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The Effects of Poverty on Childhood Brain Development: The Mediating Effect of Caregiving and Stressful Life Events

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Abstract

Importance—The study provides novel data to inform the mechanisms by which poverty negatively impacts childhood brain development.

Objective—To investigate whether income to needs ratio experienced in early childhood impacts brain development at school age and to explore the mediators of this effect.

Design—Data from a prospective longitudinal study of emotion development in preschool children who participated in neuroimaging at school age were used to investigate the effects of poverty on brain development. Children were assessed annually for 3-6 years prior to the time of a MRI scan during which they were evaluated on psychosocial, behavioral and other developmental dimensions.

Setting—An academic research unit at the Washington University School of Medicine.

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Participants—Preschoolers 3- 6 years of age were ascertained from primary care and day care sites in the St. Louis metropolitan area and annually assessed behaviorally for 5-10 years. Healthy preschoolers and those with clinical symptoms of depression participated in neuroimaging at school age/early adolescence.

Main Outcome Measure(s)—The main outcomes of interest were brain volumes of children's white matter and cortical gray matter as well as hippocampus and amygdala obtained using MRI. Mediators of interest were caregiver support/hostility measured observationally during the preschool period and stressful life events measured prospectively.

Results—Poverty was associated with smaller white and cortical gray matter and hippocampal and amygdala volumes. The effects of poverty on hippocampal volume were mediated by caregiving support/hostility on the left and right as well as stressful life events on the left.

Conclusions and Relevance—The findings that exposure to poverty in early childhood materially impacts brain development at school age further underscores the importance of attention to the well established deleterious effects of poverty on child development. Findings that these effects on the hippocampus are mediated by caregiving and stressful life events suggest that attempts to enhance early caregiving should be a focused public health target for prevention and early intervention. Findings substantiate the behavioral literature on the negative effects of poverty on child development and provide new data confirming that effects extend to brain development. Mechanisms for these effects on the hippocampus are suggested to inform intervention.

INTRODUCTION

The deleterious effects of poverty on child development have been well established in psychosocial research, with poverty identified as among the most powerful risk factors for poor developmental outcomes.^{1,2} Children exposed to poverty have poorer cognitive outcomes and school performance as well as higher risk for antisocial behaviors and mental disorders.³ Notably, developmental deficits associated with poverty have been detected as early as infancy.^{4,5} Despite these established and alarming poor developmental outcomes, to date there has been little neurobiological data in humans to inform the mechanism(s) of these relationships. This represents a critical gap in the literature and an urgent national and global public health problem based on statistics that over one in five children are now living below the poverty line in the United States alone.⁶

The tangible effect of early environmental exposures on brain development has been well established in laboratory animals. Animals exposed to enriched environments high in stimulation have been shown to display increased hippocampal cell proliferation and neurogenesis compared to those reared in relative deprivation.⁷ Poverty represents a form of human deprivation that may parallel this animal model, raising the question of whether low levels of stimulation and relative psychosocial neglect associated with poverty have a similar negative effect on human brain development. A few studies have directly investigated the relationship between poverty and childhood brain development. Consistent with animal data, Noble and colleagues detected smaller hippocampus and amygdala in 5-17 year old children living in poverty.⁸ In a large community sample, Hanson et al., reported smaller hippocampal gray matter volumes among children from lower income

backgrounds.⁹ Lower socioeconomic status was associated with smaller hippocampal gray matter volumes bilaterally in a small sample of healthy 10 year olds.¹⁰

These findings suggest that exposure to poverty has deleterious effects on human amygdala and hippocampal development. These brain regions, involved in stress regulation and emotion processing, are known to be sensitive to environmental stimuli. However, what remains unclear, and critical to addressing this public health problem, are the specific factors that mediate this association in humans. Poverty is strongly associated with a number of risk factors implicated in poor developmental outcomes in behavioral studies, such as unsupportive parenting, poor nutrition and education, lack of caregiver education, and high levels of traumatic and stressful life events, making the income to needs ratio a good proxy for cumulative developmental stress.¹¹ These as well as other associated factors could serve as mechanisms mediating the negative impact of poverty on brain development. Whether such mediators of risk are also operative at the neurobiological level in humans remain unclear.

