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Exposure to Violence as an Environmental Pathway Linking Low Socioeconomic Status with Altered Neural Processing of Threat and Adolescent Psychopathology

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Abstract

Low childhood socioeconomic status (SES) is associated with increased risk for psychopathology, because in part of heightened exposure to environmental adversity. Adverse experiences can be characterized along dimensions, including threat and deprivation, that contribute to psychopathology via distinct mechanisms. The current study investigated a neural mechanism through which threat and deprivation may contribute to socioeconomic disparities in psychopathology. Participants were 177 youths (83 girls) aged 10–13 years recruited from a cohort followed since the age of 3 years. SES was assessed using the income-to-needs ratio at the age of 3 years. At the age of 10–13 years, retrospective and current exposure to adverse experiences and symptoms of psychopathology were assessed. At this same time point, participants also completed a face processing task (passive viewing of fearful and neutral faces)during an fMRI scan. Lower childhood SES was associated with greater exposure to threat and deprivation experiences. Both threat and deprivation were associated with higher depression symptoms, whereas threat experiences were uniquely linked to posttraumatic stress disorder symptoms. Greater exposure to threat, but not deprivation, was associated with higher activation in dorsomedial pFC to fearful compared with neutral faces. The dorsomedial pFC is a hub of the default mode network thought to be involved in internally directed attention and cognition. Experiences of threat, but not deprivation, are associated with greater engagement of this region in response to threat cues. Threat-related adversity contributes to socioeconomic disparities in adolescent psychopathology through distinct mechanisms from deprivation.

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INTRODUCTION

About one in seven children in the United States are estimated to live in poverty as of 2019 (U.S. Census Bureau, 2019a). The resulting strain that this lack of financial resources places on families and the communities in which they live increases the likelihood that children raised in families with a low socioeconomic status (SES) will experience environmental adversities, including exposure to violence, family conflict, parental separation, low cognitive stimulation, and a less predictable environment (Rosen et al., 2020; Evans, 2004). These adverse childhood experiences have potent and enduring influences on children's development, contributing to SES-related disparities in mental health (McLaughlin, Green et al., 2012; Green et al., 2010; Kessler, Davis, & Kendler, 1997). However, the associations between adversity and psychopathology involve a complex and varied set of mechanisms that may differ depending on the nature of the adverse experience. Understanding the neural mechanisms linking SES and co-occurring experiences of environmental adversity with psychopathology may help generate novel targets for interventions aimed at reducing socioeconomic disparities in mental health. Here, we focus on neural responses to threat-related stimuli as a potential mechanism underlying socioeconomic disparities in psychopathology specifically among children who have been exposed to violence.

Children raised in families with a low SES are more likely to develop psychopathology in childhood and adolescence than those from higher SES backgrounds (Peverill et al., 2021), including mood, anxiety, behavior, and substance use disorders (McLaughlin, Costello, Leblanc, Sampson, & Kessler, 2012). Low SES is associated with increased likelihood of experiencing many forms of environmental adversity (Rosen et al., 2020; Evans & Cassells, 2014; McLaughlin et al., 2011; Evans, 2004), and adverse experiences are strongly related to the emergence of psychopathology across the lifespan (McLaughlin, Green, et al., 2012; Green et al., 2010; Kessler et al., 1997). Therefore, exposure to adversity is an environmental pathway through which low childhood SES is likely to contribute to risk for psychopathology in children and adolescents. Indeed, cumulative exposure to adversity mediates the association between childhood poverty and psychopathology in early adulthood (Evans & Cassells, 2014). Existing work on this topic has relied on aggregate measures of adversity—often termed cumulative risk or an adverse childhood experience score. This approach involves creating a count of the different types of adverse experiences to which a child has been exposed (Evans, Li, & Whipple, 2013; Felitti et al., 1998). Cumulative risk scores reflect the fact that negative developmental and mental health outcomes are more likely among children who have experienced multiple co-occurring adversities that impact developmental outcomes through their impact on physiological stress response systems (Evans et al., 2013). However, such an approach precludes the ability to examine the potential for different types of adverse experiences influencing developmental outcomes through unique neurobiological mechanisms, which appears increasingly likely (see McLaughlin, Sheridan, Humphreys, Belsky, & Ellis, 2021, for a review).

The dimensional model of adversity (McLaughlin & Sheridan, 2016; McLaughlin, Sheridan, & Lambert, 2014) proposes that complex environmental experiences can be distilled into core underlying dimensions that cut across many forms of adversity, and these dimensions

have differential influences on cognitive, emotional, and neural development. Two initial dimensions proposed by the theory are threat and deprivation. Threat is characterized by experiences involving harm or threat of harm to the physical integrity of the child, such as exposure to abuse or violence. The dimensional model argues that experiences characterized by threat are associated with heightened behavioral and neural sensitivity to potential danger cues, including heightened neural response in the amygdala and broader salience network (McLaughlin & Sheridan, 2016; McLaughlin, Sheridan, & Lambert, 2014; Sheridan & McLaughlin, 2014). Deprivation, in contrast, is characterized by the absence of social and cognitive inputs that the brain has evolved to expect during development, including cognitive stimulation and the presence of a responsive caregiver (McLaughlin & Sheridan, 2016; McLaughlin, Sheridan, & Lambert, 2014). The dimensional model posits that environments characterized by deprivation constrain children's learning opportunities leading to pronounced changes in higher-order cognitive functioning, including difficulties with language and executive function. Moreover, the model posits that children raised in deprived environments demonstrate altered structure and function of brain circuits underlying higher-order cognition, including the fronto-parietal network (Sheridan & McLaughlin, 2016). Here, we focus on neural mechanisms proposed in the dimensional model to be specifically related to experiences of threat.

Existing evidence on exposure to violence and developmental outcomes is largely consistent with the predictions of the dimensional model of adversity. Youth exposed to threat can detect anger with less perceptual information (Pollak, Messner, Kistler, & Cohn, 2009; Pollak & Sinha, 2002) and exhibit heightened attention to threat-related cues (Pollak, Vardi, Putzer Bechner, & Curtin, 2005; Pollak & Tolley-Schell, 2003) than youth never exposed to threat. Furthermore, youth exposed to threat, but not deprivation, are more likely to perceive neutral or ambiguous expressions as angry (Pollak, Cicchetti, Hornung, & Reed, 2000). In a recent systematic review, we found that threat exposure is consistently associated with elevated activation in amygdala and anterior insula to negative emotional cues in children and adolescents; in contrast, studies based on cumulative measures of adversity or deprivation experiences like early institutionalization have not found heightened neural responses to negative emotional cues with the same consistency (McLaughlin, Weissman, & Bitrán, 2019). Increased salience network reactivity to threat-related cues is associated with depression, anxiety, and posttraumatic stress disorder (PTSD; Swartz, Williamson, & Hariri, 2015; McLaughlin, Busso, et al., 2014; Pagliaccio, Luby, Luking, Belden, & Barch, 2014), and may therefore be an important mechanism linking threat-related adversity with psychopathology.

