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The Association between Exposure to Fine Particulate Air Pollution and the Trajectory of Internalizing and Externalizing Behaviors during Late Childhood and Early Adolescence: Evidence from the Adolescent Brain Cognitive Development (ABCD) Study

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Background: Exposure to high levels of fine particulate matter (PM) with aerodynamic diameter ≤2.5 μm ($PM_{2.5}$) via air pollution may be a risk factor for psychiatric disorders during adulthood. Yet few studies have examined associations between exposure and the trajectory of symptoms across late childhood and early adolescence.

Objective: The current study evaluated whether $PM_{2.5}$ exposure at 9–11 y of age affects both concurrent symptoms as well as the longitudinal trajectory of internalizing and externalizing behaviors across the following 3 y. This issue was examined using multiple measures of exposure and separate measures of symptoms of internalizing disorders (e.g., depression, anxiety) and externalizing disorders (e.g., conduct disorder), respectively.

Methods: In a sample of more than 10,000 youth from the Adolescent Brain Cognitive Development (ABCD) Study, we used a dataset of historical $PM_{2.5}$ levels and growth curve modeling to evaluate associations of $PM_{2.5}$ exposure with internalizing and externalizing symptom trajectories, as assessed by the Child Behavioral Check List. Three distinct measures of $PM_{2.5}$ exposure were investigated: annual average concentration during 2016, number of days in 2016 above the US Environmental Protection Agency (US EPA) 24-h $PM_{2.5}$ standards, and maximum 24-h concentration during 2016.

Results: At baseline, higher number of days with $PM_{2.5}$ levels above US EPA standards was associated with higher parent-reported internalizing symptoms in the same year. This association remained significant up to a year following exposure and after controlling for $PM_{2.5}$ annual average, maximum 24-h level, and informant psychopathology. There was also evidence of an association between $PM_{2.5}$ annual average and externalizing symptom levels at baseline in females only.

Discussion: Results suggested $PM_{2.5}$ exposure during childhood is associated with higher symptoms of internalizing and externalizing disorders at the time of exposure and 1 y later. In addition, effects of $PM_{2.5}$ exposure on youth internalizing symptoms may be most impacted by the number of days of exposure above US EPA standards in comparison with annual average and maximum daily exposure. https://doi.org/10.1289/EHP13427

Introduction

Fine particulate matter (PM) with aerodynamic diameter ≤2.5 μm ($PM_{2.5}$) air pollution is one of the leading contributors to disease burden in the modern world.[1] To date, much of the research on the adverse health effects of $PM_{2.5}$ exposure has focused on impacts on cardiopulmonary health in adults,[2] yet a growing body of evidence suggests that $PM_{2.5}$ may also directly impact the brain, increasing both short- and long-term risk for mental illness in both children[3–9] and adults,[10–12] as well as in samples including both children and adults.[13–16] Dynamic neurodevelopmental processes that unfold across late childhood and early adolescence may make this developmental stage a particularly sensitive period for adverse impacts of $PM_{2.5}$ exposure on mental health.[17–19] Despite general improvements in air quality over recent decades,[20] over 90% of children worldwide were exposed to unsafe levels of $PM_{2.5}$ at some point during 2016 alone,[21] and critical questions remain as to the impacts of such exposure. Evidence suggests that prenatal exposure is associated with poor outcomes later in childhood,[5] but the degree to which the temporal pattern of $PM_{2.5}$ exposure during late childhood is associated with symptoms of internalizing and externalizing disorders as youth transition from childhood into adolescence is unclear. We investigate this issue using growth curve modeling in a large-scale, longitudinal dataset of adolescent health to test for effects of multiple measures of $PM_{2.5}$ exposure at 9–11 y of age on the trajectory of internalizing and externalizing symptoms across the ensuing 3 y as participants transition into adolescence.

$PM_{2.5}$ Exposure Levels during Adulthood Affect Psychopathology

Though several common air pollutants negatively impact health, $PM_{2.5}$ may be particularly detrimental to mental health because its component particles are small enough to pass through the blood–brain barrier and impinge on neural tissue.[22] Epidemiological research investigating effects of exposure on psychopathology suggests that short- and long-term exposure to high levels of $PM_{2.5}$ elevates both immediate and future risk for mental illness during adulthood.[15,23–30] Supporting immediate effects, several studies have found increased hospital admissions for a range of psychiatric conditions on days with high levels of ambient $PM_{2.5}$, including hospitalizations for depression, suicide attempts, and psychotic episodes.[15,23–25] Supporting effects of long-term exposure, higher average exposure from the months to years prior has been associated with an increased risk for depression and anxiety, among other disorders, including a higher probability of a diagnoses, higher symptom levels, and higher rate of psychiatric medication use and

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services.[26–30] Thus, it appears that high $PM_{2.5}$ exposure during adulthood may affect mental health on multiple levels. Yet important questions remain as to the long-term effects of $PM_{2.5}$ exposure during brain development, including whether exposure during late childhood is associated with altered trajectories in psychopathology across adolescence.

$PM_{2.5}$ Exposure and Psychopathology during Childhood

Exposure to high levels $PM_{2.5}$ during childhood may have particularly long-lasting and detrimental effects. Evidence in rodents suggests high exposure disrupts a range of neurodevelopmental processes that set the stage for brain structure and function in adulthood, with notable effects on behavior.[31] To date, the developmental literature of $PM_{2.5}$ exposure in humans has focused on prenatal exposure, with high exposure during this critical developmental period associated with a range of poor outcomes years later in childhood, including alterations in brain structure, motor deficits, and cognitive impairments.[32–34] Yet far fewer studies have investigated how exposure during late childhood may affect the trajectory of internalizing and externalizing symptoms as children transition into adolescence, the focus of the current study.

Internalizing and externalizing symptom trajectories during adolescence have been shown to be predictive of problems later in life, even when symptom levels do not reach criteria for clinical disorder during adolescence.[35–36] Thus, understanding effects of air pollution on symptom trajectories during late childhood and adolescence is of considerable importance when it comes to both public policy and personal health decisions aimed at reducing the long-term impacts of air pollution exposure. To date, a handful of studies have investigated the effects of exposure during late childhood on later development of psychopathology, with evidence that exposure at 12 y of age is associated with increased risk for major depression at age 18, but not at age 12,[12,37] whereas exposure during late childhood was associated with an altered trajectory of conduct problems, with high exposure associated with less of a normative reduction in symptoms over time.[38] Yet important questions remain, including whether $PM_{2.5}$ exposure differentially affects symptoms of internalizing or externalizing disorders and the degree to which associations between exposure and symptom trajectories may differ between the sexes. These issues are investigated in the current study.

Current Study

Using data from the Adolescent Brain Cognitive Development (ABCD) Study, the current study implemented latent growth curve modeling to investigate several unanswered questions regarding associations between $PM_{2.5}$ exposure during late childhood and the trajectory of internalizing and externalizing symptoms into early adolescence. Specifically, we used two broadband measures that differentially capture symptoms of internalizing (e.g., anxiety and depression) and externalizing (e.g., conduct disorder) disorders. We hypothesized that associations between $PM_{2.5}$ exposure and symptom trajectories will be observed for both internalizing and externalizing disorders and that these associations would be observed both during the year of exposure, as well as for multiple years following exposure. In addition, we tested for associations between symptom trajectories and three distinct measures of $PM_{2.5}$ exposure, allowing us to evaluate the unique impacts of different patterns of exposure (e.g., acute vs. chronic) on mental health.[39] Finally, we tested for sex differences in both the underlying trajectories of symptoms as well as the association of exposure levels with individual differences in these trajectories. We hypothesized that, despite differences in internalizing and externalizing trajectories between the sexes, the associations between these trajectories and exposure will be consistent across females and males.

