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Archival Report

Neurobiological Markers of Resilience to Depression Following Childhood Maltreatment: The Role of Neural Circuits Supporting the Cognitive Control of Emotion

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ABSTRACT

BACKGROUND: Childhood adversity is strongly linked to negative mental health outcomes, including depression and anxiety. Leveraging cognitive neuroscience to identify mechanisms that contribute to resilience in children with a history of maltreatment may provide viable intervention targets for the treatment or prevention of psychopathology. We present a conceptual model of a potential neurobiological mechanism of resilience to depression and anxiety following childhood adversity. Specifically, we argue that neural circuits underlying the cognitive control of emotion may promote resilience, wherein a child's ability to recruit the frontoparietal control network to modulate amygdala reactivity to negative emotional cues—such as during cognitive reappraisal—buffers risk for internalizing symptoms following exposure to adversity.

METHODS: We provide preliminary support for this model of resilience in a longitudinal sample of 151 participants 8 to 17 years of age with (n = 79) and without (n = 72) a history of childhood maltreatment who completed a cognitive reappraisal task while undergoing functional magnetic resonance imaging.

RESULTS: Among maltreated youths, those who were better able to recruit prefrontal control regions and modulate amygdala reactivity during reappraisal exhibited lower risk for depression over time. By contrast, no association was observed between neural functioning during reappraisal and depression among youths without a history of maltreatment.

CONCLUSIONS: These preliminary findings support the hypothesis that children who are better able to regulate emotion through recruitment of the frontoparietal network exhibit greater resilience to depression following childhood maltreatment. Interventions targeting cognitive reappraisal and other cognitive emotion regulation strategies may have potential for reducing vulnerability to depression among children exposed to adversity.

Keywords: Adolescence, Adversity, Depression, Emotion regulation, Neurobiological, Resilience

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Childhood adversity, which robustly predicts psychopathology (1–3), refers to negative experiences that deviate from the expectable environment, requiring meaningful adaptation by an average child (4). These experiences can reflect either threat, defined as relating to harmful experiences, or deprivation, the absence of expected environmental inputs, such as caregiver support and cognitive stimulation (5–7). This paper focuses on childhood adversity in the form of threat, specifically maltreatment (e.g., physical or sexual abuse), as it has particularly strong ties to depression and anxiety (3,8–10).

Although childhood adversity is a powerful predictor of psychopathology, this relationship is not deterministic; many children who have encountered severe forms of adversity demonstrate resilience and do not go on to develop mental health problems (11–15). Resilience involves processes that buffer children from risk for these negative consequences (16). Identifying mechanisms of resilience may reveal targets for preventative interventions designed to protect children following adversity (4). Considerable work examines factors that promote resilience (15,16), but few studies examine neurobiological mechanisms conferring resilience among children exposed to threat-related adversity. Here, we advance a neurobiological model of resilience, focusing on neural circuits underlying the cognitive control of emotion. Specifically, we posit that a child's ability to recruit the frontoparietal control network to modulate amygdala reactivity to negative emotional cues—such as during cognitive reappraisal and other effortful forms of emotion regulation—buffers risk for internalizing symptoms following exposure to adversity. We provide preliminary data testing this proposed framework using

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neuroimaging data of cognitive reappraisal in a longitudinal sample of children and adolescents exposed to maltreatment.

DEFINING RESILIENCE

Developmental and clinical psychologists have long been interested in resilience, and various definitions have been proposed. Some have conceived of resilience as a fixed trait or set of traits that are immutable (17–19) and may be present within an individual whether or not they have experienced adversity (20). Instead, we utilize the definition that resilience reflects an absence of negative outcomes despite exposure to adversity (15,16,21). To study this form of resilience from an empirical perspective, one must identify specific factors or developmental processes that moderate the association between adversity and negative outcomes, such that the adversity-negative outcome relationship is weaker among those who have higher levels of the resilience factor.

