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Residential proximity fine particles related to allergic sensitisation and asthma in primary school children

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Summary
Background: Fine particulate matter has been linked to allergies by experimental and epidemiological data having used aggregated data or concentrations provided by fixed-site monitoring stations, which may have led to misclassification of individual exposure to air pollution.
Methods: A semi-individual design was employed to relate individual data on asthma and allergy of 5338 school children (10.4 ± 0.7 years) attending 108 randomly chosen schools in 6 French cities to the concentrations of $PM_{2.5}$ (fine particles with aerodynamic diameter $\leqslant 2.5\,\mu m$) assessed in proximity of their homes. Children underwent a medical visit including skin prick test (SPT) to common allergens, exercise-induced bronchial (EIB) reactivity and skin examination for flexural dermatitis. Their parents filled in a standardised health questionnaire.
Results: After adjustment for confounders and NO_2 as a potential modifier, the odds of suffering from EIB and flexural dermatitis at the period of the survey, past year atopic asthma and SPT positivity to indoor allergens were significantly increased in residential settings with $PM_{2.5}$ concentrations exceeding $10\,\mu g/m^3$ (WHO air quality limit values). The relationships were strengthened in long-term residents (current address for at least 8 years).

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Conclusions: Findings support the hypothesis that changes in allergy prevalence observed in recent decades might be partly related to interactions between traffic-related air pollution and allergens. Further longitudinal investigations are needed to corroborate such results.
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Introduction

Various experimental data have shown a link between traffic-related air pollution and allergy.[1,2] *In vitro*, diesel exhaust particulates (DEPs) have been shown to promote immunoglobulin E (IgE) synthesis.[3] *In vivo*, DEPs are at the origin of inflammatory response in target organ tissues and specific immunoglobulin E production (marker of allergy) by modulating immune response.[4–7] Traffic-related pollutants have also been revealed to have an indirect effect on allergic response by influencing quantitatively and qualitatively allergens. In addition, modified antigenicity and production of pollens by allergenic plants due to DEPs might enhance allergic sensitisation in predisposed individuals.[8]

At the population level, there is also evidence of an association between allergy and increased atmospheric concentrations of $PM_{2.5}$ (particles with aerodynamic diameter $\leqslant 2.5\,\mu m$ which are fine and thus highly penetrable in the airways), to which production mostly contributes diesel fuel. An increased prevalence of allergic diseases has been found in urban areas of industrialised countries with heavy truck traffic.[9,10] Moreover, more allergic sensitisation was found in individuals living in heavily polluted urban areas.[11–14] However, traffic-related air pollution has not been associated with allergic diseases in all population-based studies.[15–17] The lack of consistency in population settings could be due to inaccurate assessments of air pollution exposure (through traffic counts or concentrations provided by fixed-site monitoring stations of the Air Quality Monitoring Networks), which may have led to misclassification of individual exposure to air pollution.

In the frame of The French Six City study, a semi-individual design was used to relate individual data on allergic sensitisation and morbidity of children drawn from large population-based samples to concentrations of $PM_{2.5}$, an appropriate surrogate measure of diesel exhaust, assessed in proximity of their residences. A sensitivity analysis was repeated in the children for whom exposure to air quality was likely to have been relatively stable during lifespan in order to limit exposure misclassification. Potential confounders and NO_2, another major traffic-related pollutant, as potential modifier were, taken into account in the study of the relationship.

Methods

Participants

The French Six City (6C) study was intended to estimate the prevalence and the severity of asthma and allergies and identify the associated risk factors in 6 French cities (Bordeaux, Clermont-Ferrand, Créteil, Marseille, Strasbourg, Reims) chosen for their differences in the quality of air. Between March 1999 and October 2000, all children in the relevant school classes from a random sample of schools in each city were recruited and contacted for participating in the survey; namely 9615 children aged 10.4 years in mean.

