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Community and Household-Level Socioeconomic Disadvantage and Functional Organization of the Salience and Emotion Network in Children and Adolescents

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Abstract

Socioeconomic disadvantage (SED) during childhood has been linked to disparities in physical and mental health. A growing body of research has focused on identifying neurodevelopmental consequences of SED, commonly measured using within-household factors (e.g., household income), to better understand the processes underlying SED-related disparities. These studies suggest that childhood SED has a widespread impact on brain development, altering development of multiple brain regions simultaneously. These findings also raise the possibility that childhood SED impacts development of key brain systems, such as the salience and emotion network (SEN), which is positioned at the intersection of brain systems involved in cognitive and emotion-related functioning and is thought to mediate information flow within and between these networks. The present study tests for associations between household- and community-level SED, as well as their interaction, and measures of SEN-based functional neural organization in 57 children and adolescents (ages 6–17). We applied graph theoretical analyses to resting-state functional magnetic resonance imaging (fMRI) to examine SEN-based functional network topology. Results showed that youth residing in more distressed communities demonstrate lower hub-like properties (i.e., less efficient global information transfer and fewer connections) of two core SEN nodes – the anterior cingulate cortex and the left supramarginal gyrus. Household income had an opposite effect on efficiency of the anterior cingulate, but no effect on the supramarginal gyrus. There was,

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however, an interaction between income and community SED in the rostral prefrontal cortex, such that higher income was associated with higher clustering coefficient and lower betweenness centrality, suggesting greater local processing and lower influence of this region on information flow across the network. These effects were significant only among youth living in low (but not high) SED communities, suggesting that within-household SED factors may not protect against the detrimental effects of a disadvantaged community context. Similarly, the age-related increase in average path length of the left rostral prefrontal cortex was only significant among youth living in low (but not high) SED communities. Given that maturation of the SEN is considered to be a critical functional backbone supporting the development of more flexible cognitive and emotional processes into adulthood, we tested for links between SEN graph metrics and measures of cognitive and emotion-related functioning. We found that higher community SED and lower income were both associated with lower IQ. Lower IQ, in turn, was associated with global efficiency of the left supramarginal gyrus. Observed effects of SED on SEN-based functional neural organization may help to explain the strong and pervasive link between childhood SED and disparities in cognitive and emotional outcomes.

Keywords

Socioeconomic status; salience network; graph theory; resting-state; functional connectivity; income

1. Introduction

A wealth of research demonstrates a link between childhood socioeconomic disadvantage (SED) and a range of poor outcomes (Boardman & Saint Onge, 2005). As a group, children reared in socioeconomically disadvantaged environments are at greater risk of behavioral and emotional problems, perform worse on cognitive and achievement tests, and are more likely to experience developmental delays than their more advantaged counterparts (Brooks-Gunn & Duncan, 1997; Duncan, Brooks-Gunn, & Klebanov, 1994). In addition, childhood SED is linked to lower occupational and educational attainment and poorer physical and mental health, even decades later into adulthood (Guralnik, Butterworth, Wadsworth, & Kuh, 2006; Minkler, Fuller-Thomson, & Guralnik, 2006; Zeki Al Hazzouri, Haan, Galea, & Aiello, 2011). With approximately 41% of U.S. children under 18 years old living in poor or near-poor families (Koball & Jiang, 2018), there is a need to identify the neurocognitive domains that underlie the pervasive disparities in outcome.

A growing body of behavioral research demonstrates that the consequences of childhood SED may be mediated via detrimental effects on several core cognitive and emotion-related domains, including executive functioning, language, memory, and social-emotional processing (see review by Farah, 2017). Neuroimaging studies have demonstrated SED-related structural and functional changes in brain areas implicated in executive functioning (e.g., prefrontal cortex; Noble et al., 2015), language (e.g., left superior temporal gyrus; Noble, Houston, Kan, & Sowell, 2012), memory (e.g., hippocampus; Hanson, Chandra, Wolfe, & Pollak, 2011), and socio-emotional processing (e.g., amygdala; Gianaros et al., 2008). As a group, these studies suggest that childhood SED has widespread impact on brain development, altering development of multiple brain regions simultaneously. These findings also raise the possibility that childhood SED impacts development of key brain systems that are positioned as integrated hubs in the brain and play a central role in larger-scale patterns of neural integration across several cognitive or emotion-related domains.

One intriguing possibility is that childhood SED influences the development of the salience and emotion network (SEN), a brain network positioned at the nexus of cognitive, homeostatic, motivational and emotional systems in the brain. Importantly, the SEN has been shown to play a critical causal role in switching between large-scale brain networks involved in higher-order cognitive and emotion-related processes, including executive functioning and memory (Menon, 2015). Key regions of the SEN include the anterior cingulate cortex, anterior insula, rostral prefrontal cortex, and supramarginal gyrus. Studies have consistently identified SEN regions as ‘hub’ regions, which are highly interconnected regions of the brain that are engaged in a wide range of cognitive and emotion-related processes and plays a prominent role in global communication processes by linking functionally segregated remote brain regions (van den Heuvel, Kahn, Goñi, & Sporns, 2012). This is in contrast to regions such as the primary visual cortex, which participate in one or a small number of functional networks and have little cross-talk with regions in other networks. Further, prominent neurodevelopmental models consider maturation the SEN to be a critical functional backbone supporting the development of more flexible cognitive and emotional processes into adulthood (Menon, 2015). Given this protracted development and functional significance, the SEN may be particularly sensitive to potent developmental exposures, such as childhood SED. Exposure to SED during childhood may lead to altered development of the SEN, which may help to explain the strong and pervasive link between childhood SED and a wide range of disparities (e.g., mental health, academic and occupational performance). In support of the notion that the SEN is affected by childhood SED, the largest structural neuroimaging study on SED in a pediatric sample published to date (N = 1,099) found that SED (as measured by family income) accounted for a significant portion of the variation in cortical surface area of several brain regions, including the anterior cingulate cortex, supramarginal gyrus, insula, and rostral frontal regions (Noble et al., 2015). However, no studies to date have examined the impact of childhood SED on connectivity of the SEN or its functional properties within the brain (e.g., integration of the SEN with other key brain regions, importance of SEN regions in the context of the whole brain as a network).

Moreover, childhood SED is most commonly measured using within-household factors, such as family income and parental education. However, compelling research demonstrates the importance of broader, community-level SED factors such as community poverty levels or unemployment rates, on child development and health outcomes. For example, Leventhal & Brooks-Gunn (2000) estimated that neighborhood- and community-level SED accounts for up to 10% of variation in child development, well-being, and health. A recent neuroimaging study by Gianaros and colleagues (2017) demonstrates that community SED can impact whole-brain organization in adults. In particular, the authors found that midlife adults residing in more distressed communities demonstrated lower cortical gray matter volume (Gianaros et al., 2017). Interestingly, they found no direct effects of household-level SED, or household x community SED interaction on cortical morphology. These results suggest unique effects of SED measured at the household and community level on brain organization (see Figure 1), which may help to extend epidemiological studies of community SED disparities to the level of the brain. Gianaros and colleagues (2017) hypothesized that the adverse effects of community SED on brain morphology may have originated during development; however, at the time no studies had been conducted to evaluate the potential effects of community SED on brain organization in children or adolescents. In a recent study, we showed that corticostriatal resting-state functional connectivity was differentially affected by community-versus household-level SED in children and adolescents (Marshall et al., 2018). Together, these studies support the notion that the effects of different environmental levels of SED are distinct (Figure 1).

