**An empirical assessment of cognitive, affective, and developmental mechanisms by which threat and deprivation impact adolescent psychopathology.**

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**Abstract** (184 words)

Early life adversity is a major predictor of psychiatric dysregulation over the lifecourse, but the mechanisms are likely complex and differential depending on the specific adversity experiences. This analysis strives to empirically determine the most salient mediating phenotypes connecting childhood threat and deprivation experiences to internalizing and externalizing symptoms in adolescence. Candidate mediating phenotypes considered cover domains of attention bias to threat, emotion regulation, theory of mind, fear conditioning, pubertal timing, inhibitory control, language and reasoning ability, and reward sensitivity. High-dimensional mediation analysis (HIMA), combining minimax concave penalty and joint significance testing, was used to identify phenotypes linking deprivation and threat to psychopathology. Reward sensitivity and pubertal timing were retained as jointly significant predictors of internalizing symptomatology, and inhibitory control in addition to pubertal timing and reward sensitivity were jointly predictive of externalizing symptomatology. Reward sensitivity was a significant mediator of the relationship between threat and internalizing psychopathology, explaining 15.29% of threat’s total effect after controlling for pubertal timing. While deprivation was a strong independent predictor of both internalizing and externalizing psychopathology, none of the cognitive, affective, and developmental phenotypes considered mediated its effect.

**Introduction**

Adversity experienced early in life is a well-established predictor of psychopathology, explaining roughly 30% of the liability for lifetime psychiatric disorders (Kessler et al., 2010; McLaughlin et al., 2012). Early life 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 (McLaughlin, 2016). Adversity is, however, not monolithic. The dimensional model of adversity and psychopathology proposes that threat (harm or threat of harm) and deprivation (lack of social or cognitive stimulation and nurturing support) influence cognitive, affective, and neurodevelopmental phenotypes in ways that are at least partially distinct (McLaughlin & Sheridan, 2016; McLaughlin et al., 2014; Sheridan & McLaughlin, 2014).

Mechanisms by which early life adversity impacts psychopathology are a focus of investigation, following the seminal work that showed a dose-response relationships between the cumulative number of adverse childhood experiences and psychiatric disorders (Edwards et al., 2003). A growing body of literature explores disruptions in executive functioning, emotion regulation, social information processing, accelerated pubertal development, and fear learning as precursors to psychopathology in response to adverse circumstances in early life. Many recent studies focus on validating the dimensional model for adversity and psychopathology and determining whether experiences of deprivation and threat affect psychiatric wellbeing via distinct mechanisms.

Executive functioning, a complex domain that includes language ability, reasoning ability, memory, and inhibitory control, has been repeatedly implicated as a mechanism connecting deprivation experiences to psychopathology over the lifecourse. Significant indirect effects of institutional rearing, parental neglect, caregiver change, and financial difficulties were found with respect to internalizing and externalizing psychopathology via memory problems and inhibitory control (Carozza et al., 2022; McNeilly et al., 2021; Wade et al., 2020). Detriments in language ability were found in several large longitudinal samples to mediate deprivation’s impact on internalizing and externalizing psychopathology in adolescents (Miller et al., 2021; Miller et al., 2018).

Aspects of emotion regulation and social information processing – encompassing allocation of attention towards emotionally-valenced stimuli, reward processing, and theory of mind among other constructs – have more often been found to be related to experiences of threat than deprivation. Excessive rumination, a maladaptive emotion regulation strategy, has been shown to mediate the relationship between child maltreatment and general psychopathology (Weissman et al., 2019). Poor accuracy on cognitive and affective theory of mind tasks was reported as a link between violence exposure in childhood and the development of externalizing behaviors (Heleniak & McLaughlin, 2020). The relationship between adversity and reward sensitivity appears complex, with some studies citing it as a moderator of the effect of threat on externalizing symptoms, and others as a suppression mechanism for threat but a mediating mechanism for deprivation with respect to depressed mood in adolescents (Dennison et al., 2016; Kasparek et al., 2020; Sheridan et al., 2018).

Enhanced threat detection and greater attention bias to threatening stimuli have been shown to mediate the relationships between abusive and threatening early life experiences and psychopathology transdiagnostically (Pollak et al., 2000; Shackman et al., 2007; Weissman et al., 2019). Children exposed to trauma demonstrate reduced fear extinction and have a lower skin conductance response to stimuli paired with aversive stimuli vs unpaired stimuli during conditioning compared to children who have not been exposed to trauma, mediating trauma’s impact on externalizing psychopathology (McLaughlin et al., 2016). Underlying the impacts of adversity on cognitive and emotional functioning are potentially altered developmental trajectories measured by acceleration or deceleration of pubertal timing in response to adverse experiences. Threatening experiences early in life have been shown to accelerate pubertal timing, exacerbating externalizing symptoms in adolescent girls (Colich et al., 2020).

The cited findings about cognitive, affective, and developmental mechanisms spanning the domains of emotion regulation, social information processing, fear learning, executive functioning, and biological aging are supported by neuroimaging data. A review of 109 imaging studies found divergent associations of threat and deprivation with structural and functional neurodevelopmental outcomes in children (McLaughlin, Weissman, et al., 2019). Exposure to threat, but not deprivation, predicts reduced amygdala and hippocampal volume, as well as elevated activation in the amygdala to negatively-valenced stimuli (Brooks et al., 2014; Hanson et al., 2015; McLaughlin et al., 2016; David G. Weissman et al., 2020). These findings comport with threat having been found to enhance threat detection, attention bias to threat, and sharpen emotional reactivity. Experiences of deprivation, but not threat, are associated with the volume and function of frontoparietal cortical regions, suggesting deprivation’s likely effects on executive functioning (Mueller et al., 2010). Findings about the relationships between early life adversity and striatal reward circuits are less clear but suggest that deprivation and threat may impact reward sensitivity in divergent ways (Dennison et al., 2016; Mehta et al., 2010).

In summary, there is a complex and growing literature investigating mechanisms linking dimensions of adversity to psychopathology. We propose a rigorous analysis to synthesize this literature using penalized regression techniques to empirically identify intermediate phenotypes with the strongest indirect pathways linking threat and deprivation to adolescent psychopathology. The novelty of this analysis is in the availability of detailed threat and deprivation accounts, a comprehensive assessment of cognitive, affective, and developmental phenotypes that have been proposed as precursors to psychiatric disorders, and an assessment of adolescent internalizing and externalizing psychopathology. We hypothesize that threat and deprivation have at least partially distinct mechanisms of impact with respect to adolescent psychopathology. Learning about such mechanisms can help epidemiologic efforts to measure early signs of psychiatric dysregulation on a broader scale and inform strategies to prevent onset of psychiatric disorders.