Protocol

The timetable of the school visits for air quality assessment and simultaneous medical examination of the children was randomly chosen. Children were invited to undergo objective evidence of visible flexural dermatitis,[18] skin prick tests (SPTs) to common aeroallergens (*Dermatophagoides pteronyssinus*, *Dermatophagoides farinae*, cat fur, *Alternaria tenuis*, *Blatta germanica*, mixed grass, *betullaceae* pollens (Stallergènes laboratories, France) and positive and negative controls) and exercise-induced bronchial (EIB) reactivity, provided that parental consent was obtained. SPT positivity was defined as a wheal at least 3 mm greater than that of the negative control for any of the allergens 15 min after the pricks. EIB was defined using a peak flow (PF) according to the standardised protocol of the run test[1] meter as follows: PEFin–PEFfin/PEFin $\geqslant$ 10%.[19] The parents were also asked to complete the questionnaire used in phase II of the International Study of Asthma and Allergies in Childhood (ISAAC).[20] All elements of the study protocol obtained approval of the National Ethics Board (CCPPRB).

Health outcomes

Health outcomes were classified according to the time of their occurrence on the basis of parental responses to the questionnaire as follows:

- *At the period of the survey*: EIB and visible flexural dermatitis according to the physician.
- *Past year*: Asthma (wheezing or whistling in the chest), rhinoconjunctivitis, atopic dermatitis

Past year asthma was separated in atopic, when accompanied by SPT positivity to at least 1 allergen, and non-atopic asthma, otherwise.

- *Lifetime*: Asthma, allergic rhinitis, atopic dermatitis, SPT positivity. Monosensitisation was successively distinguished from polysensitisation. Allergens were grouped in outdoor (mixed grass and tree pollens) and indoor

(house dust mites, cat, and *B. germanica*) allergens, and moulds (*A. tenuis*).

Potential confounders included gender, family history of allergic diseases, passive smoking during pregnancy and later (maternal, paternal, of others), socio-economic status (in 8 classes according to the INSEE), parental education and ethnic group. NO_2 was considered as a potential modifier.

Air pollutants

$PM_{2.5}$ and NO_2 assessments were performed using the same methods and simultaneously in both schoolyards (proximity level) and fixed-site monitoring stations (city level). Five weekdays (from Monday to Friday) were monitored in order to obtain typical traffic volumes. Assessments were scattered over between a minimum of a 13-week span (in 3 cities) and a maximum of a 24-week span (in 1 city) trough all seasons of the year. Data collection was avoided during summer vacations (8 weeks), end-of-the-term vacations and weekends in order to reduce exposure misclassification. Air monitors of $PM_{2.5}$ consisted of 4 l/min battery-operated sampling pumps (Gillian model Gil-Air 5; Gillian Instrument Corp., W. Caldwell, NJ) attached by flexible tubing to polyethylene filter sampling cartridges (University Research Glassware, Carrboro, NC). The cartridge had an inlet nozzle and a greased impactor plate, which eliminated particles $>2.5\,\mu m$ in aerodynamic diameter from the air stream before collection on the filter. The pump/cartridge sampling contained a pre-weighed Teflon filter for gravimetric $PM_{2.5}$. Passive diffusion samplers were used to assess concentrations of NO_2 (Radiello, Padua, Italy). Analyses were centralised in Paris for $PM_{2.5}$ and in Padua for NO_2, respectively. The reproducibility of air pollution assessments using pumps was determined in Strasbourg. NO_2 concentration values obtained with passive diffusion samplers at monitoring stations were compared to those obtained by Air Quality Monitoring Networks by chemiluminescence. Detailed methods were presented elsewhere.[21]

- *Proximity level:* To represent traffic-related air quality at residential proximity, the concentrations of $PM_{2.5}$ and NO_2 were measured in the schoolyards of the schools attended by the children during the week, when possible, of the medical examination according to the timetable of the survey. It must be noted that in urban France almost all children live within 500 m of their elementary school.
- *City level:* To represent traffic-related air quality at city level, the concentrations of $PM_{2.5}$ and NO_2 were measured on fixed-site monitoring stations. This allowed determining the reliability of the study methods compared with assessments provided by Air Quality Monitoring Networks. In each city, fixed-sites monitoring stations considered as the most representative of the global background pollution by experts of the networks were chosen. They were 2 at maximum.

