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Associations between air pollution and surrounding greenness with internalizing and externalizing behaviors among schoolchildren

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Background: Air pollution and greenness are emerging as modifiable risk and protective factors, respectively, in child psychopathology. However, research shows inconsistencies. Here, we examined associations between air pollution and surrounding greenness with internalizing and externalizing behaviors. In addition, the potential modifying role of the genetic susceptibility for these traits and socioeconomic status (SES) was explored. **Methods:** This population-based study included 4485 schoolchildren aged 5–18 years from Spain. Internalizing and externalizing behaviors were assessed using the Child Behavior Checklist (CBCL). Average air pollution (NO_2, $PM_{2.5}$, PM_{10}, PM_{coarse}, and $PM_{2.5}$ absorbance) and surrounding greenness (NDVI within 100-m, 300-m, and 500-m buffers) school exposure were estimated for 12 months before outcome assessment. Genetic liability was assessed by computing polygenic risk scores (PRS) and SES was calculated using the Hollingshead Four-Factor Index. Associations were analyzed using negative binomial mixed-effects models. **Results:** Although no associations survived multiple testing, we found that increases of 5.48 μg/m^3 in PM_{10} and 2.93 μg/m^3 in PM_{coarse} were associated with a 6% (Mean Ratio (MR) = 1.06; 95% CI: 1.01–1.12) and a 4% (MR = 1.04; 95% CI: 1.00–1.09) increase in internalizing behavior scores. A 0.1 increase in NDVI within a 100-m buffer was associated with a 6% decrease in externalizing behavior (MR = 0.94; 95% CI: 0.89–0.99). Neither differences by sex or age, or moderation effects by PRS or SES, were observed. **Conclusions:** We found preliminary evidence of detrimental effects of air pollution on internalizing behavior and protective effects of greenness on externalizing behavior, which were not modified by sex, age, SES, or genetic liability. If confirmed, these results

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reinforce the need for improving air quality, especially around schools, as part of preventive strategies focused on childhood psychopathology.

Key Practitioner Message

What is known?

- Air pollution and greenness are emerging as modifiable risk and protective factors, respectively, in child mental health. However, research shows inconsistencies and potential differential effects depending on factors such as sex, age, socioeconomic status (SES) or genetic liability remain largely unknown

What is new?

- We observed preliminary evidence of detrimental effects of 12 months exposure at the school level to PM_{10} and PM_{coarse} on internalizing behavior and protective effects of school surrounding greenness (NDVI 100 m) on externalizing behavior
- These associations did not differ by sex or age group and were not moderated by SES or the genetic liability for depression, anxiety, ADHD, or externalizing traits

What is significant for clinical practice?

- Our results support policies aimed at protecting air quality in schools as preventive strategies for mental health. We need more research to identify potential high-risk groups and understand the mechanisms underlying these associations

Keywords: Air pollutants; green spaces; polygenic risk scores; child mental health; anxiety; aggressive

Introduction

Early manifestation of psychopathology during childhood and adolescence involves emotional and behavioral problems that can persist into adulthood and cause significant suffering in affected individuals, their families, and their scholarly and social contexts (Thapar & Riglin, 2020). Behavioral and emotional problems and mental disorders are common among young individuals, with an average of 13.4% of children and adolescents being affected by mental health problems worldwide (Polanczyk, Salum, Sugaya, Caye, & Rohde, 2015).

Childhood psychopathology can be split into two broad categories, namely internalizing and externalizing behaviors or disorders. The internalizing domain includes behaviors directed toward the self (e.g., emotional disorders such as depression and anxiety), while externalizing behaviors are characterized by behaviors directed outward at an individual's environment (e.g., disruptive behaviors such as attention deficit/hyperactivity disorder (ADHD) and conduct disorder) (Ogundele, 2018). These behaviors are complex traits with both genetic and environmental factors involved in their etiology (Faraone & Larsson, 2019; Polderman et al., 2015).

Twin and family studies show a strong genetic component underlying internalizing and externalizing behaviors, with reported heritability estimates around 50% and 80%, respectively (Franić, Dolan, Borsboom, Van Beijsterveldt, & Boomsma, 2014; Hicks, Krueger, Iacono, McGue, & Patrick, 2004). To date, large genome-wide association studies (GWAS) have been conducted on relevant components of internalizing behavior such as anxiety and depression, and externalizing behavior and ADHD (Als et al., 2023; Demontis et al., 2023; Karlsson Linnér et al., 2021; Purves et al., 2020), which can be used to construct genome-wide polygenic risk scores (PRS) that capture the cumulative effect of genetic risk variants inherited by an individual. So far, studies on PRS associated with internalizing and externalizing behaviors show evidence of association with a wide range of traits and disorders (Abdellaoui & Verweij, 2021).

