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Individual Differences in Biological Stress Responses Moderate the Contribution of Early Peer Victimization to Subsequent Depressive Symptoms

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Abstract

Rationale—Some children who are exposed to early peer victimization become depressed, whereas others are resilient. Understanding individual differences in responses to early adversity, such as victimization, is critical for developing both comprehensive theoretical models and effective interventions.

Objectives—This study examined whether individual differences in biological stress responses (i.e., activation of the hypothalamic-pituitary-adrenal axis and autonomic nervous system) moderated the contribution of peer victimization to depressive symptoms across a one-year period.

Methods—Children (N = 132; M age = 9.46 years, SD = .33) completed measures of peer victimization and depressive symptoms, and rated their ruminative responses (i.e., persistent thoughts about negative task-related emotion and experiences) to a laboratory-based social challenge task involving two conflict-of-interests situations with an unfamiliar peer. Children's saliva was collected prior to, and following, participation in the task, and was later assayed for cortisol and alpha amylase [sAA].

Results—Victimization interacted with levels of cortisol measured in anticipation of the task to predict task-related rumination and depressive symptoms one year later, adjusting for initial symptoms. Specifically, victimization served as a risk factor for rumination and depressive symptoms in children with heightened but not dampened anticipatory cortisol; yet, heightened anticipatory cortisol was protective against rumination and depressive symptoms in low-victimized children. Victimization also predicted subsequent depressive symptoms in girls with high sAA reactivity across the task.

Conclusions—This study advances contemporary theory and research by implicating individual variation in biological stress responses as one determinant of sensitivity to the mental health effects of early adversity.

Keywords

peer victimization; biological sensitivity to context; cortisol; sAA; depression

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In the past few decades, increasing attention has focused on the long-term psychological consequences of early adversity (Boyce et al. 1998; Boyce and Ellis 2005; Fox and Rutter 2010; O'Connor 2003). In this context, development scientists have shown that early exposure to peer victimization (i.e., physical, verbal, or psychological abuse by peers) can compromise children's mental health (for a review, see Hawker and Boulton 2000); in particular, both a meta-analysis (Hawker and Boulton 2000) and a qualitative review (Juvonen et al. 2003) suggest a strong link between peer victimization and depression both concurrently (Nadeem and Graham 2005; Prinstein et al. 2001) and over time (Boivin et al. 1995; Rudolph et al 2010). However, not all victimized children become depressed. To fully understand the psychological impact of early adversity, such as peer victimization, it is critical to elucidate why some children suffer adverse consequences whereas others are resilient. The present study tested the proposal that individual differences in the activity of the hypothalamic-pituitary-adrenal (HPA) axis and the autonomic nervous system (ANS)—help to account for variations in the contribution of peer victimization to subsequent depression.

The HPA axis is a slow-acting stress response system; activation of this system triggers a cascade of events that begins with the secretion of corticotropin releasing hormone by the hypothalamus and culminates in the release of glucocorticoids (cortisol in humans) by the adrenal glands into the bloodstream. The sympathetic branch of the ANS is a fast-acting stress response system that is responsible for the classic "fight or flight" response (Chrousos and Gold 1992), eventuating in the release of catecholamines into the bloodstream. The HPA axis and ANS are distinct but interrelated systems; together they provide specialized responses to stress (Chrousos and Gold 1992). Although both systems respond to psychological stressors involving challenge, novelty, and social-evaluative threat (Chrousos et al. 1988; Lundberg and Frankenhaeuser 1980) and have implications for physical and mental health, there are some key differences across the two systems.

HPA activation is thought of as a "defeat action," or a passive response to novel or unpredictable stressors, particularly those perceived as uncontrollable (Lundberg and Frankenhaeuser 1980). HPA over-activation is linked to avoidance, withdrawal, and negative emotions such as anxiety and depression (Buss et al. 2004; Fortunato et al. 2008; Gunnar and Vazquez 2006; Gunnar et al. 2009b; Kalin et al. 1998). Moreover, elevated basal cortisol levels (Goodyer et al. 2000) and heightened cortisol reactivity to social challenge (Susman et al. 1997) predict depressive symptoms over time, although the evidence for links between heightened cortisol and depression has been mixed in children (Kaufman et al. 2001).

