Ambient air pollution and overweight and obesity in school-aged children in Barcelona, Spain

Jeroen de Bont[a,b,c], Maribel Casas[a,b,c], Jose Barrera-Gómez[a,b,c], Marta Cirach[a,b,c], Ioar Rivas[d], Damaskini Valvi[e], Mar Álvarez[a,b,c], Payam Dadvand[a,b,c], Jordi Sunyer[a,b,c], Martine Vrijheid[a,b,c,*]

[a] ISGlobal, Barcelona Institute for Global Health, Spain
[b] Universitat Pompeu Fabra (UPF), Barcelona, Spain
[c] CIBER Epidemiología y Salud Pública (CIBERESP), Barcelona, Spain
[d] MRC-PHE Centre for Environment & Health, Environmental Research Group, King's College London, SE1 9NH London, United Kingdom
[e] Department of Environmental Health, Harvard T.H. Chan School of Public health, Boston, MA, United States

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ABSTRACT

Background: Ambient air pollution may increase the risk of overweight and obesity in children. However, available evidence is still scarce and has mainly focused on ambient air pollution exposure occurring at home without considering the school environment. The aim of this study is to assess whether exposure to ambient air pollution at home and school is associated with overweight and obesity in primary school children.

Methods: We studied 2660 children aged 7–10 years during 2012 in Barcelona. Child weight and height were measured and age- and sex-specific z-scores for body mass index (zBMI) were calculated using the WHO growth reference 2007. Overweight and obesity were defined using the same reference. Land use regression models were used to estimate levels of nitrogen dioxide (NO_2), particulate matter < 2.5 μm ($PM_{2.5}$), < 10 μm (PM_{10}) and coarse (PM_{coarse}) at home. Outdoor levels of NO_2, $PM_{2.5}$, elemental carbon (EC), and ultrafine particles (UFP) were measured in the schoolyard. Multilevel mixed linear and ordered logistic models were used to assess the association between ambient air pollution (continuous per interquartile range (IQR) increase and categorical with tertile cutoffs) and zBMI (continuous and ordinal: normal, overweight, obese), after adjusting for socio-demographic characteristics.

Results: An IQR increase in PM_{10}-home (5.6 μg/m^3) was associated with a 10% increase in the odds of being overweight or obese (odds ratio (OR) = 1.10; 95% CI = 1.00, 1.22). Children exposed to the highest tertile of UFP-school (> 27,346 particles/cm^3) had a 30% higher odds of being overweight or obese (OR = 1.30; 95%CI = 1.03, 1.64) compared to the lowest tertile of UFP exposure. We also observed that exposure to NO_2, $PM_{2.5}$ or EC at schools was associated with higher odds of overweight or obese at medium compared to low levels of exposure. Home and school exposures did not show any significant associations with zBMI (except $PM_{2.5}$-school comparing tertile 2 vs tertile 1) but were similar in direction.

Conclusions: This study suggests that exposure to ambient air pollution, especially at school, is associated with childhood risk for overweight and obesity. A cautious interpretation is warranted because associations were not always linear and because school and home air pollution measurements were not directly comparable.

1. Introduction

The prevalence of childhood obesity has risen substantially in most industrialised countries during the last decades ((NCD-RisC), 2017). In Europe, the highest rates of childhood overweight and obesity are found in southern countries (20–40%) (Moreno Aznar et al., 2011). In Catalonia (Spain) for example, around 30% of children between 6 and 12 years old were overweight or obese in 2015 (Generalitat de Catalunya, 2016). Childhood obesity is associated with several health consequences such as cardiovascular diseases, metabolic complications, gastrointestinal disorders, pulmonary dysfunction, and musculoskeletal diseases (Daniels, 2009; Han et al., 2010) and therefore the early prevention of disease is critical.

Childhood obesity is a multifactorial condition resulting from the interaction between multiple genetic and non-genetic risk factors (Han et al., 2010), with the imbalance between energy intake and energy

expenditure as primary cause. During the last decade there has been increasing interest in whether environmental chemical exposures may contribute to the rising prevalence of obesity (Holtcamp, 2012). Ambient air pollution is one of the suspected environmental obesogens (McConnell et al., 2016). Some studies in animals suggest that ambient air pollution can alter the metabolism and increase weight gain (Bolton et al., 2012; Sun et al., 2009; Xu et al., 2010).

