The Journal of Child Psychology and Psychiatry

Journal of Child Psychology and Psychiatry **:* (2024), pp **–** doi:10.1111/jcpp.14067

Identifying cognitive, affective, and developmental mechanisms linking threat and deprivation with adolescent psychopathology

Ekaterina Sadikova,[1] David G. Weissman,[2] Maya L. Rosen,[3] Elise Robinson,[4,5] Liliana J. Lengua,[6] Margaret A. Sheridan,[7] Henning Tiemeier,[1] and Katie A. McLaughlin[2,8]

[1]Department of Social and Behavioral Sciences, Harvard T.H. Chan School of Public Health, Boston, MA, USA; [2]Department of Psychology, Harvard University, Cambridge, MA, USA; [3]Program in Neuroscience, Smith College, Northampton, MA, USA; [4]Stanley Center for Psychiatric Research, Broad Institute of MIT and Harvard, Cambridge, MA, USA; [5]Center of Genomic Medicine and Department of Psychiatry, Massachusetts General Hospital and Harvard Medical School, Boston, MA, USA; [6]Department of Psychology, University of Washington, Seattle, WA, USA; [7]Department of Psychology and Neuroscience, University of North Carolina at Chapel Hill, Chapel Hill, NC, USA; [8]Ballmer Institute, University of Oregon, Eugene, OR, USA

Background: The mechanisms linking early-life adversity with psychopathology over the life-course are complex. In this prospective study, we collectively examined cognitive, affective, and developmental mediators previously found to individually link childhood threat and deprivation experiences to adolescent psychopathology to identify the most potent mechanisms. **Methods:** Data came from a community sample of 227 children (mean child age 11.5 ± 0.5 years, 48.5% female) from the Seattle metro area with recruitment designed to reflect diversity in family income. Candidate mechanisms included self-rated pubertal development and task-measured attention bias to threat, emotion regulation, theory of mind, fear learning, inhibitory control, language ability, reasoning, and reward sensitivity. Using a high-dimensional mediation approach, we determined which mediating pathways linking threat and deprivation to psychopathology persisted after controlling for all candidate mechanisms associated with psychopathology. Models additionally controlled for the child's age, sex, early-childhood emotional and behavioral symptoms, poverty, and maternal depression. **Results:** Blunted reward sensitivity mediated the prospective relationship between threat and internalizing psychopathology, explaining 17.25% (95% CI 1.08%, 69.96%) of this association. Advanced pubertal development was associated with increases in internalizing and externalizing symptoms (standardized associations of 0.16 (95% CI 0.03, 0.29) and 0.17 (95% CI 0.05, 0.29), respectively), but not with adversity. Although deprivation was strongly related to psychopathology, no mechanisms were empirically identified. **Conclusions:** In a well-characterized community sample, we isolated reward sensitivity as a robust mediator of the prospective association between early-life threat and adolescent internalizing psychopathology. Interventions aimed at bolstering reward sensitivity may mitigate the impact of early-life threat experiences on internalizing problems. **Keywords:** Adversity; threat; deprivation; psychopathology; high dimensional mediation analysis; reward sensitivity; pubertal development.

Introduction

Experiences of early life adversity are powerfully associated with psychopathology over the lifecourse (Francis, Tsaligopoulou, Stock, Pingault, & Baldwin, 2023; Kessler et al., 2010; McLaughlin et al., 2012). Early-life adversity, either chronic or singular but severe, is a deviation from a nurturing environment conducive to normative development and likely requires adaptation on the part of an average child (McLaughlin, 2016). The dimensional model of adversity and psychopathology proposes that adversity can be conceptualized across dimensions of experience that share common features including threat—which involves harm or threat of harm to the child's physical integrity, and deprivation—which involves reduced social or cognitive stimulation. The dimensions of threat and deprivation have been argued to influence a child's cognitive, affective, and developmental characteristics in ways that are at least partially distinct, potentially requiring different interventions (McLaughlin & Sheridan, 2016; McLaughlin, Sheridan, Humphreys, Belsky, & Ellis, 2021; McLaughlin, Sheridan, & Lambert, 2014; Sheridan & McLaughlin, 2014).

For instance, disruptions in social information processing, emotion regulation, and pubertal development have been proposed as mechanisms linking threat with psychopathology (McLaughlin, Colich, Rodman, & Weissman, 2020; McLaughlin & Lambert, 2017). Specifically, enhanced threat detection and greater attention to threatening stimuli—aspects of social information processing—were shown to mediate associations between abusive and threatening early-life experiences and psychopathology transdiagnostically (Pollak, Cicchetti, Hornung, & Reed, 2000; Shackman, Shackman, &

Conflict of interest statement: No conflicts declared.

Pollak, 2007; Weissman et al., 2019). Children exposed to trauma also demonstrate a lower skin conductance response (SCR) during fear conditioning—a pathway linking trauma to externalizing symptoms (McLaughlin et al., 2016). In addition, poor cognitive and affective theory of mind were found to mediate association between violence experiences and externalizing behaviors (Heleniak & McLaughlin, 2020). Threat has been linked to depression symptoms via sensitivity to reward value (Kasparek et al., 2023). Moreover, threatening experiences early in life may accelerate pubertal development, which has been linked to psychopathology in adolescents (Colich et al., 2023; Colich, Rosen, Williams, & McLaughlin, 2020; Hamlat, Snyder, Young, & Hankin, 2019; Platt, Colich, McLaughlin, Gary, & Keyes, 2017).

On the other hand, deprivation has been linked to psychopathology primarily via difficulties with executive functions, such as inhibitory control, language, and other higher order cognitive abilities. Indirect effects of institutional rearing, parental neglect, caregiver disruptions, and material deprivation on psychopathology have been reported via difficulties with working memory and inhibitory control (Carozza, Holmes, & Astle, 2022; McNeilly, Peverill, Jung, & McLaughlin, 2021; Wade, Zeanah, Fox, & Nelson, 2020). Large longitudinal samples demonstrate that difficulties with language ability in early childhood mediate deprivation's association with adolescent internalizing and externalizing symptoms (Miller et al., 2018; Miller, Machlin, McLaughlin, & Sheridan, 2021). In addition, increased caregiver support following experiences of deprivation have been linked to bolstered reward sensitivity—a potential mechanism of resilience to psychopathology risk (Colich et al., 2021).

The complex evidence known to date has been assembled into theoretical models for how threat and deprivation operate to relate to psychopathology. For instance, a transdiagnostic model for risk and resilience in response to childhood trauma identified social information processing, emotion processing, and accelerated biological aging as the prominent pathways linking trauma with internalizing and externalizing psychopathology (McLaughlin et al., 2020). A large review of studies on childhood adversity and neurodevelopment endorsed associations between deprivation and altered function of the frontoparietal network—the network responsible for executive function and cognitive processes that can shape psychopathology (McLaughlin, Weissman, & Bitran, 2019). However, thus far, an empirical approach to validate such models has not been undertaken. Since many of the tested mediators are understood to be interrelated (Menon, 2011; Pessoa, 2008), studying each phenotype in isolation may be obscuring a fuller mechanistic picture, hindering our ability to detect which pathways inform interventions to improve mental health among adolescents who experience early-life adversity.

In this study, we examine a broad set of theorized mechanisms to identify which emerge as robust mediators linking threat and deprivation with psychopathology when putative mechanisms are collectively considered. Specifically, we assess aspects of social information processing (attention bias to threat and theory of mind), reward sensitivity, fear learning and pubertal development—all hypothesized to relate to threat—and inhibitory control, language and reasoning abilities—which have been linked to deprivation. We apply a novel statistical approach to explore this question in data with dimensional measures of threat and deprivation, a broad set of largely task-measured candidate mediators, and an assessment of internalizing and externalizing psychopathology in adolescence. We capitalize on early childhood data to adjust for important confounders—including the severity of maternal depression symptoms, emotional and behavioral symptoms. and experiences of poverty in early life.

