PNAS

Supplementary Information for
Prenatal Exposure to Maternal Social Disadvantage and Psychosocial Stress and Neonatal White Matter Connectivity at Birth

Rachel E. Lean*, Christopher D. Smyser, Rebecca G. Brady, Regina L. Triplett, Sydney Kaplan, Jeanette K. Kenley, Joshua S. Shimony, Tara A. Smyser, J. Phillip Miller, Deanna M. Barch, Joan L. Luby, Barbara B. Warner, and Cynthia E. Rogers.

*Corresponding Author: Rachel E. Lean. Washington University School of Medicine, Campus Box 8514, St. Louis, MO 63110.
Email: rachel.lean@wustl.edu

This PDF file includes:

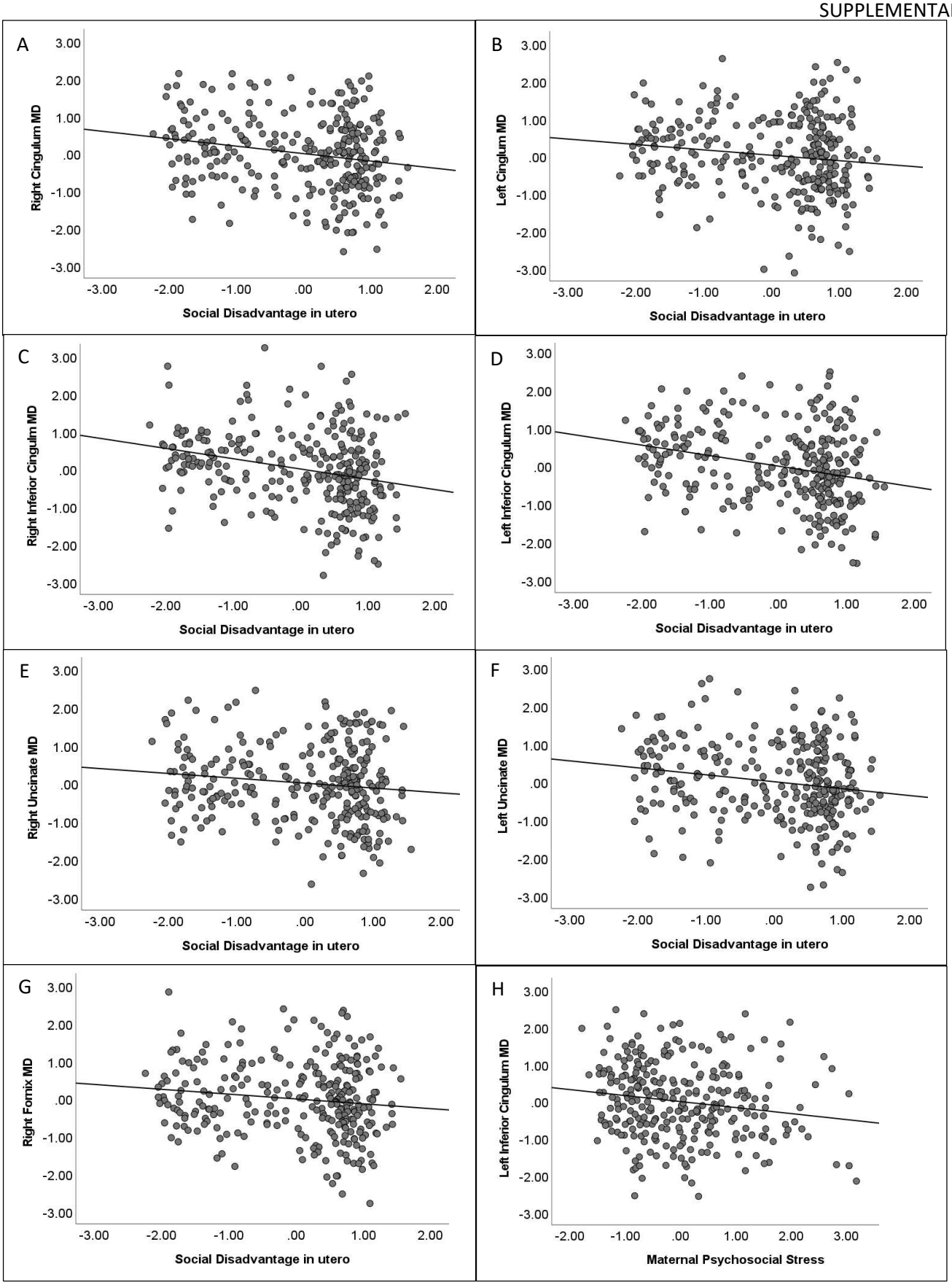

Figure S1. Key Latent Factor and MD/FA Associations. Panels A – G correspond with Table S1 and panel H corresponds with Table S2. MD/FA values shown as standardized residuals adjusted for sex and infant PMA at MRI scan.

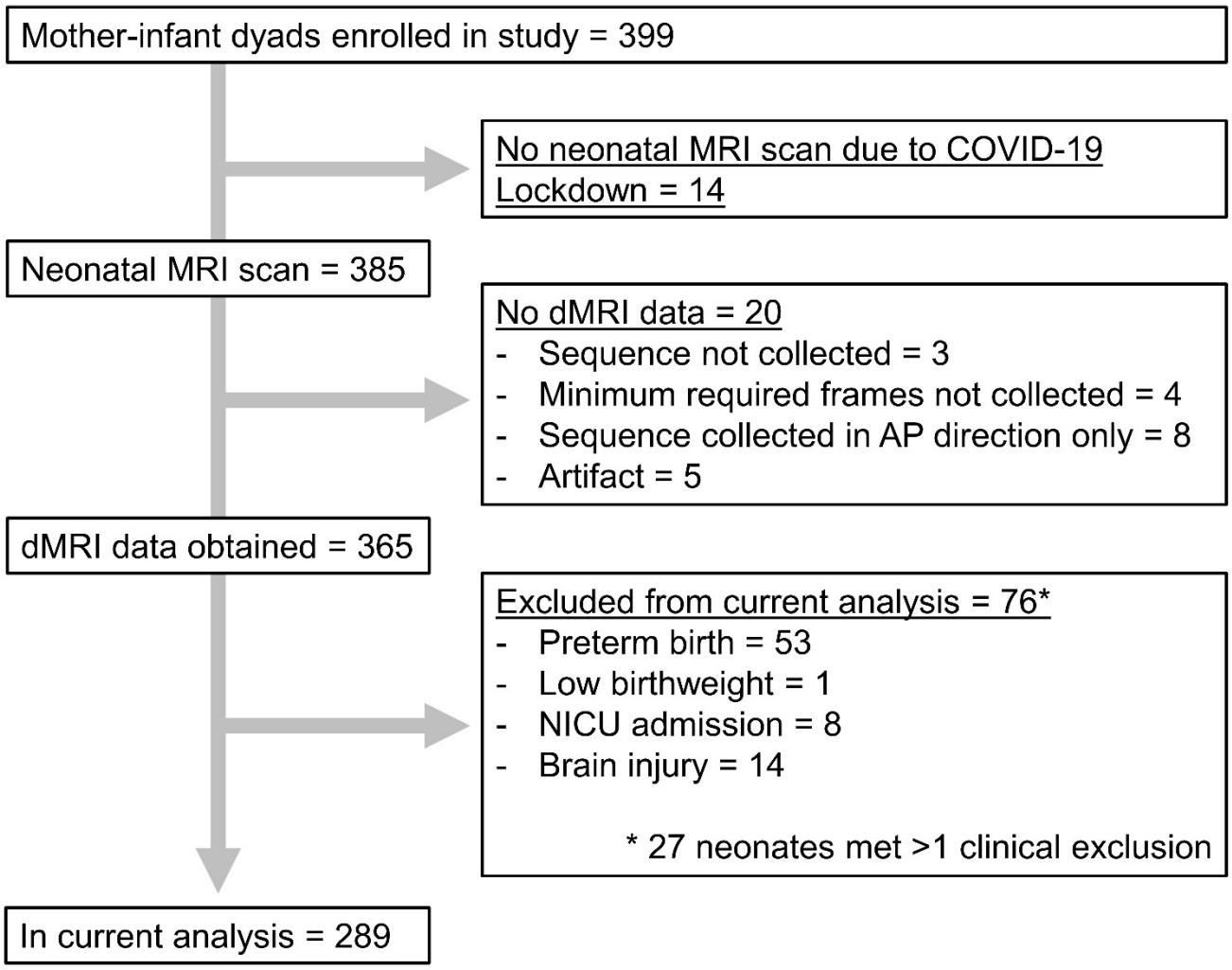

Figure S2. Participant flow diagram from study enrollment (*n* = 399) through to inclusion in final reported data analysis (*n* = 289).
dMRI, diffusion magnetic resonance imaging; AP, Anterior-to-Posterior direction; NICU, Neonatal Intensive Care Unit

Structural Equation Modelling (SEM) of Social Disadvantage and Psychosocial Stress.
As described in Luby et al. (1), SEM was performed in MPLUS (version 8.4) to group the observed prenatal adversity variables into a maternal Social Advantage latent factor (Income-to-Needs Ratio, Area Deprivation Index, health insurance status, highest level of education, and Healthy Eating Index) and a Psychosocial Stress latent factor (depression symptoms, perceived stress, racial discrimination, and lifetime measures of trauma and life events) (Figure S2, adapted from Luby et al.). The SEM was performed using maximum likelihood estimation with robust standard errors to create latent factor scores for all 399 mothers, including those with partial data on observed variables. As described in Luby et al., a two-factor model provided the best fit of the data with all fit statistics in an acceptable range (RMSEA = 0.042, SRMR = 0.055, CFI/TU = 0.995/0.946). Additionally, there were low correlations between the observed variables for one factor (*e.g.*, Social Advantage) with the other factor (*e.g.,* Psychosocial Stress), supporting the grouping of the observed variables. An alternative three-factor model was performed, but the three-factor model did not provide an adequate fit of the data (RMSEA = 0.080 and SMSR = 0.080 were in an acceptable range but CFI/TLI = 0.844/0.808 was not in an acceptable range) and variable loadings on the third factor were all low. Thus, the two-factor model was selected for analyses. We also opted to use latent factors to account for multiple, correlated socio-economic or psychosocial variables rather than to examine interactions between observed variables within a latent factor. Note that for the purposes of the current study, standardized Social Advantage values were reverse scored and termed Social Disadvantage to (a) correspond with the direction of Psychosocial Stress (higher z-scores = greater adversity) and (b) allow for easier interpretation of associations with MD and FA, which are typically inversely related in neonates (2). In the current study sample (n = 289), Social Disadvantage and Psychosocial Stress were positively correlated (Pearson r = .40, p <.001).