A few epidemiological studies have analyzed the association between exposure to ambient air pollution and childhood obesity and most of these report increases in body mass index (BMI) associated with increasing levels of nitrogen dioxide (NO_2), nitrogen oxides (NO_x), particulate matter < 2.5 μm ($PM_{2.5}$), < 10 μm (PM_{10}) and coarse (PM_{coarse}) (Dong et al., 2015; Jerrett et al., 2010, 2014; McConnell et al., 2014). However, a recent birth cohort study in Italy including 499 children at 8 years of age did not find association between exposure to traffic-related air pollution (TRAP) and BMI, blood lipids, or abdominal adiposity (Fioravanti et al., 2018). There is no evidence on the impact of other ambient air pollution such as ultrafine particles (UFP) and elemental carbon (EC) on childhood obesity. Further, these previous studies have assessed exposure to ambient air pollution exclusively at the home address. However, school-aged children spend between 23% and 35% of the day at school including morning hours when the highest peaks in ambient air pollution are noted (Mazaheri et al., 2014; Nieuwenhuijsen, 2015; Pañella et al., 2017). In fact, a personal monitoring study of 45 schoolchildren in Barcelona found out that 37% of their daily integrated BC dose was received at school (Rivas et al., 2016). There is thus a need for studies including an evaluation of the role of ambient air pollution exposure at schools in childhood obesity risk.

We aimed to assess whether exposure to ambient air pollution at home and school (the two micro-environments where schoolchildren spend much of their time) is associated with overweight and obesity risk in children aged 7 to 10 years.

2. Methods

2.1. Design and study population

This cross-sectional study was conducted in the context of the BREATHE (BRain dEvelopment and Air polluTion ultrafine particles in scHool childEn) study that aimed to evaluate the impact of long-term exposure to TRAP in schools on cognitive development (Sunyer et al., 2015). Forty primary schools were selected in Barcelona (2012) in order to maximize the contrast in exposure based on modeled traffic-related NO_2 concentrations (Wang et al., 2013). Low- and high-polluted schools were matched by a neighborhood socioeconomic indicator (Ministry of Public Works, 2015), and type of school (i.e., public/private). A total of 39 schools agreed to participate and were included in the study (Supplementary Fig. S1). Participating schools were similar to the remaining schools in Barcelona in terms of socioeconomic vulnerability index and NO_2 levels (Sunyer et al., 2015). All school children (n = 5019) without special needs in grades 2th through 4th of primary school (7–10 years old) were initially invited and 2897 (59%) children agreed to participate. To be included in the BREATHE study, children had to be enrolled at the school for at least 6 months before the beginning of the study (98% of our final sample were at the same school for more than one year). All parents or tutors/guardians signed the informed consent form approved by the Clinical Research Ethical Committee (No. 2010/41221/I) of the IMIM-Parc de Salut MAR, Barcelona, Spain (Sunyer et al., 2015).

2.2. Outcome assessment

Child height (nearest 0.1 cm) and weight (nearest 0.1 kg) were measured at enrollment, between January 2012 and June 2013. All measurements were taken without shoes and in light clothing by specially trained personnel following a standardized protocol. Height and weight were used to calculate BMI (kg/m^2) and age-and-sex specific BMI z-scores (zBMI, in standard deviation units) were then calculated using the WHO Growth Reference 2007 (de Onis et al., 2007). Overweight and obesity status were defined following the WHO Child Growth Standards where overweight is > +1 z-score (equivalent to BMI 25 kg/m^2 at 19 years) and obesity > +2 z-score (equivalent to a BMI equal to 30 kg/m^2 at 19 years).

2.3. Ambient air pollution assessment: residential levels

We estimated residential levels of NO_2, NO_x, PM_{10}, $PM_{2.5}$, PM_{coarse} and PM_{abs} for the geocoded postal address of each participant using a land-use-regression (LUR) model; a detailed description can be found elsewhere (Cyrys et al., 2012; Eeftens et al., 2012; Wang et al., 2013). Briefly, this model was developed within the European Study of Cohorts for Air Pollution Effects (ESCAPE) project that measured several pollutants of interest in 36 European study areas. The monitoring campaign in Barcelona was developed between January 2009 and January 2010 during 3 seasonal periods of two weeks, in the cold, warm and intermediate temperature seasons per each of the 40 monitoring sites for NO_x and 20 for PM. Several predictor variables such as traffic intensity, population, and land-use were used to model spatial variation of annual average concentrations for each study area (Beelen et al., 2013; Eeftens et al., 2012). Adding traffic predictors improved the models in Barcelona (Beelen et al., 2013; Eeftens et al., 2012). Therefore, the LUR model developed within ESCAPE predicted air pollutants levels at children's residential addresses for the year 2009. We estimated the annual average pollutant levels in 2011 (the year before the BREATHE study was conducted), by temporally adjusting the spatial estimates using a ratio method, according to the ESCAPE guidelines (Beelen et al., 2013; Eeftens et al., 2012). These models predicted (R^2) 75% and 83% of variation in annual levels (2009) of NO_2 and $PM_{2.5}$, respectively.

