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Socioeconomic disparities in academic achievement: A multi-modal investigation of neural mechanisms in children and adolescents

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ABSTRACT

Growing evidence suggests that childhood socioeconomic status (SES) influences neural development, which may contribute to the well-documented SES-related disparities in academic achievement. However, the particular aspects of SES that impact neural structure and function are not well understood. Here, we investigate associations of childhood SES and a potential mechanism—degree of cognitive stimulation in the home environment—with cortical structure, white matter microstructure, and neural function during a working memory (WM) task across development. Analyses included 53 youths (age 6–19 years). Higher SES as reflected in the income-to-needs ratio was associated with higher parent-reported achievement, WM performance, and cognitive stimulation in the home environment. Although SES was not significantly associated with cortical thickness, children raised in more cognitively stimulating environments had thicker cortex in the frontoparietal network and cognitive stimulation mediated the association between SES and cortical thickness in the frontoparietal network. Higher family SES was associated with white matter microstructure and neural activation in the frontoparietal network during a WM task, including greater fractional anisotropy (FA) in the right and left superior longitudinal fasciculi (SLF), and greater BOLD activation in multiple regions of the prefrontal cortex during WM encoding and maintenance. Greater FA and activation in these regions was associated higher parent-reported achievement. Together, cognitive stimulation, WM performance, FA in the SLF, and prefrontal activation during WM encoding and maintenance significantly mediated the association between SES and parent-reported achievement. These findings highlight potential neural, cognitive, and environmental mechanisms linking SES with academic achievement and suggest that enhancing cognitive stimulation in the home environment might be one effective strategy for reducing SES-related disparities in academic outcomes.

Introduction

Growing evidence indicates that brain development varies as a function of family socioeconomic status (SES; Brito and Noble, 2014; Noble et al., 2015; Ursache and Noble, 2016). These neural differences may play a role in the well-documented academic achievement gap between children raised in high-compared to low-SES households (Baydar et al., 1993; Brooks-Gunn and Duncan, 1997). SES-related differences in cognitive and brain outcomes are particularly pronounced in the domains of executive functions (EF) and language (Noble et al., 2005, 2007). EFs are a set of cognitive functions including inhibition, cognitive flexibility, and working memory (Miyake and Friedman, 2012). Here, we focus

specifically on SES-related differences in working memory (WM), which involves the ability to hold in mind, manipulate, and update information in memory.

Children growing up in low-SES households exhibit worse WM than children raised in higher-SES families; these differences have been observed across the SES gradient and are not limited to children living in poverty (Hackman and Farah, 2009; Noble et al., 2005, 2007). EF abilities broadly, and WM specifically, are strongly associated with academic achievement (Best et al., 2011; Blair and Diamond, 2008; Finn et al., 2016). Understanding how the neural networks that support WM vary as a function of SES may shed light on neural pathways that explain the achievement gap. To that end, the present study uses a multi-modal

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approach to investigate SES-related differences in brain structure and function in neural systems involved in WM and the links between these neural systems and cognitive and academic performance in children.

Why might childhood SES influence brain development? It is likely that many aspects of SES produce differences in neural structure and function, and ultimately academic achievement, including cognitive and social stimulation, environmental predictability, parenting, exposure to toxins, nutrition, and exposure to violence (Johnson et al., 2016). Here, we focus on whether SES-related differences in neural structure and function are driven by differences in the degree of cognitive stimulation in the home environment—a modifiable factor that could be targeted with early intervention.

Children raised in low-SES families, on average, experience lower levels of cognitive stimulation, interaction with adults, linguistic complexity, and access to enriching experiences at home and school than children raised in high-SES families (Hart and Risley, 1995; Bradley et al., 2001; Bradley and Corwyn, 2002; Hackman et al., 2015). This reduction in cognitive and social stimulation is argued to constrain early forms of learning that rely on rich sensory, linguistic, and social input, resulting in accelerated synaptic pruning throughout the cortex (McLaughlin et al., 2017; McLaughlin and Sheridan, 2016; Sheridan and McLaughlin, 2016). These patterns could produce age-specific reductions in cortical thickness and surface area among children from low-SES backgrounds.

Existing research on SES and neural structure is consistent with these predictions (Jednoróg et al., 2012; Lawson et al., 2013; Mackey et al., 2015; Noble et al., 2012, 2015; Piccolo et al., 2016). Lower parental education and family income are associated with reduced cortical thickness and surface area throughout the cortex (Mackey et al., 2015; Noble et al., 2015), with the strongest association between SES and cortical surface area at the lowest levels of income (Noble et al., 2015). SES-related differences are particularly pronounced in regions underlying WM and language, including dorsolateral prefrontal cortex (dlPFC), superior temporal cortex, and superior parietal cortex (Noble et al., 2012, 2015). Cortical thickness in dlPFC and superior temporal cortex decreases more rapidly in children from low-SES backgrounds followed by an attenuation of this thinning in adolescence (Piccolo et al., 2016), consistent with the idea that children in low-SES environments exhibit accelerated pruning of synaptic connections early in life that produces more rapid declines in cortical thickness and surface area across childhood (McLaughlin et al., 2014, 2017; Sheridan & McLaughlin, 2014, 2016). Although accumulating evidence demonstrates reductions in cortical thickness and surface area among children raised in low-SES environments, we are unaware of prior research directly examining the hypothesis that these differences are driven by the reductions in cognitive stimulation experienced by low-SES children. We provide the first empirical test of this hypothesis in the current paper.

Differences in cortical structure may have implications for cognitive and academic outcomes. Longitudinal data indicate that accelerated cortical thinning in childhood followed by attenuated thinning in adolescence—a pattern observed among low-SES children (Piccolo et al., 2016) is associated with lower cognitive ability (Shaw et al., 2006). Similarly, greater thickness in temporal, parietal, and occipital cortex is associated with better standardized test scores in adolescents (Mackey et al., 2015). Thus, reductions in cortical thickness may be a mechanism linking low-SES with poor academic outcomes.

Although SES-related differences in cortical structure are well documented, few studies have examined the associations of SES with white matter microstructure, particularly in children. White matter microstructure in fronto-striatal and fronto-temporal tracts is reduced in children who have experienced adverse environments characterized by deprivation in cognitive and social stimulation, such as institutional rearing and neglect (Eluvathingal et al., 2006; Kumar et al., 2014; Hanson et al., 2013; Bick et al., 2015). Because children raised in low-SES families also are likely to experience lower levels of cognitive stimulation than children raised in high-SES families (Bradley and Corwyn, 2002), it is possible that SES may have similar influences on white matter

microstructure, although this is largely untested. Evidence from adults is somewhat consistent with this hypothesis: global white matter integrity follows an SES gradient in adults, such that greater education, income, and community-level SES are associated with higher fractional anisotropy (FA) across the entire brain (Gianaros et al., 2013). Variability in white matter structure, in turn, influences cognitive outcomes. In particular, greater integrity of the superior longitudinal fasciculus (SLF), a tract that connects the lateral PFC to the parietal cortex, has been linked to better WM (Mabbott et al., 2009; Vestergaard et al., 2011) and higher educational attainment in adolescents (Noble et al., 2013), suggesting that this tract may play an important role in SES-related variation in WM and academic achievement.

Few studies have examined SES-related differences in neural function during WM tasks in children, although such differences in neural function have been observed in relation to language processing (e.g. Raizada et al., 2008), emotion regulation (e.g. Kim et al., 2013), and academic subjects including mathematics and reading (e.g. Demir-Lira et al., 2016; and Noble et al., 2006). Existing evidence suggests that SES is associated with PFC function during multiple forms of EF. During novel rule-learning, low-SES children perform more poorly and exhibit a more diffuse pattern of PFC activation than higher-SES children (Sheridan et al., 2012). Additionally, SES is related to reduced inhibitory control in adolescents and greater recruitment of the dorsal anterior cingulate cortex, coupled with reduced connectivity between the dorsal anterior cingulate and dorsolateral PFC specifically among low SES girls (Spielberg et al., 2015). During a WM task, children from lower-income backgrounds exhibit reduced PFC and superior parietal recruitment than children from higher-SES families (Finn et al., 2016). In that study, WM capacity and fronto-parietal recruitment mediated the association between SES and performance on a statewide mathematics exam. These findings suggest that differences in neural recruitment in the frontoparietal network observed among low-SES children may contribute directly to academic performance.