Methods

Study overview

Data were sourced from a longitudinal cohort study that recruited 306 dyads of 3-year-old children and their mothers from the Seattle metropolitan area (Lengua et al., 2020). Families were recruited to obtain diversity in income at the start of the study. Children with developmental disabilities and insufficient English proficiency were excluded. Informed consent and assent were appropriately obtained, and all procedures were approved by Institutional Review Boards of the University of Washington and Harvard University.

Our analysis included 227 mother–child dyads who provided data at the early adolescent visit (age ranging from 10.9 to 13.0 years, mean = 11.5, *SD* = 0.5). At this visit, participating children and their mothers provided retrospective accounts of threat and deprivation experiences and the children completed behavioral tasks to assess cognition and affect. Psychopathology was assessed approximately 2 years later (age ranging from 13.1 to 15.1 years, mean = 13.7, *SD* = 0.4).

To control for confounding, we included the child's age at the early adolescent visit, biological sex, and measures of early-life poverty, child emotional and behavioral problems, and maternal depression symptoms collected across four early childhood assessments, conducted between child ages 3 and 6 years at 9-month increments. Experiences of poverty were captured by the number of visits (0–4) when the participating child's family income was at or below 150% of the national poverty line. Early childhood emotional and behavioral problems were measured by the total score on the child behavioral checklist (CBCL), augmented for this study with 11 behavioral problem items from the preschool instrument validated among children aged 2–3 (Moran, Lengua, & Zalewski, 2013). We summed parental responses on a 3-point scale from 0 = *not true* to 2 = *very/often true* for each problem for a total score at each visit. The maximum total problem score across the four assessment waves was used. Maternal depression symptoms were captured by the maximum score on the Center for Epidemiologic Studies Depression Scale (CES-D) across the four early childhood assessments (Radloff, 1977). The early adolescent sample was 48.5% female, with 38.1% having experienced

poverty. Total problem scores ranged from 5 to 112 (mean = 40.7, *SD* = 16.9) and maternal CES-D depression symptom scores ranged from 12 to 56 (mean = 23.9, *SD* = 7.6).

Measures

Threat and deprivation experiences. Dimensional variables for threat and deprivation were constructed as described in a preregistration and done in this cohort (https://osf.io/6yf4p/) (Kasparek et al., 2023; Weissman et al., 2022). The continuous threat experiences variable was a composite of the count of distinct types of interpersonal violence as well as the frequency and severity of violence experienced. Distinct types of interpersonal violence—physical abuse, sexual abuse, domestic violence, witnessing a violent crime, or being a victim of a violent crime—were endorsed either by the child or the parent on the UCLA PTSD Reactions Index (Steinberg et al., 2013; Steinberg, Brymer, Decker, & Pynoos, 2004). Physical abuse, sexual abuse, and domestic violence could be additionally endorsed by the child on the Childhood Experiences of Care and Abuse Interview (CECA) or by the parent on the Juvenile Victimization Questionnaire (JVQ) (Bifulco, Brown, & Harris, 1994; Finkelhor, Hamby, Ormrod, & Turner, 2005). The frequency of violent experiences was measured by the summed frequency ratings of witnessing or experiencing violence on the Violence Exposure Scale for Children-Revised instrument (VEX-R) (Raviv et al., 2001; Raviv, Raviv, Shimoni, Fox, & Leavitt, 1999). The severity of violent experiences was measured by the physical and sexual abuse subscales of the Childhood Trauma Questionnaire (CTQ) (Bernstein, Ahluvalia, Pogge, & Handelsman, 1997; Kaufman Kantor et al., 2004). The count of the types of violent experiences was strongly correlated with frequency (r = .46) and severity (r = .40) of violence experiences, while frequency and severity were more modestly correlated (r = .11). The correlations reflect that the sources of information complement each other to comprehensively characterize the burden of threat experiences using a multi-informant approach. The count, frequency, and severity of violence experiences were each standardized to mean of 0 and standard deviation of 1 and averaged to create the composite threat experience variable.

The continuous deprivation construct comprised cognitive, emotional, and material deprivation measures. Cognitive deprivation was measured using maternal responses on the Home Observation Measurement of the Environment-Short Form (HOME-SF) instrument (Mott, 2004). The 19 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, etc.) were counted and reverse-scored so higher scores reflected greater cognitive deprivation. Emotional deprivation was the average of standardized scores on emotional neglect subscales of the CECA and Multidimensional Neglectful Behavior Scale (MNBS) (Bifulco et al., 1994; Kaufman Kantor et al., 2004). Lastly, material deprivation was the standardized average of a food insecurity score, measured by parental report on the four-item Household Food Insecurity Scale, the child-reported physical needs subscale score of MNBS, and the child-reported physical neglect subscale score of the CTQ (Bernstein et al., 1997; Kaufman Kantor et al., 2004). Cognitive deprivation was moderately correlated with emotional (r = .09) and physical deprivation (r = .22), while emotional and physical deprivation were more strongly correlated (r = .37). Thus, the subdomains of deprivation together generated a comprehensive overall deprivation construct, which was operationalized as the average of the cognitive, emotional, and material deprivation measures. Higher values on the composite threat and deprivation measures conveyed greater levels of experience.

Candidate mediators. Candidate mediators were scoped from a review of emotional, social, cognitive, and neurobiological mechanisms that mediate the effects of childhood adversity and psychiatric sequelae in youth (McLaughlin, 2020), conceptual models of pathways linking threat with psychopathology (McLaughlin et al., 2020), a synthesis of findings on early-life deprivation from the Bucharest Early Intervention Project (Wade et al., 2022), and a review of potential intervention targets to prevent adverse psychiatric consequences of childhood deprivation and threat experiences (McLaughlin, DeCross, Jovanovic, & Tottenham, 2019). The putative mediators cover the domains of attention bias to threat, emotion regulation, theory of mind, fear learning, pubertal development, inhibitory control, language ability, reasoning, and reward sensitivity. See Table 1 for an overview of the 15 variables considered, grouped by domain, and refer to Appendix S1 for detailed descriptions of the administered tasks.

Attention bias to threat was captured by differences in reaction times to neutral versus angry faces displayed by the visual Dot-probe task (Briggs-Gowan et al., 2015; Pérez-Edgar et al., 2010; Waters, Henry, Mogg, Bradley, & Pine, 2010; Weissman et al., 2019). Greater values signify shorter response times to angry rather than neutral expressions and reflect greater attention bias to threat.

Emotion regulation was captured by several metrics from the Emotional Stroop task (Ben-Haim et al., 2016; Egner, Etkin, Gale, & Hirsch, 2008; Etkin, Egner, Peraza, Kandel, & Hirsch, 2006). Each trial on the task consisted of an image with a happy or fearful facial expression displayed with the word "happy" or "fear" overlaid over the image. In congruent trials, the emotional valence of the face matched the label displayed, whereas in incongruent trials, the emotion label was inconsistent with the facial expression, and required the child to correctly identify the valence of the facial expression despite a conflicting label. We used three measures of emotion regulation derived from this task. Using only trials with correctly identified facial expressions, we contrasted reaction times on incongruent versus congruent trials with fearful faces and happy faces separately. We also included a variable for adaptation to emotional conflict—a measure of implicit emotion regulation. Faster reaction times are expected on incongruent trials that are preceded by incongruent trials rather than congruent trials, since cognitive control over emotional conflict is expected to be elicited. Adaptation to emotional conflict was operationalized as the difference in reaction times on incongruent trials that were preceded by congruent trials versus reaction times on incongruent trials preceded by incongruent trials (Kim, Weissman, Sheridan, & McLaughlin, 2021). Higher values on this contrast signal greater adaptation to emotional conflict.

Theory of mind was measured with a Theory of Mind task, adapted from a task to detect differences between cognitive and affective theory of mind dimensions (Heleniak & McLaughlin, 2020; Schlaffke et al., 2015). Vignettes depicting several interaction scenarios were shown to children who were asked to predict the conclusion of each story and respond to questions about the story. In cognitive trials, children were asked to correctly identify the thoughts, beliefs, and intentions of the characters in the cartoon while in affective trials, the participants needed to accurately interpret the emotional state of the characters. Average accuracy metrics were calculated as the proportion of correct responses on cognitive and affective theory of mind trials.

