Traffic-related Air Pollution and Attention in Primary School Children

Short-term Association

Jordi Sunyer,[a,b,c,d] *Elisabet Suades-González,*[a,b,c,e,f] *Raquel García-Esteban,*[a,b,c] *Ioar Rivas,*[a,b,c,f]
Jesús Pujol,[g] *Mar Alvarez-Pedrerol,*[a,b,c] *Joan Forns,*[a,b,c] *Xavier Querol,*[f] *and Xavier Basagaña*[a,b,c]

Background: Although air pollution's short-term effects are well understood to be marked and preventable, its acute neuropsychological effects have, to our knowledge, not yet been studied. We aim to examine the association between daily variation in traffic-related air pollution and attention.

Methods: We conducted a follow-up study from January 2012 to March 2013 in 2,687 school children from 265 classrooms in 39 schools in Barcelona (Catalonia, Spain). We assessed four domains of children's attention processes every 3 months over four repeated visits providing a total of 10,002 computerized tests on 177 different days using the child Attention Network test (ANT). Ambient daily levels of nitrogen dioxide (NO_2) and elemental carbon (EC) in particulate matter <2.5 µm ($PM_{2.5}$) filters were measured at a fixed air quality background monitoring station and in schools.

Results: Daily ambient levels of both NO_2 and EC were negatively associated with all attention processes (e.g., children in the bottom quartile of daily exposure to ambient NO_2 levels had a 14.8 msecond [95% confidence interval, 11.2, 18.4] faster response time than those in the top quartile, which was equivalent to a 1.1-month [0.84, 1.37] retardation in the natural developmental improvement in response speed with age). Similar findings were observed after adjusting for the average indoor (classroom) levels of pollutants. Associations for EC were similar to those for NO_2 and robust to several sensitivity analyses.

Conclusions: The short-term association of traffic-related air pollutants with fluctuations in attention adds to the evidence that air pollution may have potential harmful effects on neurodevelopment. See video abstract at, http://links.lww.com/EDE/B158.

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Urban air pollution is associated with acute (short-term) and chronic (long-term) stroke and other cardiovascular and respiratory effects.[1–4] Chronic exposure to urban air pollutants have also been associated with neuropsychological and behavioral effects.[5] In addition to vascular effects, air pollution could cause brain damage through neuroinflammation, glial activation, and white matter injury.[6] While air pollution is believed to have a marked preventable acute impact in addition to chronic effects,[7] its acute neuropsychological effects have to our knowledge not yet been studied.

We previously reported an association between long-term exposure to traffic pollution and attention and working memory development in school children.[8] Attention processes fluctuate daily in response to individual characteristics (e.g., medications and other central nervous system stimulants like glucose or caffeine) and environmental or situational variables, such as noise, temperature, and time of day.[9,10] These acute fluctuations may have an important impact on learning and academic achievement in school children by fostering inattention, forgetfulness, disorganization, and careless errors.[10,11]

The hypothesis that air pollution is a neurodevelopmental toxicant has not yet been properly evaluated because of the limitations of conducting studies in the general population (e.g., exposure assessment and residual confounding).[12] Assessment of acute associations is more robust to exposure misclassification and to residual confounding than chronic associations.[13] The analysis of acute associations has the advantage that it is not sensitive to participants' individual or social characteristics, because these characteristics do not change over time.[13]

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From the [a]ISGlobal, Centre for Research in Environmental Epidemiology (CREAL), Barcelona, Catalonia, Spain; [b]Pompeu Fabra University, Barcelona, Catalonia, Spain; [c]Consortium for Biomedical Research in Epidemiology and Public Health (CIBERESP), Madrid, Spain; [d]Institut Hospital del Mar d'Investigacions Mèdiques–Parc de Salut Mar, Barcelona, Catalonia, Spain; [e]Learning Disabilities Unit (UTAE), Neuropediatrics Department, Hospital Sant Joan de Déu, Universitat de Barcelona, Catalonia, Spain; [f]Institute of Environmental Assessment and Water Research (IDAEA-CSIC), Barcelona, Catalonia, Spain; and [g]MRI Research Unit, CRC Mar, Hospital del Mar, Barcelona, Spain.

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Correspondence: Jordi Sunyer, Doctor Aiguader, 88, 08003 Barcelona, Catalonia, Spain. E-mail: jordi.sunyer@isglobal.org.