**Methods**

Study overview:

Data for this analysis was sourced from a longitudinal cohort study - the Deprivation and Threat (DT) study. DT recruited 306 dyads of 3-year-old children and their mothers from the Seattle metropolitan area. The aim of DT was 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 (Zalewski et al., 2012). From the original cohort, 227 mother-child dyads were recruited into a second phase of data collection when the children were between 10.9 and 13 years of age. The main aim of the second phase of the study 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.

Chronicity of poverty and reports of the mother’s depressed mood were captured from 4 early childhood assessments (between ages 3 and 6) to control for confounding of the relationships between adversity and subsequent outcomes. Chronicity of poverty was defined as the number of visits out of 4 when the participating child’s family income was at or below 1.5 times the national poverty line (to account for higher living expenses in the Seattle metro area). Maternal depression was captured by the maximum CES-D score across the four pre-baseline visits. At the baseline assessment of the second phase of data collection, participating children and their mothers provided retrospective information on threat and deprivation experiences and the children underwent behavioral tasks and structural and functional MRI assessments to capture cognitive, affective, and developmental phenotypes. Psychopathology outcomes were collected at a follow-up assessment conducted approximately 2 years post-baseline.

Key constructs:

*Deprivation and threat exposures*:

The continuous deprivation measure comprises domains of cognitive, emotional, and physical deprivation. Cognitive deprivation was measured using maternal responses on the Home Observation Measurement of the Environment-Short Form (HOME-SF) instrument (Mott, 2004). 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, among others) were counted and 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) (Bifulco et al., 1994; Kaufman Kantor et al., 2004). 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) (Bernstein et al., 1997; Kaufman Kantor et al., 2004). 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 (Bifulco et al., 1994; Steinberg et al., 2004). Frequency of violence exposure was measured by the Violence Exposure Scale for Children-Revised instrument (VEX-R) (Raviv et al., 1999). Severity of violent exposures was measured by the physical and sexual abuse subscales of the CTQ (Bernstein et al., 1997).

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/>.

*Candidate mediators:*

Candidate mediators of the impact of deprivation and threat on psychopathology were scoped from a review of neurodevelopmental mechanisms that mediate the effects of childhood adversity and psychiatric sequelae in youth (Sheridan & McLaughlin, 2020), the conceptual model of the pathways linking the effects of threat on psychopathology (McLaughlin et al., 2020), and the review of potential intervention targets to prevent adverse psychiatric consequences of childhood deprivation and threat experiences (McLaughlin, DeCross, et al., 2019). The available phenotypes comprehensively cover the domains of attention bias to threat, emotion regulation, theory of mind, fear conditioning, pubertal timing, inhibitory control, language ability, reasoning ability, and reward sensitivity. Except for pubertal timing, these phenotypes were objectively captured by tasks rather than questionnaires, minimizing the influence of shared method variance on the identification of indirect effects.

Attention bias to threat was captured by the difference in reaction times to neutral vs angry faces displayed by the Dot Probe task (Amin et al., 2004). Each trial consisted of a pair of faces of different emotional valence and a brief flash of a dot behind one of them. The participating child was instructed to press a button to identify behind which face the dot flashed – faster reaction times to correctly identify the dot behind angry faces rather than neutral faces signaled greater attention bias to threat.

Emotion regulation was captured by several metrics from the Emotional Stroop task (Ben-Haim et al., 2016). In congruent trials, the emotional valence of the face matched the emotion label displayed, whereas in incongruent trials, the emotion label was inconsistent with the facial expression, and required the child to correctly read the label despite a distracting conflicting visual stimulus. To capture emotion regulation, we used the difference in reaction times incongruent vs congruent trials with fearful faces and happy faces (correct trials only). We also included a variable for adaptation to emotional conflict, operationalized as the difference in reaction times on incongruent trials that were preceded by congruent trials vs reaction times on incongruent trials preceded by incongruent trials (Kim et al., 2021).

Cognitive and affective theory of mind was measured with a 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 can accurately interpret the emotional state of the characters. Accuracy on cognitive and affective theory of mind trials was recorded.

Fear conditioning was measured by the skin conductance response (SCR) captured during the first block of the acquisition phase of the fear conditioning task (Shechner et al., 2015). Greater SCR is expected on trials where the neutral stimulus is coupled with an aversive stimulus (loud sound) as opposed to when an alternative neutral stimulus is not coupled with any aversive signal.

Pubertal timing was assessed using the Tanner staging method (Marshall & Tanner, 1969, 1970). Children were shown sex-specific line drawings conveying stages of development of sexual characteristics (breasts for girls, testes/scrotum/penis for boys, and pubic hair for both). Pubertal timing was the average of the two sex-specific ratings.

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 (Brooks et al., 2009). The Stroop task measured the ability of the participating children to accurately read words for colors, even if the color with which the word is presented doesn’t match, with greater accuracy conveying greater inhibitory control (Stroop, 1935). Additionally, reaction times and accuracy on the Go/No-Go task were recorded for clicking a button when presented with “Go” stimuli (a set of specific shapes) and withholding clicking when other shapes were presented (Verbruggen & Logan, 2008).

Language ability and reasoning ability were measured using the Wechsler Abbreviated Scale of Intelligence (WASI) task (Wechsler, 1999). Language ability was measured with the t-score on the WASI vocabulary subtest. The vocabulary subtest was 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.

Lastly, reward sensitivity was assessed using the Piñata task, a child-friendly version of a monetary incentive task (Helfinstein et al., 2013). 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 is sufficiently quick. The total earned stars and the contrast in reaction times on no-reward (0-star) vs high-reward (4-star) trials measure reward sensitivity, with greater total stars and a greater reaction time contrast conveying greater reward sensitivity.

Overall, 19 variables capture cognitive, affective, and developmental characteristics hypothesized to mediate the relationships between adverse experiences and adolescent psychopathology. A summary of the constructs, measurement tools, and specific metrics can be found in **Table 1**.