2.4. Ambient air pollution assessment: school levels

We measured levels of NO_2, $PM_{2.5}$, elemental carbon (EC) and ultrafine particles (UFP) in schoolyards during two 1-week campaigns separated by 6 months from January to June 2012, and from September 2012 to February 2013, covering the warm and cold seasons for each school (Rivas et al., 2014). Four weekday average of NO_2 was obtained with passive dosimeter (Gradko Environmetal). $PM_{2.5}$ was measured using a High-Volume sampler (MCV SA, Spain) during 8 h of school (09:00 h to 17:00 h). Filter chemical analysis was used to measure the concentration of EC that was analyzed via a Thermal-Optical Transmission technique (Sunset Laboratory OCEC Analyzer). Details on the $PM_{2.5}$ filter analyses can be found elsewhere (Amato et al., 2014). Real-time UFP numbers concentrations (10–700 nm in this study) were measured during class time in real-time concentration using a DiSCmini (Matter Aerosiol) meter. Outdoor school levels were then obtained by averaging the results of the two campaigns. NO_2 and EC were adjusted also for temporal variability. Seasonalized levels were obtained by multiplying the daily concentrations at each school by the ratio of annual average to the same day concentration at a fixed air quality background monitoring station in Barcelona (Rivas et al., 2014). The main source of the pollutants is from traffic, except $PM_{2.5}$ for which the main source was mineral dust (Rivas et al., 2014). Therefore, we only included the proportion $PM_{2.5}$-school concentration that originated from traffic sources – including organic particles from motor exhaust, EC, and metals from brake wear (copper, antimony, tin, and iron) – as obtained from a previous source apportionment analyses (Amato et al., 2014).

2.5. Covariates

Data on socio-demographic and lifestyle factors were collected from parents through questionnaires. These included parental education, employment status, and country of birth, maternal smoking during pregnancy, child's adopting status, exposure to environmental tobacco smoke (ETS) at home, number of siblings, and physical activity. To measure this last variable, parents were asked how frequently the child did physical exercise outside school enough to make out of breath or get sweaty. It had six categories: every day, from 4 to 6 times a week, from 2 to 3 times a week, once a week, once a month, less than once a month. In addition to the indicators of household levels of socioeconomic status (i.e. parental education and employment), we also assigned each participant the Urban Vulnerability Index which is an indicator of neighborhood socioeconomic status. This indicator is based on level of education, unemployment, and occupation in each census tract, the finest spatial census unit, with median area of $0.08 \, km^2$ (Ministry of Public Works, 2015). Noise levels in the classroom before children arrived (as a measure of traffic-related noise) were also measured (Sunyer et al., 2015). Residential noise levels were obtained from the Catalan regional government (Generalitat de Catalunya, n.d.) and expressed as L_{den} (day, evening and night). Further, school and residential surrounding greenness was measured in buffers of 50 m and 250 m respectively, around the address based on the Normalized Difference Vegetation Index (NDVI) derived from Landsat 5 Thematic Mapper data.

2.6. Statistical analyses

Because of missing data in covariates multiple imputation was performed. Five imputed datasets were created based on a predictive stepwise distribution from the observed data on determinants covariates, outcomes, and other characteristics used in the models (White et al., 2011) (Supplementary Material Table S1). Distributions of covariates in imputed datasets were similar to those observed (Supplementary Table S2). The exposure and outcome variables were not imputed.

Due to the multilevel nature of the data (i.e. children within schools) we used linear mixed effect models to assess the association between ambient air pollution and zBMI, whereas multilevel mixed effects ordered logistic regression models were used to assess the association between ambient air pollution and zBMI categories (normal weight, overweight, obese). In all models, we firstly treated ambient air pollution as a continuous variable (interquartile increase) and secondly we categorized ambient air pollution using tertiles as cutoff points. We used directed acyclic graphs (DAGs) to determine covariates included in the multivariate models and minimize overadjustment bias (Shrier and Platt, 2008) (Supplementary Fig. S2). Once the potential confounders were identified, we included each of them one by one in the model and we selected those that had a better fit of the model based on the Wald test. The final adjusted model included maternal and paternal education (primary education or lower, secondary education, university education or higher), maternal and paternal country of birth (Spain, other), paternal employment status (self-employed, employed, unemployed), number of siblings, household status (bi-parental, mono-parental) and maternal smoking during pregnancy (no, yes). The proportional odds assumption was evaluated using likelihood ratio test. Results are expressed as beta coefficients for continuous zBMI and as odds ratios (OR) for the overweight/obesity categories, were the normal weight category was the comparison group. The proportional odds assumption assumes that the OR that describes the relationship between normal weight versus overweight or obesity is the same as those that describes the relationship between normal weight or overweight versus obesity none of the fitted model violated such assumption. Because the relationship between all pairs of groups is the same, there is only one set of coefficients.