Experimental studies of the neurobiological impact of poverty cannot be conducted in humans for obvious ethical reasons. However, the negative effect of early unsupportive parenting in the form of maternal deprivation and stress on hippocampal and amygdala development has been well established in rodents. Stress paradigms in rodent models have been associated with elevated anxiety and contrasting alterations in neuronal morphology in the hippocampus and amygdala, with dendritic atrophy observed in the hippocampus and increased dendritic arborization in amygdala.^{12,13} Developing rodents deprived of maternal nurturance show decreased hippocampal volume and altered stress reactivity.¹⁴ An epigenetic mechanism for this effect has been elaborated.¹⁵ Importantly, controlled trials that have randomized institutionalized toddlers to early therapeutic foster care versus institutionalization have documented the deleterious effects of early relative deprivation on cognitive outcomes.¹⁶

A few studies have investigated the effects of early caregiving on amygdala and hippocampal volumes in children. Consistent with animal data, Tottenham et al., showed an association between early institutional rearing and larger amygdala volumes.¹⁷ While animal data would suggest that institutional rearing would lead to reduced hippocampal volume, some investigators have suggested that such effects may not become evident in humans until later in life.¹⁸ Consistent with this, decreased hippocampal volumes have been found in numerous studies of adults who experienced high levels of childhood stress/trauma.^{19,20} In spite of this hypothesized delayed hippocampal effect, a positive impact of early supportive parenting on hippocampal development has been detected as early as school age.²¹

To investigate the effects of poverty on childhood brain development and to begin to inform the mediating mechanisms of these negative effects, we investigated associations between poverty and total white and total cortical gray matter volume, as well as hippocampus and amygdala volumes in a sample of children ages 6 to 12 years followed longitudinally since the preschool period. Based on the behavioral data in humans and the neurobiological data in animals, we hypothesized that an effect of poverty on these brain volume outcomes would be found. We also hypothesized that key variables associated with poverty and known to

negatively impact child development outcomes, including caregiving support, caregiver education and stressful life events, would mediate the association between poverty and brain volumes.

METHODS

Participants

A total of n=145 right-handed children were obtained from a larger sample enrolled in the 10-year longitudinal Preschool Depression Study (PDS, N=305 at baseline). The larger sample was recruited from metropolitan St. Louis daycares and preschools using a screening checklist to include healthy children and to oversample preschoolers with depressive symptoms. Subjects and their caregivers participated in 3-6 comprehensive annual diagnostic and developmental assessments prior to the first neuroimaging session (see ²² for full description). Subjects were screened for standard imaging contraindications. There were no significant differences on demographic variables between the imaging sub-sample and the original sample. Table 1 shows the characteristics of the study sample. All study procedures were reviewed and approved by the IRB.

Measures

Income to Needs—Income-to-needs ratio was operationalized as the total family income divided by the federal poverty level based on family size in the year most proximal to data collection.²³ The value was calculated through baseline PDS data of caregiver reported total family income and total number of people living in the household.

Psychiatric Diagnostic Status/Stressful Life Events/Caregivers' Education—Subjects were assessed annually using Preschool Age Psychiatric Assessment (parent interview, age 3-8) and Child and Adolescent Psychiatric Assessment (parent/child interview, age 9).²⁴ Both measures also reliably capture experiences of stressful and traumatic life events.^{25,26} Life events between baseline and time of scan were used for the current analysis.

Tanner Staging Questionnaire—The Tanner was used to measure children's pubertal status at the time of scan.^{27,28}

Parental Supportive/Hostile Caregiving—At the second assessment wave (ages 4 -7 years), parent-child dyads were observed interacting during the “waiting task,” a structured task designed to elicit mild dyadic stress²⁹. This laboratory task requires the child to wait for 8 min before opening a brightly wrapped gift within arm's reach. Children are told that they can open the gift once their caregiver completes questionnaires. Blind raters, trained to reliability coded the interaction for caregivers' use of both supportive (e.g., praising the child for waiting) and hostile (e.g., threats about negative consequences) strategies. This task has acceptable psychometric properties and is a well-validated and widely used parenting measure.²⁹⁻³² Hostility scores were subtracted from support scores to provide a difference score.

