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Association of lead-exposure risk and family income with childhood brain outcomes

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Socioeconomic factors influence brain development and structure, but most studies have overlooked neurotoxic insults that impair development, such as lead exposure. Childhood lead exposure affects cognitive development at the lowest measurable concentrations, but little is known about its impact on brain development during childhood. We examined cross-sectional associations among brain structure, cognition, geocoded measures of the risk of lead exposure and sociodemographic characteristics in 9,712 9- and 10-year-old children. Here we show stronger negative associations of living in high-lead-risk census tracts in children from lower- versus higher-income families. With increasing risk of exposure, children from lower-income families exhibited lower cognitive test scores, smaller cortical volume and smaller cortical surface area. Reducing environmental insults associated with lead-exposure risk might confer greater benefit to children experiencing more environmental adversity, and further understanding of the factors associated with high lead-exposure risk will be critical for improving such outcomes in children.

Childhood lead exposure is associated with lower cognitive functioning and socioeconomic status. Eleven-year-old children with elevated blood lead levels show reductions in their own social standing 27 yr later relative to their parents' standing.[1] Higher concentrations of lead in blood, bone or deciduous teeth have been linked to decrements in intellectual functioning (even at very low levels)[2–6], juvenile delinquency and criminal activity[7,8], and the pathogenesis of neuropsychiatric disorders[9–12]. In 2012, the National Toxicology Program concluded that blood lead concentrations below 5 μg dl^{-1} were associated with diminished intelligence quotient (IQ) and academic performance, attentional problems and problem behaviors[13].

Socioeconomic status (for example, family income) also influences brain development and cognitive functioning[14]. Past research has suggested that total brain volume is positively associated with intelligence[15], and children from high-income families have significantly larger volumes of gray matter than children from low-income families[16]. Small increases in family income lead to proportionally larger increases in cortical surface area in children from the poorest families than in children from higher-income families[17]. Further, the association between family income and neurocognitive and academic ability is mediated by brain structure[17,18]. However, these previous studies have not accounted for lead exposure, which is often elevated in children in lower-income households[4,19]. Importantly, animal studies have shown that postweaning exposure to enriched environments can alleviate the negative effects of preweaning[20] and postweaning lead exposure[21] in rats housed in isolated and deprived environments. Thus, the neurotoxic effects of lead exposure may be exacerbated in low-income children, who may have less access to environmental enrichment[22,23].

Early childhood lead exposure has been linked to reduced frontal-lobe gray-matter volume in young men[24,25] and disrupted white-matter connectivity in young men and women[26], but blood lead concentrations were much higher in those studies than would be observed in contemporary children[24–26]. Given that these studies analyzed lead exposure during childhood but brain structure during adulthood, little is known about how lead exposure impacts brain structure in today's developing children and adolescents. The present study sought to quantify the relationship between geocoded lead-exposure risk and family income on brain structure and cognitive function in children in the Adolescent Brain Cognitive Development (ABCD) Study. We hypothesized that higher risk of lead exposure[27,28] and lower family income would be negatively associated with brain structure and cognitive function and that these associations would be greater in children from low-income families.

Results

The ABCD cohort and lead-exposure risk. The ABCD Study is an ongoing, large-scale, 10-yr longitudinal study involving 21 data collection sites across the United States[29]. The data from the ABCD Study are annually made public via the National Institute of Mental Health (NIMH) Data Archive[30]. Of the 11,875 children with baseline data, there were complete data for the variables of interest (Supplementary Table 1) for 9,712 children (Table 1). Endogenous lead exposure levels have not yet been measured in the ABCD participants, so we instead used geocoded lead-risk scores for each ABCD participant's census tract[27,28]. These risk estimates, computed by the Washington State Department of Health for 72,305 census tracts in the United States, reflect deciles of a weighted sum of two derived census-tract values from the American Community Survey: the ages of homes and poverty rates, two well-established correlates of lead exposure[31,32] (Fig. 1a), with housing age being more strongly weighted (0.58) than poverty rates (0.42) in these lead-risk estimates. While 40.8% of ABCD children are at a low risk for lead exposure (lead risk ≤ 3; $n = 3{,}967$), 31.8% of the children are living in intermediate-risk tracts (4 ≤ lead risk ≤ 7; $n = 3{,}088$) and 27.4% are living in high-risk tracts (lead risk ≥ 8; $n = 2{,}657$) (Table 1 and Fig. 1c). Across 13 states and two cities (Supplementary Table 2), elevated-blood-lead-level rates were significantly associated with higher lead risk (un-standardized regression coefficient (b) = 0.32, $F(1, 3{,}886{,}935) = 39.52$, $P < 0.001$), indicating that lead risk serves as a valid proxy for endogenous lead exposure (Fig. 1b and Extended Data Fig. 1)[33].

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Lead risk, cognition and brain structure. Cognition was operationalized by the total composite uncorrected standard score from the National Institutes of Health (NIH) Toolbox[34]. Cognitive test scores were significantly greater at higher income levels ($F(2, 9{,}699) = 49.62$, $P < 0.001$), and significantly lower with higher lead-risk levels ($F(1, 9{,}699) = 4.70$, $P = 0.030$) (Fig. 2, Extended Data Fig. 2 and Supplementary Table 3), and there was a significant family income × lead risk interaction ($F(2, 9{,}699) = 7.34$, $P = 0.001$). Specifically, the negative association between lead risk and cognitive test scores was significant in the low-income group ($P < 0.001$), but not in the mid- or high-income groups ($P \geq 0.127$). Further, while mean (95% confidence interval) cognitive test scores of the low-income group were 9.0% (8.6%, 9.5%) lower than those of the high-income group, the low-income group living in areas with the highest lead-risk scores (lead risk = 10) exhibited an additional 3.1% (2.2%, 4.0%) reduction in cognitive testing performance.

Measures of cortical thickness, cortical surface area and cortical volume were obtained using FreeSurfer v.5.3.0 on acquired T_1-weighted magnetic resonance imaging volumes from ABCD participants[35]. There were no main effects of lead risk on cortical thickness, surface area or volume ($P \geq 0.699$) (Supplementary Tables 4–6), but there were main effects of income (thickness: $F(2, 9{,}699) = 3.07$, $P = 0.047$; surface area: $F(2, 9{,}699) = 11.00$, $P < 0.001$; volume: $F(2, 9{,}699) = 16.50$, $P < 0.001$). As predicted, there were significant family income × lead risk interactions (Fig. 3 and Extended Data Figs. 3 and 4). Associations between brain structure and lead risk differed as a function of family income for cortical surface area ($F(2, 9{,}699) = 3.95$, $P = 0.019$) and cortical volume ($F(2, 9{,}699) = 3.03$, $P = 0.048$), but not cortical thickness ($F(2, 9{,}699) = 1.46$, $P = 0.232$). For cortical surface area, the lead-risk slope was significantly less than 0 for the low-income group ($P = 0.033$), but not for the mid- and high-income groups ($P \geq 0.101$). Mean cortical surface area of the low-income group was 4.5% (4.1%, 5.0%) lower than that of the high-income group, but the children in the low-income group living in the highest lead-risk tracts exhibited an additional 2.1% (1.3%, 2.9%) reduction in cortical surface area relative to the low-income group mean.

For cortical volume, the lead-risk slopes did not significantly differ from 0 for any of the groups (low-income: $P = 0.060$; mid-income: $P = 0.255$; high-income: $P = 0.369$), but the negative slope for the low-income group was significantly different from those of the mid- and high-income groups ($P \leq 0.039$); the mid- and high-income groups did not differ from each other ($P = 0.770$). While the children across the low-income group exhibited a 5.6% (5.2%, 6.1%) reduction in cortical volume compared with those of the high-income group, the mean cortical volume of the children living in the highest lead-risk tracts was 9.6% (8.1%, 11.1%) smaller in the low-income group than in the high-income group. Vertex maps, in which the means of participants living in high-lead-risk census tracts (lead risk ≥ 8) were subtracted from the means of those living in low-lead-risk census tracts (lead risk ≤ 3), demonstrated global decreases in cortical surface area and volume across the entire cortex in participants in the low-income group relative to those in the high-income group (Fig. 3c,d).

Cortical volume–cognition associations. To provide a conceptual overview of the patterns in the data as well as context for the meaningfulness of individual differences in brain structure (that is, how they relate to cognitive test scores), we conducted a set of post hoc analyses to determine the relationships between cognition and brain structure[17] and how they were associated with lead risk and family income. Bivariate correlational analyses indicated that all cortical measures were significantly and positively related to cognitive test scores ($P < 0.001$). While cortical surface area and volume were positively correlated (Pearson's correlation coefficient $(r) = 0.87$), cortical volume accounted for the most variance in cognitive test scores (thickness: coefficient of determination $(R^2) = 0.003$; surface area: $R^2 = 0.036$; volume: $R^2 = 0.042$), so it was used here as the primary structural predictor of cognition.

Table 1 | Demographics of the ABCD cohort

	Release 2.0 (*n* (%))	Sample with complete data used in this study (*n* (%))	ACS target (%)
Sex			
Male	6,188 (52.1)	5,106 (52.6)	N/A[a]
Female	5,681 (47.8)	4,606 (47.4)	N/A[a]
Missing/undefined	6 (0.1)	0 (0)	-
Income bracket			
<$50,000 (low)	3,222 (27.1)	2,825 (29.1)	39
$50,000–100,000 (mid)	3,070 (25.9)	2,783 (28.7)	30
>$100,000 (high)	4,565 (38.4)	4,104 (42.3)	31
Missing/Undefined	1,018 (8.6)	0 (0)	-
Lead risk			
Low (1–3)	4,373 (36.8)	3,967 (40.8)	N/A
Intermediate (4–7)	3,544 (29.8)	3,088 (31.8)	N/A
High (8–10)	3,258 (27.4)	2,657 (27.4)	N/A
Missing/undefined	700 (5.9)	0 (0)	-
Race/ethnicity			
Asian	252 (2.1)	188 (1.9)	5
Black	1,779 (15.0)	1,279 (13.2)	17
Hispanic	2,407 (20.3)	1,881 (19.4)	23
Other	1,245 (10.5)	1,012 (10.4)	5
White	6,174 (52.0)	5352 (55.1)	49
Missing/undefined	18 (0.2)	0 (0)	-
Total	11,875	9,712	100

Lead risk was categorized as being low (lead risk ≤ 3), intermediate (4 ≤ lead risk ≤ 7) or high (lead risk ≥ 8) (Fig. 1). The targeted percentages at each level of the demographics were based on the American Community Survey (ACS). N/A, not applicable. [a]While there were no explicit targets for sex, it was generally assumed that the ABCD sample would be split evenly between sexes. Recruitment was consistently monitored for any critical deviations from this assumption.

The subgroups of interest were children from low- and high-income families living in low- and high-lead-risk census tracts (Table 1 and Fig. 3c,d). For each subgroup, we regressed cognitive test scores on cortical volume via simple linear regression. For groups experiencing at least one environmental insult (that is, high lead risk and/or low income), there were significant positive relationships between cognitive test performance and cortical volume (low income, high risk: standardized regression coefficient $(\beta) = 1.55$, $P < 0.001$; low income, low risk: $\beta = 1.47$, $P < 0.001$; high income, high risk: $\beta = 0.91$, $P = 0.003$). This was not true for the high-income, low-risk group ($\beta = 0.06$, $P = 0.731$). Thus, these positive associations decreased in strength with decreasing levels of environmental adversity (that is, higher incomes and/or lower lead risk) (Fig. 4).

Area deprivation, cognition and brain structure. To evaluate whether lead risk was associated with brain and cognitive outcomes using a more comprehensive measure of socioeconomic status, we conducted secondary analyses using the area deprivation index (ADI) instead of income[36]. The use of ADI in place of family income worsened the fit of the model of cognitive function (ΔAkaike information criterion $(AIC)_{Income\text{-}ADI} = -51.8$; Supplementary Table 7).

