Family income buffers the relationship between childhood adverse experiences and putamen volume

Max P. Herzberg 1 | Laura Hennefield 1 | Katherine R. Luking 2 | Ashley F. P. Sanders 1 | Alecia C. Vogel 1 | Sridhar Kandala 1 | Rebecca Tillman 1 | Joan Luby 1 | Deanna M. Barch 1,2,3

1 Department of Psychiatry, Washington University in St. Louis, St. Louis, Missouri, USA
2 Department of Psychological & Brain Sciences, Washington University in St. Louis, St. Louis, Missouri, USA
3 Department of Radiology, Washington University in St. Louis, St. Louis, Missouri, USA

Correspondence
Max P. Herzberg, Department of Psychiatry, Washington University in St. Louis, St. Louis, MO, USA.
Email: maxherzberg@wustl.edu

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Abstract
Adverse experiences and family income in childhood have been associated with altered brain development. While there is a large body of research examining these associations, it has primarily used cross-sectional data sources and studied adverse experiences and family income in isolation. However, it is possible that low family income and adverse experiences represent dissociable and potentially interacting profiles of risk. To address this gap in the literature, we examined brain structure as a function of adverse experiences in childhood and family income in 158 youths with up to five waves of MRI data. Specifically, we assessed the interactive effect of these two risk factors on six regions of interest: hippocampus, putamen, amygdala, nucleus accumbens, caudate, and thalamus. Adverse experiences and family income interacted to predict putamen volume ($B = 0.086$, $p = 0.011$) but only in participants with family income one standard deviation below the mean (slope estimate $= -0.11$, $p = 0.03$). These results suggest that adverse experiences in childhood result in distinct patterns of brain development across the socioeconomic gradient. Given previous findings implicating the role of the putamen in psychopathology-related behaviors, these results emphasize the importance of considering life events and socioeconomic context when evaluating markers of risk. Future research should include interactive effects of environmental exposures and family income to better characterize risk for psychopathology in diverse samples.

KEYWORDS
adverse experiences, poverty, brain structure, psychopathology, early childhood

1 INTRODUCTION

Adverse events in childhood are associated with alterations across a broad array of domains, including physical and behavioral health and brain development (Afifi et al., 2016; Lupien et al., 2009; Taillieu et al., 2016; Teicher et al., 2016). Unfortunately, experiencing adverse events, such as poverty, parental maladjustment, interpersonal loss, or maltreatment, is common in childhood. More than half of the children in the United States will experience an adverse event prior to adulthood and are more likely to go on to develop psychopathology as a result (J. G. Green et al., 2010; McLaughlin et al., 2012). In fact, it has been suggested that adverse experiences (AEs) in childhood may be responsible for nearly 30% of all psychopathology (Kessler et al., 2010). The mechanisms by which AEs in childhood lead to increased rates of...
psychiatric illness have long been sought and a number of theories tested, including alterations to stress physiology, increased levels of inflammation, and modification of brain structure and function (Danese & McEwen, 2012). Of particular interest to this investigation, stressful experiences in early life have been consistently linked to altered brain structure years after the adverse event.

Research on the neurobiological effects of AEs has found global changes in brain development and more specific regional differences (Edmiston et al., 2011; Gold et al., 2016; Kelly et al., 2013; Luby et al., 2019; Teicher et al., 2016). Youth exposed to adversity have exhibited smaller whole brain volumes compared to control groups at 8–21 years of age, with gray matter variations reported in frontal, temporal, parietal, and occipital regions (De Brito et al., 2013; Gur et al., 2019; Kelly et al., 2015; Lim et al., 2014). These structural abnormalities extend to subcortical areas where AEs have been associated with morphological differences in limbic structures. Infants and children exposed to different forms of AEs (i.e., maltreatment, neglect, institutionalization) have exhibited smaller hippocampal volumes in late childhood, including specific reductions in stress sensitive CA1 and CA3 subfields, compared to children with no history of adversity (Dahmen et al., 2018; Hanson et al., 2015). Volumetric differences have also been reported in the amygdala following adversity, though the nature of these variations is inconsistent. For example, early childhood maltreatment and neglect has been linked to larger (Mehta et al., 2009; Tottenham et al., 2010), smaller (Edmiston et al., 2011), and equivalent amygdala volumes compared to youth without AEs (Carrion et al., 2001; McLaughlin et al., 2014; Sheridan et al., 2012). While existing studies have largely focused on the effects of adversity on the amygdala and hippocampus, recent reports have also associated AEs with smaller putamen, caudate, and thalamus volumes and stress hormones related to adverse experiences with smaller nucleus accumbens volumes, highlighting the need for further investigation into subcortical structures (Gehred et al., 2021; C. Green et al., 2021). Notably, early AEs have been linked to structural brain alterations in adulthood (Mackes et al., 2020; Tomalski & Johnson, 2010), suggesting that these early traumatic and stressful events have lasting effects on brain development.