MRI Acquisition

Two 3D T1-weighted magnetization prepared rapid gradient echo (MPRAGE) scans were acquired on a Siemens 3.0-T Tim Trio scanner without sedation (sagittal acquisition, repetition time 2,300ms, echo time 3.16ms, inversion time 1,200ms, flip angle 8°, 160 slices, 256 × 256 matrix, field of view 256mm, 1.0-mm³ voxels, total time 12:36min).

Image Analyses: Whole Brain

Total gray and white matter volumes were obtained using FreeSurfer (v5.1). The white and pial FreeSurfer surfaces were visually inspected and were regenerated with manual intervention when necessary. Cortical gray matter volume was defined as the volume between the pial and white matter surfaces. White matter volume was calculated by subtracting the subcortical and ventricular volumes from the volume bounded by the white matter surface.

Image Analyses: Amygdala and Hippocampus

The hippocampus was segmented by an automated high-dimensional template-based transformation. The manual template, delineated on one subject with typical anatomy, was reviewed by neuroanatomical gold standard experts following boundary definitions.^{33,34} The gold template surface, generated from the manual template, included grey and white matter. Subject images, landmarked by an experienced rater blind to subject characteristics, were aligned to the template through an affine transformation followed by a non-linear large deformation transformation to increase alignment precision. After matching subject-template voxel intensities, a high-dimensional subject-template transformation was generated through large deformation diffeomorphic metric mapping³⁵. Results were blindly reviewed (C.B.) for surface quality. The reliability of this process is well established.³⁴ The amygdala segmentation paralleled the methodology of the hippocampus.

Statistical Analyses

Potential Covariates—T-tests and Pearson Correlations were conducted to explore variation in brain volumes related to children's gender, age, pubertal status, history of psychiatric disorders (Y/N), and children's history of psychotropic medication (Y/N) use. Covariates were included in the final analyses if significant for that particular region.

Associations between income-to-needs ratio and brain volume—Hierarchical multiple linear regression analyses were conducted to test whether income-to-needs ratio predicted brain volumes. For all models, covariates were entered at step 1 and income-to-needs ratio was entered at step 2.

Mediators of the hypothesized associations between income-to-needs & brain volumes—Three variables were tested as possible mediators of the relations between baseline income-to-needs ratios and children's brain volumes (see Figure 1). Mediators were tested by calculating bias-corrected 95% confidence intervals using bootstrapping with n = 10,000 resamples via the PROCESS procedure for SPSS.^{36,37} Given our data cannot

establish temporal precedence between caregivers' income-to-needs ratio and highest level of education, we chose to use baseline data for both variables.

RESULTS

Table 1 shows the results of analyses testing potential covariates. Based on these results, gender was included as a covariate in all analyses except those examining right hippocampal volume. For analyses of white matter volume, children's age and pubertal status were also included as covariates. None of the brain volumes differed significantly in relation to children's history of DSM-IV Axis I disorder or psychotropic medication exposure. For all analyses examining hippocampus or amygdala volumes, children's total cortical brain volume (total white + total cortical grey) was included as a covariate to assess specificity.

Income-to-Needs Predicting Total White and Cortical Gray Matter Volumes

White Matter Volume—Children's age, gender, and pubertal status were entered at step 1. Income-to-needs ratio was entered at step 2 and was a positive predictor of white matter volume, accounting for a significant increase in variance, $F_{change}(1,137) = 8.12, p = .005$. The $R^2_{adjusted}$ for each step of the model as well as the unstandardized regression coefficients (B), standard error (SE), and standardized regression coefficients (β) are reported in Table 2.

Cortical Gray Matter—Gender was included at step 1 of the model. Income-to-needs ratio was entered at step 2 and was a positive predictor of gray matter volume, accounting for a significant increase in variance, $F_{change}(1,142) = 21.79, p < .001$ (Table 2).