ANS activation is thought of as the body's active, defensive reaction to imposing threats, particularly those perceived as controllable (Henry 1992), and is believed to reflect generalized alertness, arousal, or vigilance and active engagement with one's environment (Schachter and Singer 1962). Consistent with this more generalized response, research links activation of various components of the ANS with approach behavior and positive affect (Adam and Granger 2010; Fortunato et al. 2008) as well as withdrawal behavior and negative affect (Buss et al. 2004; Kagan et al 1987); the specific type of response may depend on children's social motivation (approach vs. avoidance; Beauchaine et al. 2007) or the context of the behavior (Fortunato et al. 2008). With regard to depression, heightened sympathetic nervous system activation (reflected in 24-hour norepinephrine levels) is associated with more depressive symptoms in women (Hughes et al. 2004).

In the context of developmental science, there has been renewed interest in the utility of salivary alpha amylase [sAA] as a minimally invasive surrogate marker of ANS activation (e.g., Granger et al. 2007a). Controlled pharmacological studies employing adrenergic

agonists and antagonists specifically link individual differences in sAA to activity of the SNS (Nater et al., 2006; Nedefors and Dahlof, 1992; Speirs et al., 1974). It should be noted, however, that the salivary glands that secrete sAA are innervated by both the SNS and PNS, and therefore sAA secretion also may partially reflect PNS activation (Nater and Rohleder 2009). Research links heightened sAA levels with an excessive focus on negative affect (Byrd-Craven et al. in press), internalizing symptoms (when combined with high cortisol levels; El Sheikh et al. 2008), and depression (Vigil et al. in press).

The present study examined whether cortisol and sAA levels measured in the context of a laboratory social stressor (i.e., a conflict-of-interests interaction with an unfamiliar peer) moderated the contribution of peer victimization to depression over a one-year period. To provide a comprehensive assessment of biological stress responses, we assessed children's level of *anticipatory cortisol and sAA* while awaiting the stressor as well as their *task-related reactivity* over the course of the stressor. Although most research on biological stress responses focuses on task-related reactivity, increasing evidence underscores the importance of the anticipatory phase of the stress response, particularly in the context of naturalistic stressors (Afifi et al. 2009; Klimes-Dougan et al. 2001; Powers et al. 2009; Stroud et al. 2009). In this case, children's level of pre-task cortisol/sAA reflected regulation while awaiting an impending interaction with an unfamiliar peer, which had the potential to trigger a sense of uncertainty, uncontrollability, and potential social threat.

To formulate specific predictions, we drew from the biological sensitivity to context (BSC) theory (Boyce and Ellis, 2005; Obradovic et al. 2010). According to this theory, high biological reactivity to stress fosters maladaptive outcomes (i.e., health risks) under conditions of adversity but positive outcomes (i.e., health benefits) under conditions of support. Individuals with high BSC are therefore believed to be more attuned to both negative and positive aspects of their social contexts. Accordingly, we predicted that exposure to peer victimization would predict subsequent depressive symptoms in children with high biological sensitivity to context, as reflected in heightened levels of cortisol and sAA both in anticipation of, and response to, a social stressor. However, we expected that biological sensitivity to context would be innocuous (i.e., unrelated to depressive symptoms) or even beneficial (i.e., protective against depressive symptoms) in children exposed to low levels of peer victimization. In these children, biological sensitivity to context may allow them to reap the benefits of living in a low-stress environment. We also examined whether exposure to victimization and biological stress responses jointly contributed to specific responses to social challenge during the task. In particular, we anticipated that victimization would predict rumination (i.e., a perseverative, excessive focus on negative emotions and experiences; Nolen-Hoeksema 2000) in children with high but not low biological sensitivity to context.

Method

Participants

Participants were 132 children (68 girls; 64 boys; *M* age = 9.46 years, *SD* = .33; 71.2% White, 28.8% minority; 50% of families with an annual income below $60,000) recruited from a larger study of peer victimization. Families were invited to participate in a supplemental study involving an interaction with an unfamiliar peer. Parents completed a survey of children's use of over-the-counter and prescription medications; usage during the past 24 hours was confirmed at the assessment. Participants from different school districts were paired to ensure lack of familiarity between partners; otherwise, children were randomly assigned to same-sex dyads.