Similar gray matter changes have been reported in children experiencing poverty, an environmental risk factor for adversity. Low family income-to-needs ratio (INR), or poverty, in childhood has been associated with reduced gray matter volume (Dufford et al., 2020). Consistent with AE findings, associations with poverty are often observed at the whole brain level, but it is also observed within subcortical regions, particularly the hippocampus (Brody et al., 2017; Hair et al., 2015; Jednoróg et al., 2012; McDermott et al., 2019; Noble et al., 2015; Staff et al., 2012). Recently, work from the same sample used in the present study reported smaller cortical and subcortical gray matter volumes in children and youth with lower family INR (Barch et al., 2021). Among the subcortical regions implicated in this research, the hippocampus, caudate, and thalamus showed specific associations with family INR. Further, subcortical gray matter volume mediated the association between childhood INR and cognition and high-risk behaviors in adolescence, highlighting the importance of these alterations in brain development on adaptive outcome following AEs. The few other longitudinal studies that have been completed suggest that low INR affects brain volumes as early as the first year of life (Lawson et al., 2013), may contribute to slower gray matter growth (Hanson et al., 2013), and exerts effects from childhood into young adulthood (McDermott et al., 2019). Other work has begun to investigate potential mediators of the relationship between poverty and neural outcomes, including stress, caregiving, or environmental toxin exposure (Avants et al., 2015; Luby et al., 2013). Critically, however, there is still relatively little longitudinal work investigating how INR impacts the development of specific subcortical structures and how it interacts with other environmental factors, like AEs, to elucidate differences in brain development.

Whereas both childhood poverty and experiencing AEs have been consistently associated with alterations in brain structure, the relationship between these constructs, including whether they interact to predict unique associations with brain volume, is not yet known. Making the relationship between poverty and adversity more complicated, it is widely understood that there is an association between lower family income and experiencing more AEs in childhood. Data from a recent nationally representative sample indicate that children who live at or below the poverty line are three times more likely to have experienced 2+ adverse events relative to children living at or above 400% of the poverty line, and five times as likely to have experienced 4+ adverse events (Halfon et al., 2017). Nonetheless, AEs are not unique to children living below the poverty threshold but are distributed across income strata, though some types of AEs may be more common in lower-income contexts (e.g., exposure to neighborhood violence) while others are experienced more equally (e.g., death of a loved one). This distribution of AEs implies that higher income may not necessarily buffer against the deleterious health outcomes associated with experiencing adverse events in childhood (Halfon et al., 2017). Despite clear links between poverty and AEs, and the key role that both appear to play in brain development and health outcomes, research on these constructs is not well integrated (see Walsh et al., 2019 for a review). Further, research on the relationships between early AEs and negative health outcomes, for example, persist after adjusting for socioeconomic characteristics suggest that these constructs may capture dissociable aspects of risk (e.g., Kelly-Irving et al., 2013).
The possibility that low family income and AEs represent unique profiles of risk is especially important when identifying targets for intervention and prevention efforts related to the development of psychopathology. Investigations focused on associations between family income or AEs and total brain volume in isolation need more specificity to further inform clinical translation. Recent theoretical work in developmental psychopathology suggests that, just as pathways to depression and behavior problems are diverse, the interventions that will be most effective for individuals need to recognize diverse developmental pathways to risk (Doom & Cicchetti, 2020). Interventions specific enough to address heterogeneous pathways to risk may have the added benefit of interrupting developmental cascades that can lead to amplified negative outcomes (Masten & Cicchetti, 2010). Approaches that focus on interactive effects are consistent with this idea, as they better characterize individual experiences and may provide multifaceted risk profiles better suited to effective intervention and prevention. Further, targeting more specific brain regions of interest impacted by family income and AEs may shed light on the kinds of behavioral outcomes associated with their combined impact. Consistent with this idea, meta-analytic work has suggested that the inclusion of neuroimaging data can improve accuracy in studies predicting clinical outcomes better than behavioral data alone (Jollans & Whelan, 2016).