*Psychopathology outcomes*:

Internalizing symptoms of depression, anxiety, and post-traumatic stress disorder (PTSD) were 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 (Birmaher et al., 1997; Kovacs; Steinberg et al., 2004). 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) (Achenbach, 1991; Liu et al., 1997). We focused on latent internalizing and externalizing psychopathology outcomes, constructed using a confirmatory factor analysis performed in MPlus Version 8.1 (Muthén & Muthén, 2017) on deciles of scores for depression, anxiety, PTSD, attention problem, rule-breaking, and aggression. The algorithm for these internalizing and externalizing composites has been previously described by Weissman et al (D. G. Weissman et al., 2020).

--- Table 1 here ---

Statistical analysis:

For the 227 participants with baseline data, we imputed missing values on covariates, exposures, mediators, and outcomes using hot-deck imputation (Ono & Miller, 1969). We reported proportions of missing values and distributions of key variables in **Table A.1** in the Appendix.

We ran an analysis of the mediator space using the 3-stage high-dimensional mediation algorithm executed using the ‘HIMA’ R package (Zhang et al., 2016). Stage 1 uses sure independent screening to select candidate mediators that are most strongly individually associated with the outcome, selecting *d=[2n/log(n)]* variables with the largest coefficients, where n is the sample size (Fan & Lv, 2008). In our analysis, Stage 1 is not applicable given that *d* = 84 is far greater than the number of mediators considered (19). Stage 2 is a minimax-concave penalty (MPC) regularized regression to consider all candidate mediators selected by the screening, identifying significant predictors of the outcome from a correlated set. Stage 3 is joint significance testing, requiring that both the exposure-mediator and mediator-outcome relationships are statistically significant, with a family-wise type I error rate of 5% maintained by the implementation of the Benjamini-Hochberg procedure (Benjamini & Hochberg, 1995). All exposure, candidate mediator, and outcome variables involved in this analysis were continuously measured and standardized to mean 0 and standard deviation 1 to facilitate interpretable comparisons of effect sizes.

We evaluated the main and mediated effects of threat and deprivation on the internalizing and externalizing adolescent psychopathology outcomes. Exposure-mediator and exposure-outcome relationships were adjusted for age at baseline, biological sex, chronicity of poverty, and the severity of the mother’s depression symptoms in the child’s early life. Mediator-outcome models were additionally adjusted for both adversity exposure types. In a sensitivity analysis for the HIMA procedure, exposure-mediator and exposure-outcome models for threat were also adjusted for deprivation and models for deprivation were adjusted for threat to account for unmeasured common causes of adversity.

Lastly, for any significant mediator, we estimated its natural indirect effect on the outcome, quantifying the impact of increasing the mediator phenotype to the level it would naturally take on if the aversity exposure is increased by a standard deviation. For natural indirect effects and the proportions of the total effect explained by the mediating path, we used bootstrapping to calculate standard errors using the CMAverse package in R (Shi et al., 2021).

**Results**

The data was imputed to reconstruct the sample of 227 children for whom a detailed characterization of early life adversity, candidate mediating phenotypes, and psychiatric outcomes was collected. Overall sample statistics and proportions of missing data across the key study variables are summarized in **Table A.1** in the Appendix. The average age of the participating children was 11.47 (SD=0.48) at baseline and 14.XX at follow-up. The sample was 48.5% female, with 38.1% having experienced poverty at some point in childhood. Early childhood maternal CES-D depression symptom scores ranged from 12 to 56 (mean=23.94, SD=7.55). Approximately 84% reported having threatening experiences, while all children had at least some deprivation experiences.

Pearson correlation coefficients for exposures, candidate mediators, and adolescent psychopathology outcomes are reported in **Table 2**. Adversity types were modestly correlated (ρ=0.32). Positive univariate correlations were observed between both types of adversity and internalizing and externalizing adolescent psychopathology, with threat correlated more strongly with externalizing symptoms (ρ=0.22 for internalizing vs ρ=0.35 for externalizing) and deprivation similarly associated with both psychopathology outcomes (ρ=0.30 for internalizing and ρ=0.29 for externalizing). Correlations between adversity exposures and candidate mediators were modest, with strongest negative correlations emerging with respect to theory of mind, language, and reasoning ability. Despite prior findings of deprivation-specific effects, both threat and deprivation were associated with detriments in these characteristics. Reactivity to fearful faces had discrepant associations with threat and deprivation – reaction times on incongruent vs congruent trials with fearful faces decreased with increasing threat (ρ=-0.12) but increased with increasing deprivation (ρ=0.08). Tanner stage, reward sensitivity, and theory of mind metrics were estimated to have the strongest crude relationships with the adolescent psychopathology outcomes, but there were few notable correlations between candidate mediators and outcomes. Correlations among candidate mediators are summarized in Appendix **Table A.2**.

--- Table 2 here ---

**Table 3** summarizes the results of the HIMA analysis. After adjustment for age, biological sex, poverty chronicity, and severity of maternal depression in early life, the standardized associations between adversity dimensions and psychopathology outcomes remained similar to the crude associations, with deprivation’s impact on internalizing symptoms becoming more pronounced (β = 0.34, 95% CI (0.20,0.48)) and threat’s impact on externalizing symptoms diminishing slightly (β = 0.31, 95% CI (0.18,0.44)). The contrast in reaction times on no-reward vs high-reward trials (a measure of reward sensitivity) and pubertal timing were retained as having non-zero associations with internalizing symptoms by the MCP-regularization step of the HIMA algorithm. Greater reward sensitivity emerged as protective against internalizing symptoms (standardized β = -0.15, 95% CI (-0.27,-0.03)), and accelerated pubertal timing exacerbated internalizing symptoms (standardized β = 0.19, 95% CI (0.06,0.32)). However, the only significant association between adversity and the retained candidate mediator phenotypes was between threat and reward sensitivity, with a 1-SD increase in threat experiences decreasing reward sensitivity by 0.20 standard deviations on average (95% CI (-0.33,-0.07)).

A similar set of phenotypes was selected as mutually predictive of adolescent externalizing symptoms. A measure of inhibitory control (the accuracy on No-Go trials), pubertal timing, and an alternative measure of reward sensitivity (total stars earned during the Piñata task) were retained in the regularized regression. Accelerated pubertal timing was predictive of greater externalizing symptoms in adolescence (standardized β = 0.21, 95% CI (0.08,0.34)), and greater inhibitory control and reward sensitivity were associated with diminished adolescent externalizing symptoms (standardized β = -0.14, 95% CI (-0.26,-0.02) and standardized β = -0.19, 95% CI (-0.31,-0.07), respectively). Neither threat nor deprivation was significantly associated with any of the phenotypes selected as predictive of externalizing symptoms.