In the present study we used a multi-modal neuroimaging approach to investigate the associations of parental SES with brain structure and function, including cortical structure, white matter microstructure, and neural function during a WM task. We focused on SES-related differences in the frontoparietal network because of its known role in WM (Corbetta and Shulman, 2002; Curtis & D'Esposito, 2003), which was the focus of our behavioral and fMRI task. Moreover, previous studies have found SES-related differences in neural structure and function in the frontoparietal network (Sheridan et al., 2012; Noble et al., 2013; Finn et al., 2016). For structural region of interest (ROI) analyses, we focused on the middle frontal gyrus (MFG) and superior parietal lobule/intraparietal sulcus (SPL/IPS), key frontoparietal regions that are recruited during WM tasks (Corbetta and Shulman, 2002). For white matter analyses, we examined the superior longitudinal fasciculus (SLF) because it connects the prefrontal and parietal cortices and is associated with WM performance (Mabbott et al., 2009; Vestergaard et al., 2011). In our fMRI approach, we used a conservative whole brain approach to examine SES-related differences in neural recruitment, which demonstrated clear differences in our frontoparietal regions. We then extracted ROIs from frontoparietal regions to examine associations with task performance and academic achievement.

We hypothesized that SES would be associated with frontoparietal structure and function, including positive associations with cortical thickness in the MFG and SPL/IPS; positive associations with white matter integrity in the SLF; and positive associations with BOLD signal in the prefrontal and parietal cortex during a WM task. We expected that cortical thickness, white matter microstructure, and BOLD signal in these frontoparietal regions would be associated not only with SES, but also with parent-reported academic achievement. Importantly, we also predicted that SES-related differences in neural structure and function would be driven by differences in the degree of cognitive stimulation in the home environment. Together, we expected that WM performance, cognitive stimulation, and neural structure and function would be mechanisms

explaining the income-achievement gap. Critically, low-SES is associated not only with lower levels of cognitive stimulation but also higher levels of exposure to violence, which has distinct influences on neural development (McLaughlin et al., 2014). To date, only one study examining SES-related differences in neural measures has measured and controlled for violence exposure (Sheridan et al., 2017). We did so in the present study to isolate the links between SES and neural structure and function that are not explained by exposure to violence.

Materials and methods

Participants

A sample of 66 participants aged 6–19 years ($M = 13.68$ years, $SD = 3.23$ years; 35 male) participated. The sample was recruited in Seattle, WA between February 2014 and February 2015. Youths were recruited at schools, after-school and prevention programs, medical clinics, and in the general community. Half of the sample was recruited based on exposure to violence in order to test additional questions about how environmental experience is associated with neural processes involved in memory for emotional information (Lambert et al., 2017). We controlled for violence exposure by including it as a covariate of non-interest in all analyses that included SES or cognitive enrichment as the predictor variable. The study sample was racially and ethnically diverse (53.5% White, 6.25% Black, 14.55% Hispanic, 2.1% Asian, 23.6% Multiracial or Other). The Institutional Review Board at the University of Washington approved all procedures. Participants were compensated and written informed consent was obtained from legal guardians; youths provided written assent.

Five participants were excluded from all analyses. One subject (female, 15 years) had an incidental neurological finding, one subject got out of the scanner (female 8 years), and three subjects had excessive motion for all three scan types (female, 6 years, male 6 years, male, 9 years). For functional MRI analyses, seven additional participants (5 female, mean age: 11.43 ± 3.11 years) were excluded from analyses due to below-chance performance on the task and two participants (females, 9 and 12 years) were excluded due to excessive motion ($>20\%$ TRs with framewise displacement outliers). For DTI analyses, nine subjects (6 female, mean age 10.92 ± 2.76 years) were excluded due to poor quality assurance on DTI images. The final analytic sample after the above exclusions and missing data was 49 for structural MRI analyses, 43 for DTI, and 47 for fMRI. Importantly, exclusion from analyses did not vary as a function of income-to-needs ratio ($ps > .250$).

Measures

Socioeconomic status

We used the income-to-needs ratio as a measure of SES. The income-to-needs ratio captures the amount of annual income that a family earns

relative to the federally-defined poverty threshold for a family of that size. Income-to-needs is a widely used measure of SES that allows associations to be examined across the entire SES gradient. Parents reported annual income in 10 bins, and the median of the income bins was used except for the lowest and highest bins, which were assigned \$5000 and \$200,000 respectively. The median income was \$42,500. Income-to-needs ratio was calculated by dividing the total household income by the 2014 U.S. census-defined poverty line for a family of that size, with a value of 1 or less indicating income below the poverty line. The range of income-to-needs was 0.13–8.33. See Table 1 for income-to-needs ratio distribution across age. Median income-to-needs was 1.77, and 21 participants (38.18%) were living in poverty. Six participants (mean age 16.85 ± 2.32 years, 4 female) had missing income data. These participants were included for analyses where they had available data (e.g., those examining cognitive stimulation and neural structure and function). The income-to-needs ratio was log-transformed for all analyses, following prior work documenting that associations between income and neural measures exist across the SES distribution but are stronger at lower levels of income (Noble et al., 2015). Additionally, we examined whether the best fitting model included income-to-needs as a linear or log-transformed variable, and the logarithmic model was a better fit to the data for all analyses.

Parent-reported academic achievement

To assess academic achievement, parents completed the Child Behavior Check List (CBCL; Achenbach et al., 1991). Parents reported their child's performance in four academic subjects (Reading, English, or Language Arts, History or Social Studies, Arithmetic or Math, and Science) choosing from four options. Each of these options was assigned a numerical value (1 = Failing, 2 = Below Average, 3 = Average, 4 = Above Average) and we used this value to compute a composite score for each participant by taking the mean performance level for all four academic subjects. Three subjects were missing parent-reported achievement data (2 males 18 years, 1 female 18 years).

Cognitive stimulation

To assess the degree of cognitive stimulation in the home environment, parents completed the Home Observation for Measurement of the Environment-Short Form (HOME-SF; Mott, 2004). The HOME-SF has slightly different versions for children aged 6–9 and 10–15 years, with 16 items that are identical across these age ranges. We used only the 16 questions that are present in the HOME-SF for both younger and older children. This assessment included items that assess cognitive stimulation and exposure to varied learning experiences. Example items included: “About how many books does your child have?”; “How many times does your child get out of the house per week for activities (e.g., sports, extracurricular activities, activities with the family)?”; and “Did you and/or your partner teach your child numbers at home?”. The measure was scored using the cut-offs used in the original HOME

Table 1
Income-to-needs ratio distribution across age.