Fear learning was measured by the difference in the amplitude of SCR during the early acquisition phase of a fear learning and extinction task that has been adapted to the early adolescent population (Machlin, Miller, Snyder, McLaughlin, & Sheridan, 2019; Shechner et al., 2015). Fear learning was captured by the difference in SCR on CS+ trials (where an

Table 1 Candidate mediator constructs and how they were measured

Domain (abbreviation)	Measurement tool	Tool type	Candidate mediator constructs
1. Attention bias to threat (AB)	Dot Probe task	Behavioral task	• Difference in reaction times on accurate trials with neutral faces versus 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 correctly identified incongruent versus congruent fear trials • Difference in reaction times on correctly identified incongruent versus congruent happy trials
3. Theory of mind (ToM)	Theory of Mind task	Behavioral task	• Accuracy on trials to identify emotions (affective trials) • Accuracy on trials to identify thoughts, beliefs, or intensions (cognitive trials)
4. Fear learning (FL)	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 development (PD)	Tanner staging	Self-report	• Mean of testes/scrotum/penis and pubic hair development stages for biologically male participants and mean of breast and pubic hair development stages for biologically female participants
6. Inhibitory control (IC)	NEPSY Circles and Squares task	Behavioral task	• Reaction times on "inhibit" trials relative to baseline reaction time • Reaction times on "switch" trials relative to baseline reaction time
	Stroop task	Behavioral task	• Accuracy on all trials
7. Language ability (LA)	Wechsler Abbreviated Scale of Intelligence	Behavioral task	• T-score on the vocabulary subset
8. Reasoning (R)	Wechsler Abbreviated Scale of Intelligence	Behavioral task	• T-score on the matrix reasoning subset
9. Reward sensitivity (RS)	Piñata task	Behavioral task	• Difference in reaction time on no-reward (0-star) trials and reaction time on high-reward (4-star) • Overall performance on the task—total stars earned

orange diamond was initially paired with an aversive stimulus (a loud sound) and later presented without it) versus CS- trials (where a blue square was presented and never paired with the aversive stimulus).

Pubertal development 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 stage 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 two tasks. NEPSY Circles & Squares task tested the children's reaction time on "inhibit" and "switch" tasks (Brooks, Sherman, & Strauss, 2009). The participants were shown a series of circle and square shapes, with some of them shaded and others left blank. Baseline reaction times were established when participants simply read through the series of shapes. In the "inhibit" trials, the participants were asked to say the opposite of the shape presented, regardless of whether it was shaded in or blank. In the "switch" trial sequence, they were asked to say the opposite of the shape if it was blank, and the true shape if it was shaded. Greater differences in reaction times on "inhibit" and "switch" trial sequences relative to baseline reaction times indicate poorer inhibitory control. The Stroop task measured the ability of participants to accurately identify the color of ink with which words for incongruent colors were displayed, with greater accuracy conveying greater inhibitory control (Stroop, 1935).

Language ability and reasoning 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, which was designed to measure word knowledge and verbal concept formation. Reasoning 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). Animal-shaped piñatas were displayed on a screen and were previewed as having 0, 1, 2, or 4 stars inside to cue the participants, who were asked to press the spacebar on a keyboard as quickly as possible once each piñata dropped to the middle of the screen. The total earned stars and the contrast in average reaction times on no-reward (0-star) versus high-reward (4-star) trials measured reward sensitivity. The contrast in reaction time to no- versus high-reward trials on the Piñata task is considered a measure of behavioral sensitivity to reward value, while the total stars earned in the task is interpreted as approach motivation – or the ability to exert effort to maximize reward (Kasparek et al., 2023; Kasparek, Jenness, & McLaughlin, 2020; Olino, 2016; Sheridan et al., 2018). Participants more sensitive to reward were expected to collect more stars and exhibit faster reaction times on trials with greater reward, yielding greater average reaction times on no-reward versus high-reward trials (Wang, Liu, & Shi, 2017).

Psychopathology symptoms. At the 2-year follow-up, 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, 2011; Steinberg et al., 2004). Externalizing psychopathology was captured using the maximum of parent and child reports on attention problem, rule-breaking, and aggression subscales of the CBCL and the Youth Self-Report (YSR), respectively (Achenbach, 1991; Liu et al., 1997). Latent internalizing and externalizing psychopathology outcomes were constructed using a confirmatory factor analysis performed in MPlus Version 8.1 (Muthén & Muthén, 2017) on deciles of scores for depression, anxiety, PTSD, attention problems, rule-breaking, and aggression (Weissman et al., 2020). More details are provided in Appendix S2.

Statistical analysis

We imputed missing values on covariates, exposures, mediators, and outcomes with hot-deck imputation (Ono & Miller, 1969). In a sensitivity analysis, we additionally tested imputation using expectation maximization. Proportions of missing values and distributions of key variables are outlined in Table S1.

We examined the mediator space using the three-stage high-dimensional mediation algorithm implemented by the "HIMA" R package (Zhang et al., 2016). Stage 1—only applicable when the number of considered mediators exceeds $2n/\log(n)$ where n represents the sample size—uses sure independent screening to select $d = 2n/\log(n)$ variables with the largest coefficients (Fan & Lv, 2008). In Stage 2, a minimax-concave penalized regression is run with all candidate mediators selected by Step 1. Coefficients for variables not contributing to outcome prediction are driven down to zero. Stage 3 is joint significance testing, requiring that both the exposure-mediator and mediator–outcome relationships are significant, with a 5% family-wise type I error rate maintained by the Benjamini–Hochberg procedure (Benjamini & Hochberg, 1995). In our analysis, Stage 1 was not applicable given that $d = 2*227/\log(227) = 84$ exceeds the 15 mediators considered. All exposure, candidate mediator, and outcome variables involved in this analysis were standardized to mean 0 and standard deviation 1 to facilitate interpretable comparisons of effect sizes.

Exposure–mediator, exposure–outcome, and mediator–outcome relationships were adjusted for age at baseline, biological sex, poverty, child emotional and behavioral symptoms, and maternal depression symptoms. Exposure–mediator and exposure–outcome models were additionally adjusted for the other adversity dimension (deprivation for threat and threat for deprivation). We checked whether removing the other adversity dimension from exposure–mediator and exposure–outcome models changed the results and assessed any identified mediating pathways within strata of biological sex. Lastly, for significant mediators, we estimated indirect effects and proportions mediated using the CMAverse package in R (Shi, Choirat, Coull, VanderWeele, & Valeri, 2021; Valeri & Vanderweele, 2013). Standard errors were bootstrapped.

Imputation was completed using SAS Software (SAS Institute Inc., Cary, NC, USA) and all other analyses were carried out using R Statistical Software (version 4.1.2). Please refer to the following programming repository: https://github.com/katsadikova/Aim1_DT.git.

Results

Sample overview

In Table 2, we demonstrated that threat and deprivation were significantly correlated with both internalizing and externalizing psychopathology. The two dimensions of adversity had similar patterns of association with candidate mediators. Namely, we see that threat and deprivation were crudely associated with poorer cognitive and affective theory of mind, language ability and reasoning. Threat was additionally correlated with diminished inhibitory control and reward sensitivity. Psychopathology outcomes were related to more advanced pubertal development and blunted reward sensitivity, with externalizing symptoms additionally related to lower scores on the cognitive theory of mind task. Pairwise associations among candidate mediators are presented in Table S2.

