Supplementary Online Content

Hair NL, Hanson JL, Wolfe BL, Pollak SD. Association of child poverty, brain development, and academic achievement. *JAMA Pediatr*. Published July 20, 2015. doi:10.1001/jamapediatrics.2015.1475.

eAppendix 1. Imaging Appendix.
eAppendix 2. Statistical Appendix.
eFigure 1. Normative Developmental Curve: Total Gray Matter.
eFigure 2. Normative Developmental Curve: Frontal Lobe Gray Matter.
eFigure 3. Normative Developmental Curve: Temporal Lobe Gray Matter.
eFigure 4. Normative Developmental Curve: Hippocampus Gray Matter.
eTable 1. Recruitment Summary by SES, NIH MRI Study of Normal Brain Development.
eTable 2. Exclusion During Early Screening, NIH MRI Study of Normal Brain Development.
eTable 3. Predicted Probability of Incomplete Neuroimaging Data.
eTable 4. Normative Developmental Curves for Regions of Interest.
eTable 5. Summary of Normed Developmental Measure.
eTable 6. SES and Brain Development: Sensitivity to Alternative Measures of Low SES.
eTable 7. SES, Brain Development, and Achievement (Regional Specificity, WASI).
eTable 8. SES, Brain Development, and Achievement (Regional Specificity, WJ-III).
eTable 9. SES, Brain Development, and Achievement (Mediation Regressions).

This supplementary material has been provided by the authors to give readers additional information about their work.

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eAppendix 1: Imaging Appendix.

To examine the neurobiological correlates of socioeconomic status, regions of interest were quantified by registering a parcellated brain template via diffeomorphic warping to each individual subject. The wrapping algorithm used symmetric normalization (SyN; Avants and Gee (2004)) which was recently judged as one of the best available in a comparison of fourteen nonlinear registration routines (Klein et al., 2009).

The approach used consisted of the following steps: first T1-weighted images were checked for scanner artifacts (such as extreme field inhomogeneity). Next, these volumes were segmented using custom a priori brain tissue segmentations generated by the Template-o-Matic toolbox (Wilke et al., 2008). These custom segmentations were based on the age and sex distributions of the full sample. Structural neuroimaging expert Jamie Hanson then checked the accuracy of each subject's segmentation. If any errors were present, the bounding box or image matrix was adjusted and MRI images reprocessed. If after this correction segments still contained errors, they were corrected by hand to remove skull, dura, and other nonbrain matter. Once segmentation was completed successfully, each subject's tissue segments were registered to a template where brain regions were previously quantified (Davatzikos et al., 2001). This procedure yielded an individual subject's MRI with ninety possible regions of interest across the brain. Amount of gray or white matter was then summed in each region of interest.

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eAppendix 2: Statistical Appendix.

Modeling Normal Brain Development. To account for the non-monotonic "inverted U" shaped trajectories of gray matter volumes, we first establish a reference of typical development for each brain area of interest. We use mixed effects linear models, a statistical analysis technique that combined cross-sectional and longitudinal data and accounts for both intrasubject correlation and unbalanced panel design, to estimate a series of growth curves.

$$ROI_{ist} = \beta_{0s} + \beta_{1s}Age_{ist} + \beta_{2s}Age_{ist}^2 + b_{0i} + b_{1i}Age_{ist} + \epsilon_{it} \quad (1)$$

The dependent variable, ROI_{ist}, is the volume, measured in cubic centimeters, of a brain region of interest for subject i of sex s at sample period t. The estimated developmental curves are sex-specific and quadratic in age. The terms b_{0i} and b_{1i} allow for subject-specific random intercept and slope components.

Using the estimated developmental trajectories (eTable 4, eFigures 1- 4), we construct an index of structural brain development based on an adjusted or "normed" measure of regional GM volume: subject regional volume expressed as a percentage of an expected volume given sex and age.

$$ROI_{it}^* = \frac{ROI_{ist}}{E[ROI_{ist}|sex_i, Age_{ist}]} * 100 \quad (2)$$

This index reflects deviations from normative development. Primary analyses consider whether a region is smaller or larger than expected comparing a child to others of the same sex and age. Basic summary statistics related to developmental indices (ROI_{it}^*) are available in eTable 5.

Modeling Brain Development and Poverty. Using the constructed indices, we examine the influence of socioeconomic status, specifically growing up in or near poverty, on development within focal areas of the brain.

$$ROI_{it}^* = \beta_0 + \beta_1 LowIncome_{it} + [\beta_2 X_{it} +]\epsilon_{it} \quad (3)$$

The dependent variable (ROI_{it}^*) is defined as in equation (2). $LowIncome_{it}$ is an indicator of family financial resources or socioeconomic status. Several classifications of SES are evaluated. We introduce binary (e.g., an indicator equal to 1 if household income below 1.5 times FPL) as well as categorical measures of income and consider the sensitivity of estimates to the selection of particular income threshold. Specifications with an extended set of covariates control for birth weight, race/ethnicity, family size, and maternal education. Standard errors are clustered at the individual level.