Age	Income-to-Needs Ratio										Total
	<0	1–2	2–3	3–4	4–5	5–6	6–7	7–8	>8		
8	3	2	1	0	0	0	0	0	0	0	6
9	0	0	0	0	0	0	0	1	0	1	2
10	2	0	0	0	0	0	1	0	0	0	3
11	3	1	0	0	0	0	2	0	0	0	6
12	2	0	1	1	0	0	1	1	0	0	5
13	2	1	0	1	0	0	1	1	0	0	6
14	1	0	1	0	1	0	1	0	1	0	5
15	3	1	2	0	0	1	1	0	2	0	10
16	2	0	0	0	0	0	0	2	0	0	4
17	2	1	0	0	1	0	2	0	0	0	6
18	0	1	0	0	0	0	0	0	0	0	1
19	1	0	0	0	0	0	0	0	0	0	1

assessment, where one point is assigned for each item where age-appropriate experiences are met (e.g., 1 point is assigned if a child leaves the house at least once a week for an activity; 0 is assigned if the child leaves the house less than once a week for an activity); for a total possible score of 16. While this assessment has not been validated in youths over 15, it has been used in older adolescents in prior studies (Cleveland et al., 2000). In the present study, the HOME-SF had good internal consistency ($\alpha = .75$) and the subscale assessing cognitive stimulation used in the present study has adequate internal consistency ($\alpha = .62$). The mean score on the cognitive stimulation sub-scale was 13.05 ± 2.15 , and scores were normally distributed. Seven subjects were missing cognitive stimulation data (4 male, mean age = 14.5 years).

Violence exposure

Violence exposure was assessed with the Childhood Experiences of Care and Abuse (CECA) interview (Bifulco et al., 1997), the Childhood Trauma Questionnaire (CTQ) (Bernstein et al., 1997) and the UCLA PTSD Reaction Index (PTSD-RI) trauma screen (Steinberg et al., 2004). Each of these measures assesses exposure to violence, including child abuse and domestic violence. Participants who reported physical abuse, sexual abuse, witnessing domestic violence, or directly experiencing other violence, or who had a score on the CTQ physical or sexual abuse sub-scales above a validated threshold (Walker et al., 1999) were classified as exposed to violence and this dichotomous variable was included as a covariate in all analyses investigating SES-related differences including behavioral, parent-reported achievement, cognitive stimulation, cortical thickness, white matter integrity, and functional MRI analyses. Because this study included youths exposed to different types of violence (e.g., abuse, domestic violence, community violence) and no single scale captures all of these exposures, a dichotomous variable for violence exposure was used. As a sensitivity analysis, we constructed a continuous variable reflecting a sum of the standardized scores of multiple violence measures as a covariate rather than a dichotomous variable. Using this continuous measure of violence exposure as a covariate in our analyses did not alter any of our results.

Working memory task

Participants completed a delayed-match to sample WM task (Supplemental Fig. 1) using emotional faces as stimuli. Faces were drawn from a standardized stimulus set (Tottenham et al., 2009). Stimuli were neutral, happy, and angry faces, distributed evenly across trials and presented in a counter-balanced order across participants. Participants were instructed to attend and respond to the faces and their emotional expressions. The delayed-match-to-sample (DMS) task consisted of two runs of 50 trials. Each trial involved Encoding (2000 ms), Delay (1000 or 5000 ms), and Probe (2000 ms) and an inter-trial interval (ITI) of 500 ms (67% of trials) or 2000 ms (33% of trials). Each actor was presented 6–7 times for each facial expression. During the Encoding, facial stimuli were embedded in realistic background scenes to investigate implicit context encoding for another study that involved a memory test outside the scanner for contextual information (Lambert et al., 2017). This made encoding more similar to real-world facial encoding. During the Probe, an image of a face without a background scene was presented, and participants were asked to indicate whether the Probe face matched the Encoding face. On 1/3 of trials, the Probe face presented matched the Encoding face (i.e. was the same person showing the same emotion) and on the other 2/3 of trials, the Probe did not match. There were two types of mismatches: Emotion Mismatch (same person, different emotion), Identity Mismatch (different person). Each subject had 30 trials of each mismatch type (16–17 per run, for a total of 100 trials). All trial types were interspersed throughout the 2 task runs. Subjects completed two runs of the WM task, with the exception of one subject that completed only one run.

Behavioral performance was assessed using d' , which was calculated using the following formula:

$$d' = z(\text{hit rate}) - z(\text{false alarm rate})$$

where z is the standardized score, as a measure of the sensitivity to detect matches.

Image acquisition and processing

Image acquisition

Before undergoing scanning, children 12 years and younger and older children exhibiting anxiety about the scan were trained to minimize head movements in a mock scanner with a motion tracker that stopped playing a movie if a movement of >2 mm occurred. This method has been shown to significantly reduce head motion once children are in the scanner (Raschle et al., 2012). In the scanner, we used a head-stabilizing pillow to further restrict movement.

Scanning was performed on a 3T Phillips Achieva scanner at the University of Washington Integrated Brain Imaging Center using a 32-channel sensitivity-encoding (SENSE) head coil. T1-weighted multi-echo MPRAGE volumes were acquired (TR = 2530 ms, TE = 1.64–7.04 μ s, flip angle = 7°, FOV = 256 mm², 176 slices, in-plane voxel size = 1 mm³). Blood oxygenation level dependent (BOLD) signal during functional runs was acquired using a gradient-echo T2*-weighted EPI sequence. Thirty-two 3 mm thick slices were acquired parallel to the AC-PC line (TR = 2000 ms, TE = 30 ms, flip angle = 90°, bandwidth = 2300, echo spacing = 0.5, FOV = 256 × 256, matrix size = 64 × 64). Prior to each scan, four images were acquired and discarded to allow longitudinal magnetization to reach equilibrium. DTI was acquired using a single-shot echoplanar imaging sequence (TR = 8165 ms, TE = 75 ms, flip angle = 90°, FOV = 256 × 256 mm, 72 slices, in-plane voxel size = 2 mm³). Diffusion-weighted images were acquired along 64 non-collinear and non-coplanar directions with a b value of 1000 s/mm² and 1 image with a b value of 0 s/mm².

Structural image processing

Cortical surface of each hemisphere was computationally reconstructed using FreeSurfer software (Dale et al., 1999; Fischl et al., 1999). ROI analyses of the prefrontal and parietal cortex were conducted by extracting the mean cortical thickness value for each subject for predetermined regions in the frontoparietal network defined by the FreeSurfer 2005 parcellation (left and right MFG and SPL/IPS). We focus here on hypothesized differences in the frontoparietal network, but present a whole-cortex exploratory analysis in the Supplemental Materials.

DTI processing

DTI pre-processing included skull-stripping and correction for distortion due to eddy currents in FSL and registration using non-linear symmetric diffeomorphic transformation in Advanced Normalization Tools (ANTS) (Avants et al., 2011). Head motion and eddy current correction were conducted with the 'eddy' tool in FSL (Andersson and Sotiropoulos, 2016). The diffusion tensor was calculated per voxel using conventional reconstruction methods in FSL's dtifit. From these maps, FA was calculated. The temporal signal-to-noise ratio and estimates of subject movement (from the eddy tool) were calculated for quality assurance purposes (Roalf et al., 2016). Subjects with values greater than 2.5 standard deviations from the mean of these metrics were excluded from the analyses.

We then examined FA in the SLF. To extract FA values, we used a standardized protocol developed by the ENIGMA consortium; this protocol is described in detailed elsewhere (Jahanshad et al., 2013). Briefly, FA images were nonlinearly registered to the ENIGMA-DTI target brain using FNIRT. The data were then processed using a modified version of FSL's tract-based spatial statistics (TBSS) (Smith et al., 2006) to project individual FA values on the hand-segmented ENIGMA-DTI skeleton mask rather than the TBSS skeleton. After extracting the skeletonized white matter and the projection of individual FA values, ENIGMA tract-wise

regions of interest, derived from the Johns Hopkins University white matter parcellation atlas (Mori et al., 2008), were transferred to extract the average FA values for the SLF tract for each hemisphere. The protocol, target brain, ENIGMA-DTI skeleton mask, source code and executables are all publicly available (<http://enigma.ini.usc.edu/ongoing/dti-working-group/>).