High-dimensional mediation

Table 3 summarizes the results of the HIMA analysis. The contrast in reaction times on no-reward versus high-reward trials and Tanner stage were selected as having non-zero associations with an increase in internalizing symptoms when all candidate mediators were collectively considered. After adjustment, greater reward sensitivity was associated with a decrease in internalizing symptoms (standardized β = −.14, 95% CI (−0.26, −0.02)), and more advanced pubertal development was associated with an increase in internalizing symptoms (standardized β = .16, 95% CI (0.03, 0.29)). Pubertal development and the total stars earned in the Piñata task were associated with an increase in externalizing symptoms. Greater reward sensitivity was associated with diminished adolescent externalizing symptoms (standardized β = −.18, 95% CI (−0.29, −0.07)) and more advanced pubertal development was associated with increases in externalizing symptoms in adolescence (standardized β = .17, 95% CI (0.05, 0.29)). However, the only significant association between adversity and the retained candidate mediators was between threat and the contrast in reaction times on no-reward versus high-reward trials. A 1-*SD* increase in threat experiences was associated with a 0.18-*SD* decrease in this reward sensitivity measure (95% CI (−0.32, −0.04)). Removing adjustment for the other adversity dimension did not change the mediation results. We confirmed these findings using the expectation–maximization imputation technique in a sensitivity analysis (a 1-*SD* increase in threat was associated with a 0.19-*SD* decrease in reward sensitivity (95% CI (−0.05, −0.33))) and a 1-*SD* increase in reward sensitivity was associated with a 0.15-*SD* decrease in internalizing symptoms (95% CI (−0.26, −0.04)).

In sum, threat was associated with significantly lower reward sensitivity, which in turn was associated with increases in internalizing symptomatology after controlling for age, sex, poverty, childhood emotional and behavioral problems, maternal depression, and pubertal development. A 1-*SD* increase in threat was estimated to increase internalizing symptoms by 0.15 *SD*, and reward

Table 2 Product–moment correlations between threat, deprivation, candidate mediators, and adolescent psychopathology outcomes

	Dimensions of adversity		Psychopathology symptoms	
	Threat	Deprivation	Internalizing	Externalizing
Threat	1		0.22***	0.35***
Deprivation	0.32***	1	0.29***	0.30***
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**	−0.10	−0.16*
FL: SCR to CS+ vs. CS−	0.08	0.02	0.03	0.09
PD: Tanner stage	−0.05	−0.09	0.15*	0.13*
IC: Reaction time on inhibit trials	0.14*	−0.01	0.00	0.04
IC: Reaction time on switch trials	0.09	0.04	0.09	0.09
IC: Accuracy on Stroop task	−0.10	−0.02	−0.03	−0.08
LA: Language ability	−0.14*	−0.26***	−0.01	−0.07
R: Reasoning	−0.18**	−0.13*	−0.08	−0.14*
RS: Reaction time no- vs. high-reward trials	−0.16*	−0.07	−0.21**	−0.12
RS: Total stars	−0.04	−0.08	−0.06	−0.22**
Internalizing symptoms			1	0.72***
Externalizing symptoms				1

AB, attention bias to threat; ER, emotion regulation; FC, fear conditioning; IC, inhibitory control; LA, language ability; PD, pubertal development; R, reasoning; RS, reward sensitivity; ToM, theory of mind.
Two-sided *p*-value *** <.001, ** <.01, * <.05.

sensitivity was estimated to explain 17.25%, 95% CI (1.08%, 67.95%) of the association with threat. Figure 1 illustrates the identified mediating pathway between threat and internalizing symptoms via reward sensitivity.

Discussion

In this application of a high-dimensional mediation algorithm we considered 15 cognitive, affective, and developmental mediators, which are theorized to link threat and deprivation with psychopathology. We found that the empirically strongest mediating pathway connecting threat to changes in internalizing psychopathology was through reward sensitivity, consistent with recent findings of a reward sensitivity pathway connecting threat to depression symptoms (Kasparek et al., 2023). Specifically, threat was associated with lower reward sensitivity, which was in turn associated with greater adolescent internalizing symptoms. More advanced pubertal development and diminished reward sensitivity were associated with greater adolescent internalizing and externalizing symptoms. No significant mediating mechanisms were identified for the relationship between deprivation and psychopathology.

Facets of reward processing have been consistently implicated in major depression, bipolar disorder, anxiety, and externalizing behaviors (Alloy, Olino, Freed, & Nusslock, 2016; Cardoso Melo, Groen, & Hartman, 2022; Nusslock & Alloy, 2017). This is in line with fMRI and EEG studies, which show that blunted striatal activity may constitute a reward-related neurobiological vulnerability to the onset and severity of depression (Toenders et al., 2019). Small but consistent associations have been found between threat and reward processing (Kasparek et al., 2023; Oltean, Şoflău, Miu, & Szentágotai-Tătar, 2022). Greater exposure to threat in childhood often co-occurs with greater unpredictability in parenting behavior, which may foster inconsistent positive reinforcement and blunt reward-seeking behavior (Pollak, 2015). We add to the existing literature by isolating the reward sensitivity pathway in a data-driven analysis and highlight the potential of supportive interventions, such as behavioral activation, that bolster reward learning and approach motivation in those experiencing early-life threat (Dimidjian et al., 2006; McCauley et al., 2016; McLaughlin, DeCross, et al., 2019).

Contrary to what has been previously reported (Colich et al., 2020; Platt et al., 2017; Sumner, Colich, Uddin, Armstrong, & McLaughlin, 2019), threat experiences were not associated with advanced pubertal development in this sample. Stratification by sex (Table S3) showed that among

doi:10.1111/jcpp.14067

Table 3 Relationships between adversity, mediator, and outcome measures for the mediating variables selected as significant predictors of psychopathology by the high-dimensional mediation (HIMA) algorithm

	Adversity Exposure	Mediator	Adversity-psychopathology[a] Standardized β (95% CI)	Adversity-mediator[a] Standardized β (95% CI)	Mediator-psychopathology[b] Standardized β (95% CI)	p^c
Internalizing	Threat	PS: Tanner stage	.15 (0.02, 0.28)*	.01 (−0.12, 0.14)	.16 (0.03, 0.29)*	.8656
	Threat	RS: Reaction time on no- vs. high-reward trials	.15 (0.02, 0.28)*	−.18 (−0.32, −0.04)*	−.14 (−0.26, −0.02)*	.0241
	Deprivation	PS: Tanner stage	.32 (0.18, 0.46)***	−.12 (−0.26, 0.02)	.16 (0.03, 0.29)*	.1898
	Deprivation	RS: Reaction time on no- vs. high-reward trials	.32 (0.18, 0.46)***	−.08 (−0.23, 0.07)	−.14 (−0.26, −0.02)*	.2933
Externalizing	Threat	PS: Tanner stage	.26 (0.14, 0.38)***	.01 (−0.12, 0.14)	.17 (0.05, 0.29)**	.8887
	Threat	RS: Total stars	.26 (0.14, 0.38)***	−.01 (−0.15, 0.13)	−.18 (−0.29, −0.07)**	.8887
	Deprivation	PS: Tanner stage	.23 (0.1, 0.36)***	−.12 (−0.26, 0.02)	.17 (0.05, 0.29)**	.1898
	Deprivation	RS: Total stars	.23 (0.1, 0.36)***	−.04 (−0.19, 0.11)	−.18 (−0.29, −0.07)**	.6252

Standardized β coefficients represent the change in the standardized outcome associated with a 1-*SD* change in the independent variable. PT, pubertal timing; RS, reward sensitivity.
[a]Adjusted for age, biological sex, early life poverty, CBCL total problems, and maternal depression.
[b]Adjusted for threat, deprivation, age, biological sex, early life poverty, CBCL total problems, and maternal depression.
[c]Two-sided *p*-value for the mediating pathway, adjusted for multiple testing using the Benjamini–Hochberg method to preserve the false discovery rate at .05.
Two-sided *p*-value *** <.001, ** <.01, * <.05; not corrected for multiple testing.