Statistical and epidemiological analyses

Air pollutants: At the school level, the inter-variability of $PM_{2.5}$ and NO_2 assessments during the survey span was estimated using the coefficient of variation (CV), i.e. the ratio of the standard deviation to the mean of the concentrations. In the case of several schools located closely (according to the experts of the monitoring stations), a unique CV was estimated. Correlations between concentration values obtained with our instruments at both proximity and city levels were performed by computing the Spearman coefficient. NO_2 concentration values obtained with passive diffusion samplers at monitoring stations were compared to those obtained by chemiluminescence by computing the corresponding regression equation.

Relation of $PM_{2.5}$ to health outcomes: The 5-day means of $PM_{2.5}$ and NO_2 levels were used in the analyses. In the case of 2 fixed-site monitoring stations the mean of the concentrations was computed to assess the city level. Due to inter and intra-cities heterogeneity (Fig. 1), a two-class variable of exposure (high vs. low) to $PM_{2.5}$ and NO_2 was defined with respect to the median value of the distribution of the concentrations in the schoolyards and on monitoring stations, respectively, independent of the city. Logistic regression analysis was used to obtain the odds-ratio (OR) of each health outcome for high vs. low pollutant exposure adjusted for potential confounders and NO_2 as a potential modifier.[22] A marginal model[23] was applied in order to take into account the non-independence of data in children living in the same city, as they share the same environment in terms of climate, pollens, food products, diet and socio-cultural factors. The parameters of the marginal model were estimated by the generalised estimating equation (GEE) approach using SAS GENMOD with independent working

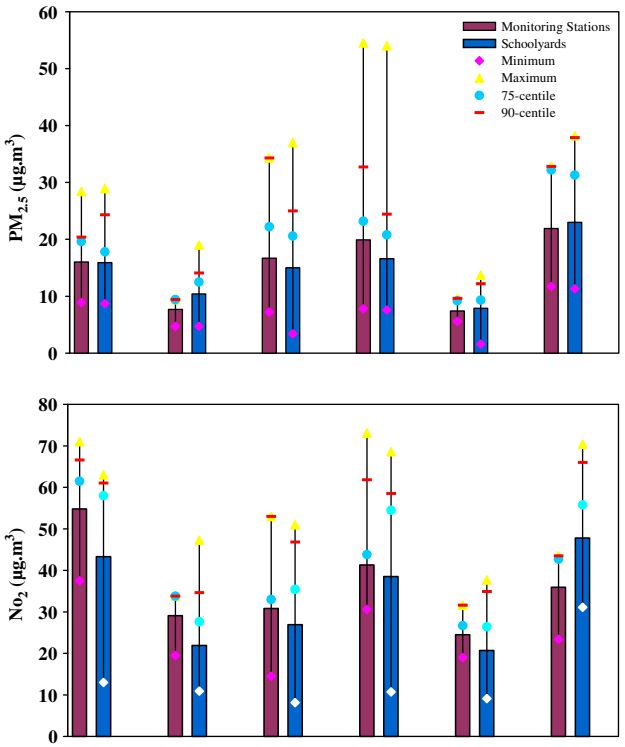

Figure 1 Distribution of 5-day mean NO_2 and $PM_{2.5}$ concentrations at monitoring stations, schoolyards and classrooms in the French Six Cities Study.

correlation structure using the city as stratum. Version 8.2 of SAS System for AIX was used for statistical analyses. Statistical significance was provided by a p-value <0.05. In order to limit exposure misclassification, a sensitivity analysis was repeated in the children for whom exposure to air quality was likely to have been relatively stable during life as they had spent the last 8 years at the same address (long-term resident children).