The present study tested the effect of household- and community-level SED, and their interaction, on SEN-based functional neural organization in children and adolescents. Importantly, the present study was centrally located in Detroit, Michigan, a city with the highest proportion of the population living within a distressed zip code (98.9%) within the US (http://eig.org/dci). Thus, we tested these associations in a racially and economically diverse sample of youth. We used resting-state functional magnetic resonance imaging (fMRI), and focused on the functional role of the SEN in relation to the rest of the brain, given that brain hubs and their role in information processing can best be understood by examining their connections and properties of network organization (Cohen & D'Esposito, 2016; Sporns, 2013). To achieve this, we used graph theoretical analyses to examine the impact of household- and community-level SED on complementary measures of SEN-based functional segregation (i.e., independent, specialized networks) and functional integration (i.e., dependent, interconnected networks) (Cohen & D'Esposito, 2016; Sporns, 2013). Of note, both segregation and integration of brain networks are considered critical for higher-order cognitive and emotion-related functioning (Cohen & D'Esposito, 2016). Following previous studies demonstrating unique effects of household- and community-level SED on brain structure and function (Gianaros et al., 2017; Marshall et al., 2018), we hypothesized distinct effects of household and community SED on functional properties of the SEN in youth. In particular, we hypothesized that youth residing in lower income families or more distressed communities would show a lower number of connections of SEN regions (i.e., lower degree), lower importance of SEN regions to information flow across the whole brain network (i.e., lower betweenness centrality), lower extent of information transfer across regional neighbors and across the network (i.e., lower global and local efficiency), lower communication efficiency of SEN regions (i.e., longer average path length), and/or more segregated, 'cliquey', processing (i.e., higher clustering coefficient). Given that connectivity of the SEN has been shown to shift between childhood and adulthood (Uddin, Supekar, Ryali, & Menon, 2011), age was controlled for in all analyses and we examined potential age x household or community SED interactions on brain metrics. To explore brain substrates that may underlie SED-related disparities in psychological health, we tested for potential effects of household- and community-level SED on behavioral measures of cognitive and emotion-related functioning, and potential associations with brain metrics.

2. Materials and Methods

2.1 Participants

This study reports on 57 children and adolescents (30 females) between the ages of 6 and 17 (*M*=10.41, *SD*=2.89). FMRI data were collected in three additional youth, but these individuals were excluded from the study due to poor fMRI data quality (see 'Motion' section below). Participants were recruited from the greater Detroit Area through printed advertisements displayed around Wayne State University (WSU) and local clinic waiting rooms; electronic advertisements on the WSU online bulletin board and Craigslist; and in-person via local clinic waiting rooms and word-of-mouth. Exclusion criteria included past or current neurological injuries, significant learning disability, and English as a second-language. All participants and their parents provided written consent or assent following approval by the Institutional Review Board (IRB) of WSU. Although participants were not recruited for race or economic standing, the sample was racially and economically diverse (see Table 1). Pubertal development was measured using the self-reported Tanner stages questionnaire (Marshall & Tanner, 1968).

2.2 Socioeconomic Disadvantage Measures

Within-household SED was estimated using annual household income, reported by the parent within various categories (see Table 1). Community SED was estimated using participant zip codes, via the 2016 Distressed Communities Index (DCI; available at https://eig.org/wp-content/uploads/2016/02/2016-Distressed-Communities-Index-Report.pdf; see Figure 2a). The 2016 DCI combines seven socioeconomic indicators based on data from the US Census Bureau and business patterns from the year 2011 to 2015. The seven DCI metrics are weighted equally, and include: (1) percent of the population that are ages ≥25 years and without a high school diploma, (2) percent of the population living under the poverty line, (3) prime-age (ages 25–64) adults that are unemployed, (4) percent of habitable housing that is unoccupied, (5) median income ratio, (6) percent change in the number of jobs from 2011 to 2015, and (7) percent change in the number of business establishments from 2011 to 2015. Community SED scores range from 0 (least distressed) to 100 (most distressed). See Figure 2b for distribution of community scores and Table 1 for household income, across the sample. Consistent with the study location, as a group our sample was more likely to reside in more distressed communities ($M = 60.26$, $SD = 36.2$, $p = 0.019$ [one-sample *t*-test from mean value, 50]). However, there was significant variation in the sample, with ~30% of participants living in less distressed communities (i.e., scores < 30) and ~30% of participants living in households with annual incomes $100,000+. Not surprising, income and distress were negatively correlated ($r[57] = -0.7$, $p < 0.001$). In addition, given evidence that interpersonal threat-related adversity (e.g., violence, abuse) impacts SEN-based functional neural organization (e.g., Marusak, Etkin, & Thomason, 2015), and that threat-related adversity is more prominent among more disadvantaged communities (Rosenfeld, Edberg, Fang, & Florence, 2013), we measured and controlled for threat-related adversity in our sample using self- and parent-reports via the standardized Juvenile Victimization Questionnaire (Finkelhor, Hamby, Turner, & Ormrod, 2011). In this sample, threat-related adversity exposure was not associated with household or community SED (*p*'s > 0.2). In addition, to examine threat-related adversity at the community level, we examined objective city crime rates obtained via www.city-data.com. However, crime rate was collinear with community SED ($r(57) = 0.873$, $p < 0.001$), and was thus not entered as nuisance covariates.

2.3 Neurocognitive and Emotional Measures

To examine potential links between SED and cognitive functioning in the sample, child IQ was estimated using the K-BIT v.2 (Kaufman & Kaufman, 2004). To examine emotion-related functioning, parents completed the Child Behavior Checklist (CBCL) (Achenbach, Dumenci, & Rescorla, 2001), a widely used measure with excellent psychometric properties (Achenbach et al., 2001). We focused on T-scores for the broad-band internalizing (e.g., "unhappy, sad, or depressed") and externalizing (e.g., "impulsive or acts without thinking") scales of the CBCL, which have been shown to correspond with mood and anxiety disorders, and disruptive behavior disorders, respectively, among children and adolescents (Nakamura, Ebesutani, Bernstein, & Chorpita, 2009). Internalizing and externalizing behavior problems have both been linked to SED (Dearing, McCartney, & Taylor, 2006; Gilliom & Shaw, 2004).

2.4 Neuroimaging Data Acquisition

Ten minutes of eyes-closed resting-state data were acquired for each participant, using a research-dedicated 3.0 Tesla Siemens MAGNETOM Verio system (WSU School of Medicine MRI Research Facility). Blood-oxygen level-dependent (BOLD) fMRI data were collected using a multi-echo/multi-band (ME/MB) echo-planar imaging sequence, customized for the scanner and for pediatric imaging: 51 slices, 186 mm field of view (FOV), 64 × 65 matrix size yielding 2.9 mm isotropic resolution, in-plane GRAPPA acceleration factor 2, flip angle (FA) = 83 degrees, repetition time (TR) = 1.5 s, and echo time triplet (TEs) = 15, 31, 46 ms. ME fMRI is a bottom-up revision to fMRI methodology that allows for more principled removal of non-BOLD artifacts (Kundu et al., 2015; Lombardo et al., 2016). Effective denoising is particularly important for pediatric neuroimaging, given potential influence of excess head motion on results (Kotsoni, Byrd, & Casey, 2006). A high-resolution T1-weighted image was obtained for anatomical reference within the same session, using a magnetization prepared rapid acquisition gradient-recalled echo (MP-RAGE) sequence: 128 slices, 256 mm FOV, 384 × 384 matrix size yielding 0.7 × 0.7 × 1.3 mm resolution, in-plane GRAPPA acceleration factor 2, FA = 9 degrees, TR = 1.68 s, TE = 3.51 ms.

2.5 Neuroimaging Data Preprocessing

ME/MB fMRI data were submitted to ME-ICA software v3 (beta 1; https://bitbucket.org/prantikk/me-ica) for preprocessing and denoising. ME-ICA represents a significant advance in fMRI methodology that allows for enhanced detection and removal of head motion and other non-BOLD artifacts (e.g., cardiopulmonary physiology) via independent components analysis (ICA) (Kundu, Inati, Evans, Luh, & Bandettini, 2012). ME-ICA allows for more principled removal of non-BOLD signals from fMRI data via decomposition of ME fMRI datasets into independent components that are then categorized as BOLD or non-BOLD based on their TE-dependence (Kundu et al., 2012). In particular, whereas BOLD signal shows linear dependence of percent signal change on TE, non-BOLD signal amplitudes are TE-independent. ME-ICA has been applied to resting-state fMRI datasets and has been shown to be superior to several conventional fMRI and arbitrary denoising strategies (e.g., motion regression, band-pass filtering, removal of datapoints [“scrubbing”]) in terms of signal-to-noise ratio, fMRI effect sizes, and denoising (Dipasquale et al., 2017; Kundu et al., 2013, 2015; Lombardo et al., 2016; Power et al., 2018). Preprocessing in ME-ICA includes, in brief: (1) skull-stripping and warping of the anatomical image to the MNI template, (2) co-registration of the first echo timeseries for motion correction and for anatomical-functional co-registration, (3) de-obliquing of the functional data, and (4) 12-parameter affine anatomical-functional co-registration. In addition, the first 15 s of data were removed to allow for signal equilibration. No temporal filtering or smoothing was applied to the data. See Kundu et al. (2012) for further information.

