is a growing body of evidence on associations between pre- and postnatal exposure to traffic-related air pollutants (TRAPs) and adverse impacts on cognitive development in children (Block and Calderón-Garcidueñas 2009; Guxens et al. 2012; Guxens and Sunyer 2012; Suglia et al. 2008). Air pollution is considered as a suspected cause of developmental neurotoxicity (Grandjean and Landrigan 2014). In this context, TRAPs may also impact on behavioral development. The available evidence for such an effect is limited and mostly focused on attention deficit and hyperactivity disorder (ADHD) symptomatology, suggesting a positive association between prenatal (Perera et al. 2006, 2012) and early-life exposure to TRAPs (Newman et al. 2013) and ADHD. Only one study has reported a positive cross-sectional association between ADHD and TRAPs exposure during childhood (Siddique et al. 2011).

Like air pollution, noise is a ubiquitous environmental pollutant, mostly generated by traffic in urban areas (Moudon 2009). Noise has been associated with adverse impacts on quality of life and health, including mental health (Basner et al. 2014). It has been suggested that children are vulnerable to noise due to their reduced ability to manage environmental stressors (Ben-Shlomo and Kuh 2002). Therefore, efforts have been made to understand the impact of noise exposure on cognitive development (Stansfeld et al. 2005). Some studies have suggested that the negative impact of road traffic and aircraft noise at school and aircraft on cognitive development in children may exceed that of air pollution (Clark et al. 2012; Hygge et al. 2002; van Kempen et al. 2010, 2012). The available body of evidence on the associations of noise exposure on child behavioral development is limited, but associations have been reported between increased

hyperactive symptomatology and both traffic noise at home (Tiesler et al. 2013) and aircraft noise at school (Crombie et al. 2011; Stansfeld et al. 2005).

Most of the literature in this field is focused on children's residential exposures to these pollutants. However, children spend long periods of time at school, where levels of TRAPs and noise peak during the day (Kim et al. 2002; Ning et al. 2007). Teaching requires a quiet environment in classrooms. According to the World Health Organization's recommendation, a noise level < 35 dB in classrooms is considered as optimal. However, it is not unlikely that the noise levels exceeds this levels in some schools. (Berglund et al. 1999) The physical activity of children at school may be increased due to physical education classes, sports or play activities, and their breathing rates and dose of inhaled pollutants to the lungs may increase during school hours (McConnell et al. 2010). The present study aimed at investigating the association between levels of TRAPs and noise at school and behavioral developmental in schoolchildren.

## **METHODS**

### *Study setting*

This study was carried out as part of the BRain dEvelopment and Air polluTion ultrafine particles in scHool childrEn (BREATHE) project, which aims to study associations between air pollution and neuropsychological development of schoolchildren. Schools were selected based on modeled levels of traffic-related nitrogen dioxide (NO<sub>2</sub>) in order to achieve maximum contrast in TRAP levels (Wang et al. 2013). Thirty-six of the 416 schools in Barcelona were selected. Three additional schools in an adjacent municipality, Sant Cugat del Vallès, were included in BREATHE (39 schools in total). All participating schools were similar to the

remaining schools in Barcelona in terms of the socioeconomic vulnerability index (0.66 versus 0.62,  $p=0.20$ ) and  $\text{NO}_2$  levels (51.5 versus  $50.9 \mu\text{g}/\text{m}^3$ ,  $p=0.81$ ).

All families of children without special needs from these 39 schools in the 2<sup>nd</sup>, 3<sup>rd</sup> and 4<sup>th</sup> primary grades were invited to participate in the study by letter and/or presentations in schools. A total of 2897 (59%) enrolled in the study. All children had been at the school for more than 6 months (and 98% for more than one year) before the beginning of the study. We observed similar participation rates across classes. Participation rates were similar across classes (62%, 61%, and 62% for 2<sup>nd</sup>, 3<sup>rd</sup>, and 4<sup>th</sup> grades, respectively,  $p = 0.96$ ). Participation rates were similar according to the school vulnerability index (62% and 61% for higher and lower school vulnerability index, respectively,  $p = 0.326$ ), but not between public (52%) and private schools (66%) ( $p<0.01$ ). Parents or legal guardians of all participating children gave their informed consent as approved by the IMIM-Parc Salut Mar Ethical Committee (No. 2010/41221/I).