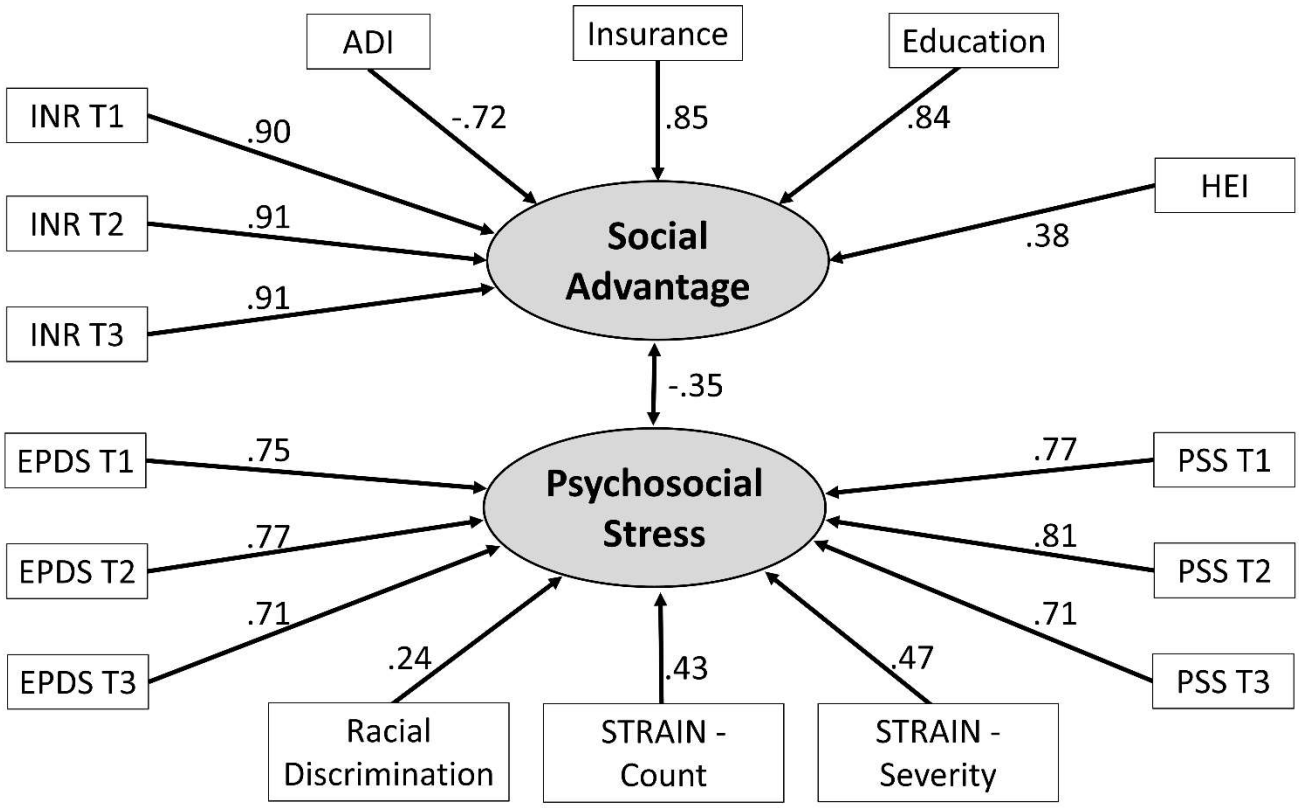

Figure S3. Structural Equation Model of Latent Factors. Adapted from Luby et al. (1), Figure S3 illustrates the latent prenatal Social Advantage and Psychosocial Stress factors and their observed components (n = 399). Standardized estimates between observed and latent variables, as well as between latent variables, are shown.
T1, Trimester 1; T2, Trimester 2; T3, Trimester 3; INR, Income-to-Needs Ratio; ADI, Area Deprivation Index; HEI, Healthy Eating Index; EPDS, Edinburgh Postnatal Depression Scale; STRAIN, Stress and Adversity Inventory for Adults; PSS, Perceived Stress Scale.

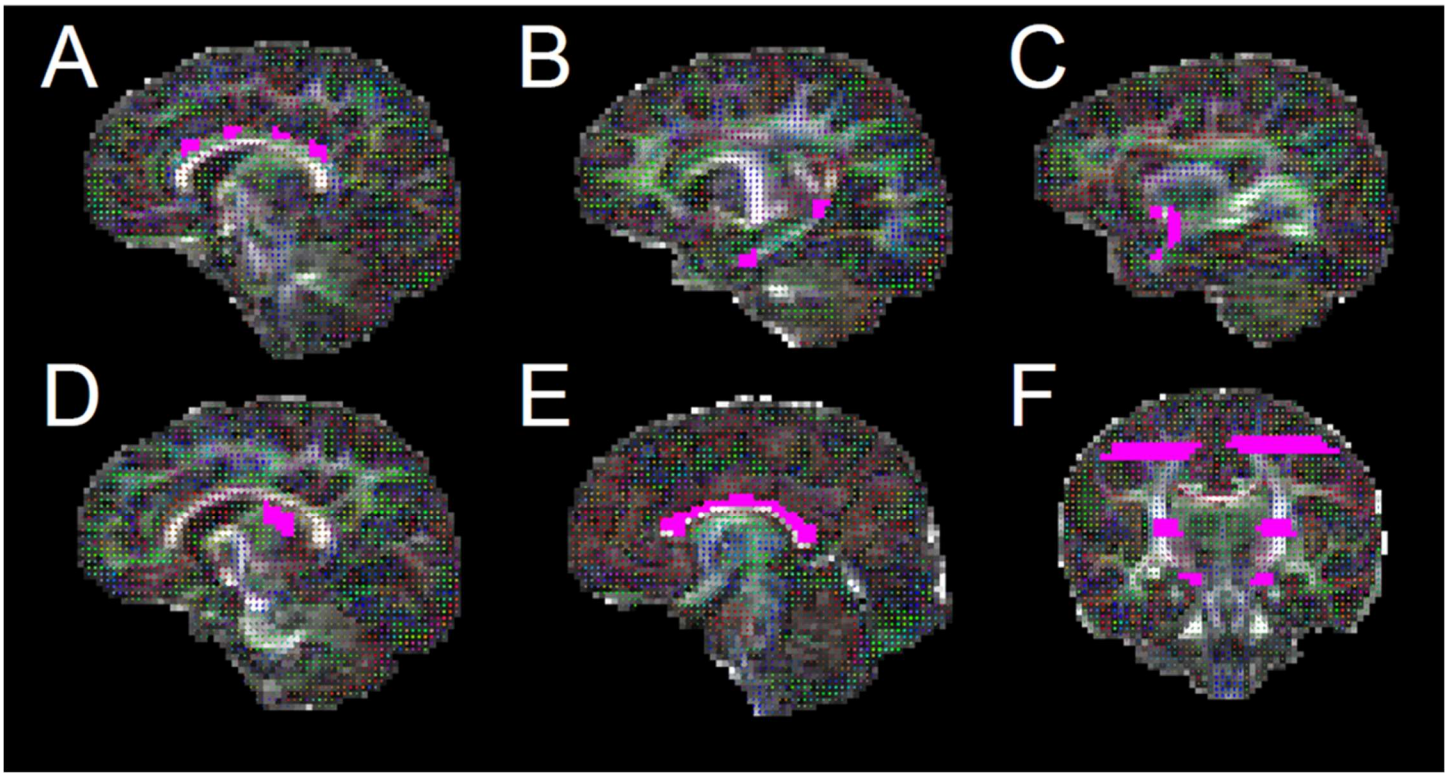

Figure S4. Probabilistic Tractography Methods. Start-, way-, end-point seeds placed using standard anatomical landmarks for the dorsal (A) and inferior (B) cingulum bundle, uncinate (C), fornix (D), corpus callosum (E), and cortico-spinal tract (F). Seeds shown on a FA/F1 image in a representative healthy, term-born infant.

Table S1. Summary of associations between Social Disadvantage and neonatal mean diffusivity (MD), radial diffusivity (RD), axial diffusivity (AD), and fractional anisotropy (FA) (*n* = 289).

