Neighborhood air pollution is negatively associated with neurocognitive maturation in early adolescence

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Abstract

The ability to maintain focus and process task-relevant information continues developing during adolescence, but the specific physical environmental factors that influence this development remain poorly characterized. One candidate factor is air pollution. Evidence suggests that small particulate matter and NO2 concentrations in the air may negatively impact cognitive development in childhood. We assessed the relationship between neighborhood air pollution and the changes in performance on the *n*-back task, a test of attention and working memory, in the Adolescent Brain Cognitive Development (ABCD) Study's baseline (ages 9-10) and two-year-follow-up releases (Y2, ages 11-12; n = 5,256). In the *behavioral* domain, multiple linear regression showed that developmental change in n-back task performance was negatively associated with neighborhood air pollution ($\beta = -.044$, $t = -3.11$, $p = .002$), adjusted for covariates capturing baseline cognitive performance of the child, their parental income and education, family conflicts, and their neighborhood's population density, crime rate, perceived safety, and Area Deprivation Index (ADI). The strength of the adjusted association for air pollution was similar to parental income, family conflict, and neighborhood ADI. In the *neuroimaging* domain, we evaluated a previously published youth cognitive composite Connectome-based Predictive Model (ccCPM), and again found that decreased developmental change in the strength of the ccCPM from pre- to early adolescence was associated with neighborhood air pollution ($\beta = -.110$, $t = -2.69$, $p = .007$), adjusted for the covariates mentioned above and head motion. Finally, we found that the developmental change in ccCPM strength was predictive of the developmental change in n-back performance ($r = .157$, $p < .001$), and there was an indirect-only mediation where the effect of air pollution on change in n-back performance was mediated by the change in the ccCPM strength ($\beta_{\text{indirect effect}} = -.013$, $p = .029$). In conclusion, neighborhood air pollution is associated with lags in the maturation of youth cognitive performance and decreased strengthening of the brain networks supporting cognitive abilities over time.

Keywords: Air pollution, Neurocognitive development, Functional brain connectivity, Early adolescence

Introduction

The ability to maintain focus and process task-relevant information continues to develop during adolescence [Fortenbaugh et al., 2015; Isbell et al., 2015; Theodoraki et al., 2020; Ferguson et al., 2021] and predicts desirable educational and health outcomes [Rogers et al., 2011; Alloway & Alloway, 2010; Allan et al., 2016; Ahmed et al., 2021]. The marked improvement in performance on sustained attention and working memory tasks from pre- to early adolescence [Fortenbaugh et al., 2015; Heyes et al., 2016] makes this period of lifespan particularly important for studying environmental factors that may be detrimental to the maturation of these abilities. Many aspects of cognitive development are associated with the neighborhood one lives in [Tucker-Drob et al., 2013; Meredith et al, 2022], but the specific physical environmental factors that influence cognitive development above and beyond socioeconomic factors remain poorly characterized [Berman et al., 2019]. One candidate factor is exposure to air pollution.

Lower neighborhood air quality has been associated with negative impacts on children's cognitive development. Specifically, higher concentrations of fine particulate matter (particles smaller than 2.5 micrometers, i.e., PM 2.5) in the air and indicators of burned fuel such as nitrogen dioxide (NO2) have been linked to worsened child cognitive performance [Forns et al., 2017; Alvarez-Pedrerol et al., 2017; Rivas et al., 2019; Ni et al., 2022; but also see Luminati et al., 2022]. Small particles (i.e., PM2.5) may have a wider impact on the body through blood circulation due to being smaller than red blood cells [Wang et al., 2021; Thiankhaw et al., 2022], and may impact the brain by traveling through the nasal cavity to the olfactory bulb and beyond [Underwood, 2017; Chen et al., 2020]. While growing evidence suggests that small air pollutants can adversely affect cognitive development, the precise mechanisms are still unknown.

Network neuroscience proposes that cognitive and attentional processes are emergent properties of interactions between brain regions [Bassett & Sporns, 2017]. In other words, the degree to which activity is coordinated across large-scale brain networks may better characterize cognitive processes than the magnitude of activity in singular brain regions in isolation [Smith et al., 2013; Medaglia et al., 2015]. Connectome-based predictive modeling (CPM) is an approach that identifies functional connectivity networks (here connectivity is correlated fMRI activity time-courses of pairs of brain regions) that are related to behavior and measures the strength of these networks in previously unseen individuals to make predictions about their behavior [Shen et al., 2017]. Since adolescence is a critical period for the development of attention and working memory and the brain networks supporting them [Spear,

2013; Keller et al., 2022; Kardan et al., 2022], it is possible that environmental influences such as exposure to PM2.5 and NO2 may influence this protracted [Keller et al., 2022] neurobehavioral development.

The current study seeks to bridge these literatures by assessing the relationship between neighborhood air pollution and developmental change in attention and working memory performance, as well as the brain networks that support general cognitive performance in youth, from pre- to early adolescence. We utilized neighborhood socioeconomic and air pollution variables in conjunction with behavioral and neuroimaging measures of attention and memory from the baseline time-point (ages 9-10) and the two-year follow-up time-point (Y2; ages 11-12) releases of the Adolescent Brain Cognitive Development™ Study (ABCD Study® data Releases 2.0.1 and 4.0, respectively). Change in performance on the *n*-back task was used to operationalize change in cognitive processes including aspects of attention and memory performance from baseline to Y2 for each participant. To capture the neural development of the brain networks supporting cognitive performance, we quantified the change in the strength of a pre-registered predictive brain network, the cognitive composite Connectome-based Predictive Model (ccCPM; Kardan et al., 2022), from baseline to Y2 for each participant using their fMRI connectivity at each time-point. To ensure independent associations with air pollution are assessed, we included other family and environmental factors that may predict individual differences in neurocognition [Viner et al., 2012; Vargas et al., 2020; Sripada et al., 2021] as covariates in our models. Because neighborhood variables for participants prior to baseline were not available, we also included baseline cognitive performance as a covariate to isolate the developmental change in neurocognition related to environmental exposure within the two-year period between baseline and Y2. Our hypothesis was that lower neighborhood air quality would be negatively associated with youth's developmental change from pre- to early adolescence in both behavioral performance and brain network connectivity that supports those psychological functions, the ccCPM.