## *Exposure*

### **School air pollution measurement**

For each school, TRAP levels were measured twice during one-week periods separated by six months, in the warm and cold periods of the year 2012. In each campaign week, we measured TRAP levels in two schools simultaneously: one located in an area with high levels of pollution, and one in area with low levels. Levels of TRAPs were measured simultaneously indoors in a single classroom and outdoors in the school yard. We selected measured elemental carbon (EC), black carbon (BC), and  $\text{NO}_2$ , given their relation high correlation to road traffic emissions in Barcelona (Amato et al. 2014; Reche et al. 2014; Rivas et al. 2014). Initially, we also considered

concentrations of traffic-related particulate matter with aerodynamic diameter  $\leq 2.5\mu\text{m}$  ( $\text{PM}_{2.5}$ ) (composed of organic particles from motor exhaust, EC, and metals from brake wear (Cu, Sb, Sn and Fe)) as another measure of exposure to TRAPs. However, given the high correlation between EC and traffic-related  $\text{PM}_{2.5}$  concentration (Spearman Rho = 0.93) and the consistency of our results for these two measures, only the results for EC are included in this manuscript. EC levels were determined based on chemical analysis of daily 8-hour  $\text{PM}_{2.5}$  samples collected by high volume ( $30\text{ m}^3/\text{h}$ ) MCV samplers. Real time concentrations of BC were measured using the MicroAeth AE51 aerosol monitor (AethLabs). Weekly averaged  $\text{NO}_2$  concentrations were measured using Gradko Environmental passive dosimeters.

Annual outdoor and indoor school levels were obtained by averaging the results of the two campaigns. Since different schools were monitored in different weeks during each campaign period, we adjusted the levels of each TRAP for the weekly average level of that TRAP (during the corresponding sampling week for each school) measured by a background monitoring station in Barcelona to remove temporal fluctuation in background TRAP levels from our analyses (Rivas et al. 2014).

### **Noise measurement**

Traffic noise in the classroom (from now on referred to as noise) was selected as a surrogate of noise exposure because children spend most of their time at school in the classroom, and also because susceptibility to the cognitive effects of traffic noise might be greater during teaching sessions (Basner et al. 2014). Data was obtained from comprehensive noise measurements taken during the second one-week air pollution sampling period. Noise measurements were conducted during the second week of the air pollution sampling period in a single classroom for each

school. We installed the noise monitoring instrument in a classroom next to the classroom where the TRAPs measurement was performed to avoid the noise from the TRAPs monitors while having comparable measures in terms of orientation and floor. Three consecutive 10-minute measurements of equivalent sound pressure levels (in dB(A)) at different distributed locations within the classroom were performed over two consecutive days, following recommended protocols (Decret 176/2009 de la Generalitat, Annex 7.II.B, ISO 1996, and ISO 140-4) using a calibrated SC-160 sound level meter (CESVA, inc;  $\pm 1.0$  dB tolerance (type 2), range: 30-137 dB). As we aimed to register traffic and background noise levels, any unusual sounds were deleted and measurements were done before children arrived (before 9am). For robustness, we averaged the 30-minute measurements from the two consecutive days, though they showed high reproducibility.

### ***Behavioral development***

General behavioral development was assessed using the strengths and difficulties questionnaire (SDQ) (Goodman 1997) which was filled out by parents. The SDQ is comprised of five separate sub-scales, each including five questions (25 questions in total) covering different behavioral aspects including emotional symptoms, conduct problems, hyperactivity/inattention, peer relationship problems and prosocial behavior. Each question can be rated on a 3-point Likert scale (not true (0), somewhat true (1), and certainly true (2)) and each subscale can therefore be scored between 0 and 10. A total difficulties score (ranging from 0 to 40) is then generated by summing the scores for all subscales except the prosocial behavior scale, with higher scores indicating more behavioral problems. Prosocial subscale is considered as a behavioral strength.

We inverted the original distribution of the prosocial behavior scale in order to harmonize the interpretation of the sub-scales (higher score meaning less prosocial behavior).