In the last decade, physical environmental factors such as air pollution or lack of greenness exposure have emerged as modifiable risk factors for brain health, including childhood psychopathology. A growing body of research has linked air pollution with symptoms of depression, anxiety, and childhood aggressive behavior, as well as increased risk for ADHD and delinquency problems (Margolis et al., 2016; Newman et al., 2013; Younan et al., 2018). However, most studies, especially for anxiety and depression, have focused on adult or elder populations (Kim et al., 2016; Power et al., 2015; Pun, Manjourides, & Suh, 2017; Zhao et al., 2020). In parallel, exposure to natural outdoor environments has been linked to improvements in mental health (WHO Regional Office for Europe, 2016) and there is evidence supporting an inverse relationship between green space exposure and behavioral problems in children, particularly in externalizing behaviors (Zare Sakhvidi et al., 2022).

However, a large study reported no association between early life residential exposure to air pollution and depression, anxiety or aggressive behavior assessed in 13,182 children from eight European cohorts in mid-to-late childhood (Jorcano et al., 2019). Similarly, null findings were reported for the impact of greenness on mental health. For instance, neither access nor use of green spaces was associated with well-being among 497 students from Singapore (Srugo et al., 2019). Another study examining school greenness also reported no

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association with mental health among 6313 students from Canada (Saw, Lim, & Carrasco, 2015).

In the present study, we sought to address some gaps and inconsistencies in the literature regarding physical environmental factors and mental health. More specifically, previous studies were primarily conducted in adults, focused on a limited range of pollutants, and did not consider potential effect modifications by genetic factors, socioeconomic status (SES), or sex. Herein, we aimed to examine the association between exposure to a wide range of air pollutants and surrounding greenness around the school with internalizing and externalizing behaviors among children and adolescents over two time periods (12 months and 4 years before the behavioral assessment). We also investigated whether these associations differ by sex or age group. Additionally, we assessed the potential modifying role of SES and polygenic risk for proxy phenotypes for internalizing and externalizing behaviors in these associations.

Methods

Sample

The study included 4485 individuals recruited in the 2013–2019 period from 48 different schools in Catalunya, Spain. Participants were of European ancestry, with data available on physical environmental exposure, genetics, and behavioral outcomes drawn from the INSchool project (Bosch et al., 2021). All variables included in the analysis (i.e., behavioral measures and sociodemographic variables) were assessed at the time of recruitment.

Behavioral measures

Participants' internalizing and externalizing behaviors were assessed using the Child Behavior Checklist (CBCL) (Achenbach, 1991; Achenbach & Rescorla, 2001). The CBCL is a standardized screening questionnaire internationally used to identify mental health problems in children and adolescents reported by parents. The CBCL has a total of 112 different items that each caregiver answers about their child using a 3-point Likert-type scale (0 = Not True, 1 = Somewhat or Sometimes True, and 2 = Very True or Often True). These answers are then used to calculate summary scores that can be grouped into broadband and syndrome scales. In the current study, we examined internalizing and externalizing broadband scales, which combine items from the withdrawn/depressed, somatic complaints, and anxious/depressed syndrome scales for internalizing behavior and items from the rule-breaking behavior and aggressive behavior syndrome scales for externalizing behavior. Higher scores indicate more emotional/behavioral problems.

Physical environmental exposures

Air pollution exposure assessment. Air pollution measurements were collected within the air pollution monitoring campaign of the European Study of Cohorts for Air Pollution Effects (ESCAPE; http://www.escapeproject.eu/). A Land Use Regression (LUR) model from 2009 was used to estimate average school exposure to air pollutants. LUR models were based on geographical information systems and statistical methods. This model has been validated and extensively used as a surrogate of long-term exposure for data collection periods between 2009 and 2019 (Alemany et al., 2021; Gascon et al., 2018; Vert et al., 2017). Air pollutants included nitrogen dioxide (NO_2) and particulate matter [$PM_{2.5}$ (PM with aerodynamic diameter < 2.5 μm), PM_{10} (< 10 μm), PM_{coarse} (2.5–10 μm), and $PM_{2.5}$ absorbance ($PM_{2.5}$ light absorption)] that were measured in three different seasons (warm, cold, and one intermediate temperature season). All pollutants are reported in micrograms per meter cubed (μg/m^3) except $PM_{2.5}$ absorbance (10^{-5}/m). We considered the time of assessment as reference to estimate the exposure to air pollutants over (a) 12 months and (b) the preceding 4 years.