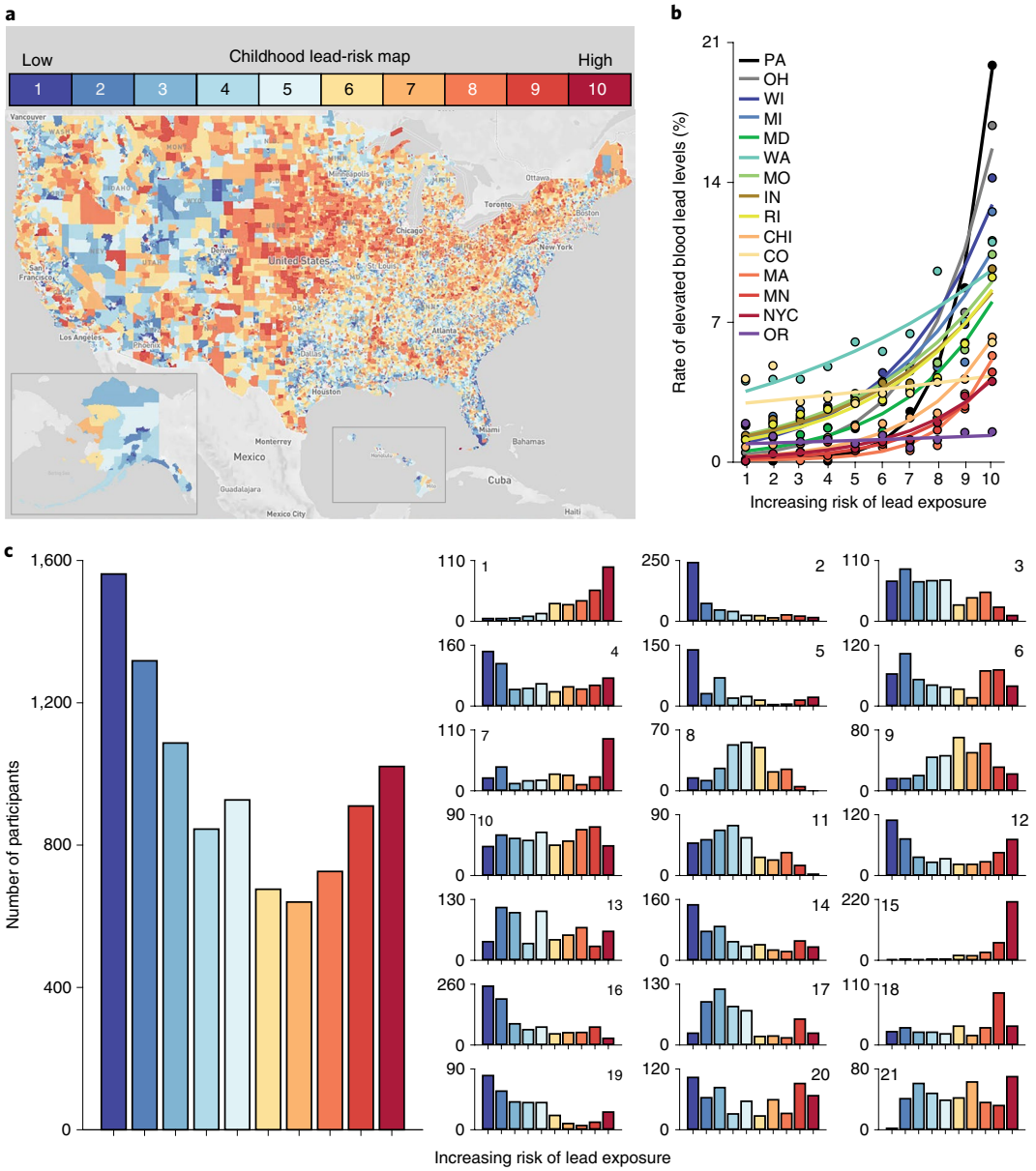

Fig. 1 | Lead-exposure risk scores predict elevated-blood-lead-level rates at the census tract level. a, The estimated risk of lead exposure by US census tract. Lower values reflect lesser risk. Map adapted with permission from ref. [27]. **b**, Rates of elevated blood lead levels globally increased with estimates of lead risk across 13 states and two cities. Analysis employed generalized linear mixed-effects models, which tested the statistical significance of coefficients against a *t*-distribution. **c**, Number of children in the ABCD cohort by lead-risk score. Geocoded data were based on current primary residential addresses provided by participants' caregivers. The smaller subpanels represent individual ABCD Study data-collection sites. Per the terms of the data release, sites are arbitrarily numbered. Site number is shown in the upper right or left of each subpanel. Alphabetically, the ABCD Study data-collection-site cities are Ann Arbor, Michigan; Baltimore, Maryland; Boulder, Colorado; Burlington, Vermont; Charleston, South Carolina; Gainesville, Florida; Los Angeles, California; Menlo Park, California; Miami, Florida; Milwaukee, Wisconsin; Minneapolis, Minnesota; New Haven, Connecticut; Pittsburgh, Pennsylvania; Portland, Oregon; Richmond, Virginia; Rochester, New York; Salt Lake City, Utah; San Diego, California; St. Louis, Missouri; and Tulsa, Oklahoma. ABCD Study data-collection sites are present in 8 of the 13 states including in the analysis in **b**. CHI, Chicago; CO, Colorado; IN, Indiana; MA, Massachusetts; MD, Maryland; MI, Michigan; MN, Minnesota; MO, Missouri; NYC, New York City; OH, Ohio; OR, Oregon; PA, Pennsylvania; RI, Rhode Island; WA, Washington; WI, Wisconsin.

The ADI×lead risk interaction was significant but more moderate compared with the family-income analyses ($F(2, 9{,}699) = 3.29$, $P = 0.037$). However, similar to family income, higher cognitive test scores were significantly associated with lower ADI scores (that is, less disadvantage) ($F(2, 9699) = 25.68$, $P < 0.001$).

Similarly, the ADI models of brain structure fit the data somewhat worse than the family-income models ($\Delta AIC_{Income\text{-}ADI} \leq -6.2$; Supplementary Tables 8–10). ADI had a main effect on cortical surface area and cortical volume (thickness: $F(2, 9{,}699) = 0.92$, $P = 0.398$; surface area: $F(2, 9{,}699) = 5.57$, $P = 0.004$; volume: $F(2, 9{,}699) = 7.24$, $P = 0.001$), but there were no main effects of lead risk ($P \geq 0.344$) or significant ADI×lead risk interactions ($P \geq 0.321$).

Discussion

Socioeconomic factors (for example, family income, poverty) have a considerable influence on child development and brain

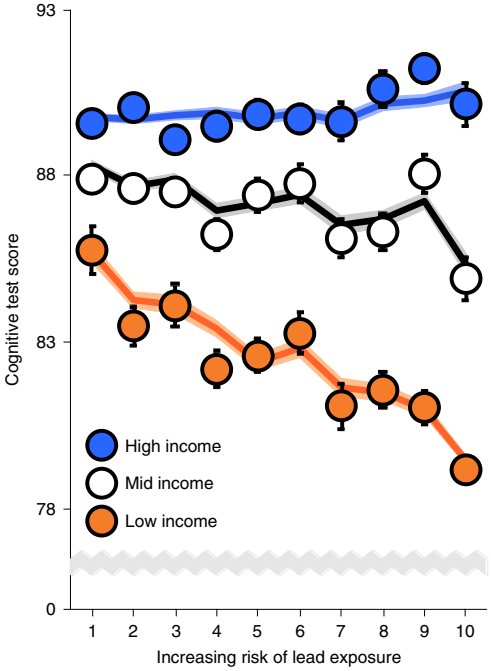

Fig. 2 | Risk of lead exposure and cognition. Overall cognitive function declined most steeply with increasing risk of environmental lead exposure in children of low-income parents. Error bars represent ±1 between-subjects standard error of the observed means. The solid lines represent means of the marginal fitted values of the model; the shaded areas surrounding the solid lines represent ±1 between-subjects standard error of those means. Analysis employed linear mixed-effects models, which tested the statistical significance of coefficients against a *t*-distribution. Age, sex, parental education and race/ethnicity were included as covariates in this analysis.

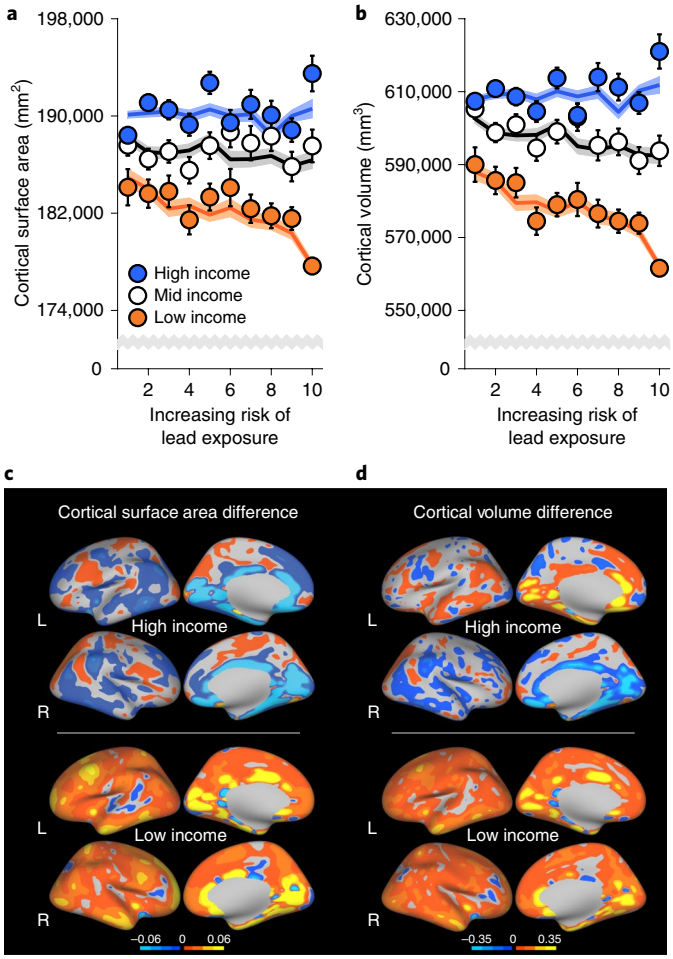

Fig. 3 | Negative associations of increased risk of lead exposure are greater for children from lower-income families. a,**b**, Whole-brain cortical surface area (**a**) and cortical volume (**b**) declined most steeply with increasing risk of lead exposure in children of low-income parents. Error bars represent ±1 between-subjects standard error of the observed means. The solid lines represent means of the marginal fitted values of the model; the shaded areas surrounding the solid lines represent ±1 between-subjects standard error of those means. Analysis employed linear mixed-effects models, which tested the statistical significance of coefficients against a *t*-distribution. Age, sex, parental education and race/ethnicity were included as covariates in this analysis. **c**,**d**, Regional cortical vertex maps of differences in cortical surface area (**c**) and cortical volume (**d**) for the high- and low-income groups. For each vertex, the means of participants living in high-lead-risk census tracts (lead risk ≥ 8) in each income group were subtracted from the means of those living in low-lead-risk census tracts (lead risk ≤ 3) in that same income group. Warmer colors (yellow, orange) represent greater negative differences in participants living in high- versus low-lead-risk tracts. L, left hemisphere; R, right hemisphere.

structure[37], but many studies have overlooked neurotoxic insults that impair neurocognitive development, such as lead exposure[2,38]. It is important to note that causality cannot be inferred because of the cross-sectional, observational nature of the ABCD Study's baseline data and because we do not currently have direct data on participants' lead exposure levels. However, our results suggest that US children from low-income families might be more vulnerable to environmental insults associated with high risks of lead exposure. The negative association between lead risk and cognitive test performance was stronger in the low-income group and not statistically significant in the middle- or high-income groups. Such effects of income disparity were also evident in brain structure. The stronger associations between cognition and cortical volume in children from low-income families living in high-lead-risk tracts suggest that reductions in environmental insults associated with lead-exposure risk might more greatly benefit children experiencing higher overall environmental adversity. This finding is consistent with the steep decrements in IQ scores observed among children at blood lead concentrations below 5 μg dl^{-1} (refs. [3,38]). While neighborhood poverty has also been shown to influence a variety of outcomes in children[39,40], as it did here in the context of ADI, neighborhood poverty is an independent construct compared with family poverty[39]. Here, neighborhood poverty was operationalized by census-tract-level ADI, while family poverty was operationalized by parent-report household/family income. That the family-income models provided better fits to the data than the ADI models further reflects the intricate yet complex interactions between the socioeconomic standing of a child's family and of the neighborhood in which the family resides.