When the exposure and mediator models in the HIMA procedure for threat were additionally adjusted for deprivation, the reward sensitivity mediating pathway connecting threat and internalizing symptoms remained significant, and no new mediating pathways were found. Interestingly, the overall effect of threat on internalizing symptoms diminished with the addition of deprivation in the model for this outcome, with a 1-SD increase in threat resulting in a 0.16-SD increase in internalizing symptoms (95% CI (0.02,0.29)), down from β=0.22, 95% CI (0.09,0.36). Please refer to **Tables A.3a and A.3b in the Appendix** for a comprehensive comparison of results with and without mutual adjustment for the other type of adversity.

--- Table 3 here ---

--- Figure 1 here ---

Figure 1 highlights the identified mediating pathway for threat and internalizing symptoms via reward sensitivity. Threat significantly diminishes reward sensitivity, and in turn, diminished reward sensitivity increases internalizing symptomatology. If the reaction time contrast to no- vs high-reward tests were set to the natural value it would be expected to have if threat is increased by 1 standard deviation, internalizing symptoms would be expected to increase by 0.04 standard deviations, 95% CI (0.01,0.08), p-value=0.01. A 1-standard deviation increase in threat expected to increase internalizing symptoms by 0.22 standard deviations, and reward sensitivity is estimated to explain 15.29%, 95% CI (3.31%,38.91%) of threat’s impact.

**Discussion**

In this application of a high-dimensional mediation algorithm to a sample with longitudinally measured accounts of childhood threat and deprivation exposures, 19 cognitive, affective, and developmental phenotypes, and adolescent internalizing and externalizing symptom measures, we found that the empirically strongest mediating pathway connecting threat to internalizing psychopathology is through reward sensitivity. Specifically, threat significantly decreased reward sensitivity, as measured by the contrast in reaction time in no-reward vs high-reward Piñata trials, which increased internalizing symptomatology at follow-up. Accelerated pubertal timing and diminished reward sensitivity significantly predicted greater adolescent internalizing and externalizing symptoms, and externalizing symptoms were additionally significantly increased by diminished inhibitory control. No significant mediating mechanisms were identified for deprivation’s impact on psychopathology.

Facets of reward processing, including sensitivity to reward value, have been consistently implicated in psychopathology, such as major depression, bipolar disorder, anxiety, and externalizing behaviors (Alloy et al., 2016; Cardoso Melo et al., 2022; Nusslock & Alloy, 2017). Costello’s seminal work identified that anhedonia and a reduction in reward’s effectiveness are critical in the etiology of major depression, and Gray’s Behavioral Approach System emerged as a leading model for understanding the neurobiology of mood dysregulation (Costello, 1972; Gray et al., 1994). A recent meta-analysis indeed found small but consistent associations between childhood adversity and impaired reward processing – specifically deficits in reward learning and valuation – and confirmed that multidimensional reward processing is a likely mechanism by which adversity increases the risk for psychopathology (Oltean et al., 2022). Fewer studies have investigated specific relationships between dimensions of adversity and reward sensitivity, and the evidence has not been definitive, with some studies findings that reward sensitivity moderates the relationships between threat and psychopathology, while others finding suppression of threat’s impact on adolescent depression through dampened reward sensitivity (Dennison et al., 2016; Kasparek et al., 2020; Sheridan et al., 2018).

Overall, we found that few of the cognitive, affective, and developmental candidate mediator phenotypes were strongly associated with the early-life adversity exposures and adolescent psychopathology outcomes in this sample. While the literature purports that several of these phenotypes are expected to have differential relationships with dimensions of adversity, we observed few disparate associations between the dimensions of adversity and the metrics of attention bias to threat, emotion regulation, theory of mind, fear conditioning, pubertal timing, inhibitory control, language ability, reasoning ability, and reward sensitivity. Accuracy on “No-Go” trials, a metric that was retained as a significant predictor of externalizing psychopathology, was weakly disparately associated with both dimensions of adversity, with threat slightly increasing and deprivation slightly decreasing it when crude associations were considered. In models adjusted for age, sex, poverty, and family history of depressed mood, however, point estimates for both threat and deprivation were in the same direction.

Unlike in other studies, pubertal timing was not associated with greater threat exposure in this sample (Colich et al., 2020; Sumner et al., 2019). When we stratified the HIMA results by biological sex, however, we saw an interesting contrast - threat slightly advanced pubertal timing for boys in this sample but slowed it down for girls, although the associations were underpowered (see Appendix **Table A.4**). In fact, the emergence of pubertal timing as a significant predictor of internalizing symptomatology appears to be driven by girls – despite the indication that threat may be slowing pubertal timing among girls in this population, girls who were advanced in their pubertal development relative to their peers had greater liability for internalizing psychopathology compared to boys who were advanced for their age.

Another surprising finding in this study was that threat was less strongly associated with adolescent internalizing psychopathology than deprivation. It has been a consistent finding that traumatic experiences – exuding harm or a threat of harm to the individual’s physical well-being – approximately double the risk of developing psychopathology in adolescence and the impact does not attenuate over the lifecourse (Kessler et al., 2010; Lewis et al., 2019; McLaughlin et al., 2012). When we stratify the sample by biological sex, we see that threat has a greater influence on both types of adolescent psychopathology among girls (**Appendix** **Table A.4**), but girls experienced less threat in this sample than boys (**Appendix Table A.5**). Given that the prevalence of internalizing psychopathology among biologically male vs female adolescents is generally lower, it’s possible that the observed dampening of threat’s impact on internalizing disorders stems from the confluence of these factors (Hankin et al., 1998; Van de Velde et al., 2010).

This study had notable strengths and limitations. The DT study collected detailed accounts of adverse experiences from multiple informants (mother and child) that were summarized into composites of threat and deprivation. All candidate mediators selected for the analysis (with the exception of pubertal timing) were measured with tasks, greatly reducing the concern for finding a mediating pathway solely because of correlation of errors that would be expected if exposures, mediators, and outcomes were all collected via self-report. The candidate mediators comprehensively spanned the domains of attention bias to threat, emotion regulation, theory of mind, fear learning, pubertal timing, inhibitory control, language and reasoning ability, and reward sensitivity.