Although prior studies provide preliminary support for the dimensional model, most studies examining childhood adversity and neural functioning recruit children with a particular type of adversity, such as physical abuse or neglect, without careful measurement and control of co-occurring adversity. These exposures are typically measured dichotomously as the presence or absence of adversity—rather than as dimensions and typically in small samples (McLaughlin et al., 2019, 2021). One prior study has simultaneously examined the associations of threat and deprivation with neural responses to emotional faces (Hein et al., 2020). No significant differences were observed in this study between threat-related adversity and neural responses to fearful or angry faces (relative to implicit baseline).

However, contrasting the face stimuli with implicit baseline makes it difficult to determine whether the associations with adversity are specific to those emotions, to the emotional valence, or to faces in general. In this study, we contrasted fearful faces with neutral faces to evaluate if stimuli that specifically reflect the presence of environmental threat elicit differential neural responses in youth exposed to violence. We examined continuous indicators of threat and deprivation, thereby quantifying a fuller range of variability across these dimensions than dichotomous indicators of exposure to a particular category of adversity. Moreover, we included measures of threat and deprivation in the same analysis, to evaluate whether associations with neural response to fearful versus neutral faces are specific to threat-related adversity. Finally, we determined whether these neural responses were related to symptoms of internalizing psychopathology. We focused on internalizing problems because associations between neural responses to threat-related cues and externalizing problems are more complex and heterogenous depending on the presence or absence of callous–unemotional traits (Dotterer, Hyde, Swartz, Hariri, & Williamson, 2017; Blair, Veroude, & Buitelaar, 2016; Viding et al., 2012), which were not measured in this study.

In the current study, we examined the distinct role of environmental experiences of threat and deprivation in explaining socioeconomic disparities in mental health and a potential neural mechanism that may contribute to these disparities. We expected that low SES would be associated with higher exposure to both threat and deprivation and that experiences of threat and deprivation would mediate the associations between early childhood SES and symptoms of depression and anxiety. In addition, we anticipated that only threat, controlling for deprivation, would be associated with PTSD symptoms as well as elevated neural response in the amygdala and salience network (e.g., anterior insula) to fearful relative to neutral faces. Finally, we predicted that heightened neural responses to threat cues would be associated with greater symptoms of depression, anxiety, and PTSD and would mediate the prospective association between low SES and symptoms of psychopathology, suggesting a neural mechanism through which threat uniquely contributes to internalizing psychopathology.

METHODS

Participants

Participants were drawn from a longitudinal study of youth followed since the age of 36 months in the Seattle, Washington area (Lengua et al., 2015). Children were recruited from a university-hospital birth registry, day-cares, preschools, health clinics, and charitable agencies to have a uniform distribution across SES based on family income. The current report focuses on a subsample who participated in a follow-up neuroimaging session performed when children were aged 10–13 years (M = 11.0 years, SD = 0.59 years). One hundred seventy-seven youth (83 female) completed the face processing fMRI task with useable data (see fMRI Preprocessing for details). Comprehensive assessments of adversity experiences and symptoms of psychopathology were also completed at this time point. The racial/ethnic composition of the sample approximates the broader Seattle area: White (n =

116, 66%), Black (*n* = 21, 12%), Latinx (*n* = 18, 10%), Asian (*n* = 15, 8%), and other (*n* = 7, 4%).

Measures

SES—When participants were 3 years old, mothers reported on family income and the number of people in the household. Income-to-needs ratio was calculated by dividing the parent-reported family income by the poverty threshold for a family of that size for the year of data collection, as indicated by the U.S. Census Bureau (2019b). Consistent with prior work on childhood SES and neurodevelopment (Rosen et al., 2018; Noble et al., 2015), the natural log of income-to-needs ratio was used as a measure of family income in all analyses to reflect that associations of income with neural outcomes are stronger at the lower end of the SES distribution.

Threat Experiences—To quantify threat experiences, we used a composite reflecting the number of distinct types of violence the child had experienced, the frequency of violence exposure, and the severity of violence exposure, all reported when participants were aged 10–13 years.

First, we used a count of exposure to five types of interpersonal violence—physical abuse, sexual abuse, domestic violence, witnessing a violent crime, or being a victim of a violent crime. Each exposure was counted if it was endorsed by the parent or child on the UCLA PTSD Reaction Index (RI; Steinberg, Brymer, Decker, & Pynoos, 2004); physical abuse, sexual abuse, and domestic violence were coded as present if they were endorsed by the child on the Childhood Experiences of Care and Abuse (CECA) Interview (Bifulco, Brown, & Harris, 1994) or by the parent on the Juvenile Victimization Questionnaire (JVQ; Finkelhor, Hamby, Ormrod, & Turner, 2005). The PTSD-RI includes a trauma screen that assesses exposure to numerous traumatic events, including physical abuse, sexual abuse, and domestic violence, and additionally assesses PTSD symptoms. The PTSD-RI has good internal consistency and convergent validity (Steinberg et al., 2013). The CECA assesses caregiving experiences, including physical, sexual, and emotional abuse. We modified the interview to ask parallel questions about witnessing domestic violence (e.g., “When you were a child or teenager, did you ever see or hear your parents or caregivers hit each other repeatedly with something like a belt or stick or hit, punch, kick, or burn each other?”). Interrater reliability for maltreatment reports on the CECA is excellent, and validation studies suggest high agreement between siblings (Bifulco, Brown, Lillie, & Jarvis, 1997). The JVQ has excellent psychometric properties, including test–retest reliability and construct validity (Finkelhor et al., 2005).

Second, to assess the frequency of violence exposure, we used the summed frequency ratings of witnessed and experienced violence on the Violence Exposure Scale for Children-Revised (VEX-R; Raviv et al., 2001; Raviv, Raviv, Shimoni, Fox, & Leavitt, 1999). The VEX-R assesses the frequency of exposure to different forms of violence. Children are presented with a cartoon and caption depicting a child of the same sex witnessing a type of violence (e.g., “Chris sees a person slap another person really hard”) and experiencing that same type of violence (e.g., “A person slaps Chris really hard”). Children are then asked to

report how frequently they have witnessed or experienced that type of violence (e.g., “How many times have you seen a person slap another person really hard?”, “How many times has a person slapped you really hard?”) on a Likert scale ranging from 0 (*never*) to 3(*lots of times*). The VEX-R demonstrates good reliability and has been validated with children as young as second grade (Raviv et al., 1999, 2001).