Resiliency factors can occur at multiple interacting levels of the bioecological milieu (22–24), from entire cultures (25) to neighborhoods (26), to families (27), to children's temperaments (28), all the way down to individual genes (29). In addition, the factors that lead to resilience may depend on the nature of the adversity experienced and the social and cultural context to which an individual must adapt (24). Developmental cognitive neuroscience may generate unique insights into resiliency factors. Work in this area can be leveraged to identify resilience mechanisms at the level of specific cognitive-affective processes and their underlying neural networks that confer protection against psychopathology following experiences of adversity. Moreover, a rich history in this area informs research performed at the therapeutic level (30). Identifying specific neurobiological, cognitive, and affective mechanisms of resilience that are modifiable is critically important for informing models of risk and resilience, as well as identifying viable targets for intervention to treat or prevent psychopathology (4).

Here, we advance the possibility that the effective engagement of cognitive control networks in service of modulating negative emotions may be a neurobiological mechanism of resilience to depression and anxiety following childhood adversity. Neural circuits underlying the cognitive control of emotion, including the frontoparietal control network, have been most studied in relation to the emotion regulation strategy of cognitive reappraisal.

COGNITIVE REAPPRAISAL

Cognitive reappraisal involves thinking about a stimulus in a way that changes the meaning to modify one's emotional response (e.g., to reduce negative or enhance positive emotion) (31–36). Cognitive reappraisal has been shown to modulate emotional responses in experimental settings (31,32,37–40), real-world settings (38,41), and clinical intervention studies, where training to enhance reappraisal is associated with reductions in symptoms of depression and anxiety in children and adults (42–44).

Functional magnetic resonance imaging studies reveal a network of brain regions recruited during cognitive reappraisal that modulate amygdala activation (45). These studies typically use specific reappraisal strategies, such as psychological distancing or reinterpretation, as tactics for reducing emotional responses to negative stimuli (e.g., images of a car crash) (31,34,35,46–49). Meta-analysis shows that during cognitive reappraisal compared with passive viewing of emotional stimuli, regulatory regions of the frontoparietal network are engaged and modulate amygdala activity (50). The frontoparietal regions recruited during cognitive reappraisal are broadly involved in cognitive control (51,52) and include multiple prefrontal regions in both dorsal and ventral areas, the dorsal anterior cingulate, as well as posterior association cortex encompassing inferior parietal sulcus (31,34,50,53–57). Recruitment of the frontoparietal network during reappraisal may serve to select and maintain reappraisal-related features and goals while engaging in and monitoring progress of the construction of a new appraisal (45,56).

Studies examining reappraisal in youths have shown that children as young as 6 years old can successfully employ this technique (57). Moreover, the extent of reappraisal success appears to improve linearly with age (36,57–59) in association with increasing recruitment of prefrontal regions (57). It should be noted, however, that some studies show that behavioral indices of reappraisal success appear similar across development (60,61), which could be explained by the type of reappraisal tactic being used (e.g., reinterpretation vs. distancing), as reinterpretation requires more complex, higher-order thinking.

Both adults and youths express patterns of frontoparietal recruitment during reappraisal in ways that modulate amygdala activation (36,57,59,62–64). Given the amygdala's role in the processing of salient events (65–67), levels of amygdala modulation may reflect successful regulation of affective responding, although the specific patterns of connectivity that underlie this modulation remain a source of debate. Because lateral prefrontal regions have sparse direct projections to the amygdala, some studies suggest that activation in these regions modulates amygdala function via projections through the more densely connected medial prefrontal cortex (53,57,68–72). Alternatively, lateral prefrontal regions may modulate amygdala activity via projections through lateral temporal cortex regions involved in semantic representation (34,39,50,64). In either case, stronger inverse coupling between the prefrontal cortex and the amygdala is believed to produce greater reductions in negative emotion during reappraisal (53,55). Below, we argue that the ability to successfully modulate the amygdala by recruiting this cognitive control circuitry in the service of reappraisal is a key neurobiological mechanism of resilience to depression and anxiety following experiences of adversity.