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We hypothesize that daily variations on traffic pollution could be associated with daily fluctuations in attention, independent of its long-term association with attention development. Thus, the aim of this study, which we have carried out within the context of the BREATHE (Brain Development and Air Pollution Ultrafine Particles in School Children) project, is to examine the daily association of traffic air pollution on attention among school children, and the extent to which these associations are independent of its chronic relationship. To assess the robustness of our methodology, we performed the same analysis using working memory as an outcome. Working memory, a brain system involved in maintenance and manipulation of information, is more stable over time in front of ongoing interference from environment triggers and can serve as a negative control.[14]

METHODS

Design

We selected 40 schools in Barcelona (Catalonia, Spain) based on modeled values of traffic-related nitrogen dioxide (NO_2),[8] and paired low- and high-NO_2 schools according to a socioeconomic vulnerability index and type of school (i.e., public/private). A total of 39 schools agreed to participate and were included in the study. School children (n = 5,019) without special needs in grades 2–4 (7–10 years of age) were invited to participate, and the families of 2,897 (59%) children agreed. Participants did not differ in terms of age and sex but had a higher good or excellent school achievement rate (53.5% vs. 39.3%) and a lower prevalence of criteria of attention deficit and hyperactivity disorder (ADHD; 8.1% vs. 11.4%). However, the participation rate was equal for high-(59.0%) and low-(59.2%) exposed schools. All parents or guardians signed the informed consent form, and the study was approved by the Clinical Research Ethical Committee (No. 2010/41221/I) of the Institut Hospital del Mar d'Investigacions Mèdiques–Parc de Salut Mar, Barcelona, Spain.

Outcomes: Attention and Working Memory

Cognitive development was assessed through change in attention and working memory functions. We selected these functions because they undergo considerable development between the ages of 6 and 10 years[8] and are strongly related to intelligence and learning.[15] In addition to its age-related development, attention shows daily fluctuations that allow testing short-term associations, in contrast to working memory that is more stable over short periods of time.[14] Between January 2012 and March 2013, the children were assessed in four repeat visits, every 3 months, in ~40-minute sessions with computerized tests. The validated tests chosen were the original child attention network test (ANT)[16] to assess attention, and the *n*-back task[17,18] to assess working memory. These tests have shown good discriminative ability in previous studies.[15–18] Among the ANT measures, we calculated inattentiveness scores according to the continuous performance test formulas[19]: hit reaction time, a measure of response speed; standard error of hit reaction time (SE of hit reaction time for correct responses), a measure of response speed consistency throughout the test; omissions rate, a measure of missed targets (i.e., stimulus without clicking response); and commissions rate, a measure of incorrect responses to nontargets. Inattention is indicated by higher values of hit reaction time and SE of hit reaction time, and by higher numbers of omissions and commissions.[19] Reaction time measures were calculated using reaction times associated with a correct response in 128 trials. Reaction times shorter than 100 msecond (5.80%) in each trial were excluded from reaction time calculations because of their physiological implausibility, implying that these responses are perseverative or anticipatory.[19] We excluded data from children with >30% errors in any visit from the analysis (1.4%) due to poor performance of the test because of uncontrolled factors.[16] For the *n*-back task, we examined response to numbers and words stimuli challenged in the two-back preceding loads. We analyzed the *d* prime (d') *n*-back parameter, a measure of detection obtained by subtracting the normalized false alarm rate from the hit rate [$(Z_{\text{hit rate}} - Z_{\text{false alarm rate}}) \times 100$]. Higher d' values indicate more accurate test performance. We report results for two-back numbers but the findings were similar for three-back parameters (http://links.lww.com/EDE/B143). Tasks were created using the psychology experiment computer program E-Prime version 2.0 (Psychology Software Tools Inc., Sharpsburg, PA), and were performed on laptops with standard 15″ screens.

Traffic-related Air Pollution

We measured short-term exposures based on the daily ambient levels of NO_2 (real-time chemiluminescence using model SIR-5012) and elemental carbon (EC) measured using particulate matter <2.5 μm ($PM_{2.5}$) filters (high volume samples, quartz microfiber filters for sampling, and the thermo optical method for EC determinations); measures were taken at a fixed air quality background monitoring station in Barcelona (Palau Reial air quality monitoring station; Figure 1) operating continuously throughout the year, as detailed elsewhere.[20,21] Daily values refer to the 09:00- to 17:00-hour period. In addition, we measured long-term school exposure based on average indoor pollution levels in classrooms, using direct measurements conducted in schools in days not coinciding with the outcome assessment that cover the entire year 2012. We measured each pair of schools simultaneously during four complete days (from Monday to Friday) on two occasions 6 months apart, during the warm and cold periods of the year 2012. We measured indoor air in a single classroom and outdoor air in the courtyard simultaneously. We measured the following pollutants during class time in schools: 4-day NO_2, measured using one passive tube (Gradko), and EC in $PM_{2.5}$ filters measured daily for 8 hours (09:00 to 17:00) on each of the 4 days of the two campaigns using the same protocol as for the reference site, described above. Using data on classroom floor level, orientation (toward indoor area, outdoor

