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Multilayer network associations between functional brain development and home and neighborhood exposomes

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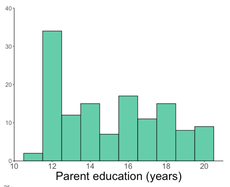
Introduction

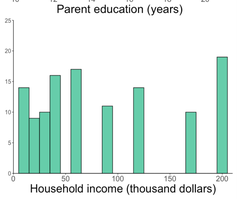
- Early-life stress (ELS) and socioeconomic status (SES) are associated with changes in the pace of brain maturation[1]
- Neighborhood-level stressors and household SES show effects on functional brain development[1]
- Functional systems undergo segregation into modular and clustered networks throughout early childhood[2,3]
- To date, research shows neighborhood deprivation index is associated with decreased global system segregation in adolescence[4] but has not been studied in childhood
- Studies of ELS & SES effects on the brain show univariate associations with ELS or SES exposure sum scores[4-6] but not multivariate associations with individual indices, such as crime, inequality, pollution
- In this study, we take a data-driven approach to reveal the multivariate associations between functional system measures and exposures to SES and ELS at the home and neighborhood levels (exposome[7]).

Methods

Sample. Children ages 4 to 10 recruited from the Philadelphia area (N = 131)

Demographics	
Age (SD)	6.7 (1.4) | 4.1– 10.6
Sex	53% F, 47 % M, 0% other
Parental education (years)	15.1 (2.7) | 11 – 20
Ethnicity & Race ** (sum > 100% because of > 1 race)*	11.5% Hispanic 51.2% Black 42.8% White 13.7% Asian 2.3% Native Hawaiian or Other Pacific Islander 1.5% American Indian/Alaska Native 3.1% Other
Household income (thousand dollars)	85.7 (68.0) |2.5 – 200
Average motion (mm)	0.30 (0.18)





Inclusion criteria: full-term (> 34 weeks) and birthweight > 5 lbs, no diagnosed neurological or psychiatric conditions, no learning disabilities, FD lower than 1mm, more than 135 volumes, fewer than 30% scans with lower than 0.5mm FD

Parent-reported home exposome measures

- ***Household SES measures:*** *parental education* and *household income*
- ***Adverse Childhood Experiences score*** (ACEs)***:*** Parent's report on their child's lifetime exposure to traumatic events

Geocoded neighborhood (census-tract) exposome measures

- ***Unemployed people above the age of 16***[8]
- ***People with a Bachelor's degree above the age of 25***[8]
- ***Gini Inequality Index****:* Summary measure of the distribution of income[8]
- ***Incidence of high blood lead levels****:* Percentage of children tested with a blood lead level concentration higher than 5 µg/mL[9].
- ***Total Crime Index:*** Regression-model predicted crime index in a census tract from FBI National Crime Data[10].
- ***Particulate matter concentration****:* Measure of concentration of fine inhalants[11,12].

Neuroimaging: resting-state functional connectivity (FC)

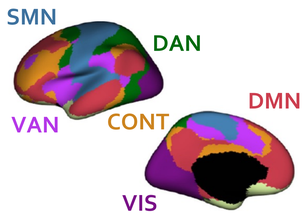
- Preprocessing and QA checks conducted using MRIQC[13], fMRIPrep[14], and xcpEngine[15]
- All neuroimaging measures were residualized for age, average edge weight, FD and % of spikes above 0.5 mm, FD, and total number of volumes

Multilayer network models: graphical LASSO model

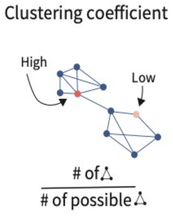
- Multilayer networks were modelled using an EBIC graphical LASSO partial correlation approach (EBICglasso in *glasso*[16] and *bootnet*[17] R package)
- Graphical LASSO models regularize partial correlation matrices by removing weak edges and then pick the model with the lowest Bayesian Information Criterion – both of which reduce False Discovery Rate (FDR)[16-18]
- Although we modelled networks with bilateral intra- and inter-system FC and individual system FC network models for other systems, we only include those with bridge edges