Our results suggest that children from high-income families may be relatively protected from lead-associated brain and cognitive deficits. At the highest risk level (lead risk = 10), the children from low-income families exhibited 12.2% lower total cognitive test scores, 9.6% smaller cortical volumes and 8.2% smaller cortical surface areas than the children from high-income families also living in highest-risk areas. The magnitudes of these decrements between the low- and high-income groups were consistently reduced at the lowest risk level (lead risk = 1; cognitive test scores: 4.2%; cortical volume: 2.9%; cortical surface area: 2.3%). Comparably, though not controlling for lead risk, children of families who make less than $25,000 per year have

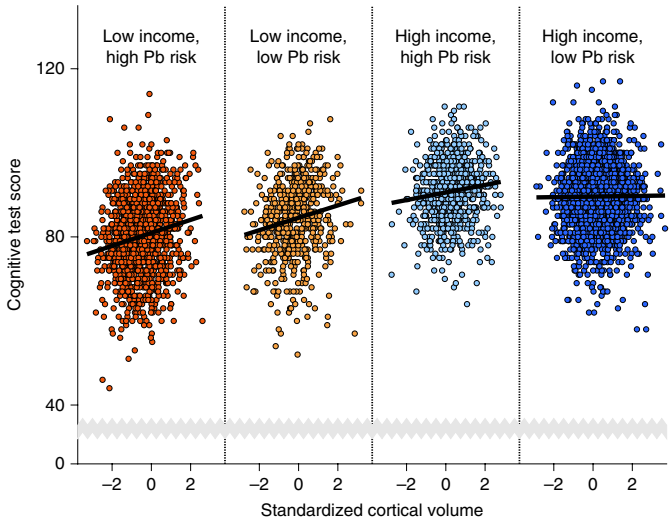

Fig. 4 | Cortical volume–cognition associations are strongest in the most-at-risk children. Cognitive test scores increased most steeply with increases in cortical volume in children from lower-income families living in census tracts with greater risks of lead (Pb) exposure. Each data point is an individual participant. The individual panels, delineated by vertical dotted lines, incorporate identical abscissa scales and are ordered left to right with respect to the strength of the standardized regression coefficient of cortical volume. Cortical volume was standardized to ease interpretation. Analysis employed simple linear regression, which tested the statistical significance of coefficients against an *F*-distribution.

been reported to exhibit cortical surface areas that are approximately 6% smaller than children of families who make at least $150,000 per year[17]. Overall, our results are also consistent with studies showing that the negative effects of preweaning[20] and postweaning lead exposure[21] observed in rats housed in isolated and deprived environments are alleviated by postweaning exposure to enriched environments. Thus, environmental enrichment and stimulation[41] may serve as potential mechanisms to ameliorate the negative effects of environmental insults associated with risk of lead exposure.

We have earlier reported a nonlinear, decelerating relationship between higher family income and larger cortical surface area[17]. The data presented here similarly convey patterns of deceleration, in that the strength of the associations between lead risk and either cognition or brain structure decreased in the children from higher-income families. While differences in cortical volume were not meaningfully associated with cognitive performance in high-income/low-risk children, a 1-s.d. increase in cortical volume in low-income/high-risk children (that is, ~9.6% increase in cortical volume) was associated with a 1.55-unit increase in cognitive performance in these children. Overall, the relationships between cortical volume and cognitive test scores were stronger in children exposed to more potential environmental insults (low income and/or high lead risk), in that the meaningfulness of how children's cortical volume relates to cognition may partially depend on environmental factors. Actions taken to reduce environmental insults associated with risk of lead exposure could potentially confer greater benefits on brain and cognition in children from low-income families than in those from high-income families.

While there were significant family income × lead risk interactions on cognitive function, cortical surface area and cortical volume, there was only evidence for an ADI × lead risk interaction on cognition. These discrepancies may reflect socioeconomic influences specific to each family rather than their home census tract, such as the relative affordability of lead remediation within a family's own home. Alternatively, ADI may capture more of the risk for childhood lead exposure than parent-report family income (Extended Data Figs. 5 and 6). However, unlike ADI, the lead-risk metric incorporates a strong predictor of lead exposure in age of housing. Lead-based paint in older housing units may continue to pollute the home environment[31], and wealthier families may have greater financial resources to maintain or remediate their homes. Future research should delineate the strength of different environmental predictors on different public health issues.

Overall, our results corroborate the unfortunate circumstances facing American children: low-income groups have more negative outcomes associated with lead exposure[42]. Relatedly, previous research has shown that children exposed to lead and whose parents had less than a high-school education showed significantly lower reading scores relative to children who met one or neither of those criteria[43]. Childhood blood lead concentrations are higher in low-income than high-income populations[4,19]. Because lead-based paint was banned in 1978, children who live in older, poorly maintained housing units are at an increased risk for lead exposure from lead-based paint[31,42,44]. Low-income populations are more likely to occupy older homes that contain lead hazards[31] and may be disproportionately more affected by lead exposure[22,23]. Efforts to reduce the risk of lead exposure and improve a child's living environment may ultimately improve cognitive and brain development.

While census-tract-level lead-risk scores predicted blood lead concentrations in children included in public databases from the same census tracts and were associated with brain and cognitive outcomes in the ABCD cohort, lead-risk scores are not an internal dosimeter of body lead burden. All children in high-risk tracts do not necessarily have an elevated blood lead level, but some children in low-risk tracts might. The nonsignificant associations of lead risk with brain structure and cognition among children in high-income families may indicate that some of these children have lower blood lead levels or, alternatively, were exposed to fewer lead hazards, as older housing units that are well maintained have fewer lead hazards than poorly maintained units.

In December of 2018, a US federal action plan was released to identify and aid communities at risk for lead exposure[45]. This goal is achievable by knowing lead exposure in all US children (that is, which regions to target), but only some states require universal children's screening[46]. While a reasonable alternative for pinpointing the 'hot zones' of lead exposure is to use archival environmental data associated with elevated exposure[32], such identification of high-risk areas is only beneficial if risk scores map onto actual blood-lead-level rates. In conjunction with a recent report on Minnesota blood-lead-level data[33], we show that the described model of lead-exposure risk[27,28] serves as a reasonable proxy for actual census-tract-level exposure rates in 14 additional states and cities (also see Extended Data Fig. 7), corroborating a rich literature on the applicability of community-level data to develop lead-exposure detection, mitigation and prevention strategies[32,47,48]. Unfortunately, while census tract and census block are more optimal spatial resolutions for geocoded health data[49], government agencies tend to only report such data, at best, for individual zip codes, and zip-code-level geocoding of blood-lead data almost resulted in officials 'missing' the Flint water crisis[50]. Thus, publicly available lead-risk maps with high spatial resolution fill a void in research practice and policy implementation, as they may be used to sensibly gauge lead exposure levels, identify at-risk regions and evaluate environmental influences on health-related outcomes in epidemiological and nonepidemiological research projects.

Lead-risk scores used here were primarily a function of housing age (weight = 58%), but it is possible that these factors may have differential strengths of prediction depending on region[33,51] (for example, very few homes in Alaska were built before the lead-paint ban in 1978 (ref. [52])). Whereas the contribution of housing age to the lead-risk score was primarily driven by age of homes given the lead-paint

ban[27,31], older homes may also be less likely to have lead-free plumbing[53]. With continued research, census-tract-level lead-risk scores could be adjusted to account for unique or multiplicative effects of housing age given the potential for drinking-water lead exposure.

While poverty rates accounted for 42% of the lead-risk score, some correlates of poverty (for example, lower parental education, less enrichment, malnutrition, subcomponents of ADI) may more strongly contribute than others to the associations between lead exposure/risk and neurocognitive development, or they may be more directly associated with neurocognitive development. Similarly, the Home Observation for Measurement of the Environment (HOME) inventory (an assessment of the emotional, social and cognitive qualities of a child's home environment[54]) may also have accounted for key variance in the data, as it has in other lead studies[38], but this metric was not measured in the ABCD cohort. The lead-risk and ADI metrics are functions of 2 and 17 individual census-tract-level predictors, respectively, and, even though over 85% of the variance in lead-risk scores cannot be accounted for by ADI (Extended Data Figs. 5 and 6), each of these individual predictors may also be capturing residual variance of the other predictors. To elucidate how brain and cognitive development are generally associated with neurotoxicant vulnerability (that is, lead risk) and neighborhood poverty (ADI), as well as family poverty (household income), our analyses included the two composite indices. Given that (1) family-level poverty and neighborhood-level poverty can have distinct effects on developmental outcomes[39], (2) children from both high- and low-income families live in low- and high-risk tracts (Fig. 4) and (3) the effects of lead persist after adjustment for multiple covariates[5,8,25,38], it will be critical to continue to evaluate how poverty and poverty-related factors (for example, heightened risk of lead exposure) collectively influence brain and cognitive development in children. Obtaining measures of lead exposure in the ABCD cohort will also provide key information with respect to how lead exposure influences child development (for example, whether higher incomes reduce the risk of lead exposure or are protective against the actual effects of bodily lead levels).

In the current report, each participant's lead-risk score was based on their primary residential address at study entry (that is, when children were 9–10 yr old). Blood lead levels tend to peak when children are 2–3 yr old[3], but it has been reported that IQ in older children is better predicted by concurrent than past blood lead levels[38,55]. Indeed, even at very low levels of exposure, IQ is associated with concurrent blood lead levels in school-aged children[56,57]. While the age at which children are most vulnerable to lead toxicity remains uncertain, evidence has suggested that school-age lead exposure may be more predictive of developmental outcomes than early childhood exposure[58]. Full address histories of the ABCD participants, which are actively being collected from the participants' parents, would further elucidate these questions.

Conclusions and future directions. Childhood lead exposure is a reflection of community predictors, such as poverty rates and age of housing[32]. However, the evidence presented here should not be taken to imply that a child's socioeconomic circumstances or lead-risk status create an immutable trajectory of brain and cognitive development. We do not yet know actual body burdens of lead exposure in the ABCD cohort, yet we found that children from higher-income families in high-risk geographical locations exhibit fewer negative brain and cognitive outcomes compared with the children from lower-income families. The ABCD consortium is exploring ways to enhance the measure of the body burden of lead in the cohort using past medical records, shed deciduous teeth[59] and blood. The open-data framework of the ABCD Study will allow researchers to disentangle the effects of family poverty, neighborhood poverty and lead exposure on the dynamics of brain, cognitive and behavioral development during childhood and adolescence.

Online content

Any methods, additional references, Nature Research reporting summaries, source data, extended data, supplementary information, acknowledgements, peer review information; details of author contributions and competing interests; and statements of data and code availability are available at https://doi.org/10.1038/s41591-019-0713-y.

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Methods

Participants. The ABCD Study is a large-scale, 10-yr longitudinal study involving 21 data collection sites across the United States[29]. Using school-based enrollment[60], the consortium successfully recruited and enrolled over 11,800 9- and 10-year-old children. The demographics of the ABCD cohort (Table 1) correspond well with the American Community Survey[61]. Our data came from the most recent April of 2019 ABCD 2.0 data release[30], which included baseline data for 11,875 children. For the variables of interest (Supplementary Table 1), there were complete data for 9,712 children. At present, there are no blood-lead data from the ABCD cohort.

Centralized institutional review board (IRB) approval was obtained from the University of California, San Diego IRB. Study sites obtained approval from their local IRBs. Written, informed consent was provided by each parent; each child provided written assent. All ethical regulations were complied with during data collection and analysis.

Lead exposure and elevated blood-lead-level data. We used a high-resolution nationwide map of lead-risk metrics to obtain a geocoded lead-risk score for each ABCD participant's census tract[27,28]. These risk estimates, generated by the Washington State Department of Health for 72,305 census tracts in the United States, reflect deciles of a weighted sum of two derived census-tract values from the American Community Survey: the ages of homes and poverty rates, two well-established correlates of lead exposure[31,32] (Fig. 1a). Housing age is more strongly weighted (0.58) than poverty rates (0.42) in the lead-risk estimates.