Modeling Brain Development in Relation to Poverty and Academic Achievement. As hypothesized, childhood poverty was associated with lower WASI and WJ-III scores. To better inform our understanding of the relationship between poverty and impaired academic performance, we conduct mediation analyses (Preacher and Hayes, 2004).

$$Achievement_{it} = \beta_0 + \beta_1 LowIncome_{it} + [\gamma X_{it} +]\epsilon_{it} \quad (4)$$

$$Achievement_{it} = \beta_0 + \beta_1 LowIncome_{it} + \beta_2 ROI_{it}^* + [\gamma X_{it} +]\epsilon_{it} \quad (5)$$

We test each focal area – where we report structural differences among low income children – as a possible mediator of the income-achievement gap. The outcome of interest is a child's performance on an index of academic ability or achievement: the Wechsler Abbreviated Scale of Intelligences (Full IQ, Performance IQ, Verbal IQ) or Woodcock-Johnson III Tests of Achievement (Math Computation, Letter-Word Identification, Passage Comprehension). All specifications adjust for sex and age. Specifications with an extended set of covariates additionally control for birth weight, race/ethnicity, family size, and maternal education. Standard errors are clustered at the individual level.

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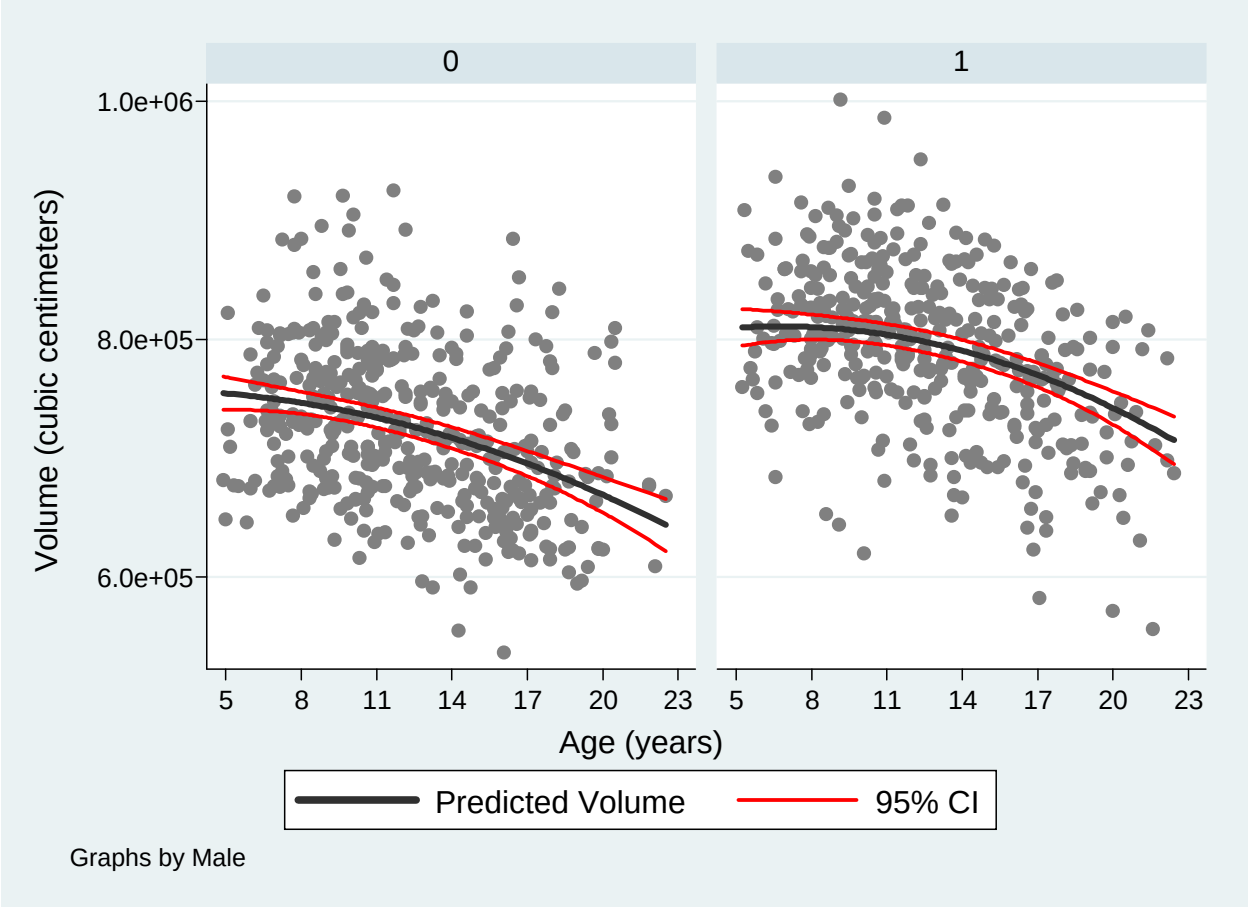
eFigure 1: Normative Developmental Curve: Total Gray Matter.



