

Original article

The relationships between ambient air pollutants and childhood asthma and eczema are modified by emotion and conduct problems

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ABSTRACT

Purpose: This study examined the hypothesis that emotion and conduct problems (ECPs) may modify the relationships between ambient air pollutants and childhood asthma and eczema.

Methods: In the cross-sectional study, 4209 French schoolchildren (aged 10–12 years) were investigated between March 1999 and October 2000. Ambient air pollutants exposures were estimated with dispersion modeling. Health outcomes and ECPs were evaluated by validated questionnaires, completed by the parents. Marginal models were used to analyze the relationships of exposures to ambient air pollutants and/or ECPs to asthma phenotypes and current eczema, adjusting for potential confounders.

Results: In our population, interactions were found between ECPs and exposures to ambient air pollutants (benzene, carbon monoxide, nitrogen dioxide, nitrogen oxides, particulate matter with an aerodynamic diameter below 10 μm , volatile organic compounds) ($P < .20$). In addition, ECPs were related to current wheezing (adjusted prevalence odds ratio [aOR], 2.35; 95% confidence interval [CI], 1.59–3.47), current doctor-diagnosed asthma (aOR, 1.82; 95% CI, 1.25–2.66), and current eczema (aOR, 2.21; 95% CI, 1.61–3.02). Children with ECPs had 1.17–1.51 times higher aORs for the associations between ambient air pollutants and asthma phenotypes and current eczema than those without ECPs.

Conclusions: ECPs may modify the relationships between ambient air pollutants and childhood asthma and eczema.

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Introduction

Increasing evidence has indicated that social environment could alter susceptibility to ambient air pollution in relation to health outcomes [1–4]. Psychological features as an important social environmental factor that impacts on the development of childhood asthma and eczema have been well documented in literature [5–9]. However, few studies have included ambient air pollutants

and psychological disorders together to gain a more comprehensive picture of how ambient air pollutants contribute to childhood asthma and eczema. Now a small but growing number of scientists are investigating whether chronic psychological stress interacts with pollutants to produce adverse health effects [10]. In North America, Chen et al. [2] found that there was an interaction between chronic stress (measured by the University of California Los Angeles Life Stress Interview) and chronic traffic-related air pollution in relation to asthma outcomes in 9- to 18-year-old Canadian children. Later, data investigating on the first grade schoolchildren (5–9 years) in 13 southern California communities of America indicated that the risk of asthma attributable to traffic-related air pollution was significantly higher for children with

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higher parental stress than for children with lower stress [3]. However, these studies did not consider internalizing and externalizing disorders together.

In the present study, we hypothesize that both emotional symptoms (internalizing disorders) and conduct problems (externalizing disorders) interact with ambient air pollutants in relation to schoolchildren's asthma phenotypes (current wheezing and current doctor-diagnosed asthma) and current eczema. We used the data set of the French Six Cities Study to examine this hypothesis.

Methods

Study population

Between March 1999 and October 2000, 9615 children were recruited from 108 randomly selected elementary schools to participate in the French Six Cities Study (the six cities included Creteil, Reims, Marseille, Strasbourg, Clermont-Ferrand, and Bordeaux) [11]. Our study population included only those children aged 10–12 years that resided at their current address for more than 3 years and without missing data on emotion and conducts problems (ECPs) (total sample of 4209). Children's parents filled standard questionnaires to measure health outcomes and ECPs after having signed an informed consent for the survey. All the questionnaires were completed by the parents of the children between 1999 and 2000. The study protocol was approved by French National Ethics Board (*Comité Consultatif de Protection des Personnes se prêtant à des Recherches Biomédicales*, approval number: 01/07, Marseille, France).

Exposure and health data collection

Long-term exposures to ambient air pollutants were estimated by a dispersion model through the STREET 5 software (Kunz Technologie Transfer [KTT] Umweltberatung in cooperation with Targeting; Versailles, France), using data of the 3-year average (from 1998 to 2000) concentrations of benzene, carbon monoxide (CO), nitrogen dioxide (NO₂), nitrogen oxides (NO_x), particulate matter with an aerodynamic diameter below 10 μm (PM₁₀), (volatile organic compounds (VOCs) at 108 school addresses, and were described in more detail previously [12]. Because in urban France almost all children live within 500 m of their elementary schools, the exposure to ambient air pollutants estimated in school addresses was considered as a satisfactory assessment of proximity to exposure to ambient air pollutants in residential addresses. Data on asthma phenotypes, current eczema, and covariates were collected by an enriched version of the International Study of Asthma and Allergies in Children questionnaire [13]. ECPs were investigated by Strengths and Difficulties Questionnaire (SDQ) [14].