2.6.1. Sensitivity analyses

Sensitivity analyses were performed to assess the robustness of our results: i) we checked whether the association between ambient air pollution and zBMI varied by child's sex, physical activity level, exposure to ETS at home, and maternal education through inclusion of interaction terms in the models and stratified analyses; ii) we checked the role of confounding by socio-economic status by evaluating how the removal of these variables (maternal and paternal education and country of birth and paternal employment status) from the main models affected the main effect estimates; and iii) we repeated all analyses using the complete case dataset without imputations. Analyses were conducted with the statistical software Stata 14 (StataCorp). Statistical significance level was set up as $\alpha = 0.05$.

3. Results

From the 2897 school children participating in BREATHE, 2660 (92%) had complete information on ambient air pollution concentrations and zBMI, and were included in the present analysis (Supplementary Fig. S3). Children included in the analysis were more likely to have parents who were born in Spain, and to have parents with higher educational level and lower rates of unemployment, than the excluded children (Supplementary Table S3). Included and excluded children did not differ in terms of age, sex, number of sibling, maternal smoking during pregnancy, and exposure to ETS at home (Supplementary Table S3). Table 1 shows the characteristics of the children included in this study stratified by zBMI categories. Children with underweight represented only 0.2% of the final sample and were included in the normal weight category. The prevalence of overweight and obesity was 26% and 16%, respectively. Girls were more likely to be overweight whereas boys were more likely to be obese. Children who had obesity were more likely to have parents who were born outside Spain, who were less educated, and who were more likely to be unemployed compared to non-obese children. They were also more likely to have fewer siblings and live in mono-parental families.

Table 2 shows the ambient air pollution concentrations at home and school. > 50% of children were exposed to NO_2 levels that exceeded the annual mean WHO guidelines ($40 \, \mu g/m^3$) both at home and at school. > 75% of children were exposed to levels of $PM_{2.5}$ (home and school) and PM_{10} (home) higher than 10 and $20 \, \mu g/m^3$, respectively, as recommended by the WHO. NO_2 levels were similar at homes and schools (median = 44.4 and $48.5 \, \mu g/m^3$, respectively) whereas $PM_{2.5}$ levels at schools (median = $25.0 \, \mu g/m^3$) were substantially higher than at homes (median = $13.4 \, \mu g/m^3$). NO_x and PM_{abs} at home level were excluded from the final analyses as they were highly correlated with NO_2 levels at home (r = 0.92 and r = 0.93, respectively) (Supplementary Table S4). At school, all correlations were below 0.9 and all pollutants were thus included in the final analyses.

Ambient air pollution concentrations at home and school were generally not associated with child's BMI when zBMI was treated as a continuous variable (Table 3). Among the different pollutants, we only observed that children exposed to levels of $PM_{2.5}$ at school in the second tertile had increased BMI z-scores (β = 0.02; 95% CI = 0.04, 0.29) compared with children in the lowest tertile (Table 3).

When comparing overweight and obese children with normal weight children, we observed that an IQR ($5.61 \, \mu g/m^3$) increase in the PM_{10} level at home was associated with a 10% increase in the odds of being overweight or obese (OR = 1.10; 95% CI = 1.00, 1.22) (Table 4). No further associations were found at homes exposure level. At schools, children exposed to levels of NO_2, $PM_{2.5}$, and EC at school in the second exposure tertile had a higher odds of being overweight or obese, versus normal weight children, compared to the first tertile of exposure (NO_2-school OR = 1.28, 95% CI = 1.03, 1.61, $PM_{2.5}$-school OR = 1.35, 95% CI = 1.01, 1.60, $PM_{2.5}$-school OR = 1.26, 95% CI = 1.01, 1.60) (Table 4). Children exposed to levels of UFP in the highest tertile of exposure had a 30% higher risk of being overweight or obese (OR for

Table 1

Population characteristics by zBMI categories in the 2660 children included in the study.