	MD	RD	AD	FA
Right Dorsal Cingulum				
Social Disadvantage	**-.162 (.05)****	**-.181 (.05)****	-.083 (.05)	.152 (.06)**
Left Dorsal Cingulum				
Social Disadvantage	**-.127 (.05)***	**-.145 (.05)****	-.049 (.06)	.125 (.06)*
Right Inferior Cingulum				
Social Disadvantage	**-.244 (.05)*****	**-.212 (.05)*****	**-.186 (.05)****	.056 (.06)
Left Inferior Cingulum				
Social Disadvantage	**-.234 (.05)*****	**-.208 (.05)*****	**-.204 (.05)*****	.034 (.06)
Right Uncinate				
Social Disadvantage	**-.115 (.05)***	-.096 (.05)	-.120 (.06)*	-.002 (.05)
Left Uncinate				
Social Disadvantage	**-.171 (.06)****	**-.114 (.05)***	**-.135 (.06)***	.049 (.05)
Right Fornix				
Social Disadvantage	**-.129 (.05)****	**-.149 (.05)****	-.079 (.06)	.113 (.06)*
Left Fornix				
Social Disadvantage	-.091 (.05)	**-.122 (.05)***	-.020 (.05)	.122 (.06)*

Note. All models adjusted for sex and postmenstrual age at scan. Standardized regression coefficients and standard errors shown.

* p <.05, ** p <.01, *** p <.001

Bold values indicate significant results (q <.05) after multiple comparison correction using Benjamini-Hochberg False Discovery Rate procedure.

Table S2. Summary of associations between maternal Psychosocial Stress and neonatal mean diffusivity (MD), radial diffusivity (RD), axial diffusivity (AD), and fractional anisotropy (FA) (*n* = 289).

	MD	RD	AD	FA
Right Dorsal Cingulum				
Psychosocial Stress	-.051 (.05)	-.041 (.05)	-.059 (.05)	.002 (.06)
Left Dorsal Cingulum				
Psychosocial Stress	-.100 (.05)	-.086 (.05)	-.094 (.05)	.028 (.06)
Right Inferior Cingulum				
Psychosocial Stress	-.093 (.05)	-.082 (.05)	-.062 (.06)	.040 (.06)
Left Inferior Cingulum				
Psychosocial Stress	**-.134 (.05)****	**-.150 (.05)****	-.064 (.06)	.099 (.06)
Right Uncinate				
Psychosocial Stress	-.056 (.05)	-.033 (.05)	-.068 (.06)	-.010 (.05)
Left Uncinate				
Psychosocial Stress	-.071 (.06)	-.063 (.05)	-.017 (.06)	.088 (.05)
Right Fornix				
Psychosocial Stress	-.026 (.05)	-.027 (.05)	-.045 (.05)	-.011 (.06)
Left Fornix				
Psychosocial Stress	-.025 (.05)	-.049 (.05)	.021 (.05)	.081 (.06)

Note. All models adjusted for sex and postmenstrual age at scan. Standardized regression coefficients and standard errors shown.

* p <.05, ** p <.01, *** p <.001

Bold values indicate significant results (q <.05) after multiple comparison correction using Benjamini-Hochberg False Discovery Rate procedure.

Table S3. Full results of hierarchical regression models linking prenatal adversity factors with neonatal mean diffusivity (*n* = 289).

	Step 1			Step 2				Change Statistics	
	β (95% CI)	SE	*p*	β (95% CI)	SE	*p*	*q*	R^2	*p*
R Dorsal Cingulum	R^2 = .23, *p* <.001			R^2 = .25, *p* <.001					
Sex	-.028 (-.13 - .07)	.052	.58	-.022 (-.12 - .08)	.051	.66	.87		
PMA at scan	-.478 (-.58 - -.38)	.052	<.001	-.504 (-.61 - -.40)	.052	<.001	**<.001**		
Social Disadvantage	-	-	-	-.168 (-.28 - -.06)	.056	.003	**.008**	.03	.007
Psychosocial Stress	-	-	-	.015 (-.09 - .12)	.055	.79	.94		
L Dorsal Cingulum	R^2 = .21, *p* <.001			R^2 = .22, *p* <.001					
Sex	-.029 (-.13 - .08)	.052	.59	-.022 (-.13 - .08)	.052	.67	.87		
PMA at scan	-.454 (-.56 - -.35)	.053	<.001	-.471 (-.58 - -.37)	.053	<.001	**<.001**		
Social Disadvantage	-	-	-	-.103 (-.22 - .01)	.057	.07	.07	.02	.03
Psychosocial Stress	-	-	-	-.059 (-.17 - .05)	.056	.29	.94		
R Inferior Cingulum	R^2 = .23, *p* <.001			R^2 = .29, *p* <.001					
Sex	-.114 (-.22 - -.01)	.052	.03	-.104 (-.20 - .01)	.051	.04	.16		
PMA at scan	-.478 (-.58 - -.37)	.053	<.001	-.516 (-.62 - -.41)	.052	<.001	**<.001**		
Social Disadvantage	-	-	-	-.246 (-.36 - -.14)	.055	<.001	**<.001**	.06	<.001
Psychosocial Stress	-	-	-	.004 (-.10 - .11)	.055	.94	.94		
L Inferior Cingulum	R^2 = .31, *p* <.001			R^2 = .36, *p* <.001					
Sex	-.119 (-.22 - -.02)	.050	.02	-.109 (-.20 - -.02)	.048	.02	.16		
PMA at scan	-.555 (-.65 - -.46)	.050	<.001	-.588 (-.68 - -.49)	.049	<.001	**<.001**		
Social Disadvantage	-	-	-	-.214 (-.32 - -.11)	.052	<.001	**<.001**	.06	<.001
Psychosocial Stress	-	-	-	-.050 (-.15 - .05)	.052	.33	.94		
R Uncinate	R^2 = .20, *p* <.001			R^2 = .21, *p* <.001					
Sex	-.060 (-.17 - .05)	.053	.26	-.056 (-.16 - .05)	.053	.30	.69		
PMA at scan	-.446 (-.55 - -.34)	.054	<.001	-.464 (-.57 - -.36)	.054	<.001	**<.001**		
Social Disadvantage	-	-	-	-.110 (-.22 - .01)	.058	.06	.07	.01	.10
Psychosocial Stress	-	-	-	-.012 (-.13 - .10)	.057	.84	.94		
L Uncinate	R^2 = .13, *p* <.001			R^2 = .16, *p* <.001					
Sex	-.060 (-.17 - .05)	.055	.28	-.051 (-.16 - .06)	.055	.35	.69		
PMA at scan	-.368 (-.48 - -.26)	.056	<.001	-.396 (-.51 - -.29)	.056	<.001	**<.001**		
Social Disadvantage	-	-	-	-.169 (-.29 - -.05)	.060	.005	**.01**	.03	.009
Psychosocial Stress	-	-	-	-.006 (-.12 - .11)	.059	.91	.94		
R Fornix	R^2 = .30, *p* <.001			R^2 = .32, *p* <.001					
Sex	.003 (-.09 - .10)	.050	.95	.008 (-.09 - .11)	.049	.87	.87		
PMA at scan	-.547 (-.65 - -.45)	.050	<.001	-.569 (-.67 - -.47)	.050	<.001	**<.001**		
Social Disadvantage	-	-	-	-.141 (-.25 - -.04)	.054	.009	**.01**	.02	.03
Psychosocial Stress	-	-	-	.029 (-.08 - .13)	.053	.59	.94		
L Fornix	R^2 = .30, *p* <.001			R^2 = .31, *p* <.001					
Sex	.007 (-.09 - .10)	.049	.89	.010 (-.09 - .11)	.049	.84	.87		
PMA at scan	-.549 (-.65 - -.45)	.050	<.001	-.564 (-.66 - -.47)	.050	<.001	**<.001**		
Social Disadvantage	-	-	-	-.096 (-.20 - .01)	.054	.07	.07	.01	.18
Psychosocial Stress	-	-	-	.013 (-.09 - .12)	.053	.80	.94		

Note. CI, Confidence Intervals; SE, Standard Error; *q,* significance value adjusted for multiple comparisons using Benjamini-Hochberg False Discovery Rate procedure (**Bold** values indicate significant results after correction); R, right; L, left; PMA, postmenstrual age.

Table S4. Full results of hierarchical regression models linking prenatal adversity factors with neonatal radial diffusivity (*n* = 289).