2.6 Head Motion

To mitigate the potential influence of motion artifact in the data, we implemented several complementary approaches. First, prior to scanning, participants viewed a video to prepare them for their scan (available at www.tnp2lab.org/think-study-video) and underwent training on a kid-friendly mock scanner. Second, a trained member of the research staff remained in the room during the scan with a hand on the child’s leg to ensure comfort and adherence. Third, ME fMRI acquisition and ME-ICA denoising strategies were applied, as described above (Kundu et al., 2012). A recent study found that ME-ICA denoising was more effective than traditional denoising procedures (e.g., regression of motion parameters, white matter, or cerebrospinal fluid, FMRIB’S FIX, and ICA-AROMA) at reducing the impact of head motion on functional connectivity, even for high motion participants, and better preserved resting-state network structure (Dipasquale et al., 2017). Here, to quantify head movement across participants during the resting-state scan and to examine the impact of ME-ICA on movement, we calculated DVARS, a measure of frame-to-frame root mean square head change in BOLD signal (Power, Barnes, Snyder, Schlaggar, & Petersen, 2012). There was a significant reduction in head movement following ME-ICA denoising in the included 57 participants (pre $M \pm SD$: 0.99 ± 0.30% BOLD vs. post $M \pm SD$: 0.21 ± 0.05% BOLD, $p < 0.001$). In addition, no participants had DVARS values ≥ 0.5% BOLD following ME-ICA denoising, a threshold suggested for detecting excess head movement (Power et al., 2012). Of note, DVARS was not related to variables of interest, including household income or community SED (p’s > 0.5). Fourth, participants with low dimensionality fMRI datasets (<10 BOLD components) estimated using ME-ICA were excluded from the study (n = 3), leaving a total sample of N = 57. We excluded low dimensionality datasets given that low dimensionality may reflect poor image quality (for further discussion, see Marusak et al., 2017).

2.7 Construction of the Functional Brain Network

Resting-state functional connectivity was estimated using the ME-ICA processed data, following a technique developed by Kundu and colleagues (Kundu et al., 2013). This technique estimates functional connectivity between brain regions by measuring correlations between the coefficients of the BOLD ICA components derived from ME-ICA. This technique uses the number of independent BOLD components estimated via ME-ICA as the effective degrees of freedom for each subject, and thus controls for false positives in connectivity estimation. BOLD component data were submitted to CONN Functional

Connectivity Toolbox (v.17.f; www.nitrc.org/projects/conn) to perform connectivity analyses and to construct a functional brain network. The network consisted of the SEN and other brain regions of interest (ROIs, or ‘nodes’), and the functional connectivity (correlation) between ROIs (‘edges’). First, based on recent data suggesting that graph measures with nodes based on ICA are more accurate than graphs with anatomical-atlas based nodes (Yu et al., 2017), we used a set of 31 functionally-defined brain ROIs based on an ICA analysis of N = 497 participants from the Human Connectome Project Dataset available through the CONN Toolbox. Seven ROIs were from our primary network of interest, the SEN (also known as the cingulo-opercular network; Seeley et al., 2007): the anterior cingulate cortex (1,063 voxels), left anterior insula (446 voxels), right anterior insula (388 voxels), left rostral prefrontal cortex (1,166 voxels), right rostral prefrontal cortex (581 voxels), left supramarginal gyrus (233 voxels), and right supramarginal gyrus (284 voxels). Four ROIs were from the default mode network (DMN; Raichle, 2013); three from the sensorimotor network (Smith et al., 2009); four from the visual network (Smith et al., 2009); four from the dorsal attention network (Vossel, Geng, & Fink, 2014); four from the CEN (also known as fronto-parietal network; Zanto & Gazzaley, 2013); four from the language network (Smith et al., 2009); and two from the cerebellar network (Smith et al., 2009). Second, Pearson Bivariate correlation was used to compute functional connectivity, as the correlation of ICA coefficients between each ROI-ROI pair. Third, the resulting correlation matrix (reflecting functional connectivity between each ROI-ROI pair, for each subject) was normalized using a Fisher r-to-z transformation. Finally, to remove spurious connections and to obtain a sparsely connected correlation matrix, we applied an edge defining threshold of costs > 0.15 (one-sided; i.e., positive values). The cost (also known as connection density) of a network is the total number of edges in a network divided by the maximum possible number of edges. This threshold was chosen to ensure that each participants’ network has the same number of connections, which reduces the impact of network density on the computation and comparison of different graph metrics (Achard & Bullmore, 2007; van den Heuvel, Stam, Boersma, & Pol, 2008).

2.8 Extraction of Functional Brain Network Measures

Our main analyses focused on the regional properties of SEN ROIs. Thus, we extracted, for each participant, six network measures of functional integration and segregation for each SEN ROI with the rest of the brain network: (1) global efficiency and (2) local efficiency, which are widely used measures of communication efficiency and ability to integrate distributed information. Whereas global efficiency measures the extent of information transmission of a given ROI with all other ROIs in a network, local efficiency estimates the extent of information transmission among neighbors of the ROI. Global efficiency was calculated as the average inverse shortest path length between all nodes in the network. Local efficiency was calculated as a ratio of number of connections between a given ROI’s neighbors to the total number of possible connections. (3) Degree, defined as the number of connections at a particular node and indicates how well connected an ROI is (for e.g., hub regions are highly connected with a high degree). (4) Betweenness centrality, defined as the number of shortest paths that pass through a certain ROI and indicates the importance of the ROI to the information flow through the network (for e.g., hub regions contribute to a high number of paths and have a high betweenness centrality). (5) Average path length, defined as the distance (i.e., number of edges) between any pairs of ROIs in a network. Path length reflects the overall communication efficiency of a network, with shorter distance corresponding with more efficient information routing (i.e., fewer steps required for information exchange). (6) Clustering coefficient, a measure of network segregation calculated by the fraction of the ROI's neighbors that are also neighbors of each other. Brain networks that are more segregated therefore have more clustered connectivity around individual ROIs. For more information on network measures, see (Rubinov & Sporns, 2010).

2.9 Group-level Analyses

Using IBM SPSS v. 24 ($p < 0.05$ significance threshold), our primary analyses tested for correlations between the six graph metrics and household- and community-level SED, and their interaction (i.e., household income x community SED), for each ROI. Given the relatively wide age range, age was controlled for in all analyses (i.e., partial correlation). Secondary analyses tested for main effects of age on SEN graph metrics, and age x SED interactions. Given that six graph metrics were assessed for each ROI, we indicate in the Results section the effects that additionally survive a familywise Bonferroni correction (α = 0.008). All statistical tests were two-tailed. We also evaluated potential links among SED, brain measures, and measures of cognitive and emotion-related functioning using Pearson Bivariate correlation in SPSS. For graph measures that are related to SED, and also related with cognitive or emotion-related functioning, we further tested for potential mediating effects. In particular, we tested for potential mediating effects of SEN graph metrics on the link between SED and cognitive or emotional outcomes using the SPSS PROCESS macro. Five thousand bootstrap samples were used to create 95% confidence intervals. Mediation (i.e., the indirect effect) is considered significant if the lower level (LLCI) and upper level confidence intervals (ULCI) do not include zero.