Characteristics	Normal weight N = 1537 (58%)	Overweight N = 702 (26%)	Obesity N = 421 (16%)
Child characteristics			
Age, years (IQR)	8.4 (7.7, 9.1)	8.5 (7.6, 9.2)	8.5 (7.7, 9.3)
Sex %			
Male	57.0	23.8	19.3
Female	58.6	29.1	12.4
Number of siblings, (SD)	1.1 (0.8)	1.0 (0.7)	0.9 (0.7)
Family characteristics			
Country of birth mother, %			
Spain	60.4	25.7	13.9
Other	41.8	30.5	27.6
Maternal education, %			
Primary or less	47.1	29.2	23.7
Secondary school	50.8	28.6	20.3
University studies	64.1	24.7	11.2
Country of birth father, %			
Spain	60.2	25.7	14.0
Other	44.6	29.6	25.8
Paternal education, %			
Primary or less	47.3	26.6	26.1
Secondary school	51.3	29.8	18.9
University studies	65.6	23.9	10.4
Paternal employment status, %			
Self-employed	62.3	24.9	12.7
Employed	59.5	25.8	14.8
Unemployed	40.4	32.5	27.2
Household status, %			
Bi-parental	60.0	25.8	14.3
Mono-parental	48.3	28.9	22.8
Family lifestyle			
Maternal smoking during pregnancy %			
No	58.5	26.3	15.2
Yes	50.6	28.0	21.3
Environmental tobacco smoke at home %			
Nobody smokes	59.3	26.7	14.1
Yes, but not inside home	56.7	25.6	17.6
Yes, smokes inside home	54.5	25.8	19.8
Physical activity			
Every day	43.4	34.3	22.2
From 4 to 6 time/week	58.2	23.1	18.8
From 2 to 3 time/week	57.9	26.9	15.2
Once a week	60.3	25.0	14.7
Once a month	55.8	34.9	9.3
Less than once a month	63.5	24.5	12.0

Values are mean (Standard deviation (SD)) for continuous normal distributed variables, median (interquartile range) for continuous non-normal distributed variables, and percentage for categorical variables. Pearson chi² was used to calculate *p*-value.

Table 3

Association between ambient air pollution concentrations at home and at school and continuous zBMI.

Pollutant	Adjusted coefficient	95% Confidence interval
Home:		
NO₂		
T2 vs T1	0.05	(−0.06, 0.16)
T3 vs T1	0.04	(−0.07, 0.15)
Per 13.7 μg/m³[a]	0.01	(−0.03. 0.05)
PM₂.₅		
T2 vs T1	0.02	(−0.09, 0.12)
T3 vs T1	0.05	(−0.06, 0.16)
Per 2.7 μg/m³[a]	0.01	(−0.03, 0.06)
PM₁₀		
T2 vs T1	0.01	(−0.10, 0.11)
T3 vs T1	0.07	(−0.03, 0.18)
Per 5.6 μg/m³[a]	0.05	(−0.01, 0.09)
PMcoarse		
T2 vs T1	0.02	(−0.09, 0.13)
T3 vs T1	0.04	(−0.08, 0.15)
Per 3.7 μg/m³[a]	0.03	(−0.03, 0.10)
School:		
NO₂		
T2 vs T1	0.09	(−0.03, 0.21)
T3 vs T1	0.07	(−0.05, 0.20)
Per 22.3 μg/m³[a]	0.04	(−0.05, 0.12)
PM₂.₅		
T2 vs T1	0.17	(0.04, 0.30)
T3 vs T1	0.06	(−0.06, 0.18)
Per 10.7 μg/m³[a]	< 0.01	(−0.03. 0.04)
EC		
T2 vs T1	0.10	(−0.03, 0.22)
T3 vs T1	0.08	(−0.05, 0.21)
Per 0.9 μg/m³[a]	0.03	(−0.03, 0.10)
UFP		
T2 vs T1	0.03	(−0.09, 0.15)
T3 vs T1	0.11	(−0.02, 0.24)
Per 13,010 particles/cm³[a]	0.03	(−0.05, 0.11)

Adjusted for maternal and paternal education, maternal and paternal country of birth, paternal employment status, number of siblings, household status and maternal smoking during pregnancy.