However, deep phenotyping like what was done in this study is seldom possible in large samples. Thus, grappling with a small sample size, we hope to validate these findings in the future using a similarly detailed data set, or a harmonized compilation of data sources. We attempted to overcome the paucity of power with an analytic approach designed to deal with high-dimensional data to detect the statistically strongest mediating pathways. Identification of large effect sizes often results in missing relationships that have a small or medium statistical effect sizes, but which may be biologically influential – an issue that permeates many disciplines including various ‘omics research fields and brain-wide association studies (Marek et al., 2022). Indeed, we see that multiple associations presented in **Table 3** are just shy of statistical significance. For instance, we may have seen deprivation indeed associated with deceleration of pubertal timing and reductions in reward sensitivity if we had a larger sample size.

A confirmation of diminished reward sensitivity as an impactful precursor of internalizing psychopathology impacted by early life experiences of threat is required for our findings to be conclusive. If, indeed, reward sensitivity emerges as an early sign of psychiatric dysregulation, intervention strategies can be implemented to bolster valuation of rewards and behavioral sensitivity to reward value among children and adolescents with a history of traumatic and threatening experiences. Task-based measurement of reward sensitivity can be challenging if the aim is to validate this mechanism in a representative epidemiologic sample. However, a number of validated self-rated scales are available to measure responsiveness to rewards, including the Monetary Choice Questionnaire, Behavioral Activation System (BAS) scale, and Reward Responsiveness (RR) scale (Carver & White, 1994; Kirby & Petry, 2004; Van Den Berg et al., 2010). While this sample did not provide empirical confirmation of mechanisms connecting deprivation to adolescent psychopathology, prior work has consistently identified detriments in facets of executive functioning – such as language ability – as likely phenotypes to target to ameliorate the impact of deprivation. In sum, we have identified one significant mediating pathway for threat’s effect on adolescent internalizing symptoms, but larger data is required for its validation.

**Table and Figures**

Table 1: Candidate mediator constructs and how they were measured.

|  |  |  |  |
| --- | --- | --- | --- |
| **Construct (abbreviation)** | **Measurement tool** | **Tool type** | **Variable(s)** |
| 1. Attention bias to threat (AB) | Dot Probe task | Behavioral task | • Difference in reaction times on accurate trials with neutral faces vs angry faces |
| 2. Emotion regulation (ER) | Emotional Stroop task | Behavioral task | • Adaptation to emotional conflict - the difference in reaction times on incongruent trials that were preceded by congruent trials and reaction times on incongruent trials preceded by incongruent trials • Difference in reaction time on incongruent vs congruent correct fear trials • Difference in reaction times on incongruent vs congruent correct happy trials |
| 3. Theory of mind (ToM) | Theory of Mind task | Behavioral task | • Accuracy on affective and cognitive trials |
| 4. Fear conditioning (FC) | Fear conditioning task | Physiologic response | • Difference between skin conductance response to CS+ and CS- in the first acquisition block of the task, adjusted for baseline conductance |
| 5. Pubertal timing (PT) | Tanner staging | Self-report | • Mean of testes/scrotum/penis & pubic hair development stages for biologically male participants and mean of breast and pubic hair development stages for biologically female participants |
| 6. Language ability (LA) | Wechsler Abbreviated Scale of Intelligence | Behavioral task | • T-score on the vocabulary subset |
| 7. Reasoning ability (RA) | Wechsler Abbreviated Scale of Intelligence | Behavioral task | • T-score on the matrix reasoning subset |
| 8. Inhibitory control (IC) | NEPSY Circles and Squares task | Behavioral task | • Reaction times relative to baseline on "inhibit" tasks • Reaction times relative to baseline on "switch" tasks |
| Stroop task | Behavioral task | • Accuracy on all trials |
| Go/No-Go task | Behavioral task | • Accuracy on "Go" trials • Accuracy on "No-Go" trials • Reaction time on accurate "Go" trials • Reaction time on inaccurate "No-Go" trials |
| 9. Reward sensitivity (RS) | Pinata task | Behavioral task | • Difference in reaction time on high-reward (4-start) trials and reaction time on no-reward (0-star) trials • Overall performance (total stars earned) |

AB=Attention bias to threat; ER=Emotion regulation; ToM=Theory of Mind; FC=Fear conditioning; PT=Pubertal timing; IC=Inhibitory control; AL=Language ability; AR=Reasoning ability; RS=Reward sensitivity

Table 2: Correlations between adversity exposures, candidate mediators and adolescent psychopathology outcomes.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | | Adversity | | Psychopathology | |
|  | | Threat | Deprivation | Intern. | Extern. |
| Threat | 1 | |  | 0.22 | 0.35 |
| Deprivation | 0.32 | | 1 | 0.29 | 0.3 |
| AB: Attention bias threat | -0.01 | | -0.02 | 0.02 | -0.03 |
| ER: Adaptation to emotional conflict | 0.03 | | 0.05 | -0.03 | 0.02 |
| ER: Stroop - fear | -0.12 | | 0.08 | -0.02 | -0.02 |
| ER: Stroop - happy | -0.05 | | -0.03 | 0.01 | -0.02 |
| ToM: Accuracy on affective trials | -0.13 | | -0.19 | -0.05 | -0.13 |
| ToM: Accuracy on cognitive trials | -0.17 | | -0.18 | -0.1 | -0.16 |
| FC: Skin conductance response to CS+ vs CS- | 0.08 | | 0.02 | 0.03 | 0.09 |
| PT: Tanner stage | -0.05 | | -0.09 | 0.15 | 0.13 |
| IC: Reaction time on inhibit trials | 0.14 | | -0.01 | 0 | 0.04 |
| IC: Reaction time on switch trials | 0.09 | | 0.04 | 0.09 | 0.09 |
| IC: Accuracy on Stroop task | -0.1 | | -0.02 | -0.03 | -0.08 |
| IC: Accuracy on 'Go' trials | -0.13 | | -0.03 | 0.01 | -0.12 |
| IC: Accuracy on 'No-Go' trials | 0.06 | | -0.04 | -0.08 | -0.14 |
| IC: Reaction time on accurate 'Go' trials | 0.14 | | 0.03 | -0.02 | 0 |
| IC: Reaction time on inaccurate 'No-Go' trials | 0.02 | | 0.1 | -0.03 | 0.03 |
| LA: Language ability | -0.14 | | -0.26 | -0.01 | -0.07 |
| RA: Reasoning ability | -0.18 | | -0.13 | -0.08 | -0.14 |
| RS: Reaction time on high- vs low-reward trials | -0.16 | | -0.07 | -0.21 | -0.12 |
| RS: Total stars | -0.04 | | -0.08 | -0.06 | -0.22 |
| Internalizing psychopathology |  | |  | 1 | 0.72 |
| Externalizing psychopathology |  | |  |  | 1 |