Results

1. Neighborhood air quality predicts behavioral performance improvement

We first assessed the change in *n*-back task [Casey et al., 2018] performance from participants' baseline to two-year follow-up study sessions (i.e., ages 9-10 to 11-12 years; n = 7,278 with complete *n*-back task behavioral at both time-points; 53% Male, 47% Female; 55% non-Hispanic White, 20% Hispanic, 13% Black, 12% Asian/Other). The *n*-back task (see

Methods) includes 0-back task blocks, in which participants are asked to indicate via button press whether every image in a series matches a target image, and 2-back blocks, in which participants indicate whether every image matches the image seen two trials before (26 sec per block; 8 blocks per run; two approximately 5-min runs per participant at each time-point). The *n*-back task is thought to assess cognitive processes including sustained attention, working memory, and cognitive control [Barch et al., 2013; Kardan et al., 2022], and is reliably related to other measures of childhood cognitive performance (e.g., the NIH-Toolbox; Rosenberg et al., 2020) and attentional problems (e.g., the Child Behavior Checklist attention subscale; Kardan et al., 2022). We found that n-back accuracy significantly improved from baseline to Y2 (mean Δ Acc = +7.3%, t = 45.80, p < .001). As shown in **Figure 1**, however, there is large variability in the amount of change in *n*-back accuracy across participants (SD of Δ Acc = 13.5%).

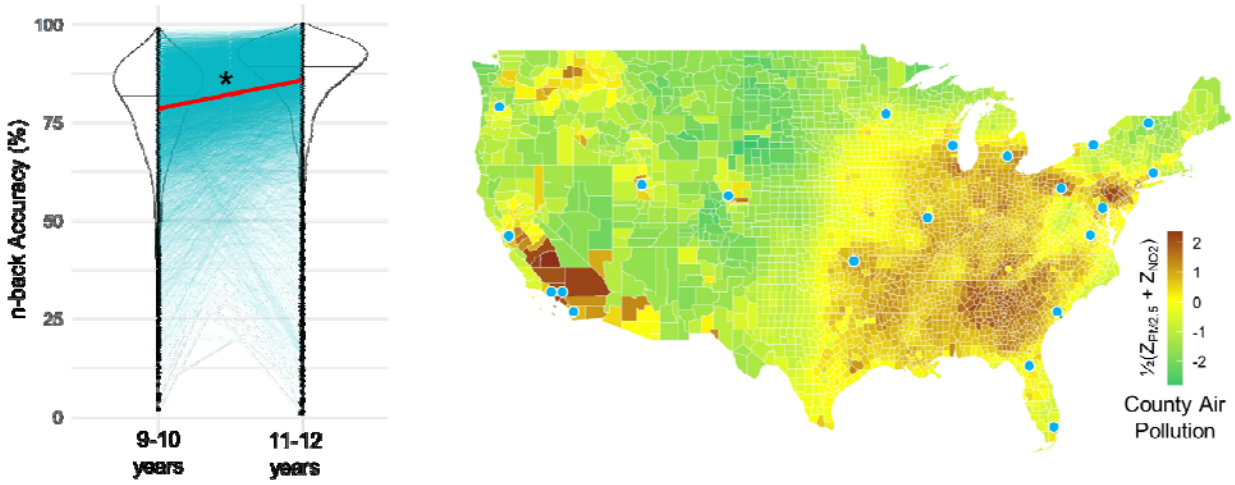

Figure 1. Left: Performance in the *n*-back task improved from ages 9-10 to ages 11-12 in the ABCD Study sample. Each blue line represents a participant. The red line connects the means. Violins cover the entire data range, with medians indicated as black horizontal lines. **Right:** The concentrations of PM2.5 and NO2 across the United States (based on the 2016-2018 average US Environmental Protection Agency Air Quality Database to match the dates of ABCD Study data collection). This map is at the county level and only included for visualization purposes. Data in the analyses were used at the 10x10 Km^2 square around residence level as released by the ABCD Study Consortium [see Fan et al., 2021] using [Geddes et al., 2017] and [van Donkelaar et al., 2018]. The blue circles show approximate locations of ABCD data collection sites. **Supplementary Figure S1** shows separate maps for concentrations of PM2.5 and NO2.

Next, we tested whether variations in neighborhood air pollution explained some of the variability in *n*-back task performance change across youth. **Figure 1** shows county-level air pollution in the United States based on PM2.5 and NO2 concentrations. There was a small but significant negative correlation between air pollution and change in *n*-back task accuracy from ages 9-10 to ages 11-12 (*r* = -.055, t = -4.00, p < .001, n = 5,256 participants with complete n-

back and environmental data; 53% Male; 59% non-Hispanic White, 19% Hispanic, 11% Black, 11% Asian/Other). This relationship, however, is confounded by other variables that are related to air pollution and cognitive development, such as socioeconomic factors.

Multiple linear regression showed that change in n-back task accuracy was negatively associated with neighborhood air pollution (β = -.044, t = -3.11, p = .002, n = 5,256; **Table 1**) when controlling for potential confounds from multiple domains (see *Methods* for details of the variables). Model covariates included participants' baseline cognitive performance (operationalized by Bayesian PCA weights published by Thompson et al., 2019 for ABCD Study baseline cognition), baseline *n*-back accuracy (which additionally removes variance due to regression to the mean), sex assigned at birth, race/ethnicity, caregiver income and education, degree of family conflict, neighborhood population density, neighborhood crime rate, perceived neighborhood safety, and neighborhood's economic resources indexed by the first principal component of the Area Deprivation Index (ADI, [Kind & Buckingham, 2018]). These measures are from baseline due to their sparseness in subsequent data releases. Caregiver-reported race and ethnicity are included as proxies of structural factors that differentially affect racial and ethnic groups in the United States [Meredith et al., 2022].

