Supplementary Materials

Timing-specific associations between income-to-needs ratio and hippocampal and amygdala volumes in middle childhood: A preliminary study

Supplementary Methods

Data collection

Income-to-needs ratio, material hardship, and maternal demoralization were collected at all timepoints (third trimester, 6 months, 1, 2, 3, 5, and 7 years). Maternal perceived stress was collected at all timepoints except the prenatal visit. See Table S1 for a timeline of data collection.

Income-to-needs ratio

Parents reported total household income in $10,000 bins ranging from $0-10,000 up to >$90,000 and household income was estimated as the midpoint of the indicated bin. For example, if household income was indicated as "$30,000-40,000," INR was calculated based on an estimated household income of $35,000 (and $95,000 for the highest income bin). The federal poverty threshold for each participant at each time point was determined from census records (based on family size and household income during that year)(Bureau, 2020). Across 246 unique INR measurements (41 participants; 6 ages), INR was missing at 10 instances (1, 0, 1, 1, 1, and 6 participants missing INR at 6 months, 1, 2, 3, 5, and 7 years, respectively).

Mediators of INR-brain associations

The material hardship questions sought to identify unmet basic needs (food, housing, clothing, healthcare)(Meyer, Castro-Schilo, & Aguilar-Gaxiola, 2014):

1. Think about where you live, the food you eat, and the things you can afford to do and buy. How do you feel about your overall living condition? Would you say?
2. In the last year, has there been a time when you and your family needed food but couldn't afford to buy it?
3. In the last year, has there been a time when you couldn't afford a place to stay, or when you couldn't pay the rent?
4. In the last year, has your gas or electricity been turned off because you couldn't afford to pay the bill?
5. In the last year, have you needed to buy any type of clothing for yourself or your family but didn't buy it because you couldn't afford to pay for it?
6. In the last year, has there been a time when you or a member of your family needed medicine or medical care but didn't get the treatment because you couldn't afford it?
7. Do you currently receive Medicaid?
8. Do you currently receive any type of public assistance?

The maternal demoralization questions were from the Psychiatric Epidemiology Research Instrument Demoralization Scale (Dohrenwend, Shrout, Egri, & Mendelsohn, 1980):

1. During the past year, how often have you felt you were bothered by all different kinds of ailments in different parts of your body…
2. During the past year, how often have you been bothered by feelings of sadness or depression – feeling blue…
3. In general, how satisfied have you been with yourself in the last year...
4. During the past year, how often have you had attacks of sudden fear or panic...
5. During the past year, how often have you felt confident...
6. During the past year, how often have you felt lonely...
7. During the past year, how often have you been bothered by feelings of restlessness
8. During the past year, how often have you felt useless...
9. During the past year, how often have you feared going crazy; losing your mind
10. During the past year, how often have you felt anxious...
11. During the past year, how often have you feared something terrible would happen to you...
12. During the past year, how often have you felt confused and had trouble thinking
13. During the past year, how often have you had trouble concentrating or keeping your mind on what you are doing
14. During the past year, how often have you felt that nothing turns out for you the way you want it to...
15. During the past year, how often have you felt completely hopeless about everything...
16. During the past year, how often have you felt completely helpless....
17. During the past year, how often have you had times when you couldn't help wondering if anything was worthwhile anymore...
18. During the past year, how often have you been bothered by cold sweats...
19. During the past year, how often have you had trouble with headaches or pains in the head...
20. During the past year, how often has your appetite been poor....
21. In general, if you had to compare yourself with the average woman your age, what grade would you give yourself for the past year....

Are you the kind of person

1. *Who feels she has much to be proud of ...*
2. Who is the worrying type...
3. Who feels that she is a failure generally, in life...
4. When you have gotten angry in the last year, how often have you felt uncomfortable, like getting headaches, stomach pains, cold sweats and things like that...
5. During the past year, how often have you feared being left all alone or abandoned...
6. During the past year, how often have you been bothered by nervousness, being fidgety or tense.

The maternal perceived stress questions were adapted from the Perceived Stress Scale and measured subjective stress and coping capacity (Cohen, Kamarck, & Mermelstein, 1994):

1. In the last month, how often have you felt that you were unable to control the important things in your life?
2. In the last month, how often have you felt confident about your ability to handle personal problems?
3. In the last month, how often have you felt that things are going your way?