COGNITIVE REAPPRAISAL NEURAL CIRCUITRY IN DEPRESSION AND ANXIETY

Behaviorally, children and adults with depression and anxiety report similar reductions in negative emotion following reappraisal as those without psychopathology (31,48,73–77). However, those with depression and anxiety appear to use less-efficient reappraisal strategies (73,74). Disruptions in neural activation of frontoparietal and limbic regions involved in cognitive reappraisal have also been associated with depression and anxiety. However, findings vary across age and

diagnosis. Some studies find affected relative to unaffected individuals to show greater recruitment of frontoparietal regions and heightened amygdala activity during cognitive reappraisal (48,69,73,76), whereas others find affected individuals to show reduced recruitment across prefrontal regions (77,78) or no amygdala differences (31,75,78). Taken together, data suggest that affected individuals manifest some form of disrupted prefrontal capacity to modulate the amygdala, which may reflect less-efficient recruitment of regions supporting reappraisal processes.

COGNITIVE CONTROL CIRCUITRY AS A MECHANISM OF RESILIENCE FOLLOWING CHILDHOOD ADVERSITY

The ability to effectively recruit frontoparietal circuitry in support of effortful emotion regulation strategies, such as cognitive reappraisal, could be a critical compensatory mechanism that may help to buffer against the heightened emotional and neurobiological reactivity commonly observed following childhood adversity. Prior work consistently demonstrates that children exposed to adversity, particularly experiences of threat, exhibit elevated emotional responses to negative stimuli assessed at multiple levels of analysis, including subjective report (79–82), autonomic nervous system response (83,84), and amygdala reactivity (49,85–89), the latter of which has also been confirmed in meta-analysis (90). Heightened emotional reactivity is a well-established risk factor for the emergence of depression and anxiety in youths (80,81,91–96). The ability to recruit frontoparietal circuitry to modulate amygdala reactivity may buffer children from internalizing problems that arise following these adversity-related increases in emotional reactivity. Indeed, among children exposed to adversity, a growing body of evidence links greater structural and functional integrity within emotion regulatory circuits—encompassing connections between multiple regions of the medial prefrontal cortex and the amygdala—to resilience, in the form of lower risk for negative mental and physical health outcomes (97–100). These studies provide preliminary support for the notion that the ability to recruit prefrontal circuitry to modulate amygdala responses may be a neurobiological mechanism underlying adaptation to childhood adversity that dampens emotional and neurobiological hyperreactivity, ultimately contributing to lower risk for psychopathology.

Effective cognitive reappraisal capacity may also be particularly important for children who have experienced adversity, owing to the strong continuity between exposure to adversity and subsequent exposure to stressful life events. Experiences of childhood adversity are highly co-occurring, such that children who experience one form of adversity (e.g., sexual abuse) typically experience several others (e.g., neglect and domestic violence) (1,3). In addition, children exposed to adversity experience higher levels of stressful life events and chronic stress across academic, peer, and family domains (98,101). Exposure to stressful life events and chronic stressors are well-established risk factors for depression and anxiety (102–105), and the link between stressful life events and internalizing psychopathology is stronger among those who have experienced childhood adversity (101,106–109). The ability to effectively utilize cognitive reappraisal may protect children from the negative mental health consequences of ongoing exposure to stressors, as has been shown in adults (110). Indeed, animal models of stress in nonhuman primate research support the notion that enhanced recruitment of regulatory circuits may promote resilience following early life stress (e.g., maternal separation) (111). For children who have experienced maltreatment, the capacity to flexibly deploy cognitive reappraisal and underlying control circuitry may be all the more important, considering the high likelihood that these children live in chronically stressful environments that frequently elicit negative emotions. However, no study to date has explicitly tested whether children's ability to explicitly engage effortful regulation strategies and recruit prefrontal circuitry to modulate amygdala responses to negative emotional cues moderates risk for depression and anxiety following adversity.