	Outcome: n-back ΔAcc			
Predictors	*β*	*t*	*CI*	*p*
(Intercept)	*(0.565)*	*(53.65)*	*(0.55 – 0.57)*	***<0.001***
n-back accuracy at baseline	-0.691	-52.57	-0.72 – -0.67	**<0.001**
Baseline Cognitive Ability				
BPPC 1 Gen Ability	0.154	11.39	0.13 – 0.18	**<0.001**
BPPC 2 Exec Function	0.113	9.66	0.09 – 0.14	**<0.001**
BPPC 3 Learn Mem	0.099	8.08	0.07 – 0.12	**<0.001**
Sex & Race/Ethnicity				
Male	-0.005	-0.41	-0.03 – 0.02	0.681
White	0.018	0.95	-0.02 – 0.06	0.344
Black	-0.071	-4.42	-0.10 – -0.04	**<0.001**
Hispanic	0.007	0.41	-0.03 – 0.04	0.685
Asian/Other	-0.004	-0.33	-0.03 – 0.02	0.738
Family				
Income	0.048	2.93	0.02 – 0.08	**0.003**
Education	0.005	0.35	-0.02 – 0.03	0.725
Conflict	-0.029	-2.54	-0.05 – -0.01	**0.011**
Neighborhood				
Residential Density (log)	0.043	3.38	0.02 – 0.07	**0.001**
Perceived Safety	0.007	-0.57	-0.03 – 0.02	0.571
Crime Rate	-0.014	-0.99	-0.04 – 0.01	0.323
Area Deprivation Index PC1	-0.034	-2.29	-0.06 – -0.00	**0.022**
Air Pollution	-0.044	-3.11	-0.07 – -0.02	**0.002**
Observations (subjects)	5,256			

R^2 / Adjusted R^2	0.354 / 0.352

Table 1. Regression results showing associations of air pollution and other variables with change in n-back performance from baseline to Y2 in the ABCD Study sample. For the overall model, F(18, 5238) = 168.8, p < .001. *β* coefficients are standardized to unit variance in predictor and outcome. CI shows 95% confidence intervals, and p-values smaller than .05 are in bold.

The strength of the adjusted effect of air pollution was small but similar to parental income (β = +.047, t = 2.93, p = .003), family conflict (β = -.029, t = -2.54, p = .011), and neighborhood ADI (β = -.034, t = -2.29, p = .022). Excluding baseline *n*-back accuracy from the model did not change the air pollution's relation with change in *n*-back accuracy (β = -.047, t = -2.60, p = .009) but did make the coefficients for some of the covariates statistically non-significant (**Supplementary Table S1**).

In summary, we found a negative association between neighborhood air pollution and the degree to which performance on a task assessing sustained attention, working memory, and cognitive control improved from 9-10 to 11-12 years of age. Importantly, the strength of association was comparable to effects of family and neighborhood socioeconomic factors on change in *n*-back accuracy.

2. Neighborhood air quality predicts strengthening of a brain network associated with cognitive performance

To capture the development of brain networks supporting cognitive performance, we quantified the strength of an existing predictive brain network, the cognitive composite Connectome-based Predictive Model (ccCPM). This "publication-preregistered" network model was defined in Kardan et al. (2022) and shared at https://nda.nih.gov/study.html?id=1849. The strength of expression of ccCPM was measured using each participant's fMRI connectivity during the *n*-back task at both baseline and Y2 (n = 1,159 with sufficient fMRI data at both timepoints; see *Methods* for fMRI exclusion criteria). This sample was 48% Male, 52% Female; 65% non-Hispanic White, 17% Hispanic, 7% Black, 11% Asian/Other, which underrepresents US Black or African American population.

The ccCPM includes two sets of functional brain connections (**Figure 2**) that predict higher or lower performance on the out-of-scanner NIH Toolbox Cognitive Battery (Weintraub et al, 2013; see *Methods*). The ccCPM was previously trained in ABCD Study baseline fMRI connectivity data using leave-one-site-out cross-validation (Kardan et al, 2022). Here, the ccCPM brain expression score was calculated from baseline and Y2 data iteratively for participants from the left-out sites to estimate the neurodevelopmental change in network

predictors of general cognitive performance between the two ages. This approach ensures full independence between model training and testing data. A single ccCPM strength is calculated for each time point by averaging the two sets of connections shown in Figure 2.

The ccCPM strength values were normalized to unit variance (Z) for interpretability. First, we found that the ccCPM strength significantly increased from the baseline to Y2 (mean of ΔZ_{ccCPM} = +0.172, t = 5.32, p < .001, n = 1,159). There was, however, large variability in changes in ccCPM strength across participants (SD of ΔZ_{ccCPM} = 1.103; **Figure 2**). Both of these findings mirror results from the *n*-back behavioral analyses.

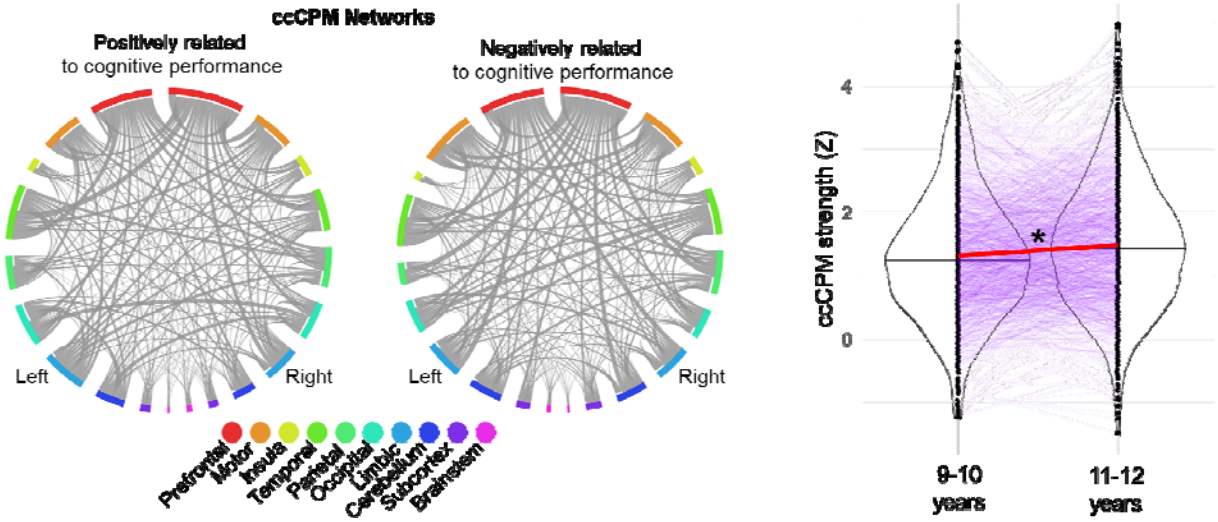

Figure 2. Left: The ccCPM networks from Kardan et al., 2022, where each grey arc shows one or more functional connections between macroscale brain regions. Line width corresponds to the number of connections between two regions included in the network. Macroscale regions are organized by brain hemisphere. For visualization, all the models (one applied to each site) are averaged into one for this figure. **Right:** ccCPM expression scores across participants and ages shown as normalized ccCPM strength in baseline and two-year follow-up of the ABCD Study sample. Each purple line represents a participant.