Specific ADHD symptomatology was reported by teachers filling out the ADHD Criteria of Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (ADHD-DSM-IV) list (American Psychiatric Association 2002). ADHD-DSM-IV consists of 18 symptoms categorized into two separate groups: inattention (nine symptoms) and hyperactivity/impulsivity (nine symptoms). Each ADHD symptom is rated on a 4-point scale (0 = never or rarely, 1 = sometimes, 2 = often, or 3 = very often) and subscales can therefore be scored from 0 to 27 and the global ADHD symptomatology score can range from 0 to 54, where higher numbers indicate more problems.

### ***Other variables***

Sociodemographic data including child age, sex (male and female) and maternal education (primary, secondary and university) were collected by the BREATHE baseline questionnaire, which was filled out by parents. In the same questionnaire, parents were asked whether their children had been clinically diagnosed with ADHD by a medical doctor. We also included a question regarding traffic noise annoyance at home using a 11-point scale question developed by the International Commission on the Biological Effects of Noise (ICBEN) (Fields et al. 2001). For each home and school address, we extracted the Urban Vulnerability Index, which is a measure of neighborhood SES at the census tract level (median area of 0.08 km<sup>2</sup> for the study area). This index is based on 21 indicators of urban vulnerability grouped into four themes that has been developed based on the 2001 Spanish census data: sociodemographic vulnerability (five indicators), socioeconomic vulnerability (six indicators), housing vulnerability (five indicators),

and subjective perception of vulnerability (five indicators). Annual air pollution concentrations (BC) at the participants' home addresses were estimated by temporally-adjusted land-use regression (LUR) models developed as part of the European Study of Cohorts for Air Pollution Effects (ESCAPE) project (Beelen et al. 2013; Eeftens et al. 2012). To explore the comparability of levels of TRAPs measured by BREATHE monitors at schools and levels of TRAPs estimated using ESCAPE LUR mod

els, we applied ESCAPE LUR models to estimated NO<sub>2</sub> and BC outdoor levels at schools during the corresponding BREATHE sampling weeks for that school. We observed Spearman's correlation coefficients of 0.81 and 0.75 for NO<sub>2</sub> and BC, respectively, measured by BREATHE monitors and estimated by ESCAPE LUR models.

### ***Statistical analysis***

#### **Main analyses**

We estimated associations of indoor and outdoor levels of TRAPs (EC and NO<sub>2</sub>) and noise on the total difficulties score from SDQ and on the total ADHD symptomatology from ADHD-DSM-IV list (one at a time) in two sets of models: single-exposure models, using noise and TRAP levels as the exposure one at a time in separate models; and multi-exposure models, which included each TRAP and noise together in the same model. Negative binomial mixed effects models (including school and teacher as random effects for SDQ and ADHD-DSM-IV list, respectively) were used to address the multilevel nature of the data and to account for over-dispersion of the outcomes. Negative binomial model models the ratio of the mean score among exposed and non-exposed. The results are presented as adjusted mean ratios (aMR) with

corresponding 95% confidence intervals (95% CI). In all of these models, the exposure estimate was reported for one interquartile range (IQR) increase in exposure levels, e.g. a ratio of mean score of 1.15 for an IQR increase in EC exposure meant that those with an EC exposure at the 75th percentile had a 15% higher mean score, as compared with those with an EC exposure at the 25th percentile. The analyses were adjusted for a number of covariates identified *a priori*: child's sex (male/female), child's age (continuous in years), BC concentrations at home (continuous as  $\mu\text{g}/\text{m}^3$ ), traffic noise annoyance at home (continuous ranging from 0 to 10, from the less to the highest annoyance), home tobacco use (no, yes but not inside home, yes), and indicators of SES at the individual level [maternal education (primary or less, secondary, or high educational level) and the Urban Vulnerability Index at home address (continuous variable ranging from 0 to 1, with 1 indicating the highest level of deprivation)] and the area level [Urban Vulnerability Index for the child's school and the type of school (public/private)].

### **Further and sensitivity analyses**

Because of the rather high correlation between TRAPs and noise, we evaluated the potential multicollinearity using the Multilevel Variance Inflation Factors (MVIFs). In addition, we tested for potential effect modification by noise (low noise ( $<35\text{dB}$ ); high noise ( $\geq 35\text{ dB}$ )) in the association between TRAPs and the total difficulties score from SDQ and on the total ADHD symptomatology from ADHD-DSM-IV list. We included the product term between TRAPs and the effect modifier, considering  $p < 0.05$  as the cut-off for interaction.