Methods

Participants

All data were drawn from the ABCD Study National Data Archive (NDA) data release 4.0 (NDA 4.0). The ABCD Study is a longitudinal project following 11,876 youth from the general population, with yearly assessments for 10 y, beginning at 9–10 y of age. Data used in the current project were collected between 2016 and 2021. ABCD participants were recruited from 21 sites across the United States, with sampling techniques designed to reflect the sociodemographic variability of the United States in regard to age, gender, race/ethnicity, socioeconomic status, and urbanicity, with target demographic distributions derived from the American Community Survey and third and fourth grade enrollment data from the National Center for Education Statistics.[40] Specifically, recruitment was done through probability sampling of schools within the 21 research site catchment areas, and the demographic distribution of the resulting sample was monitored during initial recruitment. If the sample was found to deviate from the target demographic distributions, recruitment was increased in schools with overrepresentation of the specific demographic in question. A listing of participating research sites can be found at https://abcdstudy.org/consortium_members/. In addition to the environmental and psychopathology measures used in the current report, the ABCD protocol includes an array of other measures, including neuroimaging and genetic and cognitive variables, collected at yearly longitudinal intervals.[41]

Analyses in the current report used data on internalizing and externalizing behaviors from four distinct time points, restricting the sample to participants with at least a single time point of internalizing and externalizing symptom data as well as data for all three of the $PM_{2.5}$ measures of interest, measured at the baseline time point (see section " $PM_{2.5}$ Exposure Estimation" for information on the measures of interest). Of the 11,876 participants with data in the ABCD Study, two were excluded due to missing internalizing and externalizing symptom data at all time points, and 649 were excluded because of missing data on all three $PM_{2.5}$ measures of interest. In addition, we elected to exclude data from any participant who was missing any of the three $PM_{2.5}$ measures used in the current study, which resulted in the exclusion of an additional 442 subjects. These additional subjects were excluded because all three $PM_{2.5}$ measures were drawn from the same source datasets, meaning quality control issues for a one $PM_{2.5}$ measure likely applied to the other measures. However, the measures were released in different data releases, and it is unclear the degree to which they underwent the same or distinct quality control procedures. As a result, we assumed that missing data on any of the three $PM_{2.5}$ measures indicated potential quality control issues across all three $PM_{2.5}$ measures. After these exclusions, the final sample in the current project consisted of data on 10,783 participants. To determine the degree to which these exclusions resulted in sampling bias, we used Mann-Whitney–Wilcoxon tests, comparing the analysis sample ($n = 10{,}783$) to the excluded sample ($n = 1{,}093$) on continuous covariates of interest (see Table S1; see Table S2 for information comparing analysis and excluded samples on distribution of categorical variables).

Because all participants were under 18 y old, written, informed consent was obtained from a parent or guardian, and assent was obtained from the participant. Research protocols across the 21 ABCD sites were approved by the University of California–San Diego institutional review board (IRB; protocol

number 160091), the IRB of record for the entire ABCD Study. Data from the baseline time point through year 2 were drawn from parent-report questionnaires, which were administered via a computer tablet, except for address history, which was obtained through an interview with the parent, and pubertal status, which was completed by the youth participant on a computer tablet. Some year 3 data were collected from an online form due to a pause in on-site data collection resulting from the COVID-19 pandemic. All parent responses were obtained from a single parent or guardian.

$PM_{2.5}$ Exposure Estimation

We used three measures of $PM_{2.5}$ exposure based on participants' home addresses at baseline available in the ABCD NDA 4.0 release: annual average of daily ambient $PM_{2.5}$ levels across 2016, number of days during 2016 with ambient $PM_{2.5}$ levels above the US Environmental Protection Agency (US EPA) National Ambient Air Quality Standard for mean 24-h $PM_{2.5}$ exposure ($>35\ \mu g/m^3$), and maximum 24-h $PM_{2.5}$ level in 2016. Estimates of $PM_{2.5}$ exposure were calculated based on participants' primary address as reported by their parent or caregiver. Addresses were geocoded to latitude and longitude coordinates and then linked to a preexisting spatiotemporal $PM_{2.5}$ dataset from Di et al.[42] that provides daily historical estimates of ambient $PM_{2.5}$ across the United States at a 1-km^2 resolution from 2000 to 2016. $PM_{2.5}$ exposures were derived based on the spatial intersection of this 1-km^2 grid with geocoded primary addresses during 2016, the year of the baseline ABCD assessment.

Longitudinal Indicators of Internalizing and Externalizing Symptoms

Internalizing and externalizing symptom levels were measured through the parent-reported Child Behavior Checklist (CBCL), with outcomes of interest including the internalizing subscale, which measures symptoms related to anxiety and depression, as well as the externalizing subscale, which measures symptoms related to conduct disorder and related disorders.[43] Parental informants rated the degree to which specific statements were true for their child using a three-point Likert scale: "0 - not true", "1 - sometimes true", or "2 - always true." Subscales were calculated by adding informant responses on the relevant items, with the internalizing score as the sum of all items related to "withdrawn," "somatic complaints," and "anxious/depressed problems" and the externalizing score as the sum of all items related to "rule breaking" and "aggressive behaviors." Raw scores can range between 0 and 64 for the internalizing scale and 0 and 56 for the externalizing scale. For the internalizing subscale, in children 6–11 y of age, raw scores of 12 or greater in boys and 14 or greater in girls are indicative of a clinical disorder, whereas in children 12–18 y of age, scores of 14 or greater in boys and 15 or greater in girls are indicative of a clinical disorder. For the externalizing subscale, in children 6–11 y of age, scores of 16 or greater in boys and 15 or greater in girls are indicative of a clinical disorder, whereas in children 12–18 y of age, scores of 19 or greater in boys and 16 or greater in girls are indicative of a clinical disorder. The ABCD NDA 4.0 release contains CBCL data across four time points, including a baseline timepoint in 2016, as well as three follow-up time points roughly a year apart, herein referred to as baseline, year 1, year 2, and year 3. Mean scores in general population samples for the current age group across multiple countries have been shown to range between 6.0 and 6.5 for the internalizing subscale and 7.0 and 7.5 for the externalizing subscale.[44–45]