In this study, we extended the prior literature by investigating family income-to-needs ratio as a moderator of the relationship between AEs in childhood and subcortical brain structures. Specifically, we assessed the interactive effect of AEs and family INR on six subcortical regions of interest: the hippocampus, amygdala, nucleus accumbens, caudate, putamen, and thalamus. These regions of interest were chosen due to prior research demonstrating their association with socioeconomic status and AEs. We completed these analyses using data from a large longitudinal study spanning nearly two decades, which included five waves of neuroimaging assessment spanning childhood through late adolescence. To leverage the longitudinal data available and test for developmental timing effects, separate models were run using AEs experienced in the preschool, school-age, and early adolescent periods. Given the paucity of research regarding the interaction of family INR and AEs in childhood, we made no specific predictions regarding the direction of effects prior to beginning the analyses.

2 | METHODS

2.1 | Participants

Participants were 158 youth that took part in the larger preschool depression study, a 17-year longitudinal study that began when participants were 3–5 years of age and includes five waves of brain imaging data. Youth and their primary caregivers were recruited from the St. Louis metropolitan area and oversampled for depression symptoms using the Preschool Feelings Checklist (Luby et al., 2004). When the original participants were 7–12 years of age, those who were either healthy or had any depression history were invited to participate in brain imaging. An additional 42 new healthy children were also recruited to participate in neuroimaging (N = 210 at scan wave 1). Children were excluded at study entry for head injury with loss of consciousness for 5+ minutes, diagnosis of an autism spectrum disorder, neurological illness, treatment for lead poisoning, or contraindications for MRI scanning (scan wave 1 specific). All participants included in this analysis provided complete data for baseline INR, usable imaging data from at least one scan wave, and AE data in each developmental period of interest. See Table 1 for demographic information. Caregivers and participants provided informed consent and assent, respectively. All methods were approved by the Washington University Institutional Review Board (IRB #201502094).

2.2 | Income-to-need ratio

Family INR was defined as total family income at baseline (T1) divided by the federal poverty level associated with the appropriate family size such that an INR of 1 is equal to the poverty line (McLoyd, 1998). For the additional 42 participants recruited at scan wave 1, INR was calculated using parent retrospective report of family income in 2003 (the first year of the study).

2.3 | Adverse experiences

AE scores were created using parent-reported variables from the life events section of the preschool age psychiatric assessment (PAPA, when participants were 3–7 years; Egger, 2009; Egger et al., 2006) or child and adolescent psychiatric assessment (CAPA, 8 years and older; Angold & Costello, 2000), and family interview for genetic studies (for parental psychopathology; Maxwell, 1992). The number of AEs endorsed on each assessment were summed to create a single score at each wave and standardized within that wave. AE scores were then created for each developmental period by averaging sum scores for each assessment that fell within the age range for each period: preschool age (3;0–5;11 years), school-age (6;0–9;11 years), early adolescence (10;0-14;11 years). See Supporting Information Appendix 1 for variables included in the AE scores and methods used to create these scores.
### TABLE 1  Participant demographics