Third, to assess the severity of violence exposure, we used the physical and sexual abuse subscales from the Childhood Trauma Questionnaire (CTQ; Bernstein, Ahluvalia, Pogge, & Handelsman, 1997). The CTQ is a 28-item scale that assesses the severity of maltreatment during childhood, including physical and sexual abuse (e.g., “People in my family hit me so hard that it left me with bruises or marks.”). The CTQ has excellent psychometric properties including internal consistency, test–retest reliability, and convergent and discriminant validity with interviews and clinician reports of maltreatment (Bernstein et al., 1994, 1997).

Number of violence exposure types was significantly correlated with the severity of violence exposure ($r = .283$) and the frequency of violence exposure ($r = .411$), but the frequency of violence exposure and the severity of violence exposure were not significantly correlated ($r = .114$). To create a threat composite, we first standardized each of these three subscales of (1) number of violence exposure types, (2) frequency of violence exposure, and (3) severity of physical or sexual abuse exposure and averaged them together. The construction of this composite has been preregistered (osf.io/6yf4p/).

The goal for the threat composites was to combine well-established measures of violence exposure into a single score reflecting the severity and frequency of violence participants had experienced. The measures of violence exposure included in this study each provide unique, valuable information for this goal, and each approaches the task of quantifying violence exposure in a slightly different way. The UCLA PTSD-RI, CECA, and JVQ each include dichotomous items that indicate whether or not a participant has experienced several different types of violence. In contrast, the CTQ and VEX-R involve Likert-scale ratings. The CTQ includes items ranging from 1 to 5 reflecting the frequency and severity of physical and sexual abuse. The VEX-R involves ratings from 0 to 3 of the frequency of experiencing different forms of violence. Thus, in addition to measuring slightly different aspects of violence experiences conceptually (i.e., exposure, severity, and frequency), the number and variety of experiences, the type of rating, and the range of those ratings vary between each of these measures. Because the CTQ included only physical and sexual abuse, and the VEX-R was the only measure to include witnessed violence, experiences like physical and sexual abuse ultimately received greater weight in the overall score. However, these experiences are more severe, so their relatively greater weight in the composite is consistent with a dimensional approach to conceptualizing childhood adversity, with higher scores reflecting experiences of threat that are more frequent or severe (see McLaughlin et al., 2021).

Deprivation Experiences—To quantify deprivation, we used a composite composed of cognitive, emotional, and physical forms of deprivation, all reported when participants were aged 10–13 years. We created composites for these subdomains of deprivation, given

the possibility for specificity in their associations with some developmental domains (e.g., cognitive deprivation may be more strongly related to aspects of cognitive development like language and executive functioning than emotional deprivation). Therefore, we aimed to create a composite that reflected not only deprivation broadly but also faces of deprivation that could be evaluated separately. For the purposes of this study, however, we did not have specific hypotheses about subdomains of deprivation and thus focus on the broad composite.

Cognitive deprivation was assessed using the Home Observation Measurement of the Environment–Short Form (Mott, 2004). This measure assesses numerous forms of cognitive stimulation, including the presence of learning materials in the home, the child's engagement with activities outside the home, the degree of caregiver involvement in learning, and the complexity of the linguistic environment. To assess cognitive stimulation, Home Observation Measurement of the Environment items are scored dichotomously such that the presence of a stimulating activity or experience is coded as 1 and the absence is coded as 0. Because we were interested in quantifying cognitive deprivation, we reverse-scored the measure. To create a cognitive deprivation measure, we created a binary score of the 19 cognitive stimulation items (e.g., "Did you and/or your partner teach your child colors at home?") such that the presence of each item reflecting cognitive stimulation was scored as a 0 and the absence was scored as a 1. We then standardized this summed variable to create a continuous measure of cognitive deprivation.

Emotional deprivation was assessed with several scales measuring emotional neglect of the child by caregivers. These included the emotional neglect subscale of the Multidimensional Neglectful Behavior Scale (MNBS; Kantor et al., 2004) and the emotional neglect items from the CECA Interview. The MNBS includes subscales for emotional needs (e.g., "helped you when you had problems"), physical needs, cognitive needs, and supervision needs. It has good internal consistency and convergent validity with related measures of exposure to neglect and other adversity and mental health (Kantor et al., 2004). The CECA neglect scale includes items that assess both emotional and physical neglect by the child's primary male and female parental figures. We included only the eight items assessing emotional neglect (e.g., "she was concerned about my worries"). For participants who reported on both a female and male parental figure, the higher of the two scores was used. We created a total sum score for each of these scales, standardized each scale, and averaged these z scores together to create the final composite score of emotional deprivation.

Physical deprivation was quantified using the physical needs subscale of the MNBS (e.g., "Make sure you bathed regularly"), the four-item Household Food Insecurity Scale as completed by a caregiver (e.g., "How often in the past 12 months did you not have enough money to buy food?"), and the physical neglect subscale of the CTQ (e.g., "I had to wear dirty clothes"). Because these measures utilize the same scoring scale and had a nearly identical range in our data set, we took the mean of these three scales and standardized it to create a composite score of physical deprivation.

Physical deprivation was significantly correlated with cognitive deprivation ($r = .223$) and emotional deprivation ($r = .373$), but cognitive deprivation and emotional deprivation were not significantly correlated ($r = .086$). To create a composite reflecting all three types

of deprivation, we took the mean of the cognitive, emotional, and physical deprivation standardized scores. The construction of this deprivation composite has been preregistered (osf.io/6yf4p/).

Symptoms of Psychopathology—Depression symptoms were assessed by self-report with the Children's Depression Inventory-2 (CDI), a recently revised version of the widely used self-report measure of depressive Symptoms in children and adolescents (Kovacs, 1992, 2011). The CDI has demonstrated good reliability and validity in children and adolescents (Craighead, Smucker, Craighead, & Ilardi, 1998). The CDI demonstrated good internal consistency in our sample (α = .87).

Anxiety symptoms were assessed by self-report with the Screen for Child Anxiety Related Emotional Disorders (SCARED), which measures anxiety disorder symptoms across five domains: panic/somatic, generalized anxiety, separation anxiety, social phobia, and school phobia (Birmaher et al., 1997). The SCARED has sound psychometric properties (Birmaher et al., 1997, 1999) and good internal consistency in our sample (α = .90).