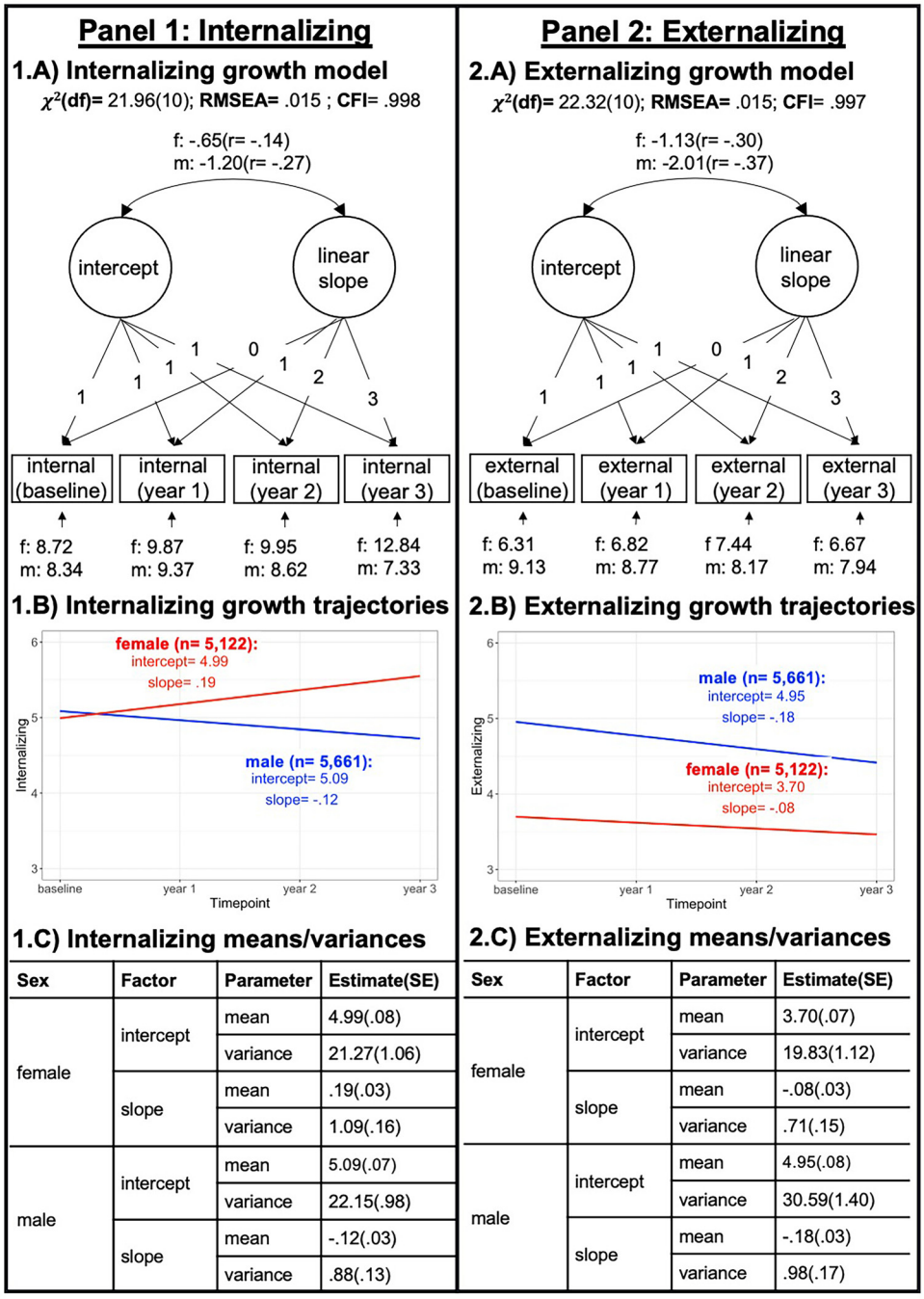
Covariates

In the analyses testing for associations between internalizing and externalizing symptom trajectories and $PM_{2.5}$ exposure, we used time invariant covariates from the baseline time point, including continuous measures of pubertal level, Area Deprivation Index (ADI)[46] total score for participants' home address, and total psychopathology problems of the parent caregiver, as gleaned from the Achenbach System of Empirically Based Assessment Adult Self Report.[47] Categorical covariates included child race (White, Black, Asian, Hispanic, and mixed/other), parental combined income ("<USD $25,000," "USD $25,000–$49,999," "USD $50,000–$74,999," "USD $75,000–$99,999," "USD $100,000–$200,000," and "above USD $200,000"), parental marital status (married, not married, missing information), and parental maximum education level ["did not complete high school/GED" (12th grade or below), "completed high school" (high school graduate or GED), "some college," "completed associate degree," "completed bachelor's degree," and "completed graduate degree" (professional, master's, or doctoral degree)]. Age was used as a continuous time-varying covariate and was regressed from CBCL symptom levels at all four time points. Although there is considerable debate over what racial categories are measuring beyond social constructions,[48] we elected to control for race because previous evidence suggests racial differences in both $PM_{2.5}$ exposure[49] and CBCL scores,[50] even after accounting for confounding variables such as socioeconomic status. Pubertal level was quantified as an average of the five items on the Pubertal Development Scale (PDS), including three general items, as well as two sex-specific items.[51] Pubertal level was included as a covariate to block puberty as a pathway driving $PM_{2.5}$–symptom trajectory associations, allowing us to test for the existence of other pathways. The ADI, an aggregate measure developed to quantify socioeconomic disadvantage within an area, was derived using census tract data from the 2011–2015 American Community Survey.

Although the original income data had 10 different income bins, we collapsed "<USD $5,000," "USD $5,000–$11,999," "USD $12,000–$15,999," and "USD $16,000–$24,999" into a single bin of "<USD $25,000" as well as collapsed "USD $25,000–$34,999" and "USD $35,000–$49,999" into a single bin of "USD $25,000 – $49,999," resulting in six bins: "<USD $25,000," "USD $25,000–$49,999," "USD $50,000–$74,999," "USD $75,000 – $99,999," "USD $100,000–$200,000]," "above USD $200,000." Marital status originally had seven bins, including "married," "widowed," "divorced," "separated," "never married," "living with partner," and "refuse to answer." These seven bins were collapsed into three, with "married" treated as one bin, "refuse to answer" treated as its own bin, and all other responses collapsed into a "not married" bin. Race, income, and parental maximum education were all deviation coded, comparing each group (minus one) to the unweighted mean of all groups. Informants reported participants' race as being either White, Black, Asian, Hispanic, or Other/Mixed race, and this variable was contrast coded, treating White as the "minus one" group, meaning we did not include a code comparing White with the grand mean. For parental combined income and maximum education, participants with missing responses were treated as their own group, and these groups were not compared with the grand mean. Participant sex was based on parent report of their child's sex at birth.

Statistical Analysis

The MPlus software package was used to conduct latent growth curve modeling of internalizing and externalizing trajectories (MPlus; version 7.1.4).[52] To account for missing continuous data and nonnormality, all analyses used robust full information maximum likelihood



Sex	Factor	Parameter	Estimate(SE)
female	intercept	mean	4.99(.08)
		variance	21.27(1.06)
	slope	mean	.19(.03)
		variance	1.09(.16)
male	intercept	mean	5.09(.07)
		variance	22.15(.98)
	slope	mean	-.12(.03)
		variance	.88(.13)

Sex	Factor	Parameter	Estimate(SE)
female	intercept	mean	3.70(.07)
		variance	19.83(1.12)
	slope	mean	-.08(.03)
		variance	.71(.15)
male	intercept	mean	4.95(.08)
		variance	30.59(1.40)
	slope	mean	-.18(.03)
		variance	.98(.17)

Figure 1. Latent growth curves for Child Behavior Checklist internalizing and externalizing subscales in full sample ($n = 10{,}783$) of ABCD cohort. Panels 1 and 2 show growth curves for internalizing and externalizing, respectively, unconstrained across the sexes. All estimates are unstandardized. Estimated trajectories for females and males are shown. Note: CFI, Comparative Fit Index; χ^2, chi-square; df, degrees of freedom; RMSEA, root mean square error of approximation; SE, standard error; f, female; m, male; *r*, standardized correlation coefficient.

estimation through the "ESTIMATOR = MLR" option, and sandwich estimation was used to adjust the fit and standard errors for the nonindependence of participants from the same family through the "TYPE = complex" option. Because robust estimation can account for nonnormality often present in CBCL scores, we measured CBCL levels using raw, untransformed scores.[53] Growth curve models included latent intercept and slope factors of CBCL subscales, with all latent factors specified to have both means and variances, as well as covariance between them, and all indicators specified to have residual variances (see Figure 1 for schematic and Supplemental Material for relevant MPlus syntax). Loadings between the longitudinal CBCL indicators and the intercept factor were all set to 1, whereas loadings between the indicators and the slope factors were specified as linear (i.e., 0, 1, 2, 3). With these loadings, the intercept factor captured symptom levels at the baseline time point, and the slope factor captured the linear rate of change of symptoms over the following three time points, measured in raw CBCL scores.

Participants were excluded if they were missing CBCL scores at all time points or did not have all three $PM_{2.5}$ measures of interest. However, as the MLR estimator in MPlus uses full information maximum likelihood and hence can accommodate different patterns

of missing data, participants were not excluded due to missing covariate data. Instead, continuous covariates were brought into the model by specifying a latent mean and variance for each covariate, whereas for categorical covariates, participants with missing data were treated as their own level (see Tables 1 and 2 for information on demographics, covariates, and data missingness).

To first characterize the trajectories of internalizing and externalizing behaviors, and whether they differed between the sexes, we used chi-square difference tests (appropriately scaled for MLR)[54] comparing multigroup models in which model parameters of interest were constrained to be equal across females and males with models in which these parameters were allowed to differ between the sexes (parameters of interest include covariance between intercept and slope factor, means of the intercept and slope factors, and residual variances for the four timepoints of CBCL data). After determining whether females and males should be modeled as having distinct trajectories, we then evaluated the degree to which individual differences in the intercept and slope of these trajectories were associated with the $PM_{2.5}$ exposure at the baseline time point while controlling for several potentially confounding covariates (see "Covariates" section). Associations between $PM_{2.5}$ exposure levels and the intercept factor would suggest that exposure during childhood is associated with concurrent levels of internalizing or externalizing symptoms at the baseline time point, whereas associations between exposure and the slope factor would suggest that exposure levels at the baseline time point may influence the rate of change in internalizing and externalizing symptoms in the years that follow as children enter adolescence.