<table>
<thead>
<tr>
<th>Overall (N = 158)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sex</strong></td>
</tr>
<tr>
<td>Male</td>
</tr>
<tr>
<td>Female</td>
</tr>
<tr>
<td><strong>Race/Ethnicity</strong></td>
</tr>
<tr>
<td>White</td>
</tr>
<tr>
<td>Black</td>
</tr>
<tr>
<td>Other</td>
</tr>
<tr>
<td><strong>Baseline INR</strong></td>
</tr>
<tr>
<td>Mean (SD)</td>
</tr>
<tr>
<td>Median [Min, Max]</td>
</tr>
<tr>
<td><strong>Age at Scan 1</strong></td>
</tr>
<tr>
<td>Mean (SD)</td>
</tr>
<tr>
<td>Median [Min, Max]</td>
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<tr>
<td>Missing</td>
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<tr>
<td><strong>Age at Scan 2</strong></td>
</tr>
<tr>
<td>Mean (SD)</td>
</tr>
<tr>
<td>Median [Min, Max]</td>
</tr>
<tr>
<td>Missing</td>
</tr>
<tr>
<td><strong>Age at Scan 3</strong></td>
</tr>
<tr>
<td>Mean (SD)</td>
</tr>
<tr>
<td>Median [Min, Max]</td>
</tr>
<tr>
<td>Missing</td>
</tr>
<tr>
<td><strong>Age at Scan 4</strong></td>
</tr>
<tr>
<td>Mean (SD)</td>
</tr>
<tr>
<td>Missing</td>
</tr>
<tr>
<td><strong>Age at Scan 5</strong></td>
</tr>
<tr>
<td>Mean (SD)</td>
</tr>
<tr>
<td>Median [Min, Max]</td>
</tr>
<tr>
<td>Missing</td>
</tr>
</tbody>
</table>

#### Putamen Volume at Scan 1

- **Mean (SD)**: 6.31 (0.597)
- **Median [Min, Max]**: 6.27 [4.38, 8.47]
- **Missing**: 14 (8.9%)

#### Putamen Volume at Scan 2

- **Mean (SD)**: 6.30 (0.589)
- **Median [Min, Max]**: 6.26 [4.53, 8.47]
- **Missing**: 28 (17.7%)

#### Putamen Volume at Scan 3

- **Mean (SD)**: 6.21 (0.596)
- **Median [Min, Max]**: 6.15 [4.52, 7.41]
- **Missing**: 44 (27.8%)

#### Putamen Volume at Scan 4

- **Mean (SD)**: 6.71 (0.682)
- **Median [Min, Max]**: 6.70 [4.85, 8.64]

#### AE Sum Score During Preschool

- **Mean (SD)**: 0.107 (0.975)
- **Median [Min, Max]**: 0.0117 [−1.42, 3.09]

#### AE Sum Score During School Age

- **Mean (SD)**: 0.0907 (0.954)
- **Median [Min, Max]**: −0.0826 [−1.23, 3.20]

#### AE Sum Score During Early Adolescence

- **Mean (SD)**: 0.119 (0.938)
- **Median [Min, Max]**: 0.0226 [−1.57, 3.34]

### TABLE 1 (Continued)  Overall (N = 158)

<table>
<thead>
<tr>
<th>Overall (N = 158)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Missing</strong></td>
</tr>
</tbody>
</table>

#### Putamen Volume at Scan 5

- **Mean (SD)**: 6.63 (0.676)
- **Median [Min, Max]**: 6.60 [4.64, 8.59]
- **Missing**: 53 (33.5%)

#### AE Sum Score During Preschool

- **Mean (SD)**: 0.107 (0.975)
- **Median [Min, Max]**: 0.0117 [−1.42, 3.09]

#### AE Sum Score During School Age

- **Mean (SD)**: 0.0907 (0.954)
- **Median [Min, Max]**: −0.0826 [−1.23, 3.20]

#### AE Sum Score During Early Adolescence

- **Mean (SD)**: 0.119 (0.938)
- **Median [Min, Max]**: 0.0226 [−1.57, 3.34]

### 2.4  Structural MRI acquisition and processing

Scan waves 1–3 were collected using a 3.0T Siemens Trio whole-body scanner with a 12-channel head coil. Scan waves 4–5 were collected using a 3.0 T Siemens Prisma whole-body scanner with a 32-channel head coil. The FreeSurfer Longitudinal processing stream was used to process the structural imaging data (v 5.3 http://surfer.nmr.mgh.harvard.edu; Reuter et al., 2012). Specific MRI acquisition parameters and data processing information can be found in the appendix. Scanning sessions also included task-based and resting-state scans that are not considered here.