Symptoms of PTSD were assessed using child- and parent-report versions of the UCLA PTSD-RI (Steinberg et al., 2004). The PTSD-RI assesses PTSD reexperiencing, avoidance/numbing, and hyperarousal symptoms according to DSM-IV criteria. A total symptom severity score is generated by summing all items. The higher score of the parent- and child-reported symptom severity was used. The use of the higher score of parent or child report on the is an implementation of the standard "or" rule used in combining parent and child reports of psychopathology. In this approach, if either a parent or child endorses a particular symptom, it is counted, and the reporter endorsing the higher level of symptoms or impairment is used. This is a standard approach in the literature on child psychopathology—for example, it is how mental disorders are diagnosed in population-based studies of psychopathology in children and adolescents (e.g., Kessler et al., 2012; Merikangas et al., 2010). The PTSD-RI has sound psychometric properties (Steinberg et al., 2013) and had excellent internal consistency in our sample (α = .89).

The distribution of psychopathology in the sample was predominantly subclinical and reflective of the general population. Although they are not diagnostic measures, cutoff scores of 19 for the CDI (Kovacs, 1992) and 25 for the SCARED (Birmaher et al., 1999) have been proposed for these measures, respectively. On the basis of these cutoffs, six participants met criteria for clinical depression, and 35 met criteria for general anxiety disorder. Seven participants met criteria for a PTSD diagnosis on either the parent or child report of the PTSD-RI.

Emotional Faces Task

The face processing task consisted of two runs of a face-viewing task in which participants passively viewed emotional face stimuli. Faces were drawn from the NimStim stimulus set (Tottenham, Borscheid, Ellertsen, Marcus, & Nelson, 2002). The "calm" faces from this data set were used as neutral expressions, as these expressions are potentially less emotionally evocative than neutral faces, which can be perceived as negatively valenced (Tottenham et al., 2009). Fearful faces were used to elicit negative emotional responses and suggest

the presence of potential threat. Fearful faces were used as they have been found to elicit amygdala activation more consistently than other emotion expressions (Fusar-Poli et al., 2009). Each run consisted of three blocks of calm, fearful, and scrambled faces and three fixation blocks displayed in a pseudorandom order that ensured that no block type was displayed twice in a row. During each 18-sec block, 36 faces of different actors expressing the same emotion were displayed for 300 msec each, with 200 msec between each face, based on prior face processing tasks (Somerville, Kim, Johnstone, Alexander, & Whalen, 2004). At one point during each block, participants were prompted to indicate by an index or middle finger button press whether the last face they saw was male or female (or whether a dot appeared on the left or right side of the screen for scrambled face blocks) to ensure they were paying attention to the stimuli. Three participants performed below chance on this attention check and were excluded from analyses.

fMRI Data Acquisition

Before undergoing scanning, youth were trained to minimize head movements in a mock scanner. They watched a movie with a head-mounted motion tracker that stopped playing if a movement of over 2 mm occurred. This method has been shown to significantly reduce head motion once children are in the scanner (Raschle et al., 2012). In the scanner, an inflatable head-stabilizing pillow was used to restrict movement. During the task, mean frame-wise displacement ranged from 0.05 to 1.43 mm with a mean of 0.26 mm.

Scanning was performed on a 3-T Phillips Achieva scanner at the University of Washington Integrated Brain Imaging Center using a 32-channel head coil. T1-weighted magnetization prepare rapid gradient echo volumes were acquired (repetition time = 2530 msec, echo time = 3.5 msec, flip angle = 7°, field of view = 256 × 256, 176 slices, in-plane voxel size = 1 mm^3) for coregistration with fMRI data. BOLD signal during functional runs was acquired using a gradient-echo T2*-weighted EPI sequence. Thirty-seven 3-mm-thick slices were acquired sequentially and parallel to the AC–PC line (repetition time = 2 sec, echo time = 25 msec, flip angle = 79°, interslice gap = 0.6 mm, field of view = 224 × 224 × 132.6, matrix size = 76 × 74, voxel size = 2.8 × 2.8 × 3.6 mm). Before each scan, four images were acquired and discarded to allow longitudinal magnetization to reach equilibrium.

fMRI Preprocessing

Preprocessing and statistical analysis of fMRI data was performed in a pipeline using GNU Make, a software development tool designed for building executables from source files that can be used to create neuroimaging workflows that rely on multiple software packages. The following preprocessing steps were applied: (1) motion correction followed by slice-time correction in FMRIB Software Library (FSL), (2) skull-stripping using FSL's bet tool, (3) despiking using AFNI's 3dDespike tool, and (4) smoothing with a 6-mm FWHM kernel using SUSAN in FSL. Outlier volumes in which framewise displacement exceeded 1 mm, the derivative of variance in BOLD signal across the brain exceeded the upper fence (above 75th percentile + 1.5 × interquartile range), or signal intensity was more than 3 *SD*s from the mean were regressed out of person-level models. Six rigid-body motion regressors and the time series extracted from white matter and ventricles were included in person-level models to reduce noise associated with motion and physiological fluctuations. Person-

and group-level models were estimated in FSL. After estimation of person-level models, the resulting contrast images were normalized into standard space (Montreal Neurological Institute, 2 × 2 × 2 mm voxels), and anatomical coregistration of the functional data with each participant's T1-weighted image was performed using Advanced Normalization Tools software.

Data were visually inspected for the presence of major artifacts or abnormalities in the structural and functional images by two trained researchers. After person-level analyses, four participants were excluded from group-level analyses because of substantial signal dropout in the ventromedial pFC, indicating distortion of data in relevant brain regions for this analysis. One was excluded because of an incidental finding indicating a major structural abnormality, and one participant's data were unusable because of a data storage error. One run of data was excluded for four additional participants: two because of excessive motion (more than 20% of volumes censored), one because of a data acquisition error, and one because the scan was interrupted after the first run.

fMRI Analysis

fMRI data processing was performed using FSL FEAT Version 6.0.0. Regressors were created by convolving a boxcar function of phase duration with the standard double-gamma hemodynamic response function for each phase of the task (fearful, neutral, and scrambled faces). A general linear model was constructed for each participant. Higher level analysis was carried out using FLAME1.

To investigate study hypotheses, we first conducted a single whole-brain multiple regression analysis using AFNI's 3dttest++, with threat and deprivation composites as the primary predictors; early childhood SES, age, and sex as covariates; and neural activation to fearful versus neutral faces as the outcome variable. Recommended cluster corrections at a number of voxel-wise thresholds were obtained from this program using "Clustsim," which has been shown to maintain false-positive rates around 5% (Cox, Chen, Glen, Reynolds, & Taylor, 2017). On the basis of output from this program, a voxel-wise threshold of $z = 3.615$ ($p < .0003$) with a minimum cluster size of 75 voxels was used, to set the corrected FWE rate at .05.

Because multiple comparison correction in whole-brain analysis limits power, and given substantial evidence for differences in amygdala response to threat cues in children exposed to violence (McLaughlin et al., 2019), we also conducted an ROI analysis with the amygdala. Bilateral amygdala ROIs were constructed in FSL based on the Harvard Oxford subcortical probabilistic structural atlas, thresholded at 20% probability, and warped back into each participant's native space. The mean of the z scores of every voxel within the bilateral amygdala ROI was then extracted for the fear-versus-neutral contrast for each participant. Differences in amygdala response as a function of threat and deprivation were examined using linear regression, controlling for age, sex, and log income-to-needs, using R Version 4.0.0.