Six sets of models were run, regressing the two growth curve factors (internalizing symptoms, externalizing symptoms) on the three exposure measures (annual average, days above EPA standards, maximum), separately. Within each set, we tested for sex differences in effects of exposure on internalizing and externalizing symptoms through chi-square difference tests, comparing models with the $PM_{2.5}$ regression coefficient constrained to be equal and unequal across males and females.

To test for nonlinear associations between $PM_{2.5}$ exposure and symptom trajectories, we ran initial models in which we included independent variables for both $PM_{2.5}$ exposure (i.e., linear term) and that exposure squared (i.e., quadratic term) for each $PM_{2.5}$ measure separately. We then evaluated the degree to which the quadratic term was significantly associated with the intercept and slope of the symptom trajectories. In the absence of significant associations, we dropped the quadratic term from the model and proceeded with models that included only linear associations between $PM_{2.5}$ exposure and symptom trajectories.

We used a combination of model fit indices including root mean square error of approximation (RMSEA), comparative fit index (CFI), and standardized root mean square residual (SRMR). Models were deemed a good fit if they had RMSEA <0.06, CFI >0.95, and SRMR <0.08.[55] To investigate sex differences in individual parameters, including $PM_{2.5}$-symptom regression coefficients, we carried out chi-squared differences tests (appropriately scaled for MLR),[54] comparing a model in which all growth and regression parameters were allowed to differ between females and males to a model in which the parameter of interest was constrained to be equal across the sexes. The standard chi-square significance threshold of $p < 0.05$ was used to determine the significance of chi-squared differences tests of sex differences.

To determine the statistical significance of regression analyses while accounting for multiple comparisons, we used false discovery rate (FDR).[56] FDR correction was carried out across p-values for the twelve coefficients of interest [two psychopathology subscales (internalizing and externalizing) by three $PM_{2.5}$ exposure measures (average, days above US EPA standard, and maximum)

Table 1. Descriptive statistics for continuous variables of the ABCD cohort.

	Full ABCD sample ($n = 10,783$)					Female-only ABCD sample ($n = 5,122$)					Male-only ABCD sample ($n = 5,661$)				
Variable	Mean (SD)	Median	Min	Max	*n* (%)	Mean (SD)	Median	Min	Max	*n* (%)	Mean (SD)	Median	Min	Max	*n* (%)
Psychopathology (CBCL raw scores)															
Internal: baseline	5 (5.5)	3	0	51	10,779 (99%)	5 (5.5)	3	0	51	5,120 (>99%)	5.1 (5.5)	3	0	49	5,659 (>99%)
Internal: 1 y	5.1 (5.5)	3	0	48	10,204 (94%)	5.2 (5.6)	3	0	45	4,839 (94%)	5 (5.5)	3	0	45	5,365 (95%)
Internal: 2 y	4.9 (5.6)	3	0	50	7,448 (68%)	5.1 (5.7)	3	0	38	3,529 (69%)	4.8 (5.4)	3	0	50	3,919 (69%)
Internal: 3 y	5.1 (5.8)	3	0	44	5,757 (53%)	5.6 (6.1)	4	0	40	2,709 (53%)	4.7 (5.4)	3	0	44	3,048 (54%)
External: baseline	4.4 (5.8)	2	0	49	10,779 (99%)	3.7 (5.1)	2	0	40	5,120 (>99%)	5 (6.3)	3	0	49	5,659 (>99%)
External: 1 y	4.1 (5.6)	2	0	47	10,204 (94%)	3.6 (5)	2	0	47	4,839 (94%)	4.7 (6)	3	0	46	5,365 (95%)
External: 2 y	3.9 (5.5)	2	0	50	7,448 (68%)	3.4 (5.1)	1	0	43	3,529 (69%)	4.4 (5.8)	2	0	50	3,919 (69%)
External: 3 y	3.9 (5.3)	2	0	43	5,757 (53%)	3.4 (4.8)	2	0	43	2,709 (53%)	4.4 (5.7)	2	0	41	3,048 (54%)
$PM_{2.5}$ exposure															
$PM_{2.5}$ avg. ($\mu g/m^3$)	7.7 (1.6)	7.7	1.7	15.9	10,783 (100%)	7.7 (1.6)	7.8	2.1	14.5	5,122 (100%)	7.6 (1.6)	7.7	1.7	15.9	5,661 (100%)
$PM_{2.5}$ days US EPA (no. of days)	1.2 (2.5)	0	0	20	10,783 (100%)	1.2 (2.4)	0	0	20	5,122 (100%)	1.3 (2.6)	0	0	20	5,661 (100%)
$PM_{2.5}$ Max. ($\mu g/m^3$)	39.9 (27.5)	27.8	5.7	199.3	10,783 (100%)	39.9 (27.4)	27.9	6.1	188.8	5,122 (100%)	40 (27.7)	27.5	5.7	199.3	5,661 (100%)
Covariate															
Area Deprivation Index	94.5 (21.2)	98.7	1.1	125	10,562 (97%)	94.6 (21.5)	98.9	1.1	125.8	5,017 (98%)	94.4 (21)	98.4	1.1	125.8	5,545 (98%)
Age: baseline (months)	119.1 (7.5)	119	107	133	10,783 (99%)	118.9 (7.5)	119	107	132	5,122 (100%)	119.2 (7.5)	119	107	133	5,661 (100%)
Age: 1 y (months)	131.2 (7.7)	131	116	149	10,218 (94%)	131 (7.7)	131	117	149	4,844 (95%)	131.3 (7.7)	131	116	149	5,374 (95%)
Age: 2 y (months)	144.1 (7.9)	144	127	168	9,472 (87%)	144 (8)	144	128	168	4,484 (88%)	144.2 (7.9)	144	127	166	4,988 (88%)
Age: 3 y (months)	154.8 (7.7)	155	137	174	5,865 (54%)	154.6 (7.6)	155	137	171	2,757 (54%)	155 (7.7)	155	138	174	3,108 (55%)
Pubertal Development Scale (sum)	1.7 (0.5)	1.6	1	4	10,721 (99%)	1.7 (0.5)	1.6	1	4	5,092 (99%)	1.7 (0.5)	1.6	1	4	5,629 (99%)
Adult self-report: parent total problems (raw)	21 (17.8)	16	0	141	10,780 (99%)	20.6 (17.6)	16	0	141	5,120 (>99%)	21.4 (18)	16	0	132	5,660 (>99%)

Note: ABCD, Adolescent Brain and Cognitive Development Study; CBCL, Child Behavior Checklist; Max, maximum value; Min, minimum value; *n* (%), number of participants and percentage of sample with nonmissing data; PM, particulate matter; $PM_{2.5}$, fine particulate matter with aerodynamic diameter ≤2.5 μm; $PM_{2.5}$ avg., annual average of $PM_{2.5}$ air pollution at participants' home address in 2016 ($\mu g/m^3$); $PM_{2.5}$ Days US EPA, number of days in 2016 with $PM_{2.5}$ levels at participants' home address above US Environmental Protection Agency standards for ambient $PM_{2.5}$ (>35 $\mu g/m^3$); $PM_{2.5}$ max., maximum daily level of $PM_{2.5}$ at participants' home address during 2016 ($\mu g/m^3$); SD, standard deviation.

Table 2. Descriptive statistics for categorical variables of the ABCD cohort at baseline.