3. Results

Global Topological Organization of the Functional Connectome in Children and Adolescents

Figure 3 is a visualization of whole-brain network organization across the entire pediatric sample, with size of the circle representing the efficiency of each node and SEN regions shown in red. Larger circles therefore denote ROIs with higher efficiency, and thus higher importance of that ROI for integration across the whole brain network. Of the 31 ROIs, the SEN right anterior insula and right supramarginal gyrus ranked 3rd and 5th highest, respectively, in terms of global efficiency (9th, left supramarginal gyrus; 10th, right rostral prefrontal cortex; 15th, left rostral prefrontal cortex, 16th left anterior insula; 21st, anterior cingulate cortex). For local efficiency, the SEN left supramarginal gyrus ranked 3rd highest (9th, right supramarginal gyrus; 12th, right rostral prefrontal cortex; 16th, left anterior insula; 18th, right anterior insula; 19th, left rostral prefrontal cortex; 24th, anterior cingulate cortex). Figure 4 is a visualization of the strength of SEN nodal connections with the other ROIs, using the right anterior insula as an example. Of note, the right anterior insula shows strong patterns of within- and between-network connectivity, with positive connectivity with other areas of the SEN, and negative connectivity with areas of the DMN and CEN. Similar patterns were observed for other SEN nodes, supporting the notion that the SEN is a highly connected, critical region for whole-brain network integration in children as well as adults (Uddin et al., 2011).

Effects of Household- and Community-level SED on SEN-Based Functional Neural Organization

Controlling for age, we found that children reared in higher distress communities showed lower global efficiency ($r[54] = -0.36$, $p = 0.006$; Figure 5a and Figure 6a) and lower degree ($r[54] = -0.28$, $p = 0.034$) of the anterior cingulate cortex. The former passed correction for multiple comparisons. Similar patterns were observed for the left supramarginal gyrus (global efficiency, $r[54] = -0.29$, $p = 0.042$, Figure 5b and Figure 6a; degree, $r[54] = -0.28$, $p = 0.036$). Conversely, higher income was associated with higher global efficiency of the anterior cingulate cortex ($r[54] = 0.29$, $p = 0.028$). Higher income was also associated with higher global efficiency of the left supramarginal gyrus, but this effect did not reach significance ($r[54] = 0.26$, $p = 0.05$). There was no interaction between community SED and household income for global efficiency or degree of any SEN region. The community SED x income interaction was, however, significant for betweenness centrality of right ($r[54] = 0.328$, $p = 0.014$) and left ($r[54] = 0.32$, $p = 0.017$) rostral prefrontal cortex, and also for clustering coefficient of the left rostral prefrontal cortex ($r[54] = -0.275$, $p = 0.042$). Follow-up analyses in low and high community SED groups (median split) suggested that the interaction is driven by an association between higher income and lower betweenness centrality of the left rostral prefrontal cortex among children who live in low ($r[26] = -0.401$, $p = 0.034$) but not high ($r[25] = 0.196$, $p = 0.328$) SED communities (Figure 7a and Figure 6b). For betweenness centrality of the right rostral prefrontal cortex, correlations between income and centrality did not reach significance in either low or high community SED groups (low community SED, $r[26] = -0.297$, $p = 0.125$; high SED, $r[25] = 0.356$, $p = 0.068$).

The effect of community SED on betweenness centrality of the left and right rostral prefrontal cortex did not reach significance in low or high income groups (median split, ps > 0.1). For clustering coefficient, higher income was associated with higher clustering of the left rostral prefrontal cortex, among children in low SED ($r[26] = 0.437$, $p = 0.023$) but not high SED communities ($r[25] = -0.164$, $p = 0.414$). In addition, when instead split by income group, higher community SED was associated with higher clustering coefficient of the left rostral prefrontal cortex among youth living in low ($r[33] = 0.4$, $p = 0.02$) but not high income households ($r[23] = -0.11$, $p = 0.63$).

Effects of Age on SEN-Based Functional Neural Organization

Older age was associated with higher average path length of the left rostral prefrontal cortex ($r[57] = 0.284$, $p = 0.032$) and right supramarginal gyrus ($r[57] = 0.288$, $p = 0.03$), and lower local efficiency of the right rostral prefrontal cortex ($r[57] = -0.275$, $p = 0.039$).

Age x Household/Community SED Interactions and Salience Network-Based Functional Neural Organization

There was a significant age x community SED interaction for average path length of the left rostral prefrontal cortex ($r[57] = -0.385$, $p = 0.003$) and the anterior cingulate cortex ($r[57] =$

−0.289, $p = 0.029$; see Figure 7b). The former survived correction for multiple comparisons. Follow-up analyses in low and high community SED groups (median split) suggested that the interaction was driven by an association between higher age and higher average path length of the anterior cingulate cortex among children who live in low ($r[29] = 0.454$, $p = 0.013$) but not high ($r[28] = -0.104$, $p = 0.6$) SED communities (Figure 6b). Similar findings were observed for the left rostral prefrontal cortex, such that higher age was associated with higher average path length among children from low ($r[29] = 0.414$, $p = 0.025$) but not high ($r[28] = 0.028$, $p = 0.886$) SED communities. The effect of community SED on average path length of the anterior cingulate cortex was not significant in low or high income groups (median split, ps > 0.1). There were no significant age x household income interactions.

Correlations between SED, Brain Functioning, and Measures of Cognitive- and Emotion-related Functioning

Lower IQ was associated with higher community SED ($r[57] = -0.484$, $p < 0.001$) and lower income ($r[57] = 0.417$, $p = 0.001$). The community SED x household income interaction was also significant ($r[57] = -0.262$, $p = 0.049$) such that higher income was associated with higher IQ among children living in low ($r[29] = 0.416$, $p = 0.025$) but not high distress communities ($r[28] = -0.023$, $p = 0.906$; Figure 8a). Next, we tested for correlations between IQ and SEN measures that were associated with community or household SED. Lower IQ was also associated with lower global efficiency of the left supramarginal gyrus ($r[57] = 0.265$, $p = 0.047$; Figure 8b). Given that global efficiency of the left supramarginal gyrus was also associated with higher community SED (see above), we tested whether global efficiency mediated the link between higher community SED and lower IQ. The indirect effect was not significant (LLCI = −0.01, ULCI = 0.043), suggesting no evidence of mediation. In this sample, parent reports of child internalizing and externalizing problem behavior were not associated with household income or community SED (p's > 0.1). There was, however, a correlation between higher externalizing problems and lower clustering coefficient of the right anterior insula ($r[54] = -0.347$, $p = 0.01$), suggesting more segregated processing.

4. Discussion

The notion that living in a relatively socioeconomically-distressed community may be bad for your health and child development is not new (Robert, 1999). This study examined the impact of household- and community-level SED, as well as their interaction, on SEN-based functional neural organization in a racially and economically diverse sample of children and adolescents. Our results (summarized in Figure 6) show that youth living in more distressed communities have lower global efficiency and degree of two core SEN nodes – the anterior cingulate cortex and left supramarginal gyrus. This suggests that SED measured at the community level may result in lower hub-like properties of core SEN regions, characterized by less efficient global information transfer and a fewer number of connections. There was an opposite effect of household income on efficiency of the anterior cingulate cortex, however the effect of income on the supramarginal gyrus did not reach significance. There was an interaction between income and community SED in the rostral prefrontal cortex, such that higher income was associated with lower betweenness centrality and higher clustering coefficient. These effects were only significant among youth living in low SED communities, suggesting that effects of within-household SED may be blunted by low community SED. Similarly, we observed that effects of age on average path length were only significant among youth living in low (but not high) SED communities. Taken together, our data suggest that community SED impacts the development of the SEN, a key brain network involved in the integration of sensory, cognitive, and emotional information to support the development of complex cognitive and emotion-related processes (Menon, 2015). Given that maturation of the SEN is considered to be a critical functional backbone supporting the development of more flexible cognitive and emotional processes into adulthood (Menon, 2015), we performed exploratory analyses to test for links between SEN graph metrics and measures of cognitive and emotion-related functioning. We found that higher community SED and lower income were both associated with lower IQ. Lower IQ, in turn, was associated with global efficiency of the left supramarginal gyrus. Although the mediation model was not significant, the observed effects of community SED on SEN-based functional neural organization may contribute to SED-related disparities in cognitive and emotional development.