Procedure

All procedures for this study were approved by the [*institution omitted for blind review*] Institutional Review Board. Children completed measures of peer victimization (3rd grade; Wave 1 [W_1]) and depressive symptoms (3rd grade and 4th grade; Wave 2 [W_2]). During the summer and fall between the two assessments, children participated in a 3–4 hour session. Sessions occurred between 1:00 pm and 5:00 pm due to evidence that the HPA axis is more sensitive to stimulation later in the day (Gunnar et al. 2009b). Upon arrival, project staff described the study, and parents and children provided written consent/assent for participation. Children then completed some questionnaires and neutral activities (e.g., art projects) while awaiting their turn to participate in the social challenge task. Immediately prior to their participation, children provided a saliva sample.[1]

In the first phase of the social challenge task (Rudolph et al. 2009), children were told that whoever constructed a copy of a block model would win a prize. They were given a set of blocks that was sufficient to complete only one model, and were allowed to build for nine minutes. In the second phase of the task, children were informed that they would each receive a prize for their efforts, and were instructed to decide on the distribution of two prizes of noticeably unequal value. It was expected that this task would trigger individual differences in children's anticipation of a social stressor (i.e., an impending interaction with an unfamiliar peer) and reactivity to a social stressor (i.e., potential conflict and perceptions of threat, frustration, and uncontrollability). Given the distinct differences in the kinetic reactivity profiles for cortisol (Dickerson and Kemeny 2004) and sAA (Gordis et al. 2006; Nater et al. 2006), children provided two saliva samples within a short time frame after the task: 5 min. post-task to assess the peak sAA response and 20 min. post-task to assess the peak cortisol response. On average, the time difference between the pre- and 5-minute post-task samples was 26 min. (*SD* = 5). Following the task, children reviewed a videotape of the interaction, and provided ratings of the extent to which they engaged in rumination during the interaction (see Measures). Participants were then debriefed and the one who had received the less valuable prize was given the opportunity to exchange it for a higher valued prize.

Measures

Peer victimization—Children completed a revision (Rudolph et al. 2010) of the Social Experiences Questionnaire (Crick and Grotpeter 1996) to assess their exposure to overt victimization (11 items; e.g., "How often do you get pushed or shoved by another kid?") and relational victimization (10 items; e.g., "How often do other kids leave you out on purpose when it's time to play or do an activity?"). Scores were computed as the mean of the items (α = .93). Research supports the validity of self-reports of victimization (Bollmer et al. 2006; Graham and Juvonen 1998; Ladd and Kochenderfer-Ladd 2002).

Depressive symptoms—Children completed the Short Mood and Feelings Questionnaire (Angold et al. 1995) to assess their recent depressive symptoms (13 items; e.g., "I felt unhappy or miserable."). Scores were computed as the mean of the items (α = .88). This measure shows moderately high correlations with the Children's Depression Inventory and the Diagnostic Interview Schedule for Children (Angold et al. 1995), and differentiates depression from other psychiatric disorders (Thapar and McGuffin 1998).

Rumination—Following the task, children watched a videotape of their interaction and rated three items reflecting their engagement in rumination during the task (α = .79; e.g., "I

[1]On average, the time difference between when children were informed about the study and the pre-task sample was about 55 minutes (*SD* = 42), with a minimum of 20 minutes.

kept thinking about how this was way too hard." "I kept thinking, 'I hate this'."). Prior research supports the validity of self-reported responses to laboratory social stressors (Stroud et al. 2009). Moreover, in another study using the same task as the present one (Rudolph et al. 2009), self-reported rumination was significantly associated [$r(99) = .48$, $p < .001$] with observer reports of emotion dysregulation. Thus, these self-reports appear to be valid indicators of responses to a laboratory challenge.

Medication usage—Parents completed a checklist of medication usage. Children were assigned a score of 1 if they had taken medications (e.g., steroidal or psychotropic) within the past 24 hours that may interfere with the biological assessments and a score of 0 if they had not. A few children ($n = 7$) received scores of 1 despite the original exclusionary efforts; these children were included in the study, but all analyses adjusted for medication usage.

Saliva sample collection and analysis—Saliva samples were collected and handled following Granger and colleagues (2007b). All assessments were conducted between 1:00 pm and 5:00 pm to control the influence of the natural diurnal variation in cortisol production. To ensure against contamination from food consumption, children were instructed not to eat for 1 hour prior to their assessment (Gibson et al. 1999). Children provided three saliva samples: immediately prior to the task (pre-task), 5 min. after the task (to tap sAA reactivity), and 20 min. after the task (to tap cortisol reactivity). On average, the pre-task sample was collected at 2:19 pm (*SD* = 33.87 minutes). Children donated whole saliva by passive drool into a 2 mL cryogenic vial. Samples were frozen at −20 to − 80 C until shipped overnight on dry ice to Salimetrics laboratories where they were stored at − 80 C. On the day of assay, samples were brought to room temperature, centrifuged at 3,000 RPM for 15 min., and the clear top-phase of the sample was pipetted into appropriate test tubes. All samples were assayed for salivary cortisol using a highly sensitive enzyme immunoassay US FDA (510k) cleared for use as an in vitro diagnostic measure of adrenal function (Salimetrics, State College, PA). The test used 25 μl of saliva, had a lower limit of sensitivity of .007 μg/dl, with a range of sensitivity from .007 to 3.0 μg/dl. Samples were assayed in duplicate; average intra-and inter-assay coefficients of variation were less than 5% and 10%, respectively. Averaged duplicate scores were used in all statistical analyses.