We further adjusted (one at a time) our main analyses for maternal occupation (self-employed, employee, housewife, student, on work leave, unemployed or unknown), paternal education (primary or less, secondary, or higher educational level), siblings at birth (no/yes), smoking

during pregnancy (no/yes), alcohol consumption during pregnancy (no/yes) and duration of breastfeeding (no breastfeeding, <1 week, 1week to 3 months, 3 months to 6 months, and >12 months) to evaluate the robustness of our findings to inclusion of more SES-related or biologically-relevant covariates. We repeated the main models, stratifying by high- and low-polluted schools based on the previously modeled NO<sub>2</sub> to explore a potential variation in the associations across these schools. ESCAPE land use regression models (Beelen et al. 2013) were applied to estimate the annual (2009) NO<sub>2</sub> levels at schools and schools were categorized as high or low polluted if their NO<sub>2</sub> levels were below or above the median of all the schools participating in the BREATHE project

We also estimated associations between TRAPs and noise at school with the five SDQ sub-scales and the two ADHD-DSM-IV list subscales. We further estimated associations with BC at each child's home address using estimates from ESCAPE land use regression models (Eeftens et al. 2012).

Finally, we repeated the main analysis but restricted it to those children attending the same school from the age of 3 years and younger (n=2192 (81%)), to explore possible chronic associations of the reported associations.

Statistical analyses were carried out with Stata 12 (Stata Corporation, College Station) and R (R Core Team 2013).

## **RESULTS**

Sociodemographic characteristics of the study sample are presented in table 1. Six percent of children were reported as clinically diagnosed with ADHD. The median scores for SDQ total

difficulties was 8 and for SDQ subscales ranged from 1 to 3 (Table 2). For ADHD symptomatology, the median score was 5 for total, 3 for inattention, and 1 for hyperactivity-impulsivity (Table 2).

Regarding the exposure, EC and BC concentrations were almost the same indoors and outdoors while the outdoor concentrations of NO<sub>2</sub> were higher than the indoor concentrations (Table 2). The median (IQR) indoor noise was 38 (8) dB. The Spearman correlation coefficient between school TRAPs levels ranged between 0.71 and 0.97 (Table 3). Noise showed moderate correlations with school TRAPs levels with correlation coefficients ranging between 0.38 and 0.45 (Table 3).

Median SDQ total difficulties scores were higher for children attending public versus private schools (9.03 and 7.80, respectively,  $p = 0.017$ ) (see Supplemental Material, Table S1). We found higher scores in SDQ for those children attending schools with medium vulnerability index values (median SDQ score = 9.17) compared to those children attending school with low (median SDQ score = 7.77) and high (median SDQ score = 8.58) values. ADHD symptomatology scores were not significantly associated with the type of school or school vulnerability index.

### ***Main analysis***

In single-exposure models (Table 4), higher levels of TRAPs were generally associated with higher SDQ total difficulties scores with statistically significant associations for an IQR increase in indoor EC (IQR = 1.01  $\mu\text{g}/\text{m}^3$ ) (adjusted Mean Ratio (aMR) = 1.07; 95% Confidence Interval (CI): 1.01, 1.12), outdoor EC (IQR = 0.85  $\mu\text{g}/\text{m}^3$ ) (aMR = 1.07; 95%CI: 1.03, 1.12) and outdoor

NO<sub>2</sub> (IQR = 22.26 µg/m<sup>3</sup>) (aMR = 1.07; 95%CI: 1.01, 1.14). Noise was not associated with the SDQ total difficulties score (Table 4). In the multi-exposure models, we observed the same pattern of results. Because of the high correlation between EC and BC (Spearman Rho = 0.97), and since associations for BC were identical than those obtained for EC, we only present associations for EC.

We observed higher ADHD symptomatology in association with an IQR increase in noise (IQR = 7.60 dB)(aMR = 1.22; 95%CI: 1.11, 1.34) in the single-exposure models (Table 4). None of the TRAPs were statistically associated with ADHD symptomatology in the single-exposure models. In the multi-exposure models, we observed a stronger positive association between noise (an IQR increase) and ADHD symptomatology (aMRs = 1.24 to 1.29). The associations for TRAPs remained non-significant in the multi-exposure models with the exception of the association with indoor EC, for which a statistically significant inverse relationship was found (Table 4). Results for BC were the same as the results obtained for EC (data not shown).