Results

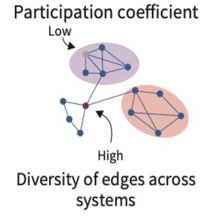
Functional network development



We used the Yeo 7 networks[19] to extract BOLD functional connectivity with N = 400 Schaefer parcels[20]



↑ with age[2]



↓ with age[2]

Node & edge legend

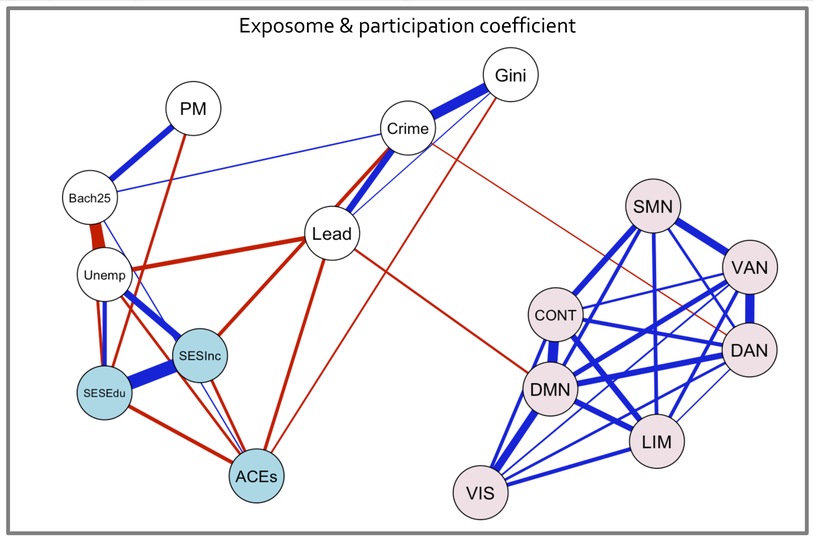
NODE LABELS:

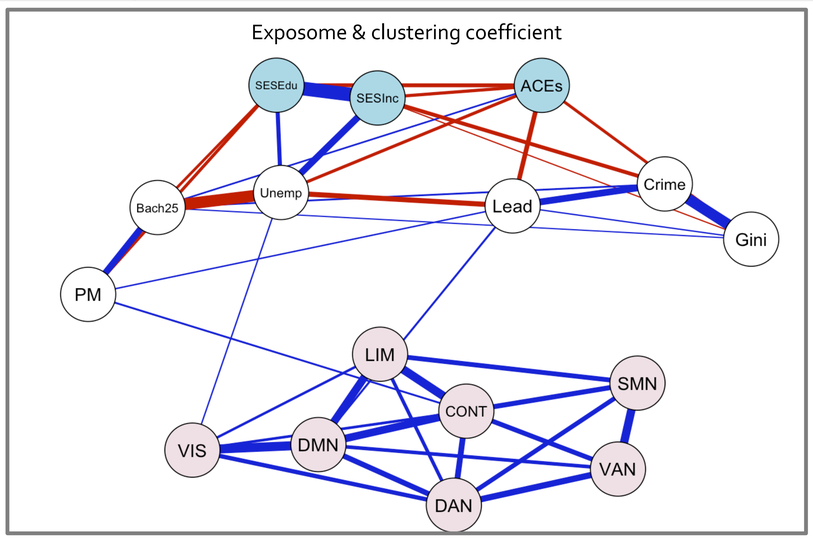
Lead: High blood lead level incidence
PM: Particulate Matter
Bach25: People 25+ with higher education
Unemp: Unemployment
Crime: Total Crime index
Gini: Inequality index
ACES: Adverse Childhood Experiences
SESEdu: Parent Education
SESInc: Household Income
VIS: Visual network
SMN: Somatomotor network
DAN: Dorsal attention network
VAN: Ventral attention network
LIM: Limbic network
DMN: Default mode network
CONT: Control network