The assay for sAA employed a chromagenic substrate, 2-chloro-p-nitrophenol, linked to maltotriose. The enzymatic action of sAA on this substrate yields 2-chloro-p-nitrophenol, which can be spectrophotometrically measured at 405 nm using a standard laboratory plate reader. The amount of sAA activity present in the sample is directly proportional to the increase (over a 2 min. period) in absorbance at 405 nm. Results are computed in U/mL of sAA using the formula: [Absorbance difference per minute x total assay volume (328 ml) x dilution factor (200)]/[millimolar absorptivity of 2-chloro-p-nitrophenol (12.9) x sample volume (.008 ml) x light path (.97)]. Following Granger and colleagues (2007), all samples were assayed in singlet. When samples and controls are assayed in duplicate using this protocol, intra-and inter-assay coefficients of variation are less than 5% and 10%.

Because pre-task cortisol and sAA distributions were positively skewed, cortisol scores were log-transformed and sAA scores were subjected to a square-root transformation. Two statistical outliers (+3 *SD* from the mean) for cortisol were then recoded to the next highest value (−1.06) in the distribution. To ease interpretation, descriptive statistics (see Table 1) are provided on the raw scores. Analyses of anticipatory levels are based on the transformed scores. Cortisol reactivity was computed as the difference between the raw cortisol scores from the third (20 min. post-task) and first (pre-task) assessments, and sAA reactivity was computed as the difference between the raw sAA scores from the second (5 min. post-task) and first (pre-task) assessments (Gordis et al. 2006). Higher scores reflected more reactivity.

Results

Overview of Analyses

For descriptive purposes, we examined mean level and individual differences in cortisol and sAA change across the task, as well as bivariate correlations among the variables.[2] We conducted hierarchical multiple regression analyses to examine the independent and interactive contributions of W_1 victimization and pre-task cortisol/sAA to W_2 depressive symptoms and task-related rumination. Because post-task scores were nested within dyad (Kenny et al. 2006), we conducted hierarchical linear modeling (HLM; Bryk and Raudenbush 1992) analyses to examine the independent and interactive contributions of W_1 victimization and cortisol/sAA reactivity to W_2 depressive symptoms and rumination. Dyad served as the grouping variable. Intercepts were set as random factors; slopes were set as fixed factors. All analyses predicting W_2 depressive symptoms adjusted for W_1 depressive symptoms, allowing us to determine whether victimization and cortisol/sAA predicted symptoms over time.

Each analysis adjusted for medication status (0 = no medication; 1 = medication; Granger et al. 2009) and time of day. Mean-centered W_1 victimization and cortisol/sAA scores and their interaction were included as predictors. Separate analyses were conducted for cortisol and sAA. Significant interactions were decomposed by conducting simple slope analyses for victimization at +1, 0, and −1 *SD* from the mean of the moderator (cortisol or sAA) (Aiken and West 1991; Bauer and Curran 2005). To quantify the effects, we examined the *SD* difference in depressive symptoms and rumination for high versus low levels of cortisol/sAA at low and high levels of victimization. Because some research suggests possible sex differences in the association between cortisol (Gunnar et al. 2009b) and sAA (Vigil et al. in press) activation and depression, we included relevant interactions with sex in the analyses. When nonsignificant, results are collapsed across sex. Of the 132 participants, four were missing pre-task cortisol and sAA, and were omitted from the regressions. Because HLM can accommodate missing data, all children were included in those analyses.

Mean Levels and Individual Differences in Reactivity of Cortisol and sAA

Table 1 presents the means and *SD*s of cortisol and sAA for the two measurements. Paired-samples *t*-tests revealed no mean change from pre- to post-task for cortisol, $t(126) = 1.35$, *ns*, or sAA, $t(126) = 1.25$, *ns*. This absence of mean level increases is consistent with research examining cortisol and sAA responses to peer rejection (Stroud et al., 2009) and social-evaluative threat (Yim et al. 2010) in children. Given our focus on individual variation in stress responses, we also examined individual differences in change across the task by computing how many children showed a substantive (at least 10%) change. For cortisol, 42 (32.1%) showed an increase and 57 (43.5%) showed a decrease at 20 minutes post-task. For sAA, 49 (37.4%) children showed an increase and 48 (36.6%) children showed a decrease at 5 minutes post-task. These results are consistent with research suggesting that only a subset of children show reactivity to laboratory tasks (Gunnar et al. 2009a), as well as with the fact that anticipatory activity may have triggered increases in cortisol and sAA prior to the task, thus tempering task-related reactivity (Stroud et al. 2009). Although the sample as a whole did not show significant reactivity, the fact that a subset of children showed an increase enabled us to examine the effect of individual differences in reactivity.