AB=Attention bias to threat; ER=Emotion regulation; ToM=Theory of Mind; FC=Fear conditioning; PT=Pubertal timing; IC=Inhibitory control; LA=Language ability; RA=Reasoning ability; RS=Reward sensitivity

Table 3: HIMA results

|  |  |  |
| --- | --- | --- |
|  | Pathway | Standardized β  (95% CI) |
| Internalizing | Threat -> Internalizing a | 0.22(0.09,0.35)\* |
| Threat -> Tanner Stage a | -0.01(-0.13,0.11) |
| Threat -> Reward Sensitivity a | -0.20(-0.33,-0.07)\* |
| Deprivation -> Internalizing a | 0.34(0.20,0.48)\* |
| Deprivation -> Tanner Stage a | -0.12(-0.25,0.01) |
| Deprivation -> Reward Sensitivity a | -0.12(-0.26,0.02) |
| Tanner Stage -> Internalizing b | 0.19(0.06,0.32)\* |
| Reward Sensitivity -> Internalizing b | -0.15(-0.27,-0.03)\* |
| Externalizing | Threat -> Externalizing a | 0.31(0.18,0.44)\* |
| Threat -> Tanner Stage a | -0.01(-0.13,0.11) |
| Threat -> Inhibitory Control (No-Go) a | 0.11(-0.02,0.24) |
| Threat -> Reward Sensitivity (Total stars) a | -0.02(-0.15,0.11) |
| Deprivation -> Externalizing a | 0.28(0.14,0.42)\* |
| Deprivation -> Tanner Stage a | -0.12(-0.25,0.01) |
| Deprivation -> Inhibitory Control (No-Go) a | 0.04(-0.11,0.19) |
| Deprivation -> Reward Sensitivity (Total stars) a | -0.04(-0.19,0.11) |
| Tanner Stage -> Externalizing b | 0.21(0.08,0.34)\* |
| Inhibitory Control (No-Go) -> Externalizing b | -0.14(-0.26,-0.02)\* |
| Reward Sensitivity (Total stars) -> Externalizing b | -0.19(-0.31,-0.07)\* |

\*p-value<0.05

a Adjusted for age, biological sex, early life poverty chronicity, and maternal depression

b Adjusted for threat, deprivation, age, biological sex, early life poverty chronicity, and maternal depression

Standardized beta coefficients represent the change in the outcome associated with a 1-SD change in the predicting variable

Figure 1: Mediating pathway connecting threat to internalizing psychopathology via reward sensitivity.

Diagram

Description automatically generated

AB=Attention bias to threat; ER=Emotion regulation; ToM=Theory of Mind; FC=Fear conditioning; PT=Pubertal timing; IC=Inhibitory control; LA=Language ability; RA=Reasoning ability; RS=Reward sensitivity

**Appendix**

Table A.1: Distributions of key variables in the overall sample

|  |  |  |
| --- | --- | --- |
| Characteristic | Overall | % Missing |
| n | 227 |  |
| Age, baseline, mean(SD) | 11.47 (0.48) | 0 |
| Female biological sex, n(%) | 110 (48.5) | 0 |
| Chronicity of poverty, early childhood, mean(SD) | 0.92 (1.40) | 7.5 |
| Ever poverty, early childhood, n(%) | 80 (38.1) | 7.5 |
| Maternal depression, early childhood, mean(SD) | 23.94 (7.55) | 0 |
| Threat, mean(SD) | 0.01 (0.77) | 0 |
| Any threat, n(%) | 191 (84.1) | 0 |
| Deprivation, mean(SD) | 0.01 (0.71) | 0 |
| AB: Attention bias threat, mean(SD) | -4.91 (35.02) | 5.3 |
| ER: Adaptation to emotional conflict, mean(SD) | 8.07 (126.39) | 6.6 |
| ER: Stroop - fear, mean(SD) | -7.40 (88.52) | 6.6 |
| ER: Stroop - happy, mean(SD) | -5.31 (85.37) | 6.6 |
| ToM: Accuracy on affective trials, mean(SD) | 0.91 (0.10) | 10.6 |
| ToM: Accuracy on cognitive trials, mean(SD) | 0.79 (0.10) | 10.6 |
| FC: Skin conductance response to CS+ vs CS-, mean(SD) | 0.18 (0.19) | 15.4 |
| PT: Tanner stage, mean(SD) | 2.21 (0.85) | 15 |
| LA: Language ability, mean(SD) | 60.06 (8.98) | 0 |
| RA: Reasoning ability, mean(SD) | 55.56 (9.27) | 0 |
| IC: Reaction time on inhibit trials, mean(SD) | 5.02 (4.17) | 18.9 |
| IC: Reaction time on switch trials, mean(SD) | 26.64 (8.89) | 18.9 |
| IC: Accuracy on Stroop task, mean(SD) | 0.33 (0.09) | 10.6 |
| IC: Accuracy on 'Go' trials, mean(SD) | 0.91 (0.09) | 24.2 |
| IC: Accuracy on 'No-Go' trials, mean(SD) | 0.63 (0.16) | 24.2 |
| IC: Reaction time on accurate 'Go' trials, mean(SD) | 491.41 (41.60) | 24.2 |
| IC: Reaction time on inaccurate 'No-Go' trials, mean(SD) | 418.97 (40.64) | 24.2 |
| RS: Reaction time on high- vs low-reward trials, mean(SD) | -28.98 (56.85) | 7.5 |
| RS: Total stars, mean(SD) | 59.82 (14.47) | 7.5 |
| Internalizing symptoms, mean(SD) | 0.00 (1.19) | 6.6 |
| Externalizing symptoms, mean(SD) | 0.04 (2.14) | 6.6 |