	Step 1			Step 2				Change Statistics	
	β (95% CI)	**SE**	***p***	**β (95% CI)**	**SE**	***p***	***q***	**R^2**	***p***
R Dorsal Cingulum	R^2 = .21, *p* <.001			R^2 = .24, *p* <.001					
Sex	.010 (-.09 - .11)	.052	.84	.017 (-.08 - .12)	.052	.74	.78		
PMA at scan	-.456 (-.56 - -.35)	.053	<.001	-.486 (-.59 - -.38)	.053	<.001	**<.001**		
Social Disadvantage	-	-	-	-.196 (-.31 - -.09)	.056	.001	**.003**	.03	.002
Psychosocial Stress	-	-	-	.036 (-.07 - .15)	.056	.52	.97		
L Dorsal Cingulum	R^2 = .19, *p* <.001			R^2 = .22, *p* <.001					
Sex	.038 (-.07 - .14)	.053	.47	-.022 (-.06 - .15)	.052	.40	.54		
PMA at scan	-.436 (-.54 - -.33)	.053	<.001	-.471 (-.56 - -.35)	.054	<.001	**<.001**		
Social Disadvantage	-	-	-	-.103 (-.24 - -.02)	.057	.02	**.03**	.02	.02
Psychosocial Stress	-	-	-	-.059 (-.15 - .08)	.057	.54	.97		
R Inferior Cingulum	R^2 = .25, *p* <.001			R^2 = .30, *p* <.001					
Sex	-.129 (-.23 - -.03)	.051	.01	-.150 (-.22 - .02)	.050	.02	.14		
PMA at scan	-.501 (-.60 - -.40)	.052	<.001	-.534 (-.64 - -.43)	.051	<.001	**<.001**		
Social Disadvantage	-	-	-	-.213 (-.32 - -.11)	.055	<.001	**<.001**	.04	<.001
Psychosocial Stress	-	-	-	.002 (-.11 - .11)	.054	.97	.97		
L Inferior Cingulum	R^2 = .32, *p* <.001			R^2 = .36, *p* <.001					
Sex	-.077 (-.17 - .02)	.049	.12	-.069 (-.16 - .03)	.048	.16	.52		
PMA at scan	-.569 (-.67 - -.47)	.050	<.001	-.597 (-.69 - -.50)	.049	<.001	**<.001**		
Social Disadvantage	-	-	-	-.176 (-.28 - -.07)	.052	.001	**.003**	.05	<.001
Psychosocial Stress	-	-	-	-.080 (-.18 - .02)	.052	.12	.96		
R Uncinate	R^2 = .26, *p* <.001			R^2 = .27, *p* <.001					
Sex	-.018 (-.12 - .08)	.051	.72	-.014 (-.11 - .09)	.051	.78	.78		
PMA at scan	-.513 (-.61 - -.41)	.052	<.001	-.528 (-.63 - -.43)	.052	<.001	**<.001**		
Social Disadvantage	-	-	-	-.098 (-.21 - .01)	.056	.08	.08	.01	.17
Psychosocial Stress	-	-	-	.005 (-.10 - .11)	.055	.93	.97		
L Uncinate	R^2 = .18, *p* <.001			R^2 = .19, *p* <.001					
Sex	-.065 (-.17 - .04)	.054	.23	-.060 (-.17 - .05)	.054	.26	.52		
PMA at scan	-.424 (-.53 - -.32)	.054	<.001	-.440 (-.55 - -.33)	.055	<.001	**<.001**		
Social Disadvantage	-	-	-	-.106 (-.22 - .01)	.059	.07	.08	.01	.10
Psychosocial Stress	-	-	-	-.022 (-.14 - .09)	.058	.71	.97		
R Fornix	R^2 = .29, *p* <.001			R^2 = .31, *p* <.001					
Sex	.047 (-.05 - .15)	.050	.35	.052 (-.05 - .15)	.049	.30	.52		
PMA at scan	-.531 (-.63 - -.43)	.050	<.001	-.556 (-.66 - -.46)	.051	<.001	**<.001**		
Social Disadvantage	-	-	-	-.165 (-.27 - -.06)	.054	.003	**.006**	.02	.009
Psychosocial Stress	-	-	-	.038 (-.07 - .14)	.053	.48	.97		
L Fornix	R^2 = .31, *p* <.001			R^2 = .32, *p* <.001					
Sex	.043 (-.05 - .14)	.049	.38	.048 (-.05 - .14)	.049	.33	.52		
PMA at scan	-.551 (-.65 - -.45)	.049	<.001	-.570 (-.67 - -.47)	.050	<.001	**<.001**		
Social Disadvantage	-	-	-	-.121 (-.23 - -.02)	.053	.02	**.03**	.02	.05
Psychosocial Stress	-	-	-	-.002 (-.11 - .10)	.052	.97	.97		

Note. CI, Confidence Intervals; SE, Standard Error; *q,* significance value adjusted for multiple comparisons using Benjamini-Hochberg False Discovery Rate procedure (**Bold** values indicate significant results after correction); R, right; L, left; PMA, postmenstrual age.

Table S5. Full results of hierarchical regression models linking prenatal adversity factors with neonatal axial diffusivity (*n* = 289).

	Step 1			Step 2				Change Statistics	
	β (95% CI)	**SE**	***p***	**β (95% CI)**	**SE**	***p***	***q***	**R^2**	***p***
R Dorsal Cingulum	R^2 = .17, *p* <.001			R^2 = .17, *p* <.001					
Sex	-.100 (-.21 - .01)	.054	.06	-.096 (-.20 - .01)	.054	.08	.15		
PMA at scan	-.404 (-.51 - -.30)	.054	<.001	-.415 (-.52 - -.31)	.055	<.001	**<.001**		
Social Disadvantage	-	-	-	-.071 (-.19 - .05)	.059	.23	.31	.01	.27
Psychosocial Stress	-	-	-	.031 (-.15 - .08)	.058	.59	.82		
L Dorsal Cingulum	R^2 = .13, *p* <.001			R^2 = .14, *p* <.001					
Sex	-.153 (-.26 - -.05)	.055	.006	-.149 (-.26 - -.04)	.055	.007	**.03**		
PMA at scan	-.338 (-.45 - -.23)	.055	<.001	-.341(-.45 - -.23)	.056	<.001	**<.001**		
Social Disadvantage	-	-	-	-.013 (-.13 - .11)	.060	.83	.83	.01	.22
Psychosocial Stress	-	-	-	-.089 (-.21 - .03)	.059	.14	.82		
R Inferior Cingulum	R^2 = .05, *p* = .001			R^2 = .08, *p* <.001					
Sex	-.054 (-.16 - .06)	.055	.33	-.047 (-.15 - .05)	.054	.39	.45		
PMA at scan	-.202 (-.31 - -.09)	.056	<.001	-.232(-.34 - -.12)	.056	<.001	**<.001**		
Social Disadvantage	-	-	-	-.191 (-.31 - -.17)	.059	.001	**.004**	.04	.003
Psychosocial Stress	-	-	-	.014 (-.10 - .31)	.059	.82	.82		
L Inferior Cingulum	R^2 = .13, *p* <.001			R^2 = .17, *p* <.001					
Sex	-.154 (-.26 - -.05)	.055	.006	-.146 (-.25 - -.04)	.054	.007	**.03**		
PMA at scan	-.348 (-.46 - -.24)	.056	<.001	-.381 (-.49 - -.27)	.055	<.001	**<.001**		
Social Disadvantage	-	-	-	-.211 (-.33 - -.10)	.059	<.001	**<.001**	.04	.001
Psychosocial Stress	-	-	-	.019 (-.10 - .14)	.059	.74	.82		
R Uncinate	R^2 = .04, *p* = .002			R^2 = .06, *p* = .001					
Sex	-.14 (-.25 - -.03)	.056	.01	-.136 (-.25 - -.03)	.055	.02	**.04**		
PMA at scan	-.151 (-.26 - -.04)	.056	.007	-.169 (-.28 - -.06)	.056	.003	**.003**		
Social Disadvantage	-	-	-	-.110 (-.23 - .01)	.060	.07	.14	.02	.09
Psychosocial Stress	-	-	-	-.024 (-.14 - .09)	.060	.69	.82		
L Uncinate	R^2 = .02, *p* = .08			R^2 = .04, *p* = .02					
Sex	-.057 (-.17 - .05)	.055	.30	-.051 (-.16 - .06)	.055	.35	.45		
PMA at scan	-.116 (-.23 - -.01)	.056	.04	-.140 (-.25 - -.03)	.056	.01	**.01**		
Social Disadvantage	-	-	-	-.151 (-.27 - -.03)	.060	.01	**.03**	.02	.04
Psychosocial Stress	-	-	-	.041 (-.08 - .16)	.059	.49	.82		
R Fornix	R^2 = .16, *p* <.001			R^2 = .16, *p* <.001					
Sex	-.028 (-.14 - .08)	.055	.60	-.025 (-.13 - .08)	.055	.65	.65		
PMA at scan	-.403 (-.51 - -.29)	.055	<.001	-.414 (-.52 - -.30)	.056	<.001	**<.001**		
Social Disadvantage	-	-	-	-.072 (-.19 - .05)	.060	.23	.31	.01	.34
Psychosocial Stress	-	-	-	-.016 (-.13 - .10)	.059	.78	.82		
L Fornix	R^2 = .17, *p* <.001			R^2 = .17, *p* <.001					
Sex	-.053 (-.16 - .05)	.054	.33	-.053 (-.16 - .05)	.054	.33	.45		
PMA at scan	-.411 (-.52 - -.30)	.054	<.001	-.416 (-.52 - -.31)	.055	<.001	**<.001**		
Social Disadvantage	-	-	-	-.033 (-.15 - .08)	.059	.57	.65	.01	.79
Psychosocial Stress	-	-	-	.034 (-.08 - .15)	.058	.56	.82		

Note. CI, Confidence Intervals; SE, Standard Error; *q,* significance value adjusted for multiple comparisons using Benjamini-Hochberg False Discovery Rate procedure (**Bold** values indicate significant results after correction); R, right; L, left; PMA, postmenstrual age.

Table S6. Full results of hierarchical regression linking prenatal adversity factors with neonatal fractional anisotropy (*n* = 289).

