**Differential influence of deprivation and threat on adolescent psychopathology via objectively measured emotional, cognitive, and developmental mediators**

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**Introduction**

Adversity experienced in childhood is a well-established predictor of psychiatric sequelae proximally and longitudinally, explaining roughly 30% of the liability for lifetime psychiatric disorders.1,2 Adversity is defined as a circumstance (either chronic, or singular but severe) that constitutes a deviation from a nurturing environment conducive to normative development and likely requires adaptation on behalf of an average child.3 ELA is, however, not monolithic. McLaughlin and Sheridan proposed the dimensional model of ELA, dissecting adverse experiences into those of threat (harm or threat of harm) and deprivation (lack of social or cognitive stimulation and nurturing support).4-6 Neurodevelopmental outcomes reflect discrepant consequences of experiencing threat and deprivation, two domains of ELA as specified by McLaughlin & Sheridan’s dimensional model of adversity and psychopathology (DMAP).4-6 Examining mediators of the relationship between early-life adversity (ELA) and psychiatric outcomes is an important step towards alleviating the burden of adolescent-onset psychopathology.

A review of 109 imaging studies found divergent impacts of threat and deprivation on structural and functional neurodevelopmental outcomes in children.7 Experiences of deprivation, but not threat, have been found to impact the volume and function of frontoparietal cortical regions, suggesting deprivation’s likely effects on executive functioning. Exposure to threat, but not deprivation, was found to affect amygdala’s size and connectivity to the medial pre-frontal cortex, as well as the function of the salience network and hippocampal volume, explaining findings of threat’s impact on enhanced threat detection, attention bias to threat, and working memory. Findings about the relationships between ELA and striatal reward circuits were less clear but suggest that deprivation and threat may have divergent consequences. 8

Exploration of emotional, cognitive, and developmental characteristics that reflect differences in structural and functional brain development precipitated by facets of ELA is a rapidly developing area of research. Most of the published analyses test mediation of threat and deprivation by one or a small set of interrelated phenotypes at a time using path analysis methods. The impact of threat, but not deprivation, on psychopathology has been shown to be mediated by enhanced threat detection, increased attention bias to threat, cognitive and affective theory of mind, fear conditioning, disruptions in automatic emotion regulation, and earlier onset of puberty.9-15 Experiences of deprivation, but not threat, were found to be mediated by language ability and aspects of executive functioning (inhibitory control, working memory, and reasoning ability).16-19 Given that many of these cited characteristics influence one another, and are not mutually accounted for in mediation analyses, estimates of indirect effects found in analyses focusing on one emotional, cognitive, or developmental mediator at a time should not be imbued with causal interpretation.

I miss more literature on mediation, do not just push to side with saying it's all path analyses

We propose an analysis that looks at a large set of objectively measured characteristics that have been previously cited to mediate the effects of threat, deprivation, or both, and utilize penalized regression techniques to empirically identify the mediators that convey the strongest indirect pathways linking threat and deprivation to adolescent psychopathology. From an epidemiologic perspective, it is critical to establish which precursor phenotypes, measurable on a population scale and targetable with intervention, most saliently reflect biological changes precipitated by deprivation and threat. Ultimately, the completion of this analysis will add to our understanding of how emotional, cognitive, and developmental phenotypes are affected by adversity, and which constitute early signs of dysregulation that precipitates onset of psychopathology in adolescence.

At this stage I lack understanding whether you will be studying mediation by imaging parameters or cognitive/behavioral/executive phenotypes

**Methods**

Study overview:

Data for this analysis was sourced from a longitudinal cohort study that recruited 306 dyads of 36-month-old children and their mothers from the Seattle metropolitan area to assess the mechanisms through which socioeconomic status, cumulative family risk, and parenting behaviors impact the function of the hypothalamic-pituitary-adrenal (HPA) axis in children 20. The primary cohort was recruited into a second phase of data collection when the children were approximately 11 years of age. The extension cohort, comprised 227 mother-child dyads. The main aim of the second phase of data collection was to examine the associations of childhood threat and deprivation experiences, characterized in detail using a multi-informant approach, with the neural architecture governing emotion regulation and cognitive control of the developing adolescents.

Participants in the extension cohort completed a 3-session baseline assessment (together comprising timepoint T1) at the age of 10.9-13.0 at the time of the first session. All 227 completed the first session; of the 215 who completed the second session, 83.3% did so within 2 months of the first session and of the 183 who completed the third session, 79.23% did so within 3 months of the first session. At the first session, recruited children and their parents provided survey data on demographics, home environment, and the child’s psychological symptomatology. Over the 3 sessions, the children additionally underwent behavioral tasks and structural and functional MRI assessments to capture emotional, cognitive, and developmental characteristics at the brink of adolescence. Child and parent survey measures, behavioral tasks, and components of the MRI assessment conducted at each T1 session are summarized in **Table A.1** in the Appendix.

At T2, approximately 2 years after T1, a follow-up psychological assessment was conducted. Of the original 227, 14 participants did not provide follow-up data. Data from T1 and T2, along with select early childhood covariates measured on the primary cohort, will be utilized in this analysis to elucidate whether objectively measured candidate mediators of the effects of threat and deprivation on adolescent psychopathology are empirically discernable.

Do we have a mediation analyses with exposure or baseline measured at the same time point, or do you use the age 3 data for this?

Key constructs:

*Deprivation and threat exposures*:

The continuous deprivation measure comprises domains of cognitive, emotional, and physical deprivation. Cognitive deprivation is measured using maternal responses on the Home Observation Measurement of the Environment-Short Form (HOME-SF) instrument.21 It is the count of cognitive stimulation items on the HOME-SF (including the presence of learning materials in the home, the child’s engagement with activities outside the home, the degree of parent-child interaction, and parental scaffolding of the child learning), reverse-scored so higher scores reflect greater cognitive deprivation. Emotional deprivation is a standardized composite of scores on emotional neglect subscales of the Childhood Experiences of Care and Abuse Interview (CECA) and Multidimensional Neglectful Behavior Scale (MNBS).22,23 Lastly, physical deprivation is the standardized composite of food insecurity, measured by a 4-item household food insecurity scale, and physical neglect subscales of MNBS and the Childhood Trauma Questionnaire (CTQ).23,24 The continuous overall deprivation metric is the average of cognitive, emotional, and physical deprivation composites.