Assessment of asthma phenotypes and eczema

Current wheezing was defined by a “yes” response to question “In the last 12 months, had your child had wheezing in the chest?” [15]. Current doctor-diagnosed asthma was defined by (1) a “yes” response to question “Has the asthma of your child been diagnosed by a physician” and (2) parent-reported wheezing attacks in the last 12 months and/or asthma medication use in the last 12 months [16]. We also included current eczema, a disorder sharing genetic and environmental risk factors with asthma and having a causal link with asthma [17]. Current eczema was defined as itchy rash in flexural areas in the last 12 months [15].

Assessment of ECPs

ECPs (internalizing and externalizing problems, respectively) were measured by two scales (emotional symptoms and conduct problems scales, with five items for each scale) of SDQ on children's behavior in the past 6 months. Each item was scored, using a three-point Likert scale: 0 for “not true,” 1 for “somewhat true,” or 2 for “very true.” The score of each item added up to a total score of ECPs, ranging from 0 to 20. In our study, for both emotional symptoms and conducts problems, children with highest 10% scores (cut-off = 4) were defined as having difficulties [14,18]. The total scores between 0 and 8 were defined as “emotion and conduct problems (ECPs)”, whereas the score range for “no emotion and conduct problems (No ECPs)” was 9–20.

Statistical analysis

The population characteristics were provided by percentages and means. Differences of air pollutant concentrations between children with ECPs and those without and among children in the six study centers were analyzed by *t*-test and analysis of variance, respectively. To take into account the potential nonindependence of data for children living in the same community [11], marginal models [19] were used to analyze the relationships of exposures to ambient air pollutants and/or ECPs to asthma phenotypes and current eczema, controlling for the potential confounders of gender, study center, ethnic origin, parental educational attainment, siblings, family history of asthma, prenatal parental smoking, dampness in the house during the first year of life, and contact with pets during the first year of life and age. The parameters of the marginal models were estimated by the generalized estimating equation approach [19], using exchangeable working correlation matrices. Confounders were identified when the addition of a covariate to the model changed the prevalence odds ratio by 10%, without considering statistical significance. Interactions were identified when the model with a statistically significant ($P < .20$) interaction term had a smaller value of quasi-likelihood under the independent model criteria compared with the model included all other covariates of the aforementioned model except for the interaction term. In the models, ambient air pollutants were entered as continuous variables. Adjusted prevalence odds ratios (aORs) for the relationships between ambient air pollutants and asthma phenotypes and current eczema were calculated based on an interquartile increase in exposures to ambient air pollutants. When interactions between ECPs and ambient air pollutants existed, aORs and 95% confidence interval for the relationships between ambient air pollutants and asthma phenotypes and current eczema were calculated according to ECPs.

All statistical tests were performed using SAS statistical software version 9.2 (SAS Institute, Inc., Cary, NC). All values of *P* were two-tailed. A value of $P < .05$ was considered statistically significant, except for the values of *P* for interaction terms.

Results

Characteristics of study population

The characteristics of the study population were described in Table 1 and Supplementary Table S1, according to ECPs and study centers, respectively. There were 2097 (50%) boys in the study population. The mean age of the study population was 10.80 years. The prevalence of current eczema was highest (13%), followed by current wheezing (7%) and current doctor-diagnosed asthma (5%). There were significant differences for certain characteristics between children with ECPs and those without ($P < .05$), except for