	Full ABCD sample ($n = 10,783$)	Female-only ABCD sample ($n = 5,122$)	Male-only ABCD sample ($n = 5,661$)
Variable	*n* (%)	*n* (%)	*n* (%)
Sex			
Female	5,122 (48%)	5,122 (100%)	0 (0%)
Male	5,661 (52%)	0 (0%)	5,661 (100%)
Race/ethnicity			
Hispanic	2,171 (20%)	1,039 (20%)	1,132 (20%)
Black	1,536 (14%)	765 (15%)	771 (14%)
White	5,712 (53%)	2,654 (52%)	3,058 (54%)
Asian	236 (2%)	124 (2%)	112 (2%)
Multiracial	1,126 (10%)	539 (11%)	587 (10%)
Missing	2 (<1%)	1 (<1%)	1 (<1%)
Parent marital status			
Not married	3,348 (31%)	1,635 (32%)	1,713 (30%)
Married	7,353 (68%)	3,453 (67%)	3,900 (69%)
Missing	82 (1%)	34 (1%)	48 (1%)
Parent max. education			
Did not complete high school/GED	509 (5%)	264 (5%)	245 (4%)
Completed high school/GED	986 (9%)	464 (9%)	522 (9%)
Some college	1,350 (12%)	622 (12%)	728 (13%)
Completed Associate's degree	1,417 (13%)	667 (13%)	750 (13%)
Completed Bachelor's degree	2,771 (26%)	1,302 (25%)	1,469 (26%)
Completed graduate degree	3,727 (35%)	1,795 (35%)	1,932 (34%)
Missing	23 (<1%)	8 (<1%)	15 (<1%)
Parental income (USD)			
<$25,000	1,435 (13%)	668 (13%)	767 (14%)
$25,000–$49,999	1,413 (13%)	704 (14%)	709 (13%)
$50,000–$74,999	1,371 (13%)	642 (13%)	729 (13%)
$75,000–$99,999	1,443 (13%)	696 (14%)	747 (13%)
$100,000–$199,999	3,077 (29%)	1,443 (28%)	1,634 (29%)
$200,000 or greater	1,144 (11%)	549 (11%)	595 (11%)
Missing	900 (8%)	420 (8%)	480 (8%)

Note: ABCD, Adolescent Brain and Cognitive Development Study; CBCL, Child Behavior Checklist; GED, general education diploma; Max, maximum value; Mdn, median value; Min, minimum value; *n* (%), number of participants and percentage of sample with nonmissing data; PM, particulate matter; $PM_{2.5}$, fine particulate matter with aerodynamic diameter ≤2.5 μm; $PM_{2.5}$ avg., annual average of $PM_{2.5}$ air pollution at participants' home address in 2016 ($\mu g/m^3$); $PM_{2.5}$ Days US EPA, number of days in 2016 with $PM_{2.5}$ levels at participants' home address above US Environmental Protection Agency standards for ambient $PM_{2.5}$ (>35 $\mu g/m^3$); $PM_{2.5}$ max, maximum daily level of $PM_{2.5}$ at participants' home address during 2016 ($\mu g/m^3$); SD, standard deviation; USD, United States dollars.

by two growth curve factors (intercept and slope)]. FDR calculations were carried out separately for models testing for linear and quadratic associations, respectively. An FDR-adjusted *q*-value of <0.05 was used as significance threshold. Uncorrected *p*-values were determined according to the *z*-statistic of the coefficient of interest (i.e., estimate divided by standard error).

For all models with significant regression coefficients between $PM_{2.5}$ exposure and the intercept or slope growth factors, we conducted post hoc analyses evaluating whether the effects of interest remained significant when controlling for the two other $PM_{2.5}$ exposure measures, as well as the parental informant's own total psychopathology at the baseline timepoint, as measured by the Achenbach System of Empirically Based Assessment Adult Self Report. By controlling for the other two $PM_{2.5}$ measures, we can determine if associations of a given $PM_{2.5}$ measure with internalizing and externalizing trajectories are indeed unique to that measure, potential demonstrating that certain temporal patterns of exposure are particularly problematic as compared with others. For example, if both annual average of exposure and number of days of exposure above EPA standards were associated with the same aspect of symptom trajectories, it would be unclear whether the annual average association was in fact driven by the few days with exposures above the standards. By running post hoc analyses that include all three measures as simultaneous predictors, we can help address this issue as to the specificity of any observed effects.

For any significant associations between the intercept factors and $PM_{2.5}$ exposure in our main analyses, we changed the slope factor loadings, so the intercept factor was capturing means and variances in internalizing and externalizing symptoms at the later time points (i.e., years 1–3) and then reran the models for each of these later time points, separately. These analyses provided a post hoc significance test, allowing us to ascertain whether any observed association between exposure and internalizing and externalizing symptoms at the baseline timepoint remained significant at later time points.

Finally, to evaluate the degree to which any significant associations between exposures and internalizing and externalizing symptom trajectory factors may be explained by residual confounding, we computed E-values for that coefficient, which estimates the degree of unmeasured confounding needed to fully explain the observed association.[57] E-values were computed using the "Evalue" R package (version 4.0.2; R Development Core Team), using the following parameters: standardized regression coefficient, standard error of the regression coefficient, variance of the factor in question (i.e., intercept or slope), and a delta of 1.

Results

Demographics, Descriptive Statistics, and Zero-Order Correlations

For complete demographic data and descriptive statistics, see Tables 1 and 2. Comparisons of covariates between the analysis sample and the excluded sample can be seen in Tables S1 and S2. For zero-order Spearman correlations between all measures across the full sample and in females and males, separately, see Supplemental Figures S1–S3. In brief, using a standard significance threshold of $p < 0.05$, Mann-Whitney–Wilcoxon tests revealed that

Table 3. Linear growth curve model fit statistics of models in which all parameters are constrained to be equal and unequal between the sexes in the ABCD cohort ($n = 10{,}783$; female $n = 5{,}122$; male $n = 5{,}661$).

CBCL subscale	Model	χ^2 (df)	Scaling factor	Scaled $\Delta\chi^2$ (df)	RMSEA (90% CI)	CFI	TLI	SRMR
Internalizing	Equal across sexes	116.1 (19)	2.3700	83.3 (9)	0.031 (0.026, 0.036)	0.984	0.990	0.045
Internalizing	Unequal across sexes	22.0 (10)	2.0086	—	0.015 (0.006, 0.023)	0.998	0.998	0.014
Externalizing	Equal across sexes	181.4 (19)	3.2867	134.7 (9)	0.040 (0.035, 0.045)	0.966	0.979	0.106
Externalizing	Unequal across sexes	22.3 (10)	2.6585	—	0.015 (0.007, 0.024)	0.997	0.997	0.018

Note: Model fit and chi-square difference comparisons between models in which growth factor parameters are constrained or unconstrained across females and males. Growth curve parameters for the unconstrained models can be seen in Figure 1. For chi-square differences tests of individual parameters, see Table S3. 90% CI, 90% confidence interval; ABCD, Adolescent Brain and Cognitive Development study; CBCL, Child Behavior Checklist; CFI, Comparative Fit Index; CI, confidence interval; df, degrees of freedom; $\Delta\chi^2$, change in chi-square; RMSEA, Root Means Square Error of Approximation; SRMR, Standardized Root Mean Squared Residual; TLI, Tucker-Lewis Index.

the excluded sample was younger at all time points (baseline: W = 5,540,112, $p = 0.001$; year 1: W = 4,857,411, $p = 0.003$; year 2: W = 4,275,128; $p = 0.034$; year 3: W = 1,045,184; $p = 0.011$), while also having significantly higher ADI (W = 2,637,922; $p < 0.001$). In addition, we found that the excluded sample was slightly higher in $PM_{2.5}$ annual average (W = 2,515,342; $p = 0.038$) but interpret this result with caution, given the concerns regarding the quality of $PM_{2.5}$ data in the excluded sample. We did not compare the analysis sample and the excluded sample on the other two $PM_{2.5}$ measures because there were only five participants in the excluded sample with data on these measures. Notably, the excluded sample was disproportionately drawn from one site (site 19), which represented ~5% of the participants in the analysis sample but ~18% of participants in the excluded sample and had a higher percentage of Black participants (~14% in analysis sample and ~23% in excluded sample). As a result, we saw some evidence of selection when comparing the analysis sample and the excluded sample, though it is unclear as to how this selection may bias the results.