Results

The response rate to the questionnaire survey was 81% (7781/9615). 6672 children (69%) in 401 classrooms of 108 targeted schools completed the survey protocol (Table 1). Protocol completion rate among the participating children ranged from 79% (Créteil) to 98% (Strasbourg). Analyses on air pollution were restricted to the 5338 (80%) children who underwent examination the week of the air quality assessment in order to take potential short-term effects of air pollution into account. Children excluded from the analysis did not differ significantly from the others in terms of the recorded characteristics.

Atopic dermatitis had the highest lifetime cumulative prevalence followed by allergic rhinitis and asthma (25.6%, 20.0% and 9.9%, respectively) (Table 2). This trend was confirmed for symptoms in the past year. At the period of the survey, 10.6% of children suffered from flexural dermatitis as assessed by a physician and 8.7% had EIB. Twenty-eight percent of the children had at least one positive SPT; 12.3% of the children were positive to outdoor allergens, 20.9% to indoor allergens, and 2.8% to *Alternaria tenuis*. Monosensitisation was observed in 11.2% of children and polysensitisation in 16.8%.

The CVs estimated to determine the inter-variability of $PM_{2.5}$ assessments through the survey as described in the methods were always $<$ 10%. NO_2 concentration values measured with passive diffusion samplers at monitoring stations were highly related to those provided the same week by Air Quality Monitoring Networks (Regression coefficient: 0.82; $p<0.0001$). Furthermore, concentration values assessed using pumps and passive diffusion samplers in schoolyards correlated satisfactorily with those obtained at city level the same week (Spearman correlation coefficient: 0.88; $p<0.0001$ and 0.69; $p<0.0001$ for $PM_{2.5}$ and NO_2, respectively). There was no significant difference in the concentrations of $PM_{2.5}$ and NO_2 in schoolyards and city level (Table 3).

After adjusting for proven confounders (namely gender, passive smoking and family history of allergic diseases) with

Table 1 Characteristics of the children having participated in the French Six Cities Study ($n = 6672$).

Factors	Child	Mother	Father
Age (years) (m±SD)	10.4±0.7	38.4±5.1	41.5±6.3
Sex (male) (%)	49.2		
Weight (kg) (m±SD)	36.21±8.14		
Height (m) (m±SD)	1.42±0.08		
Body mass index (m/kg^2) (m±SD)	17.88±2.88		
Peak flow (ml/min) (m±SD)	330.1±49.0		
Geographical origins (%)			
Metropolitan France		74.9	73.1
French overseas departments		3.6	2.5
South Europe		3.8	4.3
Morocco, Algeria, Tunisia		8.5	10.1
Sub-Saharan Africa		3.3	3.5
Asia		2.8	3.0
Other		3.2	3.5
Education (%)			
Primary		11.7	12.5
Secondary		45.3	42.9
High school and university		37.8	39.3
Other		5.2	5.4

(m±SD): Mean±standard deviation; Body mass index: Weight/Height^2.

Table 2 Prevalence rates (%) of skin prick test positivity and allergic and respiratory morbidity in the French Six Cities Study ($n = 6672$).

Health outcome	Boys	Girls	All
During air pollution assessment			
N	3246	3357	6603
EIB	9.1	8.3	8.7
Flexural dermatitis	9.0	12.2*	10.6
Past year			
N	3141	3166	6307
Asthma	9.7	6.6*	8.1
Rhinoconjunctivitis	13.1	10.7**	11.9
Atopic dermatitis	10.8	14.1*	12.5
Lifetime			
N	3213	3336	6549
Asthma	12.7	7.1*	9.9
Atopic asthma	5.9	3.5*	4.6
Non-atopic asthma	2.8	2.5	2.6
Allergic rhinitis	22.3	17.9*	20.0
Atopic dermatitis	24.6	26.5	25.6
SPT positivity	32.4	23.7*	28.0
Monosensitisation	12.0	10.5	11.2
Polysensitisation	20.4	13.3*	16.8

EIB: Exercise-induced bronchial hyperresponsiveness as assessed by PEFin–PEFfin/PEFin$\geqslant$10% (PEF = peak expiratory flow); SPT: skin prick tests; Monosensitisation: SPT positivity to at least 1 allergen; Polysensitisation: SPT positivity to at least 2 allergens.
*$p<0.001$.
**$p<0.01$.