### ***Further and sensitivity analyses***

The MVIFs for TRAPs and noise when combined in two-exposure models for both outcomes ranged between 1.29 and 1.45 (as a rule of thumb MVIF > 10 is suggestive for multicollinearity) (See Supplemental material, Table 2). The interaction between noise and TRAP was statistically significant only for the association between indoor NO<sub>2</sub> and ADHD symptomatology [aMR = 0.93; 95% CI: 0.72, 1.19 versus 1.11; 95% CI: 1.02, 1.22 when stratified by low (< 35 dB) and high noise, respectively, p = 0.03], otherwise associations with TRAPs were similar when stratified by noise (see Supplemental material, Table S3).

Our findings did not change meaningfully after further adjusting for SES-related or biologically-relevant covariates (data not shown). When we stratified the main analyses by high and low polluted schools based on the previous measure of NO<sub>2</sub>, we observed similar results (data not shown).

We found similar positive associations for most SDQ sub-scales, particularly for hyperactivity/inattention, peer relationship problems and prosocial behavior in association with EC indoor and outdoor and NO<sub>2</sub> outdoor (See Supplemental Material, Figure S1). Similarly, the results for the ADHD-DSM-IV subscales were similar to those for the overall ADHD symptomatology scores, with positive associations between noise and both inattentiveness and hyperactivity (Supplemental Material, Figure S2). Noise was associated with increased symptomatology of inattentiveness and hyperactivity. Concentrations of BC at each child's home address using estimates from ESCAPE land use regression models were not associated with either behavioral problems or with ADHD symptomatology (See Supplemental material, Table S4). When we restricted the main analysis to those children attending the same school since 3 years of age and younger n=2192 (81%), we observed similar results to those reported for the main analysis (See Supplemental material, Table S5).

## **DISCUSSION**

To our knowledge, this is the first study to evaluate the impact of air pollution on behavioral development in schoolchildren using both indoor and outdoor air pollution levels measured at schools. We found a consistent pattern of positive associations between exposure to indoor and outdoor EC, BC, and, to a lesser extent, NO<sub>2</sub> and SDQ scores for general behavioral development. Noise was not associated with general behavioral development (i.e. SDQ) scores,

but was positively associated with ADHD symptom scores. In contrast, TRAPs exposures were not associated with ADHD symptom scores.

TRAPs concentrations at school were positively associated with SDQ scores for general behavioral development in schoolchildren after taking levels of residential air pollution into account. These results persisted after adjusting our final models by noise. The results remained unchanged after restricting the analysis to those children attending the same school since early in life. Our analytical strategy (also including subscales from SDQ and ADHD-DSM-IV in the further analysis) allowed us to conduct several comparisons. We are not aware of any available report on the negative impacts of exposure to air pollution (EC, BC and NO<sub>2</sub>) during childhood on general behavioral development assessed by SDQ scores; therefore, it is not possible to compare our findings with those of others. However, our findings are consistent with several previous observations assessing air pollution early in life. Hyperactivity symptom scores at age 7 years were higher in association with elemental carbon exposures during the first year of life in a cohort of US children (Newman et al. 2013). In a cross-sectional study conducted in India (Siddique et al. 2011), children living in urban areas (with higher concentrations of PM<sub>10</sub>) showed a fourfold rise in the prevalence of ADHD (assessed using the ADHD-DSM-IV list) compared to those children living in rural areas. ADHD symptom scores were not positively associated with TRAPs exposures in our cross-sectional study population. Unexpectedly, indoor EC exposure was negatively associated with ADHD symptom scores when adjusted for noise. We do not have a causal explanation for this finding, which may have been due to chance or bias.