Surrounding greenness assessment. Indicators of surrounding greenness exposure were calculated using the Normalized Difference Vegetation Index (NDVI). The NDVI is used to quantify vegetation greenness and is based on land surface reflectance of visible (red) and near-infrared parts of the spectrum (USGS, 2022). This index ranges between −1 and 1, with higher numbers indicating more greenness. For each participant, surrounding greenness was abstracted as the average NDVI within buffers of 100 m, 300 m, and 500 m around his/her school. We used the Landsat surface reflectance dataset from Collection 2, Tier 1, Level 2 data from USGS/NASA Landsat 5, 7, and 8 satellites at a 30 m spatial resolution. We used Google Earth Engine to make the image selection and pixel selection. We used the pixel quality attributes band provided with the Landsat products to filter invalid pixels. Those are pixels covered with clouds, cloud shadows, snow, or water. We considered the time of assessment as a reference to estimate the exposure to air pollutants over (a) 12 months and (b) the preceding 4 years.

Genotyping and polygenic scoring

Genomic DNA was isolated from saliva samples or buccal swabs collected using Oragene DNA OG-500 or OC-175 kits, respectively (DNA Genotek) and genotyped in three genotyping waves: Illumina Infinium PsychChip_v1.0 array for wave 1 (n = 824), the Infinium Global Screening Array-24 version_2 (GSA_v2) for wave 2 (n = 2844), and the Infinium Global Screening Array-24 version_3 (GSA_v3) for wave 3 (n = 1040) (Illumina, CA, San Diego, USA). Preimputation quality control was done with the PLINK 2.0 (Chang et al., 2015) and included individual and variant filtering based on the following parameters: variant call rate > 0.95 (before individual filtering), individual call rate > 0.98, autosomal heterozygosity deviation (|Fhet| < 0.2), variant call rate > 0.98 (after individual filtering), Single Nucleotide Polymorphism (SNP) Hardy–Weinberg equilibrium ($p > 1 \times 10^{-10}$), and minor allele frequency (MAF) > 0.01. Genetic outliers were identified by principal component analysis (PCA) using PLINK 2.0 and the mixed ancestry 1000G reference panel (Auton et al., 2015). Ancestry outliers were excluded if their principal component (PC) values for PC1 or PC2 were greater than 1 standard deviation from the mean-centering point for our sample, considering each GWAS wave separately. Imputation was done with McCarthy tools, for data preparation, and the Michigan Imputation Server, using the Haplotype Reference Consortium (HRC_Version_r1.1_2016) EUR reference panel (GRCh37/hg19). Postimputation quality control per wave included imputation INFO score ≥ 0.8 and MAF > 0.01 and variant call rate > 0.95. SNPs present in all GWAS waves were considered and related or duplicate individuals were removed with the 'KINGrobust kinship estimator' analysis with PLINK 2.0 considering a kinship coefficient exceeding 0.0442. We applied a final individual call rate threshold of 0.95. Dosage files we converted into best guess files with PLINK 2.0 and filtered for MAF > 0.01 and call rate > 0.95 for downstream PRS analyses (n_{SNP} = 3,726,073).

Genetic liability was assessed by computing polygenic risk scores (PRS) for depression and anxiety as proxies for internalizing and ADHD and externalizing traits as proxies for externalizing behavior using PRScs software (Ge, Chen, Ni, Feng, & Smoller, 2019) and summary statistics of the largest GWAS available to date (Als et al., 2023; Demontis et al., 2023; Karlsson Linnér et al., 2021; Purves et al., 2020) (Table S1). All PRS were computed and standardized to a mean of 0 and a standard deviation (SD) of 1.

Socioeconomic status

Parents completed a questionnaire on their educational level and occupation, which was weighted to compute the Hollingshead Four-Factor Index (Hollingshead, 2011), a measure of SES

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that ranges from 8 to 66, where higher scores reflect higher SES. In 2-parent family cases, an average of the information from both parents was used as a measure of SES.