Our findings reinforce the notion that household- and community-level SED may have distinct effects on brain development (see Figure 1). Prior studies have primarily focused on within-household measures of SED during childhood (e.g., household income), and have observed potent effects of household socioeconomic factors on the development of specialized brain areas for executive functioning (e.g., prefrontal cortex), memory (e.g., hippocampus), language (e.g., superior temporal gyrus), and social-emotional processing (e.g., amygdala). Here, we considered for the first time the effect of household and community SED on functional network interactions centered on the SEN, a critical dynamic hub for mediating interactions within and between other neurocognitive systems (e.g., DMN, CEN). We observed that some effects of community SED on two SEN regions (anterior cingulate cortex, left supramarginal gyrus) were not also associated with low household income, suggesting unique effects. In addition, we observed interactions between household income and community SED in a separate SEN region, the rostral prefrontal cortex. Given the critical importance of the SEN for whole-brain organization and its protracted maturational trajectory, examining the effects of SED on development of the SEN may provide a more integrative neurodevelopmental framework linking SED-related change across numerous cognitive and emotion-related domains. In addition, these results highlight the role of community SED in shaping neurodevelopment, and ultimately, disparities in cognitive and emotional outcomes (Chen, 2004).

Main effects of community SED on efficiency and connectivity of the SEN were observed in two regions: the anterior cingulate cortex and the left supramarginal gyrus. The supramarginal gyrus is associated with language, reading, and various executive functions (Ravizza, Delgado, Chein, Becker, & Fiez, 2004; Stoeckel, Gough, Watkins, & Devlin, 2009), and the anterior cingulate is involved in diverse functions, including attentional orienting, affective processing, behavioral selection, and error monitoring (Bush et al., 2002). These functions have been shown to covary with SED (e.g., Noble, McCandliss, & Farah, 2007). The anterior cingulate, in particular, is consistently recognized as a central and flexible network hub, with densely interconnections with other brain networks and a crucial position in terms of the whole brain network (for a review, see van den Heuvel & Sporns, 2013). In addition, the anterior cingulate integrates multimodal inputs and has direct connections with the motor system, allowing for rapid regulation of behavioral responding (Bush et al., 2002). Importantly, connectivity of the anterior cingulate undergoes dramatic reorganization during childhood and adolescence, with studies showing an age-related increase in within- and between-network connectivity (Fair et al., 2007; Uddin et al., 2011). Thus, anterior cingulate connections may be particularly sensitive to environmental exposures during development, such as socioeconomic climate. Our data suggest that children living in more distressed communities have less efficient global information transfer and a fewer number of connections of the anterior cingulate and the supramarginal gyrus. These effects were only counteracted by household income for global efficiency of the anterior cingulate and suggest that community SED may relate to lower hub-like properties of these regions during development.

Income x community SED interactions were observed in the rostral prefrontal cortex, a region that is interconnected with sensory regions and implicated in a wide variety of functions, including risk and decision making, affective processing, prospective memory, working memory, reward, and pain (Gilbert et al., 2006; Volle, Gonen-Yaacovi, de Lacy Costello, Gilbert, & Burgess, 2011). Here, we observed that higher income was associated with higher clustering coefficient and lower betweenness centrality, potentially indicating a shift towards more local segregated processing and less control of this region over information flowing through it, respectively. Interestingly, these effects were only significant among youth living in low distress communities; among high distress communities, there was no impact of income on the rostral prefrontal cortex. These observations suggest that effects of income were only observed in the absence of a distressed community environment, supporting the idea that certain environmental contexts may be necessary to mask or unmask the effects of household income on neural development.

Similarly, we observed effects of age on anterior cingulate cortex and left rostral prefrontal cortex, but only among children living in low (but not high) distress communities. In particular, among youth in low SED communities, older age was associated with higher average path length, which is consistent with a shift from short connections to longer path lengths from childhood to adulthood (Fair et al., 2007). Thus, community SED may interact with typical patterns of SEN development.

Given that the SEN is considered critical for higher-order cognitive processes, we tested for interrelations among IQ, SED, and SEN measures. We observed a significant income x community SED interaction on IQ, with low community SED and higher household income associated with the highest IQ scores. A previous study by the Infant Health and Development Program found that higher neighborhood affluence and lower family income to needs were both associated with lower children's IQ scores at age 5 (Duncan, Brooks-Gunn, & Klebanov, 1994b). Interestingly, we found that lower IQ was also associated with lower global efficiency of the left supramarginal gyrus. Lower global efficiency of the left supramarginal gyrus was also related to higher community SED, as described above. Although the mediation model was not significant, these observations may help to explain the neural substrates underlying SED-related cognitive disparities.

Although our findings shed new light onto potential environmental exposures that shape brain development, they raise further questions about potential mechanisms and functional implications of these changes. For example, a child living in a distressed community has the potential to be exposed to a large variety of environmental risk factors, including hazardous wastes, air pollution, water pollution, housing quality, and inadequate education facilities (Evans & Kantrowitz, 2002). It is unclear which factor(s) are driving observed changes. Of note, two SEN regions – the anterior cingulate cortex and the anterior insula – are the only brain areas that contains a specialized class of neurons, Von Economo neurons, that are responsible for the rapid relay of biologically-relevant information across long distances in the brain (see Ibegbu, Umana, Hamman, & Adamu, 2014 for a review). Given this critical function, and that these neurons develop rapidly during early childhood (Ibegbu et al., 2014), nutritional deficiencies, inflammation, and/or exposure to environmental toxins during childhood may be particularly detrimental to the development of the SEN. Future multi-level studies, coupled with parallel research in experimental animal models, may be better equipped to identify the mechanisms underlying the link between community SED and neurodevelopment.

Although this study had several strengths including a racially and economically diverse sample size of children, there are some limitations that warrant mention. The age range of the sample was relatively wide (ages 6–17 years). Although age was controlled for in analyses and we explored age x SED interactions, the brain continues to develop across the first two decades of life (Durston et al., 2001; Reiss, Abrams, Singer, Ross, & Denckla, 1996) which corresponds to changes in cognitive- and emotion-related functioning (Yurgelun-Todd, 2007). Larger sample sizes are needed to evaluate effects of age, pubertal development, and gender on the link between SED and brain organization. Another limitation is that SED measures were not evenly stratified across races/ethnicities. Participants were not recruited for race or economic standing, and future studies should consider recruitment into more evenly stratified groups. Further, consistent with previous observations (e.g., Hsieh & Pugh, 1993), crime rates were higher among more distressed communities. Thus, it is difficult to disentangle these complex effects. Participants were also not asked how long they have lived in their current zip codes (i.e., duration and levelof exposure to community distress), and the cross-sectional design limits our ability to examine how brain-behavior patterns unfold over time. While we found that higher community SED was associated with lower IQ, which was, in turn associated with lower global efficiency of the left supramarginal gyrus, the mediation model was not significant. Future longitudinal studies may be better suited to identify later-emerging mediation effects in cognitive outcomes, school performance, or health. In particular, inclusion of additional self- or parent-report measures, or of laboratory-based cognitive and behavioral testing may be more sensitive to these effects. Given reported links between poor neighborhood quality and higher risk of all-cause mortality (Bosma, Dike van de Mheen, Borsboom, & Mackenbach, 2001) and cardiovascular risk factors (e.g., diabetes, smoking, body mass index, blood pressure; Cubbin, Hadden, & Winkleby, 2001), future studies should examine the association between SED-related effects on the brain and measures of physical health (e.g., cardiovascular functioning).

Conclusions

We found that efficiency and connectivity of core SEN regions was altered by the community socioeconomic climate in which youth reside (see Figure 6). There were also significant community SED x household income interactions in the SEN rostral prefrontal cortex, such that effects of income were only significant among youth living in low distress communities. Similarly, there was an age-related increase in path length of SEN-based connections, but only among low SED communities. Given the critical role of the SEN in whole-brain functioning and higher-order functions, altered development of the SEN may help to explain the link between childhood SED and a range of cognitive- and emotion-related outcomes. Indeed, lower IQ was associated with lower global efficiency of the SEN left supramarginal gyrus, which was, in turn associated with higher community SED. Together, this study provides the first empirical support for the notion that community-level SED impacts SEN-based functional neural organization in a pediatric sample and may provide new insights into socioeconomic health disparities. Early intervention that targets youth living in disadvantaged neighborhoods and focus on lowering the severity and exposure of environmental factors may reduce poor health outcomes.