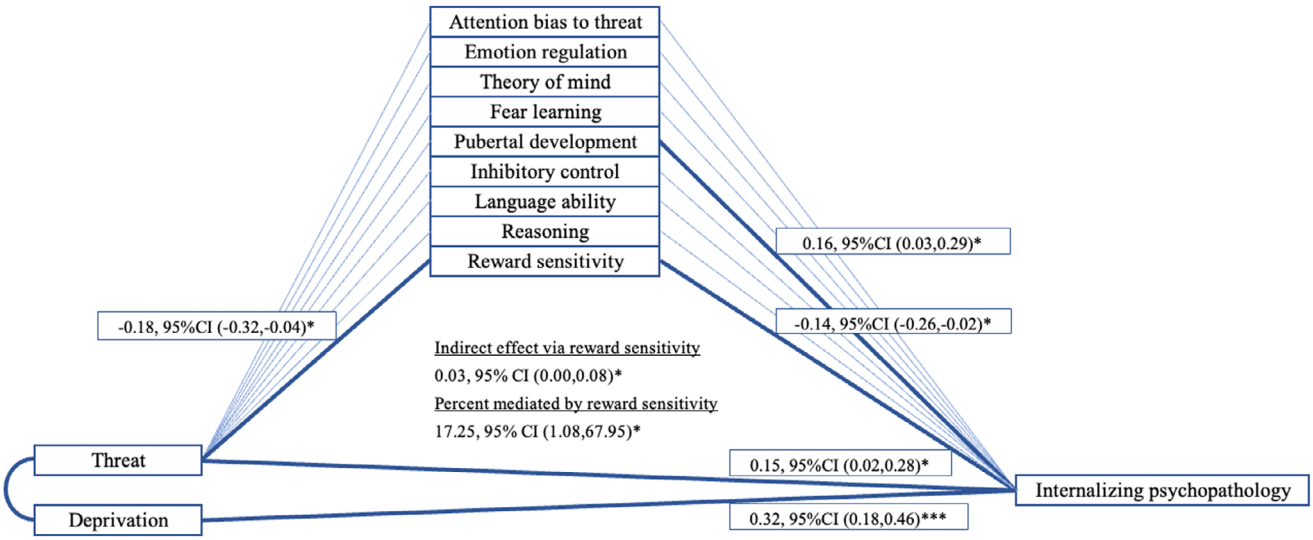

Figure 1 Representation of the tested framework and estimates of the indirect effect of threat via reward sensitivity and proportion of threat's association with internalizing psychopathology mediated by reward sensitivity. Two-sided *p*-value *** <.001, * <.05

boys, who in this sample experienced threat significantly more frequently than girls (Table S4), a 1-*SD* increase threatening experiences was associated with a 0.11-*SD* more advanced Tanner stage (95% CI (−0.04, 0.26)). The coefficient for threat in relation to Tanner stage was in the opposite direction for girls, though the associations were not significant in either sex stratum.

We did not replicate previous findings related to the mediating mechanisms for deprivation with respect to psychopathology in this sample. Associations between deprivation and language ability were evident even after adjustment for confounding, but language ability was not a strong predictor of psychopathology. Reasoning and inhibitory control were weakly associated with psychopathology and were related to threat rather than deprivation in this sample—perhaps signifying some misclassification of adversity experiences. In fact, a network analysis of threat and deprivation measures in the context of the dimensional model of adversity and psychopathology found that physical neglect—in our work part of the deprivation construct—clustered with experiences of threat rather than deprivation (Sheridan, Shi, Miller, Salhi, & McLaughlin, 2020).

Sparce replication of prior findings with respect to mechanisms linking threat and deprivation to psychopathology may be attributable to comparatively less severe experiences of adversity in our cohort but are less likely to stem from a lack of statistical power. In Appendix S3 we demonstrate that effect sizes previously found in mediation studies upon which we based our analysis are likely detectable with our sample size with 80% power (Fritz et al., 2017). We additionally emphasize that much of prior work in this field was done in sample sizes similar to ours. However, many prior studies examined experiences of adversity that were much more severe than those experienced by participants of this study (e.g., institutional rearing (Wade et al., 2022)). While the recruited sample over-represented families with low income, parental education at enrollment was representative of the Seattle metropolitan area—compared to 55.9% among the parents of recruited children, 56% of Seattle residents 25 years and older had at least a bachelor's degree according to the 2010 US census. However, the sample was not recruited to represent children with relatively severe forms of adversity (e.g., maltreatment and institutional rearing), which distinguishes it from many studies that have examined mechanisms linking childhood adversity and psychopathology.

A strength of this analysis is the collective consideration of a broad scope of candidate cognitive, affective, and developmental mechanisms. While the studied constructs are certainly distinct, we demonstrate correlations across cognitive, affective, and developmental domains (Table S2). For instance, attention bias to threat was associated with inhibitory control, language ability, and reasoning. On the other hand, total stars earned on the Piñata task, one of the reward sensitivity measures, was significantly associated with inhibitory control measured using the Stroop task but was not associated with the alternative reward sensitivity measure from the same task—the contrast in reaction time to no-reward versus high-reward trials. The latter observation may stem from the feature of the Piñata task that results in no stars earned on trials when the reward is attempted too early—children who were appropriately timing their piñata strikes exhibited greater inhibitory control. This finding is consistent with a recent validation of a titrated monetary incentive task, which failed to demonstrate divergent validity of reward sensitivity relative to inhibitory control (DelDonno et al., 2019). Our study is novel in highlighting the interrelated nature of cognitive, affective, and developmental

processes and suggests that interventions targeting multiple domains may be effective at interrupting the link between adversity and psychopathology.

In addition, this well-characterized longitudinal study included dimensional constructs of adverse experiences from multiple informants (mother and child). Except for pubertal development, all candidate mediators selected for the analysis were measured with behavioral tasks, reducing the concern for finding a mediating pathway solely due to correlation of errors that would be expected if exposures, mediators, and outcomes were all self-rated. Moreover, the recruitment oversampled families from less advantaged backgrounds and the sample remained similar in composition despite attrition through the early adolescent visit. Early childhood participant characteristics—such as income, parental education, experiences of stress and ill-health during pregnancy, and maternal and child psychiatric symptoms – were similar between the originally recruited sample and the sample that remained in the study at the early adolescence visit (see Table S5).

There were also notable limitations to our study. Most adversity experiences in this community-based sample were mild to moderate. Like in other population- or community-based studies (Ning, Gondek, Pereira, & Lacey, 2023), we observed smaller effect sizes and saw fewer associations than expected based on work carried out in studies enriched for adversity experiences. While our sample size was modest, it was consistent with prior published work and was powered to detect effect sizes previously reported. We also employed an analytic approach designed to deal with high-dimensional data to detect statistically evident mediating pathways. However, such approaches are prone to favoring relationships with larger effect sizes and lower error variance (Marek et al., 2022). We also did not consider possibly non-linear relationships or complex interactions between candidate mediators due to a lack of statistical power. Lastly, retrospective accounts of threat and deprivation experiences and candidate mediators were assessed at one study time point, obscuring the temporal ordering of exposures and mediators.

Conclusion

In this study, early-life threat and deprivation were associated with greater adolescent internalizing and externalizing psychopathology after adjustment for age, biological sex, poverty, childhood emotional and behavioral problems, and maternal depression. Fifteen candidate mediating variables, spanning domains of attention bias to threat, emotion regulation, theory of mind, fear learning, pubertal development, inhibitory control, language ability, reasoning, and reward sensitivity, were jointly assessed using a high-dimensional mediation approach. Blunted reward sensitivity and advanced pubertal development were associated with greater internalizing and externalizing psychopathology. Although deprivation was strongly related to adolescent psychopathology, none of its theorized mechanisms were empirically evident in this sample. Approximately 17% of threat's association with adolescent internalizing symptoms was mediated by blunted reward sensitivity. Our findings underscore the complexity of relationships between cognitive, affective, and developmental pathways theorized to mediate the associations between adversity dimensions and psychopathology symptoms and suggest that supportive interventions that bolster reward sensitivity in children that experience threat may protect against internalizing symptomatology in adolescence.

Supporting information

Additional supporting information may be found online in the Supporting Information section at the end of the article:

Appendix S1. Detailed descriptions of behavioral tasks.
Appendix S2. Additional details for psychopathology symptom variables.
Appendix S3. Sample size justification.