We used generalized mixed-effects models (binomial distribution, logit link) to determine how well the lead-risk scores[27] were associated with blood-lead-level data. Census-tract-level blood-lead data were available for 13 states and two cities (Supplementary Table 2). Publicly available blood-lead data are typically provided in terms of the number of individuals tested and the number of those individuals who showed elevated blood lead levels relative to some criterion (for example, 5 $\mu g\,dl^{-1}$). However, to minimize potential issues for dispersion given such count data, as well as to more effectively control for total children tested given the total number elevated, the count data (number tested, number elevated) for each tract were re-coded by test result: '0' (nonelevated) or '1' (elevated). The fixed-effects structure included an overall intercept (that is, global mean) and lead risk (centered, continuous). The random-effects structure included a random intercept and slope (as a function of lead risk) for each state/city; the by-state/city intercepts and slopes were restricted to be uncorrelated. Analyses were conducted in MATLAB v.9.6.0 (R2019a, Update 2; MathWorks) and MATLAB's Statistics and Machine Learning Toolbox v.11.5 (R2019a).

To further gauge the extent to which these lead-risk scores could predict lead exposure levels, we conducted a secondary supplemental analysis using average blood lead levels. Across the 13 states and two cities in our analysis (Supplementary Table 2), only the state of Maryland had data that incorporated actual blood lead levels at the census-tract level. Specifically, these data are published online in terms of the geometric mean of blood lead levels. Geometric means of annual blood-lead-level data were collapsed across the years 2010–2014 (Supplementary Table 2), weighted in terms of the number of children screened in each of those years. Extended Data Fig. 7 (left) shows the frequency distribution of geometric mean blood lead levels across 992 Maryland census tracts that met the following criteria: (1) the census tract had at least 1 yr of data that included both the number screened and the geometric mean blood lead level, and (2) the census tract data available from the Maryland Environmental Public Health Tracking portal were able to be merged with the lead-risk data. Extended Data Fig. 7 (right) shows the geometric mean blood lead levels for each of the 992 census tracts as a function of the census tract's estimated lead-risk score. As seen in the right panel of Extended Data Fig. 7, there was generally a positive association between lead risk and the geometric mean of blood lead levels across census tracts. Due to the positive skewness of the data and the presence of a finite lower asymptote to the data, a Spearman's rank-order correlation was performed. The analysis revealed a significant positive correlation between census tracts' lead-risk scores and geometric means of blood lead levels (Spearman's correlation coefficient (ρ) = 0.46, $P < 0.001$), further supporting the validity of the lead-risk scores as a proxy for actual lead exposure.

ABCD data. From the baseline ABCD data, we analyzed the composite uncorrected standard score within the NIH Toolbox[34] and structural brain measures (whole-brain cortical thickness, surface area and volume)[62]. Data collection procedures are described in detail elsewhere[34,62,63]. Briefly, we used NIH Toolbox measures in the ABCD Study because they harmonize data collection elements across NIH-funded projects, thereby facilitating cross-study comparisons. They have been normed for samples between the ages of 3 and 85 and comprise a standardized battery of cognitive tests administered using tablet devices that are comparable with other standardized tests of cognitive function, attesting to their validity in estimating general intellectual functioning[64]. The composite uncorrected standard score, which is automatically calculated within the NIH Toolbox, incorporates performance from seven different tests, which show good convergent validity compared with established gold standards of cognitive testing[65]: (1) the picture vocabulary test (Ages 3+, Version 2.0; a measure of language), (2) the flanker inhibitory control and attention test (Ages 8–11, Version 2.0; attention and executive function), (3) the list-sorting working memory test (Ages 7+, Version 2.0; working memory), (4) the dimensional change card sort test (Ages 8–11, Version 2.0; executive function), (5) the pattern comparison processing speed test (Ages 7+, Version 2.0; processing speed), (6) the picture sequence memory test (Ages 8+, Form A, Version 2.0; episodic memory) and (7) the oral reading recognition test (Ages 3+, Version 2.0; language). Because our analyses controlled for age, sex and race/ethnicity, which are accounted for within the age-corrected and fully corrected NIH Toolbox scores, we analyzed the uncorrected scores here.

Measures of cortical volume, cortical surface area and cortical thickness were obtained using FreeSurfer v.5.3.0 on acquired T_1-weighted magnetic resonance imaging volumes from ABCD participants[35]. ABCD data are publicly available through the NIMH Data Archive (https://data-archive.nimh.nih.gov/abcd).

Statistical analyses. We used general linear mixed-effects models to determine the relationships among lead risk, family income, brain structure and cognition and how well lead risk specifically accounted for these relationships given a second environmental-risk measure, the ADI[36]. Analyses included the 9,712 children who had complete data for the variables of interest (Supplementary Table 1). A participant's data were excluded if the primary residential address was not valid and/or was not able to be geocoded into a 1–10 lead-risk score, if a valid household/family income was not provided (answering 'Don't know' or 'Refuse to answer') or if there were missing data for sex, age, parental education, race/ethnicity, ADI, the composite uncorrected score from the NIH Toolbox or structural imaging measures (see Supplementary Table 1).

Our first set of analyses determined the extent to which family income moderated the relationship between lead risk and both cognition and brain structure. As described above, the dependent variables for these analyses were the compositive uncorrected standard score from the NIH Toolbox, mean whole-brain cortical thickness, total whole-brain cortical surface area and total whole-brain cortical volume. Given previous neuroimaging and cognitive research within the Pediatric Imaging, Neurocognition, and Genetics Study[17,66], we controlled for the following variables: age, sex, parental education, family income and race/ethnicity. Lead risk and age (in months) were centered, continuous factors. Parental education was also a centered, continuous factor, operationally defined as the maximum educational level achieved by a parent or caregiver, with seven levels (1, 6th grade or less; 2, 7th–9th grade; 3, 10th–12th grade, no diploma; 4, high-school graduate, general educational development exam (GED) or equivalent; 5, some college with no degree, Associate's degree; 6, bachelor's degree; 7, master's degree, professional degree or doctorate). Race/ethnicity was an effects-coded categorical factor with five levels: 'white', 'black', 'Hispanic', 'Asian' or 'other' (for example, Pacific Islander, multiracial). In conjunction with ABCD's NIMH-supported Data Exploration and Analysis Portal (deap.nimhda.org), family income was a categorical factor with three levels (effects-coded here), based on the parents' reported household income (low income: ≤$50,000; middle income: $50,000–100,000; high income: ≥$100,000). While lead risk was a function of a census tract's poverty rates and age of housing, family income was specific to each family (that is, from the parent's self-report).

To evaluate whether lead risk was associated with brain and cognitive outcomes using a more comprehensive measure of socioeconomic status, we conducted secondary analyses using ADI instead of income[36,67]. ADI was computed at the census-tract level in accordance with the coefficient values described by Kind et al.[36], re-coded in terms of national percentile (that is, higher values reflect greater disadvantage) and discretized into low- (ADI: 0–32), middle- (33–66) and high-ADI categories (67–100), comparable to the family-income analyses. The R code for computing the ADI and merging it into the ABCD dataset is located at the following website: https://github.com/ABCD-STUDY/geocoding/blob/master/Gen_data_proc.R. Unlike lead risk, ADI does not incorporate housing age. Additional analyses comparing lead risk and ADI are provided (see section 'Correlates of lead-exposure risk and ADI' below).

The random-effects structure in all analyses included a random intercept for study site and family identification number (that is, some ABCD participants were siblings). When relevant, significant interactions were probed using MATLAB's coefTest function. Complete model output and model-fit characteristics for each analysis are provided in Supplementary Tables 3–10. Statistical reporting in the main text is in the form of F tests computed using MATLAB's anova function, reflecting the combined statistical significance of all coefficients of the corresponding factor. When specified, model fits were compared using the AIC.

A series of post hoc analyses were also conducted to determine the associations between cognition and brain structure[17] and how these associations differed by lead risk and family income. First, we performed bivariate correlational analyses between the three whole-brain cortical measures (thickness, surface area, volume) and cognitive test scores. Because cortical volume accounted for the most variance in cognitive test scores across the three whole-brain measures, we then regressed cognitive test scores on cortical volume (standardized across the entire sample of participants) via simple linear regression for four subgroups (that is, children from low- and high-income families living in low- and high-lead-risk census tracts). As in Table 1, high risk was defined as a lead-risk score greater than or equal to 8, while low risk was operationally defined as a lead-risk score less than or equal to 3 (also see Fig. 1a). The following number of participants were in each of these subgroups: low income, high risk, $n = 1{,}329$; low income, low risk, $n = 581$; high income, high risk, $n = 697$; high income, low risk, $n = 2{,}185$.

For visualization purposes, vertex maps of regional cortical maps of differences in cortical surface area and cortical volume were also generated for the high- and low-income groups. For each vertex, the means of the participants living in high-lead-risk census tracts (lead risk ≥ 8) in each income group were subtracted from the means of the participants living in low-lead-risk census tracts (lead risk ≤ 3) in that same income group. Of the 4,792 participants composing these four subgroups, the vertex maps incorporated the participants with available vertex data (that is, 4,312 of 4,792, 90%).

Correlates of lead-exposure risk and ADI. Parent-report family income, lead risk and its two subcomponents, and ADI and its 17 subcomponents were correlated (that is, 22 total variables). Due to the mix of skewed distributions of the 22 variables, as well as the finite lower and upper asymptotes of each variable, zero-order Spearman's rank-order correlations were performed. Extended Data Fig. 5 shows the zero-order correlation matrix for these 22 variables. For ease of interpretation, Extended Data Fig. 6 shows the same correlation matrix as Extended Data Fig. 5, but the ρ values from the zero-order correlation matrix were squared (that is, pseudo-R^2 values). Notably, 11.5% of the variance of the lead-risk composite score was accounted for by parent-report household income; 14.1% of the variance of the lead-risk composite score was accounted for by the composite ADI score. Thus, while lead risk is significantly correlated with household income and ADI, there is a considerable amount of variance in the lead-risk score that is unaccounted for with respect to the family poverty (that is, income) and neighborhood poverty factors (that is, ADI).

Reporting Summary. Further information on research design is available in the Nature Research Reporting Summary linked to this article.

Data availability

ABCD data are publicly available through the National Institute of Mental Health Data Archive (https://data-archive.nimh.nih.gov/abcd). The blood-lead-level data were not collected as part of the ABCD Study and were made available by the corresponding agencies, entities or individuals identified in the Supplementary information (Supplementary Table 2); these data are, however, available from the authors upon reasonable request and with permission of each of the agencies, entities or individuals.

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Author contributions

A.T.M., R.M., B.P.L. and E.R.S. conceived and designed the experiments/analysis. A.T.M., S.B. and E.C.K. collected the data. A.T.M. and B.P.L. contributed data or analysis tools. A.T.M., S.B. and E.C.K. analyzed the data. A.T.M. and E.R.S. wrote the paper.

Competing interests

The authors declare no competing interests.