Income-to-needs Predicting Left and Right Hippocampus and Amygdala Volumes

Covariates, including whole brain volume, were entered in step 1. As seen in Table 3, for children's left hippocampus volume, including income-to-needs at step 2 resulted in a significant increase in the amount of variance accounted for, $F_{change}(1,115) = 5.76, p = .018$. Income-to-needs was a positive predictor of children's left hippocampus volumes. For right hippocampus, the increase in variance accounted for after including income-to-needs at step 2 only approached significance, $F_{change}(1,119) = 2.94, p = .09$. For children's left amygdala volume, including income-to-needs at step 2 resulted in a significant increase in the amount of variance accounted for, $F_{change}(1,120) = 6.28, p = .014$. Income-to-needs was a positive predictor of children's left amygdala volumes. For right amygdala volumes, the increase in variance accounted for after including income-to-needs at step 2 only approached significance, $F_{change}(1,127) = 2.79, p = .09$.

Caregivers' Education, Parenting, & Stressful Life Events as Mediators of the Associations Between Income-to-Needs & Brain Volumes

The analyses described above established a relationship between income-to-needs and later brain volumes. We hypothesized that there would also be indirect (i.e., mediated) effects through caregivers' education, observed use of supportive/hostile parenting, as well as children's experience of stressful life events. Figure 1 provides a conceptual diagram of the mediational analyses conducted. MacKinnon (2002) and colleagues suggest that mediation

analyses be conducted when there is a relation between a predictor and mediator (paths a1, a2, a3 in Figure 1) as well as a relation between a mediator and outcome (paths b1, b2, and b3 in Figure 1). To be considered a mediator, the strength of the direct relation between predictor and outcome (path c in Figure 1) will be diminished when the mediator is entered into the analysis (path c' in Figure 1). Covariates included in the meditational analyses were parallel with prior analyses and were only applied to outcome variables. Below we first establish the relationship between the predictor (income-to-needs) and the potential mediators (caregiver education, parenting and life events), and then examine the relationships of the mediators to the outcome (brain volume), and when significant, whether they reduce the direct effect of income-to-needs on brain volumes.

Income-to-Needs Predicting Potential Mediators—Regression analyses confirmed income-to-needs ratio: (path a1) was significantly associated with caregivers' education (ranges across all regions: *p-values* <.001 in all models), (path a2) predicted caregiving support/hostility assessed 1-year after baseline controlling for caregivers' education (*p-values* <.001), and (path a3) predicted children's experience of stressful life events between baseline and time of scan when covarying for caregivers' education and supportive/hostile parenting (*p-values* <.001 in all models).

Mediators of Total White Matter and Cortical Gray Matter Volumes—Paths b1, b2, and b3 from the mediators to white matter and cortical gray matter volume were all non-significant, *p's* > .05. Thus, neither caregiving behaviors, education, nor life stress, mediated the relationship between income-to-needs and cortical gray or white matter volume.

Mediators of Hippocampal Volumes—Figure 2 illustrates that two of the mediating variables, stressful life events (path b1) and caregiving behaviors (path b3), positively predicted children's left hippocampus volumes. For right hippocampus volume, caregiving behavior (path b3) was the only significant mediator. When mediators were included in the model, the direct paths (i.e., paths c') from income-to-needs to left hippocampus, *p* > .51, and right hippocampus, *p* > .55, volumes were no longer significant, indicating full mediation (see Figure 2). eTable 2 shows the mediated effects of income-to-needs ratio on left and right hippocampus volumes.

Mediators of Amygdala Volumes—Paths b1, b2, and b3 from the mediators to left and right amygdala volumes were all non-significant, *p's* > .14.

DISCUSSION

Study findings demonstrate that exposure to poverty during early childhood is associated with smaller white matter, cortical gray matter and hippocampal and amygdala volumes measured at school age/early adolescence. These findings extend the substantial body of behavioral data demonstrating the deleterious effects of poverty on child developmental outcomes into the neurodevelopmental domain and are consistent with prior results.^{8,9} Further, these study findings extend the available structural neuroimaging data in children exposed to poverty by informing the mechanism of the effects of poverty on hippocampal volumes. Findings indicated that the effects of poverty on hippocampal volumes were

mediated by caregiving support/hostility on both left and right hippocampus. On the left, stressful life events also emerged as a significant mediator. Caregiver education was not a significant mediator. As exposure to poverty is well known to be strongly associated with a variety of negative life experiences, the role that these risk factors appeared to play in the relationship between poverty and alterations in brain development elucidates more specific targets for prevention.