	Step 1			Step 2				Change Statistics	
	β (95% CI)	**SE**	***p***	**β (95% CI)**	**SE**	***p***	***q***	**R^2**	***p***
R Dorsal Cingulum	R^2 = .10, *p* <.001			R^2 = .13, *p* <.001					
Sex	-.106 (-.22 - .01)	.056	.06	-.111 (-.22 - -.01)	.056	.05	.13		
PMA at scan	.293 (.18 - .41)	.057	<.001	.321 (.21 - .43)	.057	<.001	**<.001**		
Social Disadvantage	-	-	-	.179 (.06 - .30)	.061	.003	**.02**	.03	.01
Psychosocial Stress	-	-	-	-.068 (-.19 - .05)	.060	.26	.57		
L Dorsal Cingulum	R^2 = .11, *p* <.001			R^2 = .13, *p* <.001					
Sex	-.156 (-.27 - -.05)	.056	.006	-.160 (-.27 - -.05)	.056	.004	**.03**		
PMA at scan	.280 (.17 - .39)	.056	<.001	.301 (.19 - .41)	.057	<.001	**<.001**		
Social Disadvantage	-	-	-	.135 (.02 - .26)	.061	.03	.07	.02	.08
Psychosocial Stress	-	-	-	-.025 (-.14 - .09)	.060	.68	.83		
R Inferior Cingulum	R^2 = .11, *p* <.001			R^2 = .11, *p* <.001					
Sex	.059 (-.05 - .17)	.056	.29	.057 (-.05 - .17)	.056	.31	38		
PMA at scan	.334 (.22 - .45)	.056	<.001	.342 (.23 - .45)	.057	<.001	**<.001**		
Social Disadvantage	-	-	-	.047 (-.07 - .17)	.061	.44	.71	<.01	.57
Psychosocial Stress	-	-	-	.021 (-.10 - .14)	.060	.72	.83		
L Inferior Cingulum	R^2 = .10, *p* <.001			R^2 = .11, *p* <.001					
Sex	-.052 (-.16 - .06)	.057	.36	-.055 (-.17 - .05)	.057	.34	.38		
PMA at scan	.305 (.19 - .42)	.057	<.001	.305 (.19 - .42)	.058	<.001	**<.001**		
Social Disadvantage	-	-	-	-.006 (-.13 - .12)	.062	.92	.97	.01	.22
Psychosocial Stress	-	-	-	.101 (-.02 - .22)	.061	.10	.57		
R Uncinate	R^2 = .26, *p* <.001			R^2 = .26, *p* <.001					
Sex	-.114 (-.21 - -.01)	.051	.03	-.114 (-.21 - -.01)	.051	.03	.11		
PMA at scan	.491 (.39 - .59)	.051	<.001	.492 (.39 - .59)	.052	<.001	**<.001**		
Social Disadvantage	-	-	-	.002 (-.11 - .11)	.056	.97	.97	<.01	.98
Psychosocial Stress	-	-	-	-.011 (-.12 - .10)	.055	.84	.84		
L Uncinate	R^2 = .18, *p* <.001			R^2 = .19, *p* <.001					
Sex	-.004 (-.11 - .10)	.053	.99	-.004 (-.11 - .10)	.053	.94	.94		
PMA at scan	.426 (.32 - .53)	.054	<.001	.429 (.32 - .54)	.054	<.001	**<.001**		
Social Disadvantage	-	-	-	.016 (-.10 - .13)	.058	.78	.97	.01	.24
Psychosocial Stress	-	-	-	.082 (-.03 - .20)	.058	.16	.57		
R Fornix	R^2 = .09, *p* <.001			R^2 = .11, *p* <.001					
Sex	-.081 (-.19 - .03)	.057	.15	-.084 (-.20 - .03)	.057	.14	.22		
PMA at scan	.289 (.18 - .40)	.057	<.001	.311 (.20 - .43)	.058	<.001	**<.001**		
Social Disadvantage	-	-	-	.140 (.02 - .26)	.062	.03	.07	.02	.08
Psychosocial Stress	-	-	-	-.066 (-.19 - .06)	.061	.28	.57		
L Fornix	R^2 = .08, *p* <.001			R^2 = .10, *p* <.001					
Sex	-.091 (-.20 - .02)	.057	.11	-.097 (-.21 - .01)	.057	.09	.18		
PMA at scan	.261 (.115 - .37)	.057	<.001	.278 (.16 - .39)	.058	<.001	**<.001**		
Social Disadvantage	-	-	-	.107 (-.02 - .23)	.062	.09	.17	.02	.08
Psychosocial Stress	-	-	-	.039 (-.08 - .16)	.061	.52	.83		

Note. CI, Confidence Intervals; SE, Standard Error; *q,* significance value adjusted for multiple comparisons using Benjamini-Hochberg False Discovery Rate procedure (**Bold** values indicate significant results after correction); R, right; L, left; PMA, postmenstrual age.

Summary of Sensitivity Analysis in Age-Restricted Subsample

Given the relatively strong associations between age at scan and white matter microstructure at birth (Tables S3 – S6), we performed supplementary sensitivity analyses in an age-restricted subsample of infants. Because the largest bolus of infants was scanned between 41- and 43-weeks PMA (n = 223, 77%), we restricted the sensitivity analysis to this two-week window. In this subsample of infants, Social Disadvantage and Psychosocial Stress were still positively correlated (r = .40, p < .001). There was no correlation between PMA at scan and either Social Disadvantage (r = -.07, p = .27) or Psychosocial Stress (r = -.05, p = .45). Consistent with results observed in the larger cohort, Social Disadvantage was associated with lower MD in the right dorsal cingulum bundle (CB), bilateral inferior CB, left and uncinate, and right fornix (all p <.05) and higher FA in the right dorsal CB (p = .004) in the age-restricted subsample (Table S7). In the age-restricted subsample, infant PMA at scan explained variance in dMRI parameters across tracts (all p <.001) although the estimates for age at scan were slightly weaker than reported for the larger cohort (compare with Tables S3 and S6).

Table S7. Summary of hierarchical regression models linking infant characteristics and prenatal adversity factors with neonatal Mean Diffusivity (MD) Fractional Anisotropy (FA) in a subsample of infants scanned 41 to 43 weeks postmenstrual age (n = 223).

	MD			FA		
	β (95% CI)	**SE**	***p***	**β (95% CI)**	**SE**	***p***
R Dorsal Cingulum	R^2 = .13, p <.001			R^2 = .10, p <.001		
Sex	-.004 (-.12 - .12)	.063	.96	-.106 (-.23 - .02)	.064	.10
PMA at scan	-.317 (-.44 - -.19)	.063	<.001	.247 (.12 - .37)	.064	<.001
Social Disadvantage	-.202 (-.34 - -.07)	.069	.004	.204 (.07 - .34)	.070	.004
Psychosocial Stress	.004 (-.13 - .14)	.069	.94	-.056 (-.19 - .08)	.070	.42
L Dorsal Cingulum	R^2 = .16, p <.001			R^2 = .12, p <.001		
Sex	-.013 (-.14 - .11)	.062	.83	-.168 (-.29 - -.04)	.064	.009
PMA at scan	-.389 (-.51 - -.27)	.062	<.001	.282 (.16 - .41)	.064	<.001
Social Disadvantage	-.083 (-.22 - .05)	.068	.22	.140 (.01 - .28)	.069	.05
Psychosocial Stress	-.089 (-.22 - .05)	.068	.19	-.026 (-.16 - .11)	.069	.71
R Inferior Cingulum	R^2 = .19, p <.001			R^2 = .14, p <.001		
Sex	-.116 (-.24 - .01)	.061	.06	.038 (-.09 - .16)	.063	.55
PMA at scan	-.363 (-.48 - -.24)	.061	<.001	.363 (.24 - .49)	.063	<.001
Social Disadvantage	-.232 (-.36 - -.10)	.067	.001	.069 (-.07 - .20)	.069	.32
Psychosocial Stress	-.026 (-.16 - .11)	.067	.70	.064 (-.07 - .20)	.069	.35
L Inferior Cingulum	R^2 = .22, p <.001			R^2 = .08, p = .001		
Sex	-.105 (-.22 - .01)	.060	.08	-.060 (-.19 - .07)	.065	.36
PMA at scan	-.400 (-.52 - -.28)	.060	<.001	.258 (.13 - .39)	.065	<.001
Social Disadvantage	-.204 (-.33 - -.08)	.066	.002	.030 (-.11 - .17)	.071	.67
Psychosocial Stress	-.088 (-.22 - .04)	.065	.18	.103 (-.04 - .24)	.071	.15
R Uncinate	R^2 = .13, p <.001			R^2 = .24, p <.001		
Sex	-.074 (-.19 - .05)	.063	.24	-.112 (-.23 - .01)	.059	.06
PMA at scan	-.347 (-.47 - -.22)	.063	**<**.001	.472 (.36 - .59)	.059	<.001
Social Disadvantage	-.101 (-.24 - .04)	.069	.15	-.022 (-.15 - .11)	.064	.73
Psychosocial Stress	-.033 (-.17 - .10)	.069	.63	.041 (-.09 - .17)	.064	.53
L Uncinate	R^2 = .11, p <.001			R^2 = .17, p <.001		
Sex	-.039 (-.17 - .09)	.064	.55	-.035 (-.16 - .09)	.062	.58
PMA at scan	-.287 (-.41 - -.16)	.064	<.001	.405 (.28 - .53)	.062	<.001
Social Disadvantage	-.152 (-.29 - -.01)	.070	.03	<.001 (-.13 - .13)	.067	.99
Psychosocial Stress	-.048 (-.19 - .09)	.070	.50	.094 (-.04 - .23)	.067	.16
R Fornix	R^2 = .17, p <.001			R^2 = .08, p = .001		
Sex	-.024 (-.15 - .09)	.062	.70	-.083 (-.21 - .05)	.065	.21
PMA at scan	-.387 (-.51 - -.27)	.062	<.001	.223 (.09 - .35)	.065	<.001
Social Disadvantage	-.175 (-.31 - -.04)	.068	.01	.173 (.03 - .31)	.071	.02
Psychosocial Stress	.013 (-.12 - .15)	.067	.84	-.057 (-.20 - .08)	.071	.43
L Fornix	R^2 = .18, p <.001			R^2 = .10, p <.001		
Sex	.025 (-.10 - .15)	.062	.69	-.158 (-.29 - -.03)	.065	.02
PMA at scan	-.413 (-.54 - -.29)	.062	<.001	.215 (.09 - .34)	.065	.001
Social Disadvantage	-.113 (-.25 - .02)	.067	.10	.134 (-.01 - .27)	.070	.06
Psychosocial Stress	.023 (-.11 - .16)	.067	.73	.060 (-.08 - .20)	.070	.39

Note. CI, Confidence Intervals; SE, Standard Error; R, right; L, left; PMA, postmenstrual age.

Multivariate Linear Regression Models using Income-to-Needs Ratio (INR).