Next, we tested whether some of the variability in the developmental change in ccCPM strength across youth is explained by variations in their neighborhood air pollution (see **Figure 1**). There was a non-significant negative correlation between air pollution and ΔZ_{ccCPM} in the subset of participants with complete fMRI and environmental data (*r* = -.042, t = -1.25, p = .213, N.S., n = 878; 48% Male, 52% Female; 68% non-Hispanic White, 18% Hispanic, 6% Black [under-represented], 8% Asian/Other). The correlation is small, similar to the behavioral results, but the sample size here is not sufficiently large for evaluating such zero-order correlation.

Next, we introduced the covariates similar to the behavioral analyses. Multiple linear regression revealed that decreased developmental change in the strength of the ccCPM from

age 9-10 to 11-2 (i.e., ΔZ_{ccCPM}) was associated with neighborhood air pollution (β = -.110, t = -2.69, p = .007, n = 878; **Table 2**). The coefficient for air pollution is adjusted for head motion, baseline cognitive performance, ccCPM strength at baseline (which additionally removes variance due to regression to the mean), caregiver income and education, family conflict, and neighborhood population density, crime rate, perceived safety, and ADI.

	Outcome: change in ccCPM strength			
Predictors	*β*	*t*	*CI*	*p*
(Intercept)	*(0.972)*	*(18.83)*	*(0.87 – 1.07)*	***<0.001***
ccCPM strength at baseline	-0.551	-17.76	-0.61 – -0.49	**<0.001**
Head Motion	-0.139	-4.51	-0.20 – -0.08	**<0.001**
Base Cognitive Ability				
BPPC 1 Gen Ability	0.165	4.67	0.10 – 0.23	**<0.001**
BPPC 2 Exec Function	0.055	1.69	-0.01 – 0.12	0.092
BPPC 3 Learn Mem	0.006	0.18	-0.06 – 0.07	0.857
Sex & Race/Ethnicity				
Male	0.032	1.07	-0.03 – 0.09	0.283
White	-0.011	-0.20	-0.12 – 0.10	0.841
Black	-0.042	-0.81	-0.14 – 0.06	0.421
Hispanic	-0.031	-0.60	-0.13 – 0.07	0.551
Asian/Other	-0.044	-1.23	-0.11 – 0.03	0.220
Family				
Income	-0.087	-1.98	-0.17 – -0.00	**0.049**
Education	0.046	1.13	-0.03 – 0.13	0.259
Conflict	0.002	0.08	-0.06 – 0.06	0.939
Neighborhood				
Residential Density (log)	0.002	0.05	-0.06 – 0.06	0.957
Perceived Safety	-0.043	1.16	-0.03 – 0.12	0.245
Crime Rate	0.031	0.82	-0.04 – 0.11	0.413
Area Deprivation Index PC1	-0.040	-0.95	-0.12 – 0.04	0.344
Air Pollution	-0.110	-2.69	-0.19 – -0.03	**0.007**
Observations (subjects)	878			
R^2 / Adjusted R^2	0.288 / 0.273			

Table 2. Regression results showing associations of air pollution and other variables with change in ccCPM network strength from baseline to Y2 in the ABCD Study sample. For the overall model, F(19, 859) = 19.31, p < .001. *β* coefficients are standardized to unit variance in predictor and outcome. CI shows 95% confidence intervals, and p-values smaller than .05 are in bold.

Aside from the air pollution, generally, associations between demographic, socioeconomic, and family environment measures observed in behavioral analyses did not replicate in the neural domain. The coefficient for family income had the opposite sign for behavior change (β = .048) and brain change (β = -0.087, t = -1.98, p = .049), and there was no significant relationship between family conflict and ΔZ_{ccCPM} in this sample. Although the association between neighborhood ADI and change was numerically similar in the behavioral (β

= -.034) and neural (β = -.040) domains, the relationship was not statistically significant in the smaller neuroimaging sample size (t = -.946, p =.344, N.S.). Finally, not including the baseline ccCPM strength in the predictors (**Supplementary Table S2**) weakened air pollution's association with ΔZ_{ccCPM} (β = -.080, t = -1.66, p = .097).

3. ccCPM networks' change mediates the association between air quality and behavioral performance change

After investigating the association between neighborhood air pollution and developmental changes of behavioral and neuroimaging markers of cognitive performance separately, we next assessed them jointly. First, we found that the change in ccCPM strength predicted change in *n*-back performance (out-of-sample *r* = .157, t = 4.72, p < .001, n = 878[1], correlation is adjusted for head motion) from baseline to the Y2 study visit. **Figure 3** depicts this relationship between *n*-back accuracy and ccCPM at baseline and the Y2 study visits as well as the association between ccCPM strengthening and *n*-back accuracy improvement (inset). This relationship (the *r* = .157 reported above) is indicated with the black arrow 'developmental gradient' starting at the medians of the distributions at baseline and ending at the medians of the distributions at Y2.