% Missing out of 227 with baseline data

Table A.2: Correlations among candidate mediators

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | AB: Attention bias threat | ER: Adaptation to emotional conflict | ER: Stroop - fear | ER: Stroop - happy | ToM: Accuracy on affective trials | ToM: Accuracy on cognitive trials | FC: Skin conductance response to CS+ vs CS- | PT: Tanner stage | LA: Language ability | RA: Reasoning ability | IC: Reaction time on inhibit trials | IC: Reaction time on switch trials | IC: Accuracy on Stroop task | IC: Accuracy on 'Go' trials | IC: Accuracy on 'No-Go' trials | IC: Reaction time on accurate 'Go' trials | IC: Reaction time on inaccurate 'No-Go' trials | RS: Reaction time on high- vs low-reward trials | RS: Total stars |
| AB: Attention bias threat | 1 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| ER: Adaptation to emotional conflict | -0.04 | 1 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| ER: Stroop - fear | -0.07 | -0.02 | 1 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| ER: Stroop - happy | 0.08 | 0.01 | 0.18 | 1 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| ToM: Accuracy on affective trials | 0.03 | 0.00 | 0.03 | 0.08 | 1 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| ToM: Accuracy on cognitive trials | 0.09 | -0.09 | -0.03 | 0.00 | 0.59 | 1 |  |  |  |  |  |  |  |  |  |  |  |  |  |
| FC: Skin conductance response to CS+ vs CS- | -0.04 | 0.02 | -0.02 | 0.03 | 0.11 | 0.09 | 1 |  |  |  |  |  |  |  |  |  |  |  |  |
| PT: Tanner stage | -0.02 | -0.01 | 0.10 | -0.02 | 0.01 | 0.03 | 0.07 | 1 |  |  |  |  |  |  |  |  |  |  |  |
| AL: Language ability | 0.22 | 0.13 | -0.12 | -0.05 | 0.08 | 0.15 | -0.04 | -0.04 | 1 |  |  |  |  |  |  |  |  |  |  |
| AR: Reasoning ability | 0.20 | 0.05 | -0.01 | 0.10 | 0.04 | 0.12 | -0.04 | -0.01 | 0.42 | 1 |  |  |  |  |  |  |  |  |  |
| IC: Reaction time on inhibit trials | -0.08 | -0.12 | 0.07 | -0.07 | -0.02 | 0.12 | -0.09 | -0.02 | -0.13 | -0.17 | 1 |  |  |  |  |  |  |  |  |
| IC: Reaction time on switch trials | -0.08 | -0.01 | 0.09 | -0.04 | 0.00 | 0.02 | -0.11 | 0.06 | -0.11 | -0.12 | 0.43 | 1 |  |  |  |  |  |  |  |
| IC: Accuracy on Stroop task | 0.15 | 0.09 | 0.11 | 0.01 | 0.08 | 0.06 | 0.13 | 0.06 | 0.32 | 0.17 | -0.18 | -0.31 | 1 |  |  |  |  |  |  |
| IC: Accuracy on 'Go' trials | 0.07 | -0.02 | 0.01 | 0.08 | 0.03 | 0.10 | -0.07 | 0.04 | 0.15 | 0.14 | -0.10 | -0.17 | 0.19 | 1 |  |  |  |  |  |
| IC: Accuracy on 'No-Go' trials | -0.04 | 0.11 | -0.04 | -0.10 | -0.01 | 0.05 | 0.06 | 0.01 | 0.05 | 0.10 | -0.03 | -0.13 | 0.21 | -0.1 | 1 |  |  |  |  |
| IC: Reaction time on accurate 'Go' trials | -0.07 | 0.06 | -0.18 | -0.09 | 0.05 | 0.02 | 0.08 | -0.01 | -0.01 | -0.01 | 0.04 | 0.14 | -0.07 | -0.52 | 0.46 | 1 |  |  |  |
| IC: Reaction time on inaccurate 'No-Go' trials | -0.06 | 0.05 | -0.05 | -0.05 | 0.00 | 0.04 | 0.09 | -0.08 | 0.00 | -0.04 | 0.12 | 0.03 | -0.05 | -0.44 | 0.16 | 0.66 | 1 |  |  |
| RS: Reaction time on no- vs high-reward trials | 0.07 | 0.05 | 0.04 | 0.04 | 0.02 | 0.07 | 0.07 | -0.08 | 0.02 | 0.08 | 0.13 | 0.13 | -0.07 | -0.01 | -0.08 | 0.02 | -0.04 | 1 |  |
| RS: Total stars | 0.13 | 0.04 | 0.06 | 0.04 | -0.01 | 0.01 | -0.01 | 0.02 | 0.16 | 0.16 | -0.03 | -0.10 | 0.29 | 0.26 | 0.07 | -0.09 | -0.09 | -0.03 | 1 |