Acknowledgements

This work was supported by the National Institute of Mental Health at the National Institute of Health, USA (R01-MH106482, R56-MH119194, and R37-MH119194), the National Institute of Child Health and Human Development (R01-HD054465), the Training Program in Psychiatric Genetics and Translational Research (T32-MH 017119) and by grant T32 HD 104612-3 from the National Institutes of Health's Eunice Kennedy Shriver National Institute of Child Health and Human Development. A special thank you to Natalie Colich and Laura Machlin for sharing their expertise. The authors have declared that they have no competing or potential conflicts of interest.

Ethical considerations

Informed consent and assent were appropriately obtained, and all procedures were approved by Institutional Review Boards of the University of Washington and Harvard University.

Data availability

Data and analysis code are available in the following repository: https://github.com/katsadikova/Aim1_DT.git.

Correspondence

Ekaterina Sadikova, 677 Huntington Ave, Boston, MA 02115, USA; Email: sadikova@hcp.med.harvard.edu

Key points

- Mechanisms linking childhood adversity to psychopathology are complex and may be specific to experiences of threat and deprivation—at least partially distinct dimensions of adversity.
- A high-dimensional mediation analysis was run with a set of 15 mostly task-measured candidate mediators spanning domains of attention bias to threat, emotion regulation, theory of mind, fear learning, pubertal development, inhibitory control, language ability, reasoning, and reward sensitivity.
- Reward sensitivity and pubertal development had robust associations with internalizing and externalizing symptoms prospectively.
- Reward sensitivity explained approximately 17.25% of threat's association with internalizing symptoms, suggesting the potential of interventions such as behavioral activation to ameliorate psychopathology following childhood adversity experiences.

References

Achenbach, T.M. (1991). *Manual for the Child Behavior Checklist/4-18 and 1991 profile*. Burlington: University of Vermont, Department of Psychiatry.

Alloy, L.B., Olino, T., Freed, R.D., & Nusslock, R. (2016). Role of reward sensitivity and processing in major depressive and bipolar spectrum disorders. *Behavior Therapy*, *47*, 600–621.

Ben-Haim, M.S., Williams, P., Howard, Z., Mama, Y., Eidels, A., & Algom, D. (2016). The emotional stroop task: Assessing cognitive performance under exposure to emotional content. *Journal of Visualized Experiments*, *112*, 53720.

Benjamini, Y., & Hochberg, Y. (1995). Controlling the false discovery rate: A practical and powerful approach to multiple testing. *Journal of the Royal Statistical Society. Series B: Methodological*, *57*, 289–300.

Bernstein, D.P., Ahluvalia, T., Pogge, D., & Handelsman, L. (1997). Validity of the Childhood Trauma Questionnaire in an adolescent psychiatric population. *Journal of the American Academy of Child & Adolescent Psychiatry*, *36*, 340–348.

Bifulco, A., Brown, G.W., & Harris, T.O. (1994). Childhood experience of care and abuse (CECA): A retrospective interview measure. *Journal of Child Psychology and Psychiatry*, *35*, 1419–1435.

Birmaher, B., Khetarpal, S., Brent, D., Cully, M., Balach, L., Kaufman, J., & Neer, S.M. (1997). The screen for child anxiety related emotional disorders (SCARED): Scale construction and psychometric characteristics. *Journal of the American Academy of Child & Adolescent Psychiatry*, *36*, 545–553.

Briggs-Gowan, M.J., Pollak, S.D., Grasso, D., Voss, J., Mian, N.D., Zobel, E., … & Pine, D.S. (2015). Attention bias and anxiety in young children exposed to family violence. *Journal of Child Psychology and Psychiatry*, *56*, 1194–1201.

Brooks, B.L., Sherman, E.M.S., & Strauss, E. (2009). NEPSY-II: A developmental neuropsychological assessment, second edition. *Child Neuropsychology*, *16*, 80–101.

Cardoso Melo, R.D., Groen, R.N., & Hartman, C.A. (2022). Reward sensitivity at age 13 predicts the future course of psychopathology symptoms. *Frontiers in Psychiatry*, *13*, 818047.

Carozza, S., Holmes, J., & Astle, D.E. (2022). Testing deprivation and threat: A preregistered network analysis of the dimensions of early adversity. *Psychological Science*, *33*, 1753–1766.

Colich, N.L., Hanford, L.C., Weissman, D.G., Allen, N.B., Shirtcliff, E.A., Lengua, L.J., … & McLaughlin, K.A. (2023). Childhood trauma, earlier pubertal timing, and psychopathology in adolescence: The role of corticolimbic development. *Developmental Cognitive Neuroscience*, *59*, 101187.

Colich, N.L., Rosen, M.L., Williams, E.S., & McLaughlin, K.A. (2020). Biological aging in childhood and adolescence following experiences of threat and deprivation: A systematic review and meta-analysis. *Psychological Bulletin*, *146*, 721–764.

Colich, N.L., Sheridan, M.A., Humphreys, K.L., Wade, M., Tibu, F., Nelson, C.A., … & McLaughlin, K.A. (2021). Heightened sensitivity to the caregiving environment during adolescence: Implications for recovery following early-life adversity. *Journal of Child Psychology and Psychiatry*, *62*, 937–948.

DelDonno, S.R., Karstens, A.J., Cerny, B., Kling, L.R., Jenkins, L.M., Stange, J.P., … & Langenecker, S.A. (2019). The Titrated Monetary Incentive Delay Task: Sensitivity, convergent and divergent validity, and neural correlates in an RDoC sample. *Journal of Clinical and Experimental Neuropsychology*, *41*, 512–529.

Dimidjian, S., Hollon, S.D., Dobson, K.S., Schmaling, K.B., Kohlenberg, R.J., Addis, M.E., … & Gollan, J.K. (2006). Randomized trial of behavioral activation, cognitive therapy, and antidepressant medication in the acute treatment of adults with major depression. *Journal of Consulting and Clinical Psychology*, *74*, 658–670.

Egner, T., Etkin, A., Gale, S., & Hirsch, J. (2008). Dissociable neural systems resolve conflict from emotional versus nonemotional distracters. *Cerebral Cortex*, *18*, 1475–1484.

Etkin, A., Egner, T., Peraza, D.M., Kandel, E.R., & Hirsch, J. (2006). Resolving emotional conflict: A role for the rostral anterior cingulate cortex in modulating activity in the amygdala. *Neuron*, *52*, 1121.

Fan, J., & Lv, J. (2008). Sure independence screening for ultrahigh dimensional feature space. *Journal of the Royal Statistical Society. Series B: Statistical Methodology*, *70*, 849–911.

Finkelhor, D., Hamby, S.L., Ormrod, R., & Turner, H. (2005). The Juvenile Victimization Questionnaire: Reliability, validity, and national norms. *Child Abuse & Neglect*, *29*, 383–412.

Francis, E.R., Tsaligopoulou, A., Stock, S.E., Pingault, J.B., & Baldwin, J.R. (2023). Subjective and objective experiences of childhood adversity: A meta-analysis of their agreement and relationships with psychopathology. *Journal of Child Psychology and Psychiatry*, *64*, 1185–1199.

Fritz, K., Russell, A.M.T., Allwang, C., Kuiper, S., Lampe, L., & Malhi, G.S. (2017). Is a delay in the diagnosis of bipolar disorder inevitable? *Bipolar Disorders*, *19*, 396–400.