Additional information

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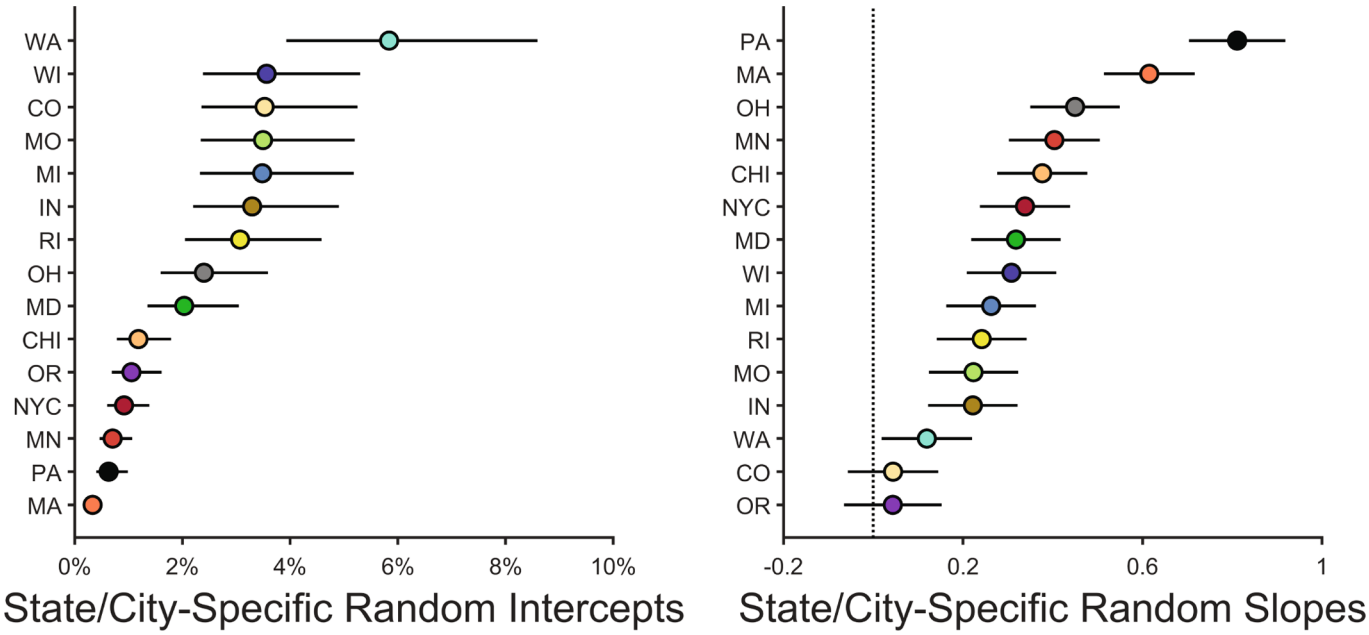
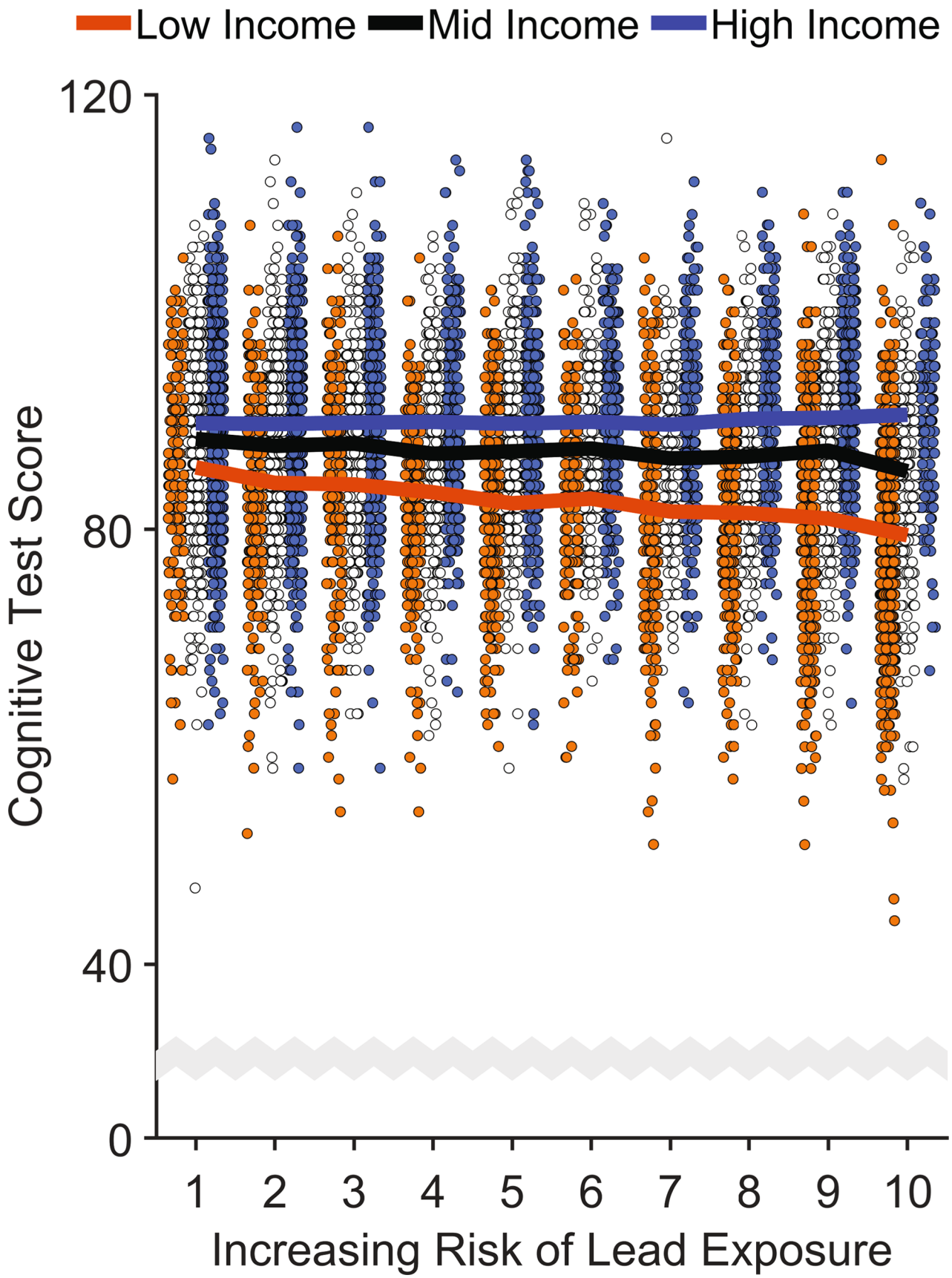
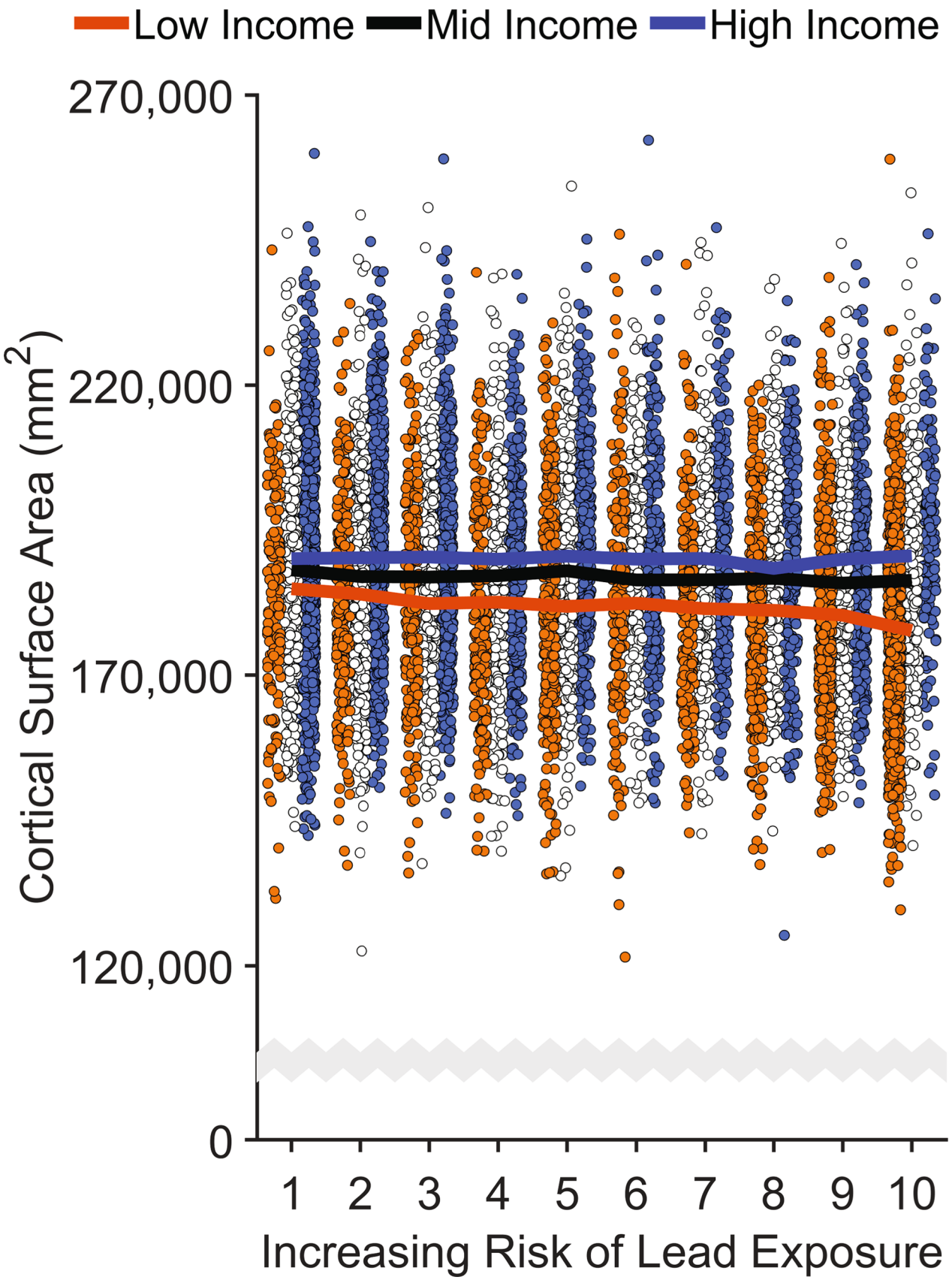


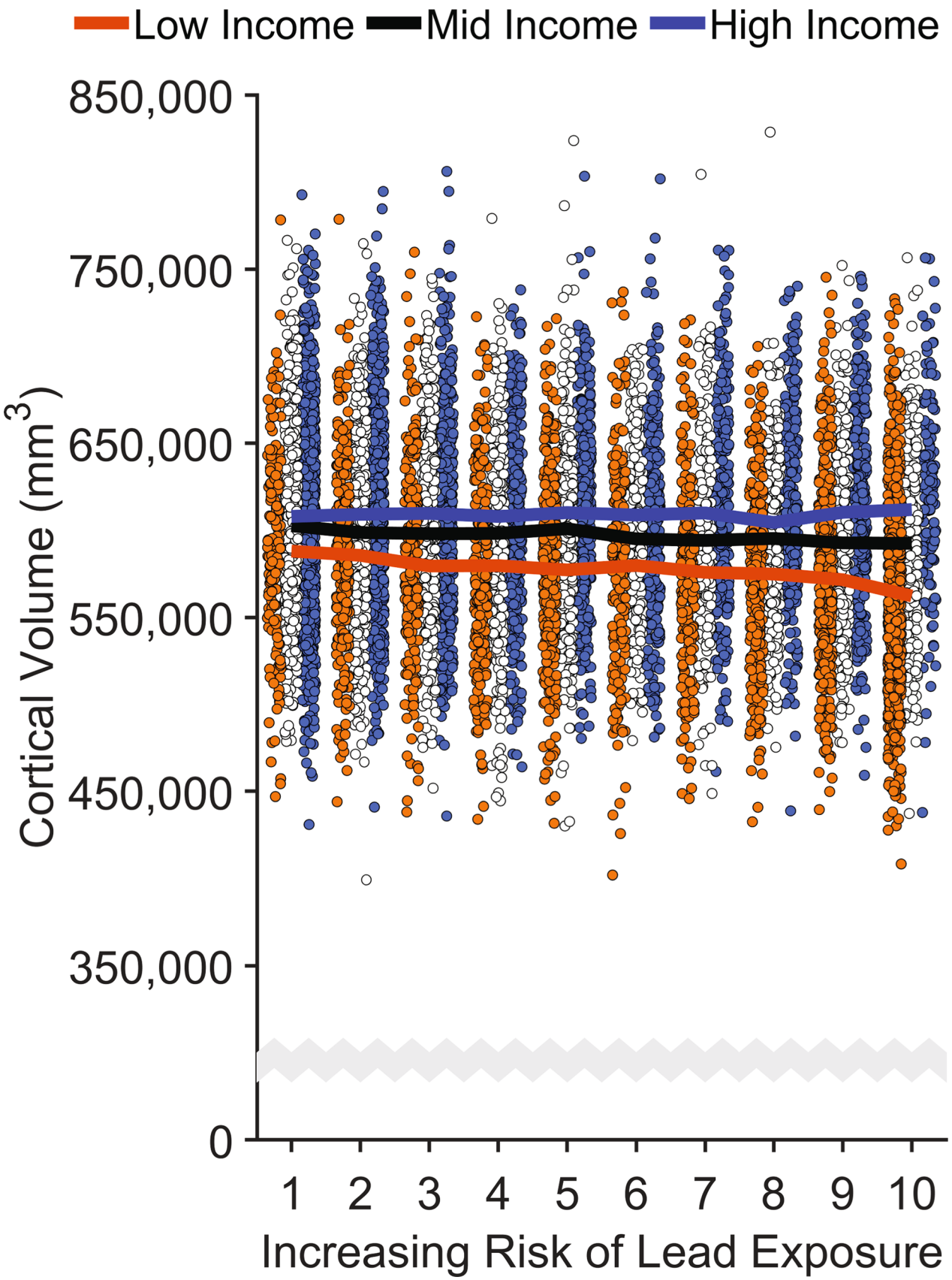
Extended Data Fig. 1 | The distribution of random coefficients for each geographic region. Each data point represents the random intercept (left) or slope (right) for each state/city (i.e., fixed effect coefficient + random effects deviation). The lines surrounding the data points represent the 95% confidence interval of the coefficient. Aside from Oregon and Colorado (for which the 95% confidence intervals included 0), there were significant increases in elevated-blood-lead-level rates with increasing lead-risk scores for each state/city (right). Analysis employed generalized linear-mixed effects models, which tested the statistical significance of coefficients against a *t*-distribution.