Notably, alterations in brain volume associated with poverty were detected more globally in cortical gray and white matter volume, although mediation in these regions was not identified. The finding that mediation associated with parenting and life stress was selective to the hippocampus suggests regional specificity to these mechanistic relationships. The key role of caregiver nurturance in hippocampal development and its relationship to adaptive stress responses has well been established in animal studies. Consistent findings have been provided from an earlier sub-group of this study sample suggesting that supportive parenting also plays a key role in child hippocampal development independent of income.²¹ Thus, the current findings add to and extend the literature underscoring the critical role of nurturance for childhood well being.³⁸ The finding that experiences of stressful life events also mediated the relationship between poverty and left hippocampal volume is consistent with the extensive body of animal data that have elucidated the negative effects of early stress on HPA function and hippocampal volume.³⁹ Understanding these mechanisms is key to the design of more targeted interventions, providing a feasible alternative to changing psychosocial status itself, a much more challenging goal that vulnerable rapidly developing young children do not have time to await.

Limitations of the current data are that the original study sample was oversampled for preschoolers with symptoms of depression, limiting generalizability. Further, the relationships in the mediation model may be bi-directional. A sample with multiple waves of imaging data starting earlier in development would be necessary to adequately test directionality. Future studies with such designs and more detailed assessments of the correlates of poverty such as nutrition, parental psychopathology and genetic factors are needed to further elucidate the mechanisms of risk.