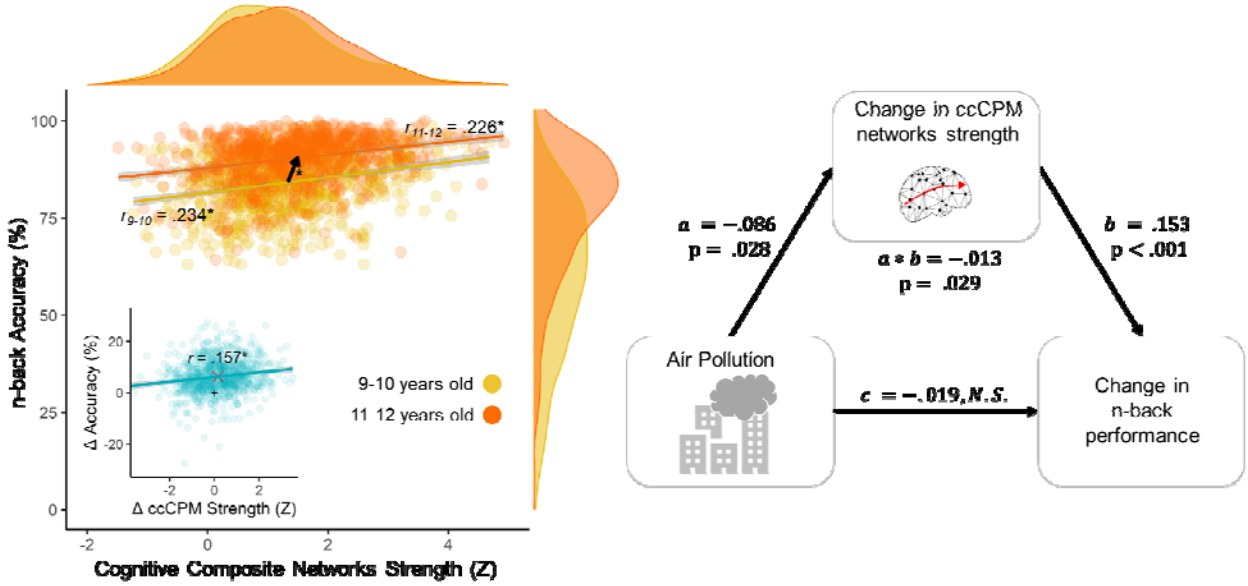

Figure 3. Left: The relationship between *n*-back accuracy and ccCPM strength at baseline (yellow; 9-10 years; *r* = .234, p < .001) and Y2 (orange; 11-12 years; *r* = .226, p < .001). Pearson correlations are adjusted for head motion. The black arrow connects the centers of the

[1] Out-of-sample *r* = .159 when using n = 1,159 participants, but for consistency with our next analysis we will use the n = 878 participants with full fMRI and environmental data in this section.

two distributions, starting at the medians of the distributions at 9-10 years of age and ending at the medians of the distributions at 11-12 years. Inset scatterplot shows the relationship between change in ccCPM strength and change in *n*-back accuracy across participants. **Right:** The proposed mediation model and resulting parameter estimates for air pollution's relationship with neurocognitive development of cognitive processes including attention and working memory from pre- to early adolescence.

Finally, we tested whether change in ccCPM strength (ΔZ_{ccCPM} adjusted for the covariates in the **Table 2** regression) mediated the effect of air pollution on change in *n*-back accuracy (ΔAcc adjusted for the covariates in the **Table 1** regression; **Figure 3**). First, the total effect of air pollution on change in *n*-back accuracy (adjusted for covariates) was not significant in the model with the limited sample, potentially due to the drop in statistical power (path c, $\beta = -.019$, $p = .623$, $n = 878$). Importantly, in a traditional mediation test (Baron & Kenny, 1986) this step would require stopping the mediation analysis. However, more modern approaches to mediation do not rely on change in path c and instead estimate a*b independently, thus permitting the estimation of the indirect effect in the absence of a significant 'total' effect [Zhao et al., 2010]. Therefore, we continued to test for the mediated effect (path a*b) and found an 'indirect-only mediation' (see [Zhao et al., 2010]) where the effect of air pollution on change in n-back performance was mediated by change in ccCPM strength ($\beta_{\text{indirect effect}} = -.013$, $p = .029$ based on 5000 bootstraps, $n = 878$). The mediated effect was such that higher air pollution was negatively associated with improvement in *n*-back task accuracy through decreased change in the strength of brain functional networks supporting general cognitive performance.

Discussion

Early adolescence is a period of growth in multiple domains, including neurocognitive performance. Understanding how environmental disparities may influence neurocognitive processes can help with identification of intervention targets and prioritization of efforts to reduce environmental disparities. In the current study, we found modest—but robust—associations between neighborhood air pollution and change in cognitive performance over a two-year period, from ages 9-10 to ages 11-12 in a large United States sample. Specifically, developmental change from pre- to early adolescence in both *n*-back task performance and the functional brain networks supporting cognitive performance were negatively associated with neighborhood air pollution, adjusted for baseline cognitive, demographic, and socioeconomic factors. Finally, we found an indirect-only mediation where the effect of air pollution on changes in *n*-back performance was mediated by the changes in functional brain connectivity strength in ccCPM networks.

Research has identified multiple pathways for air pollution to potentially impact neurocognition in aging populations [e.g., Thiankhaw et al., 2022; Shi et al., 2023] as well as in animal models [e.g., Shou et al., 2020]. One pathway that may be especially relevant during child development is the relationship between PM2.5 and NO2 exposure and sleep issues (e.g., breathing disordered sleep problems such as apnea [Billings et al., 2019]), which have been tied to negative consequences for developmental outcomes in both behavioral [Blechner & Williamson, 2016] and brain volumetric [Musso et al., 2020] domains. Another pathway is for specific neurotoxicant components like lead in PM2.5 to impact the brain potentially by traveling through the nasal cavity to the olfactory bulb and beyond [Underwood, 2017; Chen et al., 2020]. Future research should explicitly test potential pathways to shed light on how the development of functional brain architecture and cognitive performance is impacted by air pollutants during adolescence.

The study of the social determinants of healthy development has become an important focus of developmental cognitive neuroscience [D'angiulli et al., 2012; Johnson & De Haan, 2023]. One strength of our study is utilizing previously developed neuromarkers (i.e., the ccCPM) and implementing cross-validation in a large and geographically heterogeneous sample. Another is the longitudinal design of the ABCD *n*-back behavioral and fMRI connectivity data, which alleviates some of the concerns associated with cross-sectional studies of cognitive development. For example, when studying individual differences in development, low reliability of cognitive measures leads to a higher likelihood of spurious age-related associations in cross-sectional but not longitudinal samples [Lindenberger et al., 2011; Hedge et al., 2018; Karvelis et al., 2023]. Another strength of our study is the inclusion of both behavioral task and brain network measures to evaluate developmental change in neurocognitive functioning. Although behavioral measures are sufficient for establishing links between environmental factors and healthy development, assessing neuroimaging measures can complement behavioral studies and help shed light on potential neurodevelopmental mechanisms involved in these changes [Farah, 2018]. Additionally, these neuroimaging studies tend to have more traction with policy-makers in the fields of health disparities and environmental equity [Racine et al., 2010]. However, it is worth noting that studies that assess only neural indices as a function of environmental factors may suffer from reverse inference problem if their conclusions are not tied to any observed behavioral performance or self-report measures.