Latent Growth Curve Modeling of Internalizing and Externalizing Symptom Trajectories

The internalizing and externalizing symptom growth models fit well in both constrained and unconstrained models, all RMSEA <0.06, CFI >0.95, and SRMR <0.08 (see Table 3 for model fit information, Figure 1 for model parameters and estimated trajectories, and Supplemental Table S3 for chi-square differences tests of individual model parameters). Chi-square difference tests revealed that a model in which all growth curve parameters (i.e., means, variance, covariances, residual variances) were allowed to differ between the sexes provided a significantly better fit than when the parameters were constrained to be equal across the sexes for both internalizing and externalizing symptom trajectories (internalizing: $\Delta\chi^2[9] = 83.3$, $p < 0.001$; externalizing: $\Delta\chi^2[9] = 134.7$, $p < 0.001$).

As illustrated in Figure 1 and Supplemental Table S3, females and males had similar initial levels of internalizing symptoms (females: mean of intercept factor = 4.99; males: mean of intercept factor = 5.09; $\Delta\chi^2[1] = 1.336$, $p = 0.248$) but significantly diverged over time, with females showing an average increase in internalizing symptoms and males showing an average decrease (females: mean of slope factor = 0.19; males: mean of slope factor = −0.12; $\Delta\chi^2[1] = 54.311$, $p < 0.001$). For externalizing, females were lower than males at baseline (females: mean of intercept factor = 3.70; males: mean of intercept factor = 4.95; $\Delta\chi^2[1] = 115.690$, $p < 0.001$) and although both sexes decreased in externalizing symptoms over time, this decrease was significantly greater in males than females (females: mean of slope factor = −0.08; males: mean of slope factor = −0.18; $\Delta\chi^2[1] = 7.190$, $p = 0.007$). Variances and covariances of the intercept and slope factors for both internalizing and externalizing trajectories were all significant, whereas sex difference analyses revealed that the internalizing residual variance at year 3 ($\Delta\chi^2[1] = 19.876$, $p < 0.001$), as well as the externalizing slope factor variance ($\Delta\chi^2[1] = 34.775$, $p < 0.001$), and the externalizing residual variances at baseline ($\Delta\chi^2[1] = 8.630$, $p = 0.003$) and year 1 ($\Delta\chi^2[1] = 6.618$, $p = .010$) all significantly differed between females and males. As a result of the considerable sex differences in growth curve factor parameters, we allowed all growth parameters to differ between the sexes in analyses regressing the growth curve factors on $PM_{2.5}$ exposure.

Regressing Growth Curve Factors on $PM_{2.5}$ Exposure

In initial models testing for nonlinear associations between $PM_{2.5}$ exposure and symptom trajectories, there were no FDR-corrected significant regression coefficients between the quadratic exposure terms and the growth curve factors (see Supplemental Table S4 for FDR-corrected results and Excel Tables S1–S12 for results including all covariates in both constrained and unconstrained models). As a result, the quadratic term was dropped from all models, which were then rerun testing for linear associations only. See Table 4 for statistics on regression coefficients between symptom trajectory factors and $PM_{2.5}$ measures when these coefficients were constrained to be equal across the sexes. For regression coefficients of all covariates in both constrained and unconstrained models, see Excel Tables S13–S24. After FDR correction these analyses revealed that a higher number of days above US EPA standards was associated with alterations in internalizing symptom trajectories, but not externalizing. Specifically, for every additional day of exposure above the $PM_{2.5}$ standard, there was a 0.098 increase in the internalizing intercept [standardized $\beta = 0.052$; 95% confidence interval (CI): 0.027, 0.077], FDR-adjusted $p = 0.006$, E-value = 1.28), but this reduced in magnitude at a rate of −0.030 per year after exposure, as indicated by a significant association between days above the $PM_{2.5}$ standard with the internalizing slope factor (standardized $\beta = -0.069$; 95% CI: −0.108, −0.030, FDR-adjusted $p = 0.006$, E-value = 1.33). Thus, $PM_{2.5}$ exposure was more strongly associated with concurrent internalizing symptoms for time points closer to exposure.

Follow-up post hoc analyses tested whether the significant associations between $PM_{2.5}$ measures and symptom growth curves remained significant when controlling for the other two $PM_{2.5}$ measures, as well as informant total psychopathology levels (Excel Table S25). When including these measures as additional predictors of internalizing growth factors, the associations between days above the $PM_{2.5}$ standard and internalizing symptom factors remained significant and of a similar magnitude (internalizing intercept: standardized $\beta = 0.051$; 95% CI: 0.022, 0.080, unadjusted $p = 0.001$, E-value = 1.32; internalizing slope: standardized $\beta = -0.064$; 95% CI: −0.115, −0.013, unadjusted $p = 0.013$, E-value = 1.32), despite a strong association between informants' total psychopathology levels and the internalizing factors (intercept: standardized $\beta = -0.609$; 95% CI: 0.578, 0.640, unadjusted $p < 0.001$, E-value = 3.49; slope: standardized $\beta = -0.204$; 95% CI: −0.282, −0.126, unadjusted $p < 0.001$, E-value = 1.72).

Finally, we evaluated whether effects of number of days above the $PM_{2.5}$ standard at baseline on internalizing levels remained

Table 4. Regression coefficients of growth curve factors on $PM_{2.5}$ measures in full sample ($n = 10{,}783$) of ABCD cohort, constrained to be equal across the sexes.

CBCL subscale	$PM_{2.5}$ measure	Factor	Unstand. b (SE)	Stand. β (95% CI)	b/SE	FDR *p*-value
Internalizing	Average	Intercept	0.055 (0.036)	0.019 (−0.005, 0.043)	1.544	.211
—	—	Slope	−0.011 (0.014)	−0.017 (−0.059, 0.025)	−0.799	.440
Internalizing	Days US EPA	Intercept	0.098 (0.024)	0.052 (0.027, 0.077)	4.031	.006
—	—	Slope	−0.030 (0.008)	−0.069 (−0.108, −0.030)	−3.502	.006
Internalizing	Max	Intercept	0.002 (0.002)	0.012 (−0.012, 0.036)	0.975	.395
—	—	slope	−0.002 (0.001)	−0.044 (−0.083, −0.005)	−2.193	.084
Externalizing	Average	Intercept	0.053 (0.039)	0.019 (−0.009, 0.047)	1.35	.266
—	—	Slope	−0.01 (0.013)	−0.018 (−0.064, 0.028)	−0.772	.440
Externalizing	Days US EPA	Intercept	0.038 (0.022)	0.021 (−0.003, 0.045)	1.709	.209
—	—	Slope	−0.019 (0.008)	−0.055 (−0.098, −0.011)	−2.496	.052
Externalizing	Max	Intercept	−0.002 (0.002)	−0.014 (−0.038, 0.010)	−1.165	.325
—	—	Slope	−0.001 (0.001)	−0.001 (−0.002, 0.000)	−1.57	.211

Note: For regression statistics of covariates, see Excel Tables S13–S24. 95% CI, 95% confidence interval; ABCD, Adolescent Brain and Cognitive Development Study; Average, annual average of $PM_{2.5}$ air pollution at participants' home address in 2016 ($\mu g/m^3$); CBCL, Child Behavior Checklist; CI, confidence interval; Days US EPA, number of days in 2016 with $PM_{2.5}$ levels at participants' home address above US Environmental Protection Agency standards for ambient $PM_{2.5}$ ($>35\ \mu g/m^3$); FDR *p*-value, false discovery rate adjusted *p*-value; Max, maximum daily level of $PM_{2.5}$ at participants' home address during 2016 ($\mu g/m^3$); PM, particulate matter; $PM_{2.5}$, fine particulate matter with aerodynamic diameter ≤ 2.5 μm; SE, standard error; Stand. β, standardized regression coefficient; Unstand. b, unstandardized regression coefficient.

significant in the years following the measured exposure and baseline symptom measurement. To do so, we iterated through which of the year 1 to year 3 time points was the intercept in the growth curve and regressed the resulting intercept factor on the days above the US EPA $PM_{2.5}$ standard and the covariates used in the main analyses (Excel Tables S26–S28). These analyses revealed that, despite getting smaller with time, the association between days above the $PM_{2.5}$ standard and higher internalizing score remained significant 1 y after exposure (standardized $\beta = 0.036$; 95% CI: 0.012, 0.060, unadjusted $p = 0.002$) but not at the later time points. Thus, the number of days with $PM_{2.5}$ above US EPA standards is not only associated with higher concurrent internalizing symptoms in youth but also higher internalizing symptoms 1 y following exposure, and these effects appear to be unique to youth when controlling for informants psychopathology levels.