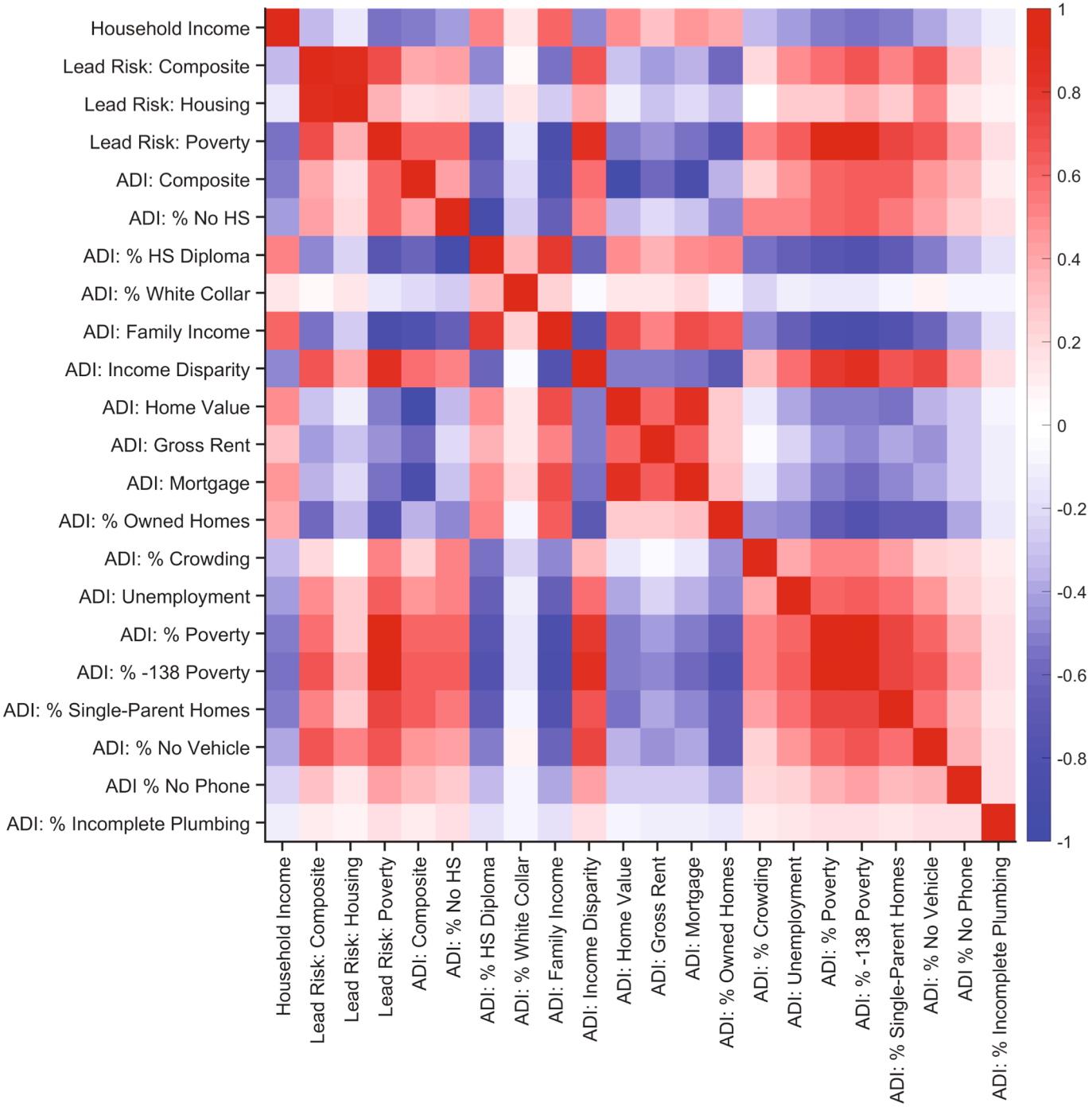
Extended Data Fig. 2 | Risk of lead exposure and cognition. Overall cognitive test scores declined most steeply with increasing risk of environmental lead exposure in children of low-income parents. The data reflect individual participants. Solid lines represent means of the marginal fitted values of the model. Analysis employed linear mixed-effects models, which tested the statistical significance of coefficients against a *t*-distribution. Age, sex, parental education, and race/ethnicity were included as covariates in this analysis. The scale of the ordinate differs from that in Fig. 2.



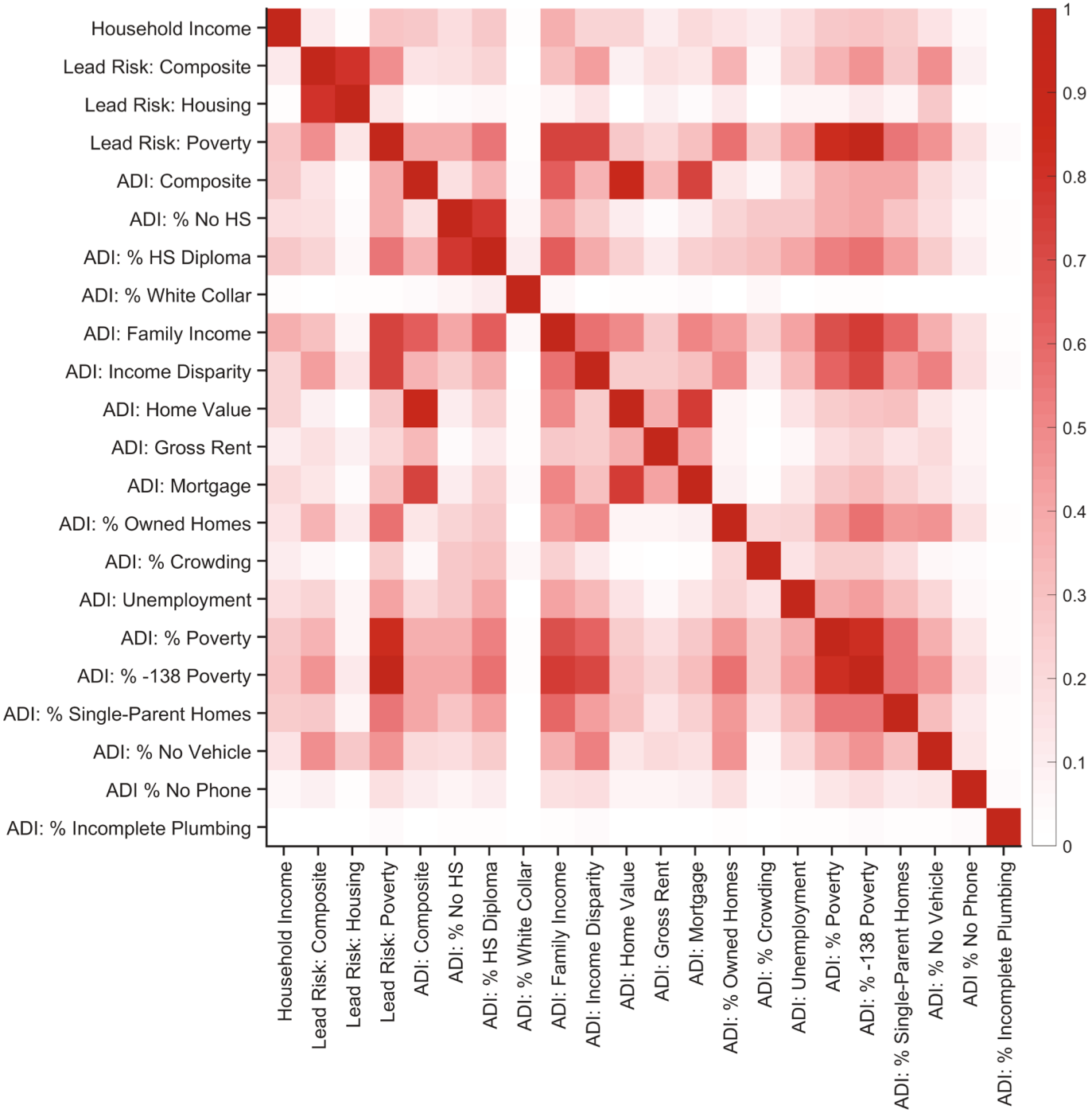
Extended Data Fig. 3 | Negative associations of increased risk of lead exposure are greater for children from lower-income families. Whole-brain cortical surface area declined most steeply with increasing risk of environmental lead exposure in children of low-income parents. The data reflect individual participants. Solid lines represent means of the marginal fitted values of the model. Analysis employed linear mixed-effects models, which tested the statistical significance of coefficients against a *t*-distribution. Age, sex, parental education, and race/ethnicity were included as covariates in this analysis. The scale of the ordinate differs from that in Fig. 3a.



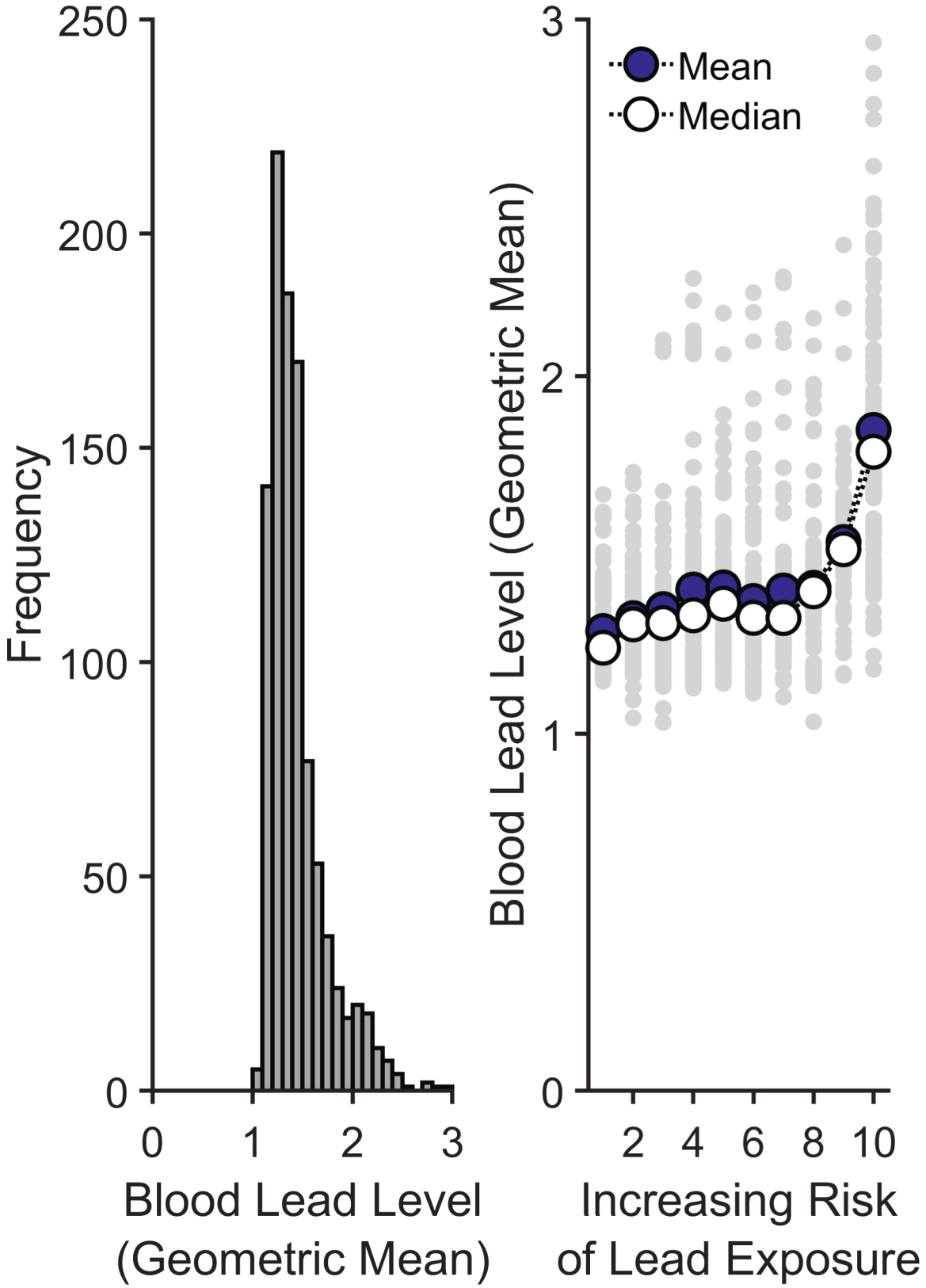
Extended Data Fig. 4 | Negative associations of increased risk of lead exposure are greater for children from lower-income families. Whole-brain cortical volume declined most steeply with increasing risk of environmental lead exposure in children of low-income parents. The data reflect individual participants. Solid lines represent means of the marginal fitted values of the model. Analysis employed linear mixed-effects models, which tested the statistical significance of coefficients against a *t*-distribution. Age, sex, parental education, and race/ethnicity were included as covariates in this analysis. The scale of the ordinate differs from that in Fig. 3b.