4. In the last month, how often have you felt difficulties were piling up so high that you could not overcome them?
5. You have been upset because of something that happened unexpectedly.
6. You have felt nervous and "stressed".
7. You have dealt successfully with irritating life hassles.
8. You have felt that you were effectively coping with important changes that were occurring in your life.
9. You have found that you could not cope with all the things you had to do.
10. You have been able to control irritations in your life.
11. You have felt that you were on top of things.
12. You have been angered because of things that happened that were outside of your control.
13. You have found yourself thinking about things that you have to accomplish.
14. You have been able to control the way you spend your time.

Statistical Analyses

To ensure the robustness of our findings on timing-specific associations between INR and subcortical volumes, we used generalized estimating equations (GEE; *geepack* R package (Højsgaard, Halekoh, & Yan, 2005)) as a complementary approach (Chen, Ferguson, Meeker, McElrath, & Mukherjee, 2015; Sánchez, Hu, Litman, & Téllez-Rojo, 2011). First, we simultaneously estimated regression coefficients relating INR at each timepoint to subcortical volumes. Next, we used a linear temporal contrast to directly test whether these regression coefficients varied linearly with the timepoint (0.5 through 7) for which the regression coefficients were estimated. As in our main analysis, this approach examines whether the association between INR and subcortical volumes varies linearly with the timepoint at which INR was measures.

Model diagnostics

We detected modest non-normality of the residuals in our main model (hippocampus: $W=.98$, $p<.001$, amygdala: $W=.98$, $p=.003$) due to slight skew in the INR distribution. To assess whether alternative specifications of the model improve the fit, we tested gamma, exponential, log-normal, and inverse gaussian regression models with a variety of link functions. All alternative specifications and link functions yielded highly convergent coefficient estimates and statistical inference, but resulted in slightly poorer model fit. This suggests that a Gaussian regression model with an identity link is the optimal modeling approach, despite modest non-normality of the residuals. We therefore continue to report this model as the primary specification.

Table S1. Data collection timeline.

	Prenatal	6 months	1 years	2 years	3 years	5 years	7 years	7-9 years
INR	✓	✓[1]	✓[1]	✓[1]	✓[1]	✓[1]	✓[1]	
Material hardship	✓	✓	✓[2]	✓	✓	✓	✓	
Maternal demoralization	✓	✓	✓[2]	✓	✓	✓[3]	✓	
Maternal perceived stress[3]		✓	✓[2]	✓	✓	✓[3]	✓	
HPC and AMYG volumes								✓

Notes:

1. Variables used to address hypothesis 1 (earlier poverty has a larger association with subcortical volumes than later poverty)
2. Variables used to address hypothesis 2 (adverse sequelae of poverty would mediate its association with subcortical volumes)
3. Prior to age 5, maternal perceived stress was measured based on the first four items (see below for questions). Stress scores based on these four questions are highly correlated with scores based on all 14 questions ($r=0.86$ $p=4.0*10^{-13}$)

INR=income-to-needs ratio; HPC=hippocampus; AMYG= amygdala

Table S2. Correlations among variables.

	1	2	3	4	5	6	7	8	9
1. INR during third trimester	1.00								
2. INR at 6 months	0.52***	1.00							
3. INR at 1 year	0.72***	0.72***	1.00						
4. INR at 2 years	0.58***	0.82***	0.76***	1.00					
5. INR at 3 years	0.60***	0.66***	0.79***	0.82***	1.00				
6. INR at 5 years	0.40*	0.67***	0.67***	0.73***	0.8***	1.00			
7. INR at 7 years	0.46**	0.71***	0.73***	0.72***	0.77***	0.69***	1.00		
8. Material hardship at 1 year	-0.43**	-0.41**	-0.32*	-0.36*	-0.31	-0.26	-0.28	1.00	
9. Maternal demoralization at 1 year	-0.14	-0.02	0.03	-0.04	0.05	0.12	-0.09	0.28	1.00
10. Maternal perceived stress at 1 year	-0.17	0.02	0.04	0.05	0.16	0.22	-0.08	0.31	0.57***

INR=income-to-needs ratio

Table S3. Parameter estimates from generalized estimating equations regressing each subcortical volume against income-to-needs ratio (INR) at all timepoints and a test examining whether these parameters vary linearly with time.