We focus here on hypothesized differences in the frontoparietal network, but present a whole-brain exploratory analysis in the Supplemental Materials.

fMRI processing

Preprocessing and statistical analysis of fMRI data was performed in a pipeline using Make, a software development tool that can be used to create neuroimaging workflows that rely on multiple software packages (Askren et al., 2016). Simultaneous motion and slice-time correction was performed in NiPy (Roche, 2011). Spatial smoothing with a Gaussian kernel (6-mm full width at half maximum [FWHM]) was performed in FSL (Jenkinson et al., 2012). Data were inspected for artifacts, and volumes with motion >2-mm or >3-SD change in signal intensity were regressed out using volume-specific covariates of non-interest. For subjects who were not specifically excluded for motion, motion was extremely low. Those with the highest motion had fewer than 10% of volumes with framewise displacement outliers across both runs, with the next highest being 3.6% of volumes with outliers. Six rigid-body motion regressors were included in person-level models. A component-based anatomical noise correction method (Behzadi et al., 2007) was used to reduce noise associated with physiological fluctuations. Person- and group-level models were estimated in FSL. Following estimation of person-level models, the resulting contrast images were normalized into standard space, and anatomical co-registration of the functional data with each participant's T1-weighted image was performed using surface-based registration in FreeSurfer version 5.3 (Dale et al., 1999), which provides better alignment than other methods in children (Ghosh et al., 2010). Normalization was implemented in Advanced Normalization Tools (ANTs) software, version 2.1.0 (Avants et al., 2011). Each participant's MRI data were first warped to a pediatric template (NIH Pediatric MRI Data Repository: <https://pediatricmri.nih.gov/nihpd/info/index.html>), then from the pediatric template to MNI space. The pediatric template was originally developed from a sample of 500 youths aged 6–18 years with a mean age of 14 years, similar to the present study.

fMRI analysis was performed using FEAT (FMRI Expert Analysis Tool) Version 6.00, part of FSL (FMRIB's Software Library, www.fmrib.ox.ac.uk/fsl). Regressors were created by convolving a boxcar function of phase duration with the standard double-gamma hemodynamic response function for each phase of the task (Encoding, Delay, and Probe). A general linear model (GLM) was constructed for each participant. Higher-

level analysis was carried out using FLAME (FMRIB's Local Analysis of Mixed Effects) stage 1, (Woolrich et al., 2004). Individual-level estimates of BOLD activity were submitted to group-level random effects models of Encoding, Delay, and Probe periods, each compared to Baseline (ITI). Whole-brain analyses were conducted using only correct trials.

We performed cluster-level correction ($z > 2.3, p < .01$) to our models run in FSL FLAME. This combination of correction and model is associated with relatively low risk of both false positive and false negative findings in recent simulations (see Eklund et al., 2016, Fig. 1). Results were then projected onto the cortical surface for visualization purposes using Connectome Workbench (Washington University, St. Louis; Marcus et al., 2013).

Results of whole-brain group average activation are displayed in Supplemental Fig. 2. ROI analyses were conducted to examine associations of neural activation with performance on the task and parent-reported achievement. ROIs were created by masking functional activation for each period of the task (i.e. Encoding, Delay, and Probe) in the group average for correct trials only and intersecting this mask with an anatomical mask (20% threshold) from the Harvard-Oxford atlas in FSL. This produced an anatomical ROI that included only task-active regions. Importantly, we used a mask based on recruitment across the whole sample to avoid double-dipping when investigating the association of activation with task performance (Vul et al., 2009).

Data analysis

Bivariate correlations between all study variables are presented in Table 2.

Associations of the income-to-needs ratio with cognitive stimulation, WM, and parent-reported achievement were assessed using linear regression, controlling for age, sex, and violence exposure. As noted earlier, the income-to-needs ratio was log-transformed in all analyses, as this provided a better fit to the data than a linear variable in every model. We use the term SES throughout results to refer to this log-transformed variable. The logarithmic association of income-to-needs with academic achievement and WM and FA in the SLF can be viewed in Supplemental Fig. 3A–B and Supplemental Fig. 4. We investigated whether the association between SES and these outcomes was moderated by age and found no evidence for moderation.

We applied the same analysis approach to each of our measures of neural structure and function. For neural structure, we investigated the association of SES and cognitive stimulation with cortical thickness and FA in our ROIs of interest. We then determined whether regions that were associated with SES were also associated with WM performance and parent-reported achievement. For neural function, we estimated a model with a mean-centered regressor for log income-to-needs and cognitive

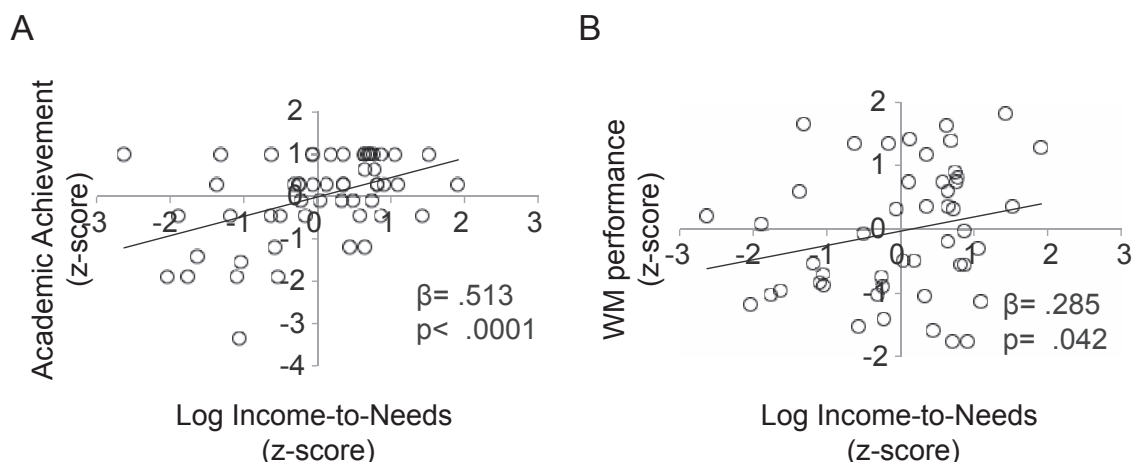


Fig. 1. Associations of SES with parent-reported achievement (A), and working memory performance (B).

Table 2
Bivariate correlations.

	Sex	Age	Violence	Log Income-to-Needs	Cognitive Enrichment	<i>d'</i>	Academic Achievement
Sex							
Age	.085						
Violence	.086	.101					
Log Income-to-Needs	-.125	.061	-.479**				
Cognitive Enrichment	.062	-.085	-.471**	.419**			
<i>d'</i>	-.105	.322*	-.259 †	.380**	.070		
Academic Achievement	-.070	-.065	-.352**	.546**	.423**	.397**	
LH MFG thick	.137	-.364**	-.075	.084	.343*	-.090	-.60
RH MFG thick	.062	-.350**	-.142	.138	.302*	-.227	.063
LH SPL thick	-.140	-.555**	-.121	.033	.349**	-.262†	-.020
RH SPL thick	-.080	-.637**	-.104	.098	.203	-.250†	-.020
L SLF	-.134	.051	-.368**	.451**	.320*	.318*	.332*
R SLF	-.243†	.151	-.412**	.459**	.143	.212	.191
LSFG Cue	.148	.124	-.165	.418**	.310*	.394**	.367*
RSFG Cue	-.019	.065	-.160	.291*	.168	.317*	.217
LMFG Cue	.078	.224	-.260†	.438**	.210	.421**	.312*
L OccFusCue	-.169	.344*	-.262†	.314*	-.019	.500**	.346*
LOFC Delay	.122	.182	-.103	.434**	.297*	.186	.340*

* $p < .05$, ** $p < .01$, † $p < .1$.

stimulation for each contrast of interest (Encoding, Delay, Probe). We then examined whether neural recruitment in regions that were associated with SES were also associated with WM and parent-reported achievement using the ROI approach described above (i.e., ROIs defined by intersecting a structural mask with task-related group average activation for the contrast of interest, to avoid double-dipping). All analysis controlled for age, sex, and violence exposure.