Statistical analysis

We analyzed the effects of physical environmental exposures on internalizing and externalizing behavior following a three-step design. First, we tested associations between physical environmental exposures (i.e., air pollutants and surrounding greenness) and internalizing and externalizing behavior using negative binomial mixed-effects models with school as random effects using the lme4 R package. Negative binomial mixed-effects models were used to account for the multilevel nature of the data, as previously described in studies examining similar outcomes (Campbell et al., 2024; González-Safont et al., 2023; Maitre et al., 2021). In all analyses, environmental exposures were the independent variables, and internalizing and externalizing behaviors were the outcomes. We fit separate models to estimate associations of each environmental exposure with each outcome. Effect estimates correspond to exponentiated regression coefficients from the negative binomial models (mean ratios or MR) that can be interpreted as the relative difference in the outcome score with one IQR increase in the exposure. We transformed the exposure variables [i.e., air pollutants (NO_2, $PM_{2.5}$, PM_{10}, PM_{coarse}, and $PM_{2.5}$ absorbance) and surrounding greenness (NDVI within buffers of 100 m, 300 m, and 500 –m)] into IQR-scaled variables by dividing them by the interquartile range (IQR), which represents the difference between the 25th percentile (Q1) and the 75th percentile (Q3). We used optimization by quadratic approximation (BOBYQA) optimizer with 1×10^5 iterations to reach valid convergence. In the event of finding warnings suggesting issues with the model fit, we used the allFit function from the lme4 R package to evaluate whether all optimizers converged to practically equivalent values (Bates, Mächler, Bolker, & Walker, 2015). We corrected for multiple testing across all exposures for association with each outcome using the false discovery rate (FDR) method (Benjamini & Hochberg, 1995). Results at a p-FDR ≤0.05 were considered statistically significant. Associations with a $p \leq .05$ were considered nominally significant. Second, we assessed whether associations found in the first step differ as a function of sex or age group. Specifically, as age groups, we considered primary and secondary school children, which starts at 12 years old, largely overlapping with the transition between childhood and adolescence. Finally, we assessed the potential moderation effects of PRS and SES on significant associations found in previous steps. Modification effects were tested by introducing a two-way interaction effect in the models.

As sensitivity analyses, we explored whether the associations identified in the broadband scales were driven by a particular group of symptoms using the different internalizing and externalizing syndrome scales. Also, for the subset of the sample where exposures were available for the previous 4 years to behavioral assessment ($n = 3454$) we assessed whether identified associations for 12 months exposure remained for 4 years exposure.

All analyses were performed using R software and adjusted by sex, age, and SES. Analyses including PRS were also adjusted by the first 10 genetic principal components.

Results

The characteristics of the sample are shown in Table 1. The mean age of the participants was 10 years ($SD = 2.98$) and approximately half of the sample was girls (45%). All environmental exposures were correlated with each other, except for $PM_{2.5}$ and PM_{coarse} (Figure S1). Positive correlations were observed within air pollutants and within surrounding greenness indicators, while there was a negative correlation between both groups of physical environmental exposures.

Table 1. Characteristics of the sample

Characteristics	INSchool sample (N = 4485)
Assessed individually	
Age [mean(min–max)]	9.94 (5–18)
Sex (female), N (%)	2019 (45.02)
Socioeconomic status [mean(min–max)]	44.76 (8–63)
Internalizing behavior [mean(min–max)]	8.03 (0–61)
Externalizing behavior [mean(min–max)]	6.89 (0–62)
Assessed at school (48 schools)	
Air pollutants	
NO_2 (μg/m^3) [mean(min–max)]	23.71 (2.07–39.61)
$PM_{2.5}$ (μg/m^3) [mean(min–max)]	12.6 (6.76–20.3)
$PM_{2.5}$ absorbance (10^{-5}/m) [mean(min–max)]	1.28 (0.73–2.09)
PM_{10} (μg/m^3) [mean(min–max)]	25.3 (16.06–37.14)
PM_{coarse} (μg/m^3) [mean(min–max)]	12.7 (5.43–21.8)
Surrounding greenness	
NDVI 100-m [mean(min–max)]	0.26 (0.13–0.45)
NDVI 300-m [mean(min–max)]	0.3 (0.13–0.46)
NDVI 500-m [mean(min–max)]	0.32 (0.14–0.45)

NDVI, normalized difference vegetation index; PM, particulate matter.

Associations of environmental exposures with internalizing and externalizing behavior

Exposure to air pollutants, namely PM_{10} and PM_{coarse}, were positively associated with internalizing behavior. Specifically, a one IQR increase in PM_{10} (5.48 μg/m^3) and PM_{coarse} (2.93 μg/m^3) was associated with an approximately 6% (MR = 1.06; 95% Confidence Interval (CI): 1.01–1.12) and 4% (MR = 1.04; 95% CI: 1.00–1.09) increase in internalizing behavior (Figure 1, Table S2). Although these associations did not survive multiple testing corrections, they were mainly driven by the withdrawn/depressed and anxious/depressed syndrome scales (Table S3).

When we considered surrounding greenness, negative associations were observed for externalizing behavior, with a 6% decrease in this outcome per one IQR increase in NDVI within a 100-meter buffer, which consisted of 0.1 units in our sample (MR = 0.94; 95% CI: 0.89–0.99). Although this association did not remain significant after multiple testing corrections, it was primarily observed in the aggressive behavior syndrome scale (Table S3).

For the subset of participants who had exposure data available for the previous 4 years to behavioral assessment ($n = 3454$), only the association between NDVI within a 100-m buffer and externalizing behavior remained significant with very similar effect size estimates (MR = 0.96; 95% CI: 0.95–0.97) (Table S4).