	Hippocampus		Amygdala	
Age of INR measurement	β		β	
6 months	0.57		0.43	
1 years	0.54		0.34	
2 years	0.49		0.42	
3 years	0.41		0.25	
5 years	0.43		0.36	
7 years	0.20		0.01	
	β	p	β	p
Linear temporal contrast	-0.05	.0002	-0.05	.04

Table S4. Parameter estimates from linear mixed-effects models delineating the interaction of timepoint of income measurement and brain volumes at age 7-9 years on binned household income values across the first seven years of life. Income was originally reported in $10,000 bins, with values ranging from 1-10 (where 1 means $0-10,000, 2 means $10,000-$20,000, and so forth. 10 corresponds to income > $90,000). Volumes for each region were summed across both hemispheres.

	Timepoint × volume	
	β	p
Hippocampus	-0.11	.004
Amygdala	-0.12	.002

Table S5. Parameter estimates from linear mixed-effects models delineating the interaction of timepoint of INR measurement and brain volumes at age 7-9 years on INR values across the first seven years of life, further residualized for maternal education. Volumes for each region were summed across both hemispheres.

	Timepoint × volume	
	β	p
Hippocampus	-0.08	.014
Amygdala	-0.11	.003

INR=income-to-needs ratio

Table S6. Parameter estimates from linear mixed-effects models delineating the interaction of timepoint of INR measurement and brain volumes at age 7-9 years on INR values across the first seven years of life. Whereas our main analyses use brain volumes that were residualized for intracranial volume, age, and sex, these results demonstrate the effect of residualizing for each covariate individually. Volumes for each region were summed across both hemispheres.

Volume definition	Hippocampus		Amygdala	
	Timepoint × volume			
	β	p	β	p
Raw subcortical volumes	-0.07	.08	-0.09	.02
Residualized for intracranial volume (ICV)	-0.08	.01	-0.11	.002
Residualized for sex	-0.06	.13	-0.08	.04
Residualized for age	-0.07	.08	-0.09	.02
Residualized for ICV and sex	-0.08	.02	-0.11	.003
Residualized for ICV and age	-0.08	.01	-0.11	.002
Residualized for age and sex	-0.06	.12	-0.08	.04

Table S7. Parameter estimates from linear mixed-effects models delineating the interaction of timepoint of INR measurement and brain volumes at age 7-9 years on INR values across the first seven years of life, including one timepoint in the third trimester of pregnancy. Volumes for each region were summed across both hemispheres.

	Timepoint × volume	
	β	p
Hippocampus	-0.075	.034
Amygdala	-0.084	.025

INR=income-to-needs ratio

Table S8. Correlations between income-to-needs-ratio at 6 months and material hardship at ages 6 months and 1 years.

	INR at 6 months	INR at 1 year
Material hardship at 6 months	-0.33	-0.16
Material hardship at 1 year	-0.41	-0.32

INR=income-to-needs ratio

Table S9. Material hardship at 1 year is a better predictor of hippocampal and amygdala volumes at age 7-9 years than material hardship in the third trimester of pregnancy and material hardship at child age 5 years. Model 1 contains parameters from a multiple linear regression model with prenatal material hardship and age one year material hardship as the independent variables; model 2 contains parameters from a multiple linear regression model with age one material hardship and age five material hardship as the independent variables.

	Model 1				Model 2			
	Prenatal material hardship		Material hardship at 1 year		Material hardship at 5 years		Material hardship at 1 year	
	β	p	β	p	β	p	β	p
Hippocampus	0.20	.25	-0.71	.0001	-0.15	.27	-0.56	.0001
Amygdala	0.06	.75	-0.54	.006	-0.01	.93	-0.50	.002