Mean z scores were extracted from clusters that were significantly associated with threat, deprivation, or early childhood SES to examine their associations with psychopathology.

Linear Regression and Mediation Analyses

Linear regression was used to investigate the associations of (1) the income-to-needs ratio in early childhood (referred to hereafter as SES) with experiences of threat and deprivation, controlling for age and sex; (2) SES with symptoms of psychopathology, controlling for age and sex; and (3) the threat and deprivation composites with symptoms of psychopathology, controlling for SES, age, and sex. Indirect effects with bootstrapped confidence intervals (10,000 iterations) were calculated using the "boot" package in R (Canty & Ripley, 2021) to evaluate whether threat and deprivation experiences mediated associations between early childhood SES and psychopathology symptoms.

Next, we examined the associations of threat and deprivation composites with neural responses during the face processing task for the contrast of fearful > neutral faces at the whole-brain level and in relation to the left and right amygdala ROIs. False discovery rate was used to control for multiple comparisons in the amygdala ROI analyses. We then examined the association of neural activity within brain regions that were significantly associated with threat or deprivation with symptoms of psychopathology, controlling for the threat and deprivation composites, age, sex, and SES. PTSD symptoms were positively skewed and zero-inflated. Furthermore, because the absence of trauma exposure that explains a large portion of the zeroes, many of the zeroes are explainable by a separate process than the positive counts of PTSD symptoms. Therefore, zero-inflated Poisson regression using the "pscl" package (Jackman et al., 2020) was used to evaluate the association between neural response to threat and PTSD symptoms. This approach uses a two-component mixture model, composed of a count model and a zero-inflation model. The count model uses Poisson regression with a log link. The zero-inflation model is binomial with a logit link. The zero-inflation model as implemented in the "pscl" package estimates whether or not the outcome variable is zero. Therefore, a positive coefficient indicates lower incidence of PTSD symptoms, and a negative coefficient indicates greater incidence of PTSD symptoms.

All regression models were checked for possible multicollinearity problems using the mctest package in R (Muhammad & Muhammad, 2020). The variance inflation factor did not exceed 1.40, and the lowest tolerance was 0.715 and so did not indicate multicollinearity problems (O'brien, 2007). To evaluate the normality of model residuals, skewness and kurtosis of model residuals were calculated for all traditional linear regression models. Skewness of residuals did not exceed 1.46, and kurtosis of residuals did not exceed 5.18 for models with depression, anxiety, deprivation, or amygdala reactivity as outcomes. Thus, the residuals of these models were considered sufficiently normal, especially for a sample of this size (Lumley, Diehr, Emerson, & Chen, 2002). Conversely, in the model with the threat composite as the outcome variable, skewness exceeded 2, and kurtosis exceeded 7. Visual inspection of the data suggested that this was largely attributable to a single outlier with a very high value on the threat composite. When this value was winsorized, skewness of this model was 1.64, kurtosis was 5.18, and neither the parameter estimates nor significance of any models was substantially altered. Final models are therefore presented with the original value for this participant.

RESULTS

Descriptive Statistics

Descriptive statistics and zero-order correlations are summarized in Table 1. Reproducible code, data, and complete results of analyses (R markdown) are available online at github.com/dgweissman/depthreat.

Early Childhood SES, Adversity Experiences, and Psychopathology Symptoms

Lower early childhood SES was associated with higher symptoms of depression (B = −1.82, SE = 0.50, p < .001) and greater incidence (B = 0.782, SE = 0.222, p < .001) and severity (B = −0.242, SE = 0.038, p < .001) of PTSD symptoms based on zero-inflated Poisson regression in early adolescence. A positive value in the zero-inflation part of the model indicates how strongly that variable corresponds with a zero on the outcome variable. Therefore, high SES is associated with having 0 PTSD symptoms, and low SES is associated with greater incidence of PTSD symptoms. Early childhood SES was not related to anxiety symptoms.

Lower early childhood SES was associated with greater exposure to threat (B = −0.331, SE = 0.067, p < .001) and deprivation (B = −0.352, SE = 0.062, p < .001) experiences.

Adversity Experiences and Psychopathology

Greater frequency and severity of threat-related experiences (B = 1.86, SE = 0.53, p < .001) and deprivation experiences (B = 2.53, SE = 0.57, p < .001) were each associated with higher depression symptoms. In a mediation analysis, higher levels of both threat (95% CI [−1.153, 0.180]) and deprivation (95% CI [−1.616, 0.462]) each mediated the association between lower childhood SES and depression symptoms (Figure 1A).

Exposure to threat, but not deprivation, was associated with greater incidence (B = −1.096, SE = 0.336, p = .001) and severity (B = 0.306, SE = 0.034, p < .001) of PTSD symptoms based on zero-inflated Poisson regression. Threat mediated the association between lower family SES and both the incidence (95% CI [0.136, 0.700]) and severity (95% CI [−0.190, 0.034]) of PTSD symptoms (Figure 1B).

Neither threat nor deprivation was significantly associated with anxiety symptoms.

Neural Activation During Emotional Face Viewing

In the entire sample, fearful relative to neutral faces elicited widespread activation, including in medial and ventrolateral pFC, precuneus, ventral temporal cortex, STS, and temporal pole (Figure 2, Table 2). Neural activation in the left (mean z score = 0.168, t = 2.39, p = .036) but not the right (mean z score = 0.112, t = 1.68, p = .096) amygdala was significantly greater in response to fearful versus neutral faces.

SES, Adversity Experiences, and Neural Response to Faces

Whole-brain multiple regression analysis revealed that more frequent and severe experiences of threat-related adversity, controlling for deprivation experiences, were associated with

higher activation in the ACC and dorsomedial pFC (dmPFC), to fearful relative to neutral faces (Table 2, Figure 3). In contrast, deprivation-related adversity experiences were not associated with neural activation to fearful relative to neutral faces, controlling for threat-related experiences. No significant associations between threat- or deprivation-related adversity and amygdala activation to fearful relative to neutral faces were observed.

Lower early childhood SES was marginally associated with greater activation in the left (B = −0.211, SE = 0.103, p =.053) and right (B = −0.190, SE = 0.097, p = .053) amygdala in ROI analyses and significantly associated with greater activation in the left uncus, proximal to the amygdala in whole-brain analyses (Table 2). Neither activation in the dmPFC or left uncus clusters that were associated with threat and SES, respectively, was associated with psychopathology when controlling for threat, deprivation, and early childhood SES.