EVALUATING A NEUROBIOLOGICAL MECHANISM OF RESILIENCE

Using preliminary data from our group, we completed a set of exploratory analyses to provide an empirical test of our proposed mechanism of resilience. Specifically, we assessed whether the ability to modulate amygdala reactivity using cognitive reappraisal is a potential neurobiological mechanism of resilience to depression and anxiety among children exposed to maltreatment, a form of adversity that has particularly strong associations with internalizing psychopathology. If the proposed neurobiological mechanism of resilience is valid, we should expect that the association between child maltreatment and depression and anxiety symptoms will be weaker among children and adolescents who exhibit 1) greater modulation of amygdala responses to negative stimuli using cognitive reappraisal; 2) greater recruitment of prefrontal regions known to be engaged during successful cognitive reappraisal; and 3)

Figure 1. Schematic representation of experimental task. While undergoing functional magnetic resonance imaging, participants were instructed to either look at an emotional image (neutral or negative) or attempt to decrease their emotional response using cognitive reappraisal (negative images only). Following the presentation of the image, participants reported the strength of emotion they experienced while viewing the image. Between trials, participants were instructed to relax.

Table 1. Summary of Participant Demographic and Clinical Characteristics

	Nonmaltreated (n = 72)		Maltreated (n = 79)			
Participant Characteristics	Mean	SD	Mean	SD	t Value	p Value
Age, Years	12.57	2.55	12.94	2.69	−0.86	.394
Pubertal Stage	2.88	0.74	3.13	0.86	−1.8791	.062
CDI at Baseline	5.54	4.27	12.16	8.72	−6.01	<.001
CDI at Follow-up	6.14	5.33	10.63	8.41	−3.37	<.001
SCARED at Baseline	26.51	15.70	15.26	10.52	−5.17	<.001
SCARED at Follow-up	21.58	15.12	16.72	9.43	−2.03	.045
ERQ—Reappraisal	27.46	6.34	27.32	8.15	0.12	.906
	n	%	n	%	χ^2	p Value
Gender, Female	33	45.83	43	54.43	0.80	.372
Attrition	15	20.83	24	30.38	1.33	.249
Race, Nonwhite	22	30.56	61	77.22	31.27	<.001
Adversity Exposure						<.001
Physical Abuse	0	0	57	72	80.41	<.001
Emotional Abuse	3	4	44	56	44.28	<.001
Sexual Abuse	0	0	36	46	40.61	<.001
Neglect	0	0	19	24	17.68	<.001

CDI, Children's Depression Inventory; ERQ, Emotion Regulation Questionnaire; SCARED, The Screen for Child Anxiety Related Disorders.

a greater tendency to use reappraisal strategies in their daily lives.

METHODS AND MATERIALS

We examined these hypotheses in a longitudinal sample of 151 participants 8 to 17 years of age with (n = 79) and without (n = 72) history of childhood maltreatment (e.g., physical or sexual abuse) who completed an emotion regulation task while undergoing functional magnetic resonance imaging. This task assessed neural activation during passive viewing and effortful attempts to regulate emotional responses to negative stimuli using cognitive reappraisal (Figure 1). Participants also reported on their tendency to engage in reappraisal in their daily lives. Symptoms of depression and anxiety were assessed at the time of the initial neuroimaging assessment and at a follow-up assessment approximately 2 years later. See Table 1 for participant characteristics. All analyses were completed controlling for gender, age, race/ethnicity, and socioeconomic status (i.e., income-to-needs ratio). We found no evidence for these patterns of resilience in relation to symptoms of anxiety. Below, we report the pattern of results for depression symptoms. For more details on participants, inclusion and exclusion criteria of the study, task design, measures, and analytical approach, see the Supplement.