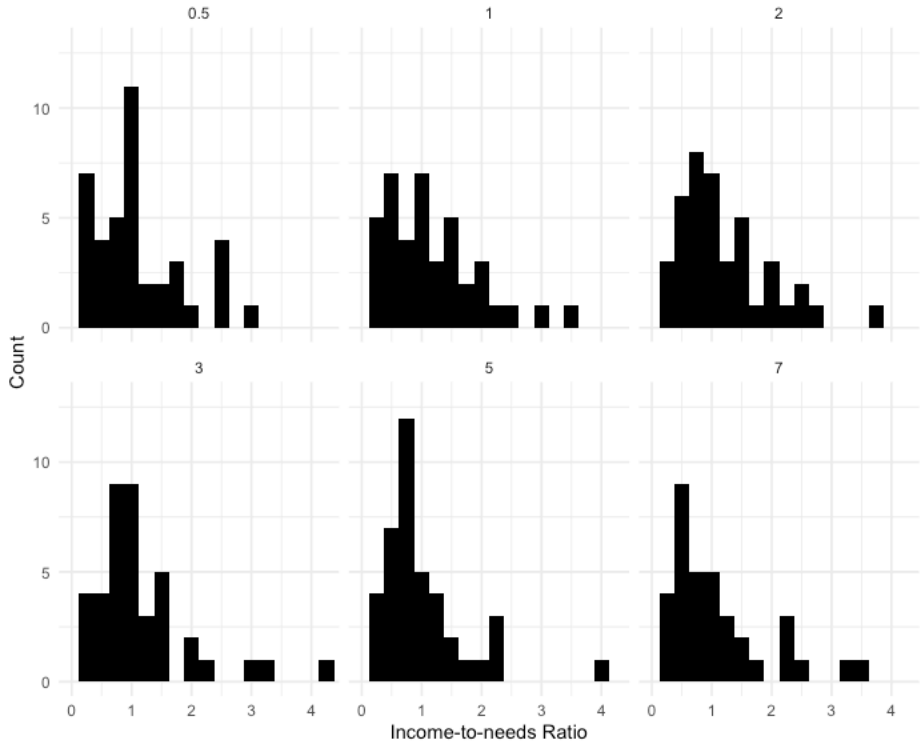

Figure S1. Histograms of income-to-needs ratio at each age (years).

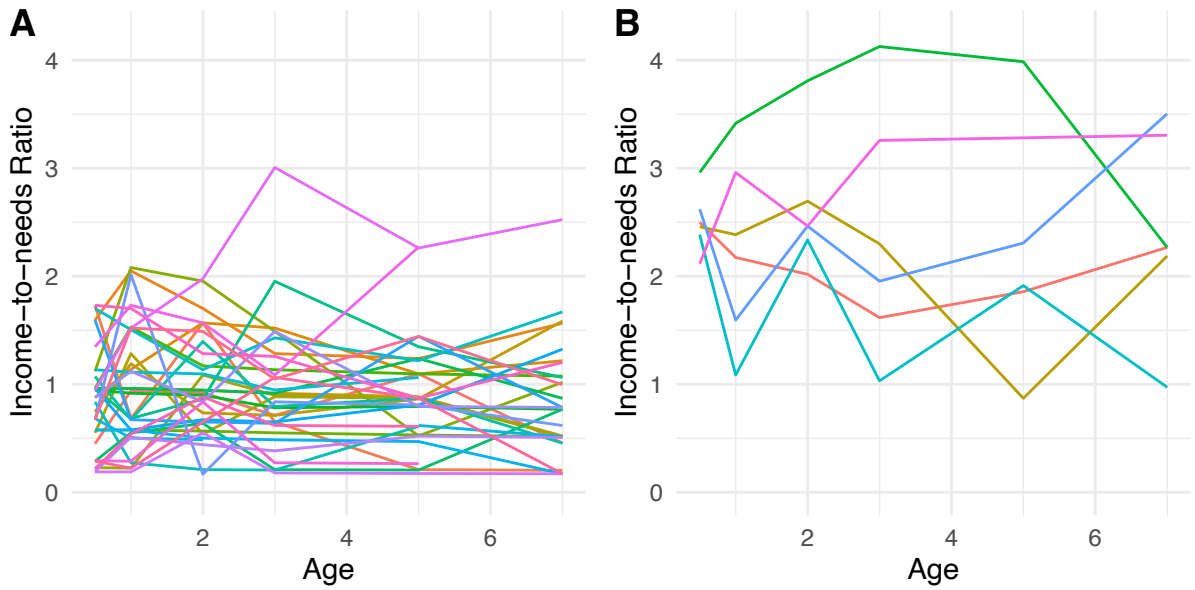

Figure S2. Dynamics of income-to-needs ratio over the first seven years of life of participants who were A) low-income and B) middle income at child age 6 months.