Notes: Sex-specific developmental trajectories estimated using mixed effects linear models. Regression coefficients are available in eTable 4.

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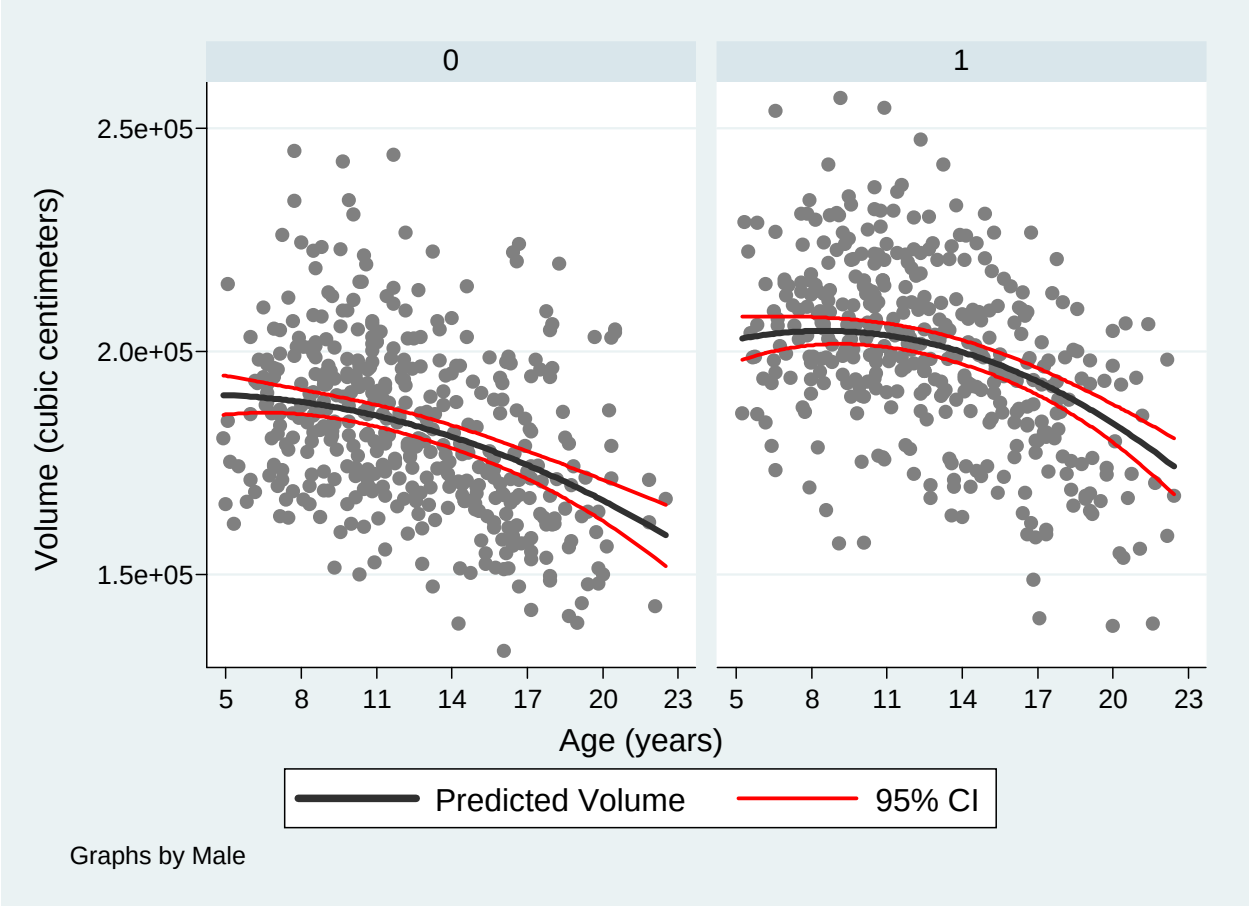
eFigure 2: Normative Developmental Curve: Frontal Lobe Gray Matter.