The continuous threat exposure variable is an average of (a) the count of distinct types of violence experienced (b) the standardized frequency of violence and (c) the standardized composite of physical and sexual abuse severity. A participating child could endorse up to 5 types of violence exposure, captured by CECA and the UCLA PTSD Reactions Index: physical abuse, sexual abuse, domestic violence, witnessing a violent crime or being a victim of a violent crime.22,25 Frequency of violence exposure was measured by the Violence Exposure Scale for Children-Revised instrument (VEX-R).8 Severity of violent exposures was measured by the physical and sexual abuse subscales of the CTQ.24

Higher values on the deprivation and threat measures convey greater levels of exposure. Algorithms used to construct the deprivation and threat measures have been detailed in a pre-registration found here: <https://osf.io/6yf4p/>.

*Psychopathology outcomes*:

Internalizing psychiatric outcomes include depression, anxiety, and post-traumatic stress disorder (PTSD) measured with total scores on child-reported Children’s Depression Inventory-2 (CDI), Screen for Child Anxiety Related Emotional Disorders (SCARED), and UCLA PTSD Reaction Index, respectively.25-27 Externalizing psychopathology outcomes were constructed using the maximum of child and parent reports on attention problem, rule-breaking, and aggression subscales of the Youth Self-Report (YSR) and the Child Behavior Checklist (CBCL).28,29 Latent internalizing and externalizing psychopathology outcomes were constructed using a confirmatory factor analysis performed in MPlus Version 8.130 on deciles of scores for depression, anxiety, PTSD, attention problem, rule-breaking, and aggression. The algorithm for the construction of internalizing and externalizing composites has been previously described by Weissman et al.31 In total, 8 psychopathology outcomes were considered.

*Candidate mediators:*

Candidate mediators of the impact of deprivation and threat on the development of psychopathology were scoped from a review of neurodevelopmental mechanisms that mediate the effects of childhood adversity and psychiatric sequelae in youth 32, the conceptual model of the pathways linking the effects of threat on psychopathology,33 and the review of potential intervention targets to prevent adverse psychiatric consequences of childhood deprivation and threat experiences 34. Potential mediators include threat detection, attention bias to threat, automatic emotion regulation, cognitive and affective theory of mind, fear conditioning, pubertal timing, language ability, facets of executive functioning (inhibitory control, working memory, reasoning ability), and reward sensitivity. In an effort to avoid undue weight that would likely be attributed by statistical models to self-reported psychosocial characteristics due to shared method variance 35, the candidate mediators considered in this analysis are measured mostly using tasks. Exceptions are self-reported Tanner pubertal stage and fear conditioning measured via skin conductance during a task – both physiologic constructs. In a sensitivity analysis, these latter 2 measures are omitted from the list of candidate mediators, resulting in a set of exclusively task-measured phenotypes.

Threat detection and automatic emotion regulation were measured using the emotional Stroop task.36 Threat detection was captured by accuracy and reaction time to identify fearful and happy faces. Those with enhanced threat detection, hypothesized to be linked to early-life threatening experiences, likely have faster reaction times and better accuracy in identifying fearful vs. neutral faces compared to happy vs. neutral faces.37 Automatic emotion regulation was captured by the difference in reaction time on incongruent trials (where the facial expression did not match the accompanying emotion word) preceded by congruent trials and the reaction time on incongruent trials preceded by incongruent trials – a measure of adaptation to emotional conflict.

Attention bias to threat was assessed using the Dot Probe task, as the difference in the reaction time on trials where the probe appeared behind the neutral face and the reaction time on trials where the probe appeared behind the angry face (both assessed only for trials with the correctly identified emotional valence).38

Cognitive and affective theory of mind was measured with the Theory of Mind task <CITE>. Cartoons depicting stories of cooperation or cooperation to deceive were shown to children who were asked to predict the conclusion of each story. Cognitive theory of mind represents their ability to understand thoughts, beliefs, and intentions of the characters in the cartoon while affective theory of mind gages whether the children could accurately interpret the emotional state of another character. Accuracy and reaction time on cognitive and affective theory of mind trials were recorded.

Language ability and reasoning ability were measured using the Wechsler Abbreviated Scale of Intelligence (or WASI) task.39 Language ability was measured with the t-score on the WASI vocabulary subtest. The vocabulary subtest is designed to measure word knowledge and verbal concept formation. Reasoning ability was measured with the t-score on the WASI matrix reasoning subtest, which gages fluid intelligence, broad visual intelligence, classification and spatial ability, knowledge of part–whole relationships, simultaneous processing, and perceptual organization.

Inhibitory control, an executive functioning ability to suppress a prepotent response to achieve a longer-term goal, was measured using several tasks. NEPSY Circles & Squares task tested the children’s reaction time on “inhibit” and “switch” tasks.40 The Stroop task measured the ability of the kids to accurately read words for colors, even if the color of the letters with which color words are presented don’t match. For example, a correct trial would have a child read “blue” even if the word “blue” is written in red color, measuring the ability of the child to suppress her initial perception of what she sees.41 Additionally, reaction times and accuracy on clicking a button when presented with “Go” stimuli (a set of specific shapes) and withholding clicking when other shapes were presented (the Go / No-Go task).42

Fear conditioning was measured by the average skin conductance response (SCR) captured during the acquisition phase of the fear conditioning task. Experiences of early-life trauma were shown to be associated with lower SCR to CS+ during conditioning compared to children who have not been exposed to trauma.13

Working memory was captured by the Working Memory Shapes task, capturing the ability to accurately remember locations of shapes briefly displayed in 9 possible locations on a 3x3 grid. High-load trials flashed 3 shapes in random locations and low-load trials flashed 1 shape. Average accuracy on both high- and low-load tasks was utilized to capture working memory.

Pubertal timing was assessed using the Tanner staging method. Children were shown sex-specific pictographs conveying stages of development of sexual characteristics (pubic hair for both, breasts for girls, and testes/scrotum/penis for boys). Tanner pubertal development stage was constructed as the average of the two sex-specific sexual characteristic ratings.

Lastly, reward sensitivity was assessed using the Piñata task, a child-friendly version of a monetary incentive task.43 A piñata appears on the screen with 0, 1, 2, or 4 stars inside, and the participating children are asked to “whack” the piñata as quickly as possible once the piñata drops to the middle of the screen. The stars are earned if the response was sufficiently quick. Total earned stars and reaction times on trials with 0, 1, 2, vs 4 stars were recorded and used to measure reward sensitivity, with greater total stars and shorter reaction times on higher-value trials conveying greater reward sensitivity.

Overall, 28 variables capture emotional, cognitive, and developmental characteristics. Prior peer-reviewed work endorsing these characteristics as candidate mediators and hypotheses drawn from the evidence are provided in **Table A.2** in the Appendix.

*Covariates:*

Exposure-outcome and exposure-mediator relationships will be adjusted for age at the first T1 session, sex, chronicity of poverty in early childhood (the count of years the child lived in a low-income household between the ages 3 and 6), severity of the mother’s depression symptoms in the child’s early life (maximum score on the CES-D reported over 4 early-life data collection waves), threat (in deprivation models) and deprivation (in threat models). Relationships between mediators and outcomes will additionally be adjusted for income-to-needs ratio and child psychiatric symptoms (maximum of the self-reported overall problem score from the YSR and parent-reported overall problem score from the CBCL), both measured at T1.