### 2.5  Statistical analysis

The volumes of the subcortical regions of interest, averaged across hemispheres at each timepoint, were investigated using multilevel modeling as implemented by the “lme4” package (Bates et al., 2015) in R (version 4.0.2; R Core Team, 2020). Volumes of the subcortical regions of interest in cubic centimeters were used as the dependent variable and the interaction of AEs and baseline INR was the predictor of interest. Covariates included sex at birth, age, the quadratic effect of age, the AE sum scores from the other developmental periods, an age by AE score interaction, and intracranial volume. Additional model information is provided in the Supporting Information Appendix. Separate models were run for each subcortical region using AE sum scores from each of three developmental periods: preschool age, school-age, and early adolescence. Missing brain volume data was handled via list wise deletion in each multilevel regression model.
TABLE 2  Means, standard deviations, and correlations with confidence intervals for the demographic and behavioral measures used in this study

<table>
<thead>
<tr>
<th>Variable</th>
<th>M</th>
<th>SD</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Sex</td>
<td>1.49</td>
<td>0.50</td>
<td>-0.02</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2. Family INR</td>
<td>2.03</td>
<td>1.15</td>
<td>0.09</td>
<td>-0.26**</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3. AEs During Preschool Period</td>
<td>0.11</td>
<td>0.96</td>
<td>0.07</td>
<td>-0.35**</td>
<td>0.61**</td>
<td></td>
</tr>
<tr>
<td>4. AEs During School Age Period</td>
<td>0.12</td>
<td>0.99</td>
<td>0.11</td>
<td>-0.41**</td>
<td>0.56**</td>
<td>0.78**</td>
</tr>
<tr>
<td>5. AEs During Early Adolescence</td>
<td>0.13</td>
<td>0.96</td>
<td></td>
<td>0.06</td>
<td>0.40</td>
<td>0.40</td>
</tr>
</tbody>
</table>

Note. M and SD are used to represent mean and standard deviation, respectively. Values in square brackets indicate the 95% confidence interval for each correlation. The confidence interval is a plausible range of population correlations that could have caused the sample correlation (Cumming, 2014), * indicates p < .05. ** indicates p < .01. INR = Income-to-Need Ratio.

A Bonferroni-adjusted alpha of α = 0.017 was used to correct for multiple comparisons (three models for each dependent variable of interest, representing the three developmental periods investigated) in the primary analyses. Follow-up analyses, which investigated whether the effects of AEs were due to different types of exposures in high- versus low-income contexts used an exploratory, uncorrected alpha of α = 0.05.

2.6  Model interpretation

Only the interactive effects were interpreted as they were the predictors of interest. The main effects of baseline INR in this sample have been reported previously (Barch et al., 2021), and the main effects of baseline INR are concordant with previous research (e.g., Hanson et al., 2011, 2015; Jednoróg et al., 2012). For completeness, the main effects of the AE sum scores are reported in the Supporting Information Appendix (see Tables A1–A6).

3  RESULTS

The means, standard deviations, and correlations among the main environmental and demographic variables are presented in Table 2. Additional tables reporting the correlation of the environmental and demographic variables with each brain region of interest can be found in the Supporting Information Appendix (Tables A7–A12).

3.1  Preschool AEs, INR, and subcortical volumes

The interaction of preschool AE sum scores with baseline INR was associated with putamen volume (see Figure 1 and Table 3). Simple slopes decomposition of the interaction effect indicated a negative relationship between AE sum scores and average putamen volume when INR was 1 standard deviation below the sample mean (slope estimate = −0.14, p = 0.02) but not at mean INR or 1 standard deviation above the sample mean (slope estimate = −0.04, p = 0.48 and slope estimate = 0.06, p = 0.40, respectively; see Figure A1). The growth curve of putamen volumes by family INR is available in the Supporting Information Appendix (Figure A2). To ensure this result was not driven by a single hemisphere, this model was also run with right and left putamen volumes separately. The hemisphere-specific results were nearly identical to those using bilateral putamen volume and can be found in the Supporting Information Appendix (Tables A13–A15). No interaction effects were found in the
other subcortical regions of interest. Main effects of INR were found, however, for both hippocampal (Table A1) and caudate volumes (A5) with higher INR associated with larger volumes.