In addition to the strengths of our study, there are also some limitations to our work. First, the ABCD Study includes a geographically diverse sample of participants, but these

participants were nested within different data collection sites. There was very little variability in air pollution metrics for participants within each ABCD Study site, as would be expected given the intrinsic spatial autocorrelation of the air pollution measures in the data (10 Km squares around address of residence). This feature of the data set led the air pollution metrics to be strongly clustered within sites and therefore prevented us from conducting a hierarchical analysis in which site effects were accounted for with random intercepts, which would likely have led any air pollution effects to be misattributed as site effects. Thus, the reported relationships may be confounded with site data collection differences. However, our use of *change* measures of behavioral performance and brain connectivity, which subtracts out data collection differences across sites from our dependent variables (assuming these site idiosyncrasies were consistent between baseline and Y2 data collection), and our inclusion of extensive covariates capturing participants' baseline cognitive ability and their neighborhood safety and economic resources, overcome some of the site-related idiosyncrasies. Nonetheless, clustering effects in multi-site data sets are likely to remain a challenge for environmental neuroscience studies moving forward given the natural spatial autocorrelation of many environmental variables of interest. Second, the final neuroimaging sample was not nationally representative of the Black or African American population. Third, as released by the ABCD Study, we used ambient air pollutant concentrations in 10 Km squares around address of residence of the participants. More precise and elaborate measures of PM2.5 and NO2 (e.g., Di et al., 2019 and Di et al., 2020) and improved linkage to individual exposures (e.g., including school area and path from home to school) can enhance the regression model estimates by reducing the measurement error for air pollution exposure. Fourth, some neighborhood features such as street tree canopy could buffer some of the impact of air pollutants at a block-level scale (e.g., see Qi & Hankey, 2021; Tian et al., 2023; Kardan et al., 2015). However, these measures were not available for the ABCD data by Release 4. Future studies using more representative samples, more precise measures of air pollutant exposure and inclusion of other related environmental factors such as urban greenspaces and tree canopy could improve our models.

In conclusion, neighborhood air pollution was associated with decreased development of youth cognitive performance. These deficits may be mediated by weakened brain network connectivity strength in functional brain networks that support these abilities over time. This work highlights the importance of examining environmental factors, such as air pollutants, for interventions aimed at improving cognitive development at large scales.

Methods

fMRI data preprocessing and exclusions:

In the ABCD Study, for both baseline and two-year follow-up neuroimaging sessions, *n*-back task fMRI was acquired in two separate runs (~5 min per run, full details are described in [Hagler et al., 2019]). Briefly, images were acquired at spatial resolution (2.4 mm isotropic) and temporal resolution (TR = 800 ms). The entire data pipeline was run through automated scripts on the University of Michigan's high-performance cluster and is described in detail in [Sripada et al., 2021]. Key features of the pipeline include FreeSurfer normalization, ICA-AROMA denoising, CompCor correction, and censoring of high motion frames with a 0.5 mm framewise displacement threshold. The key difference was that we used the Shen parcellation (including 268 parcels) which encompasses cortical, subcortical, and cerebellar regions [Shen et al., 2013], instead of the Gordon parcellation used in [Sripada et al., 2021]. This was because the ccCPM was constructed in the Shen parcellation space by Kardan et al., 2022. To be included, a participant needed to have at least 4 minutes of data below the censoring threshold (i.e., 0.5 mm) per run in both *n*-back runs, to pass visual quality control on registration and normalization, and to not have a behavioral performance flag in the curated data released by the ABCD Study consortium.

Of the 11,875 participants enrolled in the ABCD Study, n = 7,278 had completed the *n*-back task at both time-points; 53% Male, 47% Female; 55% non-Hispanic White, 20% Hispanic, 13% Black, 12% Asian/Other. Of these, n = 1,159 passed the fMRI data criteria above at both baseline and Y2 (48% Male, 52% Female; 65% non-Hispanic White, 17% Hispanic, 7% Black, 11% Asian/Other, which underrepresents the US Black or African American population.)

n-back task:

The emotional *n*-back task in the ABCD Study dataset [Casey et al., 2018; Cohen et al., 2016] includes two runs. In each run, four blocks are 2-back for which participants are instructed to respond "match" when the current stimulus is the same as the one shown two trials back. The other four blocks are 0-back for which participants are instructed to respond "match" when the current stimulus is the same as the target image presented at the beginning of the block. Example trials from the task are shown in **Supplementary Figure S2**. The stimuli include pictures of places, faces with negative emotion, positive emotion, and neutral faces.

Functional connectivity analysis and ccCPM strength:

The youth cognitive composite Connectome-based Predictive Model (ccCPM) includes two sets of functional brain connections that predict higher or lower performance in the NIH-Toolbox in ABCD baseline release (**Figure 2**; Kardan et al., 2022) in a leave-one-site out connectome-based predictive modeling approach (CPM; Shen et al., 2017). In the current study, to quantify the cognitive composite network strength for ABCD participants from site k (both their baseline and Y2), we multiplied the functional connectivity matrices (calculated from the entire *n*-back task time series) of each participant at each time-point by the ccCPM mask that was originally constructed from participants from all sites excluding k:

ccCPM network strength = $\sum_{i,j}^{268} tanh^{-1}\left(r_{i,j}\right) * w_{i,j}$

Where $r_{i,j}$ is the Pearson's correlation between fMRI timeseries of brain parcels *i* and *j*, and $w_{i,j}$ is the ccCPM network mask value (from Kardan et al., 2022) of 0, 1, or –1.

[Kardan et al., 2022] trained ccCPM to predict the cognitive composite scores of participants at ages 9-10. Cognitive composite scores are the mean performance in 5 NIH-Toolbox tasks performed out-of-scanner by the ABCD participants: the Picture Vocabulary task, Flanker inhibitory control and attention task, Pattern Comparison processing speed task, Picture sequence memory task, and Oral Reading recognition task (Weintraub et al., 2013).

Air pollution and covariates:

Air pollution was calculated as the average concentrations of PM2.5 and NO2 (Z-scored across all participants before averaging to remove differences in the units of concentration) for each participant. The concentration values were released in ABCD R4.0 abcd_rhds01.txt using [Geddes et al., 20117] and [van Donkelaar et al., 2018] (shared R scripts show details of the variable names from .txt files included in regression models, we used residential address 1, released values do not reflect families moving between data collections).

The baseline neurocognitive covariates in the multiple regressions (BPPC 1 General Ability <Gen Ability>, BPPC 2 Executive Function <Exec Function>, and BPPC 3 Learning/Memory <Learn Mem>) were from [Thompson et al., 2019], who applied Bayesian Probabilistic Principal Component Analysis (BPPCA; Tipping & Bishop, 1999) to cognitive measures with low missingness in baseline ABCD Study data including the List Sorting Working Memory Test, Picture Vocabulary Test, Flanker Task, Dimensional Change Card Sort Task, Pattern Comparison Processing Speed Test, Picture Sequence Memory Test, Oral Reading Recognition Task, the Rey Auditory Verbal Learning Test, and the Little Man Task (see

Thompson et al., 2019). BPPCA component weights for each participant were made available with the ABCD Study curated data release 2.0.1.