Missing data:

We used 20x multiple imputation with predictive mean matching using chain-linked equations to fill in missing values for covariate, exposure, candidate mediator, and outcome variables to achieve complete data for the 227 individuals who participated in the study at T1.

High-dimensional mediation analysis:

The overarching aim of the project is to explore whether mechanisms by which deprivation and threat impact adolescent psychopathology are empirically discernable, and to flag the objectively measured emotional, cognitive, and developmental markers that serve as the strongest mediators.

To achieve this, we utilized the high-dimensional mediation analysis (HIMA) framework, which combines sure independent screening, minimax concave penalty (MCP)-regularized regression modeling, and joint significance testing to identify objectively measured mediators of deprivation and threat as individual exposures, assessing one as the primary exposure while controlling for the other.44 Exposure variables (deprivation and threat), candidate mediators, and outcomes were standardized to have mean 0 and standard deviation 1 to facilitate comparison of estimates.

The HIMA algorithm comprises 3 steps. In Step 1, sure independent screening selects mediators with the strongest crude associations with the outcome, retaining the top [2*n*/log(*n*)] mediators (where *n* is the sample size) from a set of size *p* with the largest absolute values of regression coefficients.45 This is a useful initial step for scenarios where *p*>*n*. In our case, Step 1 allows for many more mediators to be considered than we have available.

Step 2 produces MCP-regularized estimates of coefficients *β1,…,βp* for mediators M1,…,Mp in a model for the outcome that is adjusted for the exposure and covariates.46 Described in detail elsewhere,44 the MCP regularization procedure is preferable to other penalties because it can select the correct model with a probability tending towards one, whereas other regularization strategies (such as elastic net) are susceptible to bias. Mediators retained in this step have non-zero *β* coefficients.

Step 3 assesses the joint statistical significance of indirect pathways through each retained mediator Mk, adjusted for all other retained mediators. For each Mk, a model is built with the deprivation and threat exposures, adjusted for early childhood characteristics. Significance of a given mediating pathway is assessed by the maximum of the p-values associated with the coefficient for the exposure in the mediator model () and the MCP-regularized coefficient for the mediator in the outcome model (). Thus, only mediators that are significantly associated with both the exposure and outcome are retained. Indirect effects of the exposure on the outcome through each mediator Mk are constructed as the product of .

This statistical approach is made available by the ‘HIMA’ R package. For the purposes of this study, the ‘HIMA’ package code needed to be modified to accommodate multiple imputed data. All regression estimates were combined using Rubin’s rules – averaging the coefficient estimates across 20 replicates, and pooling variances by combining between-imputation and within-imputation uncertainty, as described [here](https://bookdown.org/mwheymans/bookmi/rubins-rules.html). Unadjusted and multiple testing-adjusted p-values were calculated based on pooled estimates. Due to the exploratory nature of this analysis, we retained mediators with joint 2-sided p-values <0.10, and we present significance based on unadjusted p-values and p-values adjusted for multiple testing using the Benjamini-Hochberg approach based on.......

We tested the robustness of our finding by dropping the Tanner stage and fear conditioning measures from the list of candidate mediators to assess any differences in findings when only task-based phenotypes are considered.

Lastly, we repeated the HIMA analysis within strata of sex assigned at birth. Given the differences in developmental experiences associated with gender roles imbued by sex assigned at birth, we see this as an important exploratory analysis.

This series of analyses was conducted in a very well characterized, but small sample, so replication of our findings in a larger sample is a critical next step.

**Results**

The distributions of early childhood and T1 characteristics in the overall sample and by biological sex were calculated using the data prior to imputation and summarized in **Table 1**. Continuous variables were compared using t-tests and categorical variables were compared using Chi-sq tests. Almost 43% of the children in the sample experienced poverty at least at some point during early life, and at T1, the average income-to-needs ratio was 3.59, SD=1.81. 72.3% of the households having an adult with at least a college degree. The maximum of maternal depression scores recorded across the 4 early-childhood data collection waves was 23.94 on average, SD=9.4. There were few substantial differences between boys and girls, with the notable exception of greater average psychiatric symptom score at T1 of males (average score of 58.42, SD=8.33) compared to females (53.99, SD=9.10).

**Table 2** details the distributions of deprivation and threat exposures, as well as the specific measures that comprise the overall deprivation and threat constructs. Male children had greater overall deprivation and threat exposures. Boys compared to girls had notably higher ratings of emotional deprivation (standardized composite of CECA and MNBS emotional neglect measures averaging to 0.18 (SD=0.88) vs -0.18 (SD=0.80), respectively by sex) and frequency of witnessing and experiencing violence (VEX-R frequency ratings averaging to 5.56 (SD=5.92) vs 3.97 (SD=4.32), respectively by sex).

**Figure 1** displays the associations between deprivation and threat when they are considered in mutually unadjusted and mutually adjusted models. On average, internalizing disorders are more strongly associated with deprivation than threat (standardized coefficients 0.29, 95%CI (0.15,0.44) vs 0.16 95% CI (0.03,0.30)). The opposite is observed for externalizing disorders – standardized coefficients for deprivation and threat are 0.21, 95%CI (0.07,0.35) vs 0.28 95% CI (0.15,0.41), respectively. The relationships of threat and deprivation with PTSD align more closely with those for externalizing disorders rather than that for depression and anxiety, and this is the case for both boys and girls when sex-stratified samples are examined.

Among boys, there is a more pronounced discrepancy in how much more strongly deprivation predicts internalizing disorders, with threat showing no significant association with depression or anxiety. Threat and deprivation have associations of similar magnitude with externalizing disorders. Among girls, the opposite is observed. The impact of threat and deprivation on internalizing disorders is similar in magnitude, but threat is more strongly associated with externalizing disorders. This is particularly marked for rule-breaking – the lower bound of the 95% confidence interval for the standardized coefficient for deprivation is above the upper bound of the 95% confidence interval for the standardized coefficient for deprivation.

HIMA estimated several non-zero mediating pathways connecting adversity exposures and major depression, attention, rule-breaking and overall externalizing symptomatology outcomes. Results are summarized in **Table 3**. Measures of inhibitory control are selected prominently and identify a potentially discrepant mechanism by which threat and deprivation may influence psychopathology outcomes.