RESULTS

Preliminary Evidence

Across the entire sample, the use of cognitive reappraisal elicited the expected pattern of activation of frontoparietal

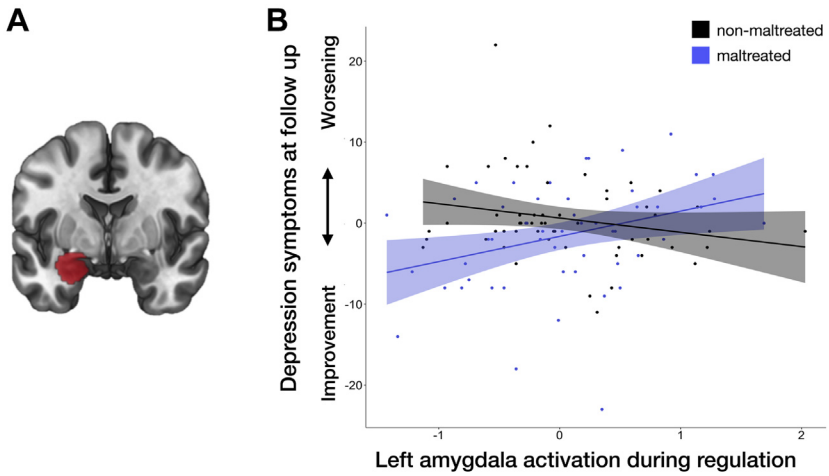

Figure 2. Amygdala activity during cognitive reappraisal moderates the association between child maltreatment and depression symptoms over time. **(A)** Red mask overlay shows left amygdala region of interest. **(B)** Greater reduction in amygdala activation during cognitive reappraisal relative to passive viewing of negative emotional stimuli (decrease negative > look negative) is associated with worsening depression symptoms over time among children who were maltreated (blue) but is unrelated to depression symptoms at follow-up among those without a history of maltreatment (black). Shaded region indicates 95% confidence interval.