We evaluated whether age moderated the association of SES and cognitive stimulation with neural structure and function and found no evidence for interactions with age for any outcome.

We tested two mechanistic hypotheses using standard tests of statistical mediation. First, we tested the hypothesis that cognitive stimulation in the home environment is a mechanism explaining the association between SES and neural structure and function; we examined this model for neural measures that were associated with cognitive stimulation. Second, we investigated potential mechanisms explaining the link between SES and parent-reported achievement; we included cognitive, neural, and environmental factors that were significantly associated with both SES and parent-reported achievement as mediators. For both models, we used the PROCESS macro to perform a test of statistical mediation that allows multiple mediators to be examined simultaneously and that uses a bootstrapping approach that provides confidence intervals for the indirect effects (Hayes, 2013). Confidence intervals that do not include 0 reflect statistically significant indirect (i.e., mediated) effects.

Results

SES, academic achievement, and working memory

Consistent with prior work, we found that SES was positively associated with parent-reported achievement ($\beta = .51$, $p < .0001$, Fig. 1A) and WM performance ($\beta = .29$, $p = .042$, Fig. 1B), such that children with higher SES had better parent-reported achievement and WM. WM performance was also positively associated with achievement ($\beta = .51$, $p = .001$).

Cognitive stimulation

Next, we investigated our hypothesis that cognitive stimulation in the home would be associated with SES as well as WM and achievement. As predicted, higher SES was associated with higher levels of cognitive stimulation ($\beta = .33$, $p = .034$), and cognitive stimulation was positively associated with parent-reported achievement ($\beta = .35$, $p = .022$). Cognitive stimulation was not associated with WM performance ($p > .8$).

SES, cognitive stimulation, and neural structure

We next tested the hypothesis that SES and cognitive stimulation would be associated with cortical thickness and FA in the frontoparietal network. With regard to cortical thickness, we observed no association between SES and cortical thickness in the MFG or SPL/IPS. In contrast, cognitive stimulation was significantly associated with cortical thickness in both left MFG ($\beta = .31$, $p = .011$) and SPL/IPS ($\beta = .29$, $p = .045$; Fig. 2), but not right MFG or SPL/IPS ($ps > .05$).

With regard to white matter microstructure, SES was positively associated with FA in both the left ($\beta = .37$, $p = .021$) and right ($\beta = .32$, $p = .032$) SLF (Fig. 3). There were no significant associations between cognitive stimulation and FA ($ps > .27$).

We next examined whether cognitive stimulation was a mechanism linking SES and cortical thickness in the frontoparietal network. Although the association between SES and cortical thickness was not statistically significant, cognitive stimulation was associated with both SES and cortical thickness, as noted above. It is well-established that requiring a significant association in the direct path in order to test statistical mediation reduces power to detect mediation, and that is appropriate to examine a mediation analysis even when the direct effect does not reach conventional thresholds of statistical significance (Hayes, 2013; MacKinnon et al., 2007). Here, we observed a significant indirect effect of SES on cortical thickness in the left MFG (95% CI: .0001-.0872) and left SPL (95% CI: .0052-.0765) through cognitive stimulation.

SES, cognitive stimulation, and neural function

We next investigated whether SES was associated with neural recruitment during the WM task in a whole-brain analysis. SES was positively associated with BOLD signal in left MFG, left occipital fusiform gyrus, and medial superior frontal gyrus (SFG) during WM Encoding, such that youths with higher SES exhibited greater activation in these regions (Table 3, Fig. 4A). During the Delay (i.e., WM maintenance), SES was positively associated with activation in left MFG, left orbitofrontal cortex (OFC), and left posterior middle temporal gyrus, again reflecting greater activation among youth with higher SES (Table 3, Fig. 4B). During the Probe, SES was positively associated with activation in left posterior middle temporal gyrus (Table 3, Fig. 4C). There were no areas where SES was negatively associated with activation. Cognitive stimulation was not associated with neural activation in frontoparietal regions.

Brain-behavior associations

Given associations of SES and cognitive stimulation with

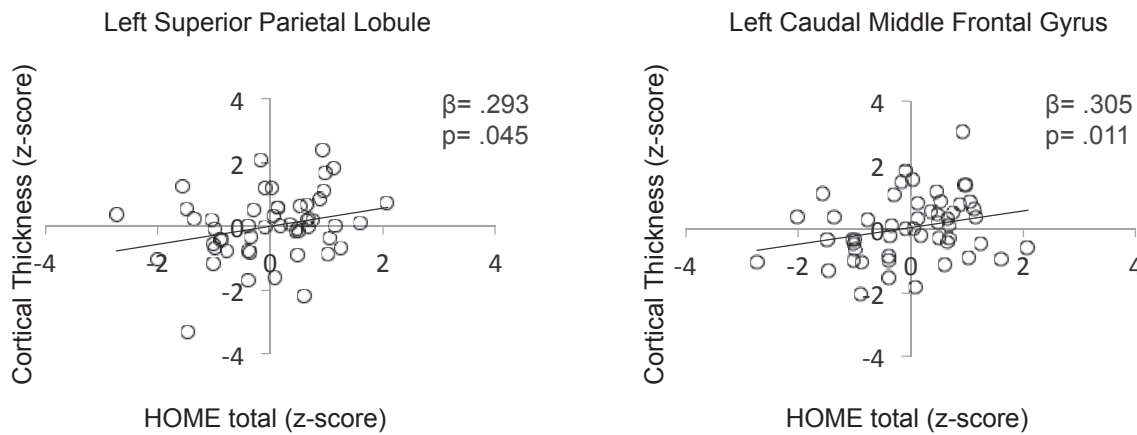


Fig. 2. Associations between cognitive stimulation in the home environment and cortical thickness in the left frontoparietal network.