The relationship between threat and depression is shown to be mediated by working memory, inhibitory control, and fear conditioning. In this population, greater working memory on high-demand tasks is shown to exacerbate depression symptoms. Threat is associated with a decrease in working memory, as measured by the hit rate on high-load tasks. This offers a protective pathway from threat to depressive symptoms. Greater reaction times to complete inhibition/switch tasks, associated with greater threat exposure, are estimated to carry 0.01/0.14=7.1% of the severity of depressive symptoms associated with threat. Shorter reaction times on 0-star reward sensitivity trials is estimated to explain 3.4% of the harmful impact of deprivation, while dampened fear conditioning is associated with a suppression of deprivation’s impact on depression symptoms.

The mediation patterns are fairly consistent across externalizing outcomes, featuring a prominent and complex role of inhibitory control. In analyses with rule-breaking and overall externalizing outcomes, threat and deprivation have opposite relationships with accuracy and reaction time on “Go” trials of the Go/No-Go task – where the child is asked to press a button each time a “Go” stimulus appears on the screen and withhold pressing the button for all other stimuli. While threat substantially decreases accuracy on these trials, deprivation in almost equal measure improves it. A 1-standard error reductions in accuracy on this task is associated with a 0.14-standard deviation exacerbation of rule-breaking and overall externalizing symptomatology, indicating a mediating pathway from threat but a suppressing one from deprivation. Interestingly, threat is also associated with a substantial and statistically significant (even after correction for multiple testing) increase in reaction time in response to “Go” stimuli, which is estimated to be protective with respect to externalizing symptoms. Overall, after adjustment for co-occurring deprivation, those who experience more threat are expected to be cautious when presented with “Go” stimuli, weighing whether to act or not and either missing the opportunity altogether, or responding accurately substantially later than those who experience lower levels of threat. Threat’s conflicting impacts on accuracy and reaction time appear to negate one another, but may warrant greater investigation in a larger data set.

Why is deprivation consistently associated with traits reducing risks, I am very surprised and if I get this right in disbelief, are we measuring and artifact of threat residual

In addition to inhibitory control, affective theory of mind is shown to suppress the impact of deprivation on rule-breaking behavior and longer reaction times to identification of fearful faces among those with greater deprivation is a fairly strong mediator of the impact of deprivation on overall externalizing symptomatology, explaining 0.02/0.21=9.5% of the overall association.

Removing Tanner stage and fear conditioning from the list of candidate mediators does not substantially alter the findings, identifying consistent pathways through inhibitory control and working memory for major depression, and through inhibitory control for attention problems, rule-breaking, and overall externalizing symptoms.

**Table A.3** in the Appendix shows the results of the HIMA analysis run within strata of biological sex. Consistently with the full-sample analysis, most mediation by the variables considered is found for externalizing disorders, although several non-zero pathways are also found for major depression. Many more mediating pathways are identified in the male sample compared to the female sample. Inhibitory control features prominently in explaining associations of threat on rule-breaking, aggression, and overall externalizing outcomes in boys?.

**Discussion points & Conclusions**

* In the population represented by this sample, deprivation has a larger impact on depression and anxiety, while threat has a greater impact on externalizing disorders such as attention problems, rule-breaking behaviors, and aggression.
* There may be additional differentiation in how threat and deprivation operate depending on biological sex or the social conditioning and gender roles that biological sex tends to prescribe.
  + Boys experience more deprivation (particularly emotional neglect) and threat (particularly more likely to witness violence)
  + For boys, the role of deprivation appears stronger in predicting internalizing disorders than threat, while for girls, threat appears to more strongly predict externalizing disorders compared to deprivation.
* HIMA run in the overall sample identified both mediation and suppression paths connecting threat and deprivation to internalizing and externalizing adolescent psychopathology.
  + Among boys, HIMA identifies many more mediating characteristics of externalizing symptoms than among girls, but none of the findings remain statistically significant after correction for multiple testing. Larger samples are needed to replicate sex-specifics mediation analyses.
* Inhibitory control appears to play a prominent but complex role in predicting externalizing symptomatology, differentially mediating experiences of threat and deprivation.
* Threatening experiences appear to result in more cautious behavior, preventing or delaying reaction to “Go” stimuli, whereas accuracy on “Go” tasks among those who experience greater deprivation appears improved.
  + More in-depth investigation into the inhibitory control construct is necessary to fully characterize the differential ways in which it carries the impacts of threat and deprivation
  + Inhibitory control, if confirmed to play an important role in determining severity of adolescent psychopathology, is an early intervention target worth exploring. Some interventions show efficacy in improving this executive function.47

**Table 1: Sample characteristics**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | Overall | Male | Female | p-value | % Missing |
| n(%) | 227 | 117 (51.5) | 110 (48.5) |  |  |
| Early childhood characteristics |  |  |  |  |  |
| Chronicity of poverty: n(%) |  |  |  | 0.673 | 7.5 |
| 0 | 130 (57.3) | 66 (56.4) | 64 (58.2) |  |  |
| 1 | 26 (11.5) | 15 (12.8) | 11 (10.0) |  |  |
| 2 | 20 ( 8.8) | 12 (10.3) | 8 ( 7.3) |  |  |
| 3 | 9 ( 4.0) | 4 ( 3.4) | 5 ( 4.5) |  |  |
| 4 | 25 (11.0) | 14 (12.0) | 11 (10.0) |  |  |
| NA | 17 ( 7.5) | 6 ( 5.1) | 11 (10.0) |  |  |
| Parents divorced: n(%) | 12 ( 5.3) | 7 ( 6.0) | 5 ( 4.5) | 0.319 | 6.6 |
| NA | 15 ( 6.6) | 5 ( 4.3) | 10 ( 9.1) |  |  |
| Number of times moved: mean(sd) | 1.32 (1.74) | 1.31 (1.75) | 1.34 (1.74) | 0.902 | 0 |
| Average number of hours per week child in preschool: mean(sd) | 13.57 (11.14) | 13.13 (10.35) | 14.03 (11.94) | 0.542 | 0 |
| Poor maternal health during pregnancy: n(%) | 34 (15.0) | 21 (17.9) | 13 (11.8) | 0.261 | 0.4 |
| NA | 1 ( 0.4) | 1 ( 0.9) | 0 ( 0.0) |  |  |
| Mother experienced some or a lot of stress during pregnancy: n(%) | 57 (25.1) | 30 (25.6) | 27 (24.5) | 0.608 | 0.4 |
| NA | 1 ( 0.4) | 1 ( 0.9) | 0 ( 0.0) |  |  |
| Mother drank beer, wine or liquor during pregnancy: n(%) | 83 (36.6) | 39 (33.3) | 44 (40.0) | 0.366 | 0 |
| Child born early or at low birth weight: n(%) | 37 (16.3) | 19 (16.2) | 18 (16.4) | 0.624 | 0.4 |
| NA | 1 ( 0.4) | 1 ( 0.9) | 0 ( 0.0) |  |  |
| Maternal depression CES-D, highest across early childhood: mean(sd) | 23.94 (7.55) | 24.65 (7.72) | 23.19 (7.31) | 0.146 | 0 |
| T1 characteristics |  |  |  |  |  |
| Child's age: mean(sd) | 11.47 (0.48) | 11.48 (0.48) | 11.47 (0.47) | 0.878 | 0 |
| Income-to-needs ratio: mean(sd) | 3.59 (1.81) | 3.44 (1.85) | 3.73 (1.76) | 0.231 | 0.9 |
| Highest levels of parental education: n(%) |  |  |  | 0.714 | 1.3 |
| High school or less | 27 (11.9) | 14 (12.0) | 13 (11.8) |  |  |
| Some college but no degree | 33 (14.5) | 18 (15.4) | 15 (13.6) |  |  |
| College degree | 69 (30.4) | 39 (33.3) | 30 (27.3) |  |  |
| Post-graduate degree | 95 (41.9) | 44 (37.6) | 51 (46.4) |  |  |
| NA | 3 ( 1.3) | 2 ( 1.7) | 1 ( 0.9) |  |  |
| Number of siblings: mean(sd) | 1.36 (1.11) | 1.43 (1.08) | 1.29 (1.14) | 0.354 | 0 |
| First-born among the siblings: n(%) | 103 (45.4) | 52 (44.4) | 51 (46.4) | 0.077 | 11.9 |
| NA | 27 (11.9) | 9 ( 7.7) | 18 (16.4) |  |  |
| Living with biological father at T1: n(%) | 175 (77.1) | 92 (78.6) | 83 (75.5) | 0.531 | 0.4 |
| NA | 1 ( 0.4) | 0 ( 0.0) | 1 ( 0.9) |  |  |
| Maximum of self- and parent-reported baseline psychiatric symptoms | 56.26 (8.97) | 58.42 (8.33) | 53.99 (9.10) | <0.001 | 1.8 |