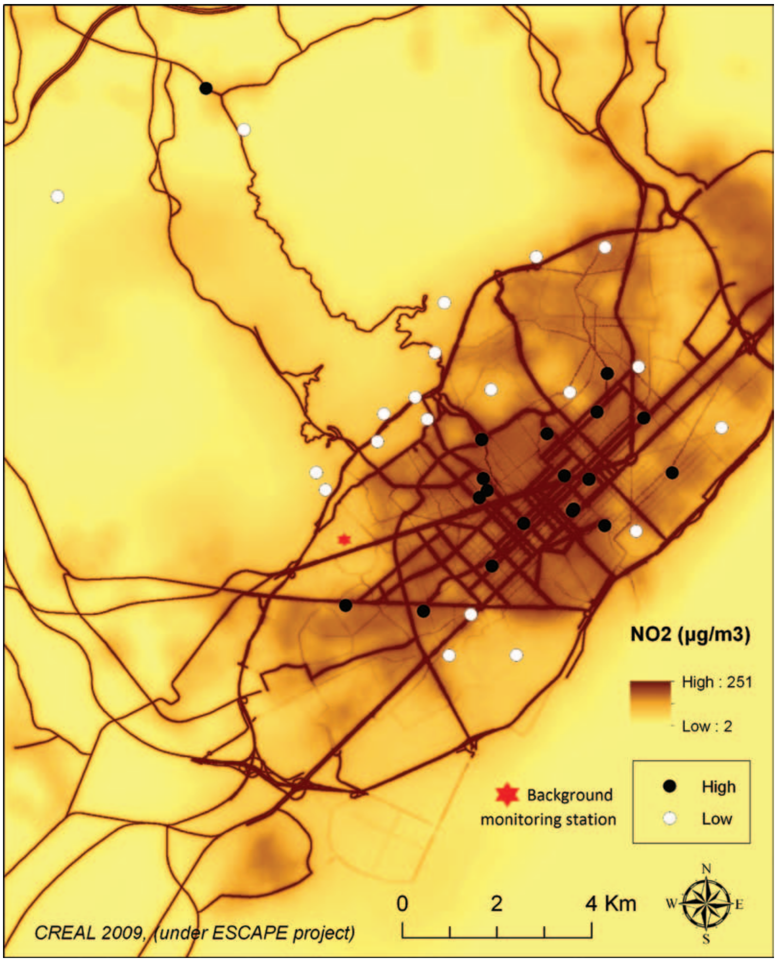

FIGURE 1. Map of Barcelona with the location of the participating schools classified by NO_2 level and the monitoring station measuring the air pollution daily levels.

playground, or directly onto the street), outdoor pollutant levels, and seasonal and meteorologic parameters such as daily temperature, relative humidity, and rainfall, we modeled average concentrations of NO_2 and EC for each classroom (eAppendix; http://links.lww.com/EDE/B143). Modeled levels of NO_2 had very good validity (correlation coefficient $r = 0.94$) with respect to a subset (n = 19) of NO_2 measurements conducted in the different classrooms of six schools at the same time. Levels of elemental carbon in $PM_{2.5}$ filters showed a high correlation with black carbon measured with aethalometers ($r = 0.95$) in the BREATHE study.[8]

Temporal, Contextual, and Individual Covariates

We obtained data on daily average temperature and humidity between 09.00 and 17.00 hours from the Faculty of Physics of the University of Barcelona. Sociodemographic status was expressed as a neighborhood socioeconomic vulnerability index (based on level of education, unemployment, and occupation at the level of census tract, the smallest spatial census unit, with a median area of 0.08 km^2) based on the home address.[22] Parental educational level was measured using the BREATHE questionnaire. Symptoms of ADHD (ADHD/DSM-IV Scales)[23] were reported by teachers. Parents completed the strengths and difficulties questionnaire (SDQ) on child behavioral problems.[24] Long-term exposure to NO_2 and EC ($PM_{2.5}$ absorbance) at home at the time of the study was estimated at the geocoded postal address of each participant using land use regression models, details of which are provided elsewhere.[25] Long-term exposure to school noise was measured directly as described elsewhere,[8] and classroom noise was modeled according to the same procedure as for NO_2, explained above. Characteristics of individuals and contextual variables were described elsewhere.[8]