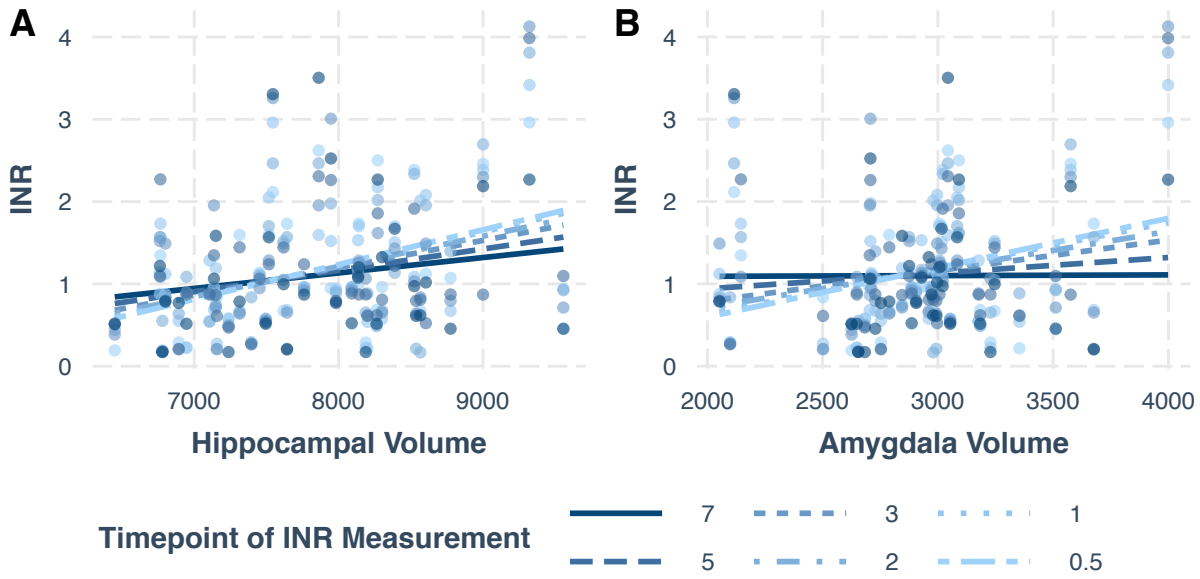

Figure S3. Graphs illustrating the interaction between subcortical volumes and timepoint of income-to-needs ratio (INR) measurement on INR value (as specified in our main model). Lines depict simple-slopes.

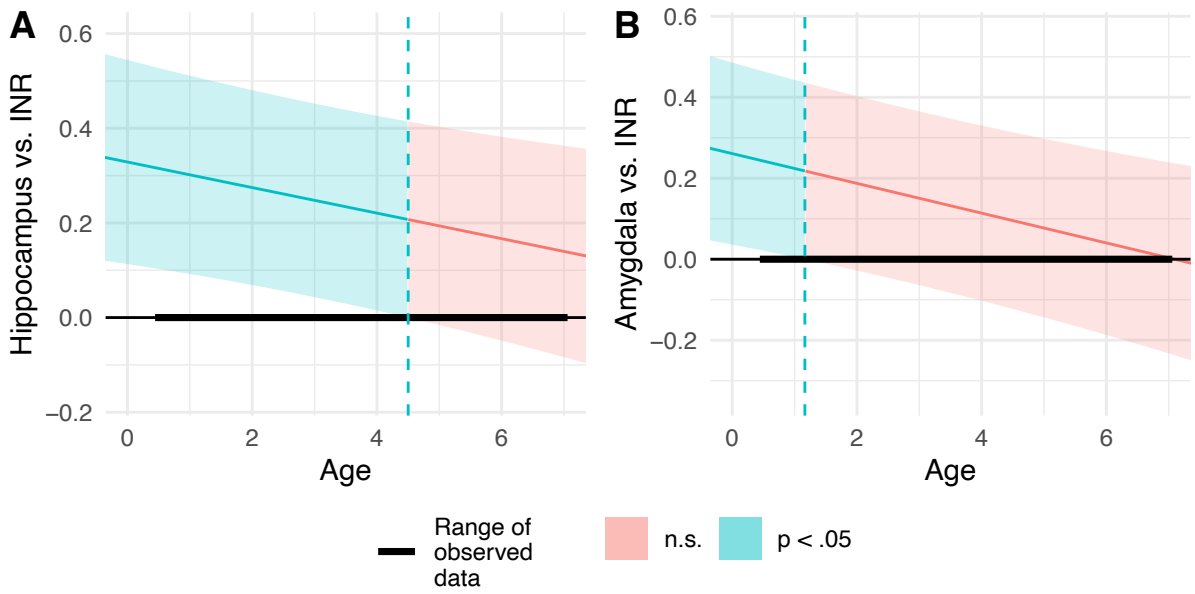

Figure S4. Johnson-Neyman analyses for repeated-measured models estimating the timing-specific association between income-to-needs ratio (INR) and hippocampal and amygdala volumes. Blue intervals denote child ages at which poverty was estimated to have a significant association with brain volumes, whereas red regions are ages at which INR-brain associations are insignificant. Interaction scatter plots are presented in Figure 1.

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