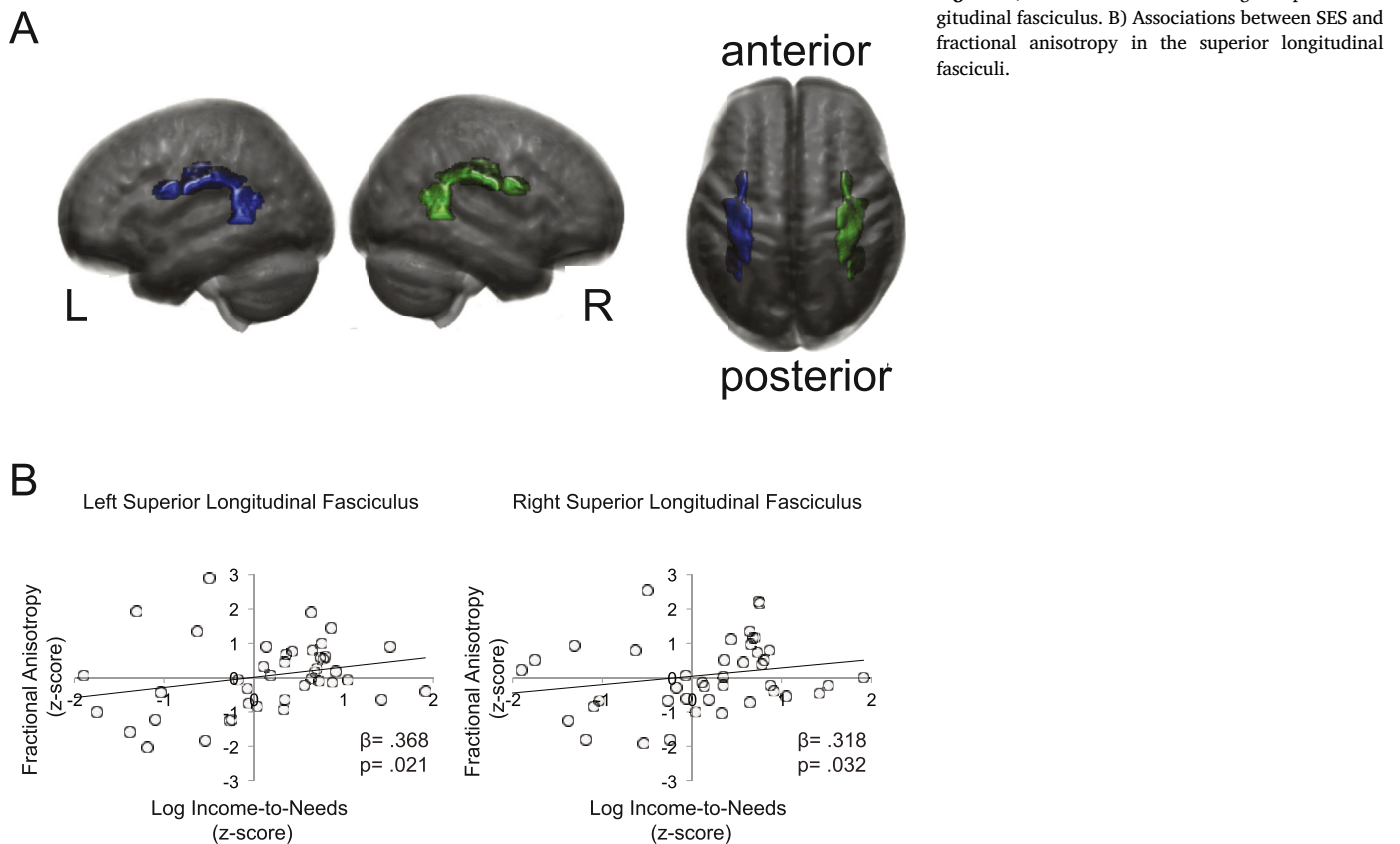


Fig. 3. A) Definitions of left and right superior longitudinal fasciculus. B) Associations between SES and fractional anisotropy in the superior longitudinal fasciculi.

frontoparietal network structure and function, we examined whether any of these neural measures were associated with WM and academic performance.

With regard to neural structure, we found no associations of cortical thickness in left MFG and SPL with WM or parent-reported achievement ($p > .30$). FA in left SLF was positively associated with WM performance ($\beta = .31, p = .042$) and parent-reported achievement ($\beta = .34, p = .034$; Fig. 5A), but FA in the right SLF was not associated with either ($\beta = .21-.26, p = .124-.192$).

For neural function, we examined regions where children with higher SES had heightened activation during the WM task and where we observed significant task-related activation within the frontoparietal network in the group average (Encoding: left MFG, left and right SFG;

Delay: left MFG). See Methods for ROI definition. Given that we examined multiple regions, including those outside of frontoparietal regions (see below), we applied FDR correction to all tests. WM performance was positively associated with neural activation in left MFG ($\beta = .38, p = .008$), left SFG ($\beta = .40, p = .008$), and right SFG ($\beta = .29, p = .038$) during Encoding, but not left MFG during the Delay ($\beta = .26, p = .076$). Academic performance was positively associated with activation during Encoding in left MFG ($\beta = .35, p = .040$), left SFG ($\beta = .36, p = .032$; Fig. 5B and C), but not right SFG ($\beta = .20, p = .120$) nor in left MFG during the Delay ($\beta = .21, p = .102$).

A significant association between SES and neural activation emerged in several regions outside of the frontoparietal network, including the left occipital fusiform cortex during Encoding, left OFC and left middle

Table 3
Log income-to-needs. MNI coordinates reflect the peak of each cluster.

Anatomical Region	x	y	z	voxels	z-max	p-value
Encoding > ITI						
Left middle frontal gyrus,	-40	10	40	199	3.32	.0005
Left occipital fusiform cortex	-14	-84	-22	148	3.85	.006
Bilateral medial superior frontal gyrus	0	10	-54	140	3.29	.009
Delay > ITI						
Left posterior middle temporal gyrus	-62	-52	2	195	4.85	.002
Left orbitofrontal cortex	-40	-26	-4	165	3.47	.007
Left middle frontal gyrus	-58	18	20	153	3.77	.009
Probe > ITI						
Left posterior middle temporal gyrus	-54	-48	16	175	3.74	.004

temporal gyrus during the Delay, and left middle temporal gyrus during the Probe. As a final step, we investigated whether any of these regions were significantly associated with WM performance or parent-reported achievement after FDR correction. We found a significant association between activation in the occipital fusiform cortex and both WM performance ($\beta = .442, p = .022$; Supplemental Fig. 5) and parent-reported achievement ($\beta = .509, p = .006$; Supplemental Fig. 6), and between activation in the left OFC during the Delay and parent-reported achievement ($\beta = .320, p = .047$; Supplemental Fig. 6).

Mechanisms linking SES and academic achievement

Finally, we examined whether the environmental, cognitive, and neural factors that were related to both SES and parent-reported achievement mediated this association. Specifically, we examined cognitive stimulation, WM performance, FA in left SLF, and activation in left MFG and left SFG during WM Encoding as mediators. Jointly, these factors significantly mediated the association between SES and parent-reported achievement, and the strong association between SES and achievement was no longer significant in the final model (c path, $B = .439, p = .007$; c' path, $B = .068, p = .67$; Fig. 6). We conducted an additional mediation analysis that included all functional ROIs that were significantly associated with both SES and parent-reported achievement (i.e., including those outside the frontoparietal network) and this mediation analysis also produced a significant indirect effect (95% CI: .105 to .800, c path, $B = .439, p = .007$; c' path, $B = .021, p = .89$; Supplemental Fig. 7).

Discussion

The present study extends the burgeoning literature on SES-related neural differences that may contribute to the achievement gap by documenting differences in brain structure and function as a function of family SES that, in turn, are related to WM and academic performance. First, although we did not find differences in cortical thickness as a function of SES, we provide novel evidence for a link between low cognitive stimulation in the home environment—which has frequently

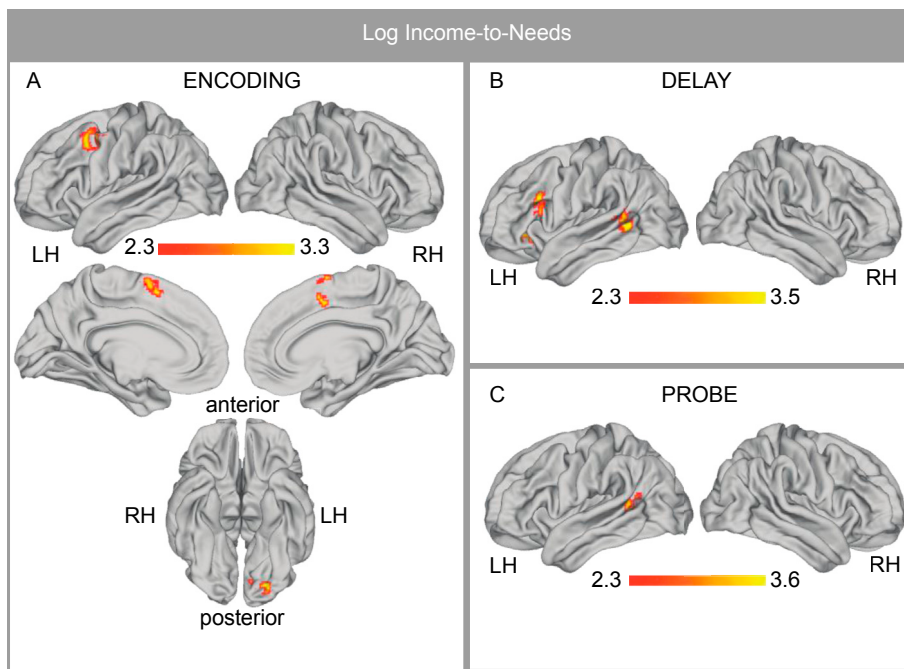


Fig. 4. Whole brain activation associations during a working memory paradigm using mean-centered predictor of log income-to-needs during: A) Encoding, B) Delay, and C) Probe.