Notes: Sex-specific developmental trajectories estimated using mixed effects linear models. Regression coefficients are available in eTable 4.

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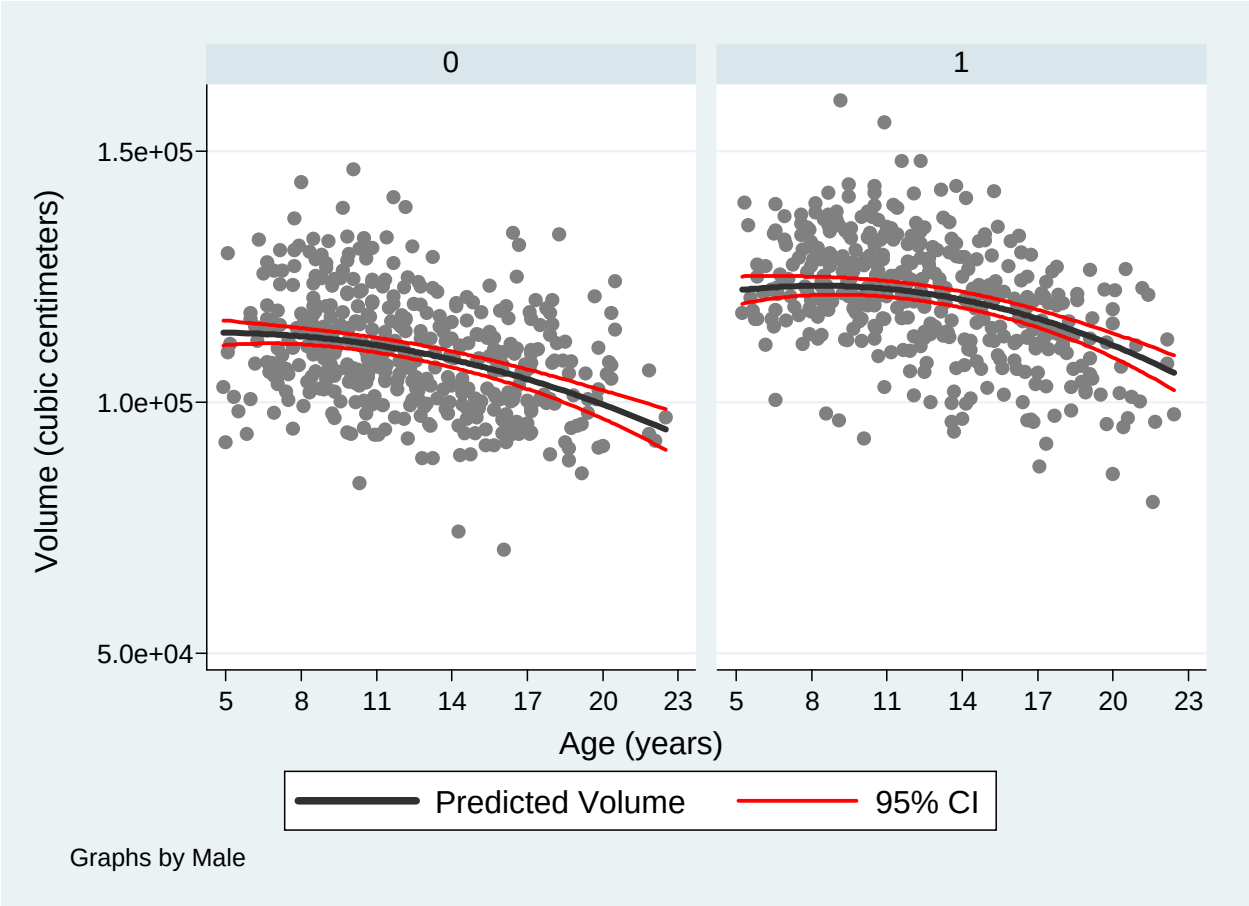
eFigure 3: Normative Developmental Curve: Temporal Lobe Gray Matter.



Notes: Sex-specific developmental trajectories estimated using mixed effects linear models. Regression coefficients are available in eTable 4.