Given that INR had the strongest loadings on the latent Social Disadvantage factor, multivariate linear regression models were performed using mean INR in place of Social Disadvantage and fitted to white matter MD and FA as key dependent variables. As shown in Table S8, key study findings using mean INR were very consistent with results using Social Disadvantage (compare with Tables S3, S6 and S10).

Table S8. Summary of hierarchical regression models linking infant characteristics and Income-to-Needs Ratio with neonatal Mean Diffusivity (MD) Fractional Anisotropy (FA) (n = 284).

	MD				FA			
	β (95% CI)	**SE**	***p***	**Δ R^2**	**β (95% CI)**	**SE**	***p***	**Δ R^2**
R Dorsal Cingulum	R^2 = .26, p <.001				R^2 = .13, p <.001			
Sex	-.020 (-.12 - .08)	.052	.70		-.114 (-.22 - -.01)	.056	.05	
PMA at scan	-.510 (-.61 - -.41)	.053	< .001		.323 (.21 - .43)	.057	< .001	
INR	.191 (.08 - .30)	.056	.001	.03 **	-.179 (-.30 - -.06)	.061	.004	.03 *
Psych. Stress	.018 (-.09 - .13)	.055	.74		-.058 (-.18 - .06)	.060	.33	
L Dorsal Cingulum	R^2 = .23, p <.001				R^2 = .13, p <.001			
Sex	-.014 (-.12 - .08)	.052	.79		-.170 (-.28 - -.06)	.056	.003	
PMA at scan	-.476 (-.58 - -.37)	.053	< .001		.303 (.19 - .42)	.057	< .001	
INR	.122 (.01 - .23)	.057	.03	.02 *	-.144 (-.26 - -.02)	.061	.02	.02
Psych. Stress	-.054 (-.16 - .06)	.056	.33		-.025 (-.14 - .09)	.060	.67	
R Inferior Cingulum	R^2 = .30, p <.001				R^2 = .12, p <.001			
Sex	-.110 (-.21 - -.01)	.051	.03		.049 (-.06 - .16)	.056	38	
PMA at scan	-.525 (-.63 - -.42)	.051	< .001		.349 (.24 - .46)	.057	< .001	
INR	.270 (.16 - .38)	.055	< .001	.07 ***	-.075 (-.20 - .05)	.061	.22	.01
Psych. Stress	.003 (-.10 - .11)	.054	.96		.014 (-.10 - .13)	.060	.82	
L Inferior Cingulum	R^2 = .40, p <.001				R^2 = .11, p <.001			
Sex	-.112 (-.21 - -.02)	.048	.02		-.055 (-.17 - .06)	.057	.33	
PMA at scan	-.597 (-.69 - -.50)	.049	< .001		.310 (.20 - .42)	.058	< .001	
INR	.222 (.12 - .33)	.052	< .001	.06 ***	-.009 (-.13 - .11)	.062	.87	.01
Psych. Stress	-.057 (-.16 - .04)	.051	.26		.104 (-.02 - .22)	.061	.09	
R Uncinate	R^2 = .21, p <.001				R^2 = .27, p <.001			
Sex	-.047 (-.16 - .06)	.054	.38		-.122 (-.22 - -.02)	.052	.02	
PMA at scan	-.466 (-.57 - -.36)	.055	< .001		.495 (.39 - .60)	.052	< .001	
INR	.127 (.01 - .24)	.058	.03	.02	-.031 (-.14 - .08)	.056	.58	<.01
Psych. Stress	-.002 (-.11 - .11)	.057	.97		-.029 (-.14 - .08)	.055	.60	
L Uncinate	R^2 = .16, p <.001				R^2 = .19, p <.001			
Sex	-.052 (-.16 - .06)	.055	.35		-.006 (-.11 - .10)	.054	.91	
PMA at scan	-.395 (-.51 - -.28)	.057	< .001		.434 (.33 - .54)	.055	< .001	
INR	.157 (.04 - .28)	.061	.01	.03 *	-.050 (-.17 - .07)	.059	.40	.01
Psych. Stress	-.015 (-.13 - .10)	.059	.80		.069 (-.04 - .18)	.057	.23	
R Fornix	R^2 = .32, p <.001				R^2 = .11, p <.001			
Sex	.004 (-.09 - .10)	.049	.93		-.088 (-.20 - .03)	.057	.13	
PMA at scan	-.575 (-.67 - -.48)	.050	< .001		.316 (.20 - .43)	.058	< .001	
INR	.155 (.05 - .26)	.054	.004	.02 *	-.151 (-.27 - -.03)	.062	.02	.02
Psych. Stress	.027 (-.08 - .13)	.052	.60		-.067 (-.19 - .05)	.061	.27	
L Fornix	R^2 = .32, p <.001				R^2 = .10, p <.001			
Sex	.009 (-.09 - .11)	.049	.86		-.094 (-.21 - .02)	.057	.11	
PMA at scan	-.569 (-.67 - -.47)	.050	< .001		.279 (.16 - .39)	.058	< .001	
INR	.107 (.01 - .21)	.054	.05	.01	-.108 (-.23 - .01)	.062	.08	.02
Psych. Stress	.015 (-.09 - .12)	.053	.78		.050 (-.07 - .17)	.061	.42	
Corpus Callosum	R^2 = .31, p <.001				R^2 = .22, p <.001			
Sex	-.001 (-.10 - .10)	.050	.99		-.099 (-.20 - .01)	.053	.06	
PMA at scan	-.560 (-.66 - -.46)	.051	<.001		.432 (.33 - .54)	.054	<.001	

Table S8. Summary of hierarchical regression models linking infant characteristics and Income-to-Needs Ratio with neonatal Mean Diffusivity (MD) Fractional Anisotropy (FA) (*n* = 284).

	MD				FA			
	β (95% CI)	**SE**	***p***	**Δ R^2**	**β (95% CI)**	**SE**	***p***	**Δ R^2**
INR	.052 (-.05 - .16)	.054	.33	.01	.072 (-.04 - .19)	.057	.21	<.01
Psych. Stress	-.029 (-.13 - .08)	.053	.58		.034 (-.08 - .14)	.056	.55	
R Cortico-Spinal Tract	R^2 = .50, *p* <.001				R^2 = .30, *p* <.001			
Sex	-.037 (-.12 - .05)	.044	.41		-.028 (-.13 - .07)	.050	.58	
PMA at scan	-.679 (-.77 - -.59)	.045	<.001		.525 (.42 - .63)	.051	<.001	
INR	.119 (.02 - .21)	.048	.02	.02 *	.086 (-.02 - .19)	.055	.12	.01
Psych. Stress	-.024 (-.12 - .07)	.047	.61		.041 (-.07 - .15)	.053	.45	
L Cortico-Spinal Tract	R^2 = .47, *p* <.001				R^2 = .25, *p* <.001			
Sex	-.047 (-.13 - .04)	.044	.28		.003 (-.10 - .11)	.052	.95	
PMA at scan	-.690 (-.78 - -.60)	.044	<.001		.495 (.39 - .60)	.053	<.001	
INR	.161 (.07 - .25)	.047	.001	.03**	.013 (-.10 - .12)	.056	.82	<.01
Psych. Stress	-.006 (-.10 - .09)	.046	.90		.063 (-.05 - .17)	.055	.25	

Note. CI, Confidence Intervals; SE, Standard Error; Δ, change; R, right; L, left; PMA, postmenstrual age; INR., Income-to-Needs Ratio; Psych., Psychosocial. INR was log10 transformed prior to analysis to reduce skew.
Model significance: * *p* < .05, ** *p* < .01, *** *p* < .001

The Corpus Callosum (CC) and Cortico-Spinal Tract (CST) as Negative Control Tracts.
In line with prior work from our group (3), the CC was selected as a negative control tract because, like the cingulum bundle (CB), the CC is long-range tract with multiple branching fibers and it has a similar anterior-posterior orientation (4). The CST forms the primary pathway with a highly directional, inferior-superior orientation (5). In contrast to the CB, uncinate, and fornix tracts, the CC and the CST do not connect limbic system structures (*i.e.,* amygdala and hippocampus) with the frontal cortex (6). Alterations in the CC and CST are typically associated with cognitive and/or motor impairment (5, 7, 8).

We performed multivariable linear regression models including Social Disadvantage, Psychosocial Stress, sex, and infant PMA at scan as independent variables fitted to CC and CST MD and FA as key dependent variables. MA and FA were extracted from the CC and CST using identical methods as the CB, uncinate, and fornix. As shown in Table S9, neither prenatal exposure to Social Disadvantage nor Psychosocial Stress were associated with MD or FA in the CC (q >.05). For the CST, there were also no associations between either of the latent factors of interest and MD in the right CST and FA in the bilateral CST (q >.05). Prenatal exposure to greater Social Disadvantage was, however, associated with lower MD in the left CST (q = .006).

Table S9. Associations between prenatal adversity factors and neonatal mean diffusivity (MD) fractional anisotropy (FA) in the corpus callosum and cortico-spinal tracts (n = 289).