The ABCD Study Consortium extracted crime rate from the adult violent crimes and drug abuse and sales using FBI data, and perceived neighborhood safety was measured using youth and caregiver reports (see [Meredith et al., 2022] for details).

Finally, the Area Deprivation Index (ADI; [Kind et al., 2014]) was constructed from 17 variables including proportion of neighborhood residents with high school diploma, unemployment rate, low income, and housing statistics from the American Community Survey (see our shared scripts for all variable names). We summarized these 17 variables into one main Principal Component using PCA, which explained 49% of variance among the variables and was related to lower socioeconomic resources in the neighborhood across all variables. The second PC (13% variance) was not significantly related to cognitive performance and therefore we did not include it as a covariate in the regression models.

Mediation analysis:

The mediation was performed using the *mediation* package in R with the built-in bootstrapping option for computing *p*-values for the coefficients and the mediated effect (5000 bootstraps). The model included air pollution as the predictor, change in *n*-back performance (ΔAcc) adjusted for all covariates (shown in **Table 1**) as the dependent variable, and change in ccCPM network strength (ΔZ_{ccCPM}) adjusted for all covariates (shown in **Table 2**) as the mediator.

Data and code availability

All ABCD Study data are available at https://nda.nih.gov. Analysis scripts to generate results and figures in the manuscript will be available on https://github.com/okardan/ABCD_Air upon publication. The ccCPM is available from Kardan et al., 2022 National Institute of Mental Health Data Archive (NDA) study 1849 doi: 10.15154/1528288.

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The ABCD data repository grows and changes over time. The ABCD data used in this report came from NIMH Data Archive Digital Object Identifier 10.15154/1523041.

Secondary analysis of ABCD Study data was approved by the relevant University of Chicago Institutional Review Board.

Competing Interests

The authors declare they have no known competing conflicts of interest, financial or personal, that could have appeared to influence the work reported in this paper.

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Supplementary Material and Results

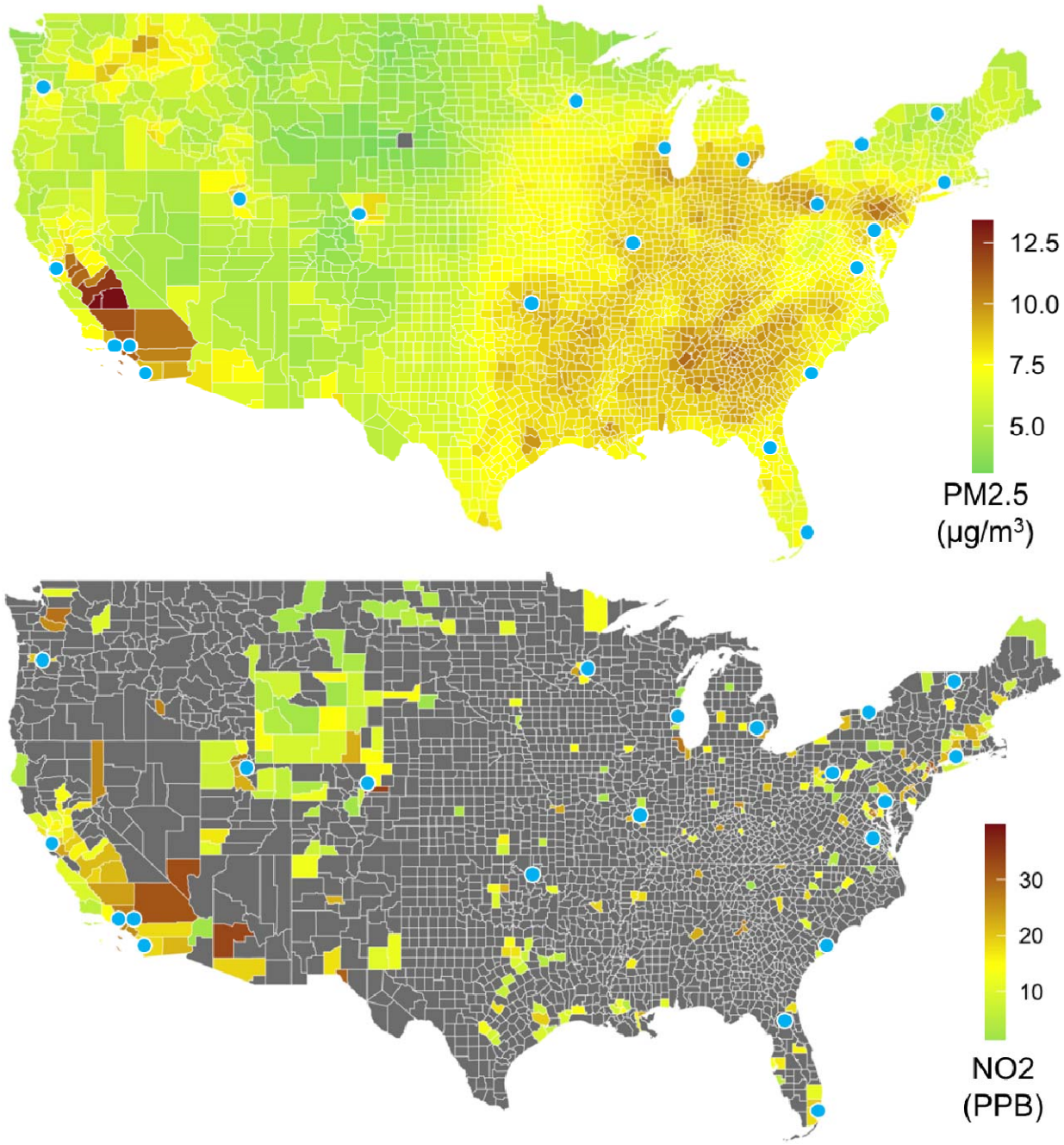

Figure S1. Separate United States county-level maps for PM2.5 concentration (top) and NO2 concentration (bottom) based on the 2016-2018 average US Environmental Protection Agency Air Quality Database. Ground-level NO2 is only measured in urban counties by the US EPA because its source is limited to burnt fuel.