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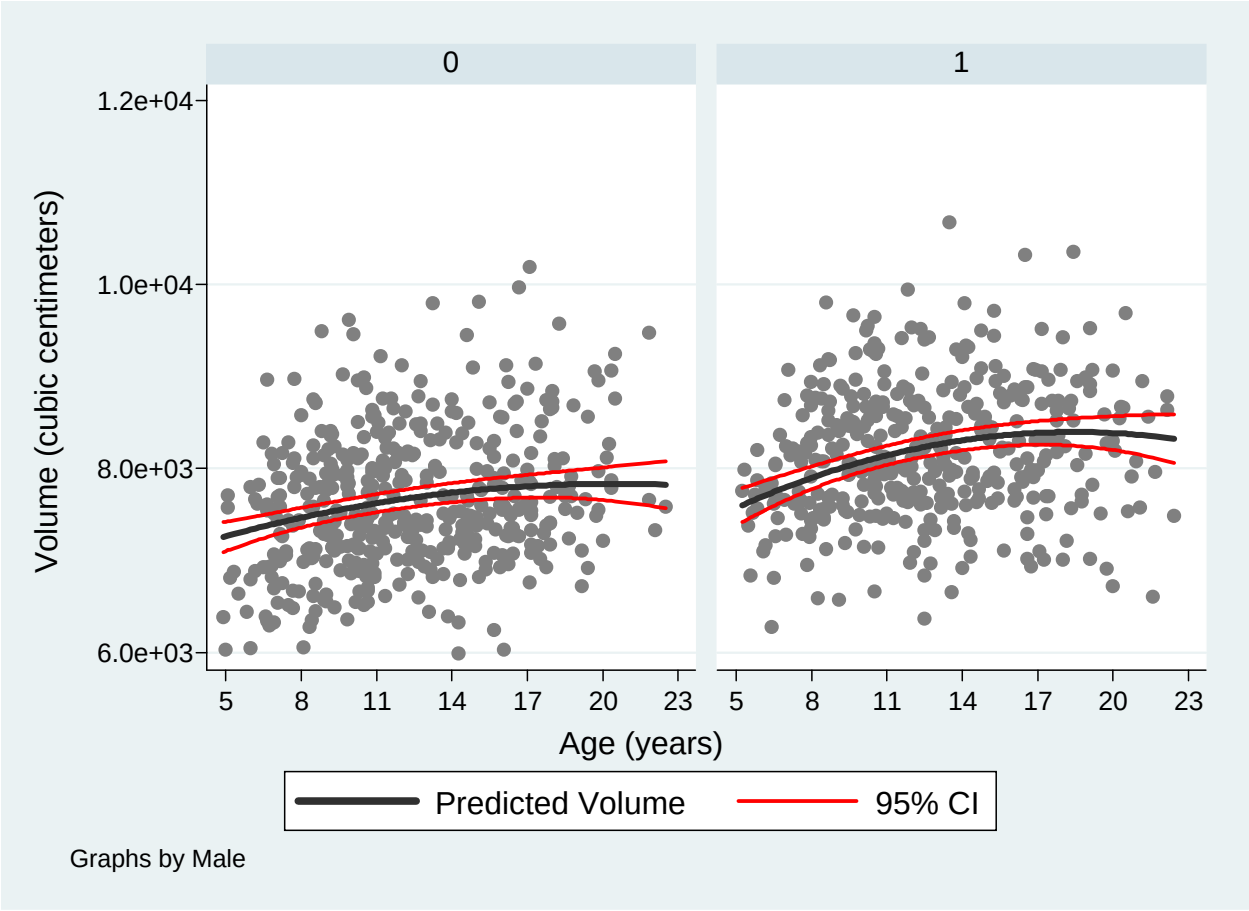
eFigure 4: Normative Developmental Curve: Hippocampus Gray Matter.



Notes: Sex-specific developmental trajectories estimated using mixed effects linear models. Regression coefficients are available in eTable 4.

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eTable 1. Recruitment Summary by SES, NIH MRI Study of Normal Brain Development.

Recruitment Summary by SES.						
NIH MRI Study of Normal Brain Development						
	Low SES		**Mid SES**		**High SES**	
Intro Letters Sent	15313		13555		6561	
Newly Contacted	10939	71.40%	10211	75.30%	4955	75.50%
Refused on Calls	3102	28.40%	3959	38.80%	2170	43.80%
Refusals	4824	44.10%	5710	55.90%	3011	60.80%
Exclusions	2565	37.90%	1410	27.00%	517	21.80%
CBCLs Sent	685	19.30%	988	32.00%	497	34.80%
CBCLs Received	418	61.00%	646	65.40%	333	67.00%
CBCLs Passed	337	80.60%	549	85.00%	304	91.30%

Source: K.N. Botteron, L.S. Freund & The Brain Development Cooperative Group (2004, October). *The NIH Study of Normal Brain Development: Objective-2 Behavior Analyses.* Poster presented at the Society for Neuroscience Annual Meeting, San Diego, CA.

eTable 2. Exclusion During Early Screening, NIH MRI Study of Normal Brain Development.