[2]Some of these means and bivariate correlations are also reported in a prior manuscript (Rudolph et al. in press).

Bivariate Correlations

Table 1 presents intercorrelations among the variables. Pre- and post-task cortisol levels and pre- and post-task sAA levels were highly correlated. Cortisol and sAA levels, as well as cortisol and sAA reactivity, were not associated across biomarker, except that pre-task cortisol was modestly correlated with post-task sAA and sAA reactivity. These modest associations are consistent with prior research (e.g., Fortunato et al. 2008; Gordis et al. 2006), and suggest that these two stress response systems provide primarily non-overlapping information. Peer victimization, rumination, and depressive symptoms were not significantly associated with any of the cortisol or sAA variables. Depressive symptoms were moderately stable from W_1 to W_2, and were significantly correlated with peer victimization at both waves. Rumination was significantly correlated with W_1 symptoms.

Anticipatory (Pre-Task) Cortisol and sAA Levels as Moderators of Peer Victimization

Cortisol and depressive symptoms—The regression analysis for anticipatory cortisol predicting W_2 depressive symptoms revealed a significant main effect of W_1 victimization and a significant Victimization × Cortisol interaction (see Table 2). Decomposition of this interaction revealed that W_1 victimization significantly predicted W_2 depressive symptoms at high, $b = .44$, $t(121) = 4.14$, $p < .001$, and average, $b = .26$, $t(121) = 3.34$, $p < .01$, but not low, $b = .08$, $t(121) = .86$, *ns*, levels of cortisol (see Figure 1a). At high levels of victimization, children with heightened anticipatory cortisol had W_2 depressive symptom scores .47 *SD*s greater than children with dampened anticipatory cortisol . At low levels of victimization, children with dampened anticipatory cortisol had depressive symptom scores . 33 *SD*s greater than children with heightened anticipatory cortisol . These effects were not significantly moderated by sex.

sAA and depressive symptoms—The regression analysis for anticipatory sAA predicting W_2 depressive symptoms revealed a significant main effect of W_1 victimization, but no significant main effect of sAA or Victimization × sAA interaction (see Table 2). These effects were not significantly moderated by sex.

Cortisol and rumination—The regression analysis for anticipatory cortisol predicting rumination revealed nonsignificant main effects of W_1 victimization and cortisol, but a significant Victimization × Cortisol interaction (see Table 2). Decomposition of the interaction revealed that victimization significantly predicted rumination at high, $b = .41$, $t(121) = 2.48$, $p < .05$, but not average, $b = .08$, $t(121) = .63$, *ns*, or low, $b = -.26$, $t(121) = -1.57$, *ns*, levels of cortisol (see Figure 1b). At high levels of victimization, children with heightened anticipatory cortisol had rumination scores .41 *SD*s greater than children with dampened anticipatory cortisol . At low levels of victimization, children with dampened anticipatory cortisol had rumination scores .60 *SD*s greater than children with heightened anticipatory cortisol. These effects were not significantly moderated by sex.

sAA and rumination—The regression analysis for anticipatory sAA predicting rumination revealed no significant main or interactive effects of W_1 victimization or sAA (see Table 2); there were no significant interactions with sex.

Task-Related Cortisol and sAA Reactivity as Moderators of Peer Victimization

Cortisol and depressive symptoms—The HLM analysis for task-related cortisol reactivity predicting W_2 depressive symptoms revealed no significant main or interactive effects of W_1 victimization or cortisol (see Table 3); there were no significant interactions with sex.

sAA and depressive symptoms—The HLM analysis for task-related sAA reactivity predicting W_2 depressive symptoms revealed no significant main or interactive effects of W_1 victimization or sAA (see Table 3). However, there was a significant Victimization × sAA × Sex interaction. Decomposition of this interaction revealed that victimization significantly predicted depressive symptoms for girls with high sAA reactivity, $b = .52$, $t(116) = 4.07$, $p < .001$, but not for girls with low sAA reactivity, $b = .10$, $t(116) = .78$, *ns*, boys with high sAA reactivity, $b = -.05$, $t(116) = -.32$, *ns*, or boys with low sAA reactivity, $b = .24$, $t(116) = 1.62$, *ns* (see Figure 2).