Table 1
Characteristics of the study population according to ECPs

Characteristics	All (n = 4209)	No ECPs (n = 3735)	ECPs (n = 474)	P*
Gender, n (%)				.02
Male	2097 (50)	1837 (49)	260 (55)	
Female	2112 (50)	1898 (51)	214 (45)	
Total	4209 (100)	3735 (100)	474 (100)	
Study center, n (%)				.39
Creteil	841 (20)	730 (20)	111 (23)	
Reims	487 (12)	431 (12)	56 (12)	
Marseille	672 (16)	599 (16)	73 (15)	
Strasbourg	778 (18)	689 (18)	89 (19)	
Clermont-Ferrand	720 (17)	649 (17)	71 (15)	
Bordeaux	711 (17)	637 (17)	74 (16)	
Total	4209 (100)	3735 (100)	474 (100)	
Ethnic origin, n (%)				.76
Metropolitan France	2618 (63)	2323 (63)	295 (64)	
French overseas departments and foreign countries	1515 (37)	1349 (37)	166 (36)	
Total	4133 (100)	3672 (100)	461 (100)	
Parental educational attainment†, n (%)				<.01
Low (primary or secondary)	1974 (50)	1721 (49)	253 (58)	
High (tertiary)	1957 (50)	1774 (51)	183 (42)	
Total	3931 (100)	3495 (100)	436 (100)	
Preterm birth‡, n (%)				.77
Yes	361 (9)	322 (9)	39 (8)	
No	3848 (91)	3413 (91)	435 (92)	
Total	4209 (100)	3735 (100)	474 (100)	
Siblings (>1), n (%)				.10
Yes	3140 (75)	2801 (75)	339 (72)	
No	1069 (25)	934 (25)	135 (28)	
Total	4209 (100)	3735 (100)	474 (100)	
Family history of asthma, n (%)				.08
Yes	890 (21)	775 (21)	115 (24)	
No	3319 (79)	2960 (79)	359 (76)	
Total	4209 (100)	3735 (100)	474 (100)	
Prenatal parental smoking, n (%)				<.01
Yes	1446 (34)	1255 (34)	191 (40)	
No	2763 (66)	2480 (66)	283 (60)	
Total	4209 (100)	3735 (100)	474 (100)	
Dampness in the house during the first year of life, n (%)				<.01
Yes	667 (18)	564 (17)	103 (24)	
No	3124 (82)	2799 (83)	325 (76)	
Total	3791 (100)	3363 (100)	428 (100)	
Contact with pets during the first year of life, n (%)				<.01
Yes	1222 (29)	1058 (28)	164 (35)	
No	2987 (71)	2677 (72)	310 (65)	
Total	4209 (100)	3735 (100)	474 (100)	
Current wheezing, n (%)				<.01
Yes	289 (7)	233 (6)	56 (12)	
No	3846 (93)	3439 (94)	407 (88)	
Total	4135 (100)	3672 (100)	463 (100)	
Current doctor-diagnosed asthma, n (%)				<.01
Yes	196 (5)	160 (5)	36 (8)	
No	3709 (95)	3302 (95)	407 (92)	
Total	3905 (100)	3462 (100)	443 (100)	
Current eczema, n (%)				<.01
Yes	518 (13)	422 (12)	96 (21)	
No	3545 (87)	3182 (88)	363 (79)	
Total	4063 (100)	3604 (100)	459 (100)	
Maternal age at recruitment (y), mean (SD)	38.84 (4.98)	38.90 (4.99)	38.42 (4.95)	.05
Age (y), mean (SD)	10.80 (0.69)	10.79 (0.68)	10.86 (0.71)	.04
Birth weight (g), mean (SD)	3261 (517)	3262 (520)	3251 (489)	.67

SD = standard deviation.

* The value of P for t-test or chi-square test between children with ECPs and those without.

† The highest educational attainment of both fathers and mothers.

‡ Maternal gestational age <37 wk and low birth weight (<2500 g).

study center, ethnic origin, preterm birth, family history of asthma, and birth weight (Table 1). There were significant differences for various characteristics among children in the six study centers ($P < .05$), except for gender, family history of asthma, birth weight, emotional symptoms, conduct problems, ECPs and prevalences of current wheezing, current doctor-diagnosed asthma, and current eczema (Supplementary Table S1).

Exposure to ambient air pollutants

Exposures to ambient air pollutants were described in Table 2 and Supplementary Table S2, according to eECPs and study centers, respectively. The concentrations of air pollutants did not differ between children with ECPs and those without ($P > .05$; Table 2). However, there were significant differences for the concentrations

Table 2

Concentrations of ambient air pollutants in study population according to ECPs, mean (SD)

Air pollutants	All (n = 4209)	No ECPs (n = 3735)	ECPs (n = 474)	P ^a
Benzene (μg/m ³)	2.41 (0.87)	2.42 (0.87)	2.39 (0.84)	.51
CO (μg/m ³)	558.94 (153.16)	559.14 (153.53)	557.36 (150.34)	.81
NO ₂ (μg/m ³)	44.19 (10.85)	44.15 (10.84)	44.56 (10.99)	.43
NO _x (μg/m ³)	78.82 (32.04)	78.80 (32.05)	78.95 (31.97)	.92
PM ₁₀ (μg/m ³)	26.68 (6.57)	26.70 (6.59)	26.48 (6.46)	.49
VOCs (μg/m ³)	17.35 (18.27)	17.41 (18.31)	16.88 (17.96)	.55

SD = standard deviation.

^a The value of *P* for the differences of air pollutants concentrations between children with ECPs and those without.

of air pollutants among children in the six study centers ($P < .01$; [Supplementary Table S2](#)).

ECPs, asthma phenotypes, and eczema

Both emotional symptoms and conduct problems were significantly related to current wheezing, current doctor-diagnosed asthma, and current eczema ([Table 3](#)).

Interactions between ECPs and ambient air pollutants

There were interactions between ECPs and ambient air pollutants in relation to current doctor-diagnosed asthma, current wheezing, and current eczema ($P < .20$). The aORs between ambient air pollutants and asthma phenotypes and current eczema were 1.17–1.51 times higher for children with ECPs than for those without. The prevalence odds ratio discrepancy attenuated to 1.15–1.43 times when comparing with the whole study population ([Table 4](#)). Both emotional symptoms and externalizing disorders conduct problems interacted with ambient air pollutants in relation to asthma phenotypes and eczema ($P < .20$; [Supplementary Figure S1A and B](#)).