A number of underlying mechanisms have been hypothesized for the observed negative associations between TRAPs and brain development (Block et al. 2012). Neuroinflammation implicating microglia has been proposed to play a central role (Block and Calderón-Garcidueñas 2009; Hanisch and Kettenmann 2007). In two studies conducted in Mexico, autopsies of 35 healthy children and young adults living in Mexico City (considered as exposed group) and about 12 healthy children and young adults living in a low polluted town (considered as control group) were evaluated. Compared to the control group, the exposed group showed a significant upregulation of some important inflammatory genes in several brain regions was found, as well as disruption of the blood-brain-barrier, endothelial activation, oxidative stress, inflammatory cell trafficking, and accumulation of ultrafine particles in the respiratory nasal epithelium, olfactory bulb neurons and the endothelium and basement membranes of olfactory bulb arterioles (Calderón-Garcidueñas et al. 2008, 2010). It has also been suggested that exposure to diesel exhaust particles may induce apoptosis of dopaminergic neurons in the presence of microglia (Block et al. 2004).

In our study, 74.4% of children were exposed to levels of noise greater than the 35dB recommended for teaching environments (Berglund et al. 1999). We detected a positive association between noise exposure at school and ADHD symptomatology. In the multi-exposure models, we detected some evidence of confounding of noise associations by TRAPs. The available evidence on the impact of noise on behavioral development is limited. In two studies, the authors found increased the SDQ hyperactivity subscale associated with aircraft noise at school in children aged from 9 to 10 years old (Crombie et al. 2011; Stansfeld et al. 2009). . In the most recent study, the authors reported an increased SDQ hyperactivity score associated with

road traffic noise exposure at home in children aged 10 years old (Tiesler et al. 2013). In our study population noise exposure was positively associated with ADHD symptom scores (ADHD-DSM-IV), but not with the SDQ hyperactivity score.

A number of mechanisms might contribute to associations between noise exposure and ADHD symptomatology (Stansfeld et al. 2005). These include noise annoyance (when noise interferes the daily activities –i.e. teaching sessions – and usually accompanied by negative responses), increased arousal and frustration (Basner et al. 2014; Evans 2006). It has also been suggested that exposure to high levels of noise may produce externalizing symptomatology (i.e. ADHD symptoms) rather than internalizing symptomatology (i.e. depressive symptoms) as a consequence of increased arousal (Haines et al. 2001).

The results of the present study should be interpreted in the context of its limitations. We could not confirm that exposure preceded the outcomes given the cross-sectional design of our study. There was a short interval between measurement of TRAPs and the assessment of behavioral development. BREATHE measurements (made at the school level) were deseasonalized according to annual levels during the same year (2012) that the questionnaires were filled out. The LUR models were developed on ESCAPE measurements conducted in 2009, prior to the start of the BREATHE project. The generalizability of our findings may have been affected by selection bias in that those children that participated in BREATHE were different to those who did not participate with respect to maternal educational level. About 60% of mothers in our study population had a university degree: higher than the regional average of 50% among women between 25 and 39 years old living in Barcelona (Ajuntament de Barcelona 2014). Although ADHD has been shown to be more prevalent among SES disadvantaged groups (Russell et al.

2013), the prevalence of ADHD cases in our sample (6.5%) was similar to the prevalence of ADHD in Spain (6.8%)(Catalá-López et al. 2012). Conversely, the sex distribution among the BREATHE participants (50%) was very similar to the regional average in the same age group (5 to 9 years), and therefore, increases the generalizability of our results. Moreover, the Urban Vulnerability Index of the schools was not associated with the school participation rate (Spearman's correlation coefficient=-0.09, p-value=0.61) which might suggest that socioeconomic status was less likely to be a major predictor of participation. Another limitation might be the potential for residual SES confounding (Klassen et al. 2004; Russell et al. 2013). However, we adjusted our analyses for indicators of SES at both individual (maternal education) and area (SES vulnerability index) levels, and adjusting for additional SES variables did not result in any notable change in associations (data not shown). As in previous studies, the quality of the assessment of noise exposure may have been limited. Because special attention is given to noise levels during teaching sessions, when noise may be most detrimental (Basner et al. 2014), we examined road traffic noise exposure in classrooms. This represented an improvement compared to previous studies, which have generally relied on a single modeled or measured outdoor noise level in front of the school. However, our noise measurements were each made in a single classroom in each school. However, in getting closer to measuring the true personal indoor environment, our assessment is also subject to exposure misclassification because of the high dependency of classroom street orientation on the actual noise exposure.