Cortisol and rumination—The HLM analysis for task-related cortisol reactivity predicting rumination revealed no significant main or interactive effects of W_1 victimization or cortisol (see Table 3); there were no significant interactions with sex.

sAA and rumination—The HLM analysis for task-related sAA reactivity predicting rumination revealed no significant main or interactive effects of W_1 victimization or sAA (see Table 3); there were no significant interactions with sex.

Discussion

This research supported the idea that individual differences in biological stress responses moderate the impact of early adversity, specifically exposure to peer victimization, on subsequent depressive symptoms in children. Specifically, victimization predicted depressive symptoms one year later in children who showed high but not low levels of anticipatory cortisol while awaiting a social challenge. However, children with this heightened biological sensitivity were protected against depressive symptoms when they were exposed to low levels of peer victimization. Victimization also predicted depressive symptoms in girls who showed high but not low sAA reactivity over the course of a stressor. Importantly, because all analyses adjusted for earlier levels of depressive symptoms, this research provided a rigorous test of the prospective, interactive contribution of peer victimization and biological stress responses to subsequent depression.

Victimized children experience a barrage of negative feedback, demeaning treatment, and even physical abuse from their peers. Those with well-regulated stress response systems may be able to cope effectively with these challenges, allowing them to maintain a healthy sense of self and emotional well-being; in contrast, those with hyper-sensitive stress response systems may engage in ineffective responses, eventually leading to depressive symptoms. Indeed, we found that exposure to victimization predicted more ruminative responses to social challenge in children with high but not low levels of anticipatory cortisol. These findings parallel those from other research linking biological stress responses with a tendency to ruminate in response to stress (Byrd-Craven et al. in press; Zaccola et al. 2008); rumination, in turn, serves as a risk factor for depression (Nolen-Hoeksema 2000). Of interest, within low-victimization contexts, children with high anticipatory cortisol actually engaged in *less* rumination than did children with low anticipatory cortisol. This pattern is consistent with research suggesting that cortisol elevation in response to cognitive tasks is associated with better executive function and self-regulatory capacity (Blair et al. 2005). In low-victimization contexts, when children are not faced with persistent social threat or harm, elevated cortisol may be linked to strong self-regulation and positive or effective engagement with the environment, whereas low cortisol may be linked to poor self-regulation and negative or ineffective engagement with the environment, as reflected in rumination.

In general, these results support the BSC theory (Boyce and Ellis 2005; Obradovic et al. 2010), which holds that heightened biological reactivity to stress serves as either a risk or a

protective factor depending on the environment in which individuals live. Whereas children living in a threatening environment, as reflected in high levels of peer victimization, suffered adverse health consequences (i.e., a heightened tendency toward rumination and depressive symptoms) as a result of their sensitivity, those living in a non-threatening environment, as reflected in low levels of peer victimization, benefited from their sensitivity. In contrast, children with low biological sensitivity to context were not significantly affected by their level of exposure to peer victimization; it will be important to investigate whether this apparent insensitivity to context holds even under extreme types of adversity (e.g., severe and persistent physical bullying by peers).

Anticipatory sAA did not moderate the contribution of victimization to subsequent depressive symptoms. The anticipatory phase of the stressor is likely marked by perceptions of uncertainty and uncontrollability as children await an unpredictable interaction with a novel peer. Because the HPA axis is particularly sensitive to uncontrollable stressors, activation of this system prior to the stressor may be more relevant than activation of the ANS to the prediction of depressive symptoms. However, victimization did pose a specific risk for depressive symptoms in girls who showed heightened sAA reactivity in response to the social stressor. These findings are consistent with prior research suggesting a positive association between sAA activation and depressive symptoms in woman but not men (Vigil et al. in press). Research suggests that girls value social connectedness (e.g., getting along with others) more than do boys (Rose and Rudolph 2006). Thus, girls who are exposed to victimization and have highly sensitive biological stress response systems (i.e., who mount a more extreme defensive response to social challenge or threat) may be least able to cope effectively with social stress and, consequently, most at risk for future depressive symptoms.