An interquartile increase in exposures to benzene, NO_x, and VOCs were found to be related to current wheezing, whereas exposure to NO_x was related to current doctor-diagnosed asthma, among children with ECPs ([Table 4](#)). However, no relationships were found between ambient air pollutants and asthma phenotypes among children without ECPs. Current eczema was found to be associated with an interquartile increase in exposures to benzene, CO, NO₂, NO_x, PM₁₀, and VOCs among children with ECPs ([Table 4](#)). The relationships persisted among children without ECPs in cases of exposures to CO, NO₂, and PM₁₀.

Discussion

Our data showed that ECPs may modify the relationships between ambient air pollutants and schoolchildren's asthma and eczema.

Increasing evidence had implicated the associations between ambient air pollutants and asthma and eczema [20–23]. Most recently, results of a large birth cohort study in Sweden showed

that exposures to PM₁₀ and NO_x from traffic in the first year of life as measured by a dispersion model were positively associated with asthma in children up to 12 years of life [22]. In two German birth cohort studies (German Infant Nutritional Intervention [GINI] and Influences of Lifestyle-related Factors on the Immune System and the Development of Allergies in East and West Germany [LISA]), results showed that long-term exposure to NO₂ assessed at residential addresses by geographic information system–based regression models and living near to the main road were related to childhood eczema [23]. In our study, there were significant relationships for benzene, NO_x, and VOCs exposures and current wheezing, and NO_x exposure and current doctor-diagnosed asthma, among children with ECPs. Current eczema was also found to be associated with exposures to benzene, CO, NO₂, NO_x, PM₁₀, and VOCs among children with ECPs. In addition, the relationships persisted among children without ECPs in cases of exposures to CO, NO₂, and PM₁₀.

Studies have also showed that psychological disorders may increase susceptibility to childhood asthma and eczema [5,7,9,24,25]. Among those psychological disorders, stress is a factor well documented in the literature [5]. In addition, stress has been observed to be related to ECPs [26,27], implicating that ECPs may be also an important psychological factor in the development of childhood asthma and eczema. The potential mechanism could be that prenatal stress is associated with fetal hypothalamic-pituitary-adrenocortical axis dysregulation, thus relating to ECPs in children [27]. Compelling evidence has indicated the association between behavior problems and childhood asthma. Calam et al. [25] have investigated behavior problems at the age of 3 years and subsequent development of wheezing by the age of 5 years; results showed that children with behavior problems (assessed by the Eyberg Child Behavior Inventory) were more likely to develop wheezing. As a disorder sharing genetic and environmental risk factors with asthma [17], eczema could be related to behavior problems through potentially overlapping mechanisms [28]. In our population, we found that both internalizing and externalizing behavior problems assessed by the SDQ were significantly related to asthma phenotypes and current eczema. However, prospective studies are needed to further examine those associations.

In our study, children with ECPs had higher prevalence odds ratios for associations between ambient air pollutants and asthma phenotypes and current eczema, compared with children without ECPs. The odds ratio differences were attenuated when compared with the whole study population. The explanation could be that ECPs play a role as social stressors and interact with air pollutants [29], one of the most important environmental stressors. ECPs as a modifier of the relationships between ambient air pollutants and asthma and eczema could also be interpreted using the conceptual framework of social determinants of health [30], indicating that the social environment is the upstream factor that determines different exposure patterns to contribute to health risk. However, the empirical evidence for psychological disorders as a modifier in the relationships between air pollutants and childhood asthma and eczema is limited. One study conducted in American implicated that parental stress interacted with traffic-related air pollution to predict childhood asthma [3]. Another study elucidated the

Table 3

The relationships between ECPs and the prevalences of asthma phenotypes and eczema

Health outcomes	Emotional symptoms (aOR, 95% CI) ^a	Conduct problems (aOR, 95% CI) ^a	All ECPs (aOR, 95% CI) ^a
Current wheezing	2.23 (1.51–3.30) [†]	1.66 (1.14–2.42) [†]	2.35 (1.59–3.47) [†]
Current doctor-diagnosed asthma	1.78 (1.26–2.50) [†]	1.63 (1.06–2.52) [†]	1.82 (1.25–2.66) [†]
Current eczema	1.95 (1.47–2.60) [†]	1.39 (1.02–1.91) [†]	2.21 (1.61–3.02) [†]

^a aORs were from the generalized estimating equation models and adjusted for potential confounders of gender, study center, ethnic origin, parental educational attainment, siblings, family history of asthma, prenatal parental smoking, dampness in the house during the first year of life, and contact with pets during the first year of life and age.