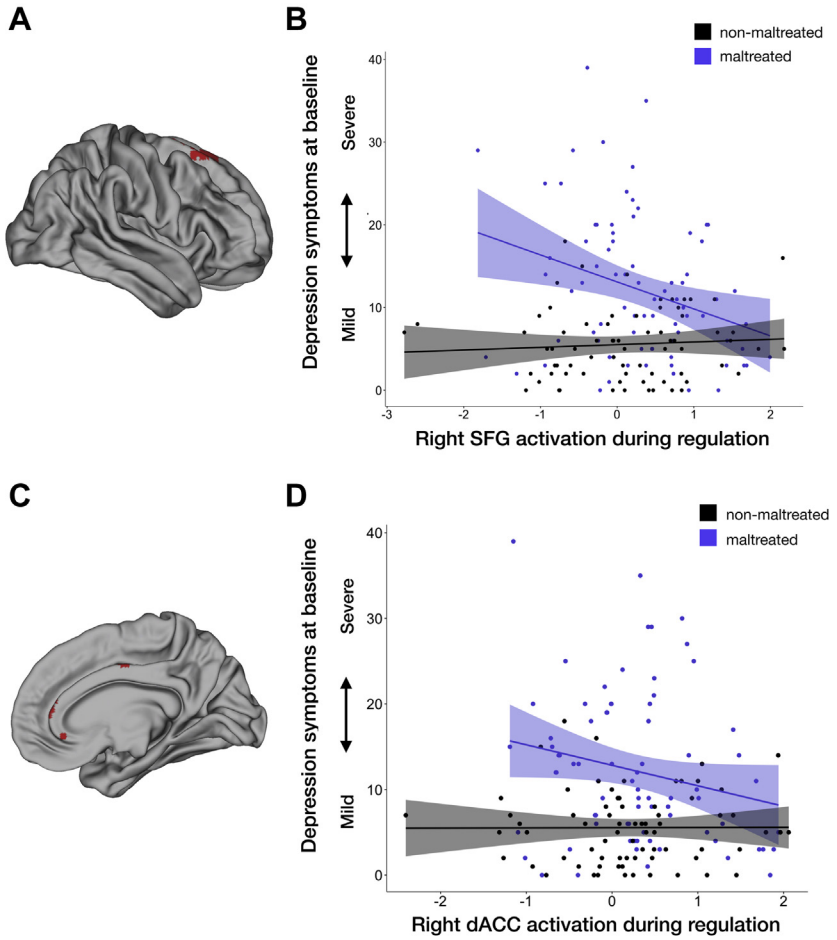

Figure 3. Association of child maltreatment with depression is moderated by prefrontal recruitment during cognitive reappraisal. **(A)** Red mask overlay shows right superior frontal gyrus (SFG) region of interest. **(B)** Greater recruitment of the right SFG during cognitive reappraisal relative to passive viewing of negative emotional stimuli (decrease negative > look negative) is associated with lower symptoms of depression among children exposed to maltreatment (blue) but is unrelated to depression symptoms among those without a history of maltreatment (black). **(C)** Red mask overlay shows right dorsal anterior cingulate cortex (dACC) region of interest. **(D)** Greater recruitment of the right dACC during cognitive reappraisal relative to passive viewing of negative emotional stimuli (decrease negative > look negative) is associated with lower symptoms of depression among children exposed to maltreatment (blue) but is unrelated to depression symptoms among those without a history of maltreatment (black). Shaded region indicates 95% confidence interval.

regions and decreased activation of the amygdala (Supplemental Figure S1). Our primary hypothesis was that maltreated children who exhibited greater modulation of the amygdala during reappraisal (i.e., lower amygdala activity during reappraisal relative to passive viewing of negative stimuli) would be at lower risk for developing depression. To evaluate this hypothesis, we examined whether reappraisal-related amygdala modulation moderated the association between child maltreatment and depression symptoms and observed a significant maltreatment-by-brain function interaction ($b = 4.20$, $t = 2.41$, $p = .018$). Greater reappraisal-related amygdala modulation predicted lower risk for depression at follow-up among maltreated youths but had no relationship to depression among those without a history of maltreatment (Figure 2), suggesting that the ability to modulate amygdala responses using cognitive reappraisal may be a marker of resilience. This finding remained significant after numerous sensitivity analyses (e.g., including pubertal stage as a covariate rather than age, including IQ as a covariate) and survived correction for multiple comparisons. Greater information on the analytical approach and sensitivity analyses can be found in the Supplement.

To follow up this finding, we conducted a set of exploratory analyses examining whether reappraisal-related recruitment of prefrontal regions moderated the association between child maltreatment and depression symptoms. To do so, we examined a set of prefrontal regions that were engaged during reappraisal relative to passive viewing of emotional stimuli in the whole sample (Supplemental Figure S1). This analysis revealed a significant maltreatment-by-brain function interaction in two regions consistently implicated in cognitive reappraisal (50): the right superior frontal gyrus (interaction: $b = -3.11$, $t = -2.50$, $p = .014$) and right dorsal anterior cingulate cortex (interaction: $b = -2.65$, $t = -1.95$, $p = .052$). In both cases, greater recruitment during reappraisal predicted lower depression symptoms at baseline, but only for those with a history of maltreatment (Figure 3). Owing to the exploratory nature of these analyses, the results presented here were not corrected for multiple comparisons. However, these patterns persist in multiple sensitivity analyses examining additional covariates (see the Supplement).