In sum, these findings contribute to emerging theory and research on the psychological legacy of early stress by providing direct empirical support for the idea that biological stress responses shape individual differences in the mental health consequences of peer adversity. More broadly, supporting the BSC theory (Boyce and Ellis 2005), this research reveals that the meaning of heightened biological stress reactivity is context-dependent: This sensitivity is health-undermining in high-risk contexts but health-promoting in low-risk contexts (Obradovic et al. 2010). Of note, the longitudinal design of this study allowed us to investigate whether the interactive contribution of peer victimization and biological sensitivity predicted depressive symptoms over time, thereby shedding light on the direction of the effects.

Despite these contributions, this research had several limitations. First, the sample size was relatively small, perhaps preventing us from detecting some small effects. Second, as in most prior research, individual differences in pre-task cortisol and sAA were measured in the same saliva samples. Given that the component subsystems of the ANS show faster reactivity than the HPA axis (Granger et al. 2007a), levels of cortisol and sAA measured at the same time prior to the task may not necessarily reflect concurrent and synchronized anticipatory activation to the same event or subjective experience. The present findings raise the possibility that future studies should explore the anticipatory phase of the stress response as a phenomenon of interest in its own right rather than merely a confound for subsequent reactivity. On the one hand, it is possible that the peak anticipatory activation occurs after children are informed about an upcoming stressor and then subsides. On the other hand, it is possible, and perhaps more likely, that anticipatory activation remains constant until children actually encounter the stressor or perhaps even increases as the stressor approaches. As the field progresses in understanding anticipatory activation of these salivary measures of psychobiological stress responses, it will be important to determine how this process unfolds for the HPA and ANS individually, as well as how anticipatory activation influences coordination between the systems, and their respective linkages to behavior and affective

states. Understanding this process is particularly critical for studies that involve other procedures (e.g., potentially stress-inducing interviews) prior to a challenge task, as it is possible that pre-task scores, typically viewed as "baseline" levels, actually reflect reactivity to stressful procedures.

Future research also would benefit from examining whether similar patterns of effects emerge in the context of different types of adversity. The observed interactive contribution of peer victimization and biological stress responses to depressive symptoms is similar to prior research examining the interactive effects of early family adversity and biological stress responses on children's socioemotional adjustment (Obradovic et al. 2010), suggesting some consistency across types of adversity. However, given that early exposure to stress is implicated as a risk factor for a wide range of physical and mental health difficulties (Boyce et al. 1998; Boyce and Ellis 2005; O'Connor 2003), it will be important to determine which types of stress and biological sensitivity confer vulnerability to which types of adverse outcomes, as well as whether certain outcomes are particularly likely to emerge when children are exposed to adversity at certain developmental stages. Moreover, although this longitudinal study built on prior research documenting concurrent associations between biological stress responses and depression, we examined only a small window of development. Further research is needed to determine the long-term effects of peer victimization and biological stress responses on emerging psychopathology.

The present findings build on prior research indicating the importance of measuring both the anticipatory and reactivity phases of biological responses to a naturalistic stressor (Afifi et al. 2009; Klimes-Dougan et al. 2001; Powers et al. 2009; Stroud et al. 2009); indeed, the anticipatory phase was particularly relevant to understanding the role of cortisol responses to stress whereas task-related reactivity was particularly relevant to understanding the role of sAA responses to stress. It would be worthwhile for future research to compare these two phases of the stress response to determine which phase is most relevant to which types of stressors, whether potentiation of anticipatory versus reactive stress responses is consistent across individuals or contexts, and whether biological sensitivity during different phases predicts different types of adjustment. Moreover, elucidating the processes that drive anticipatory activation will be critical for understanding this phase of the stress response. For example, individual differences in social-cognitive processes (e.g., anticipation of threat or harm; perceptions of control; social goals) may determine which individuals show sensitivity to anticipatory activation in the face of an impending stressor.

Finally, an intriguing direction for future inquiry is the identification of specific pathways through which early adversity and heightened biological stress responses jointly contribute to the emergence of depression. For example, HPA axis (Goodyer 2009) and ANS (Beauchaine et al. 2007) dysregulation may trigger individual differences in emotion processing and appraisals of the environment and may compromise brain regions involved in pleasure and motivation, thereby heightening risk for emotion dysregulation, anhedonia, social withdrawal, and associated symptoms of depression. Because children with a history of early adversity likely lack personal and external resources for coping, they would be particularly susceptible to these destabilizing effects of stress response dysregulation. Delineating the pathways linking early adversity, biological stress responses, and subsequent psychopathology would provide critical information for designing interventions to redirect vulnerable children toward healthier developmental trajectories.

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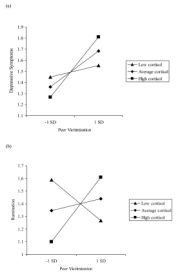

Fig 1.