3.2 | School-age AEs, INR, and subcortical volumes

Conversely, the interaction of AE sum scores during the school-age period with baseline INR was not associated with putamen volume at the alpha level used for the ROI analysis (see Table 4). Simple slopes decomposition of the interaction effect likewise showed no relationship between AE sum scores and average putamen volume at 1 standard deviation below the sample INR mean (slope estimate = −0.07, p < 0.32) nor at or above the INR mean (slope estimate = 0.02, p = 0.77 and slope estimate = 0.11, p = 0.25, respectively). There were no interaction effects found in the other subcortical regions of interest.

3.3 | Early adolescent AEs, INR, and subcortical volumes

No interaction effects were found for AE sum scores during the early adolescent period in the putamen or the other regions of interest. As some of the MRI data was collected prior to the early adolescent period, the analysis was re-run with only the final two waves of MRI data. Once again, no interaction effects were found for AE sum scores during the adolescent period in any of the regions of interest.

3.4 | Differences in AE exposure by income level

To evaluate whether the observed interaction between AE sum scores during the preschool period and baseline INR predicting putamen volume was attributable to differences in stress exposures, we compared the rates of each AE between higher and lower income groups, using a median split of INR in the sample (see Table A16). There were 10 AE items that were
Table 5: Multi-level model predicting average putamen volume with AEs that differ between INR groups during the preschool period (N = 156)

<table>
<thead>
<tr>
<th>DV: Bilateral Putamen Volume</th>
<th>Std. Beta</th>
<th>95% CI</th>
<th>t</th>
<th>df</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intercept</td>
<td>0.0357</td>
<td>[−0.0952, 0.1667]</td>
<td>6.9353</td>
<td>148.1681</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Age</td>
<td>0.2420</td>
<td>[0.2085, 0.2754]</td>
<td>10.9568</td>
<td>206.0925</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Age²</td>
<td>0.0251</td>
<td>[−0.0036, 0.0539]</td>
<td>1.7146</td>
<td>417.3482</td>
<td>0.0872</td>
</tr>
<tr>
<td>Female Sex</td>
<td>−0.1403</td>
<td>[−0.2679, −0.0127]</td>
<td>−2.1554</td>
<td>143.2283</td>
<td>0.0328</td>
</tr>
<tr>
<td>INR</td>
<td>0.1522</td>
<td>[−0.2804, 0.0241]</td>
<td>2.2680</td>
<td>143.1018</td>
<td>0.0248</td>
</tr>
<tr>
<td>Intracranial Volume (cm³)</td>
<td>0.4308</td>
<td>[0.5608, 0.3008]</td>
<td>6.4960</td>
<td>148.5122</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Preschool different AE sum score</td>
<td>0.0458</td>
<td>[−0.2266, 0.0042]</td>
<td>−1.8140</td>
<td>148.8743</td>
<td>0.0717</td>
</tr>
<tr>
<td>School-age different AE sum score</td>
<td>0.0444</td>
<td>[−0.2007, 0.1118]</td>
<td>0.5573</td>
<td>145.9661</td>
<td>0.5782</td>
</tr>
<tr>
<td>Early adolescent different AE sum score</td>
<td>0.0306</td>
<td>[−0.0542, 0.0675]</td>
<td>0.6118</td>
<td>150.8857</td>
<td>0.5416</td>
</tr>
<tr>
<td>Age x Preschool different AE sum score</td>
<td>−0.0022</td>
<td>[−0.031, 0.0354]</td>
<td>−0.1308</td>
<td>146.8829</td>
<td>0.0876</td>
</tr>
<tr>
<td>INR x Preschool different AE sum score</td>
<td>0.1353</td>
<td>[0.2592, 0.0114]</td>
<td>2.1396</td>
<td>148.3669</td>
<td>0.0340</td>
</tr>
</tbody>
</table>

Table 6: Multi-level model predicting average putamen volume with AEs that are equivalent between INR groups during the preschool period (N = 156)