Hamlat, E.J., Snyder, H.R., Young, J.F., & Hankin, B.L. (2019). Pubertal timing as a transdiagnostic risk for psychopathology in youth. *Clinical Psychological Science: A*

Journal of the Association for Psychological Science, *7*, 411–429.
Heleniak, C., & McLaughlin, K.A. (2020). Social-cognitive mechanisms in the cycle of violence: Cognitive and affective theory of mind, and externalizing psychopathology in children and adolescents. *Development and Psychopathology*, *32*, 735–750.
Helfinstein, S.M., Kirwan, M.L., Benson, B.E., Hardin, M.G., Pine, D.S., Ernst, M., & Fox, N.A. (2013). Validation of a child-friendly version of the monetary incentive delay task. *Social Cognitive and Affective Neuroscience*, *8*, 720–726.
Kasparek, S.W., Gastón-Panthaki, A., Hanford, L.C., Lengua, L.J., Sheridan, M.A., & McLaughlin, K.A. (2023). Does reward processing moderate or mediate the link between childhood adversity and psychopathology: A longitudinal study. *Development and Psychopathology*, *1-14*, 2338–2351.
Kasparek, S.W., Jenness, J.L., & McLaughlin, K.A. (2020). Reward processing modulates the association between trauma exposure and externalizing psychopathology. *Clinical Psychological Science*, *8*, 989–1006.
Kaufman Kantor, G., Holt, M., Mebert, C., Straus, M., Drach, K., Ricci, L., … & Brown, W. (2004). Development and psychometric properties of the child self-report multidimensional neglectful behavior scale (MNBS-CR). *Child Maltreatment*, *9*, 409–429.
Kessler, R.C., McLaughlin, K.A., Green, J.G., Gruber, M.J., Sampson, N.A., Zaslavsky, A.M., … & Williams, D.R. (2010). Childhood adversities and adult psychopathology in the WHO World Mental Health Surveys. *The British Journal of Psychiatry*, *197*, 378–385.
Kim, S.G., Weissman, D.G., Sheridan, M.A., & McLaughlin, K.A. (2021). Child abuse and automatic emotion regulation in children and adolescents. *Development and Psychopathology*, *1-11*, 157–167.
Kovacs, M. (2011). CDI 2: Children's depression inventory. In *Technical manual* (2nd edn). New York: Multi-health Systems.
Lengua, L.J., Thompson, S.F., Moran, L.R., Zalewski, M., Ruberry, E.J., Klein, M.R., & Kiff, C.J. (2020). Pathways from early adversity to later adjustment: Tests of the additive and bidirectional effects of executive control and diurnal cortisol in early childhood. *Development and Psychopathology*, *32*, 545–558.
Liu, X., Guo, C., Liu, L., Wang, A., Hu, L., Tang, M., … & Sun, L. (1997). Reliability and validity of the Youth Self-Report (YSR) of Achenbach's Child Behavior Checklist (CBCL). *Chinese Mental Health Journal*, *11*, 200–203.
Machlin, L., Miller, A.B., Snyder, J., McLaughlin, K.A., & Sheridan, M.A. (2019). Differential associations of deprivation and threat with cognitive control and fear conditioning in early childhood. *Frontiers in Behavioral Neuroscience*, *13*, 80.
Marek, S., Tervo-Clemmens, B., Calabro, F.J., Montez, D.F., Kay, B.P., Hatoum, A.S., … & Dosenbach, N.U.F. (2022). Reproducible brain-wide association studies require thousands of individuals. *Nature*, *603*, 654–660.
Marshall, W.A., & Tanner, J.M. (1969). Variations in pattern of pubertal changes in girls. *Archives of Disease in Childhood*, *44*, 291–303.
Marshall, W.A., & Tanner, J.M. (1970). Variations in the pattern of pubertal changes in boys. *Archives of Disease in Childhood*, *45*, 13–23.
McCauley, E., Gudmundsen, G., Schloredt, K., Martell, C., Rhew, I., Hubley, S., & Dimidjian, S. (2016). The adolescent behavioral activation program: Adapting behavioral activation as a treatment for depression in adolescence. *Journal of Clinical Child & Adolescent Psychology*, *45*, 291–304.
McLaughlin, K. (2020). 45Early life stress and psychopathology. In *The Oxford handbook of stress and mental health*. Oxford University Press, USA.
McLaughlin, K.A. (2016). Future directions in childhood adversity and youth psychopathology. *Journal of Clinical Child and Adolescent Psychology*, *45*, 361–382.
McLaughlin, K.A., Colich, N.L., Rodman, A.M., & Weissman, D.G. (2020). Mechanisms linking childhood trauma exposure and psychopathology: A transdiagnostic model of risk and resilience. *BMC Medicine*, *18*, 96.
McLaughlin, K.A., DeCross, S.N., Jovanovic, T., & Tottenham, N. (2019). Mechanisms linking childhood adversity with psychopathology: Learning as an intervention target. *Behaviour Research and Therapy*, *118*, 101–109.
McLaughlin, K.A., Greif Green, J., Gruber, M.J., Sampson, N.A., Zaslavsky, A.M., & Kessler, R.C. (2012). Childhood adversities and first onset of psychiatric disorders in a national sample of US adolescents. *Archives of General Psychiatry*, *69*, 1151–1160.
McLaughlin, K.A., & Lambert, H.K. (2017). Child trauma exposure and psychopathology: Mechanisms of risk and resilience. *Current Opinion in Psychology*, *14*, 29–34.
McLaughlin, K.A., & Sheridan, M.A. (2016). Beyond cumulative risk: A dimensional approach to childhood adversity. *Current Directions in Psychological Science*, *25*, 239–245.
McLaughlin, K.A., Sheridan, M.A., Gold, A.L., Duys, A., Lambert, H.K., Peverill, M., … & Pine, D.S. (2016). Maltreatment exposure, brain structure, and fear conditioning in children and adolescents. *Neuropsychopharmacology*, *41*, 1956–1964.
McLaughlin, K.A., Sheridan, M.A., Humphreys, K.L., Belsky, J., & Ellis, B.J. (2021). The value of dimensional models of early experience: Thinking clearly about concepts and categories. *Perspectives on Psychological Science*, *16*, 1463–1472.
McLaughlin, K.A., Sheridan, M.A., & Lambert, H.K. (2014). Childhood adversity and neural development: Deprivation and threat as distinct dimensions of early experience. *Neuroscience & Biobehavioral Reviews*, *47*, 578–591.
McLaughlin, K.A., Weissman, D., & Bitran, D. (2019). Childhood adversity and neural development: A systematic review. *Annual Review of Developmental Psychology*, *1*, 277–312.
McNeilly, E.A., Peverill, M., Jung, J., & McLaughlin, K.A. (2021). Executive function as a mechanism linking socioeconomic status to internalizing and externalizing psychopathology in children and adolescents. *Journal of Adolescence*, *89*, 149–160.
Menon, V. (2011). Large-scale brain networks and psychopathology: A unifying triple network model. *Trends in Cognitive Sciences*, *15*, 483–506.
Miller, A.B., Machlin, L., McLaughlin, K.A., & Sheridan, M.A. (2021). Deprivation and psychopathology in the fragile families study: A 15-year longitudinal investigation. *Journal of Child Psychology and Psychiatry*, *62*, 382–391.
Miller, A.B., Sheridan, M.A., Hanson, J.L., McLaughlin, K.A., Bates, J.E., Lansford, J.E., … & Dodge, K.A. (2018). Dimensions of deprivation and threat, psychopathology, and potential mediators: A multi-year longitudinal analysis. *Journal of Abnormal Psychology*, *127*, 160–170.
Moran, L.R., Lengua, L.J., & Zalewski, M. (2013). The interaction between negative emotionality and effortful control in early social-emotional development. *Social Development*, *22*, 340–362.
Mott, F.L. (2004). The utility of the HOME-SF scale for child development research in a large national longitudinal survey: The National Longitudinal Survey of Youth 1979 cohort. *Parenting*, *4*, 259–270.
Muthén, L.K., & Muthén, B. (2017). *Mplus user's guide: Statistical analysis with latent variables, user's guide*. Los Angeles, CA: Muthén & Muthén.
Ning, K., Gondek, D., Pereira, S.M.P., & Lacey, R.E. (2023). Mediating mechanisms of the relationship between exposure to deprivation and threat during childhood and adolescent