Statistical Analysis

From the 2,897 children, a total of 2,687 children were included in this study. One hundred ten (3.8%) children were excluded because of lack of complete data with which to model classroom air pollution levels. These 110 children belong to three out of the 268 classrooms. The rest of excluded children (n = 100) lack data on age, maternal education, and home address. There were no difference between included and excluded children with respect to outcomes, exposures, and key covariates. We fit linear mixed effects models to test for associations between daily levels of pollutants and the quantitative outcomes at each visit (such as hit reaction time and SE of hit reaction time, and working memory), and negative binomial mixed regression models to test for associations with semiquantitative outcomes, such as omissions and commissions rate. The child and school variables were included as random effects in the models. From the 2,687 children, only 2,086 (77.6%) did the four visits. The use of mixed models allowed handling the missing visits without excluding any child**.** To evaluate acute effects, models were adjusted for the following temporal variables: a cubic spline for daily temperature, daily relative humidity, season (cold, warm), day of the week, period (first or second school year of the study), and time of the day when the cognitive assessment was conducted. We selected three lag periods based on the a priori assumption that the effect could have very short lead time (hours): the current day of the exam (lag 0), the day before (lag 1), and the two days before (lag 2). Under this assumption, and considering that most exams were performed in the morning (76%), lag 1 is the variable that best reflects immediate exposure before the exam. Indoor levels of pollutants in classrooms were used to evaluate long-term associations, because all children had been in the same classroom for >3 months before the start of the study. To adjust the daily associations for chronic effects, we included classroom pollutant levels in the previous models together with variables previously selected[8] for assessing chronic associations: child's age and sex, maternal educational level, socioeconomic status of the residential neighborhood, and air pollution at home. Models were further adjusted for long-term exposure to school noise. As mentioned elsewhere,[8] sensitivity analysis including any of the variables in Table 1 in the multivariate models did not change the results. To assess the natural developmental improvement in attention parameters with age, we fit the models including only child's age.

TABLE 1. Description (%) of the BREATHE Population (Total No. = 2,807)

Girls	50
Foreign origin (non-Spanish)	15
Maternal education, university	59
Paternal education, university	53
Maternal occupation, unemployed	18
Paternal occupation, unemployed	10
Marital status, married	85
Walking to school	53
Overweight/obese	28
Computer games weekend, ≥1 h	70
Siblings, yes	79
Adopted child	4
Second hand smoke at home	12
Smoking during pregnancy	10
Gestational age, <37 weeks	8
Birth weight < 2,500	10
Breastfeeding, no	18

We conducted several sensitivity analyses. We stratified our analyses by sex, maternal educational level, ADHD symptoms, season, and noise to assess effect modification. Pure within-subject effects were reassessed by including the individual as a fixed instead of a random effect. Temporal trends were further adjusted using semiparametric methods.[26] Finally, analyses with lag-1 and lag-2 days (i.e., with effects preceding the exposure) was conducted. Statistical significance was set at $P < 0.05$, and all statistical analyses were carried out using Stata 12.1 (Stata Corporation, College Station, TX).

RESULTS

The 2,687 children provided 10,002 valid tests on 177 different days between January 2012 and March 2013. Characteristics of the children are shown in Table 1. The proportion of girls was 50%, 59% had a mother with university degree, 10% had a father who was unemployed, 28% were overweight or obese, and 15% were born out of country. Home SES vulnerability index mean was 1.45 (SD = 0.21), mean greenness (in terms of normalized difference vegetation index) was 0.20 (SD = 0.08), mean distance from home to school was1733 m (SD = 2381), and mean behavioral problems score was 8.4 (SD = 5.2). Table 2 shows the results of a descriptive analysis of attention and working memory, daily ambient levels of NO_2 and EC, and average indoor levels of NO_2 and EC measured in classrooms during the study. We observed higher interindividual than intraindividual variability in cognitive function, for example, the interindividual variability of hit reaction times (SD) was 163 and the intraindividual variability was 94, and the variability of the intraindividual variability was 51. The distribution of omission errors and especially of commission errors was non-normal.

The ambient levels of NO_2 and EC had a higher mean than indoor school levels (Table 2). NO_2 ambient levels were higher than average indoor school levels throughout the distribution. The bottom quartile of indoor levels of EC was higher than that of ambient levels, whereas the top quartile of daily ambient levels of EC was higher than that of indoor levels. The seasonal distributions of daily levels of both pollutants were very similar (Figure 2).