**Table 2: Distributions of Deprivation and Threat Experiences**

|  |  |  |  |
| --- | --- | --- | --- |
|  | Male | Female | p-value |
| N(%) | 117 (51.5) | 110 (48.5) |  |
| Overall deprivation: mean(sd) | 0.12 (0.73) | -0.11 (0.67) | 0.014 |
| - Cognitive deprivation - reverse-coded count of cognitive stimulation items on the HOME-SF: mean(sd) | 2.64 (1.86) | 2.43 (1.67) | 0.375 |
| - Emotional deprivation - standardized composite of the CECA and MNBS emotional neglect measures: mean(sd) | 0.18 (0.88) | -0.18 (0.80) | 0.002 |
| - Physical deprivation - standardized composite of food insecurity and physical neglect subscales of MNBS and CTQ: mean(sd) | 2.62 (0.93) | 2.47 (0.86) | 0.200 |
| Overall threat: mean(sd) | 0.09 (0.79) | -0.08 (0.74) | 0.086 |
| - Count of distinct types of violence experienced (physical, sexual, domestic violence, witnessing violent crime, victim of violent crime) : mean(sd) | 0.33 (0.84) | 0.22 (0.61) | 0.242 |
| - Summed frequency ratings of witnessed and experienced violence on VEX-R: mean(sd) | 5.56 (5.92) | 3.97 (4.23) | 0.026 |
| - Sum of physical and sexual abuse severity on CTQ: mean(sd) | 10.59 (1.36) | 10.56 (2.76) | 0.914 |

**Figure 1: Relationships\* between deprivation and threat in the full sample and stratified by sex assigned at birth**

Graphical user interface

Description automatically generated with medium confidence

\*Adjusted for the child’s age, sex, chronicity of early-life poverty, and maternal depression.

**Table 3: High-dimensional mediation analysis (HIMA) results in the full sample**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Major Depression** | | | | | |
| Mediator (Mk) | Exposure | ϒ(SE) † | α(SE) | β(SE) | α\*β |
| WM: Hit rate on high-load shapes working memory trials | Threat | 0.14 (0.07)\*\* | -0.18 (0.07) | 0.19 (0.06) | -0.03\*\* |
| Deprivation | 0.29 (0.07)\*\*\* |  |  |  |
| IC: Reaction time on switch trials | Threat | 0.14 (0.07)\*\* | 0.12 (0.07) | 0.12 (0.06) | 0.01\* |
| Deprivation | 0.29 (0.07)\*\*\* |  |  |  |
| RS: Reaction time on 0-Star trials | Threat | 0.14 (0.07)\*\* |  |  |  |
| Deprivation | 0.29 (0.07)\*\*\* | -0.13 (0.08) | -0.12 (0.06) | 0.01\* |
| FC: SCR during CS+ acquisition | Threat | 0.14 (0.07)\*\* |  |  |  |
| Deprivation | 0.29 (0.07)\*\*\* | -0.14 (0.07) | 0.16 (0.07) | -0.02\*\* |
| **Attention** | | | | | |
| Mediator (Mk) | Exposure | ϒ(SE) † | α(SE) | β(SE) | α\*β |
| IC: Reaction time on accurate Go trials | Threat | 0.21 (0.07)\*\*\* | 0.29 (0.07) | -0.26 (0.1) | -0.08\*\*\*^ |
| Deprivation | 0.18 (0.08)\*\* |  |  |  |
| **Rule-Breaking** | | | | | |
| Mediator (Mk) | Exposure | ϒ(SE) † | α(SE) | β(SE) | α\*β |
| IC: Accuracy on Go trials | Threat | 0.32 (0.07)\*\*\* | -0.16 (0.07) | -0.14 (0.07) | 0.02\*\* |
| Deprivation | 0.08 (0.07) | 0.2 (0.07) | -0.14 (0.07) | -0.03\*\* |
| IC: Reaction time on accurate Go trials | Threat | 0.32 (0.07)\*\*\* | 0.27 (0.07) | -0.27 (0.08) | -0.07\*\*\*^ |
| Deprivation | 0.08 (0.07) |  |  |  |
| IC: Accuracy on No-Go trials | Threat | 0.32 (0.07)\*\*\* | 0.13 (0.07) | -0.1 (0.06) | -0.01\* |
| Deprivation | 0.08 (0.07) |  |  |  |
| ToM: Accuracy on Affective Theory of Mind trials | Threat | 0.32 (0.07)\*\*\* |  |  |  |
| Deprivation | 0.08 (0.07) | -0.14 (0.07) | 0.11 (0.06) | -0.02\* |
| **Overall externalizing** | | | | | |
| Mediator (Mk) | Exposure | ϒ(SE) † | α(SE) | β(SE) | α\*β |
| IC: Accuracy on Go trials | Threat | 0.28 (0.06)\*\*\* | -0.19 (0.08) | -0.14 (0.07) | 0.03\* |
| Deprivation | 0.21 (0.07)\*\*\* | 0.17 (0.08) | -0.14 (0.07) | -0.02\* |
| IC: Reaction time on accurate Go trials | Threat | 0.28 (0.06)\*\*\* | 0.25 (0.07) | -0.29 (0.07) | -0.07\*\*\*^ |
| Deprivation | 0.21 (0.07)\*\*\* |  |  |  |
| TD: Reaction time to fearful faces | Threat | 0.28 (0.06)\*\*\* |  |  |  |
| Deprivation | 0.21 (0.07)\*\*\* | 0.14 (0.08) | 0.16 (0.07) | 0.02\* |
| ϒ = standardized coefficient for the association between the exposure and the outcome, adjusted for age, sex, chronicity of poverty and maternal depression | | | | | |
| α = standardized coefficient for the association between the exposure and the mediator Mk | | | | | |
| β = standardized MCP-regularized coefficient for the association between the mediator Mk and the outcome | | | | | |
| SE = standard error | | | | | |
| The maximum of p-values for α and β is \*<0.1; \*\*<0.05; \*\*\*<0.01 | | | | | |
| WM = Working Memory; IC=Inhibitory Control; RS=Reward Sensitivity; FC=Fear Conditioning; TD =Threat Detection | | | | | |
| † ϒ coefficients are averages across all 20 imputations, whereas α and β coefficients are averages of estimates from imputations where the mediator was retained by MCP-regularized regression | | | | | |