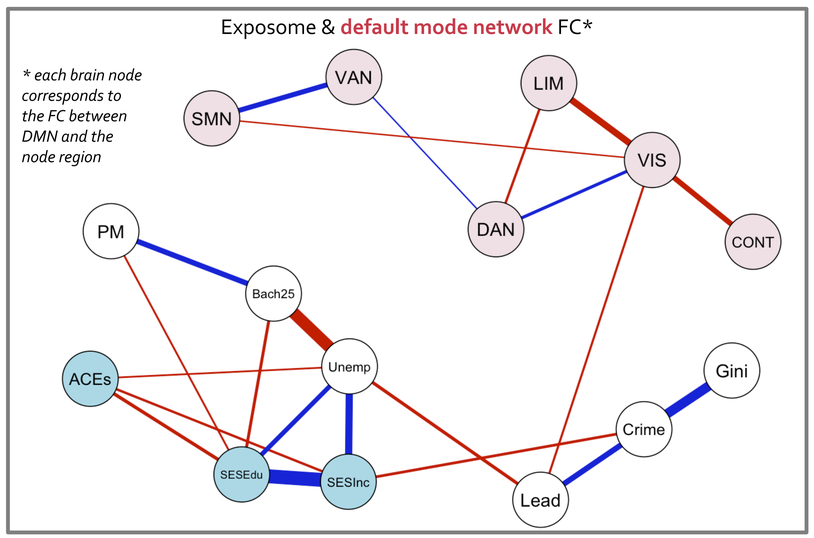
NODE COMMUNITIES: Neural Neighborhood-level Home

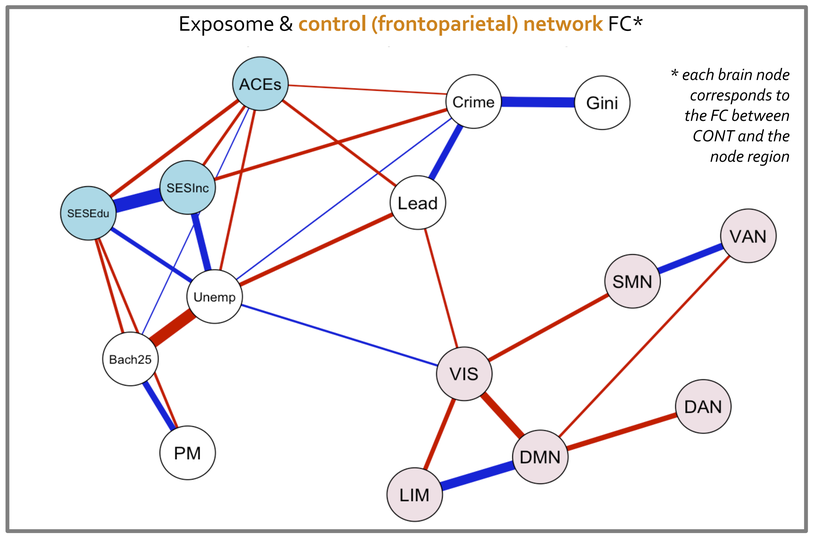
EDGE WEIGHTS: Positive weights Negative weights

Global (participation and clustering coefficient) & individual network FC bilayer network models









Discussion

- DAN participation but not clustering coefficients were associated with the crime index. Harsh environments, such as those with higher policing and crime, are associated with higher levels of vigilance and stress-adapted attention.[21] Previous resting state fMRI studies show increased DAN within-network FC with area deprivation but also other between-network FC changes.[22]
- DMN network structure was associated blood lead levels. As the DMN is located along cerebral vasculature, the association between DMN segregation with lead exposure may show a mechanism of blood toxin exposure effects on brain function; however, further research is necessary across toxins and at different developmental timepoints of exposure. For example, previous studies show increased DMN clustering coefficients in children exposed to pesticides[23]; but, air pollutants show the inverse effect[24], suggesting variations in toxin effects.
- Network models are sensitive to the choice of parameters (how conservative should the model be?) and variable sparsity (how many are independent?). For a more rigorous model of the exposome-brain relationship, further model selection analyses need to be performed.

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