Extended Data Fig. 5 | Associations between family income, lead-exposure risk, and area deprivation index. Zero-order Spearman's rank-order correlation matrix of parent-report household income, lead risk and its 2 subcomponents, and the area deprivation index (ADI) and its 17 subcomponents. Along the ordinate, from top to bottom, the variables refer to parent-report total annual household income ("Household Income"), the composite lead-risk score ("Lead Risk: Composite"), estimated percentage of homes at risk for lead exposure given lead-based paint ("Lead Risk: Housing"), percentage of individuals below –125 percent of the poverty level ("Lead Risk: Poverty"), the national ADI percentile ("ADI: Composite"), the percentage of the population at least 25 years old with less than 9 years of education ("ADI: % No HS"; HS = high school), the percentage of the population at least 25 years old with at least a high school diploma ("ADI: % HS Diploma"), the percentage of employed persons at least 16 years old in white-collar jobs ("ADI: % White Collar"), median family income ("ADI: Family Income"), income disparity as defined by Singh[67] ("ADI: Income Disparity"), median home value ("ADI: Home Value"), median gross rent ("ADI: Gross Rent"), median monthly mortgage ("ADI: Mortgage"), percentage of owner-occupied housing units ("ADI: % Owned Homes"), percentage of occupied housing units with at least 1 person per room ("ADI: % Crowding"), percentage of civilian labor force at least 16 years old who are unemployed ("ADI: Unemployment"), percentage of families below the poverty level ("ADI: % Poverty"), percentage of the population below 138% of the poverty threshold ("ADI: % –138 Poverty"), percentage of single-parent homes with children who are less than 18 years old ("ADI: % Single-Parent Homes"), percentage of occupied housing units with a motor vehicle ("ADI: % No Vehicle"), percentage of occupied housing units without a telephone ("ADI: % No Phone"), and the percentage of occupied housing units with complete plumbing ("ADI: % Incomplete Plumbing"). With the exception of parent-report household income (which was specific to each family), the lead-risk and ADI data had census-tract-level resolution.



Extended Data Fig. 6 | Associations between family income, lead-exposure risk, and area deprivation index. Zero-order Spearman's rank-order correlation matrix of parent-report household income, lead risk and its 2 subcomponents, and the area deprivation index (ADI) and its 17 subcomponents, as in Extended Data Fig. 5, except that all correlation coefficients were squared (i.e., pseudo-R^2). See Extended Data Fig. 5 caption for variable names.



Extended Data Fig. 7 | Lead exposure risk scores predict Maryland's blood lead levels at the census-tract level. Left: Distribution of the census-tract-level geometric means of blood lead levels in Maryland, collapsed across the years of 2010 to 2014. Right: Geometric mean blood lead levels as a function of the estimated risk of lead exposure. The smaller gray data points represent individual census tracts. Two measures of central tendency are provided: The larger darker data points represent the means at each risk level, while the larger open data points represent the medians at each risk level. Analysis employed a Spearman's rank-order correlation.

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Reporting Summary

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Statistics

For all statistical analyses, confirm that the following items are present in the figure legend, table legend, main text, or Methods section.

n/a	Confirmed	
☐	☒	The exact sample size (*n*) for each experimental group/condition, given as a discrete number and unit of measurement
☐	☒	A statement on whether measurements were taken from distinct samples or whether the same sample was measured repeatedly
☐	☒	The statistical test(s) used AND whether they are one- or two-sided *Only common tests should be described solely by name; describe more complex techniques in the Methods section.*
☐	☒	A description of all covariates tested
☐	☒	A description of any assumptions or corrections, such as tests of normality and adjustment for multiple comparisons
☐	☒	A full description of the statistical parameters including central tendency (e.g. means) or other basic estimates (e.g. regression coefficient) AND variation (e.g. standard deviation) or associated estimates of uncertainty (e.g. confidence intervals)
☐	☒	For null hypothesis testing, the test statistic (e.g. *F*, *t*, *r*) with confidence intervals, effect sizes, degrees of freedom and *P* value noted *Give P values as exact values whenever suitable.*
☒	☐	For Bayesian analysis, information on the choice of priors and Markov chain Monte Carlo settings
☒	☐	For hierarchical and complex designs, identification of the appropriate level for tests and full reporting of outcomes
☐	☒	Estimates of effect sizes (e.g. Cohen's *d*, Pearson's *r*), indicating how they were calculated

Our web collection on statistics for biologists contains articles on many of the points above.

Software and code

Policy information about availability of computer code

Data collection	Demographic data was collected from parent and child participants using REDCap (specifically, the REDCap software licensed to the University of California, San Diego, as they are the coordinating center in this multisite study). Cognitive data were collected using the NIH Toolbox. Measures of cortical volume, cortical surface area, and cortical thickness were obtained using FreeSurfer v5.3.0 on acquired T1w MRI volumes from ABCD participants. Geocoded data (i.e., area deprivation index, lead-exposure risk) were obtained and derived using data from the US Census Bureau's American Community Survey. Further details on data collection techniques that are part of the ABCD study but not analyzed here are available at the study's website: https://abcdstudy.org/.
Data analysis	Analyses were conducted in MATLAB 9.6.0 (R2019a, Update 2; The MathWorks, Natick MA) and MATLAB's Statistics and Machine Learning Toolbox 11.5 (R2019a). The software program R was originally used to compile the data pertaining to the area deprivation index (ADI), and the corresponding code is provided at the following website: https://github.com/ABCD-STUDY/geocoding/blob/master/Gen_data_proc.R. This R link serves as a reference for the readers, as this code was not directly used in the present manuscript. That is, this was the code used to generate the ADI data that are present in the public data release of the ABCD Study.

For manuscripts utilizing custom algorithms or software that are central to the research but not yet described in published literature, software must be made available to editors/reviewers. We strongly encourage code deposition in a community repository (e.g. GitHub). See the Nature Research guidelines for submitting code & software for further information.

Data

Policy information about availability of data

All manuscripts must include a data availability statement. This statement should provide the following information, where applicable:

- Accession codes, unique identifiers, or web links for publicly available datasets
- A list of figures that have associated raw data
- A description of any restrictions on data availability

ABCD data are publicly available through the National Institute of Mental Health Data Archive (https://data-archive.nimh.nih.gov/abcd).

Field-specific reporting

Please select the one below that is the best fit for your research. If you are not sure, read the appropriate sections before making your selection.

☐ Life sciences ☒ Behavioural & social sciences ☐ Ecological, evolutionary & environmental sciences

For a reference copy of the document with all sections, see nature.com/documents/nr-reporting-summary-flat.pdf

Behavioural & social sciences study design

All studies must disclose on these points even when the disclosure is negative.

Study description	The Adolescent Brain Cognitive Development (ABCD) study is a 10-year, longitudinal study investigating brain and cognitive development in adolescents and young adults. The children were recruited at 9-10 years old, such that the study will continue until they are 19-20 years old. The data in this manuscript are from baseline data collection (i.e., when the children were 9-10 years old). Each participant contributed one data point to each analysis, such that the present manuscript incorporates an observational, cross-sectional analysis. However, the primary analyses were in the form of mixed-effects models, with random effects of study site and family (as there were 21 study sites and some participants had siblings in the study).
Research sample	The ABCD study is a large-scale, 10-year longitudinal study involving 21 data collection sites across the U.S. Using school-based enrollment, the consortium successfully recruited and enrolled over a demographically and socioeconomically diverse sample of 11,800 9- and 10-year-old children. The demographics of the ABCD cohort are presented in the manuscript and correspond well with the American Community Survey. Our data came from the most recent April 2019 ABCD 2.0 data release, which included baseline data for 11,875 children. For the variables of interest, there were complete data for 9,712 children. ABCD data are publicly available through the National Institute of Mental Health Data Archive (https://data-archive.nimh.nih.gov/abcd).
Sampling strategy	The present report uses archival (i.e., baseline) data from the ABCD Study. Accordingly, a full description of recruitment and sampling is available in Garavan et al. (2018; DCN) as part of the 2018 special issue of Developmental Cognitive Neuroscience on the ABCD study. In brief, the sample was achieved using probability sampling of U.S. schools within the catchment areas of 21 study sites. Statisticians at University of Michigan's Institute for Social Research used geographic information software and the Common Core of Data and Private School Survey national databases from the National Center for Education Statistics to derive catchment area boundaries so as to determine school districts (private, public, and charter schools) for recruitment. These 21 catchment areas encompassed 20% of the entire US population of 9- and 10-year-olds. As described in Garavan et al. (2018; DCN), "The sample size ensures sufficient power, allowing for an anticipated 10% attrition, to detect medium to small effects over the study's duration" (p. 16).
Data collection	For the ABCD data collected in the present manuscript, child participants completed tasks on the NIH Toolbox (http://www.healthmeasures.net/explore-measurement-systems/nih-toolbox) and experienced neuroimaging sessions to derive whole-brain cortical volume, cortical thickness, and cortical surface area. During the NIH Toolbox sessions, only the researcher and child participant were present (parents are never present during the NIH Toolbox tasks). For the neuroimaging sessions, the researcher and MRI technician were in the control room while the child was in the MRI scanner. In some instances, the child's parent participant was present in the control room; in rarer instances, the parent was seated in the scanner room. Parent participants filled out questionnaires on their own, but researchers were available for questions.
Timing	Regarding the data in the current manuscript, baseline data collection across the entire sample started in September 2016 and ended in October 2018. Data are still being collected given the longitudinal nature of the study and will continue being collection for several more years.
Data exclusions	Our data came from the most recent April 2019 ABCD 2.0 data release, which included baseline data for 11,875 children. For the variables of interest, there were complete data for 9,712 children.
Non-participation	With respect to the data in the current manuscript, there were complete data for 9,712 children of the recruited sample. These data were from baseline data collection, such that retention efforts for subsequent data collection years were not an issue with respect to the current data.
Randomization	There were no experimental groups.

Reporting for specific materials, systems and methods

We require information from authors about some types of materials, experimental systems and methods used in many studies. Here, indicate whether each material, system or method listed is relevant to your study. If you are not sure if a list item applies to your research, read the appropriate section before selecting a response.