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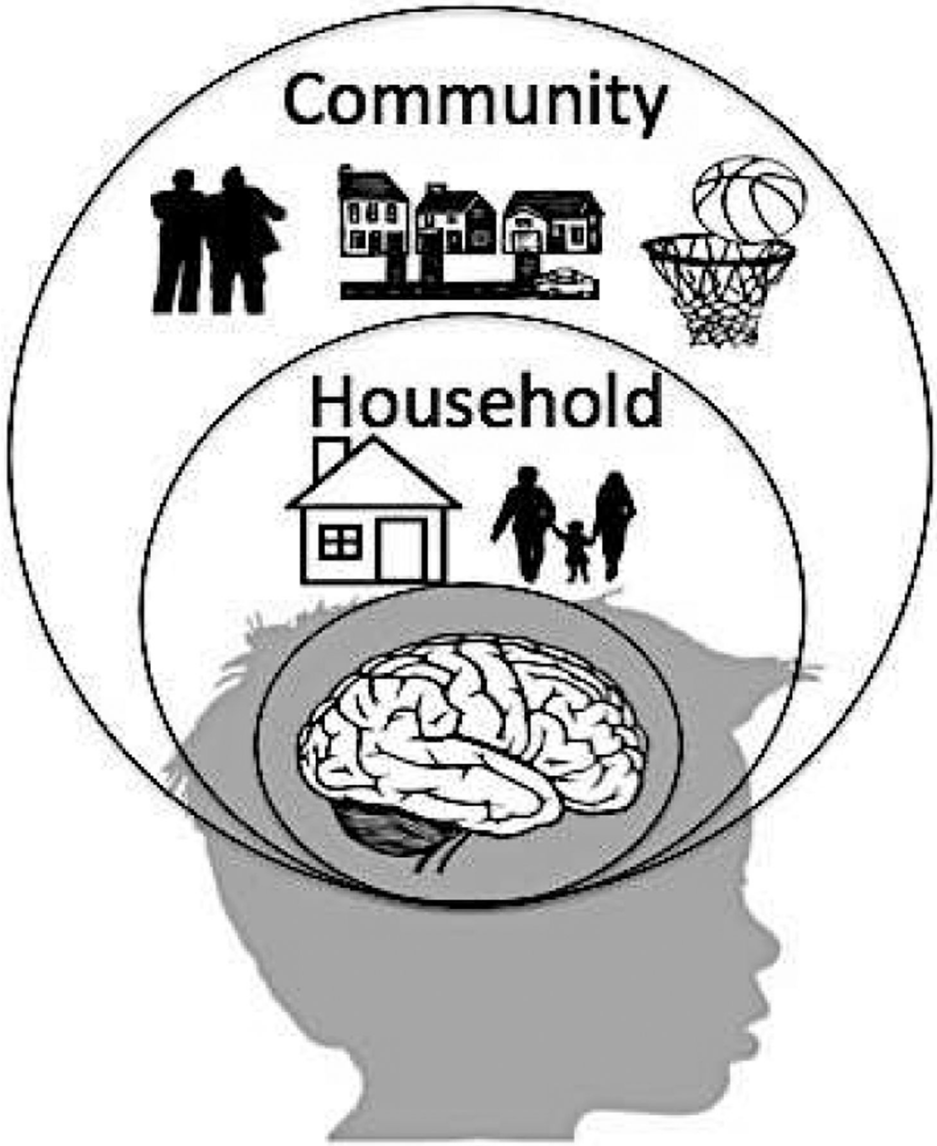

Figure 1. Community and household-level factors may have separate, interactive, or nested effects on brain development.

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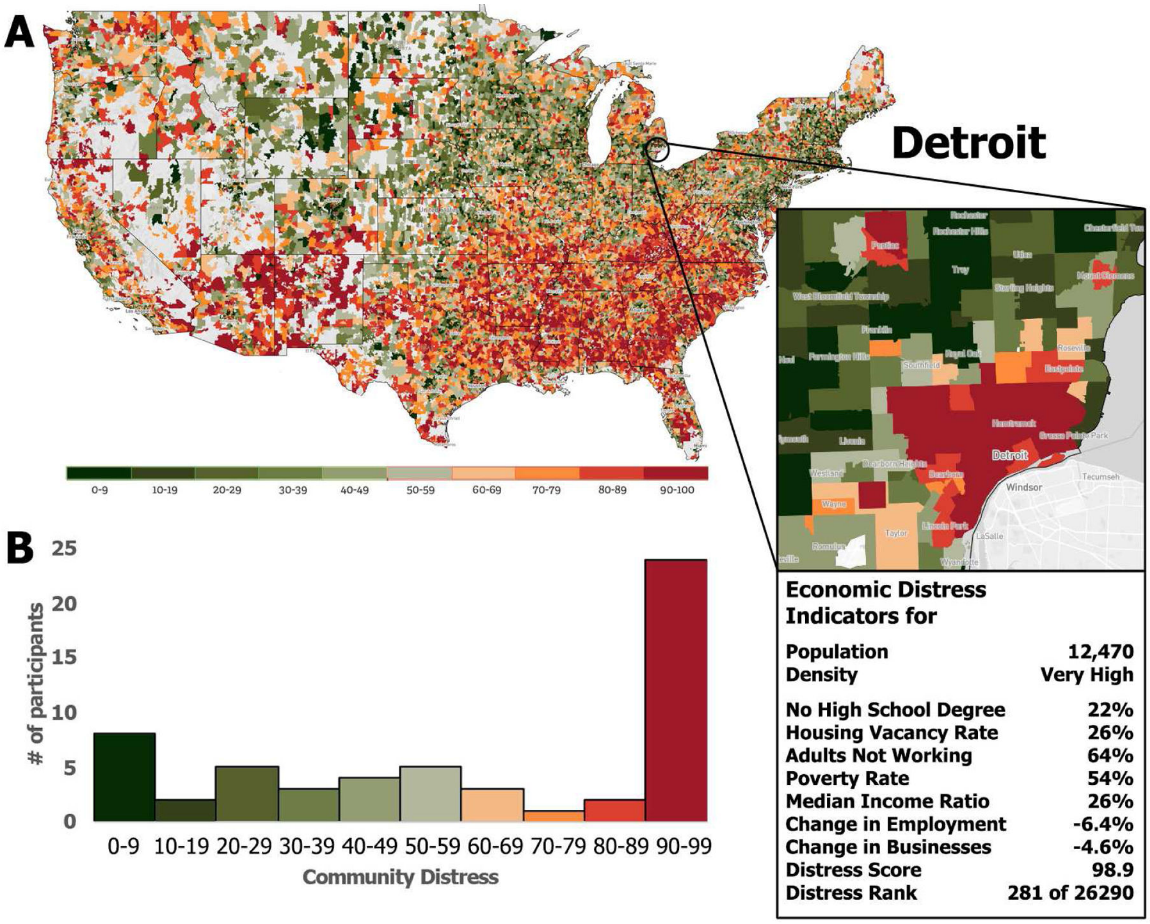

Figure 2. Community-level socioeconomic disadvantage (SED). A.

Map of community disadvantage, based on zip code and the 2016 Distressed Communities Index (DCI; available at eig.org/dci) throughout the United States. Average community distress within the study location (centrally located in Detroit, Michigan) was 98.9 out of 100 (highest possible distress). **B.** Distribution of community SED scores for included participants.