Table 3 $PM_{2.5}$ and NO_2 concentrations in residential proximity (schoolyards) and at city level as assessed by passive samplers in the French Six Cities Study (108 schools, 401 classrooms, $n = 5538$ children with clinical examination the week of air quality assessment).

	N samplers	Low concentration		High concentration		% children in settings with high concentrations
		Interval		Interval		
		Range	Mean	Range	Mean	
Pollutant						
Residential proximity level						
$PM_{2.5}$	111	[1.6–12.2][a]	8.7	[12.5–54.0]	20.7	55.4
NO_2	111	[8.1–31.0]	19.0	[31.1–70.40]	46.4	60.1
City level						
$PM_{2.5}$	51	[4.7–12.7]	9.6	[13.0–54.5]	23.0	59.0
NO_2	53	[14.5–36.9]	28.3	[37.5–73.2]	50.2	53.2

The two categories of exposure "low" vs. "high" were defined with respect to the median value of the distribution of the concentrations.

[a]Concentrations are expressed in $\mu g/m^3$.

the logistic regression model, the odds of suffering from EIB and flexural dermatitis at the period of the survey, past year atopic asthma and SPT positivity to indoor allergens were significantly higher than 1 in residential settings with $PM_{2.5}$ concentrations superior to the median value, respectively (Tables 4 and 5). A borderline significance existed in the case of lifetime allergic rhinitis. An OR higher than 1 was observed for moulds but no statistical significance was reached probably because of the small sample size. Results observed at city level confirmed these findings (Tables 4 and 5). A higher percentage of allergic polysensitisation than of monosensitisation was observed in children highly exposed to $PM_{2.5}$ (Fig. 2). The inclusion as an independent variable in the various models of NO_2 concentration, which was significantly related to EIB, flexural dermatitis and SPT to indoor allergens (Tables 4 and 5), yielded similar results for $PM_{2.5}$.

The sensitivity analysis repeated in the 1975 children for whom exposure to air quality was likely to have been stable most of life as they had spent the last 8 years at the same address (long-term resident children) displayed similar or even higher ORs, in spite of the reduction of the sample size (Tables 4 and 5). These results were unaffected when the non-independence of data was taken into account using the marginal model (data not shown).

Discussion

In this large population-based sample of 5338 school-children, the adjusted odds of suffering from exercise-induced asthma and flexural dermatitis at the period of the survey, past year asthma and SPT positivity were significantly higher than 1 in concurrence with elevated $PM_{2.5}$ concentrations in the proximity of the houses where the children lived. In the case of asthma, the risk was limited to atopic asthma. The relationships were strengthened in long-term residents (current address for at least 8 years) for whom exposure to outdoor air pollutants could be considered stable through life. Although not excessive, the mean concentrations we observed in the high exposed settings are close to the standard ($10\,\mu g/m^3$ (annual average)) the World Health Organization recommends, for long-term exposure.

Our population findings extend previous data relating vehicles counts or air pollutant concentrations provided by fixed-site monitoring stations to various respiratory and allergic health outcomes,[9,24–26] among which allergic sensitisation.[11–14,27] In one of these studies, high vehicle traffic close to home was associated with asthma, cough and wheeze and in children additionally exposed to environmental tobacco smoke also with allergic sensitization.[13] In our study, respiratory and allergic health outcomes persisted to be related to fine particulate pollution after allowing for: (1) environmental tobacco smoke and familial history of asthma, which are known risk factors of such outcomes[28] through adjusted models as well as for (2) the city through the use of a marginal model, which allowed controlling for climate, pollens, food products, diet and socio-cultural factors that are other known factors of allergic and respiratory diseases. Such factors are shared at city level. Our findings contrast with previous data.[15,16] Variations in findings might be due to exposure misclassification in these studies. In the 6C Study, we reduced potential misclassification of exposure to air pollution by employing a semi-individual design in which air quality was assessed in the proximity of the child's home and by performing a sensitivity analysis in long-term residents. Our results also show an increased risk for flexural dermatitis in children exposed to high levels of traffic-related air pollution, which to our knowledge had scarcely been reported previously.[29] However, such result deserves to be confirmed.