Attention parameters were moderately correlated with working memory while there were strong correlations between measurements of inattention, except for commission errors (Table 3, outcomes). Daily ambient levels of air pollutants were not correlated with their average indoor levels (i.e., we found no relationship between short- and long-term air pollution). There was a strong correlation between NO_2 and EC, for both daily ambient ($r = 0.50$) and indoor levels ($r = 0.76$; Table 3, exposures). In contrast, correlations between either average indoor NO_2 or EC and average indoor noise levels were weaker ($r < 0.45$). In addition, we found a correlation between daily ambient and daily indoor levels of EC ($r = 0.49$, 95% CI, 0.36, 0.61). Short-term NO_2 and short-term EC concentrations were unrelated to children's characteristics and

TABLE 2. Description of Cognitive Outcomes and Air Pollutants

			Percentile			
	Mean (SD)	**Min.**	**25th**	**50th**	**75th**	**Max.**
Outcomes for 10,002 person-days in 2,687 children						
Inattention						
Mean HRT (ms)	781 (163)	409	659	759	882	1,531
HRT-SE (ms)	249 (90)	60	180	243	312	571
Number of omission errors	1.8 (3.1)	0.0	0.0	1.0	2.0	31.0
Number of commission errors	0.3 (0.9)	0.0	0.0	0.0	0.0	21.0
Working memory						
Two-back numbers, d' × 100	237.7 (128.9)	−183.4	138.7	234.3	392.0	392.0
Intraindividual variability[a] from 2,687 children						
Inattention						
Mean HRT (ms)	94 (51)	0.1	55	86	122	363
HRT-SE (ms)	53 (26)	0.1	34	50	69	203
Number of omission errors	1.5 (1.7)	0.0	0.5	1.0	2.0	16
Number of commission errors	0.4 (0.8)	0.0	0.0	0.0	0.5	11.3
Working memory						
Two-back numbers, d' × 100	99.9 (45.9)	0.0	69.9	100.3	130.5	268.5
Indoor pollution in 265 classrooms from 39 schools						
NO_2 (μg/m^3)	30.09 (9.51)	7.79	22.82	29.43	36.13	52.56
EC (μg/m^3)	1.27 (0.42)	0.43	0.98	1.24	1.56	2.20
Ambient air pollution in 177 days						
NO_2 (μg/m^3)	37.75 (18.41)	11.69	24.75	33.50	46.44	113.00
EC (μg/m^3)	1.34 (0.84)	0.00	0.77	1.13	1.73	4.44

[a] SD for the four measurements in each child.

d', detectability; EC, elemental carbon; HRT, hit reaction time; ms: milliseconds; NO_2, nitrogen dioxide; SE, standard error.

modestly related to relative humidity ($r = 0.14$ and $r = 0.39$, for NO_2 and EC, respectively), season and day of the week; however, long-term NO_2 and EC were related to education and socioeconomic status (eTable 1; http://links.lww.com/EDE/B143).

Daily ambient levels of both NO_2 and EC were associated with impaired attention function (i.e., increased hit reaction time, SE of hit reaction time, omissions, and commissions; Table 4). Thus, an interquartile increase (a difference between 25th and 75th percentile) in daily levels of NO_2 was associated with a 14.8 (95% CI, 11.2, 18.4) msecond increase in hit reaction time or a 7% (95% CI, 3%, 12%) higher number of missing answers (omissions). This increase was equivalent to a 1.1-month (0.84, 1.37) retardation in the natural developmental improvement in response speed with age (normally 13.4 msecond per month). Similarly, age development of SE of hit reaction time was retarded by 1.45 months (0.78, 2.12) and omissions by 0.82 months (0.32, 1.32) for NO_2. We obtained similar findings after adjusting for the long-term exposure (i.e., average indoor levels of pollutants in the classroom), which indicates that daily variations in ambient levels of pollutants have a short-term association with outcomes, independent of the average level of pollution in the school. Thus, an interquartile increase in daily ambient levels of NO_2 resulted in a 9.90-msecond increase in hit reaction time, independent of average indoor levels in the classroom. We did not find any short-term association with relative humidity. We controlled for potential confounding by complex relationships between neurodevelopment and temperature by adjusting for cubic splines of temperature. We did not observe short-term associations with working memory. In contrast, long-term exposure to indoor NO_2 was associated with impaired attention processes (hit reaction time, SE of hit reaction time, and omission errors) and working memory (Table 4, eTable 2; http://links.lww.com/EDE/B143). These chronic associations did not change after adjusting for the acute relationship, except for the association between working memory and EC, which became stronger. This result also did not change after adjusting for classroom noise.

Figure 3 shows the acute associations of ambient NO_2 with SE of hit reaction time and omission errors for each of the different lags, with and without adjustment for average indoor pollutant levels. We observed the strongest association for the lag 1 period, as well as for hit reaction time and commission errors (eFigure 1; http://links.lww.com/EDE/B143). This figure also depicts a stronger association with long-term exposure than with short-term exposure. We observed similar patterns for EC, with the strongest association for the lag 1 period.