[a] Additive change in the adjusted mean of the zBMI associated to an increase in the pollutant level equivalent to a interquartile range increase.

high versus low exposure = 1.30; 95% CI = 1.03, 1.64). No significant association was found between children exposed the medium level of exposure to UFP and the odds of overweight or obesity (OR for medium versus low exposure = 1.19; 95% CI = 0.96, 1.51). None of the models violated the proportional odds assumption. Child's sex, physical activity level, exposure to ETS at home, and maternal education did not modify any of the associations between ambient air pollution and child zBMI (Supplementary Tables S5 and S6). Effect estimates did not substantially change after removing socio-economic variables from the models (Supplementary Table S7). In the complete case-analyses the associations did not change notably (Supplementary Table S8 and S9).

Table 2

Distribution of ambient air pollution concentrations at home and schools.

Air pollutants	Min	Percentile			Max	IQR	WHO guidelines
		p33.3	p50	P66.7			
NO₂ - home	1.7	39.6	44.4	47.9	97.0	13.7	40
NO₂ - school	25.9	46.1	48.5	54.4	84.6	22.3	40
PM₂.₅ - home	6.1	12.7	13.4	14.3	25.0	2.7	10
PM₂.₅ - school	10.0	20.1	25.0	28.2	85.4	10.7	10
PM₁₀ - home	15.2	28.0	30.0	31.6	45.3	5.6	20
PMcoarse - home	8.2	16.0	17.4	18.4	23.5	3.7	–
EC - school	0.6	1.1	1.3	1.5	3.9	0.9	–
UFP - school	11,939	17,612	22,157	27,346	51,146	13,010	–

Units are μg/m³ (NO₂, PM₂.₅, PM₁₀, PMcoarse, and EC) or number of particles per cubic centimeter (UFP). IQR = interquartile range.

Table 4

Association between ambient air pollution concentrations at home and school and zBMI categories.

Air pollutant	Adjusted OR	95% Confidence interval
Home:		
NO_2		
T2 vs T1	1.17	(0.95, 1.44)
T3 vs T1	1.12	(0.91, 1.39)
Per 13.7 µg/m³[a]	1.05	(0.97, 1.13)
$PM_{2.5}$		
T2 vs T1	1.05	(0.86, 1.29)
T3 vs T1	1.13	(0.92, 1.38)
Per 2.7 µg/m³[a]	1.05	(0.96, 1.15)
PM_{10}		
T2 vs T1	1.03	(0.84, 1.26)
T3 vs T1	1.19	(0.97, 1.46)
Per 5.6 µg/m³[a]	1.10	(1.00, 1.22)
PM_{coarse}		
T2 vs T1	1.07	(0.87, 1.33)
T3 vs T1	1.13	(0.92, 1.45)
Per 3.7 µg/m³[a]	1.08	(0.95, 1.22)
School:		
NO_2		
T2 vs T1	1.28	(1.03, 1.61)
T3 vs T1	1.16	(0.96, 1.42)
Per 22.3 µg/m³[a]	1.09	(0.92, 1.28)
$PM_{2.5}$		
T2 vs T1	1.35	(1.07, 1.68)
T3 vs T1	1.09	(0.87, 1.36)
Per 10.7 µg/m³[a]	1.00	(0.93, 1.08)
EC		
T2 vs T1	1.26	(1.01, 1.60)
T3 vs T1	1.23	(0.98, 1.56)
Per 0.9 µg/m³[a]	1.09	(0.97, 1.22)
UFP		
T2 vs T1	1.19	(0.96, 1.51)
T3 vs T1	1.30	(1.03, 1.64)
Per 13,010 particles/cm³[a]	1.11	(0.96, 1.29)

Adjusted for maternal and paternal education, maternal and paternal country of birth, paternal employment status, number of siblings, household status and maternal smoking during pregnancy.

[a] Adjusted OR (odds ratio) of obese/overweight versus normal weight (or, equivalently, of obese versus overweight/normal) associated to an increase in the pollutant level equivalent to a interquartile range increase.

4. Discussion

To our knowledge, this is the first study evaluating the associations of exposure to ambient air pollution at both home and school - the two main micro-environments for school-aged children - with obesity in children. It is also the first to report on such an impact for UFP and EC. We observed that children exposed to high levels of UFP at schools were more likely to be overweight or obese than those exposed to low levels. We also found that increases in NO_2, $PM_{2.5}$ and EC exposure levels at schools were associated with an increase in the odds of being overweight or obese, but only at medium levels of exposure. Sex, physical activity and maternal education did not modify these associations. Associations between ambient air pollution exposure at home and school and zBMI were similar in direction to the overweight/obesity results, but they did mostly (except $PM_{2.5}$-school comparing T2 vs T1) not reach statistical significance.