Stratification by sex and age

When stratifying the analysis by sex, protective effects were observed for NDVI within a 100-m buffer only among boys ($n = 2466$) (MR = 0.93; 95% CI: 0.88–0.98) (Figure 1, Table S5).

Stratification by age group [children (mean age = 7.87 years) vs. adolescents (mean age = 13.15 years)]

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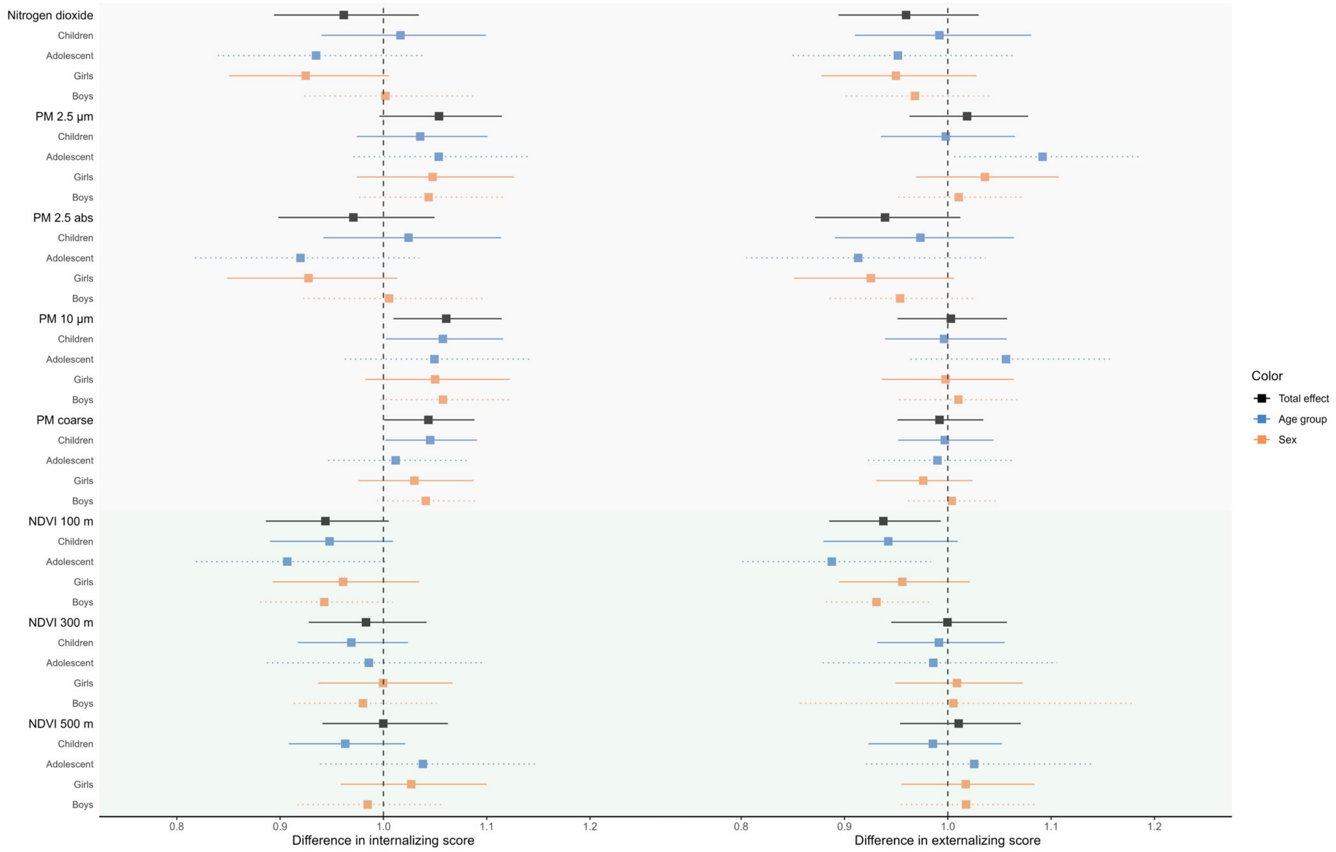

Figure 1. Forest plot depicting associations between physical environmental exposures and internalizing (left) and externalizing (right). Black color represents the results for the whole sample, sex-stratified results are shown in orange while age-stratified results are represented in blue. NDVI, normalized difference vegetation index; PM, particulate matter

revealed that the association between internalizing behavior and higher levels of PM_{10} (MR = 1.06; 95% CI: 1.00–1.12) and PM_{coarse} (MR = 1.05; 95% CI: 1.00–1.09) was limited to children (n = 2728) (Figure 1, Table S6). Also, we found new evidence of a positive association between levels of $PM_{2.5}$ and externalizing behavior (MR = 1.09; 95% CI: 1.01–1.19) among adolescents (n = 1757). The protective effect of NDVI within a 100-m buffer on externalizing behavior (MR = 0.89; 95% CI: 0.80–0.98) was also limited to adolescents. Interaction analyses, however, revealed that none of the estimates significantly differed across sexes or age groups (Tables S5 and S6).