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Exclusions During Early Screening					
NIH MRI Study of Normal Brain Development					
	Low	**Mid**	**High**	**Total**	
Size (off growth chart)	12	16	13	41	(1.30%)
Braces	19	29	15	63	(2.10%)
Chronic Medical Disorder	9	14	3	26	(0.90%)
Lead Poisoning	3	0	0	3	(0.10%)
Seisures, LOC, Neurological Disorder	28	37	11	76	(2.80%)
Psychiatric Disorders - All Sites	**Low**	**Mid**	**High**	**Total**	
Major Depression or Bipolar	10	21	8	39	(1.40%)
ADHD	75	126	60	261	(9.20%)
Autism	12	20	8	40	(1.40%)
Tourette Syndrome or OCD	2	3	1	6	
Schizophrenia	0	1	0	1	
Alcoholism	2	1	0	3	

Source: K.N. Botteron, L.S. Freund & The Brain Development Cooperative Group (2004, October). *The NIH Study of Normal Brain Development: Objective-2 Behavior Analyses.* Poster presented at the Society for Neuroscience Annual Meeting, San Diego, CA.

eTable 3. Predicted Probability of Incomplete Neuroimaging Data.

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		Logit Marginal Effects[a]	
		dy/dx	P > |z|
Male		0.0317	0.144
Non-white		0.0102	0.820
Hispanic		0.0411	0.335
Birth weight (ounces)		-0.0006	0.478
Age (years)		-0.0293	0.000
Maternal Education			
High School or less		0.0288	0.361
Some College		0.0347	0.344
College		0.0188	0.354
Household Income[b]			
Below 100% FPL		-0.0558	0.419
100 to 150% FPL		-0.0257	0.435
150 to 200% FPL		-0.0159	0.751
Observations		1019	
Pseudo R^2		0.1045	

Notes: [a] Marginal effects for birth weight and age evaluated at sample means. Estimates related to binary covariates estimated as discrete change form 0 to 1. Model additionally controls for survey time point and collection site. Robust standard errors adjust for clustering on collection site. [b] Household income adjusted for family size and expressed relative to federal poverty level (FPL).

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eTable 4. Normative Developmental Curves for Regions of Interest.

Normative Developmental Curves for Regions of Interest **NIH MRI Study of Normal Brain Development**					
	1	**2**	**3**	**4**	**5**
	Total	**Frontal**	**Temporal**	**Hippo.**	**Amyg.**
	GM	**GM**	**GM**	**GM**	**GM**
Age (months)	34.6	50.45	36.97	8.212**	3.429**
	-208.7	-67.39	-36.02	-2.483	-0.938
Age^2	-1.684**	-0.606**	-0.382**	-0.0168**	-0.00846**
	-0.663	-0.215	-0.115	-0.00795	-0.003
Male	35166.4	4015.2	4401.4	10.65	-28.86
	-23712	-7628	-4107.6	-282.3	-101.1
Age x Male	386.2	165.6*	78.37	5.807	2.748**
	-298.1	-96.27	-51.48	-3.549	-1.337
Age^2 x Male	-0.941	-0.45	-0.199	-0.0147	-0.00738*
	-0.935	-0.302	-0.162	-0.0112	-0.0043
Constant	758826.8**	189420.4**	113097.5**	6831.5**	1944.2**
	-16322	-5251.5	-2826.8	-194.3	-69.82
Observations	823	823	823	823	823

Notes: Sex-specific development trajectories (mixed effects linear models) allow for subject-specific random intercept and slope components. Growth models that additionally adjust for PSU/scanner are available upon request. We found nothing to suggest systematic differences across study sites or MRI machines.

* $p < 0.10$, ** $p < 0.05$

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eTable 5. Summary of Normed Developmental Measure.

Summary of Normed Developmental Measure NIH MRI Study of Normal Brain Development				
	Min	**Max**	**Mean**	**SD**
Full Analysis Sample				
Total GM	75.6	126.6	100.1	8.2
Frontal GM	72.5	132.2	100.0	9.4
Temporal GM	66.6	130.7	100.2	9.4
Hippo GM	77.3	130.5	100.1	9.0
Low Income[a]				
Total GM	75.6	115	96.6	9.1
Frontal GM	72.5	116.6	96.8	10.1
Temporal GM	68.5	116.5	96.4	10.8
Hippo GM	77.3	123.3	96.7	9.5
High Income[b]				
Total GM	84.4	126.6	100.8	9.1
Frontal GM	80.8	132.2	100.7	9.1
Temporal GM	77.9	127.2	101.0	8.7
Hippo GM	86.0	128.8	101.3	8.4

Notes: Full sample consists of 823 observations from 389 children and adolescents with non-missing neuroimaging and demographic information. Regional volumes are expressed as a percentage of a sex- and age-specific norm. [a] Household income below 150% of the FPL. [2] Household income above 400% of the FPL.

eTable 6. SES and Brain Development: Sensitivity to Alternative Measures of Low SES.