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Table A.3a: Not mutually adjusted | | |  |  |  |  |
| outcome | exposure | mediator | exposure- mediator | mediator- outcome | exposure- outcome | p-value (Benjamini-Hochberg) |
| Internalizing | Threat | Tanner stage | -0.01(0.1,-0.13) | 0.13(0.04,0.22) | 0.22(0.09,0.36) | 0.8319 |
| Internalizing | Threat | Reward sensitivity (reaction time contrast) | -0.2(-0.06,-0.33) | -0.07(-0.01,-0.13) | 0.22(0.09,0.36) | 0.0209 |
| Internalizing | Deprivation | Tanner stage | -0.12(0.01,-0.26) | 0.13(0.04,0.22) | 0.34(0.2,0.48) | 0.0970 |
| Internalizing | Deprivation | Reward sensitivity (reaction time contrast) | -0.12(0.02,-0.27) | -0.07(-0.01,-0.13) | 0.34(0.2,0.48) | 0.0970 |
| Externalizing | Threat | Tanner stage | -0.01(0.1,-0.13) | 0.21(0.08,0.34) | 0.31(0.19,0.44) | 0.8319 |
| Externalizing | Threat | Inhibitory control (No-Go accuracy) | 0.11(-0.03,0.24) | -0.11(-0.02,-0.21) | 0.31(0.19,0.44) | 0.3532 |
| Externalizing | Threat | Reward sensitivity (total stars) | -0.02(0.11,-0.15) | -0.19(-0.07,-0.31) | 0.31(0.19,0.44) | 0.8319 |
| Externalizing | Deprivation | Tanner stage | -0.12(0.01,-0.26) | 0.21(0.08,0.34) | 0.28(0.14,0.42) | 0.2053 |
| Externalizing | Deprivation | Inhibitory control (No-Go accuracy) | 0.04(-0.1,0.18) | -0.11(-0.02,-0.21) | 0.28(0.14,0.42) | 0.6199 |
| Externalizing | Deprivation | Reward sensitivity (total stars) | -0.04(0.1,-0.18) | -0.19(-0.07,-0.31) | 0.28(0.14,0.42) | 0.6199 |
|  |  |  |  |  |  |  |
| Table A.3b: Mutually adjusted | | |  |  |  |  |
| outcome | exposure | mediator | exposure- mediator | mediator- outcome | exposure- outcome | p-value (Benjamini-Hochberg) |
| Internalizing | Threat | Tanner stage | 0.02(-0.1,0.13) | 0.13(0.04,0.22) | 0.16(0.02,0.29) | 0.8144 |
| Internalizing | Threat | Reward sensitivity (reaction time contrast) | -0.18(-0.04,-0.32) | -0.07(-0.01,-0.13) | 0.16(0.02,0.29) | 0.0212 |
| Internalizing | Deprivation | Tanner stage | -0.13(0.01,-0.27) | 0.13(0.04,0.22) | 0.3(0.15,0.44) | 0.1373 |
| Internalizing | Deprivation | Reward sensitivity (reaction time contrast) | -0.08(0.07,-0.22) | -0.07(-0.01,-0.13) | 0.3(0.15,0.44) | 0.3115 |
| Externalizing | Threat | Tanner stage | 0.02(-0.1,0.13) | 0.21(0.08,0.34) | 0.27(0.14,0.39) | 0.8721 |
| Externalizing | Threat | Inhibitory control (No-Go accuracy) | 0.1(-0.03,0.24) | -0.11(-0.02,-0.21) | 0.27(0.14,0.39) | 0.4233 |
| Externalizing | Threat | Reward sensitivity (total stars) | -0.01(0.12,-0.14) | -0.19(-0.07,-0.31) | 0.27(0.14,0.39) | 0.8721 |
| Externalizing | Deprivation | Tanner stage | -0.13(0.01,-0.27) | 0.21(0.08,0.34) | 0.21(0.07,0.35) | 0.2059 |
| Externalizing | Deprivation | Inhibitory control (No-Go accuracy) | 0.01(-0.13,0.15) | -0.11(-0.02,-0.21) | 0.21(0.07,0.35) | 0.8574 |
| Externalizing | Deprivation | Reward sensitivity (total stars) | -0.03(0.11,-0.18) | -0.19(-0.07,-0.31) | 0.21(0.07,0.35) | 0.8574 |

Table A.4: HIMA results in the overall sample and by sex.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | Pathway | Overall Sample | Boys (n=117) | Girls (n=110) |
| Standardized Beta (95% CI) | Standardized Beta (95% CI) | Standardized Beta (95% CI) |
| Internalizing | Threat -> Internalizing a | 0.22(0.09,0.35)\* | 0.17(0,0.34)\* | 0.29(0.08,0.5)\* |
| Threat -> Tanner Stage a | -0.01(-0.13,0.11) | 0.11(-0.05,0.27) | -0.17(-0.37,0.03) |
| Threat -> Reward Sensitivity a | -0.20(-0.33,-0.07)\* | -0.19(-0.35,-0.03)\* | -0.2(-0.42,0.02) |
| Deprivation -> Internalizing a | 0.34(0.20,0.48)\* | 0.33(0.16,0.5)\* | 0.32(0.08,0.56)\* |
| Deprivation -> Tanner Stage a | -0.12(-0.25,0.01) | -0.06(-0.22,0.1) | -0.2(-0.42,0.02) |
| Deprivation -> Reward Sensitivity a | -0.12(-0.26,0.02) | -0.07(-0.24,0.1) | -0.21(-0.46,0.04) |
| Reward Sensitivity -> Internalizing b | -0.15(-0.27,-0.03)\* | -0.11(-0.29,0.07) | -0.17(-0.34,0) |
| Externalizing | Threat -> Externalizing a | 0.31(0.18,0.44)\* | 0.24(0.07,0.41)\* | 0.41(0.23,0.59)\* |
| Threat -> Tanner Stage a | -0.01(-0.13,0.11) | 0.11(-0.05,0.27) | -0.17(-0.37,0.03) |
| Threat -> Inhibitory Control (No-Go) a | 0.11(-0.02,0.24) | 0.17(-0.01,0.35) | 0.02(-0.18,0.22) |
| Threat -> Reward Sensitivity (Total stars) a | -0.02(-0.15,0.11) | -0.04(-0.23,0.15) | 0.00(-0.19,0.19) |
| Deprivation -> Externalizing a | 0.28(0.14,0.42)\* | 0.27(0.09,0.45)\* | 0.28(0.06,0.5)\* |
| Deprivation -> Tanner Stage a | -0.12(-0.25,0.01) | -0.06(-0.22,0.1) | -0.2(-0.42,0.02) |
| Deprivation -> Inhibitory Control (No-Go) a | 0.04(-0.11,0.19) | 0.00(-0.19,0.19) | 0.11(-0.12,0.34) |
| Deprivation -> Reward Sensitivity (Total stars) a | -0.04(-0.19,0.11) | -0.12(-0.31,0.07) | 0.07(-0.15,0.29) |
| Inhibitory Control (No-Go) -> Externalizing b | -0.14(-0.26,-0.02)\* | -0.19(-0.36,-0.02)\* | -0.06(-0.23,0.11) |
| Reward Sensitivity (Total stars) -> Externalizing b | -0.19(-0.31,-0.07)\* | -0.19(-0.35,-0.03)\* | -0.22(-0.39,-0.05)\* |
| \*p-value<0.05 | |  |  |  |
| a Adjusted for age, biological sex, early life poverty chronicity, and maternal depression | | | |  |
| b Adjusted for threat, deprivation, age, biological sex, early life poverty chronicity, and maternal depression | | | |  |
| Standardized beta coefficients represent the change in the outcome associated with a 1-SD change in the predicting variable | | | | |

Table A.5: Distributions of deprivation and threat experiences by biological sex.

|  |  |  |  |
| --- | --- | --- | --- |
|  | 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 |

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