Sex Differences in Associations between $PM_{2.5}$ Exposure and Symptom Trajectories

Chi-square differences tests evaluating sex differences in associations between the $PM_{2.5}$ quadratic terms and symptom trajectory found no evidence of sex differences in nonlinear associations between exposure and growth curve factors (see Supplemental Table S5). Chi-square differences tests evaluating sex differences in linear $PM_{2.5}$-symptom trajectory associations demonstrated that the association between annual average of $PM_{2.5}$ and the externalizing intercept significantly differed between the sexes, albeit weakly ($\Delta\chi^2[1] = 4.006$, $p = 0.045$) (see Supplemental Table S6). Specifically, for every increase of 1 $\mu g/m^3$ in average $PM_{2.5}$ levels, the externalizing intercept factor (i.e., externalizing levels at baseline) increased by .113 in females but not males (females: standardized $\beta = 0.040$; 95% CI: 0.003, 0.077, unadjusted $p = 0.035$, E-value = 1.24; males: standardized $\beta = -0.008$; 95% CI: −0.021, 0.037; unadjusted $p = 0.621$). No other regression coefficient of interest showed significant sex differences. Post hoc analyses revealed that the association between annual average of $PM_{2.5}$ and the externalizing intercept in females was reduced to the point of no longer being significant after controlling for the other exposure measures and informant psychopathology (standardized $\beta = 0.024$; 95% CI: −0.011, 0.059; unadjusted $p = 0.183$; Excel Table S29). Thus, although there was weak evidence of an association between annual average and externalizing in female youth, this effect does not appear to reflect unique effects of the annual average measures and was not specific to youth when controlling for informants' psychopathology levels.

Discussion

Using latent growth curve modeling in a large-scale, longitudinal dataset of youth development, the current study found evidence that a higher number of days with ambient $PM_{2.5}$ levels above EPA standards ($>35\ \mu g/m^3$ 24-h average) during late childhood was associated with higher levels of internalizing symptoms during the same year and up to 1 y later, regardless of an individual's sex. This association between number of days above US EPA standards and internalizing symptoms was found over and above associations with annual average and maximum level, suggesting that repeated high levels of $PM_{2.5}$ exposure (i.e., days above US EPA standards) may be more impactful to internalizing psychopathology than the typical level of exposure (i.e., annual average) or highest level of exposure (i.e., maximum) over the same exposure period. Finally, there was weak but notable evidence that females and males differed in their associations between annual average of $PM_{2.5}$ and externalizing symptom levels, with higher annual average associating with higher levels of externalizing symptoms at baseline in females only. In the remainder of the discussion, we integrate the current results with previous literature and highlight critical unanswered questions.

$PM_{2.5}$ Exposure is Associated with Concurrent and Future Internalizing Symptoms

Several studies have reported similar effects between $PM_{2.5}$ exposure and internalizing symptoms in adult or general population samples, including studies linking daily $PM_{2.5}$ levels to hospital admission for psychiatric episodes,[58–61] cross-sectional studies linking level of exposure to concurrent mental health,[62,63] and longitudinal studies demonstrating effects of exposure on adjacent or future mental health.[9,26,27,64] However, the current findings extend this literature in important ways. First, previous research linking childhood $PM_{2.5}$ exposure to psychopathology has found evidence of long-term associations between $PM_{2.5}$ exposure during childhood and later internalizing diagnoses,[9] as well as concurrent associations between childhood exposure in children 6–11 y of age and subclinical externalizing symptoms,[64] but there has been little evidence of effects of $PM_{2.5}$ exposure during late childhood on concurrent internalizing symptoms, as was observed in the current report. Indeed, two recent studies both suggested that air pollution exposure across adolescence was associated with internalizing and externalizing symptoms at the end of the exposure window, but that these effects were specific to NO_x exposure, not $PM_{2.5}$.[65–66] As such, the specific findings in the current report align with previous work demonstrating

effects of air pollution exposure on subclinical symptoms of psychopathology in youth but also contrast with this work as to the specific pollutant implicated, because they found no associations with $PM_{2.5}$.

It is notable that the current study failed to conceptually replicate a related study which found that higher $PM_{2.5}$ exposure during late childhood was associated with a flattening in the trajectory of conduct problems over time, a central aspect of externalizing symptoms.[38] Whereas externalizing symptoms generally have been found to decrease over time across late childhood and early adolescence,[67] Karamanos et al.[38] found that higher $PM_{2.5}$ exposure was associated with a flattening of conduct problems trajectory, with levels of conduct problems not decreasing at as fast a rate. Yet in the current study the association between annual average of $PM_{2.5}$ and the externalizing symptoms slope factor was nonsignificant. However, important methodological differences make it difficult to compare these studies, including differences in how sex was modeled, with Karamanos et al. controlling for sex, whereas the current report treated sex as a grouping variable, allowing us to test for moderating effects of sex on associations between $PM_{2.5}$ exposure and psychopathology symptoms. Indeed, as discussed in the following section, the current report found weak but notable sex differences in both the trajectory of externalizing symptoms, as well as the association between $PM_{2.5}$ exposure and initial levels of externalizing, highlighting the importance of explicitly testing for sex differences in research on youth psychopathology.

With data on more than 10,000 youth, the current study had considerably more power than previous investigations. As a result, even very small effects could be detected, effects which would be deemed nonsignificant in studies with smaller sample sizes. The association between $PM_{2.5}$ and internalizing symptoms in the current report was small in nature (standardized $\beta = 0.052$; 95% CI: 0.027, 0.077), yet in line with effect sizes observed using ABCD Study data when trying to link individual differences in behavior to biological measures.[68] However, the small effect sizes do not mean the associations between $PM_{2.5}$ exposure and internalizing symptoms are trivial. First, even if effects of $PM_{2.5}$ on mental health are small, if enough people are exposed, the cumulative societal impact of these effects may be quite large, as has been demonstrated elsewhere.[1] Second, because only a small part of the overall exposome, $PM_{2.5}$ is just one of many common pollutants that may exacerbate mental illness and, when considered together, the cumulative effect of these pollutants may add up to a substantial impact.[69] In addition, certain risk factors not investigated in the current report may moderate effects of air pollution exposure, putting specific individuals at increased risk for negative impacts of exposure, with effects of exposure being stronger in certain subpopulations. As a future direction, our research group plans to use additional environmental and genomic data within the ABCD dataset to identify genetic risk factors that may moderate effects of environmental exposures on mental health.