Five previous studies have assessed the association between exposure to ambient air pollution and childhood obesity, especially focused on TRAP (Dong et al., 2015; Fioravanti et al., 2018; Jerrett et al., 2010, 2014; McConnell et al., 2014). A cohort in 12 communities in Southern California (United States) followed 3318 children from 10 to 18 years and observed a positive association between traffic within 150 m, as proxy of TRAP, around child's home and attained BMI (Jerrett et al., 2010). The same cohort also suggested a synergistic effect between TRAP and second-hand tobacco smoke on the development of

childhood obesity (McConnell et al., 2014). It is worth mentioning that we tested whether exposure to ETS at home modified the association between ambient air pollution and childhood obesity, but we did not observe any effect modification. Another cohort in Southern California from 13 communities, followed 4550 children from 5 to 11 years and observed an annual increase of 14% in BMI, equivalent to an increase of 0.4 on attained BMI at age 10, when comparing the highest and the lowest tenth percentile of TRAP (Jerrett et al., 2014). A Chinese cross-sectional study conducted in 9354 children aged 5–17 observed that obesity modified the association between long-term exposures to ambient air pollution, especially PM_{10}, and hypertension, (Dong et al., 2015). Finally, an Italian birth cohort of 719 infants assessed the association between exposure to NO_2, NO_x, PM_{10}, $PM_{2.5}$, PM_{coarse} and PM_{abs} at home, obtained by using the same ESCAPE LUR model as us, and BMI, blood lipids, and abdominal adiposity at 4 (N = 581) and 8 years of age (N = 499) (Fioravanti et al., 2018). They did not found any association between TRAP and several obesity parameters. Although in previous studies, the NO_x concentrations were similar to those in Barcelona, except in China (US = 80.6 µg/m³, Italy = 69.2 µg/m³, China (NO_2) = 36.4 µg/m³ and Barcelona = 75.3 µg/m³), associations were only observed in the US study maybe because of the larger sample size. The Chinese study found an association using PM_{10} but not with NO_2, this is probably because the concentration of PM_{10} is three times more than our study (China = 88.9 µg/m³ and Barcelona = 29.7 µg/m³). It is important to mention that all previous studies focused on the exposure of ambient air pollution only at home address. However, school-aged children spend approximately between 23% and 35% of their time at schools at morning hours when highest ambient air pollution concentrations are observed (Mazaheri et al., 2014; Nieuwenhuijsen, 2015; Pañella et al., 2017). In our study we evaluated ambient air pollution exposures at schoolyard using in-situ measures, a more accurate measurement of air pollution compared to modeling approaches, and assessed EC and UFP in relation to childhood obesity for the first time. Indeed, the strongest association was observed in relation to UFP exposure at school level.

The health effects of air pollution have been described to follow a linear exposure-response relationship, especially in areas with low exposure levels (between 5 and 35 µg/m³ of $PM_{2.5}$) (Burnett et al., 2014; Cohen et al., 2017). In our study, the associations between ambient air pollution at home (except NO_2) and UFP at school and overweight and obesity followed a linear relationship; however, for NO_2, $PM_{2.5}$ and EC at school the strongest association with overweight or obesity was observed at the second tertile of exposure. One possible explanation of this nonlinearity could be attributable to the so-called saturation phenomenon, where relatively low levels of exposure can activate relevant biological pathways such as oxidative stress and inflammation (Arden Pope et al., 2011). Barcelona has one of the highest air pollution levels in Europe (e.g. children from the lowest tertile are already exposed to higher levels than the WHO recommendations) which could make this saturation effect a possible explanation for our findings. Further, we should consider that the pollutants have different composition, origin and toxicity (HEI, 2010; Krzyzanowski, 2005) and the saturation point maybe differ for each pollutant, leading to different shape of the exposure-response relationship.

The mechanisms underlying the effects of air pollution exposure and childhood obesity are yet to be established. Studies in animals have shown that air pollution uptake may disrupt molecular mechanisms known to underlie obesity pathogenesis including inflammation/oxidative stress and hormone disruption (Sun et al., 2009; Xu et al., 2010). One study observed that exposure to $PM_{2.5}$ could induce insulin resistance and visceral inflammation and adiposity in mice (Sun et al., 2009). A similar study reported that early-life exposure to diesel particles can induce metabolic and vascular dysfunction, inflammation, and visceral adiposity in mice (Xu et al., 2010). This could have further impact on the basal metabolic rate and appetite control of exposed individuals (Bolton et al., 2012). In this animal study they observed that