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**Appendix**

**Table A.1: T1 data collection for the Deprivation and Threat Study, by session**

|  |  |
| --- | --- |
| **Session 1:** | |
| Child Measures | Child demographics |
|  | Body Mass Index (BMI) |
|  | Children’s Depression Inventory 2 (CDI 2) |
|  | Screen for Child Anxiety Related Disorders (SCARED) |
|  | UCLA PTSD Reaction Index |
|  | Childhood Trauma Questionnaire (CTQ) |
|  | School Mindset Questionnaire |
|  | Youth Self-Report (YSL) |
|  | Children’s Response Styles Questionnaire |
|  | Tanner Pubertal Stage |
|  | Positive and Negative Affect Scale (PANAS-GEN) |
|  | Childhood Experiences of Care and Abuse Interview (CECA) |
| Parent Measures | Parent demographics |
|  | Juvenile Victimization Questionnaire (JVQ) |
|  | Conflict Tactics Scale – Family Version |
|  | CHAOS Scale |
|  | Family Routines Inventory |
|  | HOME Parent Report Measure |
|  | UCLA PTSD Reaction Index |
|  | Child Abuse Potential Inventory |
|  | Child Behavior Checklist (CBCL) |
|  | Pittsburg Sleep Quality Index (PSQI) |
|  | Family Inventory of Sleep Habits (FISH) |
|  | Epworth Sleepiness Scale (ESS) |
|  | Children’s Chronotype Questionnaire (CCTQ) |
| Behavioral Tasks | Wechsler Abbreviated Scale of Intelligence (WASI) |
|  | Dimensional Change Card Sort (DCCS) |
|  | FIT |
|  | NEPSY Auditory Attention Task |
|  | Theory of Mind Task |
|  | Dot Probe Task |
|  | Emotional Stroop Task |
| **Session 2:** | |
| Child Measures | Violence Exposure Interview (VEX-R) |
|  | Child Sleep Assessment |
|  | Multidimensional Neglectful Behavior Scale (MNBS) |
| Parent Measures | Violence Exposure Interview (VEX-R) |
|  | The Schedule for Affective Disorders and Schizophrenia for School-Aged Children (K-SADS) – clinical diagnostic interview |
| Behavioral Tasks | Stroop Task |
|  | Piñata Task |
|  | Fear Conditioning Task |
| **Session 3:** | |
| MRI Assessment | fMRI Face Reactivity Task |
|  | Working Memory Task – Shapes |
|  | Working Memory Task – Faces |
|  | Go/No-Go Task |
|  | Fear Learning Task |
|  | Resting State Scans (6 minutes of acquisition) |
|  | Diffusion Tensor Imaging (60 direction DTI sequence) |