Materials & experimental systems

n/a	Involved in the study
☒	☐ Antibodies
☒	☐ Eukaryotic cell lines
☒	☐ Palaeontology
☒	☐ Animals and other organisms
☐	☒ Human research participants
☒	☐ Clinical data

Methods

n/a	Involved in the study
☒	☐ ChIP-seq
☒	☐ Flow cytometry
☐	☒ MRI-based neuroimaging

Human research participants

Policy information about studies involving human research participants

Population characteristics	See above.
Recruitment	The present report uses archival (i.e., baseline) data from the ABCD Study. Accordingly, a full description of recruitment and sampling is available in Garavan et al. (2018; DCN) as part of the 2018 special issue of Developmental Cognitive Neuroscience on the ABCD study. In brief, the sample was achieved using probability sampling of U.S. schools within the catchment areas of 21 study sites. Statisticians at University of Michigan's Institute for Social Research used geographic information software and the Common Core of Data and Private School Survey national databases from the National Center for Education Statistics to derive catchment area boundaries so as to determine school districts (private, public, and charter schools) for recruitment. These 21 catchment areas encompassed 20% of the entire US population of 9- and 10-year-olds. As described by Garavan et al. (2018), in the ABCD Study, participants were primarily recruited through public, private, and charter elementary schools. Once schools were identified, the study sites contacted school administrators to request the dissemination of hard and electronic copies of materials pertaining to the study. Additional recruitment techniques involved use of commercialized mailing lists, referrals, and outreach at summer activities, such as Boys and Girls clubs, YMCA's, and summer meals programs. Twins were recruited through direct contact via information in birth registries and the corresponding tracking of parents and twins to their address. As described by Garavan et al. (2018), "It is well understood that self-selection by families into the study will likely be a major and unavoidable source of sampling bias. Consequently, any sampling strategy benefits from additional efforts to ensure outreach to and engagement with historically under-represented segments of the population. Knowledge, during recruitment, of how the accumulating sample might be deviating from target demographics (gender, race and ethnicity, SES, and urbanicity) helps identify when and where these outreach efforts need to be enhanced. Thus, active recruitment and monitoring of the accumulating sample go hand in hand over the two years of ABCD recruitment (September 2016–August 2018)" (p. 19). Indeed, throughout recruitment, the demographics of the recruitment sample were carefully monitored to correct any potential deviations in target recruitment. Despite the aforementioned potential biases, the ABCD Study reflects the largest longitudinal study of brain, cognitive, social, physical, and emotional development in U.S. children and adolescents, ultimately aiming to develop national standards for normal brain development. Lastly, as pointed out by Garavan et al. (2018), "Designing the ABCD sample demographics to match those of the national target population does not guarantee that the sample will be representative across all of the many dimensions (demographics, family and individual factors, community and environment, behaviors, exposures) that may influence a child's development. However by exerting control over this smaller but still important set of socio-demographic attributes in the baseline recruitment, ABCD hopes to minimize a later need to statistically adjust (e.g., through weighting, propensity score methods, statistical modeling) for selection bias due to those factors that cannot be easily assessed prior to baseline recruitment or can only be observed as the ABCD cohort ages and is repeatedly observed" (p. 18).
Ethics oversight	The central IRB was at the University of California, San Diego. The other 20 study sites were Children's Hospital Los Angeles, UCLA, University of Colorado Boulder, University of Minnesota, the Laureate Institute for Brain Research, Oregon Health and Science University, University of Vermont, University of Pittsburgh, Virginia Commonwealth University, University of Rochester, University of Florida, the Medical University of South Carolina, University of Michigan, University of Minnesota, University of Utah, SRI International, University of Wisconsin-Milwaukee, University of Maryland at Baltimore, Florida International University, Washington University in St. Louis, and Yale University. The federal partners of the ABCD study are listed at the following link: https://abcdstudy.org/federal-partners/.

Note that full information on the approval of the study protocol must also be provided in the manuscript.

Magnetic resonance imaging

Experimental design

Design type	With respect to the data in the current manuscript, all MRI data were structural MRI data of T1w and T2w image collection. dMRI and resting-state and task-based fMRI data were also collected but not analyzed in this report.
Design specifications	For structural MRI (sMRI) data, there were 2 blocks (i.e., sequences): T1-weighted and T2-weighted acquisition. T1-weighted imaging lasted for approximately 7 min while T2-weighted imaging lasted for approximately 6.5 min. Additional details on the neuroimaging parameters are provided at: https://abcdstudy.org/images/Protocol_Imaging_Sequences.pdf.
Behavioral performance measures	For the sMRI data, no behavioral performance measures were employed.

Acquisition

Imaging type(s)	Structural
Field strength	3 Tesla
Sequence & imaging parameters	As specified in Hagler et al. (2019; NeuroImage), "The T1w acquisition (1 mm isotropic) is a 3D T1w inversion prepared RF-spoiled gradient echo scan using prospective motion correction, when available (currently only on Siemens and GE scanners) (Tisdall et al., 2012; White et al., 2010). The T2w acquisition (1 mm isotropic) is a 3DT2w variable flip angle fast spin echo scan, also using prospective motion correction when available." (p. 4). The neuroimaging parameters are also available at: https://abcdstudy.org/images/Protocol_Imaging_Sequences.pdf.
Area of acquisition	For the present report, data analysis incorporated whole-brain cortical thickness, cortical surface area, and cortical volume.

Diffusion MRI ☐ Used ☒ Not used

Preprocessing

Preprocessing software

Hagler et al. (2019; NeuroImage) provides a detailed summary of the collection and processing of imaging data, which is cited in the current report. Selections from that paper are included here to provide requested information:

As specified in Hagler et al. (2019; NeuroImage), "T1w and T2w structural images are corrected for gradient nonlinearity distortions using scanner-specific, nonlinear transformations provided by MRI scanner manufacturers (Jovicich et al., 2006; Wald et al., 2001). T2w images are registered to T1w images using mutual information (Wells et al., 1996) after coarse, rigid-body pre-alignment via within-modality registration to atlas brains. MR images are typically degraded by a smooth, spatially varying artifact (receive coil bias) that results in inconsistent intensity variations (Fig. 2). Standard correction methods,such as those used by FreeSurfer (Dale et al., 1999; Fischl, 2012; Sled et al., 1998) are limited when compensating for steep spatial intensity variation, leading to inaccurate brain segmentation or cortical surface reconstruction. For example, brain tissue farther from the coils, such as the temporal and frontal poles, typically has lower intensity values,causing focal underestimation of the white matter surface, or even resulting in elimination of large pieces of cortex from the cortical surface reconstruction. Furthermore, brain tissue close to coils with extremely high intensity values may be mistaken for non-brain tissue (e.g., scalp). Intensity inhomogeneity correction is performed by applying smoothly varying, estimated B1-biasfields, using a novel implementation that is similar in purpose to commonly used bias field correction methods(Ashburner and Friston, 2000; Sled et al., 1998). Specifically, B1-bias fields are estimated using sparse spatial smoothing and white matter segmentation, with the assumption of uniform T1w (or T2w) intensity values within white matter. To normalize T1w and T2w intensities across participants, a target white matter intensity value of 110 is used so that after bias correction, white matter voxel intensities are centered on that target value and all other voxels are scaled relatively. The value of 110 was chosen to match the white matter value assigned by the standard bias correction used by FreeSurfer. The white matter mask, defined using a fast, atlas-based, brain segmentation algorithm, is refined based on a neighborhood filter, in which outliers in intensity–relative to their neighbors within the mask–are excluded from the mask. A regularized linear inverse, implemented with an efficient sparse solver, is used to estimate the smoothly varying bias field. The stiffness of the smoothing constraint was optimized to be loose enough to accommodate the extreme variation in intensity that occurs due to proximity to the imaging coils, without overfitting local intensity variations in white matter. The bias field is estimated within a smoothed brain mask that is linearly interpolated to the edge of the volume in both directions along the inferior-superior axis, avoiding discontinuities in intensity between brain and neck. Images are rigidly registered and resampled into alignment with an averaged reference brain in standard space, facilitating standardized viewing and analysis of brain structure. This pre-existing, in-house,averaged, reference brain has 1.0 mm isotropic voxels and is roughly aligned with the anterior commissure/posterior commissure (AC/PC)axis. This standard reference brain was created by averaging T1w brain images from 500 adults after they had been nonlinearly registered to an initial template brain image using discrete cosine transforms (DCT)(Friston et al., 1995). For most ABCD participants, a single scan of each type (T1w or T2w) is collected. If multiple scans of a given type are obtained, only one is used for processing and analysis. Results of manual quality control (QC) performed prior to the full image processing are used to exclude poor-quality structural scans (refer to the Protocol Compliance and Initial Quality Control section). If there is more than one acceptable scan of a given type, the scan with the fewest issues noted is used. In case of a tie, the final acceptable scan of the session is used" (p. 5).

Further, "We used a collection of processing steps contained within the Multi-Modal Processing Stream (MMPS), a software package developed and maintained in-house at the Center for Multi-modal Imaging and Genetics (CMIG) at the University of California, San Diego (UCSD) that provides large-scale, standardized processing and analysis of multimodality neuroimaging data on Linux workstations and compute clusters. This toolbox contains primarily MATLAB functions, as well as python, sh, and csh scripts, and Cþþ compiled executables and relies upon a number of publicly available neuroimaging software packages, including FreeSurfer (Fischl, 2012), Analysis of Functional NeuroImages (AFNI) (Cox, 1996), and FMRIB Software Library (FSL)(Jenkinson et al., 2012;Smith et al., 2004). The processing pipeline described in this manuscript was used for the ABCD Data Release 2.0, available in March 2019, and a beta testing version has been made publicly available as a self-contained, platform-independent executable (https://www.nitrc.org/projects/abcd_study). Imaging statistics shown here include the amended ABCD Fix Release 2.0.1 data published in July2019" (p. 3).

Lastly, "Morphometric measures include cortical thickness (Fischl and Dale,2000; Rimol et al., 2010), area (Chen et al., 2012; Joyner et al., 2009),volume, and sulcal depth (Fischl et al., 1999a). Image intensity measures include T1w, T2w, and T1w and T2w cortical contrast (normalized difference between gray and white matter intensity values) (Westlye et al., 2009). Cortical contrast measures are included because they reflect factors that impact placement of the gray-white

matter boundary, such as pericortical myelin content, that can significantly influence cortical thickness measures. ... We calculate averages for each cortical parcel in the two standard FreeSurfer parcellation schemes (Desikan et al., 2006; Destrieux et al., 2010) using unsmoothed, surface-based maps of morphometric and image intensity measures. For each of the fuzzy-cluster parcels (Chen et al., 2012), we calculate weighted averages (weighted by fuzzy cluster membership values ranging from 0 to 1) for each measure using smoothed surface maps (~66 mm FWHM, matching the level of smoothing used for derivation of the fuzzy cluster parcels). We also calculate averages of the unsmoothed intensity measures for the volumetric subcortical ROIs, in addition to the volume of each structure" (p. 6).

With respect to quality control, "Automated quality control procedures include the calculation of metrics such as signal-to-noise ratio (SNR) and head motion statistics. For sMRI series, metrics include mean and SD of brain values. ... Trained technicians visually review image series as part of our manual QC procedures, including T1w, T2w, dMRI, dMRI field maps, fMRI, and fMRI field maps. Reviewers inspect images for poor image quality, noting various imaging artifacts and flagging unacceptable data,typically those with the most severe artifacts or irregularities. For example, despite the use of prospective motion correction for sMRI scans,which greatly reduces motion-related image degradation (Brown et al., 2010; Kuperman et al., 2011; Tisdall et al., 2016), images of participants with excessive head motion may exhibit severe ghosting, blurring,and/or ringing that makes accurate brain segmentation impossible. Reviewers are shown several pre-rendered montages for each series, showing multiple slices and views of the first frame, and multiple frames of individual slices if applicable. For multi-frame images, linearly spaced subsets of frames are shown as a 9x9 matrix of 81 frames. ... All series are consensus rated by two or more reviewers. In the case of a rejection, the reviewer is required to provide notes indicating the types of artifacts observed using a standard set of abbreviations for commonly encountered artifacts. Series rejected based on data quality criteria are excluded from subsequent processing and analysis" (p. 5).

Normalization: See above.

Normalization template: See above.

Noise and artifact removal: See above.

Volume censoring: See above.

Statistical modeling & inference

Model type and settings: Whole-brain values of cortical thickness, surface area, and volume were regressed (via general linear mixed-effects models) on both relevant independent variables, controlling for covariates, with random effects of study site and family identification number.

Effect(s) tested: Whole-brain values of cortical thickness, surface area, and volume for each participant were regressed on a series of predictors, the primary ones being the risk of lead exposure in each participant's census tract and the participant's family's annual household income.

Specify type of analysis: ☒ Whole brain ☐ ROI-based ☐ Both

Statistic type for inference (See Eklund et al. 2016): Voxel-wise or cluster-wise analyses were not performed.

Correction: Voxel-wise or cluster-wise analyses were not performed.

Models & analysis

n/a	Involved in the study
☒	☐ Functional and/or effective connectivity
☒	☐ Graph analysis
☒	☐ Multivariate modeling or predictive analysis