[†] Indicates $P < .05$.

Table 4

The relationships between an interquartile increase in exposures to ambient air pollutants and asthma phenotypes and eczema in models with and without interaction terms of ECPs and ambient air pollutants

Health outcomes	IQR ($\mu\text{g}/\text{m}^3$)	Models without interaction term (aOR, 95% CI)*	Models with interaction term (aOR, 95% CI)*		Interaction $P^{\dagger}$
			No ECPs	ECPs	
Current wheezing					
Benzene	1.73–2.92	0.99 (0.84–1.15)	0.95 (0.81–1.11)	1.22 (1.00–1.50) [‡]	<.01
CO	435.36–635.93	0.97 (0.85–1.10)	0.94 (0.83–1.07)	1.15 (0.97–1.36)	<.01
NO ₂	35.77–52.18	1.00 (0.83–1.46)	0.96 (0.80–1.17)	1.21 (0.95–1.55)	<.01
NO _x	49.49–100.15	1.00 (0.84–1.19)	0.95 (0.80–1.13)	1.35 (1.06–1.72) [‡]	<.01
PM ₁₀	22.00–31.00	1.00 (0.82–1.21)	0.97 (0.79–1.18)	1.21 (0.97–1.51)	<.01
VOCs	2.05–28.04	1.00 (0.87–1.15)	0.95 (0.82–1.09)	1.43 (1.03–2.00) [‡]	.02
Current doctor-diagnosed asthma					
Benzene	1.73–2.92	0.97 (0.81–1.15)	0.94 (0.78–1.13)	1.18 (0.94–1.47)	.01
CO	435.36–635.93	0.98 (0.84–1.15)	0.96 (0.82–1.12)	1.15 (0.95–1.38)	<.01
NO ₂	35.77–52.18	1.00 (0.80–1.25)	0.97 (0.77–1.21)	1.17 (0.92–1.49)	<.01
NO _x	49.49–100.15	1.03 (0.86–1.25)	0.99 (0.82–1.21)	1.30 (1.01–1.67) [‡]	.02
PM ₁₀	22.00–31.00	1.02 (0.84–1.24)	1.00 (0.82–1.22)	1.17 (0.94–1.45)	.01
VOCs	2.05–28.04	0.98 (0.82–1.16)	0.94 (0.79–1.13)	1.24 (0.88–1.76)	.14
Current eczema					
Benzene	1.73–2.92	1.17 (1.03–1.33) [‡]	1.13 (0.99–1.29)	1.48 (1.24–1.75) [‡]	<.01
CO	435.36–635.93	1.19 (1.07–1.34) [‡]	1.16 (1.03–1.30) [‡]	1.42 (1.24–1.62) [‡]	<.01
NO ₂	35.77–52.18	1.28 (1.11–1.47) [‡]	1.24 (1.08–1.43) [‡]	1.52 (1.31–1.77) [‡]	<.01
NO _x	49.49–100.15	1.20 (1.04–1.39) [‡]	1.15 (0.99–1.34)	1.55 (1.30–1.85) [‡]	<.01
PM ₁₀	22.00–31.00	1.21 (1.07–1.38) [‡]	1.18 (1.04–1.34) [‡]	1.43 (1.24–1.66) [‡]	<.01
VOCs	2.05–28.04	1.17 (1.03–1.33) [‡]	1.12 (0.98–1.29)	1.54 (1.21–1.96) [‡]	.02

IQR = interquartile range for the concentrations of ambient air pollutants.

* aORs were based on an interquartile increase in exposures to ambient air pollutants which entered as continuous variable in the generalized estimating equation models and adjusted for the potential confounders of gender, study center, ethnic origin, parental educational attainment, siblings, family history of asthma, prenatal parental smoking, dampness in the house during the first year of life, and contact with pets during the first year of life and age.

[†] The values of P from the statistics for testing the interactions between ECPs and ambient air pollutants in the generalized estimating equation models.

[‡] Indicates $P < .05$.