**Table A.2: Candidate mediators of the effects of deprivation and threat on adolescent psychopathology**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Behavioral mediator candidates** | **Primary sources of evidence** | **Evidence** | **Hypothesis** | **In DT Data:**  Construct:  Task   * Variable(s) |
| Threat detection and attention bias to threat | 37, 10, 11 | 37 Pollak et al experimentally showed that children who experienced neglect (deprivation) have a difficult time differentiating emotional valence of facial expressions, whereas children who experienced abuse (threat) were considerably better at detecting anger in facial expressions, but were comparable to non-abused or neglected children in recognizing other emotions.  10 Weissman et al indicate that maltreatment predicted attention to threat bias in younger adolescents, which in turn was associated with increases in psychopathology (p-factor) over time.  11 Shackman et al demonstrated statistical mediation of the relationship between physical abuse and child-reported anxiety by increased attention allocated to anger cues. | It’s likely that higher accuracy and lower reaction time to the identification of fearful faces (enhanced threat detection) as well as an increased difference in reaction time to neutral vs angry faces (attention bias to threat) will serve as mediators of the effects of threat but not deprivation. | Threat Detection:  Emotional Stroop Task   * ACC\_FEAR, RT\_FEAR, ACC\_HAPPY, RT\_HAPPY   Attention to threat  Dot Probe Task   * RT\_NEUTRAL\_ACCURATE - RT\_ANGRY\_ACCURATE |
| Cognitive and affective Theory of Mind (ToM) | 12 | 12 Poor accuracy on cognitive and affective theory of mind (ToM) tasks was found to mediate the relationship between violence exposure in childhood and development of externalizing behaviors. | It is likely that affective and cognitive theory of mind mediates the effects of threatening experiences, but not the effect of deprivation on psychopathology | Cognitive and Affective Theory of Mind:  Theory of Mind Task   * ACC\_ATOM, RT\_ATOM, * ACC\_CTOM, RT\_CTOM |
| Fear conditioning | 13 | 13 Children exposed to trauma take longer to differentiate between paired and unpaired conditioned stimuli (reduced fear extinction) and have lower skin conductance response to CS+ during conditioning compared to children who have not been exposed to trauma. Fear conditioning and fear extinction were shown to mediate the effects of trauma on externalizing psychopathology. | Differential fear conditioning and extinction serve as likely mechanisms linking threat exposure (but not deprivation) and externalizing psychopathology. | Fear Conditioning:  Fear Conditioning Task   * Skin conductance response (SCR) to CS+ (Variables TBD) * Time to differentiation between CS+ and CS- (Variables TBD) |
| Automatic emotion regulation | 10, 14 | 10 Explicit emotional dysregulation (specifically engagement in rumination as a maladaptive strategy to regulate emotions) has been shown to mediate the relationship between child maltreatment and general psychopathology by Weissman et al.  14 Kim et al found that emotional and physical abuse predicted reduced automatic emotion regulation, as measured using the emotional Stroop task, but that automatic emotion regulation was not associated with specifically internalizing psychopathology. The link to externalizing psychopathology was not examined. | Given mixed evidence, we hypothesize that automatic emotion regulation, as measured by the adaptation construct from the emotional Stroop task, will likely not serve as a pathway distinguishing the effects of deprivation and threat, but may be a significant mediator of overall adversity on general adolescent psychopathology (p-factor) | Adaptation to emotional conflict:  Emotional Stroop Task   * ADAPTATION = RTci – RTii   where RTci = reaction time on incongruent trials preceded by congruent trial and RTii = reaction time on incongruent trials preceded by incongruent trial. Higher scores signal greater adaptation to emotional conflict |
| Early pubertal timing / Accelerated biological aging | 15 | 15 Used a sample of 13-18-year old girls from the National Comorbidity Survey Adolescence Supplement (NCS-A) to show that earlier age at menarche mediated the relationship between exposure to threat and externalizing psychopathology (where threat is associated with earlier age at menarche, which in turn is associated with reduced odds of externalizing pathology) | We expect that earlier pubertal maturation will mediate the relationship between threatening exposures and psychopathology, but will likely not mediate the effects of deprivation | Pubertal stage:   * TANNER\_STAGE |
| Language ability | 17, 16 | 17 In a longitudinal cohort study (Child Development Project, N=585) deprivation in early childhood (age 5-6) was shown to be associated with externalizing problems (by age 17) via effects on verbal abilities at age 14. In 16, Miller et al used a larger longitudinal study (Fragile Families and Child Wellbeing Study, N=2,301) to confirm that deprivation, but not threat, has a significant indirect effect on internalizing and externalizing pathology through language ability | Based on the findings in 17 and 16, we would expect language ability to serve as a heterogeneous mediator on the path from deprivation (but not threat) to psychopathology. | Vocabulary:  Wechsler Abbreviated Scale of Intelligence (WASI) Task:   * wasitscv |
| Executive functioning | 18, 19 | 18 In this study, executive function (EF) was measured using the Cambridge Automated Neuropsychological Test Battery (CANTAB). Four dimensions of EF were examined and combined into one latent EF variable: “(i) Delayed Matching to Sample (DMS), which assesses attention and short-term visual memory; (ii) Paired Associated Learning (PAL), which assesses visual-spatial memory and new learning; (iii) Stockings of Cambridge (SOC), which is a test of spatial planning and problem-solving; and (iv) Spatial Working Memory (SWM), which assesses the ability to continually update spatial information in memory.” (p.1688). There was a significant indirect effect of institutional rearing (deprivation) on p- factor through EF.  19 McNeilly et al examined the connection between a less extreme experience of deprivation (namely, low SES) and internalizing and externalizing psychopathology through executive function, and found that EF (behavioral regulation and inhibition) mediate the relationship between material deprivation and both internalizing and externalizing symptomatology | Executive functioning will likely serve as a mediating mechanism differentiating the effects of threat and deprivation experiences on psychopathology. We expect that the effect of deprivation specifically will be mediated by facets of EF | Inhibitory control:  NEPSY Circles and Squares Task:   * Inhibition\_inhibit\_baseline\_RT * Inhibition\_switch\_baseline\_RT   Stroop Task:   * STROOP\_ACC   Go/No-Go Task:   * BothRuns\_All\_Go\_ * Trials\_Accuracy * BothRuns\_All\_NoGo\_Trials\_Accuracy * BothRuns\_All\_Accurate\_Go\_Trials\_RT * BothRuns\_All\_Inaccurate\_NoGo\_Trials\_RT   Working memory:  Working memory shapes task   * Hit\_low * Hit\_high * Sensitivity Index (d’) = difference between standardized target hit rate and standardized false alarm rate (Maya will send). Shapes task (as opposed to faces) is most straightforward for WM because if doesn’t contain any emotional information   Reasoning / general cognitive ability  Wechsler Abbreviated Scale of Intelligence (WASI) Task:   * WASItscm |
| Reward processing | 48,49 | 48 Utilizing experimental data from the Bucharest Early Intervention Project (BEIP), investigators found that cognitive deprivation from institutional rearing in early childhood impacts depression and social problems in adolescence through reward processing and implicit learning, respectively. Reward processing was measured using a monetary incentive delay (MID) Piñata task.  49 Dennison et al found that maltreatment was associated with greater reward reactivity, which in turn is a resilience marker for depression in adolescents | Reward processing will likely mediate the associations between both threat and deprivation with psychopathology, but the mechanisms of action through reward processing will be different. Higher reward reactivity will likely explain some of the harm that stems from deprivation, whereas it is likely to buffer the deleterious effects of threat. | Reward processing:  MID Piñata task   * TotalStars * RT\_0star * RT\_1star * RT\_2star * RT\_4star |