Victimization × Anticipatory Cortisol Activation predicting (a) W_2 depressive symptoms, adjusting for W_1 depressive symptoms, and (b) task-related rumination

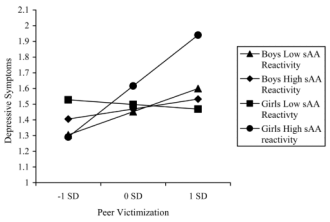

Fig 2.

Victimization × Task-Related sAA Reactivity predicting W_2 depressive symptoms, adjusting for W_1 depressive symptoms, in girls

Table 1

Descriptive Statistics and Bivariate Correlations

			Correlations									
	M	***SD***	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**
1. Pre-task cortisol	.10	.07	---									
2. Post-task cortisol	.10	.08	.57***	---								
3. Cortisol reactivity	−.01	.05	−.34***	.52***	---							
4. Pre-task sAA	100.02	72.13	.06	−.04	−.09	---						
5. Post-task sAA	94.50	71.53	.20*	.08	−.12	.78***	---					
6. sAA reactivity	−5.86	53.05	.18*	.16	−.02	−.38***	.27**	---				
7. Peer victimization	1.92	.62	.00	−.09	−.14	−.01	.04	.05	---			
8. W_1 Depressive Symptoms	1.62	.64	.08	.02	−.02	.04	−.04	−.13	.49***	---		
9. W_2 Depressive Symptoms	1.52	.55	.09	−.01	−.09	.00	.01	.01	.43**	.50***	---	
10. Rumination	1.40	.82	−.04	−.01	.04	−.15†	−.13	.03	.05	.20*	.10	---

Note. Means and standard deviations are presented for pre-task and post-task raw scores. Bivariate correlations are based on transformed, windsorized scores.

† $p < .10$.

* $p < .05$.

** $p < .01$.

*** $p < .001$.

Table 2

Contribution of Peer Victimization, Anticipatory (Pre-Task) Cortisol and sAA, and their Interaction to the Prediction of Depressive Symptoms and Rumination

	Cortisol[a]		sAA[b]	
Predictor	**β**	**ΔR^2**	**β**	**ΔR^2**
	W_2 Depressive Symptoms			
Step 1:		.26***		.26***
Medication	.12		.12	
Time of day	−.02		−.02	
W_1 Depressive Symptoms	.46***		.46***	
Step 2:		.06**		.06**
W_1 Victimization	.27**		.27***	
Anticipatory Activation	.04		−.02	
Step 3:		.04**		.00
W_1 Victimization × Anticipatory Activation	.20**		.01	
	Task-Related Rumination			
Step 1:		.01		.01
Medication	.04		.04	
Time of day	.09		.09	
Step 2:		.00		.03
W_1 Victimization	.06		.06	
Anticipatory Activation	−.04		−.16†	
Step 3:		.07**		.00
W_1 Victimization × Anticipatory Activation	.26**		−.05	

Note. Coefficients in table represent standardized values.

† $p < .10$.

* $p < .05$.

** $p < .01$.

*** $p < .001$.

[a] Units of measurement are ug/dL.

[b] Units of measurement are U/mL.

Table 3

Contribution of Peer Victimization, Task-Related Cortisol and sAA Reactivity, and their Interaction to the Prediction of Depressive Symptoms and Rumination

Predictor	Cortisol[a]	sAA[b]
	W_2 Depressive Symptoms	
Medication	.22	.16
Time of day	.00	.00
Sex	.10	.10
W_1 Depressive Symptoms	.29**	.34**
W_1 Victimization	.18	.17
Task-Related Reactivity	−.38	.00
W_1 Victimization × Reactivity	−1.86	.00
W_1 Victimization × Sex	.08	.07
Reactivity × Sex	−.45	.00
W_1 Victimization × Reactivity × Sex	−1.32	.01**
	Task-Related Rumination	
Medication	.07	−.01
Time of day	.00	.00
Sex	.15	.13
W_1 Victimization	−.03	.03
Task-Related Reactivity	1.23	.00
W_1 Victimization × Reactivity	−4.20	.00
W_1 Victimization × Sex	.13	.07
Reactivity × Sex	−1.54	.00
W_1 Victimization × Reactivity × Sex	3.35	.00

Note. Coefficients in table represent unstandardized values.

* $p < .05$.

** $p < .01$.

*** $p < .001$.

[a] Units of measurement are ug/dL.

[b] Units of measurement are U/mL.