Finally, we assessed whether greater use of cognitive reappraisal as an emotion regulation strategy in everyday life moderated the association between child maltreatment and depression

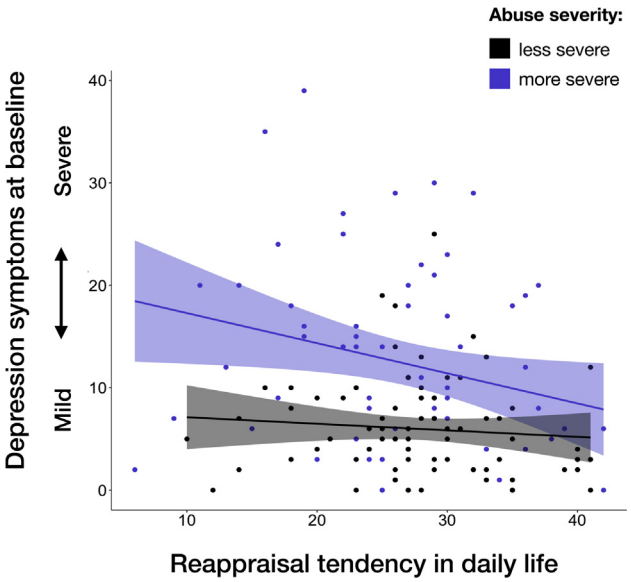

Figure 4. Association between reported tendency to engage in cognitive reappraisal in daily life and depression is moderated by severity of abuse history. Greater reported use of cognitive reappraisal strategies in response to stressful life events is associated with lower symptoms of depression, particularly among children with more severe maltreatment history (blue) compared with those with a less severe or no history of maltreatment (black). Reappraisal use measured using the Emotion Regulation Questionnaire (38). Shaded region indicates 95% confidence interval.

symptoms. Again, we observed a significant maltreatment-by-use interaction in the expected direction ($b = -.044$, $t = -2.420$, $p = .017$), whereby the association between severity of child maltreatment and depression symptoms was weaker among those who reported greater use of cognitive reappraisal (Figure 4). This finding suggests that not only is the efficacy of cognitive reappraisal associated with resilience to depression following child maltreatment, but also the tendency to use reappraisal techniques in everyday life.

DISCUSSION

The ability to modulate negative emotion using cognitive control strategies may represent a resiliency marker, which protects against depression in children who have experienced adversity. The current report finds evidence of such a relationship. Specifically, greater capacity to modulate amygdala activation using cognitive reappraisal predicts decreasing levels of depressive symptoms across a 2-year follow-up period. Similarly, greater recruitment of prefrontal regions also predicts lower concurrent symptoms of depression among children with history of maltreatment. Finally, maltreated children who reported a greater tendency to use reappraisal as a coping strategy in everyday life had lower levels of depression symptoms than those who did not. Of note, in youths unexposed to maltreatment, amygdala modulation, prefrontal function, or reported use of cognitive reappraisal in daily life was not related to symptoms of depression. These preliminary findings support the proposed model of resilience. This model underscores a specific neurobiological marker involved in the cognitive control of emotion as a potential protective factor buffering children who have experienced adversity from negative outcomes later in life.

Examining these questions in a youth sample is particularly advantageous, as insights about mechanisms of resilience can be leveraged to inform early interventions. Additionally, studies examining resilience to psychopathology in adults who experienced childhood adversity often reflect an accumulation of environmental stressors over the life course and suffer from recall biases that are mitigated, at least somewhat, when studying resilience in closer temporal proximity to the initial adversity. The key contribution from the current study relates to the contrast of brain-behavior associations in youths with and without maltreatment. Specific neural markers of effective cognitive reappraisal only related to depressive symptoms in children with a history of maltreatment. As such, the current study delineated a marker of resilience.

Resilience involves many dynamic and interacting factors that modulate risk in the face of adversity (24), including cultural (25), familial (27), and genetic (29) factors. The current study leverages advances in developmental cognitive neuroscience to examine brain function supporting specific cognitive processes as a mechanistic path to resilience. An analysis of resilience on this neuropsychological level is advantageous as it can be used to identify malleable targets for preventing the onset or progression of internalizing disorders. This approach has been successfully undertaken in the context of anxiety and posttraumatic stress disorders, wherein basic mechanistic understanding of threat-related biases in information processing and associated neural functioning has shaped therapeutic approaches (e.g., attention bias modification therapy) aimed at mitigating anxiety and trauma-related symptoms (30,112–115). Attention bias modification therapy was designed to explicitly target the types of attentional biases toward threat that characterize anxiety disorders by training subjects to orient attention away from threatening cues (116,117). As such, it is a model of how basic understanding of neurobiological mechanisms can directly inform preventative and treatment approaches (30,114,118).