The results did not change notably using alternative statistical modeling (eTable 3; http://links.lww.com/EDE/B143), or

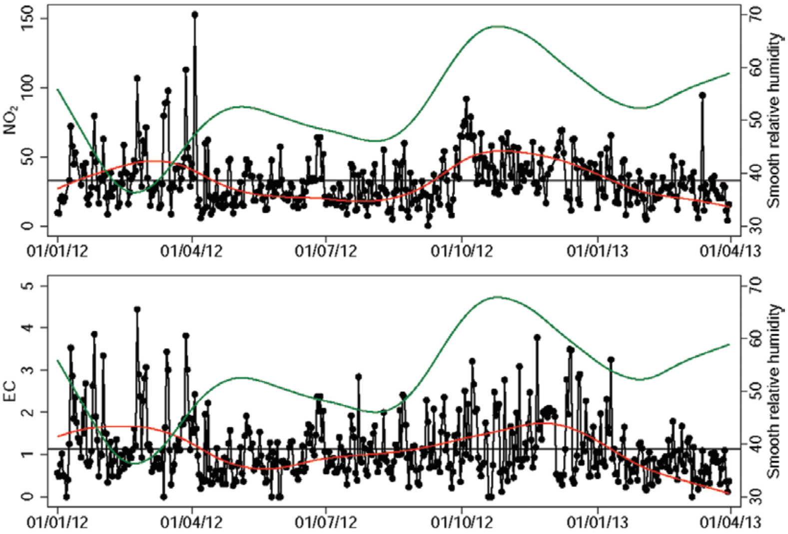

FIGURE 2. Time series of daily ambient levels of NO_2 and elemental carbon (μg/m³). Smoothed trends of the air pollutants (red line) and relative humidity (green line).

TABLE 3. Correlations Between Outcomes and Exposures (Spearman Correlation Coefficient)

Outcomes	Working Memory	Inattention		
	Two-back Numbers, *d′*	Mean HRT	HRT-SE	Number of Omission Errors
Inattention				
Mean HRT	−0.26	1.00		
HRT-SE	−0.27	0.82	1.00	
Number of omission errors	−0.25	0.56	0.65	1.00
Number of commission errors	−0.12	0.10	0.23	0.22
Exposures	Classroom NO_2	Classroom EC	Daily Levels NO_2	
Classroom EC	0.76	1.00		
Daily levels NO_2	0.03	0.01	1.00	
Daily levels EC	−0.02	0.00	0.50	

d′, detectability; EC, elemental carbon; HRT, hit reaction time; NO_2, nitrogen dioxide; SE, standard error.

stratifying by sex, maternal education, ADHD symptoms, season, or noise (eTables 4 and 5; http://links.lww.com/EDE/B143).

DISCUSSION

Daily variations in attention processes were associated with daily levels of traffic-related ambient air pollution, and this acute association was independent of the average level of pollution in the classroom. In addition to other factors previously reported as being related to short-term fluctuations, such as individual characteristics and environmental or contextual variables (e.g., temperature, time of day),[9,10] urban air pollution levels also appear to trigger daily variation in attention. Children's performance was slower and less consistent throughout the test on days with higher levels of ambient traffic-related air pollution. The size of the estimated effect was modest (around 1 month in age-related development of attention); however, common exposures with small effects on cognitive function have an important population impact, as has been shown for lead.[27] In contrast to attention, fluctuations in working memory were not associated with daily levels of ambient air pollution, even though we observed chronic associations of air pollution with the development of working memory in a previous study.[8] Our results are consistent with several studies that highlight the contribution of the central executive component of the working memory system in resisting interference by inhibiting distracters.[15,28,29]

We found that both NO_2 and EC had acute associations with inattentiveness. We selected EC and NO_2 as indicators of traffic pollution because of their link with vehicle exhaust emissions in the city of Barcelona.[30] Based on observed brain damage in animal experiments,[31–34] diesel pollutants are thought to be the most important inhaled neurotoxicants. As do many European cities, Barcelona has a diesel-dominated vehicle fleet (with very high NO_2 and EC emissions, which are responsible for the majority of these pollutants in the city air).[30,35] We did not aim to identify the specific neurotoxic

TABLE 4. Association (Difference per Interquartile Range Increase) Between Ambient Daily Levels (Short-term) and Indoor Classroom Levels (Long-term) of Traffic-related Air Pollution and Daily Cognitive Function