DISCUSSION

Low childhood SES is associated with increased risk for multiple forms of psychopathology (Peverill et al., 2021). In this study, we provide evidence for both environmental pathways that contribute to socioeconomic disparities in mental health and neural functioning. Low family SES in early childhood was associated with higher levels of depression and PTSD symptoms in early adolescence. Children raised in lower-SES families experienced higher levels of adversity involving both threat and deprivation, which each mediated the association of SES with depression symptoms. In contrast, only threat-related adversity mediated the association of SES with PTSD symptoms. Exposure to more severe and chronic experiences of threat, but not deprivation, was associated with increased neural activation in the dmPFC—a hub of the default mode network—when viewing fearful compared to neutral faces. Thus, childhood adversity characterized by threat, but not deprivation, may shift neural processing of threat-related cues in the environment. More broadly, these findings support a dimensional approach to characterizing adversity by demonstrating how experiences of threat and deprivation influence socioeconomic disparities in mental health through distinct mechanisms.

Children raised in low-SES families are more likely to experience a wide range of adverse experiences than their higher-SES peers (Rosen et al., 2020; Evans & Cassells, 2014; McLaughlin et al., 2011; Evans, 2004; Bradley, Corwyn, McAdoo, & Coll, 2001). Here, we demonstrate that experiences of both threat and deprivation were more common among children from lower SES backgrounds and contributed to socioeconomic disparities in mental health by early adolescence. Greater exposure to both threat and deprivation experiences explained higher levels of depression symptoms among children from low-SES families. This is consistent with prior work, which has demonstrated that threat and deprivation are independently associated with psychopathology (Miller, Machlin, McLaughlin, & Sheridan, 2021; Miller et al., 2018). In these studies, threat-related adversity had direct associations with psychopathology, whereas deprivation-related adversity influenced psychopathology indirectly through its impact on language functioning. In contrast, only threat-related adversity mediated the association between low SES and PTSD symptoms. Given that trauma exposure is a prerequisite for a diagnosis of PTSD, it is unsurprising that associations between income and PTSD symptoms would be mediated

solely by threat. Conversely, neither SES, threat, nor deprivation was associated with symptoms of anxiety in this sample. Nonetheless, together, these findings highlight an environmental pathway involving elevated exposure to multiple forms of adversity that contributes to socioeconomic disparities in youth mental health.

We additionally document alterations in neural responses to emotional cues associated specifically with threat-related adversity. Children who experienced more severe and frequent exposure to violence exhibited greater activation in the dmPFC when viewing fearful relative to neutral faces after controlling for both SES and experiences of deprivation. The dmPFC is a brain region involved in mentalizing (i.e., representing the thoughts and emotions of one's self and others), autobiographical memory, and prospection (Spreng, Mar, & Kim, 2009). Among youth exposed to higher levels of violence, fearful faces may evoke engagement of mentalizing to a greater degree to identify the source of the potential threat. This interpretation is consistent with evidence that children exposed to violence tend to identify threat cues, including fearful faces, faster and with less perceptual information than children who have never experienced violence (Pollak et al., 2009; Pollak & Sinha, 2002). Alternatively, fearful faces may evoke memories of one's own experiences of fear and distress to a greater extent among youth who have more varied, frequent, and severe threatening experiences, consistent with extensive work demonstrating that trauma-relevant cues trigger memory for prior traumatic events. However, future work could help validate and disentangle these potential explanations by examining whether greater activation of dmPFC to fearful versus neutral faces in youth exposed to higher levels of threat relates to behavioral measures of acuity and speed at identifying fear or anger in others, or the extent to which fear cues primed recall of autobiographical memories of one's own experiences of fear (Ehring & Ehlers, 2011; Amir, Leiner, & Bomyea, 2010; Michael, Ehlers, & Halligan, 2005).

In contrast, as expected, experiences of deprivation were not associated with neural responses to fearful relative to neutral faces. This is consistent with the predictions of the dimensional model of adversity, which suggest that although the absence of typical developmental inputs among children from deprived environments constrains learning opportunities important for cognitive development, neural responses to emotion in the absence of cognitive demands are less likely to be influenced by experiences of deprivation relative to threat (McLaughlin et al., 2021; McLaughlin, Sheridan, & Lambert, 2014). Indeed, a recent systematic review observed no association of deprivation-related adversity with neural responses to threat cues in the amygdala or salience network (McLaughlin et al., 2019). Conversely, reductions in cortical thickness and volume in the fronto-parietal control network have consistently been associated with deprivation-related adversity (McLaughlin et al., 2019; McLaughlin, Sheridan, et al., 2014; Edmiston et al., 2011) in regions that support emotion regulation processes (Niendam et al., 2012; Hartley & Phelps, 2010; Eippert et al., 2007; Levesque et al., 2004). These changes in cortical structure may be a neural pathway influencing psychopathology among youth who experience high levels of deprivation, a possibility that is important to examine in future research. Overall, these findings add to a growing body of evidence suggesting that threat and deprivation influence the emergence of psychopathology through distinct mechanisms (McLaughlin et al., 2021).

Contrary to our hypothesis, threat-related adversity was not associated with amygdala response to fearful compared with neutral faces, nor was it associated with activation in the insula or other regions of the salience network. Interestingly, lower early childhood SES was marginally associated with greater activation in both left and right amygdala and was significantly associated with greater activation in the left uncus, very proximal to the amygdala in whole-brain analyses. These associations were only observed when threat and deprivation were included in the model. This is consistent with prior findings in which low SES was found to be associated with greater amygdala reactivity specifically in youth who were not exposed to violence (White et al., 2019). However, in that same study, violence exposure was also associated with greater amygdala reactivity. Indeed, most studies examining measures of threat-related adversity have found elevated activation in amygdala and anterior insula to negative emotional cues in children and adolescents (McLaughlin et al., 2019; McLaughlin, Peverill, Gold, Alves, & Sheridan, 2015; Suzuki et al., 2014; McCrory et al., 2011, 2013). Conversely, and consistent with our findings, most studies of deprivation or cumulative measures of adversity have not found increased amygdala reactivity to negative emotional cues (McLaughlin et al., 2019). However, in recent work using this same task in a different sample, we also did not find a significant association between violence exposure and amygdala reactivity to fearful faces (Weissman et al., 2019). It is plausible that the lack of an association between threat-related adversity and amygdala reactivity in this study is attributable to task design. The task paradigm used in the current study did not constrain attention, a decision made because prior evidence indicates that attentional constraints reduce amygdala reactivity (Costafreda, Brammer, David, & Fu, 2008). However, this may have allowed for participants to divert their attention away from the faces more. Indeed, a prior study found that adults exposed to childhood adversity had greater amygdala reactivity to fearful and angry faces when attention was constrained but lower amygdala reactivity when it was not (Taylor, Eisenberger, Saxbe, Lehman, & Lieberman, 2006). In addition, that study included only fearful faces, whereas many notable studies demonstrating associations between threat-related adversity and amygdala reactivity include angry faces (e.g., McCrory et al., 2011, 2013). Fearful facial expressions indicate the presence of a potential threat in the environment, as reflected in another person's fear or distress. However, the fearful expression is not threatening in and of itself in the way that an angry expression is. Indeed, the brain regions activated by fearful relative to neutral faces in the current study overall are more consistent with engagement of social information processing in general (Fusar-Poli et al., 2009; Nelson, Leibenluft, McClure, & Pine, 2005), rather than a salience network response to threat (Menon, 2011).