interaction in terms of epigenetic mechanisms, implicating that air pollution and psychological factors interacted to impact on DNA methylation [31], a biomarker of disease risk [32]. This could be denoted that air pollution and psychological features may have overlapping biological mechanisms in relation to the development of childhood asthma and eczema [31]. Overall, psychological features and air pollution may interact to affect the structure and function of respiratory system, as well as the immune system. It has been observed that both stress and air pollution may increase the risk of asthma and eczema through altered cytokine response [28,33–36]. Wright et al. [35] found that prenatal stress was associated with altered innate and adaptive cytokine responses thus impacting on the expression of asthma and allergic diseases in children. Nakamura et al. [36] examined potential biological mechanisms for the relationship between airway inflammation and cigarette smoking, an important indoor air pollutant. Results showed that increased T helper type 2 immune response may explain the relationship between airway inflammation and cigarette smoking. Furthermore, psychological features could modify the relationships between air pollution and schoolchildren's lung function [37], thus increasing the risk of asthma and eczema. In our study, we explored the interactions between internalizing psychological disorder and externalizing psychological disorders and ambient air pollutants in relation to health outcomes in France where schoolchildren have higher scores for both emotional symptoms and conduct problem than the representative sample of schoolchildren from United States [18], adding new evidence for considering children with ECPs as a susceptible population and taking into account air pollution and ECPs simultaneously into the paradigm of childhood asthma and eczema prevention. Interestingly, we found an association of psychological disorders as defined by internalizing and externalizing behavior problems with childhood asthma and eczema. The definition of psychological disorders used in previous studies was based on violence experimented by

the child. This violence could alter the normal course of both structure and function of key organ systems (e.g., immune, respiratory) more straightforward than behavior problems through adrenaline patterns [38].

The limitation of our study is its cross-sectional design, which could not explore the etiology of childhood asthma and eczema. Future longitudinal studies are needed to elucidate how ambient air pollutants and ECPs interact to predict childhood asthma and eczema. Another limitation of our investigation derives from taking into account the air pollution at schools instead of at home, where children spend most of their time. Even if children generally live within 500 m of their schools in urban areas in France and even if exposure at school represents an important component of children's exposure experience, exposure assessments errors might have occurred. However, exposure misclassification would err toward an underestimation of the potential link, but in no way to a bias.

Strengths of our study was that our data were based on a large sample drawn from general population and collected from six cities, which could gain an overall view of the possible joint impacts of ambient air pollutants and ECPs on childhood asthma and eczema in France.

In conclusion, results of our study show that relationships between exposures to benzene, CO, NO₂, NO_x, PM₁₀, and VOCs and schoolchildren's asthma phenotypes and current eczema had different patterns among children with ECPs and those without and that ECPs might modify the relationships between ambient air pollutants and health outcomes of current wheezing, current doctor-diagnosed asthma, and current eczema.

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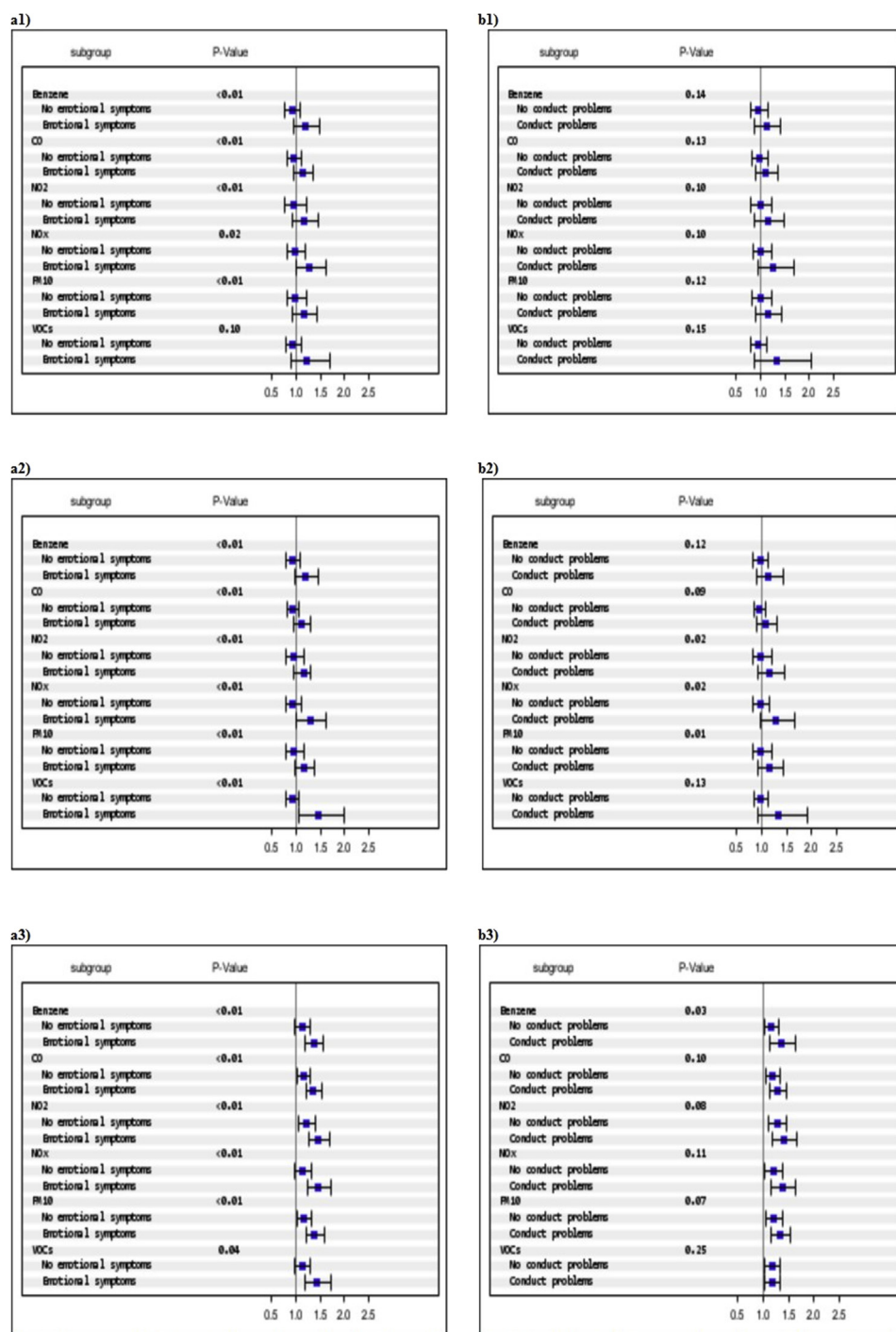