In our study population, SDQ scores were positively associated with TRAPs exposures, whereas ADHD-DSM-IV scores were positively associated with noise exposure. In our study, SDQ was rated by parents while ADHD-DSM-IV questionnaire was rated by teachers. This approach does

not allow us to compare the results obtained from the two scales. The use of two scales may, however, provide better comprehensive information on behavioral development. While ADHD-DSM-IV is a questionnaire used for in-depth assessment of ADHD symptomatology, the SDQ is a screening questionnaire used for detecting general behavioral developmental problems including hyperactivity and attentional problems as only one of several outcomes. In addition, it has been suggested that the combination of parents' and teachers' reports is more sensitive to detect behavioral problems than either alone when compared with independent psychiatric assessments (Goodman et al. 2000). Results from previous studies suggested that parents reported behavioral problems more frequently and of greater severity and therefore, the agreement between parents and teachers has been considered as poor to moderate (Dirks et al. 2011; Gomez 2007).

Estimated associations between TRAPs and the SDQ total difficulties score were statistically significant and consistent, but the magnitude of the associations were small Adjusted mean ratios used to estimate associations between behavior scores and the exposures suggest a 7–8% increase in scores with IQR increases in TRAPs, where each score can be considered a “count” of prevalent symptoms, and the median total difficulties score was 8 (range 0–32). Therefore, the results presented in this study could have a non-negligible societal impact given the link between the total difficulties score of SDQ and worse child mental health (Vostanis 2006). A similar explanation might be applied to the observed association between noise in schools and ADHD symptomatology.

## **CONCLUSION**

The results of this study suggest that higher levels of TRAPs (EC, BC and NO<sub>2</sub>) at school are associated with worse general behavioral development in schoolchildren. We also observed increased ADHD symptomatology associated with noise levels at school. Further assessments of the schools' air quality, noise level, and child behavioral development are warranted to assess the temporality of the potential causal relationship. If confirmed, the public health implications of these findings would be of great importance considering the substantial personal and societal burden accompanying such behavioral problems.

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Table 1. Characteristics of the study population of the BREATHE project:

Variables	n	(%)
Child's age (in years), <i>mean (SD)</i>	8.55	(0.88)
Child's grade		
2nd	1076	(37.4)
3rd	1028	(35.7)
4th	772	(26.8)
Sex		
Male	1446	(50.3)
Female	1430	(49.7)
Clinical diagnosis of ADHD by medical doctor		
No	2544	(93.5)
Yes	176	(6.5)
Maternal education		
Primary or less	346	(12.7)
Secondary	781	(28.7)
University	1596	(58.6)
Urban Vulnerability Index at home address		
Less deprived	1061	(37.2)
Normal deprived	1301	(45.6)
High deprived	491	(17.2)
Type of school		
Public	1031	(35.9)
Private	1845	(64.2)

Table 2. Univariate description of the outcomes (at individual level) and the exposures (at school level):

Variables	min	25 <sup>th</sup> percentile	Median	75 <sup>th</sup> percentile	Max
<b>Outcomes at individual level</b>					
SDQ (n=2.714)					
Total difficulties score	0	4	8	11	32
Emotion symptoms	0	1	2	3	10
Conduct problems	0	0	2	3	10
Hyperactivity/Inattention	0	2	3	5	10
Peer relationship problems	0	0	1	2	9
Prosocial behavior	0	0	1	2	9
ADHD-DSM-IV (n=2.805)					
ADHD symptomatology	0	1	5	12	54
Inattentive symptomatology	0	0	3	8	27
Hyperactive symptomatology	0	0	1	4	27
<b>Exposure at school level (n=39)</b>					
Indoor (µg/m <sup>3</sup> )					
EC	0.44	0.77	1.19	1.77	3.47
BC	0.60	1.00	1.37	1.86	3.30
NO <sub>2</sub>	11.47	21.58	29.82	42.60	65.65
Outdoor (µg/m <sup>3</sup> )					
EC	0.58	1.02	1.33	1.88	3.90
BC	0.65	1.13	1.33	1.75	3.38
NO <sub>2</sub>	25.92	35.10	48.46	57.37	84.55
Noise					
Indoor (dB)	28.80	34.00	38.00	42.00	51.10
<b>Exposure at home address - individual level (n=2.805)</b>					
BC (µg/m <sup>3</sup> )	0.86	2.17	2.63	3.06	5.45