This study had several strengths, including a well-powered sample recruited to ensure sufficient variability in both threat exposure and deprivation as dimensional measures and integration of multiple measures of threat and deprivation from both youths and parents. However, three primary limitations are important to consider when interpreting these findings. First, because the age range of the participants was constrained to early adolescence, we are unable to definitively characterize the specificity or generalizability of these findings across childhood and adolescence. Future work should examine these questions in a broader age range to determine how deprivation and threat exposure are differentially associated with brain function across development. Second, our measures

captured the variety, frequency, and severity of threat and deprivation experiences but may not fully capture other important characteristics such as developmental timing of these exposures or the subjective distress or interpretations of these experiences, which may be important in shaping developmental outcomes (Smith & Pollak, 2020). Finally, the stimuli in the current study included only fearful and neutral faces. Therefore, we are unable to determine whether the greater activation in dmPFC among youth exposed to higher threat characterizes a pattern of responding to expressions of fear specifically or negative emotion more generally.

In conclusion, in a prospective design, we demonstrate that experiences of threat and deprivation are environmental pathways that differentially contribute to socioeconomic disparities in mental health and alterations in neural function to affectively salient cues. Both threat and deprivation played a role in explaining socioeconomic disparities in depression, whereas only threat experiences were associated with PTSD severity. Consistent with the dimensional model of adversity, only threat-related adversity experiences were associated with neural responses to emotional cues, highlighting the importance of a nuanced approach to characterizing early environmental experiences when examining their links with neurodevelopmental processes.

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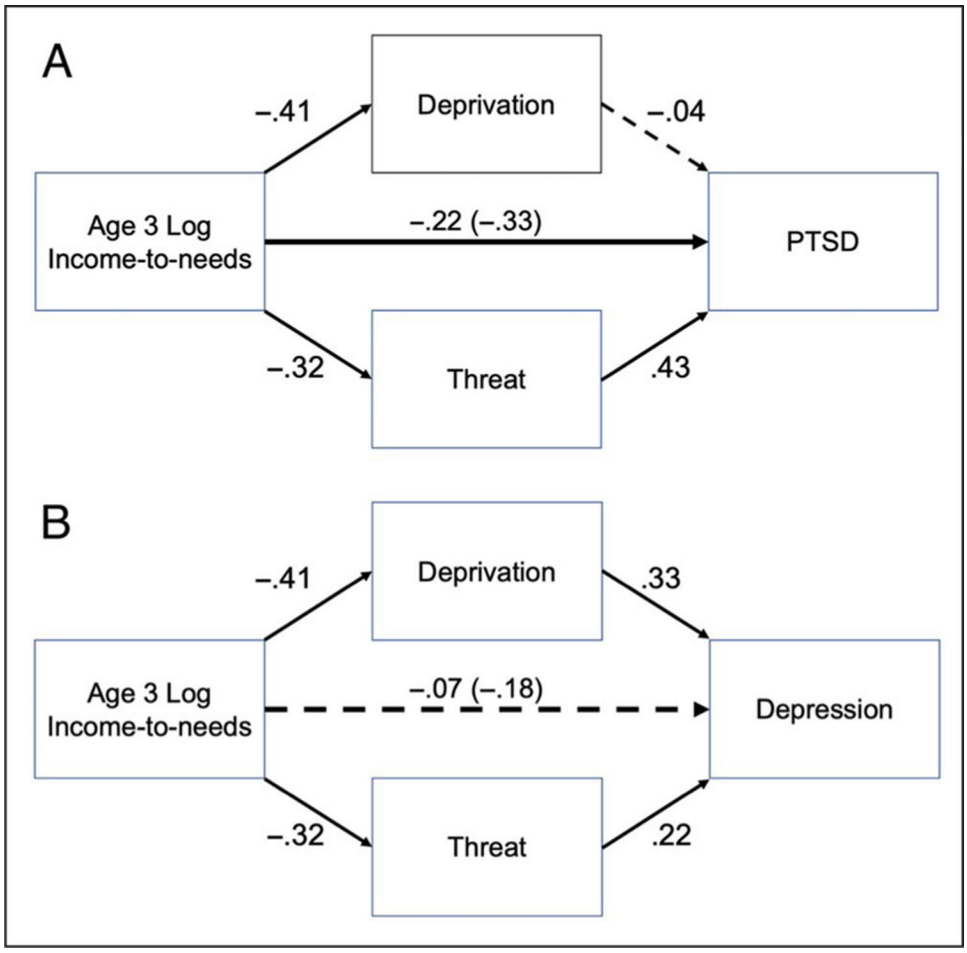

Figure 1.

Deprivation and threat mediate associations between early childhood income and psychopathology. Depiction of mediation models. All paths are standardized coefficients from regression models. Solid lines represent significant regression coefficients. Dotted lines represent nonsignificant coefficients. Coefficients for PTSD are from the count model from zero-inflated Poisson regression, which represents the severity of nonzero PTSD symptoms. Values in parentheses represent the standardized coefficient of the c path, the association between age 3 log income-to-needs and the psychopathology outcome, not controlling for mediators.