	MD				FA			
	β (95% CI)	**SE**	***p***	***q***	**β (95% CI)**	**SE**	***p***	***q***
Corpus Callosum	R^2 = .30, p <.001				R^2 = .21, p <.001			
Sex	-.005 (-.10 - .09)	.049	.91	.91	-.094 (-.20 - .01)	.053	.08	.23
PMA at scan	-.555 (-.65 - -.46)	.050	<.001	**<.001**	.426 (.32 - .53)	.054	<.001	**<.001**
Social Disadvantage	-.039 (-.15 - .07)	.054	.47	.47	-.090 (-.20 - .02)	.058	.12	.18
Psychosocial Stress	-.035 (-.14 - .07)	.053	.51	.89	-.041 (-.07 - .15)	.057	.47	.47
R Cortico-Spinal Tract	R^2 = .44, p <.001				R^2 = .30, p <.001			
Sex	-.026 (-.11 - .06)	.044	.56	.83	-.040 (-.14 - .06)	.050	.43	.64
PMA at scan	-.668 (-.76 - -.58)	.045	<.001	**<.001**	.515 (.42 - .62)	.051	<.001	**<.001**
Social Disadvantage	-.094 (-.19 - .01)	.049	.05	.08	-.124 (-.23 - -.02)	.054	.02	.06
Psychosocial Stress	-.026 (-.12 - .07)	.048	.59	.89	.054 (-.05 - .16)	.054	.31	.47
L Cortico-Spinal Tract	R^2 = .45, p <.001				R^2 = .24, p <.001			
Sex	-.039 (-.13 - .05)	.043	.37	.83	-.014 (-.12 - .09)	.052	.79	.79
PMA at scan	-.679 (-.77 - -.59)	.044	<.001	**<.001**	.484 (.38 - .59)	.053	<.001	**<.001**
Social Disadvantage	-.147 (-.24 - -.05)	.048	.002	**.006**	-.032 (-.14 - .08)	.057	.58	.58
Psychosocial Stress	-.003 (-.10 - .09)	047	.95	.95	.063 (-.05 - .17)	.056	.26	.47

Note. CI, Confidence Intervals; SE, Standard Error; *q,* significance value adjusted for multiple comparisons using Benjamini-Hochberg False Discovery Rate procedure (**Bold** values indicate significant results after correction); R, right; L, left; PMA, postmenstrual age.

Psychosocial Stress in Extremely Low and Lower-to-Higher Socioeconomic Status (SES) Groups.
Given the bivariate association between Psychosocial Stress and MD in the left inferior CB prior to accounting for broad Social Disadvantage (Table S2), we examined whether the strength of the association between maternal Psychosocial Distress and inferior CB connectivity varied depending on the socioeconomic context of the dyad. This analysis was undertaken to inform the extent that experiencing severe socioeconomic hardship may exacerbate the associations between Psychosocial Stress and aberrant white matter development.

To identify family SES groups for moderation analysis, each participant's Income-to-Needs Ratio (INR) values were averaged across trimesters and thresholded at 200% of the national poverty threshold. Average INR values below 200% of the national poverty threshold were categorized as extremely low family SES (n = 179), and values at or above 200% of the national poverty threshold categorized as lower-to-higher family SES (n = 105). INR values were missing for five mothers. The a-priori decision to use INR to identify SES groups was three-fold. First, INR is an ecologically valid metric that is used to identify families living at or close to the national poverty threshold and to determine eligibility for federally funded social welfare programs such as Medicare, Children's Health Insurance Program, and Supplemental Nutrition Assistance Program. Second, 200% INR has been used to group lower/higher SES families in multiple previous studies documenting the effects of poverty on child and adolescent health and development (including the landmark Fragile Families and Child Wellbeing and Adolescent Cognitive and Brain Development studies) (9–14) as well as national reports on low-income children (15, 16). Using consistent definitions to define lower/higher SES families is important for better comparability of findings across studies, allows for replication of moderation findings by future research, and makes recommendations for intervention more directly applicable. Third, as shown in Figure S2, INR had the highest loading values on the Social Disadvantage factor, suggesting this factor may be more reflective of INR.

As expected, mothers in the extremely low SES group had higher Psychosocial Stress scores (m = 0.68, SD = 1.02) than mothers in the lower-to-higher SES group (m = -0.46, SD = 0.80, t = -6.78, p <.001). There were also significant between-groups differences on the other observed Social Disadvantage variables (Table S10). In contrast, there was no significant between-groups difference in median MMR index scores between lower (median = 1.00, range 0 – 8) and lower-to-higher (median = 1.00, range 0 – 5) SES groups (p = .23).

Table S10. Differences in observed Social Disadvantage variables between Extremely Low SES and Lower-to-Higher Socio-economic Status (SES) groups (n = 284)

	Extremely Low SES (n = 179)	**Lower-to-Higher SES (n = 105)**	***t*/*X*²**	***p***
Education level, % (n) [a]			161.36	<.001
Less than High school	13.8 (21)	0.0 (0)		
High school graduate	78.9 (120)	15.3 (15)		
College graduate	7.2 (11)	27.6 (27)		
Post-graduate degree	0.0 (0)	57.1 (56)		
Public health Insurance, % (n)	76.0 (136)	7.6 (8)	123.73	<.001
Area Deprivation Index percentile, m (SD) [b]	81.16 (16.51)	48.12 (23.45)	12.54	<.001
Healthy Eating Index, m (SD)	55.81 (9.04)	62.17 (10.38)	-4.92	<.001

[a] Extremely Low SES group n = 152 and Lower-to-Higher SES group n = 98 due to missing education data.
[b] t statistic and corresponding p-value corrected for unequal variances between groups

To test the interaction between Psychosocial Stress and family SES group on MD in the left inferior CB, moderation analysis was performed using the PROCESS procedure for SPSS (17). Family SES group and Psychosocial Stress were included as main effects, along with a mean-centered interaction term and covariate factors (sex and infant PMA at scan). The interaction between Psychosocial Stress and family SES group was significant (p = .008), such that the association between Psychosocial Stress and MD in the left inferior CB was stronger in the lower-to-higher SES group than in the extremely low SES group (Table S11; see also Figure 2, Main Text).

Table S11. Family SES group and Psychosocial Stress on neonatal mean diffusivity (MD) in the left dorsal cingulum bundle (n = 284).

	B (95% CI)	**SE**	***p***
Left Inferior Cingulum MD	R^2 = .38, p <.001		
Sex	-.123 (-.22 - -.03)	.048	**.01**
PMA at scan	-.579 (-.67 - -.48)	.048	**<.001**
Family SES group	.319 (.10 - .54)	.111	**.004**
Psychosocial Stress	-.102 (-.20 - .01)	.052	.05
Interaction: Family SES group x Psychosocial Stress	-.305 (-.53 - -.08)	.115	**.008**

Note. Unstandardized coefficients (B) from PROCESS output. SE, Standard Error; PMA, postmenstrual age at scan

For completeness, we also performed multivariable linear regression within the lower-to-higher SES group to examine whether the association between Psychosocial Stress and MD in the left inferior CB persisted after also accounting for individual differences in general social background. As shown in Table S12, Psychosocial Stress remained significant (p = .006) among the lower-to-higher SES group even after accounting for Social Disadvantage factor scores, which were not significant (p = .67).

Table S12. Associations between prenatal adversity factors and neonatal mean diffusivity (MD) in the left dorsal cingulum bundle within family SES groups (n = 284).

	Extremely Low SES (n = 179)			**Lower-to-Higher SES (n = 105)**		
	B (95% CI)	**SE**	***p***	**B (95% CI)**	**SE**	***p***
Left Inferior Cingulum MD	R^2 = .36, p <.001			R^2 = .41, p <.001		
Sex	-.167 (-.29 - -.04)	.064	**.009**	-.060 (-.21 - .09)	.073	.41
PMA at scan	-.570 (-.69 - -.45)	.060	**<.001**	-.623 (-.79 - -.45)	.087	**<.001**
Social Disadvantage	-.283 (-.64 - .07)	.180	.12	-.057 (-.32 - .20)	.130	.67
Psychosocial Stress	.026 (-.10 - .15)	.063	.67	-.268 (-.46 - -.08)	.096	**.006**

Note. CI, Confidence Intervals; SE, Standard Error; PMA, postmenstrual age.

Confounding Factors: Supplemental Analysis Addressing Maternal Medical Risk (MMR) in Pregnancy.
Supplemental analysis was performed to account for the potentially confounding role of maternal medical co-morbidities during pregnancy on neonatal white matter connectivity at birth. A MMR index was calculated for each mother using questionnaire data and chart review (1). This validated MMR index is a weighted sum of maternal morbidities including advanced age, pre-gestational diabetes, placenta previa, asthma, hypertension, prior C-section delivery, pre-eclampsia, cardiac disease, renal disease, sickle cell disease, lupus, and human immunodeficiency virus (18–20). Higher MMR index scores indicate increased medical risk. Mothers in this study were relatively healthy with an overall mean MMR of 1.01 (SD = 1.26, range: 0 – 8).

Non-parametric spearman's rho correlations were used to screen for associations between the MMR index and neonatal white matter tract MD and FA at birth. MMR index was correlated with MD in the left dorsal CB at birth (ρ = .13, p = .03); there were no other correlations for MD or FA in any of the other white matter tracts (ρ range -.01 – .10, all p >.05). Also of note, MMR index was not associated with either Social Disadvantage (ρ = -.01, p = .84) or Psychosocial Stress (ρ = -.07, p = .23) scores.

The multivariate linear regression model for MD in the left dorsal CB was re-run including MMR index as a covariate (Table S13). After accounting for infant PMA at scan (p <.001), MMR was no longer significant (p = .49). The role of Social Disadvantage was unchanged (p >.05, compare with Table S3).

Table S13. Maternal Medical Risk, prenatal adversity factors, and neonatal mean diffusivity (MD) in the left dorsal cingulum bundle (n = 289).

	β (95% CI)	**SE**	***p***
Left Dorsal Cingulum MD	R^2 = .23, p <.001		
Sex	-.023 (-.13 - .08)	.052	.66
PMA at scan	-.468 (-.57 - -.36)	.053	**<.001**
MMR index	.029 (-.05 - .10)	.041	.49
Social Disadvantage	-.102 (-.21 - .01)	.057	.07
Psychosocial Stress	-.057 (-.17 - .05)	.056	.31

Note. CI, Confidence Intervals; SE, Standard Error; PMA, postmenstrual age.