Fig. S1. (A) Emotional symptoms as a modifier for the between ambient air pollutants and asthma phenotypes and eczema. (B) Conduct problems as a modifier for the relationships between ambient air pollutants and asthma phenotypes and eczema.

Table S1

Characteristics of the study population according to the six study centers

Characteristics	Creteil (n = 841)	Reims (n = 487)	Marseille (n = 672)	Strasbourg (n = 778)	Clermont-Ferrand (n = 720)	Bordeaux (n = 711)	P*
Gender, n (%)							.71
Male	415 (49)	257 (53)	343 (51)	383 (49)	355 (49)	344 (48)	
Female	426 (51)	230 (47)	329 (49)	395 (51)	365 (51)	367 (52)	
Total	841 (100)	487 (100)	672 (100)	778 (100)	720 (100)	711 (100)	
Ethnic origin, n (%)							<.01
Metropolitan France	462 (55)	408 (85)	0 (0)	595 (79)	549 (78)	604 (87)	
French overseas departments and foreign countries	372 (45)	71 (15)	659 (100)	161 (21)	159 (22)	93 (13)	
Total	834 (100)	479 (100)	659 (100)	756 (100)	708 (100)	697 (100)	
Parental education attainment, n (%)							
Low (primary or secondary)	407 (53)	265 (60)	302 (48)	371 (51)	370 (54)	259 (37)	<.01
High (tertiary)	367 (47)	174 (40)	323 (52)	350 (49)	310 (45)	433 (63)	
Total	774 (100)	439 (100)	625 (100)	721 (100)	680 (100)	692 (100)	
Preterm birth†, n (%)							.05
Yes	80 (10)	50 (10)	50 (7)	69 (9)	43 (6)	69 (10)	
No	761 (90)	437 (90)	622 (93)	709 (90)	677 (94)	642 (90)	
Total	841 (100)	487 (100)	672 (100)	778 (100)	720 (100)	711 (100)	
Siblings (>1), n (%)							<.10
Yes	638 (76)	377 (77)	467 (69)	605 (78)	536 (74)	517 (73)	
No	203 (24)	110 (23)	205 (31)	173 (22)	184 (26)	194 (27)	
Total	841 (100)	487 (100)	672 (100)	778 (100)	720 (100)	711 (100)	
Family history of asthma, n (%)							.13
Yes	186 (22)	121 (25)	132 (20)	168 (22)	133 (18)	150 (21)	
No	655 (78)	366 (75)	540 (80)	610 (78)	587 (82)	561 (79)	
Total	841 (100)	487 (100)	672 (100)	778 (100)	720 (100)	711 (100)	
Prenatal parental smoking, n (%)							<.01
Yes	248 (29)	158 (32)	231 (34)	277 (34)	267 (37)	265 (37)	
No	593 (71)	329 (68)	441 (66)	501 (64)	453 (63)	446 (63)	
Total	841 (100)	487 (100)	672 (100)	778 (100)	720 (100)	711 (100)	
Dampness in the house during the first year of life, n (%)							<.01
Yes	145 (20)	90 (21)	99 (16)	111 (16)	76 (12)	146 (23)	
No	595 (80)	329 (79)	533 (84)	586 (84)	578 (88)	503 (77)	
Total	740 (100)	419 (100)	632 (100)	697 (100)	654 (100)	649 (100)	
Contact with pets during the first year of life, n (%)							<.01
Yes	208 (25)	170 (35)	184 (27)	215 (28)	215 (30)	230 (32)	
No	633 (75)	317 (65)	488 (73)	563 (72)	505 (70)	481 (68)	
Total	841 (100)	487 (100)	672 (100)	778 (100)	720 (100)	711 (100)	
Emotional symptoms, n (%)							.22
Yes	142 (17)	66 (14)	97 (14)	97 (12)	102 (14)	100 (14)	
No	699 (83)	421 (86)	575 (86)	681 (88)	618 (86)	611 (86)	
Total	841 (100)	487 (100)	672 (100)	778 (100)	720 (100)	711 (100)	
Conduct problems, n (%)							.10
Yes	82 (10)	57 (12)	72 (11)	88 (11)	62 (9)	55 (8)	
No	759 (90)	430 (88)	600 (89)	690 (89)	658 (91)	656 (92)	
Total	841 (100)	487 (100)	672 (100)	778 (100)	720 (100)	711 (100)	
ECPs, n (%)							.39
Yes	111 (13)	56 (11)	73 (11)	89 (11)	71 (10)	74 (10)	
No	730 (87)	431 (89)	599 (89)	689 (89)	649 (90)	637 (90)	
Total	841 (100)	487 (100)	672 (100)	778 (100)	720 (100)	711 (100)	
Current doctor-diagnosed asthma, n (%)							.66
Yes	40 (5)	20 (4)	33 (5)	34 (5)	28 (4)	41 (6)	
No	742 (95)	434 (96)	594 (95)	694 (95)	623 (96)	622 (94)	
Total	782 (100)	454 (100)	627 (100)	728 (100)	651 (100)	663 (100)	
Current wheezing, n (%)							.29
Yes	52 (6)	32 (7)	50 (8)	47 (6)	45 (6)	63 (9)	
No	763 (94)	449 (93)	612 (92)	721 (94)	658 (94)	643 (91)	
Total	815 (100)	481 (100)	662 (100)	768 (100)	703 (100)	706 (100)	
Current eczema, n (%)							.36
Yes	114 (14)	45 (10)	83 (13)	90 (12)	97 (14)	89 (13)	
No	701 (86)	408 (90)	566 (87)	661 (88)	605 (86)	604 (87)	
Total	815 (100)	453 (100)	649 (100)	751 (100)	702 (100)	793 (100)	
Maternal age at recruitment (y), mean (SD)	39.11 (5.15)	38.32 (5.07)	38.85 (4.65)	38.67 (5.13)	38.59 (4.83)	39.34 (5.04)	<.01
Age (y), mean (SD)	10.79 (0.67)	10.57 (0.63)	11.47 (0.52)	10.68 (0.65)	10.67 (0.61)	10.60 (0.60)	<.01
Birth weight (g), mean (SD)	3259 (557)	3314 (534)	3262 (485)	3253 (542)	3242 (484)	3255 (489)	.31