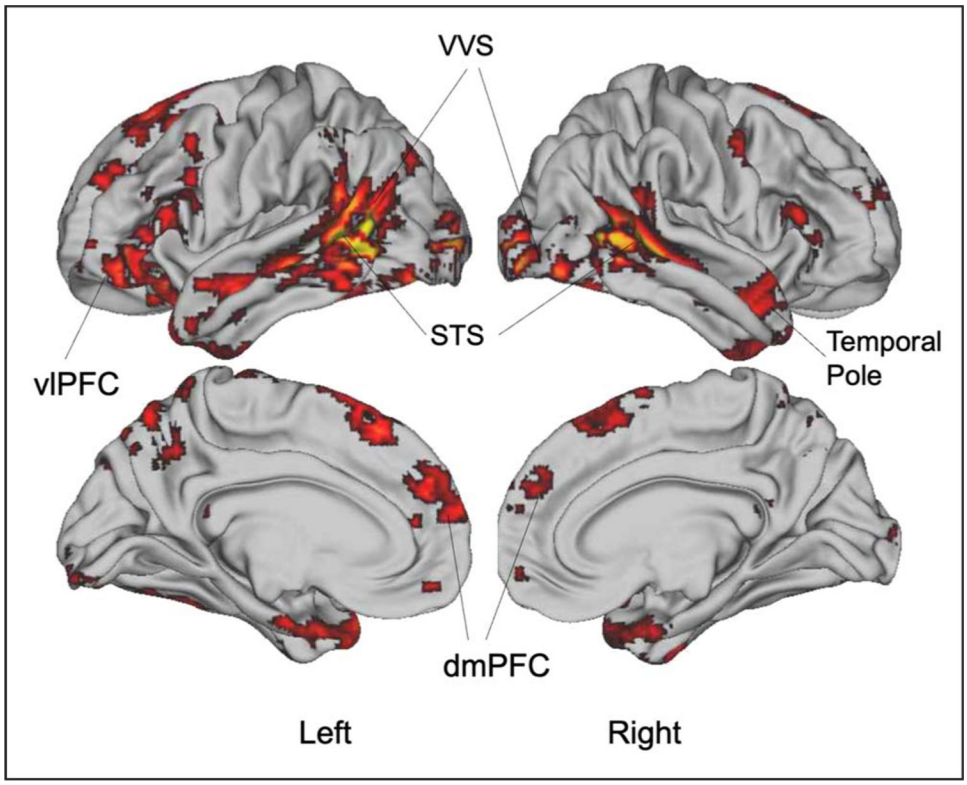

Figure 2.

Neural activation during emotional face viewing. This figure depicts significant activation in the lateral (top) and medial (bottom) surfaces of the brain when participants viewed fearful versus calm faces. vlPFC = ventrolateral pFC; VVS = ventral visual stream.

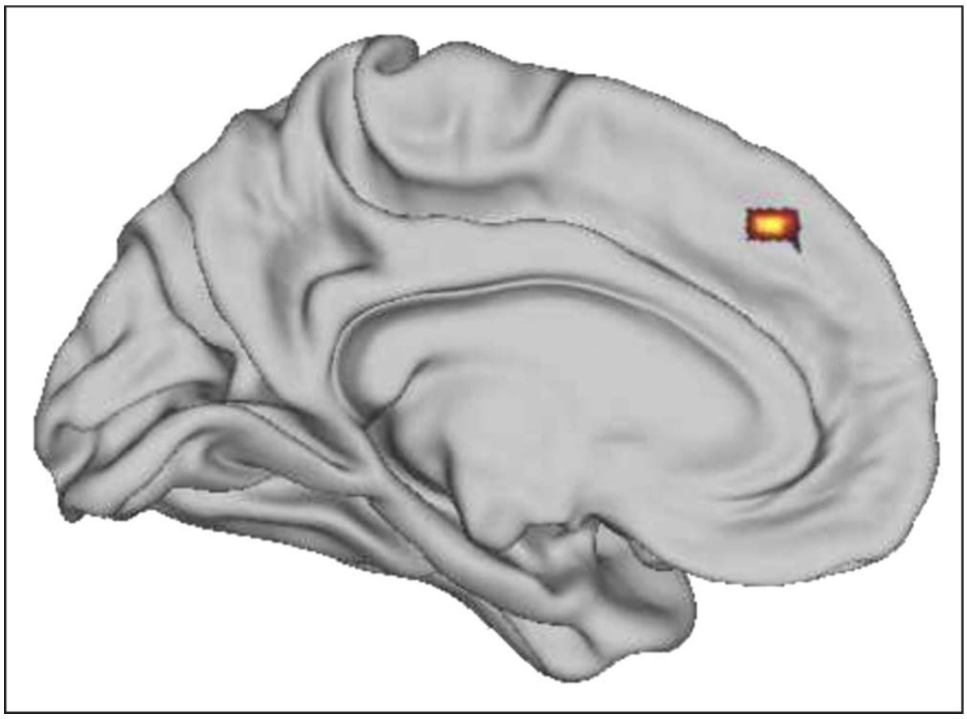

Figure 3.

Whole-brain analysis: Activity to fear versus neutral faces is associated with threat exposure. This figure depicts cluster in the dmPFC where exposure to threat-related adversity is significantly related to greater neural activation to fearful versus calm faces.

Table 1.

Descriptive Statistics and Intercorrelations

	N	*%*	*Cohen's d*	*Correlations*							
1. Sex (female)	83	46.9		–							
	M	*SD*	*Range*	*1*	*2*	*3*	*4*	*5*	*6*	*7*	*8*
2. Age	11.62	0.51	10.91–13.18	.184	–						
3. Log income-to-needs	0.89	0.77	−1.52–2.10	−.092	−.032	–					
4. Threat	0.05	0.73	−.53–4.91	.267	−.043	−.354*	–				
5. Deprivation	−0.02	0.69	−1.22–2.48	.253	−.022	−.399*	.371*	–			
6. Anxiety symptoms	17.44	10.47	1–55	.094	−.029	−.062	.187*	.168*	–		
7. Depression symptoms	4.86	5.31	0–27	.325*	−.039	−.269*	.405*	.451*	.536*	–	
8. PTSD severity	4.47	8.64	0–45	.156	−.004	−.329*	.517*	.203*	.236*	.444*	–

Cohen's *d* is provided for all variables in relation to sex. All other bivariate associations are correlations.

* $p < .05$.

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Table 2.

Results of Whole-Brain Analyses of Neural Response to Fearful vs. Neutral Faces

Voxels	Peak (x, y, z)	Region	Peak Voxel z Score
Task main effects			
4,912	−28, −84, −22	Left fusiform gyrus	5.86
3,725	30, −82, −24	Right fusiform gyrus	5.82
1,913	−30, 18, −30	Left superior temporal gyrus	5.43
785	0, −64, 54	Precuneus	4.62
779	30, 18, −30	Right superior temporal gyrus	4.68
668	−2, 22, 60	Left superior frontal gyrus	4.18
556	−6, 70, 18	Left medial frontal gyrus	4.45
389	54, 16, −6	Right inferior frontal gyrus	4.37
125	−18, 54, 32	Left superior frontal gyrus	3.70
Age 3 log income-to-needs ratio			
125	−10, −8, −32	Left uncus	−4.02
Threat			
78	2, 36, 34	Right cingulate gyrus	4.08

Peak (*x*, *y*, *z*) = Montreal Neurological Institute coordinates for the voxels with the highest coefficients within each cluster, voxel-wise *p* threshold = .0003, minimum cluster size = 75, 2 × 2 × 2 mm voxels.