Modification effects by genetic liability and SES

As expected, positive associations were found between $PRS_{anxiety}$ and $PRS_{depression}$ and internalizing behavior (MR = 1.03; 95% CI: 1.01–1.05 and MR = 1.03; 95% CI: 1.01–1.06, respectively) and between $PRS_{externalizing}$ and PRS_{ADHD} and externalizing behavior (MR = 1.10; 95% CI: 1.07–1.13 and MR = 1.11; 95 % CI: 1.08–1.14, respectively). SES was negatively associated with both outcomes, meaning lower SES was associated with higher scores for internalizing (MR = 0.89; 95% CI: 0.87–0.91) and externalizing behaviors (MR = 0.85; 95% CI: 0.82–0.88) (Table S7). However, no evidence for a modifying effect was identified for any of the PRS or SES on the associations between physical environmental exposures and internalizing or externalizing behaviors or their respective syndrome scales (Tables S8 and S9).

Discussion

We found preliminary evidence indicating that 12 months of exposure to higher levels of PM_{10} and PM_{coarse} were associated with more internalizing behavior, while higher exposure to NDVI within a 100-m buffer was associated with less externalizing behavior after controlling for age, sex, and SES. These associations were mainly driven by the withdrawn/depressed, anxious/depressed, and aggressive behavior syndrome scales. No differences were observed between sex or age groups, and no moderation effects were identified for the genetic liability or SES. These findings, together with previous evidence, support that both air pollution and greenness exert opposite effects on childhood psychopathology in the general pediatric population.

We found evidence suggesting detrimental effects of PM_{10} exposure on internalizing behavior, which is in line with several studies reporting adverse effects of air pollutants on children's behavioral and/or emotional problems. Particularly, the largest study to date performed in 1.13 million adults reported air pollution levels similar to ours (19.8 µg/m^3 PM_{10}) and showed consistent evidence for the association between higher exposure to PM_{10} and an increased risk for anxiety or depression (Zhao et al., 2020). Also, positive associations between

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PM_{10} and depression were found in 127,945 adults (S. Y. Kim et al., 2021). Other studies in children and adolescents reported higher levels of exposures, from 2 to 14 times greater than those from our study, and found that short- and long-term exposure to NO_2 and long-term exposure to $PM_{2.5}$ were positively associated with externalizing and internalizing behaviors (Qi et al., 2023), respectively, and a negative impact of PM_{10} exposure on mental health (Kim, Park, Han, & Chung, 2020).

We have not found studies investigating PM_{coarse} exposure in the context of child psychopathology, but the detrimental effects observed for this fraction of air pollutants are in line with previous research reporting associations between PM_{coarse} and self-reported history of anxiety or depression among adults (Vert et al., 2017), and with increased risk of suicide among individuals with a diagnosis of major depressive disorder (Hwang et al., 2022).

Our results also suggest a protective association between surrounding greenness and externalizing behavior, which is driven by aggressive behavior and is in line with previous evidence. Negative associations have been reported between residential green space and total problematic behavior, externalizing behavior, and internalizing behavior among children living in an urban environment (Bijnens, Derom, Thiery, Weyers, & Nawrot, 2020). Lee, Kim, and Ha (2019) also described a negative association between neighborhood greenness and total CBCL score and externalizing behavior. Together with Younan et al. (2016), these studies report that increasing the surrounding residential greenness is associated with a reduction in aggressive behavior. Exposure to greenness may exert beneficial effects on child behavior and mental health through several mechanisms such as promoting physical activity, social interaction, free play, increasing restoration/stress reduction, and reducing adverse exposures like air pollution, noise, or heat (Markevych et al., 2017). We may hypothesize that some of these beneficial aspects may be particularly relevant for externalizing behaviors characterized by poor impulse control, inattention, and aggression. For instance, systematic reviews and meta-analysis studies indicate that physical activity can reduce aggressivity in individuals with a tendency toward this behavior (Ouyang & Liu, 2023) and improve attention among schoolchildren with ADHD (Li, Li, et al., 2023).

We did not find an association between greenness and internalizing behavior, as reported by others. Higher residential greenness was associated with lower internalizing behavior scores among 2–6 aged children (Hazlehurst et al., 2024; Towe-Goodman et al., 2024). Interestingly, Towe-Goodman et al. (2024) described this association as being limited to younger children (2–5 years) since no significant results were found for children aged 6–11 years. Although further research is needed to confirm this evidence, the effects limited to younger children may explain the lack of association between greenness and internalizing behavior in our sample of schoolchildren aged 5–18 years.