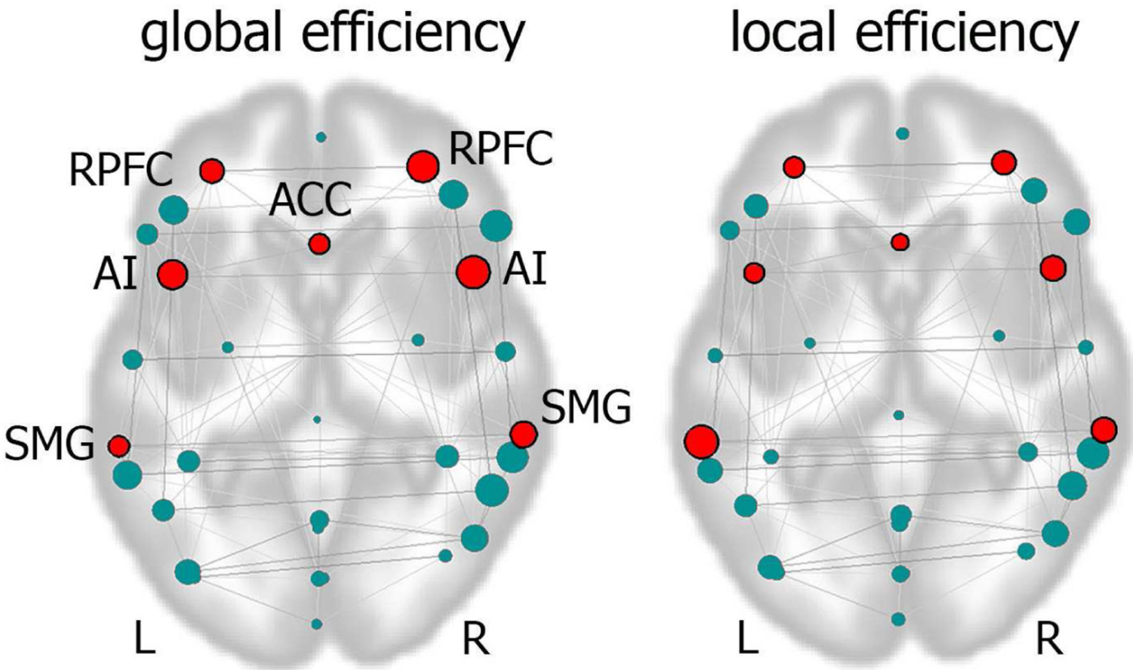

Figure 3. Global and local efficiency of salience and emotion network (SEN) regions (shown in red).

Non-SEN regions are shown in teal. The size of circle represents the degree of efficiency. Abbreviations: ACC, anterior cingulate cortex; AI, anterior insula; SMG, supramarginal gyrus; RPFC, rostral prefrontal cortex; L, left; R, right.

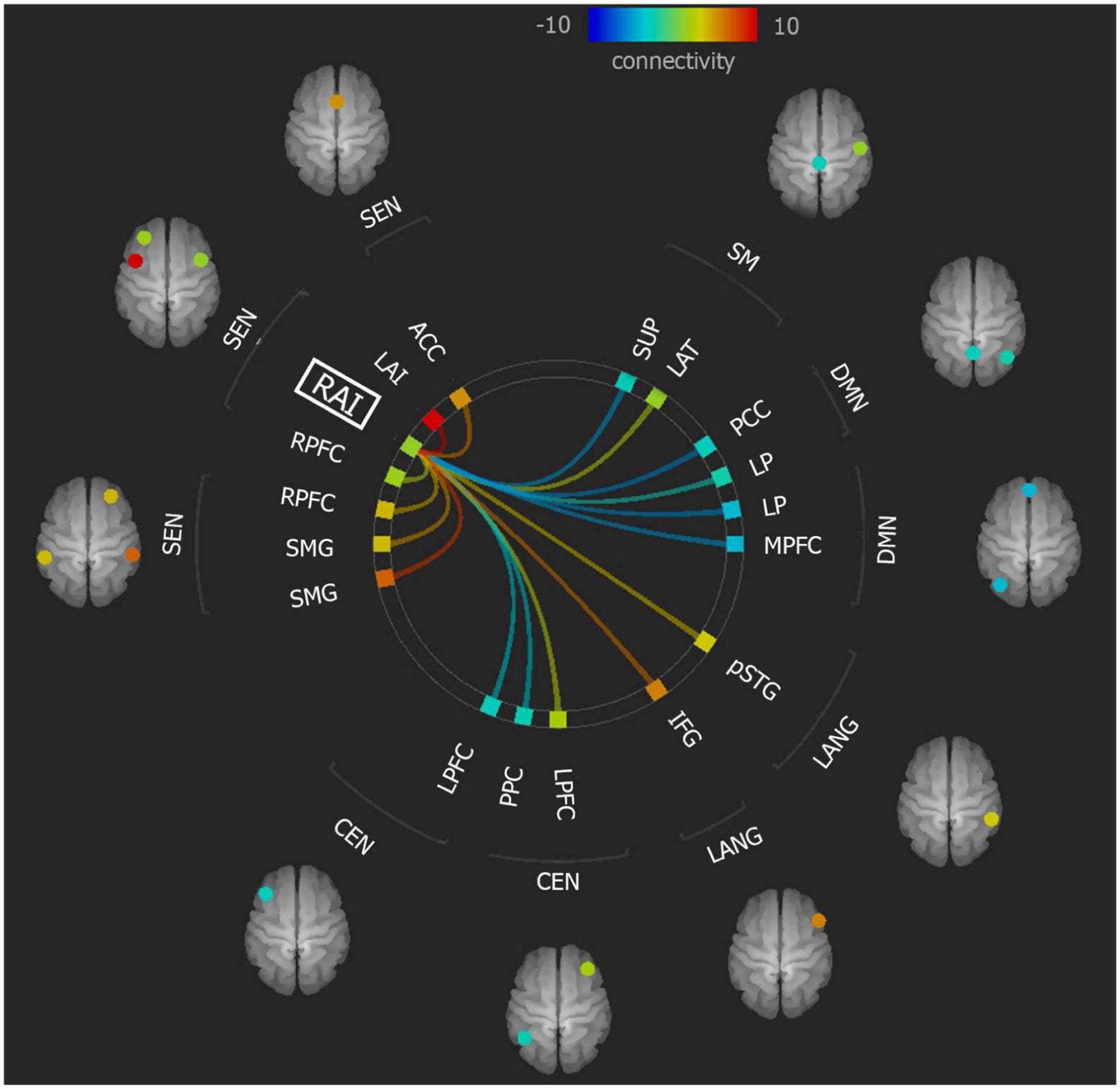

Figure 4. Within- and between-network connectivity of the salience and emotion network (SEN), using the right anterior insula (RAI) as an example node.

Warmer colors indicate positive connectivity; cooler indicates negative connectivity. ROI-ROI connectivity values are given as Z-scores. Abbreviations: ROI, region of interest; CEN, central executive network; DMN, default mode network; LANG, language network; SM, sensorimotor network, PCC, posterior cingulate cortex; MPFC, medial prefrontal cortex; pSTG; posterior superior temporal gyrus; IFG; inferior frontal gyrus; LPFC, lateral prefrontal cortex; PPC, posterior parietal cortex; SMG, supramarginal gyrus; RPFC, rostral prefrontal cortex; LAI, left anterior insula; ACC, anterior cingulate cortex; LP, lateral parietal; SUP, superior sensorimotor cortex; LAT, lateral sensorimotor cortex.

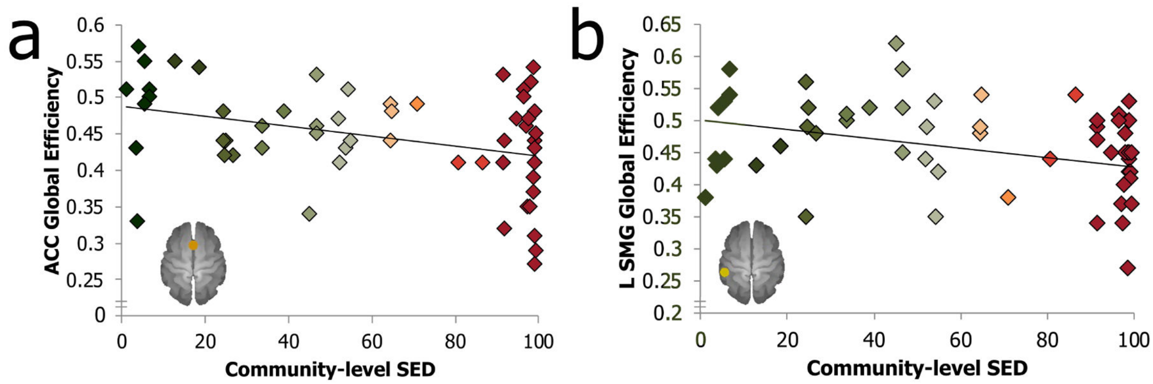

Figure 5. Higher community socioeconomic disadvantage (SED) is associated with lower global efficiency of the salience and emotion network (SEN).