			Short-term (Lag 1) Adjusted for Long-term[c]	
	Short-term (Lag 1)[a]	Long-term[b]	Short-term	Long-term
Inattention				
Mean HRT (ms)				
NO_2	14.8 (11.2, 18.4)	14.8 (4.7, 25.0)	9.9 (6.5, 13.3)	13.3 (3.1, 23.5)
EC	9.1 (5.8, 12.5)	4.6 (−5.1, 14.2)	7.9 (4.8, 11.1)	4.7 (−4.9, 14.3)
HRT-SE (ms)				
NO_2	5.0 (2.7, 7.3)	9.8 (3.4, 16.3)	2.6 (0.4, 4.8)	9.4 (2.7, 16.1)
EC	2.1 (−0.1, 4.2)	4.5 (−1.4, 10.4)	1.6 (−0.5, 3.7)	5.2 (−0.9, 11.4)
Number of omissions				
NO_2	7% (3%, 12%)	24% (16%, 33%)	4% (0%, 8%)	18% (6%, 32%)
EC	3% (−1%, 7%)	13% (4%, 22%)	2% (−2%, 6%)	10% (−1%, 22%)
Number of commissions				
NO_2	15% (9%, 22%)	4% (-9%, 18%)	12% (6%, 18%)	7% (-9%, 25%)
EC	8% (2%, 13%)	12% (-1%, 25%)	7% (1%, 12%)	11% (-3%, 28%)
Working memory				
Two-back numbers, $d' \times 100$				
NO_2	−1.62 (−5.49, 2.25)	−8.21 (−14.64, −1.79)	0.25 (−3.46, 3.96)	−8.76 (−14.78, −2.74)
EC	0.66 (−3.13, 4.45)	−4.73 (−10.80, 1.34)	0.94 (−2.72, 4.60)	−7.11 (−13.40, −0.83)

[a] Lag 1 = exposure of the day before of the attention test. Model adjusted (cubic spline) for temperature and relative humidity on the current day, season (cold, warm), day of the week and period (year 1 or 2), hour of exam.

[b] Adjusted for child's age, sex, maternal education, socioeconomic status of the neighborhood of residence, and home air pollution.

[c] Adjusted for a and b above.

d′, detectability; EC, elemental carbon; HRT, hit reaction time; ms, milliseconds; NO_2, nitrogen dioxide; SE, standard error.

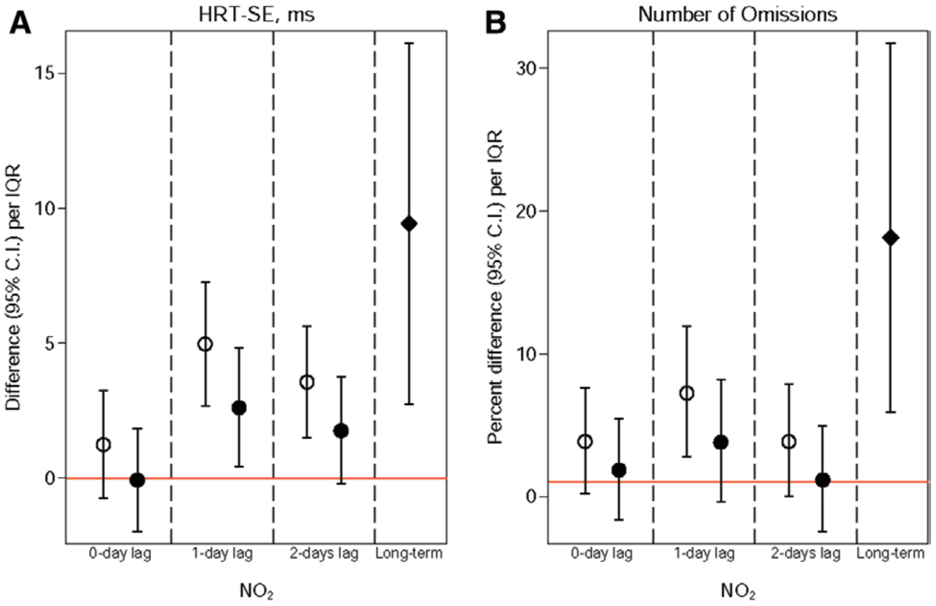

FIGURE 3. Association (difference per interquartile range width increase, IQR_w) between ambient daily levels (short-term by lag period) and indoor classroom levels (long-term) of NO_2 and inattention: (A) HRT-SE and (B) number of omission errors. Lag 0: same day exposure, lag 1: day before exposure, lag 2: 2 days before exposure. Open circle, Models were adjusted (cubic spline) for the temperature and relative humidity on the current day, season (cold, warm), day of the week, period (year 1 or 2), and the hour of the exam. Subject nested in classroom, and classroom nested in school. Filled circle, Adjusted as for the variables above, plus child's age, sex, maternal educational level, socioeconomic status of the neighborhood of residence, home air pollution, and indoor air pollution in the classroom. Filled diamond, Indoor estimate from the 1-day lag model. HRT-SE indicates standard error of hit reaction time; IQR, interquartile range.

agents that are directly responsible for neuronal damage, or to disentangle which of the different agents in the mixture of traffic-related air pollutants causes the observed associations on attentiveness, but rather used a measure that is globally representative of exposure to traffic pollution. Two recent studies in rats exposed to NO_2 that observed clear evidence of brain damage,[36,37] particularly neuron mitochondrial dysfunction,[36] raises the possibility of a specific neurotoxicity of NO_2. However, these experimental studies used high doses compared with real life.