Despite that the main analysis assessed school exposure estimations for 12 months before outcome assessment, the protective effects of school surrounding greenness on externalizing behavior remained significant after 4 years of exposure. These results highlight the importance of investing in green spaces as a strategy with positive long-term health effects and support further longitudinal studies in large cohorts to investigate the long-term effects of environmental exposures on mental health over time.

We found no evidence of moderation effects by genetic liability or SES. Few studies have assessed moderation effects of genetic liability in the association between environmental exposures and psychiatric disorders. Li, Li, et al., 2023 and Li, Xie, et al., 2023 reported that the genetic susceptibility to depression interacts with air pollution in its association with major depressive disorder. We considered PRS for multiple internalizing and externalizing-related traits, but we cannot exclude that gene–environment interaction effects underlying differential responses to physical environmental exposures are driven by SNPs involved in specific biological pathways, which may be difficult to capture using genome-wide PRS for complex traits. In this context, future studies using pathway-based PRS, which aggregate genetic variants involved in specific biological functions, may increase the likelihood of uncovering how genetic and environmental factors jointly contribute to the development of behavioral traits. For instance, some studies suggest that both exposure to air pollutants and depressive symptoms are associated with pathways of inflammatory processes (Block & Calderón-Garcidueñas, 2009; Raison, Capuron, & Miller, 2006). Thus, pathways-based PRS based on genetic variants involved in the regulation of inflammation may be a good candidate to investigate potential gene–environment interaction effects in the relationship between air pollution and the development of depressive symptoms. Also, evidence of moderating effects of SES, or its proxies, in the relationship between air pollution or greenness and child mental health is scarce. Several studies report stronger associations in the lower SES group (Balseviciene et al., 2014; Flouri, Midouhas, & Joshi, 2014; Pérez-del-Pulgar et al., 2021; Pun et al., 2017; Richardson, Pearce, Shortt, & Mitchell, 2017), but others do not find significant effects of SES (Hazlehurst et al., 2024; McEachan et al., 2018). Further research is needed to elucidate which specific factors and under which conditions they modify the link between physical environmental exposure and child mental health.

It is remarkable that even though exposure and outcome assessments, sample sizes, ethnic groups, participants' age distribution, and models used for assessing associations vary across studies, most of them, including the present study, converge in reporting that air pollution is associated with a negative impact on mental health, as opposed to greenness, which is associated with a positive impact. In addition, our findings address several key aspects. First, as most studies on physical environmental exposures are focused on adult populations, we contribute information in a schoolchildren population. Although the manifestation of internalizing and externalizing behaviors varies across age groups and certain behavioral/emotional problems may not be expressed at a very young age with the same severity as in adulthood (Cía et al., 2018; Kessler et al., 2007), we found no differences across age groups, which supports that our findings, at least, remain from childhood to adolescence. Second, we assessed two-time exposure

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periods, and we found that 12 months exposure to PM_{10} and PM_{coarse} and greenness were associated with early manifestation of psychopathology, and only the association with greenness remained significant after 4 years exposure. Further studies are needed to determine whether more recent exposures are more relevant than distant ones for childhood psychopathology. Third, we considered SES as a covariate in all the analyses, suggesting that the identified associations may not be confounded by SES, which clearly impacts mental health. Lastly, in comparison with previous reports, we considered a wide range of different air pollutants, including PM_{coarse} or $PM_{2.5}$ absorbance, which supports that further studies are required to disentangle which specific pollutants and exposure levels impact child and adolescent mental health.

Of note, in our study, environmental exposures presented small effect sizes. This finding aligns with previous research examining the relationship between physical environmental factors and health outcomes. While such modest effects might initially raise questions about the relevance of these factors, it is important to consider their broader implications. A substantial proportion of the population experiences daily exposure to these factors over extended periods of time, which may lead to cumulative effects (Nobile, Forastiere, Michelozzi, Forastiere, & Stafoggia, 2023). Consequently, even small modifications in these environmental exposures have the potential to translate into significant population-level benefits. For instance, marginal improvements in mental health, when applied to thousands of children and adolescents, could lead to relevant social and economic benefits involving improvements in the quality of life of many families and reductions in health-care costs. Furthermore, childhood and adolescence are sensitive developmental periods, and identifying and addressing modifiable factors such as air pollution or access to green spaces can contribute to preventing the escalation of mental health issues later in life.