SD = standard deviation.

* The value of *P* for the differences of characteristics of study population among children in the six study centers.

† Maternal gestational age <37 wk and low birth weight (<2500 g).

Table S2

Concentrations of ambient air pollutants according to the six study centers, mean (SD)

Air pollutants	Creteil (n = 841)	Reims (n = 487)	Marseille (n = 672)	Strasbourg (n = 778)	Clermont-Ferrand (n = 720)	Bordeaux (n = 711)	P*
Benzene ($\mu\text{g}/\text{m}^3$)	2.27 (0.51)	1.48 (0.20)	3.26 (0.85)	2.30 (0.75)	2.51 (0.87)	2.43 (0.87)	<.01
CO ($\mu\text{g}/\text{m}^3$)	608.83 (100.90)	382.84 (56.74)	631.41 (161.00)	556.06 (134.68)	595.26 (154.76)	518.39 (154.89)	<.01
NO ₂ ($\mu\text{g}/\text{m}^3$)	55.52 (4.44)	30.00 (5.39)	49.52 (5.71)	41.46 (5.56)	46.01 (10.72)	36.64 (9.38)	<.01
NO _x ($\mu\text{g}/\text{m}^3$)	102.91 (29.60)	51.04 (10.65)	84.97 (27.65)	69.93 (26.89)	83.36 (32.44)	68.66 (30.43)	<.01
PM ₁₀ ($\mu\text{g}/\text{m}^3$)	29.08 (5.84)	19.59 (1.83)	32.84 (4.27)	24.00 (5.04)	26.04 (6.77)	26.42 (6.04)	<.01
VOCs ($\mu\text{g}/\text{m}^3$)	17.23 (15.47)	3.94 (4.30)	28.91 (22.26)	9.26 (13.51)	21.86 (18.43)	20.04 (17.88)	<.01

SD = standard deviation.

* The value of *P* for the differences of air pollutants concentrations among children in the six study centers.