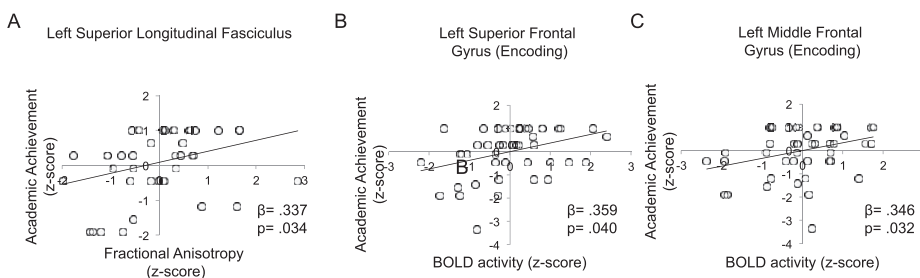


Fig. 5. Associations between FA in left SLF and parent-reported achievement (A) and between activation in regions that show whole-brain association with SES and parent-reported achievement (B and C).

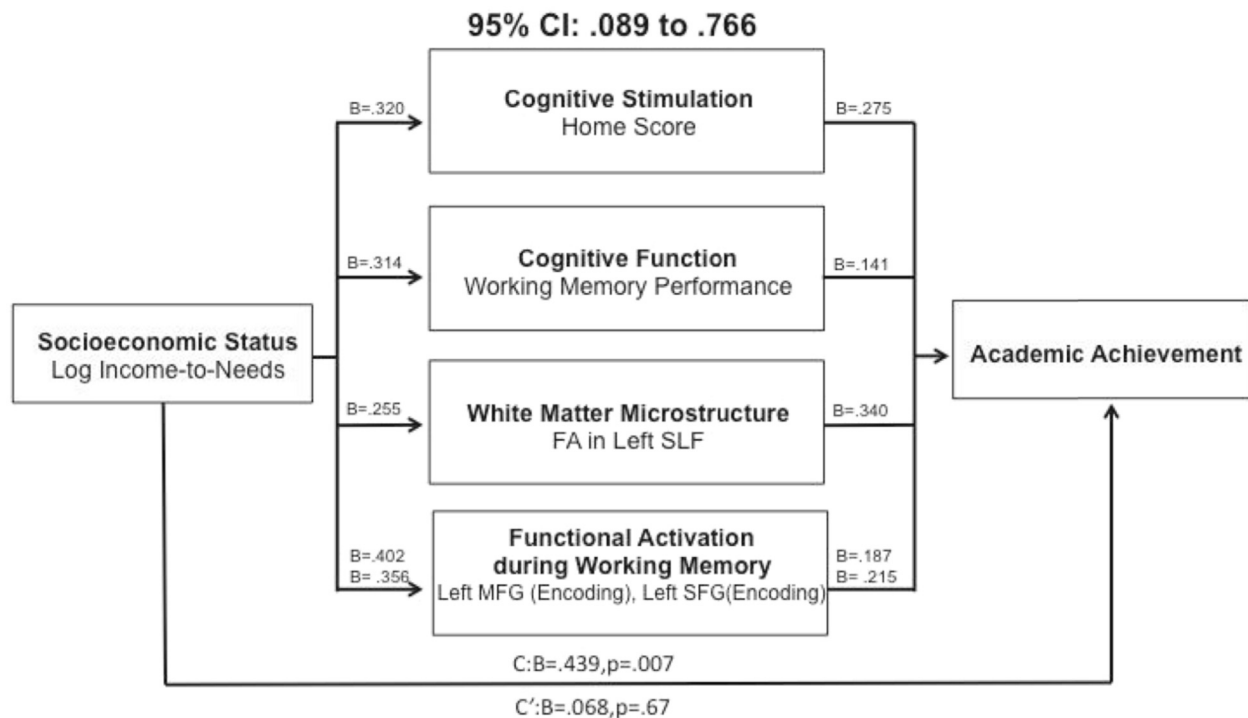


Fig. 6. Mediation model. Cognitive stimulation, WM performance, white matter connectivity in the frontoparietal network, and neural recruitment during the working memory task mediate the association between SES and parent-reported achievement (95% CI: .089 to .766).

been documented in low-SES households—and thinner cortex in frontoparietal regions. Second, we extend prior work that has focused primarily on cortical and sub-cortical structure by documenting SES-related differences in white matter microstructure in the SLF, a frontoparietal tract involved in WM (Mabbott et al., 2009; Vestergaard et al., 2011). Moreover, greater white matter integrity in this tract was associated with better academic achievement. Third, we demonstrate SES-related differences in brain activation in PFC and occipital-temporal cortex during WM encoding, maintenance, and retrieval, such that children from families with higher SES showed greater task-related activation. Greater activation in these regions was associated with improved performance on the WM task as well as better academic achievement. Finally, we found that cognitive stimulation, WM performance, and structure and function in the frontoparietal network fully mediated the association of SES with parent-reported achievement. Taken together, these findings highlight multiple links between SES and frontoparietal network structure and function and provide evidence for several environmental, neural, and cognitive factors that contribute to the SES-achievement gap.

Cognitive stimulation and cortical thickness

We extend prior work on SES and cortical thickness by documenting associations between cognitive stimulation and thickness in key nodes of the frontoparietal network and demonstrating that the degree of cognitive stimulation is a mechanism linking SES and cortical thickness. Cognitive stimulation is a key dimension of environmental experience that varies by SES (Bradley et al., 2001) and is argued to influence cortical thinning (McLaughlin et al., 2017; Sheridan and McLaughlin, 2014, 2016). Prior studies have found that low-SES and institutionalization, which are associated with low levels of cognitive stimulation, are associated with cortical thinning in the frontoparietal network (McLaughlin et al., 2014; Mackey et al., 2015; Piccolo et al., 2016; Brito et al., 2017). However, this is the first study to our knowledge to demonstrate direct associations between cognitive stimulation in the home and cortical structure in children and adolescents as well as a significant indirect effect of SES on cortical thickness that operates

through cognitive stimulation. These findings provide some support for theoretical models arguing that some forms of adversity characterized by environmental deprivation are associated with accelerated pruning of the cortex due to a lack of cognitive stimulation (McLaughlin et al., 2017; Sheridan and McLaughlin, 2014, 2016). Perhaps most importantly, these findings provide a direct target for interventions aimed at reducing the income-achievement gap, as cognitive stimulation was also related to academic achievement. Enhancing cognitive stimulation in the home environment might be one effective strategy for reducing SES-related disparities in academic outcomes.

SES, white matter microstructure, and academic achievement

Our findings also provide novel evidence for SES-related differences in white matter microstructure in the frontoparietal network. Specifically, we show that higher SES is associated with greater FA in the SLF, a tract that connects the dorsolateral PFC and posterior parietal cortex. Moreover, greater FA in the left SLF was associated with higher levels of academic achievement. Higher levels of connectivity in the SLF have been associated with better EF in children and adolescents (Urger et al., 2015), although in one study this was true only among low-SES youths (Ursache and Noble, 2016). Together, our findings suggest that greater white matter integrity in the frontoparietal network among children from higher-SES backgrounds may contribute to better WM and academic achievement and are broadly consistent with prior work demonstrating positive associations between FA in the SLF and educational attainment in late adolescence (Noble et al., 2013).