<table>
<thead>
<tr>
<th>DV: Bilateral Putamen Volume</th>
<th>Std. Beta</th>
<th>95% CI</th>
<th>t</th>
<th>df</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intercept</td>
<td>−0.0169</td>
<td>[−0.1388, 0.1049]</td>
<td>6.8314</td>
<td>148.0165</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Age</td>
<td>0.2411</td>
<td>[0.2076, 0.2747]</td>
<td>10.6768</td>
<td>212.1356</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Age²</td>
<td>0.0253</td>
<td>[−0.0037, 0.0542]</td>
<td>1.7123</td>
<td>421.8106</td>
<td>0.0876</td>
</tr>
<tr>
<td>Female Sex</td>
<td>−0.1346</td>
<td>[−0.2617, −0.0076]</td>
<td>−2.0775</td>
<td>143.9016</td>
<td>0.0395</td>
</tr>
<tr>
<td>INR</td>
<td>0.1475</td>
<td>[0.2686, 0.0263]</td>
<td>2.1242</td>
<td>145.4352</td>
<td>0.0353</td>
</tr>
<tr>
<td>Intracranial Volume (cm³)</td>
<td>0.4343</td>
<td>[0.5653, 0.3034]</td>
<td>6.5012</td>
<td>148.2758</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Preschool equivalent AE sum score</td>
<td>−0.0218</td>
<td>[−0.1021, −0.1456]</td>
<td>−2.2317</td>
<td>144.0640</td>
<td>0.0272</td>
</tr>
<tr>
<td>School-age equivalent AE sum score</td>
<td>−0.0538</td>
<td>[−0.0969, −0.1767]</td>
<td>−0.8569</td>
<td>145.2011</td>
<td>0.3929</td>
</tr>
<tr>
<td>Early adolescent equivalent AE sum score</td>
<td>0.0302</td>
<td>[0.1258, −0.0653]</td>
<td>0.6201</td>
<td>151.2177</td>
<td>0.5361</td>
</tr>
<tr>
<td>Age x Preschool equivalent AE sum score</td>
<td>0.0106</td>
<td>[−0.0423, −0.0211]</td>
<td>0.6548</td>
<td>113.3990</td>
<td>0.5139</td>
</tr>
<tr>
<td>INR x Preschool equivalent AE sum score</td>
<td>0.1456</td>
<td>[0.2667, 0.0245]</td>
<td>2.3560</td>
<td>143.0709</td>
<td>0.0198</td>
</tr>
</tbody>
</table>

more common in the lower INR group than the higher INR group, particularly items related to intentional violence or harm in the child’s environment. To address these differences in AE exposure, follow-up models assessing the interaction of AE sum scores during the preschool period with INR were run using only the AEs that were different across groups in one model (AE_INR_Diff) and equivalent across groups in a second model (AE_INR_SAME). The effect size of the interaction between AE sum scores that differ between income groups and INR was similar to those of the interaction that include only AE sum scores that are equivalent between the groups (see Tables 5–6). Both of the follow-up models were significant at the p < 0.05 level, see Figures A3–A5).

4 DISCUSSION

This study extended previous research investigating the impact of AEs on brain structure by examining the moderating role of family income. Our results indicated that low family income (i.e., at or below the poverty line) interacted with greater AEs in the preschool period to predict smaller putamen volume. The experiences of children and youth with lower income were also qualitatively different than those with higher income (i.e., higher frequency of intentional, interpersonal harm). However, when investigating models that included only AEs that were either equivalent or different between income levels, the results were largely consistent with those found when all AEs were considered together. That suggests that the interaction between income and AEs was not solely attributable to differences in the experiences reported in lower- versus higher-income youth. No interactive relationships were found when AEs in the school-age or early adolescent periods were examined, suggesting that the impact of these events is particularly important during the preschool period. Early periods of development, including the preschool period, are characterized by high levels of plasticity and serve
an important role in tuning neural systems to the kinds of environments the individual is likely to experience later in life (Lupien et al., 2009; Tottenham, 2014). In our data, only AEs reported during the preschool period interacted with family income to predict putamen volume, consistent with the importance of early experiences in development. This specificity may be further explained by the putamen’s role in learning predictable environmental contingencies and updating behavior to optimize outcomes (Birn et al., 2017; Vidal-Ribas et al., 2019). Given that low income environments can be characterized by low levels of predictability (Blair & Raver, 2016; Ellis et al., 2017), it is possible that the observed differences in putamen volume are related to the demands of unpredictable low income environments in combination with AEs in early childhood. This possibility may further explain why the putamen was the only subcortical structure to exhibit this relationship: it may be that single exposure types, like low income or AEs, are sufficient to alter the structure of the putamen was the only subcortical structure to exhibit this relationship: it may be that single exposure types, like low income or AEs, are sufficient to alter the structure of the putamen volume individually. INR has been negatively associated with putamen volume in female adolescents and morphology differences in both males and females (Jenkins et al., 2020). Similarly, stressful experiences, like peer victimization and childhood maltreatment, have also been shown to be related to reduced putamen volume (Edmiston et al., 2011; Quinlan et al., 2018). Thus, should future research aim to establish putamen volume as a potential biomarker of mal-adaptive outcomes following AEs, considering family income will be necessary for valid translation.