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SES and Brain Development: Sensitivity to Alternative Measures of Low SES

NIH MRI Study of Normal Brain Development

	1	2	3	4
	Total GM	**Frontal GM**	**Temporal GM**	**Hippo GM**
	Current Family Income (Adjusted[a])			
Below 150% FPL	-3.177	-3.075	-4.165*	-4.214**
	(1.964)	(2.206)	(2.241)	(1.988)
Above 200% FPL	0.727	0.502	0.0932	-0.553
	(1.039)	(1.206)	(1.247)	(1.322)
	Minimum Family Income			
Below $25,000	-8.614**	-6.062**	-6.332**	-5.952**
	(3.012)	(2.118)	(2.389)	(2.446)
Above $35,000	1.978	-0.659	0.501	-1.025
	(1.953)	(1.532)	(1.649)	(1.682)
	Permanent Family Income[b]			
Below $25,000	-6.421**	-8.898**	-7.175*	-6.954**
	(2.115)	(3.284)	(4.007)	(3.181)
Above $35,000	0.722	1.769	3.379	2.481
	(1.479)	(2.117)	(2.673)	(2.624)
	Minimum Family Income (Adjusted)			
Below 100% FPL	-5.240**	-5.197*	-5.230*	-6.636**
	(2.364)	(2.673)	(2.82)	(2.107)
Above 200% FPL	1.669	1.514	1.72	0.23
	(1.152)	(1.307)	(1.34)	(1.363)
	Permanent Family Income (Adjusted)			
Below 150% FPL	-4.355*	-4.688*	-2.783	-6.287**
	(2.51)	(2.795)	(3.069)	(2.788)
Above 200% FPL	-0.0305	-0.44	0.945	-1.918
	(1.821)	(2.082)	(2.244)	(2.288)
	Current Family Income (HUD Adjusted[c])			
Below $25,000	-9.076**	-9.745**	-10.13**	-4.192
	(2.979)	(3.336)	(3.614)	(3.562)
Above $35,000	-0.249	-1.291	-0.98	2.735
	(2.048)	(2.285)	(2.439)	(2.403)

Notes: Models mirror those presented in Table 2 with varying measures of parental SES. [a] Household income is adjusted for family size according to official federal poverty thresholds. [b] Household income in recorded as a categorical measure. We assign family income a numerical value at the categorical midpoint and average over all available sample periods. [c] Household income adjusted for both family size and geographic variations. Clustered standard errors in parentheses. * p < 0.10, ** p < 0.05

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eTable 7. SES, Brain Development, and Achievement (Regional Specificity, WASI).

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SES, Brain Development, and Achievement **NIH MRI Study of Normal Brain Development**												
	WASI Full IQ (n = 802)				**WASI Performance IQ (N=802)**				**WASI Verbal IQ (n = 802)**			
	1	**2**	**3**	**4**	**1**	**2**	**3**	**4**	**1**	**2**	**3**	**4**
Below 150% FPL	-8.025**	-6.474**	-6.677**	-6.680**	-6.764**	-5.241**	-5.420**	-5.411**	-7.519**	-6.302**	-6.469**	-6.480**
	(1.837)	(1.661)	(1.656)	(1.653)	(2.029)	(1.851)	(1.832)	(1.83)	(1.744)	(1.658)	(1.662)	(1.656)
Total GM		0.428**				0.387**				0.361*		
		(0.0948)				(0.101)				(0.0993)		
Total WM		-0.0523	-0.0106			0.00581	0.0302			-0.0843	-0.0384	
		(0.0879)	(0.085)			(0.0916)	(0.0899)			(0.0901)	(0.0857)	
Parietal Lobe GM			0.0996	0.0966			0.185	0.193			-0.0038	-0.0145
			(0.128)	(0.127)			(0.125)	(0.122)			(0.135)	(0.135)
Occipital Lobe GM			-0.0815	-0.0834			-0.11	-0.104			-0.0246	-0.0313
			(0.101)	(0.102)			(0.0981)	(0.0983)			(0.115)	(0.115)
Frontal Lobe GM			0.0829	0.0824			0.0126	0.0141			0.121	0.119
			(0.142)	(0.142)			(0.142)	(0.142)			(0.151)	(0.151)
Temporal Lobe GM			0.252*	0.251*			0.248*	0.253*			0.192	0.185
			(0.139)	(0.136)			(0.135)	(0.132)			(0.147)	(0.146)

Notes: Standard errors in parentheses. * p < 0.10, ** p < 0.05

eTable 8. SES, Brain Development, and Achievement (Regional Specificity, WJ-III).