A limitation of our work consists in the fact that concentrations of $PM_{2.5}$ and NO_2 we observed in the different settings could not be representative of usual concentrations in these settings. However, there was no

Table 4 Odds ratios (95% confidence interval) of allergic and respiratory morbidity by high vs. low concentrations of $PM_{2.5}$ and NO_2 in all ($n = 5338$) and long-term resident ($n = 1945$) children of the French Six Cities Study.

Site of assessments	$PM_{2.5}$ High vs. low concentrations				NO_2 High vs. low concentrations			
	All		Long-term resident		All children		Long-term residents[a]	
	OR	95% CI			OR	95% CI		
Proximity level								
Current								
EIB	1.35	1.10, 1.67	1.45	1.04, 2.01	1.52	1.21, 1.90	1.47	1.05, 2.06
Fl. atopic dermatitis	2.51	2.06, 3.06	2.97	2.14, 4.11	2.40	1.95, 2.96	3.10	2.19, 4.38
Past year								
Asthma	1.11	0.88, 1.39			1.21	0.96, 1.52		
Atopic asthma	1.43	1.07, 1.91	1.57	0.96, 2.57	1.61	1.18, 2.18	1.61	0.97, 2.67
Non-atopic asthma	0.73	0.49, 1.07			0.92	0.62, 1.36		
Rhinoconjunctivitis	0.94	0.77, 1.15			0.92	0.75, 1.12		
Atopic dermatitis	1.05	0.88, 1.27			1.05	0.86, 1.26		
Lifetime								
Asthma	1.00	0.82, 1.22			1.13	0.92, 1.40		
Allergic rhinitis	1.09	0.93, 1.27			1.08	0.92, 1.27		
Atopic dermatitis	0.94	0.82, 1.09			0.95	0.82, 1.10		
City level								
Current								
EIB	1.43	1.15, 1.78	1.42	1.01, 1.99	1.34	1.09, 1.64	1.52	1.10, 2.10
Fl. atopic dermatitis	2.06	1.69, 2.51	2.49	1.79, 3.47	1.51	1.26, 1.81	1.59	1.18, 2.13
Past year								
Asthma	1.31	1.04, 1.66	1.16	0.80, 1.70	1.16	0.93, 1.44		
Atopic asthma	1.58	1.17, 2.14	1.87	1.11, 3.14	1.18	0.89, 1.57		
Non-atopic asthma	1.00	0.68, 1.49			1.08	0.74, 1.58		
Rhinoconjunctivitis	0.98	0.80, 1.20			1.18	0.97, 1.43		
Atopic dermatitis	1.08	0.90, 1.30			0.99	0.83, 1.18		
Lifetime								
Asthma	1.09	0.89, 1.33			1.02	0.84, 1.24		
Allergic rhinitis	1.13	0.97, 1.33			1.06	0.91, 1.23		
Atopic dermatitis	0.95	0.82, 1.09			1.03	0.90, 1.17		

The two categories of exposure "low" vs. "high" were defined with respect to the median value of the distribution of the concentrations; EIB: exercise-induced bronchial hyperresponsiveness as assessed by PEFin–PEFfin/PEFin $\geqslant$10% (PEF = peak expiratory flow); SPT: skin prick tests.

Odds-ratios (ORs) were adjusted for age, sex, family history of allergy and passive smoking.