We believe these findings may be useful to inform preventive interventions for this high-risk population facing a multitude of psychosocial stressors and suggest that caregiving should be a specific target. The importance of early interventions that target caregiving is underscored by studies demonstrating high cost effectiveness through greatly enhanced long-term outcomes.⁴⁰ Further, children who receive more nurturing caregiving may also be protected from exposure to stressful life events suggesting this central target may have positive ramifications on brain development.⁴¹ Considering these issues, study findings are relevant to the public policy debate on the importance of early preschool programs for young children living in poverty. The finding that the effects of poverty on hippocampal development are mediated through caregiving and stressful life events further underscore the importance of high quality early childhood caregiving, a task that can be achieved through parenting education and support as well as through preschool programs that provide high quality supplementary caregiving and safe haven to vulnerable young children.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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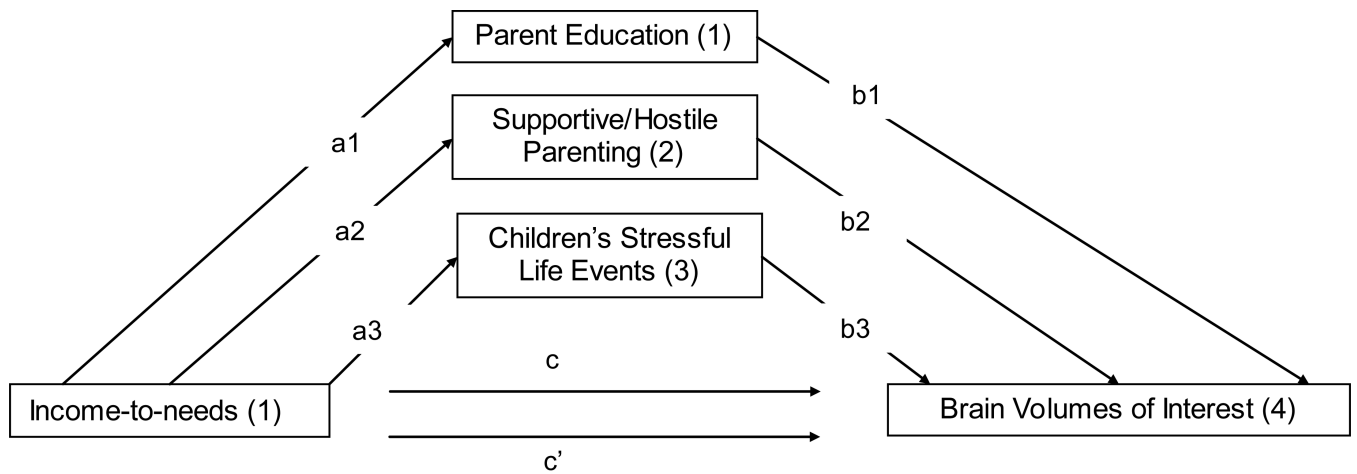
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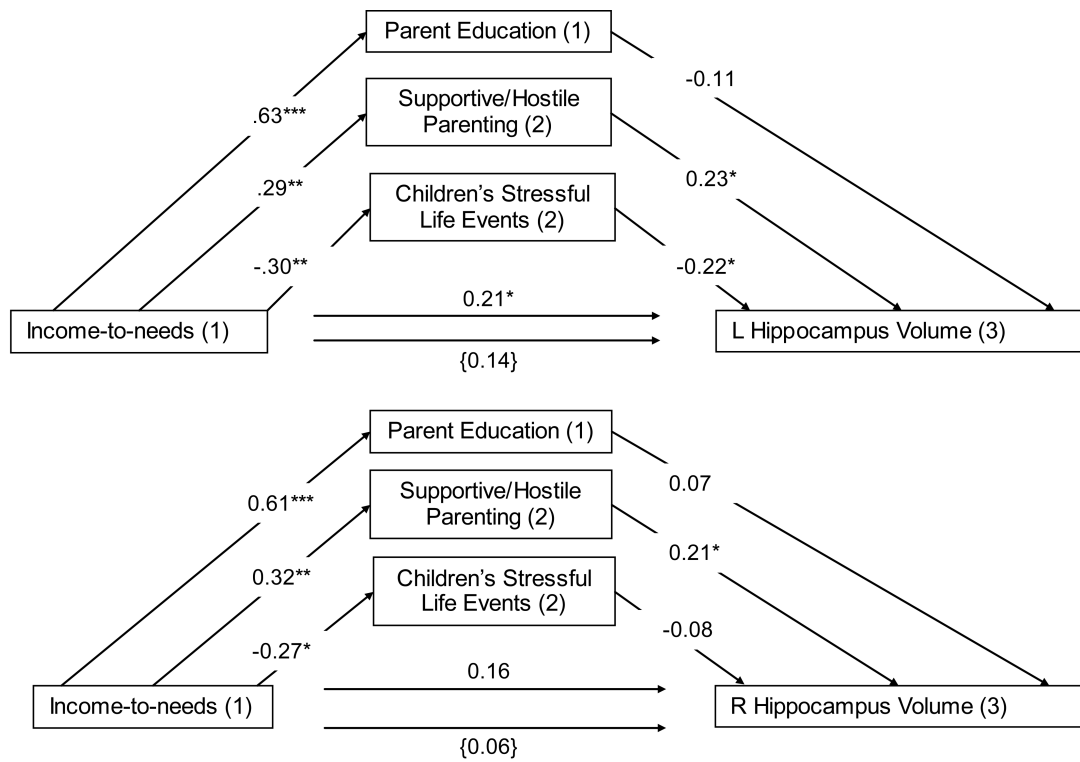
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(1) Measured at baseline (2) Measured after baseline but before scan (3) Between baseline and time of scan (4) Time of scan after (1) and (2).

Figure 1.

Conceptual Model Testing Multiple Mediators of the Hypothesized Association between Income-to-needs and Variation in Brain Volume



Values shown are standardized regression coefficients. (1) Measured at baseline (2) Measured after baseline but before scan (3) Time of scan after (1) and (2). { } after adding parents' education; supportive/hostile parenting; and children's stressful life events to the model. Both models included whole brain volume and gender as covariates. * $p < .05$, ** $p < .01$, *** $p < .001$

Figure 2.

Caregivers education, Supportive/Hostile Parenting, Children's Experiences of Stressful Life Events as Mediators of the Relation between Income-to-Needs and Hippocampus Volumes

Table 1

Demographics for current sample

| | Mean (SD; range) or N (%) |
|--|---------------------------|
| Average parent education (years) | |
| < High school diploma | 10 (7%) |
| High school diploma | 11 (8%) |
| Some college | 57 (38%) |
| College degree | 27 (19%) |
| Some graduate school or graduate/professional degree | 40 (28%) |
| Income-to-needs ratio^a | 2.14 (1.27; 0.00 – 4.74) |
| Family size | 4.27 (1.21; 2 – 8) |
| Race | |
| African-American | 47 (56%) |
| Caucasian | 81 (32%) |
| Other | 17 (12%) |
| Supportive-to-nonsupportive caregiving ratio | 0.67 (0.45; –0.44 – 1.75) |
| Children's Age (years) | 9.78 (1.29; 6 - 12) |
| Child Gender | |
| Female | 73 (51%) |

Footnote:

^aTotal family income divided by the federal poverty level for a family of that size closest to the year data were collected.