The acute association of air pollution with attention probably arises through the same mechanism as the long-term association, as do for the cardiovascular effects of air pollution.[7] There is evidence that short-term ambient PM exposure can be associated with day-to-day elevations in circulating proinflammatory biomarkers, endothelial cell activation, vascular endothelial dysfunction, blood coagulation, blood pressure, or altered heart variability.[38] Several of these effects are related to an autonomic nervous system imbalance. Whether this reaction occurred because of a generalized oxidative stress response, as a consequence of specific soluble PM constituents directly altering central nervous system activity, or via altered reflex with lung nerve receptors, remains unknown.[38] The most commonly reported brain effects involve microglia stimulation and altered innate immune response and inflammation, and synapse disruption, including dopamine dysfunction, following exposure to diesel exhaust.[6,39] Dopamine function after a stimulant medication affects the attention variability in the short term.[40] Similarly, the short-term effects of air pollution on attention could be mediated by the catecholaminergic system, although how dopamine is acutely affected by PM exposure is unknown. Interestingly, a unifying mechanism through which central dopaminergic influences might simultaneously affect vascular, neuronal, and behavioral domains has been proposed.[41] There are currently no data on the time lapse between exposure and the onset of symptoms,[7] although our observation of a lower association for 2 days' lag than for 1 day's suggests that this time lapse may be just a few hours. Note than in our study, 1-day lag is the period that best represents the period before the computer tests for both NO_2 and EC.

A secondary finding in this study is the additional chronic association observed by modeling classroom levels, in contrast to our previous study in which we only assessed indoor level in a single classroom per school.[8] Thus, we have extended the 39 different school pollution exposure contrasts to 265 classroom levels, which reduces the risk of confounding school and participant characteristics by chronic associations, given the use of different classrooms within the same schools. Interestingly, we observed stronger associations than in our previous study,[8] which suggests that any residual confounding in our previous study would lead to an underestimation of associations (e.g., increase in the association between NO_2 and SE of hit reaction time from 7.0 msecond [−1.0, 16] to 9.8 msecond [3.4, 16]).

A major shortcoming of observational studies assessing long-term associations is the potential for residual confounding by social class. Our study is unlikely to be affected by residual confounding because temporal variations in daily air pollution levels were analyzed within the same individuals. Thus, the acute association of air pollution was independent of individual and school characteristics, and could only be affected by daily variations in other variables such as temperature or season, which were included in our models. In addition, a better appreciation of attention fluctuations and their modulating factors such as traffic pollution may provide a more comprehensive understanding of the nature of inattentive classroom behavior. While fluctuations in performance and difficulties in focusing attention are widely known to be greater and more common in children with ADHD symptoms,[10,42] we found that traffic pollution is negatively associated with variability of attention irrespective of the presence or absence of this syndrome.

A potential limitation of this study is the lack of daily information on noise, which could be a source of confounding. We were unable to measure daily variation in classroom ventilation, which could also affect neuropsychological performance,[43] although adjusting for seasonal and environmental temperature makes a confounding effect unlikely. Furthermore, we did not find differences in the infiltration of NO_2 and EC between the warm and cold seasons in the BREATHE study[44] which suggests small temporal variations in ventilation. Moreover, daily levels of air pollution on the days of the computer test were obtained from a reference station and not directly from the school, so the temporal associations are unlikely to be biased, as shown elsewhere.[13] In fact, we found that there was a good correlation between ambient levels of EC at the reference site and indoor levels at the schools on the same days ($r = 0.49$). Finally, the participation rate was unrelated to the exposure, which suggests a lack of potential selection bias.

Overall, the short-term association of traffic-related air pollutants with attention fluctuations adds to the evidence that air pollution may have potential harmful effects on neurodevelopment. Our study suggests that, if shown to be a causal relationship, traffic pollution, and in particular diesel emissions addressed here by measuring NO_2 and EC, could affect the cognitive performance of school children while at the school. Attention is a key cognitive function for school success and for avoiding social and behavioral problems,[11] which highlights the importance for public health of the acute associations we observed of traffic-related air pollutants with fluctuations in attention.

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