exposure to diesel exhaust at early-ages could increase the levels of inflammatory cytokines in the brain, inducing microglial activation and anxiety in adulthood, thus predisposing offspring to diet-induced weight gain (Bolton et al., 2012). Another possibility is that effects in other tissues (e.g. the cardio respiratory system) can influence also the metabolic system through systemic inflammation or other common underlying mechanisms (Haberzettl et al., 2016; Wei et al., 2016). A study in mice suggested that the inflammatory activation and lipid oxidation of the lungs induced by long-term exposure to air pollution can, also lead to a metabolic dysfunction and weight gain (Wei et al., 2016). Finally, another experimental study showed that pulmonary oxidative stress could also be involved in the association between ambient air pollution and obesity through insulin resistance and inflammation (Haberzettl et al., 2016). In our study we observed that among pollutants, UFP particles were the pollutants that most increased the risk of overweight or obesity. This may be explained by the fact that the ultrafine fraction of the particles deposit in greater number and deeper into the lungs than do large-size particles, having more capacity to reach the circulation and induce oxidative stress and inflammation (Li et al., 2016).

The major strength of this study is the large sample size and that height and weight were measured by a specialized technician. As mentioned before, another strength is that we have objective measures of air pollution at schools. It is important to assess air pollution at schools as children receive 37% of their daily ambient air pollution dose at schools and also because children normally do physical activity and exercise during school time, thus increasing the inhalation rates (Mejía et al., 2011; Rivas et al., 2016).

Our study faced some limitations. First, given the cross-sectional design of our study, it has a limited capability to establish causality between ambient air pollution and childhood obesity. Future prospective studies with a clear temporal sequence between exposure and health outcome are needed to establish a causal link between air pollution and obesity in children, as well potential windows of exposure-effect susceptibility. Second, even though we adjusted for several socioeconomic characteristics (education, employment, and country of birth), we cannot rule out the likelihood of residual socioeconomic confounding. In our study population children whose parents had a high educational level and low rates of unemployment were exposed to lower levels of ambient air pollution both at home and school than children whose parents had a low educational level and high rates of unemployment (data not shown). However, in the sensitivity analyses we did not observe substantial changes in effect estimates after excluding these social-demographic factors from the models; also, no effect modification by maternal education was observed. Altogether these analyses suggest that residual socioeconomic confounding is unlikely to play a large role in our associations. Third, we cannot rule out residual confounding by factors such as child caloric and antioxidants intakes, but these data were not available in our study. However, child intakes could also be mediators in the associations of interest, as air pollutant exposures could influence appetite control (Bolton et al., 2012) and therefore not a necessary adjustment as shown in the DAG (Shrier and Platt, 2008). Fourth, we could not take into account time activity patterns of the children, which can have an impact on ambient air pollution inhaled doses. Fifth, BMI is not an direct measure of adiposity and therefore future studies can benefit from the use of gold-standard measures, such as Dual-energy X-ray absorptiometry (Moreno Aznar et al., 2011; Simmonds et al., 2015). Sixth, the range of air pollution exposure levels at home was narrow (i.e. the IQR of $PM_{2.5}$-home and PM_{10}-home were 2.7 and 5.6 µg/m^3, respectively) and this may explain why few significant associations were observed in this specific microenvironment. Finally, we should also consider that our home and school ambient air pollution exposures were estimated using different methods and therefore effect estimates cannot be comparable directly. We therefore recommend that future studies use the same exposure models to estimate ambient air pollution at different places. Also, we should

consider that each of these measurements may have introduced different levels of exposure measurement error (neither measure total personal ambient air pollution exposure). Indeed, the LUR model used for our home ambient air pollution measurements may be subject to measurement error due to its dependency on the number of measurement sites, the number of available predictors (Basagaña et al., 2013), and the characteristics of the study area (Mejía et al., 2011; Rivas et al., 2014). In-situ measurements at school may be subject to measurement error because the annual concentrations were only measured twice during the study year (Basagaña et al., 2016), but they are generally still considered to be more accurate (Mejía et al., 2011) and we therefore decided to use the in-situ measurements rather than LUR estimates for the school assessments. We were not able to further quantify these measurement errors as part of this study.

5. Conclusion

This study suggests that exposure to ambient air pollution, particularly at schools, was associated with higher odds of being overweight or obese in a sample ~2500 primary school children in Barcelona. However, a cautious interpretation is warranted because associations were not always linear and because school and home air pollution measurements were not directly comparable. Future studies should examine long-term effects of ambient air pollution on the development of childhood obesity using prospective designs, and taking into account diet, time-activity patterns, and levels of exposure in different environments where children spend time.

Conflict of interest statement

There is no conflict of interest to declare.

Acknowledgements

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.envint.2019.01.048.

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