[a]8 years at the same address.

evidence of unusual conditions having strongly influenced air quality at local level during the entire survey span, which was also shown by a CV$<$10%. Our results are further supported by the fact that in France air pollution emissions have been estimated to be stable at local level during the life of the children.[30] The sensitivity analysis in long-term residents and the fact that relative rankings of geographical zones with respect to various air pollutants have not changed in the past decade[31] also corroborate our findings. Unfortunately, in order not to diminish significantly the sample size, our sensitivity analysis did not take into account the first year of life which is crucial for allergic sensitisation. However, results were similar in the group of children having lived always at the same address. From the statistical point of view, the large size and spatio-temporal distribution of our sample of randomly selected schools reduced the probability of a falsely positive relationship. The consistence of a potential effect of fine particles is endorsed by findings obtained in the same sample of children, relating long-term exposure to background PM_{10} to a higher risk of allergic rhinitis, asthma and SPTs positivity.[32]

Our population-based findings are also consistent with experimental data that have demonstrated that inhalation of traffic-related air pollutants either individually or in combination, can enhance the immune responses and airway response to inhaled allergens, such as pollens or house dust mites, in atopic subjects.[1,33] There is also some evidence that DEPs can interact with aeroallergens, so enhancing their effects.[5,34,35] We found that at the population level the effects of fine particles, a good proxy of DEPs, were greater for indoor allergens than for outdoor allergens,

Table 5 Odds ratios (95% confidence interval) of allergic sensitisation by high vs. low concentrations of $PM_{2.5}$ and NO_2 in all ($n = 5338$) and long-term resident ($n = 1945$) children of the French Six Cities Study.

Site of AP assessment	$PM_{2.5}$ High vs. low concentrations				NO_2 High vs. low concentrations			
	All children		Long-term resident[a]		All children		Long-term resident[a]	
	OR	95% CI			OR	95% CI		
Proximity level								
All allergens	1.19	1.04, 1.36	1.19	0.96, 1.47	1.08	0.94, 1.25		
Indoor allergens	1.29	1.11, 1.50	1.26	1.00, 1.59	1.21	1.04, 1.41	1.13	0.89, 1.43
Outdoor allergens	1.02	0.85, 1.23			0.94	0.78, 1.13		
Moulds	1.13	0.78, 1.65			1.18	0.80, 1.73		
City level								
All allergens	1.32	1.15, 1.51	1.42	1.15, 1.76	0.92	0.81, 1.05		
Indoor allergens	1.51	1.29, 1.76	1.45	1.15, 1.84	0.96	0.83, 1.10		
Outdoor allergens	1.06	0.88, 1.28			0.86	0.72, 1.03		
Moulds	1.00	0.69, 1.46			1.14	0.79, 1.65		

Odds-ratios (ORs) were adjusted for age, sex, family history of allergy and passive smoking.
The two categories of exposure "low" vs. "high" were defined with respect to the median value of the distribution of the concentrations; EIB: PEFin–PEFfin/PEFin $\geqslant$ 10%.
[a]8 years at the same address.