Warmer colors represent more distressed communities; green represents less distressed communities (colors correspond with Figure 2). Abbreviations: ACC, anterior cingulate cortex; L SMG, left supramarginal gyrus.

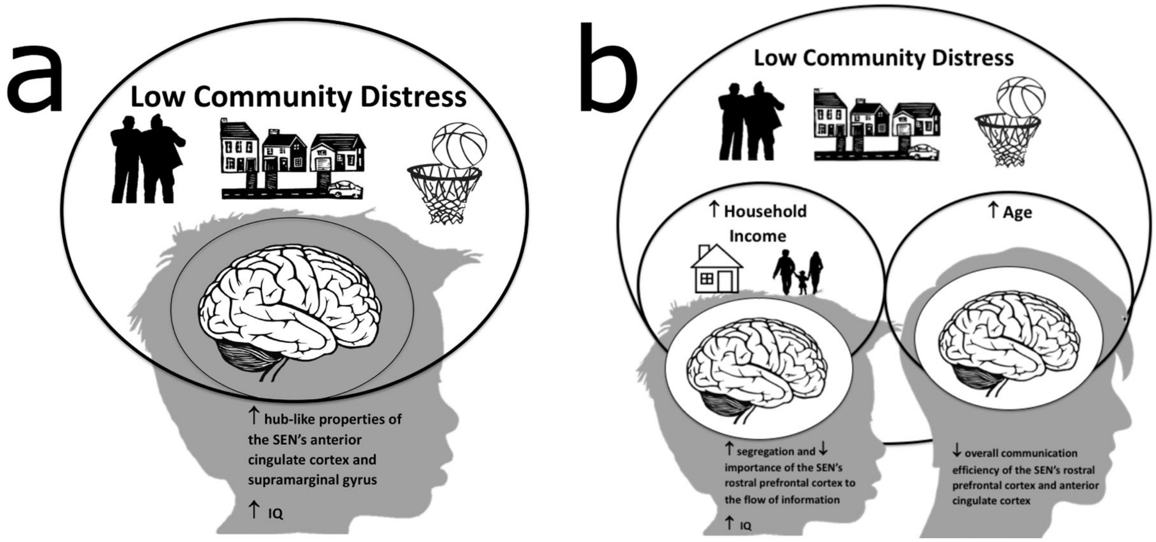

Figure 6. Summary of main and interactive effects of household income, community socioeconomic disadvantage (SED), and age on the salience and emotion network (SEN).

A, effects of community SED on the SEN and on IQ (see Figure 5). In particular, relative to more distressed communities, youth living in less distressed communities show higher IQ and more hub-like properties of two SEN regions; B, Effects of household income and age were only significant among youth living in less distressed communities. In particular, for youth living in low distress communities only, there is an effect of household income on IQ and on segregation and importance of the SEN's anterior cingulate cortex and supramarginal gyrus (i.e., household community-level SED interaction, see Figure 7a). In addition, for youth living in low distress communities only, there is an effect of age on efficiency of the SEN's rostral prefrontal cortex (i.e., age x community-SED interaction, Figure 7b).

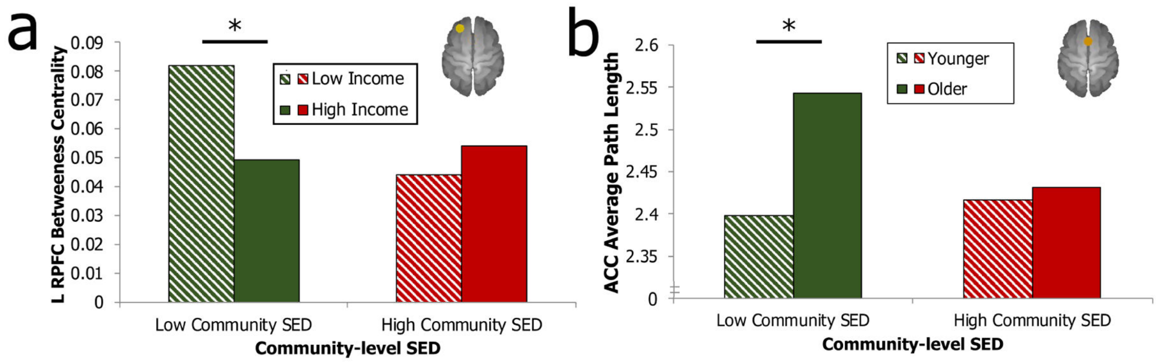

Figure 7. Interactions between community socioeconomic disadvantage (SED) and household income (a), and between community SED and age (b).

Interactions tested using variables as continuous measures. Displayed as groups, here, for visualization purposes (median split). Hatched bars refer to low income or younger age; filled bars refer to higher income or older age. Green bars correspond with low SED communities; red bars correspond with higher SED communities. Abbreviations: L RPFC, left rostral prefrontal cortex; ACC, anterior cingulate cortex.

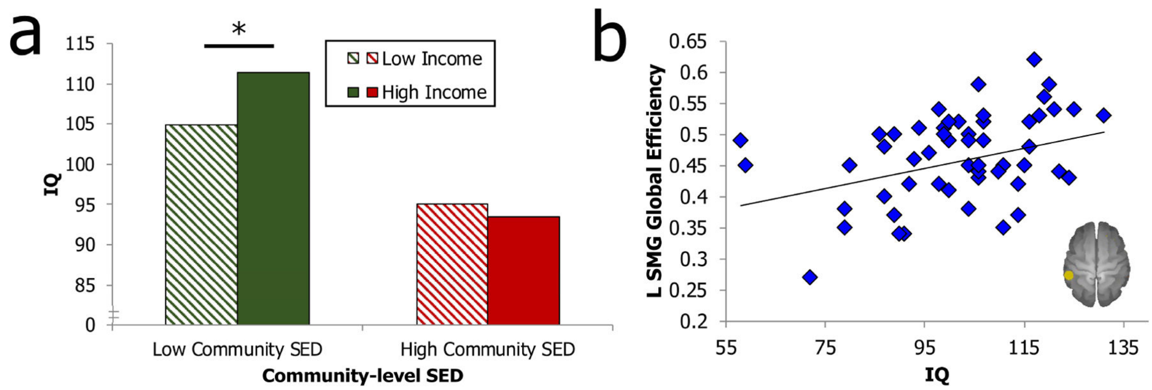

Figure 8. Interaction between income and community SED on IQ. Low IQ, in turn, was associated with lower global efficiency of the SEN.

Lower global efficiency of the L SMG was also associated with higher community SED (see Figure 5b). Displayed as groups, here, for visualization purposes (median split). Hatched bars refer to low income; filled bars refer to higher income. Green bars correspond with low SED communities; red bars correspond with higher SED communities. Abbreviations: L SMG, left supramarginal gyrus; IQ, intelligence quotient.

Table 1.

Participant demographic information (N = 57).

	N	% of total	Range	Mean (SD)
Demographic Information				
Age			6.3 – 17.7	10.41 (2.89)
Pubertal Stage (Tanner stages*)			1–5	2.44(1.28)
Sex (female)	30	52.6		
IQ			58 – 131	102(15.28)
Annual Income				
Less than $10,000	6	10.53		
$10–20,000	5	8.77		
$20–30,000	10	17.54		
$30–40,000	5	8.77		
$40–50,000	4	7.02		
$50–60,000	4	7.02		
$60–80,000	6	10.53		
$80–100,000	2	3.51		
$100–120,000	2	3.51		
$120–140,000	7	12.28		
$140–160,000	4	7.02		
$160–180,000	0	0		
$180–200,000	2	3.51		
Race**				
African American	25	45.45		
Caucasian	24	43.64		
Latino/Latina	2	3.64		
Other	4	7.27		

*Three participants did not report on Tanner Stage.

**Two participants did not report on race.