Similar translational approaches leveraging neurocognitive understanding of cognitive reappraisal could be useful in preventative and intervention efforts aimed at mitigating risk for internalizing disorders, especially in children who have experienced adversity. Cognitive reappraisal is a core intervention technique central to evidence-based psychotherapy practices for depression and anxiety, such as cognitive behavioral therapy (42). Moreover, cognitive behavioral therapy for depression and anxiety has been associated with changes in frontoamygdala neural circuitry, including reductions in amygdala hyperresponsiveness and increased engagement of medial and lateral regions of the prefrontal cortex both in resting state and during task performance (119,120). Furthermore, our findings show that in addition to cognitive reappraisal ability, the tendency to use it in everyday life may also serve as an important buffer for depression following adversity. Therefore, clinicians may incorporate training geared toward scaffolding and encouraging the use of reappraisal in the daily lives of children exposed to adversity. These strategies may be a useful component of early interventions designed to prevent the onset of internalizing psychopathology following adversity.

The present study was designed to test the proposed framework that the neurobiological underpinnings of emotion regulatory capacity may serve as a buffer against the negative mental health outcomes typically associated with adversity. However, this study should be considered in light of its limitations and the unresolved questions that remain. We focus specifically on outcomes related to early life experiences of threat or maltreatment. Given the highly overlapping experiences of maltreatment and neglect, it is important to make note that children who experience other forms of adversity, such as deprivation or neglect, could also benefit from the protective effects of successful recruitment of regulatory circuitry. Similarly, we have focused on a specific form of cognitive control of emotion—cognitive reappraisal—and it is possible that other forms of cognitive control of emotion, such as acceptance of emotional experiences, may modulate negative emotional experiences and the associated amygdala response in a similar way. Future work should investigate the boundary conditions of this model of resilience and determine whether other strategies of emotional regulation may also function as a protective factor buffering children exposed to various forms of adversity from development of psychopathology. In addition, the aim of the current study was to determine resilience factors. However, the finding that emotion regulation does not benefit those without a history of maltreatment is interesting and may reflect differential etiological mechanisms of depression in those with and without a history of maltreatment, as proposed by Teicher and Samson (121). Finally, these analyses identified markers of resilience that were specific to symptoms of depression and not anxiety, which may reflect factors specific to depression (e.g., rumination over past events) that are more readily reframed using reappraisal, as opposed to anxious worries that have yet to occur. Nonetheless, this divergence provides an important target for future research.

Conclusions

Exposure to child adversity is a potent risk factor for depression and anxiety. Here, we argue that the ability to recruit frontoparietal control networks to modulate amygdala reactivity to negative cues may be a protective factor that buffers children from developing internalizing problems following exposure to adversity. Our findings are consistent with this possibility, demonstrating that children who are more able to modulate amygdala reactivity and recruit prefrontal regions of the frontoparietal network during cognitive reappraisal are less likely to exhibit symptoms of depression following exposure to maltreatment—pointing to a potential neurobiological mechanism of resilience. Greater efforts to identify resilience factors at the neural and behavioral levels can provide mechanistic translational targets for interventions aimed at preventing or treating psychopathology among children who have experienced adversity.

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KAM, DSP, and AMR designed the research; AMR analyzed the data and drafted the manuscript; KAM, DSP, JLJ, and DGW provided critical comments and revisions. All authors approved the final version of the manuscript for submission.

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ARTICLE INFORMATION

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