Table 2

Income-to-Needs Predicting Total White Matter & Cortical Gray Matter Volume

| Region | Regression Step | $R^2_{adjusted}$ | B | SE | β |
|-----------------------------------|-----------------|------------------|----------------|------------------------|------------------|
| Total White Matter Volume | <i>Step 1</i> | | | | |
| | | .18 ^c | | | |
| | Gender | | 35825.52 | 8289.96 | .33 ^c |
| | Age | | 527.91 | 380.08 | .16 |
| | Pubertal Status | | 16157.45 | 11320.94 | .15 |
| | <i>Step 2</i> | | | | |
| | | .22 ^c | | | |
| | Gender | | 33101.50 | 8140.35 | .31 ^c |
| | Age | | 705.30 | 373.53 | .19 ^a |
| | Pubertal Status | | 11585.00 | 11155.72 | .11 |
| | | 9349.11 | 3280.85 | .22^b | |
| Total Cortical Gray Matter Volume | <i>Step 1</i> | | | | |
| | | .11 ^c | | | |
| | Gender | | 36014.24 | 8353.40 | .34 ^c |
| | <i>Step 2</i> | | | | |
| | | .22 ^c | | | |
| | Gender | | 32716.59 | 7836.99 | .31 ^c |
| | | 14828.42 | 3176.82 | .35^c | |

Footnote:

^a p < .05^b p < .01^c p < .001

Table 3

Hierarchical Regression: Income-to-Needs Variable Predicting Hippocampus and Amygdala Volumes

| Region | Regression Step | $R^2_{adjusted}$ | <i>B</i> | <i>SE</i> | β |
|-------------------|------------------------|------------------|--------------|--------------|------------------------|
| Left Hippocampus | <i>Step 1</i> | .15 ^c | | | |
| | Gender | | 7.40 | 31.83 | .02 |
| | Cortical Brain Volume | | .001 | .000 | .41 ^c |
| | <i>Step 2</i> | .19 ^c | | | |
| | Gender | | 7.19 | 31.20 | .02 |
| | Cortical Brain Volume | | .001 | .000 | .34 ^c |
| | Income-to-Needs | | 30.30 | 12.62 | .21^a |
| Right Hippocampus | <i>Step 1</i> | .27 ^b | | | |
| | Cortical Brain Volume | | .001 | .000 | .52 ^c |
| | <i>Step 2</i> | .28 ^b | | | |
| | Cortical Brain Volume | | .001 | .000 | .49 ^c |
| | Income-to-Needs | | 20.56 | 12.41 | .14 |
| Left Amygdala | <i>Step 1</i> | .25 ^c | | | |
| | Gender | | 53.65 | 26.49 | .17 ^a |
| | Cortical Brain Volume | | .001 | .000 | .42 ^c |
| | <i>Step 2</i> | .28 ^c | | | |
| | Gender | | 58.20 | 25.99 | .18 ^a |
| | Cortical Brain Volume | | .001 | .000 | .36 ^c |
| | Income-to-Needs | | 25.63 | 10.23 | .20^b |
| Right Amygdala | <i>Step 1</i> | .32 ^c | | | |
| | Gender | | 58.64 | 26.17 | .18 ^a |
| | Cortical Brain Volume | | .001 | .000 | .49 ^c |
| | <i>Step 2</i> | .33 ^c | | | |
| | Gender | | 1.11 | 26.03 | .18 ^b |
| | Cortical Brain Volume | | .001 | .000 | .44 ^c |
| | Income-to-Needs | | 17.38 | 10.41 | .13 |

Footnote:

^a
p < .05^b
p < .01^c
p < .001