This study is also subject to several limitations. Estimations of exposure to air pollutants and surrounding greenness were based on children's school location (i.e., they do not reflect individual exposures) due to the lack of available information on residential location or commuting. Thus, we cannot exclude exposure misclassification, which has been suggested to lead to underestimations of the associations between the exposures and outcomes assessed (Zeger et al., 2000). Our sample size might neither have been large enough for the associations to remain significant after FDR correction nor to detect moderating effects. Nevertheless, it has been suggested that multiple testing correction may be too restrictive and reluctance to emphasize nominally significant results may lead to missing potentially relevant findings (Feise, 2002; Rothman, 1990). The null findings concerning the moderating effects may also be related to the sample size and to the fact that we are measuring subclinical symptoms, and not clinical diagnosis, where symptoms related to internalizing and externalizing are fully expressed. The limited statistical power might similarly affect the analyses of 4-year exposures after assessment, which were only available in 70.7% of the sample. Finally, because our study participants were of European descent, the generalization of our findings on the modification effects by genetic liability should be interpreted with caution regarding other ancestries.

Conclusion

In conclusion, our results suggest that exposure to PM_{10} and PM_{coarse} at school was associated with increased internalizing behavior, whereas NDVI within a 100-m buffer was associated with reduced externalizing behavior. These associations showed no differences between sex or age groups, and neither SES nor genetic liability showed moderating effects. Effects detected were of small magnitude, but given the ubiquitous nature of these exposures and the number of people, particularly children, exposed to air pollutants on a daily basis, these results can have broad implications for public health policies. These findings reinforce the need to further investigate the role of exposure to physical environmental factors, such as air pollution and greenness, in the early manifestation of mental health problems, while highlighting the importance of improving air quality, especially around schools, as part of preventive strategies focused on childhood psychopathology.

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Conflict of interest statement

JAR-Q was on the speakers' bureau and/or acted as a consultant for Biogen, Idorsia, Janssen-Cilag, Novartis, Takeda, Bial, Sincrolab, Neuraxpharm, Novartis, BMS, Medice, Rubió, Uriach, Technofarma, and Raffo in the last 3 years. He also received travel awards (air tickets + hotel) for taking part in psychiatric meetings from Idorsia, Janssen-Cilag, Rubió, Takeda, Bial, and Medice. The Department of Psychiatry, chaired by him, received unrestricted educational and research support from the following companies in the last 3 years: Exeltis, Idorsia, Janssen-Cilag, Neuraxpharm, Oryzon, Roche, Probitas, Psious, and Rubió. The rest of the authors declare that they have no competing or potential conflicts of interest.

Ethics statement

The study was granted a full ethics approval by the ethics committees of the Hospital Universitari Vall d'Hebron and the Hospital Materno-Infantil Sant Joan de Déu (Catalonia, Spain). Written consent was obtained from all participating families.

Data availability statement

Raw data from this article are not publicly available because of limitations in ethical approvals, and the summary data will be available from the corresponding author upon reasonable request. The code used in this study is available on GitHub: https://github.com/UxueZA/Inter-Exter-Env/tree/main.

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Supporting information

Additional Supporting Information may be found in the online version of this article:

Figure S1. Correlation plot depicting the correlations between the physical environmental exposures analyzed. Inside each cell, significant correlation coefficients are shown. NDVI, normalized difference vegetation index; PM, particulate matter.

Table S1. Sample size of datasets used as discovery samples for the Polygenic Risk Score (PRS) construction.

Table S2. Associations between physical environmental exposures and internalizing and externalizing behavior adjusting by sex, age, and socioeconomic status. Nominally significant associations ($p < 0.05$) are indicated in bold.

Table S3. Effect of exposures nominally associated with internalizing and externalizing behavior on their subscales. Significant associations at $p < 0.05$ are indicated in bold.

Table S4. Effect of 4 year exposure to air pollution and surrounding greenness on nominally associations with internalizing and externalizing behavior identified in 3454 children and adolescents. Significant associations at $p < 0.05$ are indicated in bold.

Table S5. Sex stratified results for the associations between physical environmental exposures and internalizing and externalizing behavior. Significant associations at $p < 0.05$ are indicated in bold.

Table S6. Age-group stratified results for the associations between physical environmental exposures and internalizing and externalizing behavior. Significant associations at $p < 0.05$ are indicated in bold.

Table S7. Associations between Polygenic Risk Scores (PRS) and socioeconomic status (SES) on internalizing and externalizing behavior.

Table S8. Modification effects by Polygenic Risk Scores (PRS) and socioeconomic status (SES) for exposures showing nominally significant associations with internalizing and externalizing behavior.

Table S9. Modification effects by Polygenic Risk Scores (PRS) and socioeconomic status (SES) for exposures showing nominally significant associations with the specific syndrome scales composing the internalizing and externalizing behavior scores.

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