psychopathology: Evidence from the Millennium Cohort Study. *European Child & Adolescent Psychiatry*, *33*, 1907–1920.
Nusslock, R., & Alloy, L.B. (2017). Reward processing and mood-related symptoms: An RDoC and translational neuroscience perspective. *Journal of Affective Disorders*, *216*, 3–16.
Olino, T.M. (2016). Future research directions in the positive valence systems: Measurement, development, and implications for youth unipolar depression. *Journal of Clinical Child and Adolescent Psychology*, *45*, 681–705.
Oltean, L.-E., Şoflău, R., Miu, A.C., & Szentágotai-Tătar, A. (2022). Childhood adversity and impaired reward processing: A meta-analysis. *Child Abuse & Neglect*, *142*, 105596.
Ono, M., & Miller, H.P. (1969). *Income nonresponses in the current population survey*. US Bureau of the Census.
Pérez-Edgar, K., Bar-Haim, Y., McDermott, J.M., Chronis-Tuscano, A., Pine, D.S., & Fox, N.A. (2010). Attention biases to threat and behavioral inhibition in early childhood shape adolescent social withdrawal. *Emotion*, *10*, 349–357.
Pessoa, L. (2008). On the relationship between emotion and cognition. *Nature Reviews Neuroscience*, *9*, 148–158.
Platt, J.M., Colich, N.L., McLaughlin, K.A., Gary, D., & Keyes, K.M. (2017). Transdiagnostic psychiatric disorder risk associated with early age of menarche: A latent modeling approach. *Comprehensive Psychiatry*, *79*, 70–79.
Pollak, S.D. (2015). Multilevel developmental approaches to understanding the effects of child maltreatment: Recent advances and future challenges. *Development and Psychopathology*, *27*, 1387–1397.
Pollak, S.D., Cicchetti, D., Hornung, K., & Reed, A. (2000). Recognizing emotion in faces: Developmental effects of child abuse and neglect. *Developmental Psychology*, *36*, 679–688.
Radloff, L.S. (1977). The CES-D Scale: A self-report depression scale for research in the general population. *Applied Psychological Measurement*, *1*, 385–401.
Raviv, A., Erel, O., Fox, N.A., Leavitt, L.A., Raviv, A., Dar, I., … & Greenbaum, C.W. (2001). Individual measurement of exposure to everyday violence among elementary schoolchildren across various settings. *Journal of Community Psychology*, *29*, 117–140.
Raviv, A., Raviv, A., Shimoni, H., Fox, N.A., & Leavitt, L.A. (1999). Children's self-report of exposure to violence and its relation to emotional distress. *Journal of Applied Developmental Psychology*, *20*, 337–353.
Schlaffke, L., Lissek, S., Lenz, M., Juckel, G., Schultz, T., Tegenthoff, M., … & Brüne, M. (2015). Shared and nonshared neural networks of cognitive and affective theory-of-mind: A neuroimaging study using cartoon picture stories. *Human Brain Mapping*, *36*, 29–39.
Shackman, J.E., Shackman, A.J., & Pollak, S.D. (2007). Physical abuse amplifies attention to threat and increases anxiety in children. *Emotion*, *7*, 838–852.
Shechner, T., Britton, J.C., Ronkin, E.G., Jarcho, J.M., Mash, J.A., Michalska, K.J., … & Pine, D.S. (2015). Fear conditioning and extinction in anxious and nonanxious youth and adults: Examining a novel developmentally appropriate fear-conditioning task. *Depression and Anxiety*, *32*, 277–288.
Sheridan, M.A., & McLaughlin, K.A. (2014). Dimensions of early experience and neural development: Deprivation and threat. *Trends in Cognitive Sciences*, *18*, 580–585.
Sheridan, M.A., McLaughlin, K.A., Winter, W., Fox, N., Zeanah, C., & Nelson, C.A. (2018). Early deprivation disruption of associative learning is a developmental pathway to depression and social problems. *Nature Communications*, *9*, 2216.
Sheridan, M.A., Shi, F., Miller, A.B., Salhi, C., & McLaughlin, K.A. (2020). Network structure reveals clusters of associations between childhood adversities and development outcomes. *Developmental Science*, *23*, e12934.
Shi, B., Choirat, C., Coull, B.A., VanderWeele, T.J., & Valeri, L. (2021). CMAverse: A suite of functions for reproducible causal mediation analyses. *Epidemiology*, *32*, E20–E22.
Steinberg, A.M., Brymer, M.J., Decker, K.B., & Pynoos, R.S. (2004). The University of California at Los Angeles Post-traumatic Stress Disorder Reaction Index. *Current Psychiatry Reports*, *6*, 96–100.
Steinberg, A.M., Brymer, M.J., Kim, S., Briggs, E.C., Ippen, C.G., Ostrowski, S.A., … & Pynoos, R.S. (2013). Psychometric properties of the UCLA PTSD Reaction Index: Part I. *Journal of Traumatic Stress*, *26*, 1–9.
Stroop, J.R. (1935). *Studies of interference in serial verbal reactions*. Nashville, TN: George Peabody College for Teachers.
Sumner, J.A., Colich, N.L., Uddin, M., Armstrong, D., & McLaughlin, K.A. (2019). Early experiences of threat, but not deprivation, are associated with accelerated biological aging in children and adolescents. *Biological Psychiatry*, *85*, 268–278.
Toenders, Y.J., van Velzen, L.S., Heideman, I.Z., Harrison, B.J., Davey, C.G., & Schmaal, L. (2019). Neuroimaging predictors of onset and course of depression in childhood and adolescence: A systematic review of longitudinal studies. *Developmental Cognitive Neuroscience*, *39*, 100700.
Valeri, L., & Vanderweele, T.J. (2013). Mediation analysis allowing for exposure-mediator interactions and causal interpretation: Theoretical assumptions and implementation with SAS and SPSS macros. *Psychological Methods*, *18*, 137–150.
Wade, M., Parsons, J., Humphreys, K.L., McLaughlin, K.A., Sheridan, M.A., Zeanah, C.H., … & Fox, N.A. (2022). The Bucharest Early Intervention Project: Adolescent mental health and adaptation following early deprivation. *Child Development Perspectives*, *16*, 157–164.
Wade, M., Zeanah, C.H., Fox, N.A., & Nelson, C.A. (2020). Global deficits in executive functioning are transdiagnostic mediators between severe childhood neglect and psychopathology in adolescence. *Psychological Medicine*, *50*, 1687–1694.
Wang, D., Liu, T., & Shi, J. (2017). Development of monetary and social reward processes. *Scientific Reports*, *7*, 11128.
Waters, A.M., Henry, J., Mogg, K., Bradley, B.P., & Pine, D.S. (2010). Attentional bias towards angry faces in childhood anxiety disorders. *Journal of Behavior Therapy and Experimental Psychiatry*, *41*, 158–164.
Wechsler, D. (1999). *Wechsler abbreviated scale of intelligence*.
Weissman, D.G., Bitran, D., Miller, A.B., Schaefer, J.D., Sheridan, M.A., & McLaughlin, K.A. (2019). Difficulties with emotion regulation as a transdiagnostic mechanism linking child maltreatment with the emergence of psychopathology. *Development and Psychopathology*, *31*, 899–915.
Weissman, D.G., Nook, E.C., Dews, A.A., Miller, A.B., Lambert, H.K., Sasse, S.F., … & McLaughlin, K.A. (2020). Low emotional awareness as a transdiagnostic mechanism underlying psychopathology in adolescence. *Clinical Psychological Science: A Journal of the Association for Psychological Science*, *8*, 971–988.
Weissman, D.G., Rosen, M.L., Colich, N.L., Sambrook, K.A., Lengua, L.J., Sheridan, M.A., & McLaughlin, K.A. (2022). Exposure to violence as an environmental pathway linking low socioeconomic status with altered neural processing of threat and adolescent psychopathology. *Journal of Cognitive Neuroscience*, *34*, 1892–1905.
Zhang, H., Zheng, Y., Zhang, Z., Gao, T., Joyce, B., Yoon, G., … & Liu, L. (2016). Estimating and testing high-dimensional mediation effects in epigenetic studies. *Bioinformatics*, *32*, 3150–3154.

Accepted for publication: 20 August 2024