Importantly, previous research has reported differences in putamen activation and volume associated with behavioral output. The putamen has been consistently implicated in reward responses and reward learning (Pascucci et al., 2017), an effect that has been shown to be impacted by AEs. In one study, young adults with maltreatment histories exhibited marginally less activity in the left putamen in response to reward cues than controls in a monetary incentive delay task (Dillon et al., 2009). Similar results have been reported in two prospective studies linking AEs with putamen responses to reward. For example, stressful life events reported at age 7 years were associated with lower putamen responses to reward anticipation at age 10 years in a monetary delay task (Vidal-Ribas et al., 2019). The same pattern of effects has been reported in a sample of adults who completed a semi-structured life events interview when they were 10 years old and completed the monetary incentive delay task approximately 10 years later, though the altered putamen activity was specific to loss anticipation (Birn et al., 2017). Further, putamen activation during loss anticipation mediated the link between childhood stress and poor decision making, though this result was only marginally significant. In addition to functional associations, smaller putamen volumes have been associated with increased anhedonia symptoms in 12–14-year-old females (Auerbach et al., 2017). These smaller putamen volumes moderated the association between blunted responses to peer acceptance and anhedonia symptoms such that smaller putamen volume amplified the link between response to peer acceptance and anhedonia symptoms.

While our study is characterized by several strengths, including the socioeconomic diversity of the sample and the prospective nature of the associations reported, there are some limitations. First, despite the prospective design of the study,
brain imaging data was not available until after the preschool period. As such, we were unable to investigate the concurrent relationship between AEs early in development and putamen volume. Second, family INR is a proxy for the environmental features associated with poverty, not a direct measure of these exposures. Future research is needed to determine whether specific aspects of poverty, such as material deprivation, heavy metal or other environmental toxin exposure, or limited access to nutritious food, play specific roles in linking family income to brain development. Third, the sample size of this study was moderate and, despite the ROI approach taken, remains an exploratory investigation of the relationship between family INR and AEs as predictors of subcortical brain structure. Replication is needed in larger study samples. Fourth, our analysis is dependent upon the reliability of our MRI segmentations, which, though generated using a carefully designed longitudinal processing procedure, may introduce a small amount of bias in the results. However, recent work has indicated high levels of test-retest reliability in subcortical regions and confirmed the validity of investigating structural brain volumes in pediatric samples aligned to a common template (Ghosh et al., 2010; Haddad et al., 2022; Madan & Kensinger, 2017). Finally, the study sample was enriched for depression risk at the time of recruitment, which may limit generalizability.

Despite these limitations, the current study suggests an important role for family income as a moderator of the effects of AEs on subcortical brain structure. Specifically, we found that adversity during early and middle childhood was related to smaller putamen volumes but only in children from families with relatively low income. Given previous research linking the structure and function of the putamen with difficulty processing rewarding stimuli, increased anhedonia, and depression diagnosis, the current findings emphasize the importance of considering both life events and the socioeconomic context when assessing risk for psychopathology. Future research should replicate and extend this work with a particular emphasis on the early childhood period and further investigate the role of family income as an important moderator of risk for psychopathology.

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CONFLICT OF INTEREST
The authors declare no conflicts of interest.

DATA AVAILABILITY STATEMENT
Data supporting these findings are available from the corresponding author by request.

ORCID
Max P. Herzberg https://orcid.org/0000-0003-3177-7966

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