**Table A.3: HIMA analysis within strata of biological sex**

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Major Depression** | | **Males** | | | | **Females** | | | |
| Mediator (Mk) | Exposure | ϒ(SE) † | α(SE) | β(SE) | α\*β | ϒ(SE) † | α(SE) | β(SE) | α\*β |
| ToM: Accuracy on Affective Theory of Mind trials | Threat | 0.03 | -0.18 (0.1) | -0.16 (0.09) | 0.03\* | 0.26\*\* |  |  |  |
| Deprivation | 0.30\*\*\* |  |  |  | 0.29\*\* |  |  |  |
| IC: Accuracy on Go trials | Threat | 0.03 |  |  |  | 0.26\*\* | -0.22 (0.1) | 0.23 (0.09) | -0.05\*\* |
| Deprivation | 0.30\*\*\* |  |  |  | 0.29\*\* |  |  |  |
| RS: Reaction time on 0-Star trials | Threat | 0.03 |  |  |  | 0.26\*\* |  |  |  |
| Deprivation | 0.30\*\*\* | -0.13 (0.08) | -0.12 (0.06) | 0.01\* | 0.29\*\* | -0.13 (0.08) | -0.12 (0.06) | 0.01\* |
| FC: SCR during CS+ acquisition | Threat | 0.03 |  |  |  | 0.26\*\* |  |  |  |
| Deprivation | 0.30\*\*\* | -0.14 (0.07) | 0.16 (0.07) | -0.02\*\* | 0.29\*\* | -0.14 (0.07) | 0.16 (0.07) | -0.02\*\* |
| **Aggression** | |  | | | |  | | | |
| Mediator (Mk) | Exposure | ϒ(SE) † | α(SE) | β(SE) | α\*β | ϒ(SE) † | α(SE) | β(SE) | α\*β |
| IC: Reaction time on accurate Go trials | Threat | 0.18\*\* | 0.23 (0.1) | -0.17 (0.09) | -0.04\* |  |  |  |  |
| Deprivation | 0.09 |  |  |  |  |  |  |  |
| IC: Accuracy on Go trials | Threat | 0.18\*\* | -0.21 (0.1) | -0.32 (0.1) | 0.07\*\* |  |  |  |  |
| Deprivation | 0.09 |  |  |  |  |  |  |  |
| ToM: Reaction time on Affective ToM trials | Threat | 0.18\*\* | 0.21 (0.1) | 0.17 (0.1) | 0.04\* |  |  |  |  |
| Deprivation | 0.09 |  |  |  |  |  |  |  |
| PT: Tanner Stage | Threat | 0.18\*\* | 0.2 (0.1) | 0.24 (0.11) | 0.05\*\* |  |  |  |  |
| Deprivation | 0.09 |  |  |  |  |  |  |  |
| RA: Reasoning ability | Threat | 0.18\*\* | -0.23 (0.1) | -0.2 (0.08) | 0.05\*\* |  |  |  |  |
| Deprivation | 0.09 |  |  |  |  |  |  |  |
| **Rule-Breaking** | |  | | | |  | | | |
| Mediator (Mk) | Exposure | ϒ(SE) † | α(SE) | β(SE) | α\*β | ϒ(SE) † | α(SE) | β(SE) | α\*β |
| IC: Accuracy on Go trials | Threat | 0.17 | -0.23 (0.11) | -0.35 (0.13) | 0.08\*\* | 0.50\*\*\* |  |  |  |
| Deprivation | 0.13 | 0.2 (0.07) | -0.14 (0.07) | -0.03\*\* | 0.01 | 0.2 (0.07) | -0.14 (0.07) | -0.03\*\* |
| IC: Reaction time on accurate Go trials | Threat | 0.17 | 0.31 (0.1) | -0.27 (0.1) | -0.08\*\*\* | 0.50\*\*\* |  |  |  |
| Deprivation | 0.13 |  |  |  | 0.01 |  |  |  |
| ToM: Accuracy on Affective Theory of Mind trials | Threat | 0.17 |  |  |  | 0.50\*\*\* |  |  |  |
| Deprivation | 0.13 | -0.14 (0.07) | 0.11 (0.06) | -0.02\* | 0.01 | -0.14 (0.07) | 0.11 (0.06) | -0.02\* |
| WM: Hit rate on low-load shapes working memory trials | Threat | 0.17 | -0.2 (0.1) | 0.21 (0.1) | -0.04\*\* | 0.50\*\*\* |  |  |  |
| Deprivation | 0.13 |  |  |  | 0.01 |  |  |  |
| IC: Reaction time on inhibition/switch trials (NEPSY Circles&Squares) | Threat | 0.17 | 0.27 (0.1) | -0.16 (0.09) | -0.04\* | 0.50\*\*\* |  |  |  |
| Deprivation | 0.13 |  |  |  | 0.01 |  |  |  |
| PT: Tanner Stage | Threat | 0.17 | 0.22 (0.11) | 0.26 (0.13) | 0.06\*\* | 0.50\*\*\* |  |  |  |
| Deprivation | 0.13 |  |  |  | 0.01 |  |  |  |
| RA: Reasoning ability | Threat | 0.17 | -0.23 (0.1) | -0.19 (0.09) | 0.04\*\* | 0.50\*\*\* |  |  |  |
| Deprivation | 0.13 |  |  |  | 0.01 |  |  |  |
| **Externalizing** | |  | | | |  | | | |
| Mediator (Mk) | Exposure | ϒ(SE) † | α(SE) | β(SE) | α\*β | ϒ(SE) † | α(SE) | β(SE) | α\*β |
| IC: Accuracy on Go trials | Threat | 0.21\*\* | -0.19 (0.11) | -0.29 (0.12) | 0.06\* | 0.37\*\*\* |  |  |  |
| Deprivation | 0.20\*\* | 0.17 (0.08) | -0.14 (0.07) | -0.02\* | 0.21\* | 0.17 (0.08) | -0.14 (0.07) | -0.02\* |
| IC: Reaction time on accurate Go trials | Threat | 0.21\*\* | 0.23 (0.12) | -0.24 (0.09) | -0.05\*\* | 0.37\*\*\* |  |  |  |
| Deprivation | 0.20\*\* |  |  |  | 0.21\* |  |  |  |
| WM: Hit rate on low-load shapes working memory trials | Threat | 0.21\*\* | -0.2 (0.1) | 0.19 (0.09) | -0.04\*\* | 0.37\*\*\* |  |  |  |
| Deprivation | 0.20\*\* |  |  |  | 0.21\* |  |  |  |
| TD: Reaction time to fearful faces | Threat | 0.21\*\* |  |  |  | 0.37\*\*\* |  |  |  |
| Deprivation | 0.20\*\* | 0.14 (0.08) | 0.16 (0.07) | 0.02\* | 0.21\* | 0.14 (0.08) | 0.16 (0.07) | 0.02\* |
| PT: Tanner Stage | Threat | 0.21\*\* | 0.21 (0.1) | 0.2 (0.12) | 0.04\* | 0.37\*\*\* |  |  |  |
| Deprivation | 0.20\*\* |  |  |  | 0.21\* |  |  |  |
| ϒ = standardized coefficient for the association between the exposure and the outcome, adjusted for age, sex, chronicity of poverty and maternal depression | | | | | | | | |  |
| α = standardized coefficient for the association between the exposure and the mediator Mk | | | | |  |  |  |  |  |
| β = standardized MCP-regularized coefficient for the association between the mediator Mk and the outcome | | | | | |  |  |  |  |
| SE = standard error |  |  |  |  |  |  |  |  |  |
| The maximum of p-values for α and β is \*<0.1; \*\*<0.05; \*\*\*<0.01 | | | |  |  |  |  |  |  |
| WM = Working Memory; IC=Inhibitory Control; RS=Reward Sensitivity; FC=Fear Conditioning; TD =Threat Detection | | | | | | |  |  |  |
| † Coefficients for the X->Y relationships are averages across all 20 imputations, whereas estimates for the X->Mk and Mk->Y relationships are averages of estimates from imputations where the mediator retained by MCP-regularized regression | | | | | | | | | |