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SES, Brain Development, and Achievement
NIH MRI Study of Normal Brain Development

	WJ-III Math Computation (n = 787)				WJ-III Letter-Word Identification (n = 798)				WJ-III Passage Comprehension (n = 797)			
	1	2	3	4	1	2	3	4	1	2	3	4
Below 150% FPL	-7.150**	-5.905**	-6.143**	-6.149**	-4.305**	-3.666**	-3.633**	-3.625**	-5.558**	-4.966**	-4.983**	-4.952**
	(1.568)	(1.435)	(1.439)	(1.436)	(1.449)	(1.438)	(1.445)	(1.449)	(1.499)	(1.472)	(1.477)	(1.481)
Total GM		0.361**				0.158*				0.0913		
		(0.0955)				(0.0862)				(0.0738)		
Total WM		-0.0672	-0.0228			0.0093	0.0294			0.101	0.117*	
		(0.0876)	(0.0861)			(0.0808)	(0.0767)			(0.0686)	(0.0651)	
Parietal Lobe GM			-0.049	-0.055			-0.109	-0.101			0.0472	0.0765
			(0.13)	(0.127)			(0.111)	(0.111)			(0.0982)	(0.0992)
Occipital Lobe GM			-0.0085	-0.0125			0.0123	0.0176			-0.023	-0.0016
			(0.103)	(0.103)			(0.0869)	(0.0867)			(0.079)	(0.0791)
Frontal Lobe GM			0.294**	0.292*			0.0592	0.0607			-0.0911	-0.0838
			(0.149)	(0.149)			(0.116)	(0.115)			(0.119)	(0.118)
Temporal Lobe GM			0.0499	0.0458			0.167	0.173			0.131	0.153
			(0.123)	(0.123)			(0.109)	(0.107)			(0.103)	(0.101)

Notes: Standard errors in parentheses. * p < 0.10, ** p < 0.05

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eTable 9. SES, Brain Development, and Achievement (Mediation Regressions).

SES, Brain Development, and Achievement **NIH MRI Study of Normal Brain Development**					
	1	**2**	**3**	**4**	**5**
	Base	**GM**	**Frontal**	**Temporal**	**Hippo.**
	WASI Full IQ (n = 802)				
Below 150% FPL	-8.025**	-6.510**	-6.916**	-6.614**	-6.881**
	(1.837)	(1.66)	(1.688)	(1.658)	(1.679)
Brain		0.388**	0.306**	0.330**	0.303**
		(0.0718)	(0.063)	(0.0608)	(0.0713)
	WASI Performance IQ (n = 802)				
Below 150% FPL	-6.764**	-5.236**	-5.648**	-5.320**	-5.664**
	(2.029)	(1.851)	(1.878)	(1.834)	(1.929)
Brain		0.391**	0.308**	0.338**	0.291**
		(0.0758)	(0.0653)	(0.0653)	(0.0669)
	WASI Verbal IQ (n = 802)				
Below 150% FPL	-7.519**	-6.361**	-6.670**	-6.460**	-6.572**
	(1.744)	(1.652)	(1.671)	(1.664)	(1.604)
Brain		0.296**	0.234**	0.247**	0.251**
		(0.0718)	(0.064)	(0.0619)	(0.0747)
	WJ-III Math Computation (n = 787)				
Below 150% FPL	-7.150**	-5.950**	-6.180**	-6.148**	-6.268**
	(1.568)	(1.429)	(1.422)	(1.462)	(1.476)
Brain		0.308**	0.270**	0.238**	0.235**
		(0.0648)	(0.0573)	(0.0557)	(0.0603)
	WJ-III Letter-Word Identification (n = 798)				
Below 150% FPL	-4.350**	-3.659**	-3.831**	-3.647**	-3.975**
	(1.449)	(1.441)	(1.438)	(1.45)	(1.436)
Brain		0.166**	0.132**	0.154**	0.0881
		(0.0571)	(0.0489)	(0.0487)	(0.0561)
	WJ-III Passage Comprehension (n = 797)				
Below 150% FPL	-5.558**	-4.897**	-5.154**	-4.943**	-5.067**
	(1.499)	(1.467)	(1.477)	(1.477)	(1.441)
Brain		0.170**	0.113**	0.145**	0.131**
		(0.0506)	(0.0457)	(0.044)	(0.0546)

Notes: Scores on both the WASI and WJ-III are standardized with a mean of 100 and a standard deviation of 15. The "Base" specification controls for sex and age. Subsequent specifications introduce an index of structural development in a focal rain area: regional volume expressed as a percentage of a sex and age-specific norm. Clustered standard errors in parentheses.

* $p < 0.10$, ** $p < 0.05$

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