Confounding Factors: Supplemental Analysis Addressing Prenatal Cannabis and Tobacco Exposure.
Supplemental analysis was performed to account for the potentially confounding role of prenatal cannabis and tobacco exposure on white matter connectivity at birth. During pregnancy, mothers completed self-report surveys detailing the frequency of cannabis and tobacco use per trimester. When available (42.6% of the current sample), cannabis exposure information was supplemented with maternal urine drug screen (UDS) performed at the discretion of the treating physician as part of obstetric care and recorded in patient medical records. To combine self-report cannabis data with UDS positive for tetrahydrocannabinol metabolites, frequency of self-reported cannabis use was coded never = 0 and all other responses (daily, weekly but not every day, monthly but not every week) = 1. For comparability, self-report tobacco use was also binarized and coded as no use = 0 versus one or more cigarettes per day = 1. Seventy-seven (27%) mothers reported cannabis use and/or had a positive UDS. Thirty-nine (14%) mothers reported cigarette use. Independent samples *t*-tests indicated that mothers who reported cannabis use and/or had a positive UDS had higher levels of Social Disadvantage (p <.001) and Psychosocial Stress (p <.001) than mothers who had no cannabis exposure (Table S14). Similarly, mothers who reported tobacco use had higher levels of Social Disadvantage (p <.001) and Psychosocial Stress (p <.001) than mothers who reported no tobacco use.

Table S14. Comparison of prenatal adversity factors between drug exposure groups (n = 289).

	Tobacco Exposure (n = 39)	**No Tobacco Exposure (n = 250)**	***t***	***p***
Social Disadvantage, *m* (SD)	0.79 (0.43)	-0.11 (1.01)	-9.62 [a]	<.001
Psychosocial Stress, *m* (SD)	0.51 (0.99)	-0.08 (0.98)	-3.46	<.001
	Cannabis Exposure (n = 77)	**No Cannabis Exposure (n = 212)**	***t***	***p***
Social Disadvantage, *m* (SD)	0.72 (0.34)	-0.25 (1.04)	-11.85 [a]	<.001
Psychosocial Stress, *m* (SD)	0.38 (0.93)	-0.14 (0.99)	-4.00	<.001

[a] *t* statistic and corresponding *p*-value corrected for unequal variances between groups

Independent samples *t*-tests were used to screen for differences in neonatal white matter tract MD and FA at birth between drug exposure groups. Infants prenatally exposed to cannabis had lower MD in the inferior portion of the left CB (t = -2.06, p = .04) and higher FA in the left fornix (t = 2.37, p = .02) than infants with no exposure. There were no other cannabis exposure group differences in MD or FA for any of the other white matter tracts (mean difference range -.08 – .23, all p >.05). There were no tobacco exposure group differences in MD or FA for any of the white matter tracts (mean difference range -.23 – .29, all p >.05). Regression models for left inferior CB MD and left fornix FA were re-run including binarized cannabis exposure as a covariate (Table S15). After accounting for infant PMA at scan (p <.001), prenatal cannabis exposure was no longer significant (p >.05). Key study findings concerning Social Disadvantage were unchanged (compare with Tables S3 and S6).

Table S15. Prenatal cannabis exposure, prenatal adversity factors, and neonatal white matter (n = 289).

	β (95% CI)	**SE**	***p***
Left Inferior Cingulum MD		R^2 = .36, p <.001	
Sex	-.110 (-.20 - -.02)	.048	**.02**
PMA at scan	-.590 (-.69 - -.49)	.049	**<.001**
Prenatal cannabis exposure	.015 (-.09 - .12)	.052	.78
Social Disadvantage	-.221 (-.33 - -.11)	.057	**<.001**
Psychosocial Stress	-.051 (-.15 - .05)	.052	.33
Left Fornix FA		R^2 = .10, p <.001	
Sex	-.102 (-.21 - .01)	.057	.07
PMA at scan	.267 (.15 - .38)	.058	**<.001**
Prenatal cannabis exposure	.098 (-.02 - .22)	.062	.12
Social Disadvantage	.066 (-.07 - .20)	.067	.33
Psychosocial Stress	.033 (-.09 - .15)	.061	.59

Note. CI, Confidence Intervals; SE, Standard Error; PMA, postmenstrual age.

Bivariate Correlations between Observed Variables.

Social Disadvantage.

Table S16. Bivariate correlations between Social Disadvantage variables.

	1.	2.	3.	4.
1. Income-to-Needs Ratio [a,b]	-			
2. Area Deprivation Index percentile [c]	-.66 ***	-		
3. Education level [d,b]	.74 ***	-.59 ***	-	
4. Insurance status [d,b]	.65 ***	-.53 ***	.61 ***	-
5. Healthy Eating Index [b]	.32 ***	-.28 ***	.31 ***	.24 ***

[a] Average across trimesters 1, 2, 3
[b] Higher values = lower levels of adversity
[c] Higher values = higher levels of adversity
[d] Non-parametric statistic for ordinal variables
*** p <.001

Psychosocial Stress.

Table S17. Bivariate correlations between Psychosocial Stress variables.

	1.	2.	3.	4.
1. Depression symptoms [a]	-			
2. Perceived stress [a]	.70 ***	-		
3. Stressful life events - count	.33 ***	.27 ***	-	
4. Stressful life events - severity	.36 ***	.31 ***	.93 ***	-
5. Racial discrimination	.21 ***	.20 **	.23 ***	.25 ***

[a] Average across trimesters 1, 2, 3
** p <.01
*** p <.001

SUPPLEMENTARY REFERENCES

1. J. L. Luby, *et al.*, Modeling Prenatal Adversity/Advantage: Effects on Birth Weight. *medRxiv Preprint*, 1–23 (2021). doi: https://doi.org/10.1101/2021.12.16.21267938

2. R. E. Lean, J. J. Neil, C. D. Smyser, “Chapter 20 - Neuroimaging of early brain development and the consequences of preterm birth” in *Advances in Magnetic Resonance Technology and Applications*, Handbook of Pediatric Brain Imaging., H. Huang, T. P. L. Roberts, Eds. (Academic Press, 2021), pp. 429–465.

3. R. G. Brenner, *et al.*, Microstructure of the Dorsal Anterior Cingulum Bundle in Very Preterm Neonates predicts the Preterm Behavioral Phenotype at 5 Years. *Biological Psychiatry* **89**, 433–440 (2021).

4. E. J. Bubb, C. Metzler-Baddeley, J. P. Aggleton, The cingulum bundle: Anatomy, function, and dysfunction. *Neuroscience & Biobehavioral Reviews* **92**, 104–127 (2018).

5. Q. Welniarz, I. Dusart, E. Roze, The corticospinal tract: Evolution, development, and human disorders. *Developmental Neurobiology* **77**, 810–829 (2017).

6. L. J. van der Knaap, I. J. M. van der Ham, How does the corpus callosum mediate interhemispheric transfer? A review. *Behavioural Brain Research* **223**, 211–221 (2011).

7. E. G. Duerden, *et al.*, Tract-Based Spatial Statistics in Preterm-Born Neonates Predicts Cognitive and Motor Outcomes at 18 Months. *American Journal of Neuroradiology* **36**, 1565–1571 (2015).

8. M. N. Grohs, J. E. Reynolds, D. Dewey, C. Lebel, Corpus callosum microstructure is associated with motor function in preschool children. *NeuroImage* **183**, 828–835 (2018).

9. Bendheim-Thoman Center for Research on Child Wellbeing, “Disadvantaged Children who are Beating the Odds: Family, School, Neighborhood and City Contexts that Predict Academic Success among Socio-economically Disadvantaged Children” (Princeton University, New Jersey, 2019).

10. M. R. Gonzalez, *et al.*, Positive Economic, Psychosocial, and Physiological Ecologies Predict Brain Structure and Cognitive Performance in 9–10-Year-Old Children. *Front Hum Neurosci* **14**, 578822 (2020).

11. N. L. Hair, J. L. Hanson, B. L. Wolfe, S. D. Pollak, Association of Child Poverty, Brain Development, and Academic Achievement. *JAMA Pediatrics* **169**, 822–829 (2015).

12. T. Halle, *et al.*, "Disparities in early learning and development: Lessons from the Early Childhood Longitudinal Study - Birth Cohort (ECLS-B)" (Child Trends, Washington, 2009).

13. J. L. Hanson, *et al.*, Family Poverty Affects the Rate of Human Infant Brain Growth. *PLOS ONE* **8**, e80954 (2013).

14. D. E. Kendzor, M. O. Caughy, M. T. Owen, Family income trajectory during childhood is associated with adiposity in adolescence: a latent class growth analysis. *BMC Public Health* **12**, 611 (2012).

15. National Center for Children in Poverty, “Low-Income Children in the United States: National and State Trend Data, 1996-2006” (Columbia University, New York, 2007).

16. W. Engelhardt, C. Skinner, “Knowing What Works: States and Cities Build Smarter Social Policy with New and Improved Poverty Measurement” (Columbia University, New York, 2013).

17. A. F. Hayes, *Introduction to Mediation, Moderation, and Conditional Process Analysis, Second Edition: A Regression-Based Approach* (Guilford Publications, 2017).

18. B. T. Bateman, *et al.*, Development of a Comorbidity Index for Use in Obstetric Patients: *Obstetrics & Gynecology* **122**, 957–965 (2013).

19. A. Metcalfe, *et al.*, Validation of an obstetric comorbidity index in an external population. *BJOG* **122**, 1748–1755 (2015).

20. M. A. Clapp, K. E. James, A. J. Kaimal, The effect of hospital acuity on severe maternal morbidity in high-risk patients. *Am J Obstet Gynecol* **219**, 111.e1-111.e7 (2018).