Table 3. Spearman correlation coefficients between TRAPs at school ( $\mu\text{g}/\text{m}^3$ ) and the noise at school (dB):

	School TRAPs						Noise
	Indoor			Outdoor			
	EC	BC	NO <sub>2</sub>	EC	BC	NO <sub>2</sub>	
Indoor							
EC	-						
BC	0.97*						
NO <sub>2</sub>	0.78*	0.74*	-				
Outdoor							
EC	0.88*	0.88*	0.71*	-			
BC	0.89*	0.87*	0.78*	0.97*	-		
NO <sub>2</sub>	0.84*	0.82*	0.76*	0.85*	0.84*	-	
Noise	0.45*	0.40*	0.38*	0.39*	0.42*	0.42*	-

\*p-value<0.05

Table 4. Adjusted mean ratios (aMRs and 95% CIs) of SDQ total difficulties score and ADHD symptomatology (from ADHD-DSM-IV) for TRAPs exposure at school ( $\mu\text{g}/\text{m}^3$ ) and noise at school (dB) as continuous variable (based on an IQR increase):

Variables	EC and Noise		NO <sub>2</sub> and Noise	
	EC indoor IQR = 1.01 $\mu\text{g}/\text{m}^3$ EC outdoor IQR = 0.86 $\mu\text{g}/\text{m}^3$	Noise IQR = 7.60 dB	NO <sub>2</sub> indoor IQR = 21.01 $\mu\text{g}/\text{m}^3$ NO <sub>2</sub> indoor IQR = 22.26 $\mu\text{g}/\text{m}^3$	Noise IQR = 7.60 dB
<b>Total difficulties score (SDQ)<sup>a</sup></b>				
Indoor				
Single-exposure	1.07 (1.01, 1.12)*	1.01 (0.96, 1.07)	1.02 (0.96, 1.08)	1.01 (0.96, 1.07)
Multi-exposure	1.08 (1.02, 1.14)**	0.98 (0.92, 1.04)	1.02 (0.95, 1.10)	1.01 (0.94, 1.07)
Outdoor				
Single-exposure	1.07 (1.03, 1.12)**	1.01 (0.96, 1.07)	1.07 (1.01, 1.14)*	1.01 (0.96, 1.07)
Multi-exposure	1.08 (1.03, 1.13)**	0.97 (0.92, 1.03)	1.08 (1.01, 1.16)*	0.98 (0.92, 1.04)
<b>ADHD symptomatology (DSM-IV)<sup>b</sup></b>				
Indoor				
Single-exposure	0.96 (0.89, 1.03)	1.22 (1.11, 1.34)**	1.08 (0.99, 1.17)	1.22 (1.11, 1.34)**
Multi-exposure	0.89 (0.82, 0.96)*	1.29 (1.18, 1.43)**	0.98 (0.89, 1.08)	1.24 (1.12, 1.38)**
Outdoor				
Single-exposure	0.99 (0.93, 1.07)	1.22 (1.11, 1.34)**	1.03 (0.94, 1.13)	1.22 (1.11, 1.34)**
Multi-exposure	0.94 (0.87, 1.01)	1.27 (1.15, 1.40)**	0.94 (0.85, 1.04)	1.26 (1.14, 1.39)**

\*p-value<0.05; \*\*p-value<0.001

- Single-exposure models including TRAPs (EC and NO<sub>2</sub>) were adjusted for sex, child's age, maternal education, urban vulnerability index at home address, air pollution (black carbon) at home, home tobacco use, urban vulnerability index at school and type of school.
- Single-exposure models including noise were adjusted for sex, child's age, maternal education, urban vulnerability index at home address, traffic noise annoyance at home, home tobacco use, urban vulnerability index at school and type of school.

- Multi-exposure models including TRAPs and noise were adjusted for sex, child's age, maternal education, urban vulnerability index at home address, air pollution (black carbon) at home, traffic noise annoyance at home, home tobacco use, urban vulnerability index at school and type of school.

<sup>a</sup>Including school as random effect

<sup>b</sup>Including teacher as random effect