	Outcome: n-back ΔAcc			
Predictors	*β*	*t*	*CI*	*p*
(Intercept)	*(0.565)*	*(41.25)*	*(0.55 – 0.58)*	***<0.001***
Base Cognitive Ability				
BPPC 1 Gen Ability	-0.045	-2.67	-0.07 – -0.01	**0.008**
BPPC 2 Exec Function	-0.042	-2.90	-0.07 – -0.01	**0.004**
BPPC 3 Learn Mem	-0.041	-2.67	-0.07 – -0.01	**0.008**
Sex & Race/Ethnicity				
Male	-0.048	-3.35	-0.07 – -0.02	**0.001**
White	0.024	0.99	-0.02 – 0.07	0.322
Black	-0.035	-1.71	-0.07 – 0.00	0.087
Hispanic	0.028	1.26	-0.02 – 0.07	0.206
Asian/Other	0.002	0.013	-0.03 – 0.03	0.901
Family				
Income	0.003	1.46	-0.01 – 0.07	**0.003**
Education	0.016	0.83	-0.02 – 0.05	0.725
Conflict	-0.005	-0.32	-0.03 – 0.02	**0.011**
Neighborhood				
Residential Density (log)	0.026	1.62	-0.01 – 0.06	0.106
Perceived Safety	0.004	-0.22	-0.03 – 0.03	0.824
Crime Rate	-0.004	-0.23	-0.04 – 0.03	0.820
Area Deprivation Index PC1	-0.011	-0.58	-0.05 – 0.03	0.562
Air Pollution	-0.047	-3.11	-0.08 – -0.01	**0.002**
Observations (subjects)	5,256			
R^2 / Adjusted R^2	0.013 / 0.010			

Table S1. Regression results showing associations of air pollution and other variables with change in n-back performance from baseline to Y2 in the ABCD study sample without including baseline n-back accuracy in the predictors. For the overall model, $F(17, 5239) = 4.32$, $p < .001$. *β* coefficients are standardized to unit variance in predictor and outcome.

	Outcome: change in ccCPM strength			
Predictors	*β*	*t*	*CI*	*p*
(Intercept)	*(0.284)*	*(7.11)*	*(0.21 – 0.36)*	***<0.001***
Head Motion	0.004	0.11	-0.06 – 0.07	0.916
Base Cognitive Ability				
BPPC 1 Gen Ability	0.126	3.05	0.04 – 0.21	**0.002**
BPPC 2 Exec Function	0.011	0.28	-0.06 – 0.08	0.779
BPPC 3 Learn Mem	-0.009	-0.25	-0.08 – 0.06	0.806
Sex & Race/Ethnicity				
Male	-0.023	-0.67	-0.09 – 0.04	0.500
White	-0.138	-2.09	-0.27 – -0.01	**0.037**
Black	-0.031	-0.51	-0.15 – 0.09	0.608
Hispanic	-0.075	-1.24	-0.20 – 0.04	0.216
Asian/Other	-0.029	-0.69	-0.11 – 0.05	0.493
Family				
Income	-0.093	-1.81	-0.19 – 0.01	0.071
Education	0.008	0.16	-0.09 – 0.10	0.869
Conflict	0.013	0.38	-0.06 – 0.08	0.707
Neighborhood				
Residential Density (log)	-0.024	-0.68	-0.09 – 0.04	0.494
Perceived Safety	-0.042	0.97	-0.04 – 0.13	0.330
Crime Rate	0.040	0.90	-0.05 – 0.13	0.369
Area Deprivation Index PC1	-0.102	-2.06	-0.20 – -0.00	**0.040**
Air Pollution	-0.080	-1.66	-0.17 – 0.01	0.097
Observations (subjects)	878			
R^2 / Adjusted R^2	0.027 / 0.007			

Table S2. Regression results showing associations of air pollution and other variables with change in ccCPM network strength from baseline to Y2 in the ABCD study sample without baseline ccCPM included as a predictor. The model is not explaining a significant amount of variance in the dependent variable ($F(18, 860) = 1.39$, $p = 0.139$).

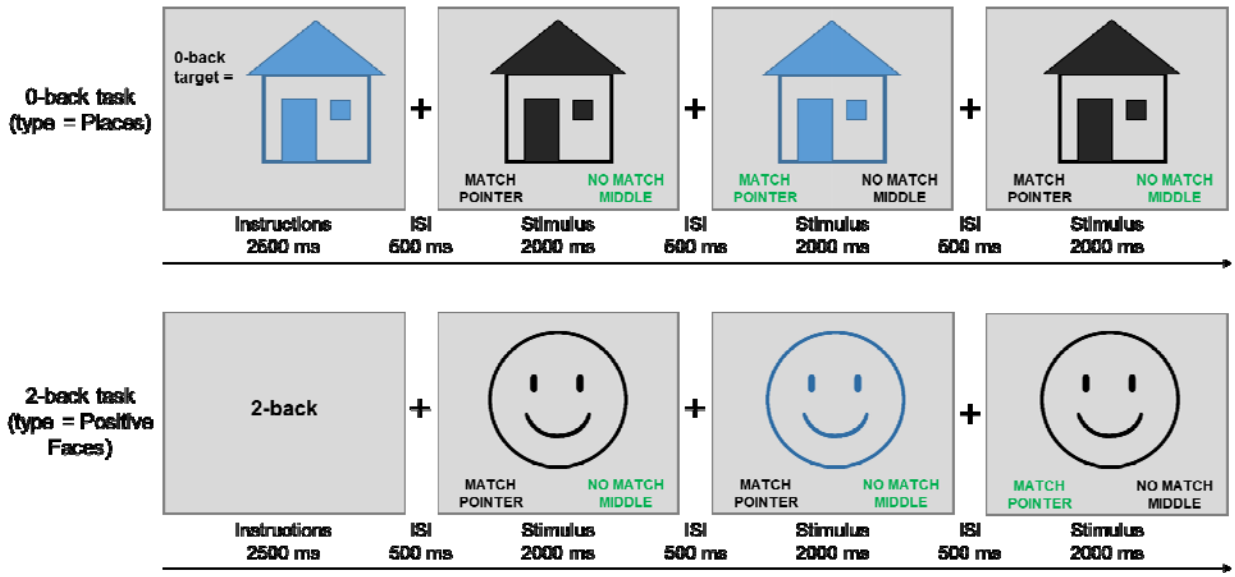

Figure S2. The instruction and first 3 trials in a block of 0-back task (top, example from Places block type) and 2-back task (bottom, example from Positive Faces block type) are shown in this figure. Real stimuli are replaced by icons to comply with bioRxiv figure policies. The correct choice for each trial is indicated in green text. The figure is adapted from [Casey et al., 2018].