In addition to demonstrating associations between $PM_{2.5}$ exposure in late childhood and concurrent internalizing symptoms, the current study also differed from previous work by using alternative measures of $PM_{2.5}$ exposure that go beyond the temporal averaging that is commonly used in the literature. A central aim of the current study was to compare different temporal models of $PM_{2.5}$ exposure to determine if youth symptom trajectories were most affected by annual average, days above EPA standards, or maximum daily level. Results suggested that youth symptoms were most affected by the number of days above US EPA standards and that these effects were independent from the other temporal patterns of exposure. Specifically, this finding suggests that persistent moderate levels of exposure (i.e., $PM_{2.5}$ annual average) and the actual level of highest exposure (i.e., $PM_{2.5}$ maximum daily exposure) are less impactful to mental health than having multiple days of relatively high exposure, even if these days are infrequent. This possibility has several important implications. First, relying solely on annual average measures of exposure, as is commonly done in the literature, likely misses effects that are unique to specific temporal patterns of exposure. Thankfully, a recent proliferation of air monitoring systems and related databases are beginning to provide researchers with a wealth of data to model different patterns of $PM_{2.5}$ exposure. Second, from a public health perspective, this finding points to a specific pattern of exposure that may put youth at heightened risk for mental health problems as they transition into adolescence, potentially providing a template for identifying youth who may particularly benefit from interventions aimed at ameliorating the long-term impacts of $PM_{2.5}$ exposure. Finally, the association between internalizing symptom trajectories and number of days of exposure above US EPA standards provides additional support to these standards. Although the nature of the ABCD dataset prevents us from comparing the specific standard of $35\,\mu g/m^3$ to other potential thresholds, the current results suggest that the current standard may be meaningful for reducing risk of symptoms of psychopathology across adolescence. A deeper understanding of the specific temporal patterns and levels of exposure that are most problematic to mental health could provide valuable information when it comes to developing prevention and intervention strategies aimed at ameliorating the psychiatric impacts of air pollution exposure.

It is important to note that the negative association between number of days above US EPA standards and the internalizing slope factor suggests that the magnitude of the association gets smaller the further in time from exposure, at least across the 3 y and outcomes investigated in the current study. This result aligns with recent research suggesting that cognitive impairments from acute $PM_{2.5}$ exposure may be temporary, at least in older adults.[70] However, other studies have demonstrated associations between childhood exposure and long-lasting psychiatric and neural outcomes, including developing a mental health disorder[9] and alterations in neuroanatomy.[4,5,71,72] These studies together suggest that effects of exposure may be diverse in both the domain affected and the timing of when they manifest. We speculate that around the time of exposure, these impacts may manifest as subtle, temporary increases in subclinical symptoms of mental illness, potentially due to an acute, transitory neuroimmune response. On a longer-term basis, however, effects may manifest as increased risk for disorders, potentially due to brain pathologies caused by chronic, elevated immune responses. This diversity in the apparent impacts of $PM_{2.5}$ exposure underscores the importance of longitudinal, multimodal datasets measuring a breadth of phenotypes to investigate the full scope of $PM_{2.5}$'s impact on youth mental health, such as the ABCD Study. A critical future direction is understanding the relationship between more immediate and long-term effects of exposure, including the degree to which they may represent common or distinct mechanisms of pathology. As additional time points of ABCD study data become available, we plan to extend this program of research to investigate additional years of internalizing and externalizing symptoms, as well as additional longitudinal outcomes, including the trajectory of brain development and cognition.

Sex Differences in Association between $PM_{2.5}$ Exposure and Externalizing Symptoms

Despite substantial differences in the trajectories of internalizing and externalizing symptoms between female and male youth, there was little evidence of sex differences in the associations of $PM_{2.5}$ exposure with these trajectories, with one exception: Females and males marginally differed in the annual average–externalizing intercept association, with higher annual average of $PM_{2.5}$ associated with higher initial levels of externalizing in females only. This finding adds to a growing body of evidence suggesting sex differences

in the impacts of air pollution on health more broadly.[73–76] One compelling mechanism potentially driving sex differences in the psychiatric impacts of $PM_{2.5}$ exposure are sex differences in immune function and inflammatory responses,[77–78] both of which are influenced by sex hormones central to puberty and thus youth development.[79–80] Immunocompetent cell function and inflammatory signals have been shown to regulate brain development and health in a partially sex-specific fashion, ultimately contributing to sexual dimorphisms in the brain and subsequent behavior.[78] Yet these same cells and signals are considered central to the deleterious neural impacts of $PM_{2.5}$, with chronic exposure leading to increased immune cell functioning and inflammatory signaling which themselves can cause neuronal damage and death.[81,82] As such, if immune cells and inflammatory signals contribute to brain development in a sex-specific fashion, are modulated by sex hormones that abound during puberty, and are affected by air pollution exposure, then the neuropsychiatric impacts of air pollution exposure during and around puberty should at least partially differ between the sexes as well. The current findings broadly align with this framework, demonstrating associations between exposure and internalizing symptoms that are consistent across the sexes, but these findings also demonstrate that associations between exposure and externalizing symptoms that are sex-specific occur only in female youth.

Limitations

This study is not without limitations. First, the lack of longitudinal $PM_{2.5}$ data limited our ability to determine whether the effects of $PM_{2.5}$ exposure at baseline were indeed specific to exposure at baseline. For instance, if there is a positive relation between $PM_{2.5}$ exposure at earlier points in development, $PM_{2.5}$ levels at baseline may be serving as a proxy for exposure during these earlier developmental stages. However, future ABCD study data releases will include estimates of $PM_{2.5}$ exposure across the entirety of participants' lives, providing an opportunity to directly address this issue. Second, there is a wide range of potential confounders of the association between $PM_{2.5}$ and behavior that were not accounted for in the current analysis. Although the authors controlled for neighborhood socioeconomic deprivation, this approach did not address all potential confounders such as additional air pollutants, noise pollution, access to green space, crime, structural racism, and more. As such, follow-up work is needed to disentangle effects of $PM_{2.5}$ from other confounding environmental variables, including understanding how multiple environmental variables may interact to compound impacts of $PM_{2.5}$ exposure on mental health. For instance, Karamanos et al. found moderating effects of ethnicity and racism on associations between exposure and symptoms, with larger associations in specific ethnic groups when compared with others. A third limitation is the reliance on parental report measures of internalizing and externalizing symptoms. Although it is standard practice to use parent reports on youth mental health symptoms, there are several potential pitfalls to this approach, including difficulties in parents' ability to recognize certain symptoms in youth,[83] as well as the potential for parent's psychopathology to distort how they perceive and ultimately report their child's internalizing and externalizing symptoms.[84] We addressed the latter concern through post hoc analyses that included informant total mental health problems as a covariate. However, we acknowledge that additional research is needed to understand how effects of exposure on internalizing and externalizing symptoms may differ according to whether symptoms are measured through parent or self-report, and whether there are unique effects of exposure depending on whether exposure occurs during youth or in adulthood. Fourth, though relatively high resolution for an area the size of the United States, the spatial resolution of the $PM_{2.5}$ estimates are not ideal for estimating precise levels of exposure, particularly in urban areas where there can be large differences in actual exposure over relatively short distances. In addition, the use of only residential home addresses does not account for the fact that many of the participants likely spent a significant amount of time during the measured exposure period at some other location or moved during the exposure period. As such, the degree to which the estimated exposures in the current report reflect actual exposure is unclear, but this is a common limitation of research into environmental exposures more broadly. Fifth, due to limitations in the curated ABCD dataset, we were unable to evaluate alternative thresholds besides 35 $\mu g/m^3$. Critically, future sensitivity analyses are needed to determine the degree to which lower thresholds may also be associated with alterations in internalizing and externalizing symptom trajectories. Finally, when comparing participants who were excluded from all analyses due to missing or incomplete $PM_{2.5}$ exposure data, we found evidence of selection that may limit the generalizability of the current findings. Specifically, excluded participants showed a higher degree of ADI and higher levels of $PM_{2.5}$ exposure, variables which have been previously linked to higher levels of psychopathology,[15,85] and we believe that this selection may weakly bias our findings by reducing the estimated associations between exposure and internalizing and externalizing trajectories.

Conclusions

The current study concluded that the number of days of $PM_{2.5}$ exposure above US EPA standards during late childhood was associated with higher concurrent levels of internalizing symptoms across females and males, even after considering effects of other temporal patterns of exposure. Notably, this association remained when accounting for parental psychopathology, suggesting $PM_{2.5}$ exposure may have specific impacts on youth distinct from impacts on their parents. Finally, results suggested a weak but notable sex difference in the association between $PM_{2.5}$ exposure and externalizing symptoms. These findings underscore the importance of considering environmental pollutants as a potential causal mechanism increasing risk for psychopathology across the lifespan, while demonstrating the utility of both dimensional models of psychopathology and alternative measures of air pollution exposure in comparison with traditional temporal average measures.

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