SES, neural function, and academic achievement

Our fMRI results replicate a previous study that found greater activation in the MFG during WM among higher as compared to lower-SES children (Finn et al., 2016), although a recent study found that lower SES was associated with greater activation in the IPS during WM (Sheridan et al., 2017). Future studies should investigate the possibility that different regions of the frontoparietal network are differentially

influenced by early SES. Also consistent with prior work (Finn et al., 2016), we find that greater left MFG activation during WM encoding was associated with both higher performance on the WM task and higher achievement. We extend this prior work in several ways. First, we show that higher SES is associated with greater activation during WM encoding in the medial SFG, a key node in the cognitive control network (Yeo et al., 2011) that is recruited for a wide range of EF tasks (e.g., Church et al., 2017; Verbruggen and Logan, 2008). Greater activation in this region was associated with better performance on the task as well as higher academic achievement. We additionally document greater recruitment of the fusiform gyrus during WM encoding among children from families with higher SES; greater activation in this region is also associated with better WM performance and academic achievement. Here, children raised in low-SES environments exhibit reduced activation in the visual association region involved in the initial encoding of the to-be-remembered stimulus—this could reflect reduced depth of perceptual processing or reduced visual attention (see Amso and Scerif, 2015; Rosen et al., 2018).

Environmental, cognitive, and neural, mechanisms in the SES-Achievement gap

Critically, we found that cognitive stimulation, WM performance, frontoparietal white matter structure, and frontoparietal recruitment during a WM task jointly mediated the association between SES and parent-reported achievement. These findings are broadly consistent with prior work showing that neural recruitment during a WM task could be a mechanism explaining the income-achievement gap (Finn et al., 2016) and that enrichment and stimulation in the home environment may explain the association between SES and EF (Hackman et al., 2015). Here, we provide evidence that multiple environmental, cognitive, and neural factors are involved in the association between SES and academic achievement.

Cognitive stimulation was not associated with white matter microstructure or functional recruitment during the WM task, although each of these measures was associated with SES. Recent work has suggested that many aspects of the home environment not measured in the present study including environmental predictability, exposure to toxins, nutrition, and parenting, may contribute SES-related neural differences (Johnson et al., 2016). It is possible that in low-SES environments, which are often characterized by lower levels of predictability (Deater-Deckard et al., 2012; Evans and Wachs, 2009), the environment produces an information processing style that prioritizes short-term goals over longer-term goals (Liu et al., 2012; Shah et al., 2012). This shift, coupled with fewer opportunities to engage in cognitively stimulating activities, may result in chronic underutilization of the frontoparietal network, which in turn may result in reduced ability to engage this network when circumstances demand it. Importantly, this strategy and resulting neural changes could be adaptive for children growing up in unpredictable environments (Ellwood-Lowe et al., 2016). However, when children encounter environments that require long-term sustained attention (e.g. school), they may be less equipped to deal with the required focus on long-term goals and associated EFs required to obtain those goals, resulting in poor performance.

Moreover, exposure to complex language is a key domain of cognitive stimulation that we did not measure directly. Differences in language exposure may have contributed to the left-lateralized pattern of SES-related differences observed here, consistent with work showing a reduced left lateralization among low compared to high SES children during a language rhyming task (Raizada et al., 2008). Language complexity and child-directed speech is reduced among children raised in low-SES environments (Hart and Risley, 1995; Walker et al., 1994; Fernald et al., 2013). While reduced language complexity and contingency has an obvious link to SES-related differences in language performance (Noble et al., 2005, 2007) and neural recruitment during language tasks (Romeo et al., 2017), a previous study found that reduced

complexity of language in the home environment was associated with differential recruitment of the PFC during an EF task among low-SES children (Sheridan et al., 2012). More complex language environments may provide greater opportunities for children to build and practice EF skills (McLaughlin, 2016) as well as early opportunities to disambiguate perceptually similar information that scaffold the development of the PFC and more complex forms of EF (see Amso and Scerif, 2015). Indeed, the PFC computations necessary for EF skills emerge much earlier in development than previously thought through the process of learning language (Werchan et al., 2016). Lower levels of caregiver interactions in low-SES households may contribute to reduced opportunities for learning categories of stimuli processed in the ventral visual stream; these differences may ultimately influence the ability to encode and sustain representations of complex visual stimuli (Amso and Scerif, 2015). Our finding that SES was positively associated with fusiform activation during WM encoding, which in turn was related to both WM and academic performance, is consistent with this possibility, and indicates that differences in early visual and linguistic processing may have meaningful implications for more complex cognitive functions. Higher SES environments, perhaps because of their higher levels of cognitive and caregiver stimulation, may enhance visual attention or perceptual processing during encoding and increase the ability to sustain these representations during maintenance, resulting in better performance. Future research should more closely examine language exposure and visual processing as potential mechanisms explaining SES related differences in neural, cognitive, and academic outcomes.

Limitations and future directions

The present findings have several notable strengths. Importantly, previous studies have used proxies for SES, including whether the child received free or reduced lunch (Finn et al., 2016), while in the present study we directly assess family SES as well as a parent report measure of cognitive stimulation. Furthermore, unlike previous studies we measure and control for childhood violence exposure to identify differences in brain structure and function that are driven by SES-related differences that are independent of violence exposure, which is known to impact neural development (McLaughlin et al., 2014). However, there are also several key limitations. First, the sample was relatively small, particularly given the large age range, which limited statistical power. Indeed, cortical thickness and white matter connectivity results only emerged in ROI analyses and not in the whole brain. A limited sample size increases the risk of both Type I and Type II errors and therefore, results should be interpreted with caution. Future studies should seek to replicate these findings with a larger sample size.

Second, unlike other studies that have found a link between SES, brain structure and function, and academic achievement (Mackey et al., 2015; Finn et al., 2016), we did not have access to statewide standardized test results, as such tests are not performed at every grade level in Washington State. Nor did we focus on actual grades, as the children in our sample came from a wide range of schools. Instead we relied on parent reports of children's academic performance across a range of subjects, which are strongly correlated with academic performance and do not vary by demographics (Maguin and Loeber, 1996). However, it is possible that SES may be related to differences in how parents perceive their children's academic performance. Parent-reports of academic achievement have been shown to be significantly related to objectively measured achievement, but are not a perfect proxy (Maguin and Loeber, 1996; Quiroga et al., 2013) and lower SES parents may be less accurate (e.g., Huston et al., 2005). Therefore, it will be critical for future studies to replicate the present findings using more objective measures of academic achievement. Additionally, while there is reason to believe that cognitive stimulation would mediate the link between SES and neural measures and those neural measures would in turn mediate the link between SES and academic achievement, the data did not support moving forward with a multilevel mediation analysis because cognitive

stimulation was associated only with cortical thickness and not the other neural measures. Any future studies that find links between SES, cognitive stimulation, neural measures, and academic achievement should explore this possibility. Furthermore, although our motion correction threshold remains common in pediatric fMRI studies, including recent studies on the development of the frontoparietal network and on SES-related differences in neural function (e.g., Peters et al., 2016; Romeo et al., 2017), even small amounts of motion can impact fMRI results (Siegel et al., 2014) and therefore results from the current study should be interpreted with caution. Additionally, it should be noted that the regions we refer to as the frontoparietal network overlap considerably with both the dorsal attention and cognitive control networks (Yeo et al., 2011). While findings for both of these networks would generate similar interpretations, future studies should focus on more fine-grained parcellation of regions within these networks. Finally, because of the cross-sectional nature of the study, replication of our findings with regard to environmental, cognitive, and neural mediators in longitudinal studies is warranted.

Conclusions

The present study adds to the growing body of literature that highlights SES-related differences in neural structure and function in children. We document multiple links between childhood SES and frontoparietal network structure and function and provide novel evidence that low cognitive stimulation, a common characteristic of low-SES households, is associated with thinner cortex in the frontoparietal network. Perhaps most importantly, we show that low cognitive stimulation, poor WM performance, reduced white matter microstructure in the fronto-parietal network, and reduced PFC recruitment during a WM task are mechanisms underlying the association between SES and academic achievement. Together, these findings suggest novel targets for reducing SES-related disparities in academic performance.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at <https://doi.org/10.1016/j.neuroimage.2018.02.043>.

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