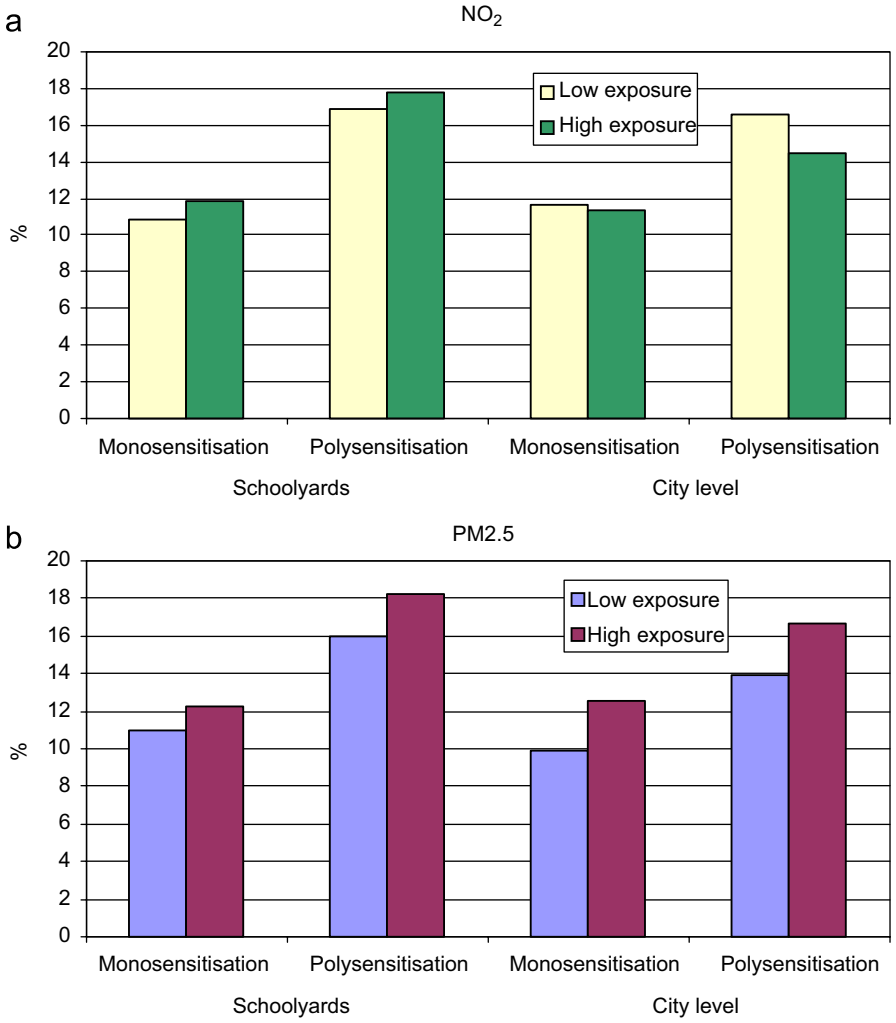

Figure 2 Prevalence rates (%) of monosensitisation and polysensitisation according to low or high exposure to NO_2 and $PM_{2.5}$ concentrations in residential proximity and at city level in the French Six Cities Study ($n = 5338$).

probably because the former allergens are ubiquitous and perennial. Consistently, we also observed that $PM_{2.5}$ concentrations were related to atopic asthma.

Contrary to what observed in experimental studies in which elevated concentrations of pollutants are necessary to obtain immediate IgE synthesis, repeated although not excessive $PM_{2.5}$ concentrations might be sufficient for the enhancement of allergic response and exacerbations at the population level.[12] In our study, the concentrations above which the effects of fine particulate were observed were close to the standards indicated by WHO. The existence of an effect at small concentrations might depend on individual susceptibility, which is modulated by various factors among which diet. Recent data have shown that antioxidant defences have a key role in controlling the allergic response to DEP as assessed by IgE production.[36] However, the mechanisms by which fine particulate and the other traffic-related pollutants might influence allergen handling by the individual and promote allergic sensitisation and morbidity can be only hypothesised. Gaseous pollutants may alter the means of defence (muco-ciliary purification and antibacterial defence), inducing development of a neutrophil inflammatory reaction and sensitisation by allergen-dependent IgE. Diesel particles have been shown to enhance inflammatory reactions and sensitisation.[37] It has been suggested that this could be due to the intervention of polycyclic aromatic hydrocarbons (PAHs) contained in particulate matter or highly related to it[38]; diesel and gasoline vehicles exhausts being the predominant local emission sources of PAHs. However, it cannot be excluded that fine particulate might also influence non-immunological properties of the allergens, such as their enzymatic activity, thus contributing to their increased penetration in the target organs. Recent data have shown that some proteolytic enzymes in allergens, house dust mites overall, are capable of increasing epithelial permeability and thereby creating conditions that favour transepithelial delivery of allergens,[39] which is also consistent with our results.

To sum up, the present population-based data support experimental and epidemiological findings according to which a complex pollution mixture associated with fine particulate matter might in part contribute to the enhancement of allergic sensitisation through interactions with allergens. Whether such phenomenon might contribute to explain the rise in allergic morbidity in children observed in recent decades cannot be answered in the absence of a more appropriate assessment of exposure. If confirmed, this will raise additional concerns about public health effects of PM, already implicated in higher rates of morbidity and mortality.[40,41]

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